ENCYCLOPEDIA OF PHARMACY PRACTICE AND CLINICAL PHARMACY

Editor in Chief
Zaheer-Ud-Din Babar

ELSEVIER

ENCYCLOPEDIA OF
PHARMACY PRACTICE AND CLINICAL PHARMACY

Page left intentionally blank

ENCYCLOPEDIA OF
PHARMACY PRACTICE AND CLINICAL PHARMACY

EDITOR-IN-CHIEF
Zaheer-Ud-Din Babar
University of Huddersfield, Huddersfield, UK

VOLUME 1

Pharmacy Practice Research Methods

SECTION EDITOR

Zaheer-Ud-Din Babar
University of Huddersfield, Huddersfield, UK

Pharmacy Practice

SECTION EDITORS

Zubin Austin
University of Toronto, Toronto, Ontario, Canada

Zaheer-Ud-Din Babar
University of Huddersfield, Huddersfield, UK

ELSEVIER

Elsevier
Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, UK
50 Hampshire Street, 5th Floor, Cambridge, MA 02139, USA

Copyright © 2019 Elsevier Inc. All rights reserved

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the publisher. Details on how to seek permission, further information about the Publisher's permissions policies and our arrangements with organizations such as the Copyright Clearance Center and the Copyright Licensing Agency, can be found at our website: www.elsevier.com/permissions.

This book and the individual contributions contained in it are protected under copyright by the Publisher (other than as may be noted herein).

Notices
Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers may always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Library of Congress Cataloging-in-Publication Data
A catalog record for this book is available from the Library of Congress

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

ISBN 978-0-12-812735-3

Publisher: Oliver Walter
Acquisitions Editor: Sam Crowe
Senior Content Project Manager: Richard Berryman
Associate Content Project Manager: Fizza Fathima
Designer: Matthew Limbert

CONTENTS OF ALL VOLUMES

VOLUME 2

VOLUME 3A

VOLUME 3B

LIST OF CONTRIBUTORS TO VOLUME 1

Nasir Abbas
University of Huddersfield, Huddersfield, West Yorkshire, United Kingdom

Yousaf Ahmad
Care UK Healthcare, London, United Kingdom

Sheraz Ali
Institute of Biomedicine, University of Eastern Finland, Kuopio, Finland

Claire Anderson
University of Nottingham, Nottingham, United Kingdom

Theo Ansong
Leicester School of Pharmacy, University of Lincoln, Lincoln, United Kingdom

Ahmed Awaisu
Qatar University, Doha, Qatar

Lilian M. Azzopardi
Faculty of Medicine and Surgery, University of Malta, Msida, Malta

Zaheer-Ud-Din Babar
Department of Pharmacy, University of Huddersfield, Huddersfield, West Yorkshire, United Kingdom

Caitlin A. Carter
University of Waterloo Library, Waterloo, ON, Canada

Nathorn Chaiyakunapruk
Center of Pharmaceutical Outcomes Research, Naresuan University, Phitsanulok, Thailand

Jie Chang
Xi'an Jiaotong University, Xi'an, China

Filipa Alves da Costa
Instituto Universitário Egas Moniz, Monte da Caparica, Portugal

Dalia M. Dawoud
Cairo University, Giza, Egypt

Piyameth Dilokthornsakul
Center of Pharmaceutical Outcomes Research, Naresuan University, Phitsanulok, Thailand

Roy Thomas Dobson
University of Saskatchewan, Saskatoon, SK, Canada

Weihua Dong
Xi'an Jiaotong University, Xi'an, China

David Dubins
University of Toronto, Toronto, ON, Canada

Greg Eberhart
Alberta College of Pharmacy, Edmonton, AB, Canada

Maguy Saffouh El Hajj
College of Pharmacy, Qatar University, Doha, Qatar

Erwin Martinez Faller
Research Management Center, Tagum Doctors College, Tagum City, Philippines

Yu Fang
Xi'an Jiaotong University, Xi'an, China

Helena Farinha
Centro Hospitalar de Lisboa Ocidental, EPE, Lisboa, Portugal

Chowdhury F. Faruquee
University of Alberta, Edmonton, AB, Canada

Kelly Grindrod
University of Waterloo, Waterloo, ON, Canada

Lisa M. Guirguis
University of Alberta, Edmonton, AB, Canada

Parthasarathi Gurumurthy
JSS College of Pharmacy, Mysore, Karnataka, India

Muhammad Abdul Hadi
School of Pharmacy, Institute of Clinical Sciences, University of Birmingham, Birmingham, United Kingdom

Syed Shahzad Hasan
University of Huddersfield, Huddersfield, West Yorkshire, United Kingdom; University of Newcastle, Callaghan, NSW, Australia

Mohamed Azmi Hassali
School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia

Helena Herrera
School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, United Kingdom

Certina Ho
University of Toronto, Toronto, ON, Canada

Sherilyn K.D. Houle
School of Pharmacy, University of Waterloo, Waterloo, ON, Canada

Rabia Hussain
School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia

Jennifer E. Isenor
College of Pharmacy, Dalhousie University, Halifax, NS, Canada

Sarah Jennings
Canadian Society of Hospital Pharmacists, Ottawa, ON, Canada

Minghuan Jiang
Xi'an Jiaotong University, Xi'an, China

Arun K.P.
JSS College of Pharmacy, Ooty, Tamil Nadu, India

Therese Kairuz
University of Newcastle, Callaghan, NSW, Australia

Dimitrios Karakitsos
University of Southern California, Los Angeles, CA, United States;

King Saud Medical City, Ministry of Health, Riyadh, Kingdom of Saudi Arabia

Nadir Kheir
The University of Auckland, Auckland, New Zealand

Puttarin Kulchaitanaroaj
Division of Health Service Research, College of Pharmacy, The University of Iowa, Iowa, IA, United States

Gregory J. Kyle
Queensland University of Technology, Brisbane, QLD, Australia

Leanne Lai
College of Pharmacy, Nova Southeastern University, Fort Lauderdale, FL, United States

Jennifer D. Lake
University of Toronto, Toronto, ON, Canada

Andreea Laschuk
University of Toronto, Toronto, ON, Canada

Asam Latif
The University of Nottingham, Queen's Medical Centre, Nottingham, United Kingdom

Esther T.L. Lau
Queensland University of Technology, Brisbane, QLD, Australia

Zongjie Li
Xi'an Jiaotong University, Xi'an, China

Miles J. Luke
University of Toronto, Toronto, ON, Canada

Catherine Lyder
Canadian Society of Hospital Pharmacists, Ottawa, ON, Canada

Dana Lyons
Alberta Health Services, Edmonton, AB, Canada

Claire Mann
Division of Pharmacy Policy and Practice, University of Nottingham, Nottingham, United Kingdom

Jennifer L. Marriott
Monash University, Parkville, VIC, Australia

Lisa M. McCarthy
Women's College Research Institute, Women's College Hospital, University of Toronto, Toronto, ON, Canada

Aleksandra B. Mejia
Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Mohamed Izham Mohamed Ibrahim
Qatar University, Doha, Qatar

Joanna C. Moullin
Curtin University, Perth, WA, Australia

Banan Mukhalalati
Qatar University, Doha, Qatar

Lotte Stig Nørgaard
Copenhagen University, Section for Social and Clinical Pharmacy, Copenhagen, Denmark

Raveena Amee Nagaria
Department of Pharmacy, University of Huddersfield, Huddersfield, West Yorkshire, United Kingdom

Nardine Nakhla
University of Waterloo, Waterloo, ON, Canada

Candace Necyk
University of Alberta, Edmonton, AB, Canada

Lisa M. Nissen
Queensland University of Technology, Brisbane, QLD, Australia

John Papastergiou
Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

Bridget Paravattil
Qatar University, Doha, Qatar

Mahendra Patel
University of Huddersfield, Huddersfield, West Yorkshire, United Kingdom

Ema Paulino
Farmácia Nuno Álvares, Almada, Portugal

Shane A. Pawluk
Qatar University, Doha, Qatar

Glen J. Pearson
University of Alberta, Division of Cardiology, Mazankowski Alberta Heart Institute, Edmonton, AB, Canada

Arjun Poudel
Queensland University of Technology, Brisbane, QLD, Australia

Oksana Pyzik
UCL School of Pharmacy, London, United Kingdom

Sara Ramzan
University of Huddersfield, Huddersfield, West Yorkshire, United Kingdom

Huma Rasheed
Institute of Pharmaceutical Sciences, University of Veterinary and Animal Sciences, Lahore, Pakistan

Cicely Roche
University of Dublin, Dublin, Ireland

Yiran Rong
University of Mississippi, Oxford, MS, United States

Meagen Rosenthal
University of Mississippi, Oxford, MS, United States

Hilary Rowe
Surrey Memorial Hospital, Surrey, BC, Canada

Myrella T. Roy
Canadian Society of Hospital Pharmacists, Ottawa, ON, Canada

Zikria Saleem
University College of Pharmacy, University of the Punjab, Lahore, Pakistan

Ratree Sawangjit
Clinical Trials and Evidence-Based Syntheses Research Unit (CTEBs RU), Mahasarakham University, Maha Sarakham, Thailand

Josie Solomon
Leicester School of Pharmacy, University of Lincoln, Lincoln, United Kingdom

Ash Soni
Royal Pharmaceutical Society, London, United Kingdom

Beth A. Sproule
Centre for Addiction and Mental Health (CAMH) & Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

Fatima Tauqeer
Institute of Health and Society, University of Oslo, Oslo, Norway

Sabrina B. Teskey
Hospital for Sick Children, University of Toronto, Toronto, ON, Canada

Kaeshaelya Thiruchelvam
University of Newcastle, Callaghan, NSW, Australia; International Medical University, Kuala Lumpur, Malaysia

Edward Agravante Tolentino
Supply Chain and Business Development, Regicon Healthcare Inc., Manila, Philippines

Janine Marie Traulsen
Copenhagen University, Section for Social and Clinical Pharmacy, Copenhagen, Denmark

Albert Wertheimer
College of Pharmacy, Nova Southeastern University, Fort Lauderdale, FL, United States

Kerry Wilbur
University of British Columbia, Vancouver, BC, Canada

Kyle J. Wilby
University of Otago, Dunedin, New Zealand

Tingting Wu
Xi'an Jiaotong University, Xi'an, China

Kangkang Yan
Xi'an Jiaotong University, Xi'an, China

Caijun Yang
Xi'an Jiaotong University, Xi'an, China

Sharon L. Youmans
Department of Clinical Pharmacy, University of California San Francisco School of Pharmacy, San Francisco, CA, United States

Maria Zhang
Centre for Addiction and Mental Health (CAMH) & Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada

Page left intentionally blank

EDITOR BIOGRAPHIES

Editor-In-Chief

Zaheer-Ud-Din Babar

Zaheer-Ud-Din Babar is Professor in Medicines and Healthcare and the Director of Centre of Pharmaceutical Policy and Practice Research at the University of Huddersfield, United Kingdom. He has worked as an academic in Pakistan, Malaysia, New Zealand, and in the United Kingdom, and understands the health systems and pharmacy globally. He is known for his work in pharmaceutical policy and practice, including quality use of medicines, clinical pharmacy practice, access to medicines, and issues related to pharmacoeconomics. Previously, he was the Head of Pharmacy Practice at the University of Auckland and received Vice Chancellor's Research Excellence Award from the University. He has published in high impact journals, such as *PLoS Medicine* and *Lancet* and has acted as a consultant for World Health Organization, Royal Pharmaceutical Society, Health Action International, International Union Against Tuberculosis and Lung Disease, World Bank, International Pharmaceutical Federation (FIP), and for the Pharmaceutical Management Agency of New Zealand.

His other work includes *Economic Evaluation of Pharmacy Services*, *Pharmaceutical Prices in the 21st Century*, *Pharmaceutical Policies in Countries With Developing Healthcare Systems*, and *Pharmacy Practice Research Methods*. Published by Elsevier and Adis/Springer, the books are used in curriculum design, policy development, and for referral all around the globe. Professor Babar is also the Editor-in-Chief of *BMC Journal of Pharmaceutical Policy and Practice* and can be contacted at z.babar@hud.ac.uk.

Section Editors

Zubin Austin

Zubin Austin BScPhm MBA MISc PhD FCAHS is Professor and Koffler Chair in Management at the Leslie Dan Faculty of Pharmacy and the Institute for Health Policy, Management, and Evaluation—Faculty of Medicine at the University of Toronto. His research focuses on the professional and personal development of the health workforce. He has published over 160 peer-reviewed manuscripts and authored four reference texts. In 2017, he was installed as a Fellow of the Canadian Academy of the Health Sciences, the highest award for health services researchers in Canada. He is the only faculty member of University of Toronto to have ever received both the President's Teaching Award for excellence in education and the President's Research Impact Award for the societal significance of his work. He has also been named undergraduate Professor of the Year by students on 18 separate occasions.

Ahmed Awaisu

Dr. Ahmed Awaisu is an Associate Professor of Clinical Pharmacy and Practice in the College of Pharmacy at Qatar University. He received his Bachelor of Pharmacy degree from Ahmadu Bello University Zaria, Nigeria in 1999, his masters and PhD degrees in Clinical Pharmacy from Universiti Sains Malaysia (USM) in 2004 and 2009, respectively. He is also a licensed pharmacist and has practiced in the hospital setting since 1999. Dr. Awaisu has a unique privilege of past academic experiences in international pharmacy degree programs. He has made substantial and tremendous contributions that impact teaching and learning, research, curriculum design, as well as professional development of students and healthcare practitioners in Qatar and other countries. He received the Qatar University Merit Award for Outstanding Faculty for 2016–17 Academic Year. He is a member of the American College of Clinical Pharmacy (ACCP), and the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), among others.

Professor Awaisu has extensive experience in the conduct of pharmacy practice and clinical research involving various types of study designs including case-control and cohort studies, quantitative surveys, mixed-methods designs, randomized control trials, and systematic reviews mostly on diabetes, cardiovascular diseases, tobacco dependence, and other chronic diseases. He has published over 100 peer-reviewed articles in internationally reputable pharmacy and healthcare journals and 10 book chapters related to the field of pharmacy. He has successfully supervised several postgraduate and undergraduate research projects, including MSc and PhD.

His research interest includes pharmacy practice especially pharmacists' expanded scope of practice, outcome-based research, pharmacoepidemiology and medication safety, and health promotion. Dr. Ahmed Awaisu has conducted training sessions and workshops on research methodology and biostatistics, drugs in sports, developing cognitive pharmacy services, and responding to symptoms in pharmacy practice. He presents regularly at continuing professional development programs for healthcare professionals in Qatar and other countries.

Timothy Chen

Professor Timothy Chen is a registered pharmacist and Professor of Medication Management, School of Pharmacy, The University of Sydney, Australia. Tim is nationally and internationally renowned for his research in medication management review and strategies to reduce medication related harm. Tim's research directly informed the Australian Government funded Home Medicines Review programme (MBS Item 903). Tim is an experienced educator and health services researcher, with experience in both community pharmacy and hospital pharmacy practice. Tim leads a productive research team (>160 peer-reviewed papers) and has completed main supervision of 15 PhDs, amongst other postgraduates. Tim has delivered >70 invited presentations at conferences and meetings across the globe. Tim has received university and national awards (Australian Government) for teaching, is an International Pharmaceutical Federation (FIP) Fellow (2016), and is President of the Social and Administrative Pharmacy Section, FIP.

Louise Curley

Louise Curley is a pharmacist and Senior Lecturer in Pharmacy practice at the School of Pharmacy. Louise's area of research focuses on the effects of recreational drug use in humans. She began her research as an undergraduate by investigating the subjective and electrophysiological effects of the Party Pill drugs using electroencephalography (EEG) and graduated with a PhD in pharmacy in 2012. Her thesis investigated the effects of the main constituents of "Party Pills" benzylpiperazine (BZP) and trifluromethylphenylpiperazine (TFMPP) on executive functioning and reward using functional magnetic resonance imaging (fMRI). Currently, her focus is developing new fMRI paradigms to investigate different aspects of risk, specifically by comparing populations of dependent versus non-dependent participants. Louise also has an interest in pharmacy practice research including innovative methods of teaching undergraduate students using different technologies and evaluating the effects of these innovations. She has recently been awarded the Butland Teaching Award: Innovation in Teaching.

Danijela Gnjidic

Dr. Danijela Gnjidic (BSc PhD MPH) is an NHMRC Dementia Leadership Fellow and Senior Lecturer at the School of Pharmacy, Faculty of Medicine and Health, University of Sydney. Her research expertise is in clinical and geriatric pharmacology, clinical studies on polypharmacy, high risk prescribing, and deprescribing in older people, pharmacoepidemiology, and the quality use of medicines. Danijela's academic track record includes 115 publications, 3-book chapters, with over 2500 citations on Scopus and $4M in research funding. Danijela was awarded the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) Denis Wade Johnson & Johnson New Investigator Award in 2012. Internationally, Danijela's contribution to the filed was recognized with the 2018 American Society of Clinical Pharmacology and Therapeutics William B. Abrams award in Geriatric Clinical Pharmacology. Danijela is an Associate Editor of the *Journal of Alzheimer's Disease* and Academic Editor of the *PloS One Journal*.

Arijana Meštrović

Dr. sc Arijana Meštrović, MPharm, FFIP has been working as a community pharmacist and she was responsible for education, services, and competency development in the biggest pharmacy chain in Croatia. She is now independent consultant and educator in Pharma Expert international agency, providing lectures and workshops in CPD programs for pharmacists, pharmacy technicians, medical representatives, implementing new services in pharmacy chains, and teaching Social Pharmacy and Pharmaceutical Care at universities in Croatia and Cyprus as Assistant Professor. Her Doctor's degree is in biomedical sciences—competency development in pharmacy. Arijana serves as member of the International Services Program Advisory Group the Accreditation Council for Pharmacy Education (ACPE, USA), member of PCNE (Pharmaceutical Care Network of Europe), ExCo member of FIP (Pharmaceutical International Federation) Academic section, and WHO international expert consultant in Pharmaceutical care field. She used to serve as Co-Chair of the FIP World Congress Programme Committee, Expert Member of the Board of Pharmacy Practice at FIP. In Croatia, she is a leader in Croatian Pharmaceutical Society and Croatian Chamber of Pharmacist as a Lecturer and Co-author of New services model in community pharmacy practice. Arijana is dedicated to promoting competency-based education in CPD cycle, so her teaching usually addresses all components of competencies—knowledge, experience, and motivation. In collaboration with ACPE International Services, she has founded and implemented SMART Pharmacy CPD model for pharmacists in more than 12 countries all over the world. She was invited speaker and consultant in more than 40 countries.

Kath Ryan

Kath is Professor of Social Pharmacy at the University of Reading, and Visiting Professor at Bournemouth University, United Kingdom. She has 45 years of experience as a pharmacist in the pharmaceutical industry, community practice, and academia. She has held posts at the University of Otago, New Zealand; Bournemouth University, United Kingdom; La Trobe University, Melbourne, Australia; and the University of Reading, United Kingdom. She also has experience in academic nursing and midwifery. Her research interests include extended roles for pharmacists, especially in general practice; application of the behavioral sciences to pharmacy practice; personal experiences of health and illness; and public and patient involvement, engagement and participation in research, and the education of health professionals. She has expertise in quantitative, qualitative, and mixed methods research. She also has an interest in infant feeding,

particularly breastfeeding research, promotion and support, from lay, professional, and academic perspectives. She has been a health advisor to La Leche League International and La Leche League New Zealand. Kath has been on Scientific Committees for the International Social Pharmacy Workshops and the Australasian Pharmaceutical Sciences Association. She has consulted for the National Institutes of Health, USA; Canadian Forces; Health Technology Assessment, NHS UK; and the NZ Ministry of Health.

Kath has over 100 publications in peer-reviewed journals and several book chapters and reports. She produced two multimedia, online resources for Health Talk: women's experiences of breastfeeding in the United Kingdom, and people's experiences of ageing in Australia. She was a Founding Co-Director of Health Talk Australia.

FOREWORD

This first edition of the Encyclopedia of Pharmacy Practice and Clinical Pharmacy is one-of-a-kind and the most comprehensive amalgamation of an inclusive range of topics relevant to the pharmacy profession brought together to ensure safe and effective provision of pharmaceutical care across the world. Professor Zaheer Babar is a Professor in Medicines and Healthcare at the University of Huddersfield and also a global expert in pharmacy practice and pharmaceutical policy. He has united over hundreds of researchers and practitioners from across the world in a collaborative endeavor to provide a unique insight into current best practice and strategies for the future for the profession of pharmacy and its practice.

As patient care becomes more complex with advances in medicines and new developments in practice, including pharmacogenomics and pharmacoeconomics, there is an ever-evolving demand for practice and policy to keep pace. This encyclopedia contains 180 chapters, from all fields of pharmacy practice and clinical pharmacy, providing an in-depth coverage of modern approaches to the practice of pharmacy and highlighting the directions that will enable advancement to continue.

This encyclopedia includes definitions, concepts, theories, and applications of clinical pharmacy and pharmacy practice, providing background knowledge of the area that will provide valuable information for students of pharmacy practice. By providing relevant and topical summaries on a broad range of subjects, this book is also an excellent resource for those seeking information beyond their specific areas of expertise. In addition, the information contained in this book and its communication is of importance to a range of stakeholders, such as physicians and other healthcare professionals, health regulatory authorities, and the pharmaceutical and health industry, in addition to patients and their caregivers.

This encyclopedia also provides an excellent insight into pharmacy practice research and methods, as well as pharmacovigilance, pharmacoeconomics, social and administrative pharmacy, public health pharmacy, pharmaceutical systems research, the future of pharmacy, and new interventional models of pharmaceutical care. In addition, new treatments, algorithms, standard treatment guidelines, and pharmacotherapies regarding diseases and disorders are also covered.

The six key strands around which this encyclopedia is arranged pay testament to the complex and broad nature of the topic and are key topics of interest in pharmacy today and drivers of change for the future, for the benefit of public health across the world.

1. Pharmacy practice
2. Pharmacy practice research methods
3. Clinical pharmacy education, professional standards, and workforce
4. Clinical pharmacy and pharmacotherapy
5. Pharmacoepidemiology and pharmacovigilance
6. Socio-behavioral and administrative pharmacy

Topics range from the education and training of pharmacists, technicians and assistants to counterfeit medicines, pharmaceutical pricing policies, and implementation of change. As pharmacy practice evolves to meet the ever-more-complex health and medicines needs of patients, practitioners need an understanding of the social, political, and economic contexts across the world, noting particular highlights and challenges in developing countries to reach high standards. While it is acknowledged that there are differences between countries in terms of legislation, regulations, and guidelines (as detailed in individual chapters), the vision for the profession must be for a world in which everyone can access safe, effective, and affordable medicines and pharmaceutical care. The chapters include many examples of innovation and best practice in delivering health

services for the future, embracing additional roles beyond the supply of medicines in a robust manner underpinned by scientific and evidenced practice. Quantitative, qualitative, and mixed methods of pharmacy practice research are presented alongside expanded and evolving roles for pharmacists and where technology may take us. More quality research and coordinating efforts will bring a range of theoretical concepts and an evidence-based practice to the forefront of our activities, to focus a global workforce to meet the challenges of this exciting new era for pharmacy practice. This timely volume exemplifies the willingness and ability of the profession to work collaboratively on global issues, representing an unprecedented opportunity to shape the future of pharmacy practice.

With ever-increasing demands on healthcare systems, alongside growing financial pressures, it is essential that we work collaboratively with other pharmacists and the wider public health workforce who have the expertise, opportunity, and capacity to support and inform development.

In this context, this encyclopedia is an important resource with far-reaching impact on global healthcare community, and I hope this will be well liked by students, researchers, and academics.

Professor Barbara Conway
Department of Pharmacy, University of Huddersfield, Queensgate, Huddersfield, United Kingdom

March 2019

PREFACE

Encyclopedia of Pharmacy Practice and Clinical Pharmacy

This encyclopedia has 180 chapters in total and it covers all domains of pharmacy practice and clinical pharmacy, including pharmacy practice research, socio-administrative and behavioral pharmacy, pharmacy education, pharmacoepidemiology, and the pharmacotherapy. One main question being asked is the need for this work. *What encyclopedia of pharmacy practice and clinical pharmacy adds to the current body of literature and what it means for global pharmacy community?* The answer to that is, though there were a number of books available on pharmacotherapy, however, current landscape lacks material comprehensively covering aspects, such as pharmacy practice, pharmacy practice research, social pharmacy, pharmacoepidemiology, pharmacy education, and the linking of clinical pharmacy with the health system. This encyclopedia aims to provide a collection of chapters on the above-mentioned areas. It also developed, synthesized knowledge, and provided policy guidance in the areas where there were gaps in the literature. For example, filling the gaps and including chapters on health systems, pharmaceutical policy, evidence and impact in pharmacy practice research, and on pharmacy education.

Here is a brief summary of what is being covered in its three volumes: Volume 1, 2, and 3.

Volume 1 includes chapters on pharmacy practice and pharmacy practice research. The pharmacy practice section starts with the historical evolution of pharmacy practice, medicines management, expanded roles of pharmacists, cognitive pharmacy services, community, and ambulatory pharmacy practice, ethics and regulation, and the new models of pharmaceutical care. There are also chapters on prescribing standards, practices, and competencies, interpersonal communication, evidence-based medicine, models on patient counseling, innovative pharmacy services, technology in pharmacy practice, and the pharmacist's role in substance misuse. The case studies chapters include pharmacy practice in high, low, and middle-income countries; United Kingdom, Western Europe, Australia, New Zealand, China, India, Gulf States, Philippines, and Portugal.

It is vital to understand and discuss the quality of evidence in pharmacy practice research, for example, how the evidence is produced and how it could impact on health outcomes. This is a niche section in the encyclopedia covering chapters on quantitative and qualitative methods in pharmacy practice research, quality of qualitative research, philosophical perspective and theories applied in pharmacy practice research, meta-synthesis, mixed methods research, discrete choice experiments, and the use of network meta-analysis in pharmacy practice. There are also chapters on evolution and definition of practice research, evidence, impact, and gaps in pharmacy practice research in low- and middle- and high-income countries.

Volume 2 covers pharmacovigilance, pharmacoepidemiology, and the socio-behavioral and administrative aspects of pharmacy and medicines use. The knowledge regarding pharmacoepidemiology and pharmacovigilance significantly impacts on medicines safety. The chapters included are on definitions, principles, and application of pharmacoepidemiology, descriptive and drug utilization studies, case-control and cohort studies, methodological challenges in epidemiological studies, data sources, and the issues related to medicines safety and comparative effectiveness research.

The socio-administrative and behavioral pharmacy section covers two broad aspects, namely, social pharmacy and pharmacy administration. Social pharmacy section covers concepts, development, and theories related to social pharmacy, public and patient engagement, sociology for pharmacists, implementation of change in pharmacy practice, and the social perspectives in addiction. There are also chapters on medicines adherence, compliance, and concordance, medication narratives, investigating medicines use among elderly

from a sociological perspective, changing nature of pharmacy as a profession, the impact of culture and religion on medicine use, and the issues related to disease mongering.

The understanding of health system is vital when promoting access and the use of medicines, hence in this context understanding administrative aspects of pharmacy are crucial. This section explores the dynamics between public policy, pharmaceutical policy, pharmacy practice, health systems, and patient-health outcomes. It covers a range of pharmaceutical policy and health system issues including access to biosimilars, access to high-cost medicines, counterfeit medicines, factors influencing pharmaceutical policy implementation, funding mechanisms for community pharmacy services, generic drug policies, national medicine policies, essential medicines list, pharmaceutical company sponsored medication assistance programs, and the pharmaceutical pricing policies.

Volume 3 covers clinical pharmacy education and pharmacotherapy. Pharmacy education training and the workforce have a great impact on global health. There are 25 chapters or more on pharmacists' training, and certification exploring the relationship between education, regulation, and practice. This is one of the largest collection of chapters covering pharmacy education and regulation at the global level. This includes chapters on pharmacist workforce, competency standards for clinical pharmacists, quality assurance in the pharmacy education, developing and evaluating clinical skills, continuing professional development, experiential education, inter-professional learning, leadership in pharmacy education, and the needs-based education. There are also case studies chapters on clinical pharmacy professional standards in the United States of America, Canada, the European Union, and in the low- and middle-income countries.

The pharmacotherapy section covers over 70 chapters discussing standard treatment guidelines, pharmacist's role in the central nervous system, infectious diseases, cardiovascular disorders, skin and endocrine disorders, musculoskeletal disorders, neurology, gastrointestinal disorders, and the respiratory disorders. The other key chapters include clinical pharmacy concepts, history, and development, clinical governance principles, pharmacokinetics, therapeutic guidelines, end of life care, palliative care, long-term care, fundamentals of pharmaceutical care planning, health outcomes and quality of life, the role of the pharmacist in the military and prisons, and the pharmacotherapy and deprescribing.

It has been a challenging task to complete this encyclopedia within a short span of 2 years. However, I am very thankful to the support of my section editors, reviewers, and hundreds of authors from all over of the world to come together and to contribute to this exciting project.

I hope you will like this effort and it will serve its purpose.

Zaheer-Ud-Din Babar, BPharm., MPharm.,PhD, SFHEA
Professor in Medicines and Healthcare
Director, Centre for Pharmaceutical Policy and Practice Research
Department of Pharmacy, University of Huddersfield, Queensgate, Huddersfield, United Kingdom

Editor-in-Chief
Encyclopedia of Pharmacy Practice and Clinical Pharmacy

March 2019

To Danyal Zaheer

Page left intentionally blank

Pharmacy Practice and Its Research: Evolution and Definitions

Syed Shahzad Hasan[*,†], **Kaeshaelya Thiruchelvam**[†,‡], **Therese Kairuz**[†], **Nasir Abbas**[*], **Zaheer-Ud-Din Babar**[*], [*]University of Huddersfield, Huddersfield, West Yorkshire, United Kingdom; [†]University of Newcastle, Callaghan, NSW, Australia; [‡]International Medical University, Kuala Lumpur, Malaysia

© 2019 Elsevier Inc. All rights reserved.

The Development of Pharmacy Practice Research

Pharmacy has traditionally been portrayed as a profession responsible for formulating and dispensing medicines. In the early 1900s, pharmacists were experts in apothecary, *secundum artem*, i.e. the art for empirical or medicinal use. As clinical pharmacy emerged as a speciality discipline, its development was influenced by the introduction of hospital pharmacy in the 1920s (Gregory, 2013). In the 1960s, clinical pharmacy started evolving and this aspect of the profession became patient-oriented rather than product-based. The significance and recognition of clinical pharmacy services were first documented in the 1970s and 1980s, respectively (International Pharmaceutical Federation, 2019; World Health Organization, 2006). This marked the beginning of the professional integration of pharmacists' roles and enhanced interactions with medical practitioners and other healthcare professionals such as nurses, physiotherapists, and dieticians (Pearson, 2007; Zermansky et al., 2006).

In 1991, Hepler proposed the concept of program evaluation for clinical pharmacy services and made useful suggestions to improve research designs (Hepler, 1991). In 1992, Ascione et al. made recommendations and provided insightful information on improving research in pharmaceutical care (Ascione et al., 1992). As pharmacy practice research continued to mature at its own pace, there was a paucity of literature in pharmaceutical care research. In 1998, Kennie et al. published a critical analysis of 12 pharmaceutical care research studies conducted between 1992 and 1998 (Kennie et al., 1998), and recommended that there was scope for improvement in study design, reporting of outcomes, and the associated relationships with structure and process, as defined by the Economic, Clinical and Humanistic Outcomes (ECHO) model (Strand et al., 1990).

The Nuffield Foundation was the first organization to advocate pharmaceutical sociology in 1986 (Deb, 1986). A few years later in 1994, Nick Mays explained that the sociological theory should be utilized to explain pharmacy practice research (Mays, 1994); however, it was not until 2001 that Bissell, Traulsen, and Haugbolle formally introduced the concepts of sociology and its importance in pharmacy practice research (Bissell et al., 2001). Morrall (2001) defined the discipline of sociology as one that reveals the nature of health and illness (Morrall, 2001). Health and illness have been identified as social phenomena and thus are susceptible to sociological analysis; for example, mortality and morbidity vary depending on the social differences such as age, gender, and ethnicity. There seems to be a social pattern associated with all forms of illness, and the analysis and elaboration of such patterns signify the importance of sociology in pharmacy practice research (Bissell et al., 2001).

Part of being diagnosed with an illness may involve taking medicines and there are many social aspects to the use and beliefs about medicines. Practice of pharmacists, use of medicines by patients, interactions between pharmacists and their patients, and the organizational and institutional structure of pharmacy services have the potential for an analysis through sociological theories (Bissell et al., 2001). Bissell et al. (2001) strongly believed that these theories directly contribute to strength, diversity, and dynamism of pharmacy practice research (Bissell et al., 2001).

Evolution of Pharmacy Practice Research and Its Literature

Pharmacy practice research continued to evolve after 2000s, particularly in the United Kingdom, the United States, Australia, Canada, and Scandinavia. In 2002, Felicity Smith published a book entitled *Research Methods in Pharmacy Practice* outlining how to conduct a practice project (Smith, 2002). These research interests also shifted from pharmacotherapy to pharmaceutical services involving education and medication advice (Fish et al., 2002). In 2015, Zaheer Babar edited *Pharmacy Practice Research Methods, an edition* that discusses theories, methodologies, models, and techniques (Babar, 2015).

In 2019, Austin and Sutton published *Research Methods in Pharmacy Practice Methods and Applications Made Easy*. This book explains basic concepts, as well as case studies outlining practice (Austin and Sutton, 2019). The current encyclopedia of pharmacy

practice and clinical pharmacy is comprehensive and has sections on pharmacy practice, covering qualitative, quantitative techniques, mixed methods approaches, meta synthesis, as well as the chapters on evidence and impact.

Definition and Evolution of Pharmacy Practice

The definition of pharmacy practice varies; in the context of this chapter, it is imperative to understand what activities or practices constitute pharmacy practice. In order to bridge this gap, a methodical and structured review of literature was performed. A summary of definitions of pharmacy practice and pharmacy practice research are presented in Table 1 and Table 2 respectively. In the process of searching for a clear and universal definition of pharmacy practice, we have identified 11 documents describing pharmacy practice published. These were all published between 1990 and 2019. The seven definitions (7/13) defined pharmacy practice as a discipline within pharmacy that involves health or pharmacy services delivery. The reason for incorporating health services provision in the definition of pharmacy practice could be increasing number of services provided by the pharmacists in both hospital and community settings.

Table 1 Summary of pharmacy practice definitions

Reference	*Relevance/ Context*	*Term used*	*Definition*	*Reference type*
Collett and Aulton (1990)	United Kingdom	Pharmaceutical practice	Pharmaceutical practice embraces the techniques of preparation and presentation of medicines, a knowledge of the biological fate of drugs and medicines, the symptomatic treatment of minor ailments, and the abilities to relate to and communicate with the patient, the prescriber, and other members of the healthcare team	Book (*Pharmaceutical Practice*)
World Health Organization (1996)	Global	Good Pharmacy Practice (GPP)	GPP is the practice of pharmacy that responds to the needs of the people who use the pharmacists' services to provide optimal, evidence-based care. The potential contribution of pharmacists extends to all levels of planning and provision of services. The mission of pharmacy practice is to provide medications and other healthcare products and services and to help people and society to make the best use of them (Pharmaceutical Care [PC] and GPP are largely identical, where GPP could be the way to implement PC)	WHO Report
RPSGB (1997a)	United Kingdom	Pharmaceutical service/ pharmacy practice	Five main areas in which pharmacy makes major contributions to health outcomes are management of prescribed medicines, management of chronic conditions, management of common ailments, promotion and support of healthy lifestyles, and advice and support for other healthcare professionals	RPSGB Report
Horne (2001)	United Kingdom	Pharmacy practice	Pharmacy practice serves to facilitate the appropriate use of medicines	Book (*Pharmacy Practice*)
Taylor and Harding (2001)	United Kingdom	Effective pharmacy practice	Effective pharmacy practice requires an understanding of the social context within which pharmacy is practiced, recognizing the particular needs and circumstances of the users of pharmaceutical services, and of pharmacy's place within health service provision	Book (*Pharmacy Practice*)
FIP/WHO (2011)	Global	Pharmacy practice	WHO described the mission of pharmacy practice as being "to provide medicines and other healthcare products and services and to help people and society to make the best use of them"	WHO Technical Report (Joint WHO/FIP Guidelines on GPP)

Table 1 Summary of pharmacy practice definitions (*cont.*)

Reference	*Relevance/ Context*	*Term used*	*Definition*	*Reference type*
American Pharmacy Association Academy of Pharmaceutical Research and Science (1998)	United States	Pharmacy practice activity	The PPAC is focused primarily on activities of licensed, practicing pharmacists across the continuum of healthcare settings. The classification captures a range of activities from traditional dispensing to direct patient care services. These include ensuring appropriate therapy and outcomes, dispensing medication and devices, health promotion and disease prevention, and health systems management	Pharmacy Practice Activity Classification (PPAC, 2019) Project
Whalley (2008)	United Kingdom	Pharmacy practice	Pharmacy practice is a discipline within pharmacy that involves developing the professional roles of the pharmacist. The critical parts of the discipline are understanding healthcare systems and public health	Book (*Foundation in Pharmacy Practice*)
Council on Credentialing in Pharmacy (2009) and National Association of Boards of Pharmacy (NABP) (2019)	United States	Pharmacy practice	NABP defines the pharmacy practice as the interpretation, evaluation, and implementation of Medical Orders; the Dispensing of Prescription Drug Orders; participation in Drug and Device selection; Drug Administration; Drug Regimen Review; the Practice of Telepharmacy within and across state lines; Drug or Drug-related research; the provision of Patient Counseling; the provision of those acts or services necessary to provide Pharmacist Care in all areas of patient care, including Primary Care and Collaborative Pharmacy Practice; and the responsibility for Compounding and Labeling of Drugs and Devices, proper and safe storage of Drugs and Devices, and maintenance of required records. The practice of pharmacy also includes continually optimizing patient safety and quality of services through effective use of emerging technologies and competency-based training	Reports (Council on Credentialing in Pharmacy, 2009; National Association of Boards of Pharmacy, 2019)
Moullin et al. (2013)	Australia	Pharmacy service/ pharmacy practice	A professional pharmacy service is defined as "an action or set of actions undertaken in or organized by a pharmacy, delivered by a pharmacist or other health practitioner, who applies their specialized health knowledge personally or via an intermediary, with a patient/client, population, or other health professional to optimize the process of care, with the aim to improve health outcomes and the value of healthcare"	Journal article
Almarsdottir et al. (2014)	Europe	Pharmacy practice	Pharmacy practice and social pharmacy are two important contemporary research areas within the field of pharmaceutical sciences, studying the role of medicines, patients, and pharmacists within the healthcare sector and society at large	Journal article
Fathelrahman et al. (2016)	Developing countries	Pharmacy practice	It is a description of what pharmacists normally do while acting in a professional context and it represents also the essential components and basic requirements for performing every job or action related to pharmacy, including where and how pharmacists do it	Book (*Pharmacy Practice in Developing Countries*)
Scahill and Babar (2017)	Global	Pharmaceutical Practice	Pharmaceutical practice encompasses everything, which is related to availability of medicines, access, and use at the individual and the population levels. This term encapsulates the research, development, formulation, distribution, access, and clinical use of medicines. It incorporates the human capital required to deliver pharmacy services and the impact on end users of pharmaceutical products and services	Journal article

Table 2 Summary of pharmacy practice research definitions

Reference	*Relevance*	*Term used*	*Definition*	*Reference Type*
Royal Pharmaceutical Society/King's Fund (RPSGB, 1997b)	United Kingdom	Pharmacy practice research	A useful definition of pharmacy practice research has been provided by the King's Fund (1997), which describes it as "research which attempts to inform and understand pharmacy and the way in which it is practiced, in order to support the objectives of pharmacy practice and to ensure that pharmacists' knowledge and skills are used to best effect in solving the problems of the health service and meeting the health needs of the population"	RPSGB Report
Smith (2010)	Global	Pharmacy practice research	Pharmacy practice research is used as an umbrella term for research into pharmacy services, medicines use, professional practice, and education. Research into the practice of pharmacy and the use of medicines is viewed as a branch of health services research	Book (*Conducting your Pharmacy Practice Research Project*)
Koster et al. (2014)/The Utrecht Pharmacy Practice network for Education and Research (2014)	Europe	Pharmacy practice research	Pharmacy practice research is necessary to generate evidence for further development of pharmacy services Pharmacy practice research can be divided in two main themes: (1) research related to the pharmacy as data source (e.g., studies regarding prescribing behavior or medication use) or (2) research related to the pharmacy as object of research (e.g., studies regarding internal pharmacy procedures, guideline adherence or quality of patient counseling)	Pharmacy Practice network for Education and Research Report
Almarsdottir et al. (2014)	Europe	Pharmacy practice research	Research within the field of pharmaceutical sciences, combining natural sciences with social and humanistic research to study the role of medicines, patients, and pharmacists within the healthcare sector and society at large	Journal article
Awaisu and Alsalimy (2015)	Global	Pharmacy practice research	"Pharmacy practice research" to be any research activity that pertains pharmacy practice or patient care, including, but not limited to, clinical and outcome research, health services research, and comparative effectiveness research	Journal article
Bond (2015)	Global	Pharmacy practice research	Pharmacy practice research, a sub-speciality within health services research, focuses on exploring how and why people access pharmacy services, the costs of pharmacy services, and the outcomes for patients as a result of these services, and comparison of these costs and outcomes compared to the same or similar services delivered by other providers	Book (*Pharmacy Practice Research Methods*)
Almarsdottir and Babar (2016)	Global	Pharmacy practice research	Many pharmacy practice researchers define their work as part of drug utilization research (DUR), clinical pharmacy, social pharmacy, pharmaceutical policy, health services research, or health economics	Journal article
Dolovich and Tsuyuki (2016)/Canadian Pharmacists Association/ Canadian Pharmacy Practice Research Group (2016)	Canada	Pharmacy practice research	Pharmacy practice research is defined as a component of health services research that focuses on the assessment and evaluation of pharmacy practice. It includes studies that evaluate pharmacists' roles in a variety of capacities. These studies include systems research, patient-centered research, and community-based research that encompasses a variety of determinants of health and their influence on patient outcomes and population health	Journal article and professional group
FIP Pharmacy Practice Research Special Interest Group (2019)	Global	Pharmacy practice research	Pharmacy practice research looks at the impact of the practice of pharmacy on healthcare systems, medicines use, and patient care. Its scope has expanded over the past 50 years to encompass aspects such as the clinical, behavioral, economic, and humanistic implications of the pharmacy practice, as well as change management and implementation	Special interest group

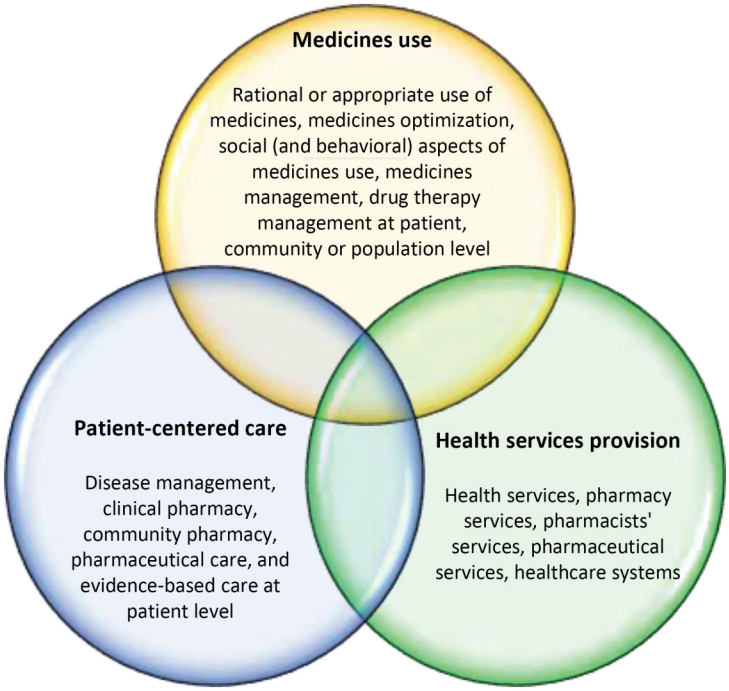

Figure 1 Diagrammatic representation of the different facets of pharmacy practice and its research.

The majority of the authors have used the term "pharmacy practice" except for a few (Collett and Aulton, 1990; Scahill and Babar, 2017) who used the term "pharmaceutical practice". The major difference between the two terms is the incorporation of pharmaceutical sciences in the definition of pharmaceutical practice.

The pharmacy practice definitions also vary according to who defines it and how they are being defined in a healthcare system. For example, in the United States, clinical pharmacy seems to be more a popular term or practice and is defined by the American College of Clinical Pharmacy as "*a health science discipline in which pharmacists provide patient care that optimizes medication therapy and promotes health, wellness, and disease prevention*" (American College of Clinical Pharmacy, 2008). In the United Kingdom, 'health services delivery' and 'medicines optimization' are more commonly used. Health services and medicines management were adopted and are widely promoted by the World Health Organization. Fig. 1 presents the three major elements (themes) which contribute to pharmacy practice and pharmacy practice research, namely medicines use, patient-centered care and health services provision.

Conclusion

It is commendable that pharmacy practice research has gained recognition in the international arena. Moving forward, pharmacy practice research should be performed in a manner which captures quality evidence on the use of medicines, patient-centered care, and provision of health services. These goals provide all the more reason to collaborate with other healthcare professionals and initiate new health services, with input from stakeholders and supported by research evidence.

List of Abbreviations

ECHO	Economic, Clinical and Humanistic Outcomes
FIP	International Pharmaceutical Federation
GPP	Good Pharmacy Practice
NABP	National Association of Boards of Pharmacy
PC	Pharmaceutical Care
RPSGB	Royal Pharmaceutical Society of Great Britain

References

Almarsdottir, A.B., Babar, Z.U., 2016. Future methods in pharmacy practice research. Int. J. Clin. Pharm. 38, 724–730.
Almarsdottir, A.B., Kaae, S., Traulsen, J.M., 2014. Opportunities and challenges in social pharmacy and pharmacy practice research. Res. Social Adm. Pharm. 10, 252–255.
American College of Clinical Pharmacy, 2008. The definition of clinical pharmacy. Pharmacotherapy 28 (6), 816–817.
Ascione, F.J., Shrimp, L.A., Opdycke, R.C., 1992. Research in pharmaceutical care: experiences from the focused drug therapy review program. Am. J. Pharm. Educ. 56, 441–447.
Austin, Z., Sutton, J., 2019. Research Methods in Pharmacy Practice Methods and Applications Made Easy. Elsevier, People's Republic of China.
Awaisu, A., Alsalimy, N., 2015. Pharmacists' involvement in and attitudes toward pharmacy practice research: a systematic review of the literature. Res. Social Adm. Pharm. 11 (6), 725–748.
Babar, Z.U., 2015. Pharmacy Practice Research Methods. Springer, New York.
Bond, C., 2015. Pharmacy practice research: evidence and impact. In: Babar, Z.U. (Ed.), Pharmacy Practice Research Methods. Springer International Publishing, Switzerland, pp. 1–24.
Bissell, P., Traulsen, J.M., Haugbolle, L.S., 2001. An introduction to sociology and what it can do for pharmacy practice research. Int. J. Pharm. Pract. 9, 289–295.
Collett, D.M., Aulton, M.E., 1990. Pharmaceutical Practice. Churchill Livingstone, New York.
Council on Credentialing in Pharmacy, 2009. A resource paper, Scope of Contemporary Pharmacy Practice: Roles, Responsibilities, and Functions of Pharmacists and Pharmacy Technicians. Available from: http://www.pharmacycredentialing.org/Contemporary_Pharmacy_Practice.pdf.
Deb, H.L., 1986. Pharmacy: Nuffield Foundation Report. The Nuffield Foundation, London 475, cc1026-1057.
Dolovich, L., Tsuyuki, R.T., 2016. Pharmacy practice research produces findings that inform how pharmacists contribute to optimal drug therapy outcomes for Canadians. Can. Pharm. J. (Ott.) 149 (5), 261–263.
Fathelrahman, A.I., Ibrahim, M.I.M., Wertheimer, A.I. (Eds.), 2016. Introduction. In: Pharmacy Practice in Developing Countries: Achievements and Challenges (pp. xxix–xxxix). Elsevier, United Kingdom.
Fish, A., Watson, M.C., Bond, C.M., 2002. Practice-based pharmaceutical services: a systematic review. Int. J. Pharm. Pract. 10 (4), 225–233.
Gregory, J.H., 2013. Evolution of pharmacy. In: Remington: The Science, Practice of Pharmacy (Vol. I: The Science and Practice of Pharmacy). 22nd ed. Pharmaceutical Press, United States of America, pp. 11–24.
Hepler, C.D., 1991. Issues and outcomes in pharmaceutical program evaluation. J. Soc. Admin. Pharm. 8, 141–149.
Horne, R., 2001. Health, illness and medicines use: compliance, adherence and concordance. In: Taylor, K., Harding, G. (Eds.), Pharmacy Practice. Taylor & Francis, United Kingdom, 2001, pp. 148–166.
Kennie, N.R., Schuster, B.G., Einarson, T.R., 1998. Critical analysis of the pharmaceutical care research literature. Ann. Pharmacother. 32 (1), 17–26.
Koster, E.S., Blom, L., Philbert, D., Rump, W., Bouvy ML, 2014. The Utrecht Pharmacy Practice network for education and research: a network of community and hospital pharmacies in the Netherlands. Int. J. Clin. Pharm. 36 (4), 669–674.
International Pharmaceutical Federation, 2019. Pharmacy practice research special interest group. Available from: https://www.fip.org/Pharmacy_Practice_Research.
Mays, N., 1994. Health Services Research in Pharmacy: A Critical Personal Review, Pharmacy Practice Research Resource Centre, University of Manchester.
Morrall, P., 2001. Sociology and Nursing. Routledge, London.
Moullin, J.C., Sabater-Hernández, D., Fernandez-Llimos, F., Benrimoj, S.I., 2013. Defining professional pharmacy services in community pharmacy. Res. Social Adm. Pharm. 9 (6), 989–995.
National Association of Boards of Pharmacy (NABP), 2019. Available from: https://nabp.pharmacy/publications-reports/.
Pharmacy Practice Research Special Interest Group, 2019. International pharmaceutical federation (FIP). Available from: https://www.fip.org/Pharmacy_Practice_Research.
Pharmacy Practice Activity Classification (PPAC), 2019. American pharmacy association academy of pharmaceutical research and science. Available from: https://www.japha.org/article/S0003-0465(16)33262-1/abstract.
Pearson, G.J., 2007. Evolution in the practice of pharmacy—not a revolution. Can. Med. Assoc. J. 176 (9), 1295–1296.
Royal Pharmaceutical Society of Great Britain (RPSGB), 1997a. Building the Future: A Strategy for a 21st Century Pharmaceutical Service. Royal Pharmaceutical Society of Great Britain, London.
Royal Pharmaceutical Society of Great Britain (RPSGB), 1997b. King's Fund. Pharmacy Practice R&D Task Force. A New Age for Pharmacy Practice Research: Promoting Evidence-based Practice in Pharmacy. Royal Pharmaceutical Society, London.
Scahill, S., Babar, Z.U., 2017. Defining pharmacy and its practice: a conceptual model for an international audience. Integr. Pharm. Res. Pract. 6, 121–129.
Smith, F., 2002. Research Methods in Pharmacy Practice. Pharmaceutical Press, London, pp. 1–160.
Smith, F., 2010. Preparation, planning & management. In: Research Methods in Pharmacy Practice. Pharmaceutical Press, London.
Strand, L.M., Morley, P.C., Cipolle, R.J., Ramsey, R., Lamsam, G.D., 1990. Drug-related problems: their structure and function. DICP 24 (11), 1093–1097.
Taylor, K.M.G., Harding, G., 2001. Preface. In: Pharmacy Practice. Taylor & Francis, United Kingdom.
Whalley, B.J., 2008. Pharmacy and the Pharmacist: What Is Pharmacy Practice. In: Foundation in Pharmacy Practice. Pharmaceutical Press, United Kingdom.
World Health Organization, 2011. Joint FIP/WHO guidelines on good pharmacy practice: standards for quality of pharmacy services [WHO Technical Report Series, No. 961, 2011]. Available from: http://apps.who.int/medicinedocs/documents/s18676en/s18676en.pdf.
World Health Organization, 1996. Good pharmacy practice (GPP) in community and hospital pharmacy settings [WHO/PHARM/DAP/96.1], WHO, Geneve. Available from: http://apps.who.int/medicinedocs/documents/s21088en/s21088en.pdf.
World Health Organization, 2006. Developing pharmacy practice: a focus on patient care (2006 Handbook) [WHO/PSM/PAR/2006.5], WHO, Geneve. Available from: https://www.fip.org/files/fip/publications/DevelopingPharmacyPractice/DevelopingPharmacyPracticeEN.pdf.
Zermansky, A.G., Alldred, D.P., Petty, D.R., Raynor, D.K., Freemantle, N., Eastaugh, J., Bowie P, 2006. Clinical medication review by a pharmacist of elderly people living in care homes-randomised controlled trial. Age Ageing 35 (6), 586–591.

Further Reading

Babar, Z.U., 2019. Encyclopedia of Pharmacy Practice and Clinical Pharmacy. Elsevier, Glasgow.
Mendes, A.E., Tonin, F.S., Fernandez-Llimos, F., 2016. Analysis of ten years of publishing in pharmacy practice. Pharm. Pract. 14 (4), 847.

Research Designs and Methodologies Related to Pharmacy Practice

Ahmed Awaisu, Banan Mukhalalati, Mohamed Izham Mohamed Ibrahim, Qatar University, Doha, Qatar

© 2019 Elsevier Inc. All rights reserved.

Learning Objectives

- Discuss the value of pharmacy practice research to evidence-based practice and policy.
- Describe the classifications and types of study designs commonly used in pharmacy practice research.
- Discuss the concepts and structure of common study designs used in pharmacy practice research including experimental, quasi-experimental, observational, qualitative, and mixed method designs.
- Discuss the important considerations for conducting pharmacy practice research in terms of study design, data collection, data analyses, and ethical considerations.

Introduction to Research Methodologies Used in Pharmacy Practice

The mission of pharmacy profession and the role of pharmacists in healthcare have evolved toward patient-centered care in the last few decades. Pharmacists with their expertise in drug therapy and accessibility to the public have unprecedented opportunities to assume increasing responsibility for direct patient care (Bond, 2006). New cognitive pharmaceutical services and new roles for pharmacists continue to emerge.

In the era of evidence-based practice and health services, it is not just adequate to propose those new pharmacy services or new roles without evidence of their benefit (Awaisu and Alsalimy, 2015; Bond, 2006). New pharmacy services and new roles must be proven to be feasible, acceptable, cost-effective, and increase health outcomes. Pharmacy practice research provides such evidence and can confirm the value of a new service, inform policy, and result in practice changes (Bond, 2006; Chen and Hughes, 2016). Research evidence should be used to identify new areas for improved health service delivery and rigorously

evaluate new services. The research used to generate such evidence should be grounded in robust and rigorous methodologies (Chen and Hughes, 2016). Traditionally, common quantitative and qualitative methods such as randomized controlled trials, cohort study, case control study, questionnaire-based surveys, and phenomenology using qualitative interviews have been used in pharmacy. However, in recent years, novel and more complex methods are being developed and utilized. Pharmacy practice researchers need to know how these old and new methodological approaches should be selected, applied, and interpreted in addressing research problems.

Various study designs, including, but not limited to experimental, quasi-experimental, observational, qualitative, and mixed method designs, have been used in pharmacy practice research. Furthermore, different classification systems (e.g., quantitative vs. qualitative, experimental vs. observational, descriptive vs. analytical study designs) have been used in the literature. The choice of a study design to answer a research question in pharmacy practice research is driven by several factors, including the type of the research question or the research hypothesis, expertise of the investigator, availability of data, and funding opportunities. Pharmacy practice researchers need to be competent in the selection, design, application, and interpretation of these methodological and analytical approaches. Today, many of the research methods used in pharmacy practice research have been adapted from fields such as sociology, anthropology, psychology, economics, and other disciplines. This paradigm shift has led to a greater emphasis on the appropriate choice of a specific research design or method to answer a specific research question (Chen and Hughes, 2016). Consequently, pharmacy practice researchers should place an emphasis on the reliability of the methods selected, the correct interpretation of their findings, the testing of a specific hypothesis, and the internal validity of their data, among other considerations. Novice and early career researchers should be familiar and have sound foundation in a variety of methods applied in pharmacy practice research, which will be covered in this chapter and other chapters in this Encyclopedia. We do believe that more experienced researchers should focus on certain methods in order to advance research in our discipline.

Core Quantitative and Qualitative Approaches Used in Pharmacy Practice Research

Traditionally, core quantitative approaches used in pharmacy practice research include nonexperiments, quasi-experimental designs, and true experimental designs such as prospective randomized controlled intervention trials. Nonexperiments also include observational study designs that are often described as pharmacoepidemiologic study designs such as case–control study, cohort study, nested case–control study, and cross-sectional study (Etminan, 2004; Etminan and Samii, 2004). In recent years, conventional qualitative approaches and their philosophical paradigms are increasingly been used in pharmacy. These include the five qualitative approaches to inquiry: narrative research, phenomenology, grounded theory, ethnography, and case study. These qualitative methods are often difficult for pharmacy practice researchers to comprehend, and researchers tend to describe the methods of data collection such as individual interviews and focus group discussions as qualitative methods of inquiry. These data collection methods are briefly described later in this chapter, among others. Furthermore, there is an increasing importance on the appropriate selection and use of mixed method approach (Hadi et al., 2013; Hadi and Closs, 2016a, 2016b), which are often designed and applied wrongly. Finally, it is worthwhile to be familiar with novel research methodologies such as discrete choice experiments, Delphi techniques, simulated client technique, and nominal group techniques, which fall between quantitative and qualitative approaches, often with no clear differentiation on where they belong. Although called "novel" in the context of this chapter, these methods are not new in other relevant disciplines, but new and not commonly used in pharmacy practice research.

Research Question and Selection of Study Design

Pharmacy practice researchers begin by conception of a research idea or identifying a research question and defining a hypothesis based on the question. The researcher then selects a study design that will be suitable to answer the research question. The study design should be appropriately selected prior to initiation of any research investigation. Selecting an inappropriate study design may potentially undermine the validity of a study in its entirety. Investigators are encouraged to critically think about the possible study designs to ensure that the research question is adequately addressed and should be able to adequately justify their choice. These study designs have been variously classified and one common classification system is quantitative vs. qualitative study designs. Study designs play a major role in determining the scientific value of research studies. Inappropriate choice of a study design is impossible to correct after completion of the study. Therefore, thorough planning is required to avoid unconvincing results and invalid conclusions. Good understanding of basic study design concepts will aid researchers in conducting robust and rigorous practice-based research. This chapter introduces the structure and the fundamentals of common study designs used in pharmacy practice research and discusses the important considerations for conducting pharmacy practice research in terms of study design, data collection, data analyses, and ethical considerations.

Classification of Research Methodologies Used in Pharmacy Practice

Various classifications for research designs and methods used in pharmacy practice have been used in the literature. The following are some of the approaches for the classification of research designs:

1. Classification based on time orientation: Retrospective vs. prospective designs

a. Retrospective design—A retrospective study design observes what has happened in the past. It begins and ends in the present. This design involves a major limitation as it looks to collect information about events that occurred in the past. An example of this design is retrospective case-control study.
Case example: Investigators were looking for the association between acute myocardial infarction and smoking status, type of tobacco, amount of smoke, etc. (Teo et al., 2006). Another example of a case–control study from published literature is the study investigating the association between the use of phenylpropanolamine and the risk of hemorrhagic stroke (Kernan et al., 2000).
b. Prospective design—A prospective study design begins in the present and progresses forward, collecting data from subjects whose outcomes lie in the future. An example of this design is prospective cohort study.
Case example: Investigators were interested to determine the long-term effectiveness of influenza vaccines in elderly people; they recruited cohorts of vaccinated and unvaccinated community-dwelling elderly (Nichol et al., 2007).

2. Classification based on study purpose: Descriptive vs. analytical designs

a. Descriptive design—A descriptive study describes a population/sample in terms of distribution of the variables, and frequency of outcomes of interest. Unlike analytical studies that include control (comparison) group, descriptive studies do not include a comparison group. Descriptive studies include case reports, case series reports, cross-sectional studies, surveillance studies, and ecological studies.
Case example: A case report was written by a physician who contracted Severe Acute Respiratory Syndrome (SARS) during an outbreak in Hong Kong (Wu and Sung, 2003). Another example is an ecological study examining diet and sunlight as risks for prostate cancer mortality (Colli and Colli, 2006). Chim et al. conducted a large population-based survey in Australia to determine what community members think about the factors that do and should influence government spending on prescribed medicines (Chim et al., 2017).
b. Analytical design—An analytical study identifies risk factors, associated factors, mediating factors, etc. Analytical studies are either experimental or observational. Case–control and cohort studies are types of observational studies.
Case example: A group of investigators carried out a study to establish an association between the use of traditional eye medicines (TEM) and corneal ulcers. In this case, both case–control and cohort study designs are applicable. In an example of a case control study, Archibugi et al. aimed to investigate the association between aspirin and statin exclusive and combined and pancreatic ductal adenocarcinoma occurrence (Archibugi et al., 2017). Another example of a cohort study is a study carried out by Wei et al. in which they investigated whether or not acid-suppression medicines increased the risk of bacterial gastroenteritis (Wei et al., 2017).

3. Classification based on investigator orientation: Experimental vs. quasi-experimental vs. observational designs

a. Experimental design—In experimental design (also known as interventional design), the investigator performs an intervention and evaluates cause and effect relationships.
Case examples: Investigators conducted a study about the newer versus older antihypertensive agents in African hypertensive patients (NOAAH) trial (nct01030458) to compare the efficacy of single-pill combinations of newer versus older antihypertensive agents (i.e., a single-pill combination of newer drugs, not involving a diuretic, with a combination of older drugs including a diuretic) (Odili et al., 2012). In a crossover design, a group of investigators evaluated the effect of spironolactone on nonresolving central serous chorioretinopathy (Bousquet et al., 2015).
b. Quasi-experimental design—The quasi-experimental design is very similar to the true experimental design described above and it involves an intervention. The design has been employed when randomization is inappropriate or impossible, especially when implementing complex interventions.
Case examples: Prashanth et al. aimed to understand if (and how) a package of interventions targeting primary health centers and community participation platforms affect utilization and access to generic medicines for people with noncommunicable diseases using quasi-experimental design approach (Prashanth et al., 2016).
c. Observational design—It involves only observation of natural phenomena and does not involve investigator intervention. Typically, this study design investigates associations and not causation. Examples include cohort study and case–control study. These studies can explore an association between a pharmacologic agent and a disease of interest. Case examples: Please see previous examples of these.

4. Classification based on question orientation: Quantitative vs. qualitative vs. mixed method designs

a. Quantitative design—This is based on measurement of quantity and it is applicable to phenomenon that can be quantified (i.e., expressed in terms of numbers).
Case examples: Please see experimental studies, and case–control and cohort study designs.
b. Qualitative design—Qualitative research is concerned with qualitative phenomenon (i.e., a phenomenon relating to or involving quality).
Case examples: Investigators in Canada explored the lived experiences of youth who are prescribed antipsychotics by conducting interpretative phenomenology study (Murphy et al., 2015).

c. Mixed method designs—Mixed method design brings together qualitative and quantitative methodologies within a single study to answer or understand a research problem (Hadi et al., 2013).
Case examples: Shiyanbola et al. combined focus group discussion with a survey tool to investigate patients' perceived value and use of quality measures in evaluating and choosing community pharmacies (Shiyanbola and Mort, 2015).

5. Classification of pharmacoepidemiologic study designs
Below is a brief description of traditional and novel pharmacoepidemiologic study designs. Several examples of pharmacoepidemiologic study designs are provided above. Some descriptive studies including case reports, case series, and ecological studies will not be described in this chapter.

a. Case–control studies—In this design, patients (those who develop the disease or outcome of interest) are identified and control patients (those who do not develop the disease or outcome of interest) are sampled at random from the original cohort that gives rise to the cases (Etminan and Samii, 2004; Newman et al., 2013). The distribution of exposure to certain risk factors between the cases and the controls is then explored, and an odds ratio (OR) is calculated.
b. Cohort studies—This can be described as a study in which a group of exposed subjects and a group of unexposed subjects are followed over time and the incidence of the disease or outcome of interest in the exposed group is compared with that in the unexposed group (Etminan and Samii, 2004; Hulley et al., 2013).
c. Case-crossover studies—The case-crossover may be considered comparable to a crossover randomized controlled trial in which the patients act as their own control (Etminan and Samii, 2004). Pattern of exposure among the cases is compared between event time and control time. The between-patient confounding that occurs in a classic case-control study is circumvented in this design. Tubiana et al. evaluated the role of antibiotic prophylaxis and assessed the relation between invasive dental procedures and oral streptococcal infective endocarditis, using a nationwide population-based cohort and a case-crossover study design (Tubiana et al., 2017).
d. Case–time control studies—This design is an extension of the case-crossover design, but includes a control group (Etminan and Samii, 2004). A group of researchers assessed medication-related hospitalization. They used the case–time control study design to investigate the associations between 12 high risk medication categories (e.g., antidiabetic agents, diuretics, benzodiazepine hypnotics) and unplanned hospitalizations (Lin et al., 2017).
e. Nested case–control studies—In this design, a cohort of individuals is followed during certain time periods until a certain outcome is reached and the analysis is conducted as a case–control study in which cases are matched to only a sample of control subjects (Etminan, 2004). de Jong et al. examined the association between interferon-β (IFN-β) and potential adverse events using population-based health administrative data in Canada (De Jong et al., 2017).
f. Cross-sectional studies—In this type of study, the investigator measures the outcome of interest and the exposures among the study participants at the same time (Hulley et al., 2013; Setia, 2016b). It provides a snapshot of a situation for a particular period.

Quantitative Research Designs in Pharmacy Practice

A wide range of quantitative methods are commonly applied in pharmacy practice research. These methods are widely used in published pharmacy practice literature to explore appropriateness of medicines use, appropriateness and quality of prescribing, and medication safety, through analyzing existing datasets, direct observation, or self-report (Green and Norris, 2015). Pharmacy practice research questions also seek to determine the knowledge, behaviors, attitudes, and practices of pharmacists, other healthcare providers, patients, policy-makers, regulators, and the general public. Quantitative methods are also used in evaluating the effect of new pharmacy services and interventions to improve medicines use. These practice research projects provide valuable insights about how medicines are used, and how to maximize their benefits and minimize their harmful effects. In the context of this chapter, quantitative study designs will be broadly classified into three: (1) observational, (2) experimental and quasi experimental, and (3) other designs.

Observational Study Designs

Pharmacoepidemiology is a "relatively new science that explores drug efficacy or toxicity using large observational study designs" (Etminan, 2004; Etminan and Samii, 2004). These study designs explore drug use studies that usually cannot be answered using randomized controlled trials or other experimental designs. In several instances, experimental study designs may not be suitable or feasible; in such circumstances, observational study designs are applied (Cummings et al., 2013). As the name implies, observational studies involve merely observing the subjects in a noncontrolled setting, without investigator intervention or manipulating other aspects of the study. Therefore, observational studies are nonexperimental. The observation of the variables of interest can be prospective, retrospective, or current depending on the type of the observational study.

In pharmacoepidemiology and other areas of pharmacy practice, researchers are often interested in measuring the relationships between exposure to a drug and its efficacy, toxicity, or other outcomes of interest using observational study designs. It is worthwhile to note that observational study designs investigate association, but, in most cases, not causation. Here, we provide descriptions of some commonly used study designs in pharmacoepidemiology and pharmacy practice research in general.

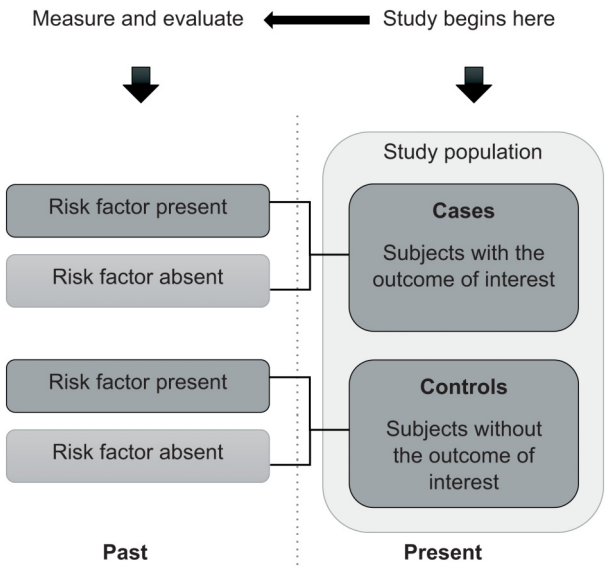

Figure 1 Case–control study design.

Case–Control Studies

Case–control study design is used to determine association between risk factors or exposures and outcomes. It is a useful design to study exposures in rare diseases or diseases that take long time to develop (Newman et al., 2013). It investigates exposures in individuals with and those without the outcome of interest. Nevertheless, case–control studies can help to identify harmful or beneficial exposures. Furthermore, the outcome of interest can be undesirable (e.g., mortality) or desirable (e.g., microbiological cure). As the name suggests, in a case–control study design, there are two groups of subjects: (1) cases (individuals with the outcome of interest) and (2) controls (individuals without the outcome of interest) (Newman et al., 2013). Cases are randomly selected based on prespecified eligibility criteria from a population of interest. Appropriate representative controls for the cases selected are then identified. The researchers then retrospectively investigate possible exposures to the risk factor. **Fig. 1** represents a schematic diagram of a case–control study.

Case–control studies are relatively inexpensive, less time-consuming to conduct, allow investigation of several possible exposures or associations, and are suitable for rare diseases. Selection of the control group is a critical component of case–control studies. Case–control studies have several drawbacks: confounding must be controlled, subject to recall, observation, and selection biases.

OR is the measure of association used for the analysis of case–control studies. This is defined as the odds of exposure to a factor in those with a condition or disease compared with those who do not have the condition or disease.

Cohort Studies

Similar to case–control studies, cohort studies determine an association between exposures/factors and development of an outcome of interest. As previously described, a cohort study is a study in which a group of exposed subjects and a group of unexposed subjects are followed over time to measure and compare the rate of a disease or an outcome of interest in both groups (Etminan and Samii, 2004; Hulley et al., 2013). A cohort study can be prospective (most common) or retrospective. While a case–control study begins with patients with and those without the outcome of interest (e.g., diseased and nondiseased patients), a cohort study begins with exposed and unexposed patients (e.g., patients with and those without certain risk factor) (Hulley et al., 2013; Setia, 2016a). In a cohort study, both the exposed and the unexposed subjects are members of a larger cohort in which subjects may enter and exit the cohort at different periods in time (Etminan and Samii, 2004; Hulley et al., 2013).

Typically, a cohort study should have a defined time zero, which is defined as the time of entry into the cohort (Etminan and Samii, 2004). The cohort (a group of exposed and unexposed subjects, who are free of the outcome at time zero) is followed for a certain period until the outcome of interest occurs. In addition, information or data related to all potential confounders or covariates should also be collected as failure to account for these can bias the results and over- or underestimates the risk estimate. There are two types of cohort studies: retrospective cohort and prospective cohort studies.

Retrospective cohort study, also known as historical cohort study, begins and ends in the present, while looking backward to collect information about exposure that occurred in the past (**Fig. 2**). Historical cohort studies are relatively less time-consuming and less expensive than prospective cohort studies (Etminan and Samii, 2004; Hulley et al., 2013; Setia, 2016a). In addition, there is no loss to follow-up and researchers can investigate issues not amenable to intervention study designs. However, these studies are only as good as the data available, the investigator has limited control of confounding variables, and it is prone to recall bias.

On the other hand, prospective cohort study, also known as longitudinal cohort study, begins in the present and progresses forward, collecting data from enrolled subjects whose outcomes fall in the future (Etminan and Samii, 2004; Hulley et al., 2013;

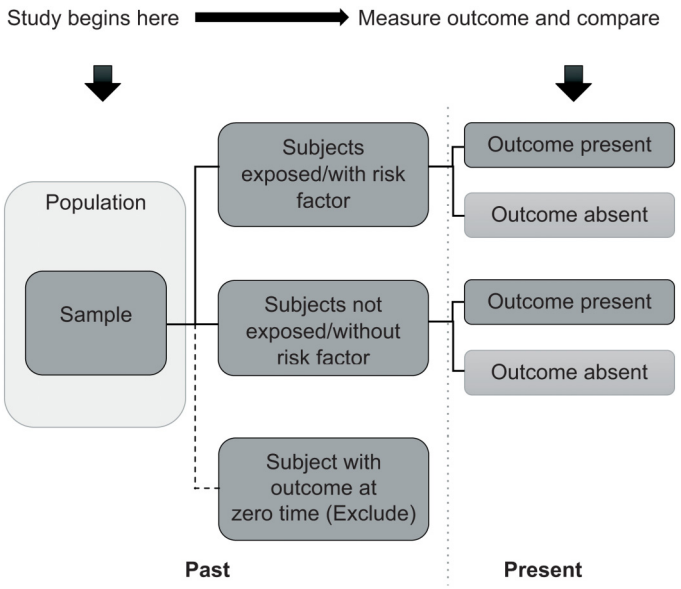

Figure 2 Retrospective (historical) cohort study design.

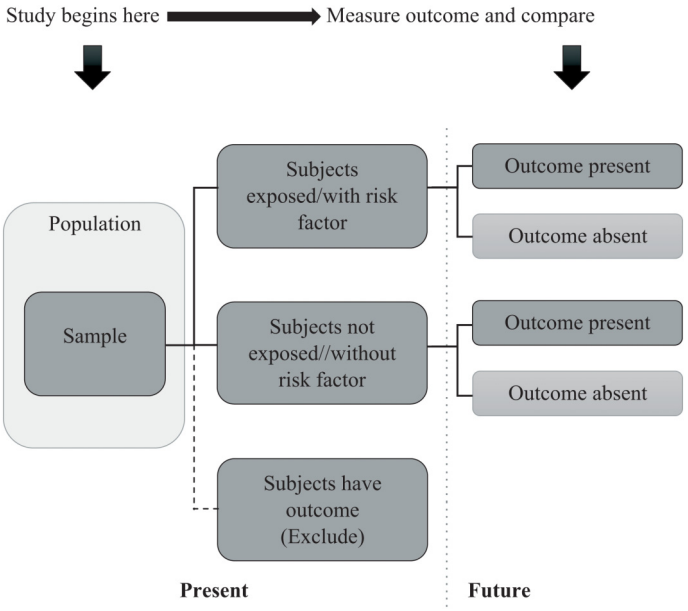

Figure 3 Prospective (longitudinal) cohort study design.

Setia, 2016a) (**Fig. 3**). Prospective cohort studies are easier to plan for data collection, have low recall bias, and the researcher has a better control of confounding factors. On the other hand, it is difficult to study rare conditions; they are more prone to selection bias, more time-consuming, expensive, and loss of subjects to follow-up is common.

Relative risk (RR) is the measure of association used for the analysis of a cohort study. This is defined as the risk of an event or development of an event relative to exposure (i.e., the risk of subjects developing a condition when exposed to a risk factor compared with subjects who have not been exposed to the risk factor).

Case-Crossover Studies

This is a relatively new design in the field of epidemiology in which the patients act as their own controls (Maclure, 1991). In this design, there is a case and a control element both of which come from the same subject. In other words, each case serves as its own control. It can be considered equivalent to a crossover RCT with a washout period (Etminan and Samii, 2004). Pattern of exposure to the risk factor is compared between the event time and the control time (Etminan and Samii, 2004). Case-crossover study design is useful to investigate triggers within an individual. For instance, it is applicable when studying a transient exposure or risk factor.

However, determination of the period of the control and case components is a crucial and challenging aspect of a case-crossover study design. Since the patients serve as their own controls, the interindividual variability that is inherent in classic case–control studies is eliminated. This is important in studies involving progressive disease states in which disease severity may differ between patients such as multiple sclerosis. OR is estimated using techniques such as Mantel–Haenszel statistics and logistic regression.

Cross-Sectional Studies

Cross-sectional studies also known as prevalence studies identify the prevalence or characteristics of a condition in a group of individuals. This design provides a snapshot of the prevalence or the characteristics of the study subjects in a single time point. The study investigator measures the outcomes and the exposures in the study subjects simultaneously (Etminan and Samii, 2004; Hulley et al., 2013; Setia, 2016b). Hence, cross-sectional studies do not follow up patients to observe outcomes or exposures of interest. Data are often collected through surveys. Cross-sectional design cannot provide cause and effect relationships between certain exposures and outcomes of interest.

Experimental and Quasi-Experimental Study Designs

In a typical experimental study design, the investigator assigns subjects to the intervention and control/comparison groups in an effort to determine the effects of the intervention (Cummings et al., 2013). Since the investigator has the opportunity to control various aspects of the experiment, this allows the researcher to determine the causal link between exposure to the intervention and outcome of interest. The researcher either randomly or conveniently assigns the subjects to an experimental group and a control group. When the investigator performs randomization, the study is considered a true experiment (see Fig. 4). On the other hand, if subjects are assigned into groups without randomization, the study is considered a quasi-experiment (refer to Fig. 5). As with experimental designs, quasi-experimental designs also attempt to demonstrate a causal link between the intervention and the outcome of interest. Due to the challenges of conducting a true experimental design, the quasi-experimental study designs have been consistently used in pharmacist intervention research.

RCTs are considered the gold standard of experimental study designs in pharmacy practice and evidence-based research (Cummings et al., 2013). The investigator randomly assigns a representative sample of the study population into an experimental group and a control group (Fig. 4). Randomization in RCT is to minimize confounding and selection bias; it enables attainment of similar experimental and control groups, thereby isolating the effect of the intervention. The experimental group receives the treatment or intervention (e.g., a new drug or pharmaceutical care for treatment of a certain disease), while the control group receives a placebo treatment, no treatment, or usual care treatment depending on the objective of the study (Cummings et al., 2013). These groups are then followed prospectively over time to observe the outcomes of interest that are hypothesized to be affected by the treatment or intervention. The result of the study is considered to have high internal validity if significant changes on the outcome variable occur in the experimental group, but not the control group. The investigator can infer that the treatment or intervention is the most probable cause of the changes observed in the intervention group. The unit of randomization in RCTs is usually the patient, but can sometimes be clusters to circumvent the drawbacks of contamination.

RCTs are very challenging to undertake and pharmacy practice researchers should ensure design of robust experiments, while considering all essential elements and adhering to best practices. For instance, to determine the impact of a cognitive pharmaceutical service, the selection of a representative sample of the population is a prime consideration in an RCT. Moreover, RCTs are expensive, labor-intensive, and highly prone to attrition bias or loss to follow-up.

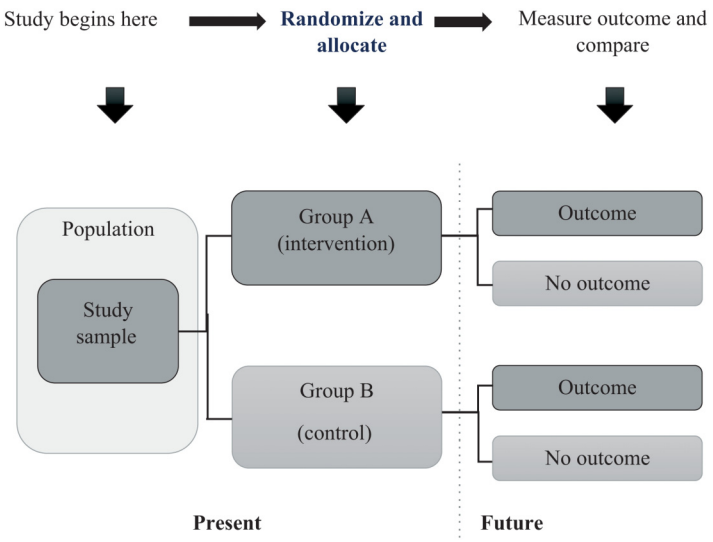

Figure 4 True experimental study design.

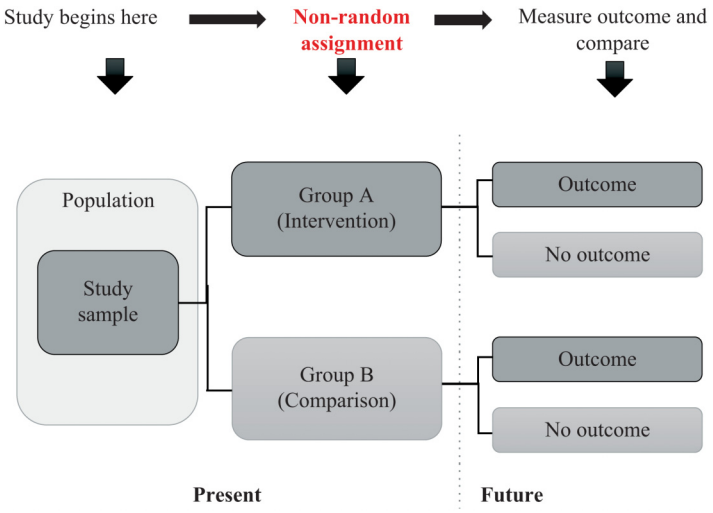

Figure 5 Quasi experimental study design.

In pharmacy practice research, it is often difficult to comply with the stringent requirements of true experimental designs such as RCTs, due to logistic reasons and/or ethical considerations (Grady et al., 2013; Krass, 2016). Whenever true experimental models are not feasible to be applied in pharmacy practice research, the researcher should endeavor to use a more robust quasi-experimental design. For instance, when randomization is not feasible, the researcher can choose from a range of quasi-experimental designs that are non-randomized and often noncontrolled (Grady et al., 2013; Krass, 2016). Quasi-experimental studies used in pharmacy literature may be classified into five major categories: (1) quasi-experimental design without control groups (i.e., one group pre–posttest design); (2) quasi-experimental design that use control groups with no pretest; (3) quasi-experimental design that use control groups and pretests (i.e., nonequivalent control group design with dependent pretests and posttests) (see **Fig. 5**); (4) interrupted time series and; (5) stepped wedge designs (Brown and Lilford, 2006; Grady et al., 2013; Harris et al., 2006).

The one group pretest posttest design and the nonequivalent control group design (**Fig. 5**) are the most commonly applied quasi-experimental designs in practice-based research literature. These designs have been commonly used to evaluate the effect of pharmacist interventions in medications management in general and specific disease states management. The lack of randomization and/or the lack of control group is a major weakness and a threat to internal validity in quasi-experimental designs (Grady et al., 2013). The observed changes could be due to some effects other than the treatment.

Other Quantitative Study Designs

In addition to the common observational, experimental, and quasi-experimental designs described above, there are other designs that are used in pharmacy. These research methods include, but are not limited to, simulated client technique, discrete choice experiments, and Delphi techniques. These methods, which are considered relatively new to pharmacy, are now commonly used in pharmacy practice research. In this chapter, we briefly describe these methods and their application in pharmacy. However, a more detailed description of their components and the nitty gritty of their application in pharmacy practice are available elsewhere within this textbook.

Simulated Client Method

The use of simulated client or simulated patient (mystery shopper) method to assess practices or behaviors in pharmacy practice has received much attention in recent times (Watson et al., 2004, 2006). "A simulated patient is an individual who is trained to visit a pharmacy (or drug store) to enact a scenario that tests a specific behavior of the pharmacist or pharmacy staff" (Watson et al., 2006). A review by Watson et al. demonstrated the versatility and applicability of this method to pharmacy practice research in both developing and developed countries (Watson et al., 2006). The investigators also identified some important characteristics that should be taken into consideration in designing studies that use this technique.

This method can be used to assess wide range of cognitive pharmacy services including counseling and advice provision, treatment of minor ailments, provision of nonprescription medicines, and public health pharmacy, among other things. This method can be a robust and rigorous method of assessing pharmacy practice if used appropriately (Watson et al., 2006; Xu et al., 2012). More recent developments have documented that the simulated patient methods have been used to provide formative feedback in addition to assessing practice behavior of pharmacists and their staff (Xu et al., 2012).

In a case example, a group of investigators evaluated Qatari pharmacists' prescribing, labeling, dispensing, and counseling practices in response to acute community-acquired gastroenteritis (Ibrahim et al., 2016). In another example, the investigators documented the state of insomnia management at community pharmacies in Pakistan (Hussain et al., 2013).

Discrete Choice Experiments

Evidence in healthcare suggests that understanding consumers' preferences can help policy-makers to design services to match their views and preferences (Ryan, 2004). Traditionally, studies to understand patients' and consumers' preferences for pharmaceutical services used opinion or satisfaction survey instruments. Nevertheless, such satisfaction surveys lack the ability to identify the drivers of satisfaction or the relative importance of the different characteristics of the service (Vass et al., 2016). Discrete choice experiments are a novel survey-based method in pharmacy that are predicated on economic theories that allow systematic quantification of preferences to help identify which attributes of a good or service consumers like, the relative value of each attribute, and the balance between the different attributes (Naik Panvelkar et al., 2010; Ryan, 2004; Vass et al., 2016). In-depth description of this method and its essential elements are described in another chapter in the Encyclopedia.

Qualitative Research Designs in Pharmacy Practice

Qualitative research methodology is applied to investigate a problem that has unmeasurable variables, to get a comprehensive understanding of the topic, through discussing it with the involved individuals, and to recognize the natural context in which the investigated issue takes place (Creswell, 2013). The use of qualitative research methodology is becoming increasingly common across diverse health-related disciplines, including pharmacy practice. This is because of its ability to describe social processes and behaviors associated with patients or healthcare professionals, which strengthen the research impact (McLaughlin et al., 2016). Therefore, pharmacy researchers and practitioners need to be better oriented to qualitative research methods (Behar-Horenstein et al., 2018).

In the following section, interpretative frameworks and philosophical orientations, methodologies, data collection and analysis methods, approaches to ensure rigor, and ethical considerations in qualitative research are briefly discussed (Cohen et al., 2013; Creswell, 2013).

Interpretative Framework and Philosophical Assumptions of Qualitative Research

Interpretative Frameworks

Interpretative frameworks are the conceptual structures for comprehension, which form researcher's reasoning and views of truth and knowledge (Babbie, 2015). Different scholars have categorized qualitative research paradigms or interpretative frameworks differently. The following are examples of interpretative framework categories that are used in health science research based on the categorization of Creswell (2013): (1) social constructivism (interpretivism) framework; (2) post-positivism framework; (3) transformative, feminist, critical frameworks and disabilities theories; (4) postmodern frameworks; (5) pragmatism frameworks.

Philosophical Assumptions

Philosophical assumptions are theories and perspectives about ontology, epistemology, axiology, and methodology, which underpin the interpretative frameworks selected by qualitative researchers (Cohen et al., 2013). As with interpretative framework, there are numerous means to categorize the philosophical assumptions that are folded within interpretative framework. The following are explanations of philosophical assumptions based on the categorization of Creswell (2013):

1. Ontological assumptions, which define the nature of reality
2. Epistemological assumptions, which clarify means for knowing reality
3. Axiological assumptions, which explain the role and influence of researcher values
4. Methodological assumptions, which identify approaches to inquiry

It is important that a qualitative researcher understands how interpretative frameworks (e.g., social constructivism, post-positivism, and pragmatic interpretative frameworks) are differentiated because of their underpinning philosophical assumptions (i.e., ontological, epistemological, axiological, and methodological assumptions).

Approaches to Inquiry (Methodology)

It is important that qualitative researchers understand the differences between the characteristics of the five qualitative approaches to inquiry, in order to select an approach to inquiry and attain methodological congruence (Creswell, 2013). The five approaches to qualitative research inquiry are:

a. Narrative research: Describes participants' written and spoken stories about their experiences with a phenomenon being investigated, while considering the chronological connection of the phenomenon's series of events (Anderson and Kirkpatrick, 2016; Creswell, 2013; Czarniawska, 2004).
b. Phenomenological research: Describes the essence of participants' common experiences of a phenomenon, so that the description is a general essence rather than an individual experience (Creswell, 2013; Giorgi, 1997; Moustakas, 1994).

c. Grounded theory research: Aims to generate a theory grounded in participants' data that conceptually explain a social phenomenon, which could involve social processes, or actions or interactions (Creswell, 2013; Strauss and Corbin, 1990; Woods et al., 2016).
d. Ethnographic research: Involves describing the shared patterns of values, behaviors, and beliefs of culture-sharing participants (Creswell, 2013; Harris, 1968; Rosenfeld et al., 2017).
e. Case study research: Provides an in-depth examination of a real-life contemporary phenomenon that researchers cannot change over time, to illustrate the significance of another general topic (Baker, 2011; Creswell, 2013; de León-Castañeda et al., 2018; Mukhalalati, 2016; Yin, 2014).

Data Collection and Analysis Methods in Qualitative Research

1. Data collection methods
   Data collection tools in qualitative research can be categorized into the following fundamental categories (Creswell, 2013):
   a. Observation
   b. Documents
   c. Individual semi-structured interviews
   d. Focus groups (FGs)
   e. Audio-visual materials
   f. Emails chat rooms, weblogs, social media, and instant messaging.
2. Common elements and steps in conducting individual interviews and focus groups
   a. Topic guides: Topic guides guide the discussions in focus groups and individual interviews, and contain open-ended questions and probes, to enable the researcher to understand the complete picture, based on participant views and experiences. They are developed based on the literature review, aim and objectives, research questions, and propositions (Kleiber, 2004).
   b. Audio recording of FGs and interviews: Audio recording of discussions that take place in interviews and FGs is essential for managing and analyzing data, and for increasing the accuracy of data collection and analysis, and ultimately enhancing the dependability and credibility of the research (Rosenthal, 2016; Tuckett, 2005).
   c. Transcription of FGs and interviews recording: Verbatim transcription refers to the word-for-word conversion of oral words from an audio-recorded format into a scripted text format. Transcribing data is considered as the first data reduction step because it generates texts that can be examined and rechecked (Miles et al., 2014; Grossoehme, 2014).
3. Data analysis
   Data analysis comprises several fundamental steps, including reading the transcribed text, arranging data, coding data deductively based on prefigured themes or inductively to produce emergent themes, and then summarizing the codes into themes, and finally presenting the analyzed data as results (Cohen et al., 2013; Crabtree and Miller, 1999; Pope et al., 2000).
   The most commonly used data analysis methods in health science research are:
   a. Thematic analysis
      Thematic analysis is characterized by identifying, analyzing, and reporting themes that are available in the data (Braun and Clarke, 2006; Castleberry and Nolen, 2018).
   b. Content analysis
      Content analysis comprises systematic coding followed by quantification of the analyzed data in a logical and unbiased way (Berelson, 1952; Vaismoradi et al., 2013).
   c. Discourse analysis
      Discourse analysis emphasizes the core format and the structure of texts to examine the assumptions and concealed aspirations behind discourses (Brown and Yule, 1983; Gee, 2004).

Quality Perspectives in Qualitative Research

Qualitative research validation involves ensuring the rigor of the utilized data collection, management, and analysis methods, by utilizing approaches to ensure the quality. In pharmacy practice research, Hadi and Closs (2016a, 2016b) argued that quality in qualitative research topic has not been discussed widely in the literature, and therefore Hadi and Closs (2016a, 2016b) suggested using several trustworthiness criteria to ensure the rigor of qualitative study. The trustworthiness criteria for ensuring quality in qualitative research (Lincoln and Guba, 1985) are:

1. The trustworthiness criteria
   a. Credibility
      This criterion aims to ensure that the results are true and increases the possibility that the conclusions are credible (Cohen and Crabtree, 2008).

b. Dependability
This criterion aims to indicate that the research results are repeatable and consistent, in order to support the conclusions of the research (Cohen and Crabtree, 2008).
c. Confirmability
This criterion aims to confirm the neutrality in interpretation by ensuring that the perspectives of participants, not the bias of researchers, influence the results (Krefting, 1991).
d. Transferability
This criterion involves identifying the contexts to which the study results can be generalized, and indicating if the study conclusions can be applied in similar setting (Yin, 2014).

2. Reflexivity in qualitative research
Reflexivity implies revealing and evaluating the effect and biases that researchers can possibly bring to research process, by explaining the researcher's opinion, feelings, and experience with the phenomenon in question, and explaining the influence of this experience on research methods, findings, and write-ups (Creswell, 2013; Krefting, 1991; Lincoln and Guba, 1985).

Ethical Considerations

Obtaining an ethical approval from the Institutional Review Board (IRB) is required before conducting the qualitative research (Creswell, 2013). The key ethical issues that need to be considered are:

a. Informed consent and participant information leaflet
Informed consent refers to the decision taken by a competent individual to voluntarily participate in a research, after adequately understanding the research. Participant information leaflet is usually distributed to participants before they consent to participate in the research to clarify them the voluntary nature of research participation, the aim and objectives of the research, the rights of the respondents and the potential risks and harms, the data collection, management and storage conditions, and the right of participants to withdraw from the research (Jefford and Moore, 2008).
b. Anonymity and confidentiality
The anonymity is usually ensured by not disclosing names of participants and by utilizing a code system to identify them during data collection, management, analysis, and in the writing up of the research. The confidentiality of participants and data is ensured by using a code system to identify participants, and by storing all data in a locked cabinet and a password-protected computer for a specified period of time (Creswell, 2013).
c. Power relations in qualitative research settings
Power imbalance is caused by the fact that participants have the experience about the investigated phenomenon, and researchers need to obtain information about these experiences. The power imbalance is usually associated with interaction between the researcher and participants during recruitment stage, and during data collection, analysis, interpretation, and validation stages. Hence, researchers should take suitable measures at each stage to decrease the influence of possible power imbalance, and should enhance trust with participants (Karnieli-Miller et al., 2009; Yardley, 2000).

Mixed Methods in Pharmacy Practice Research

Research studies in pharmacy practice usually utilize single-method research designs. However, often these report numerous limitations and may not adequately answer the research question. Therefore, the combination of more than one research method to answer certain research questions has become increasingly common in pharmacy practice research (Ryan et al., 2015). Mixed methods research design is now a popular and widely used research paradigm in pharmacy practice research fields (Hadi et al., 2013, 2014; Hadi and Closs, 2016a, 2016b; Ryan et al., 2015). Mixed methods research allows the expansion of the scope of research to offset the weaknesses of using either quantitative or qualitative approach alone (Creswell et al., 2004; Hadi et al., 2013; Hadi and Closs, 2016a, 2016b; Pluye and Hong, 2014). Typically, qualitative and quantitative data are collected concurrently or sequentially in order to increase the validity and the comprehensiveness of the study findings (Creswell et al., 2004; Hadi et al., 2013; Hadi and Closs, 2016a, 2016b; Pluye and Hong, 2014; Ryan et al., 2015). The mixed method approach provides an expanded understanding of phenomenon under investigation through the comparison between qualitative and quantitative data (Hadi et al., 2013; Hadi and Closs, 2016a, 2016b; Pluye and Hong, 2014).

This section provides an overview and application of mixed method research in pharmacy practice. However, considerations in selecting, designing, and analyzing mixed methods research studies as well as the various typologies of mixed methods research are discussed elsewhere. Johnson et al. (2007) proposed the following definition for mixed methods research: "The type of research in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purpose of breadth and depth of understanding and corroboration."

Mixed methods design allows the viewpoints of participants to be reflected, enables methodological flexibility, and promotes multidisciplinary teamwork (Ryan et al., 2015). Furthermore, the approach allows a more holistic understanding of the research

question. However, its major limitations include: need for wide range of research expertise across the research team members, highly labor-intensive, and the complexity of data integration.

Scholars believe that it is challenging to provide researchers with a step-by-step guide on how to undertake a mixed methods study and that this is driven by the specific research question (Ryan et al., 2015). Nevertheless, the investigator should precisely determine the type of qualitative and quantitative methods to be employed, the order of data collection to be undertaken, the data collection instruments to be used, and the method of data analysis (Ryan et al., 2015). This approach encompasses a synthesis of findings from both quantitative and qualitative components, which is achieved through integration of the findings from each approach (Hadi et al., 2013; Hadi and Closs, 2016a, 2016b; Pluye and Hong, 2014).

Different models or typologies for mixed methods research have been described in the literature. The most common typologies used in pharmacy practice and health services research include: concurrent or convergent parallel design, exploratory sequential design, explanatory sequential design, and the embedded design (Hadi et al., 2013; Pluye and Hong, 2014). Scholars believe that there are several factors to consider when selecting the typology or model of mixed methods research to use. These factors include: the order of qualitative and quantitative data collection (concurrent vs. sequential); priority of data (i.e., which type of data has priority between quantitative and qualitative data); purpose of integration of the data (e.g., triangulation); and number of data strands (Hadi et al., 2013; Pluye and Hong, 2014). In mixed methods research, integration of qualitative and quantitative findings is critical, and this research approach does not simply involve the collection of these data (Ryan et al., 2015).

Summary and Take-Home Messages

- In the era of evidence-based practice, it is not sufficient to propose new pharmacy services or roles without evidence of their benefit.
- New pharmacy services and new roles must be proven to be feasible, acceptable, beneficial, and cost-effective.
- Practice-based research provides such evidence and can inform policy, confirm the value of the new service, and change practice.
- Various study designs, including, but not limited to experimental, quasi-experimental, observational, qualitative, and mixed-methods designs, have been used in pharmacy practice research.
- Pharmacy practice researchers need to be competent in the selection, design, application, and interpretation of these methodological and analytical approaches.
- The choice of any study design in pharmacy practice research is driven by the expertise of the investigator, type of research question or hypothesis, data availability, time orientation, ethical issues, and availability of funding.

Conclusion

There is a great demand for innovation and quality in pharmacy practice. These can be achieved partly through robust and well-designed pharmacy practice research. Pharmacy students, practitioners, educators, and policy-makers are exposed to a variety of research designs and methods. We need to have the best evidence (e.g., in policy, regulation, practice) for making decisions about the optimal research design that ensures delivering an ultimate pharmacy practice and a quality patient care.

Glossary

Pharmacy practice research The Canadian Pharmacists Association defines pharmacy practice research as a component of health services research that focuses on the assessment and evaluation of pharmacy practice (Koshman and Blais, 2011).
Quantitative research Is simply defined as "a research in which things are counted." These things might be people, medicines, opinions, behaviors, etc. "While qualitative research is very useful for describing phenomena in depth (particularly motivations, feelings, understandings), quantitative research can tell us how common and widespread the phenomena are" (Green and Norris, 2015).
Qualitative research Qualitative research within the health sciences has developed as a means to gather an in-depth understanding of human behavior, as well as to find the underlying reasons, attitudes, and motivations that govern such behavior (Kaae and Traulsen, 2015).
Mixed methods research A mixed methods research typically involves both the components of qualitative and quantitative research approaches embedded within a single study or research program for the broad purpose of breadth and depth of understanding and corroboration (Creswell et al., 2004; Johnson et al., 2007; Tashakkori and Creswell, 2007).
Observational studies Observational studies involve merely observing the study subjects in a noncontrolled setting, without investigator intervention or manipulating other aspects of the study in order to determine an association between an exposure and an outcome of interest.

Experimental studies In experimental design (also known as interventional design), the investigator performs an intervention and evaluates cause and effect relationships between exposure to the intervention and an outcome of interest (Cummings et al., 2013). Subjects are typically randomly assigned into experimental and control groups.

Quasi-experimental studies Quasi-experimental designs are studies that aim to evaluate interventions, but that do not use randomization and at times noncontrolled (Harris et al., 2006; Krass, 2016). Similar to true experimental studies, quasi-experiments aim to determine causality between an intervention and an outcome of interest.

References

Anderson, C., Kirkpatrick, S., 2016. Narrative interviewing. Int. J. Clin. Pharm. 38, 631–634.

Archibugi, L., Piciucchi, M., Stigliano, S., Valente, R., Zerboni, G., Barucca, V., . . . , Capurso, G., 2017. Exclusive and combined use of statins and aspirin and the risk of pancreatic cancer: a case-control study. Sci. Rep. 7, 13024.

Awaisu, A., Alsalimy, N., 2015. Pharmacists' involvement in and attitudes toward pharmacy practice research: a systematic review of the literature. Res. Social Adm. Pharm. 11, 725–748.

Babbie, E., 2015. The Practice of Social Research. Nelson Education.

Baker, G.R., 2011. The contribution of case study research to knowledge of how to improve quality of care. BMJ Quality Safety 20, i30–i35.

Behar-Horenstein, L.S., Beck, D.E., Su, Y., 2018. Perceptions of pharmacy faculty need for development in educational research. Curr. Pharm. Teach. Learn. 10, 34–40.

Berelson, B., 1952. Content analysis in communication research.

Bond, C., 2006. The need for pharmacy practice research. Int. J. Pharm. Pract. 14, 1–2.

Bousquet, E., Beydoun, T., Rothschild, P.-R., Bergin, C., Zhao, M., Batista, R., . . . , Behar-Cohen, F., 2015. Spironolactone for nonresolving central serous chorioretinopathy: a Randomized Controlled Crossover Study. Retina (Philadelphia, PA) 35 (12), 2505–2515.

Braun, V., Clarke, V., 2006. Using thematic analysis in psychology. Qual. Res. Psychol. 3, 77–101.

Brown, C.A., Lilford, R.J., 2006. The stepped wedge trial design: a systematic review. BMC Med. Res. Methodol. 6, 54.

Brown, G., Yule, G., 1983. Discourse Analysis. Cambridge University Press.

Castleberry, A., Nolen, A., 2018. Thematic analysis of qualitative research data: is it as easy as it sounds? Curr. Pharm. Teach. Learn. 10 (6), 807–815.

Chen, T.F., Hughes, C.M., 2016. Why have a special issue on methods used in clinical pharmacy practice research? Int. J. Clin. Pharm. 38, 599–600.

Chim, L., Salkeld, G., Kelly, P., Lipworth, W., Hughes, D.A., Stockler, M.R., 2017. Societal perspective on access to publicly subsidised medicines: a cross sectional survey of 3080 adults in Australia. PLoS ONE 12 (3), e0172971.

Cohen, D.J., Crabtree, B.F., 2008. Evaluative criteria for qualitative research in health care: controversies and recommendations. Ann. Fam. Med. 6, 331–339.

Cohen, L., Manion, L., Morrison, K., 2013. Research Methods in Education. Routledge.

Colli, J.L., Colli, A., 2006. International comparison of prostate cancer mortality rates with dietary practices and sunlight levels. Urologic Oncol. 24, 184–194.

Crabtree, B.F., Miller, W.L., 1999. Doing Qualitative Research. Sage Publications.

Creswell, J.W., 2013. Qualitative Inquiry and Research Design: Choosing Among Five Approaches. Sage.

Creswell, J.W., Fetters, M.D., Ivankova, N.V., 2004. Designing a mixed methods study in primary care. Ann. Fam. Med. 2, 7–12.

Cummings, S.R., Grady, D., Hulley, S.B., 2013. Designing a randomized blinded trial. In: Hulley, S.B., Cummings, S.R., Browner, W.S., Grady, D., Newman, T.B. (Eds.), Designing Clinical Research. fourth ed. Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia.

Czarniawska, B., 2004. Narratives in Social Science Research. Sage.

De Jong, H.J.I., Kingwell, E., Shirani, A., Cohen Tervaert, J.W., Hupperts, R., Zhao, Y., . . . , Tremlett, H., 2017. Evaluating the safety of β-interferons in MS: a series of nested case-control studies. Neurology 88 (24), 2310–2320.

de León-Castañeda, C.D., Gutiérrez-Godínez, J., Colado-Velázquez III, J., Toledano-Jaimes, C., 2018. Healthcare professionals' perceptions related to the provision of clinical pharmacy services in the public health sector of Mexico: a case study. Res. Soc. Administr. Pharm. 15 (3), 321–329.

Etminan, M., Samii, A., 2004. Pharmacoepidemiology I: a review of pharmacoepidemiologic study designs. Pharmacotherapy 24, 964–969.

Etminan, M., 2004. Pharmacoepidemiology II: the nested case-control study—a novel approach in pharmacoepidemiologic research. Pharmacotherapy 24, 1105–1109.

Gee, J.P., 2004. An Introduction to Discourse Analysis: Theory and Method. Routledge.

Giorgi, A., 1997. The theory, practice, and evaluation of the phenomenological method as a qualitative research procedure. J. Phenomenol. Psychol. 28, 235–260.

Grady, D., Cummings, S.R., Hulley, S.B., 2013. Alternative trial designs and implementation issues. In: Hulley, S.B., Cummings, S.R., Browner, W.S., Grady, D., Newman, T.B. (Eds.), Designing Clinical Research. fourth ed. Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia.

Green, J.A., Norris, P., 2015. Quantitative methods in pharmacy practice research. In: Babar, Z.-U.-D. (Ed.), Pharmacy Practice Research Methods. first ed. Springer International Publishing, Switzerland.

Grossoehme, D.H., 2014. Overview of qualitative research. J. Health Care Chaplaincy 20, 109–122.

Hadi, M.A., Closs, S.J., 2016a. Applications of mixed-methods methodology in clinical pharmacy research. Int. J. Clin. Pharm. 38, 635–640.

Hadi, M.A., Closs, S.J., 2016b. Ensuring rigour and trustworthiness of qualitative research in clinical pharmacy. Int. J. Clin. Pharm. 38, 641–646.

Hadi, M.A., Alldred, D.P., Closs, S.J., Briggs, M., 2013. Mixed-methods research in pharmacy practice: basics and beyond (part 1). Int. J. Pharm. Pract. 21, 341–345.

Hadi, M.A., Alldred, D.P., Closs, S.J., Briggs, M., 2014. Mixed-methods research in pharmacy practice: recommendations for quality reporting (part 2). Int. J. Pharm. Pract. 22, 96–100.

Harris, A.D., Mcgregor, J.C., Perencevich, E.N., Furuno, J.P., Zhu, J., Peterson, D.E., Finkelstein, J., 2006. The use and interpretation of quasi-experimental studies in medical informatics. J. Am. Med. Inform. Assoc. 13, 16–23.

Harris, M., 1968. Emics, Etics, and the New Ethnography. The Rise of Anthropological Theory: a History of Theories of Culture. Routledge and Kegan Paul, London pp. 568–604.

Hulley, S.B., Cummings, S.R., Newman, T.B., 2013. Designing cross-sectional and cohort studies. In: Hulley, S.B., Cummings, S.R., Browner, W.S., Grady, D., Newman, T.B. (Eds.), Designing Clinical Research. fourth ed. Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia.

Hussain, A., Ibrahim, M.I., Malik, M., 2013. Assessment of disease management of insomnia at community pharmacies through simulated visits in Pakistan. Pharm. Pract. 11 (4), 179–184.

Ibrahim, M.I., Palaian, S., Al-Sulaiti, F., El-Shami, S., 2016. Evaluating community pharmacy practice in Qatar using simulated patient method: acute gastroenteritis management. Pharm. Pract. 14 (4), 800.

Jefford, M., Moore, R., 2008. Improvement of informed consent and the quality of consent documents. Lancet Oncol. 9, 485–493.

Johnson, R.B., Onwuegbuzie, A.J., Turner, L.A., 2007. Toward a definition of mixed methods research. J. Mixed Methods Res. 1, 112–133.

Kaae, S., Traulsen, J.M., 2015. Qualitative methods in pharmacy practice research. In: Babar, Z.-U.-D. (Ed.), Pharmacy Practice Research Methods. first ed. Springer International Publishing, Switzerland.

Karnieli-Miller, O., Strier, R., Pessach, L., 2009. Power relations in qualitative research. Qual. Health Res. 19, 279–289.

Kernan, W.N., Viscoli, C.M., Brass, L.M., Broderick, J.P., Brott, T., Feldmann, E., Morgenstern, L.B., Wilterdink, J.L., Horwitz, R.I., 2000. Phenylpropanolamine and the risk of hemorrhagic stroke. N. Engl. J. Med. 343, 1826–1832.
Kleiber, P.B., 2004. Focus groups: More than a method of qualitative inquiry. Foundations Res. 87–102.
Koshman, S.L., Blais, J., 2011. What is pharmacy research? Can. J. Hosp. Pharm. 64, 154–155.
Krass, I., 2016. Quasi experimental designs in pharmacist intervention research. Int. J. Clin. Pharm. 38, 647–654.
Krefting, L., 1991. Rigor in qualitative research: the assessment of trustworthiness. Am. J. Occup. Ther. 45, 214–222.
Lin, C.-W., Wen, Y.-W., Chen, L.-K., Hsiao, F.-Y., 2017. Potentially high-risk medication categories and unplanned hospitalizations: a case–time–control study. Sci. Rep. 7, 41035.
Lincoln, Y.S., Guba, E.G., 1985. Naturalistic Inquiry. Sage.
Maclure, M., 1991. The case-crossover design: a method for studying transient effects on the risk of acute events. Am. J. Epidemiol. 133, 144–153.
McLaughlin, J.E., Bush, A.A., Zeeman, J.M., 2016. Mixed methods: expanding research methodologies in pharmacy education. Curr. Pharm. Teach. Learn. 8, 715–721.
Miles, M.B., Huberman, A.M., Saldana, J., 2014. Qualitative Data Analysis: A Method Sourcebook. Sage Publications, CA, USA.
Moustakas, C., 1994. Phenomenological Research Methods. Sage.
Mukhalalati, B., 2016. Examining the disconnect between learning theories and educational practices in the PharmD programme at Qatar University: a case study.
Murphy, A.L., Gardner, D.M., Kisely, S., Cooke, C., Kutcher, S.P., Hughes, J., 2015. A qualitative study of antipsychotic medication experiences of youth. J. Can. Acad. Child Adolesc. Psychiatry 24, 61.
Naik Panvelkar, P., Armour, C., Saini, B., 2010. Community pharmacy-based asthma service-what do patients prefer? J. Asthma 47, 1085–1093.
Newman, T.B., Browner, W.S., Cummings, S.R., Hulley, S.B., 2013. Designing case-control studies. In: Hulley, S.B., Cummings, S.R., Browner, W.S., Grady, D., Newman, T.B. (Eds.), Designing Clinical Research. fourth ed. Wolters Kluwer Health/Lippincott Williams & Wilkins, Philadelphia.
Nichol, K.L., Nordin, J.D., Nelson, D.B., Mullooly, J.P., Hak, E., 2007. Effectiveness of influenza vaccine in the community-dwelling elderly. N. Engl. J. Med. 357 (14), 1373–1381.
Odili, A.N., Ezeala-Adikaibe, B., Ndiaye, M.B., Anisiuba, B.C., Kamdem, M.M., Ijoma, C.K., . . . , Ulasi, I.I., 2012. Progress report on the first sub-Saharan Africa trial of newer versus older antihypertensive drugs in native black patients. Trials 13, 59.
Pluye, P., Hong, Q.N., 2014. Combining the power of stories and the power of numbers: mixed methods research and mixed studies reviews. Annu. Rev. Public Health 35, 29–45.
Pope, C., Ziebland, S., Mays, N., 2000. Qualitative research in health care: analysing qualitative data. Br. Med. J. 320, 114.
Prashanth, N.S., Elias, M.A., Pati, M.K., Aivalli, P., Munegowda, C.M., Bhanuprakash, S., . . . , Devadasan, N., 2016. Improving access to medicines for non-communicable diseases in rural India: a mixed methods study protocol using quasi-experimental design. BMC Health Services Res. 16 (1), 421.
Rosenfeld, E., Kinney, S., Weiner, C., Newall, F., Williams, A., Cranswick, N., Wong, I., Borrott, N., Manias, E., 2017. Interdisciplinary medication decision making by pharmacists in pediatric hospital settings: an ethnographic study. Res. Social Adm. Pharm. 14, 269–278.
Rosenthal, M., 2016. Qualitative research methods: why, when, and how to conduct interviews and focus groups in pharmacy research. Curr. Pharm. Teach. Learn. 8, 509–516.
Ryan, C.A., Cadogan, C., Hughes, C., 2015. Mixed methods research in pharmacy practice. In: Babar, Z.U.D. (Ed.), Pharmacy Practice Research Methods. first ed. Springer International Publishing, Switzerland.
Ryan, M., 2004. Discrete choice experiments in health care. BMJ 328, 360–361.
Setia, M.S., 2016a. Methodology series module 1: Cohort studies. Indian J. Dermatol. 61, 21–25.
Setia, M.S., 2016b. Methodology series module 3: Cross-sectional studies. Indian J. Dermatol. 61, 261–264.
Shiyanbola, O.O., Mort, J.R., 2015. Patients' perceived value of pharmacy quality measures: a mixed-methods study. BMJ Open 5 (1), e006086.
Strauss, A., Corbin, J.M., 1990. Basics of Qualitative Research: Grounded Theory Procedures and Techniques. Sage Publications, CA, USA.
Tashakkori, A., Creswell, J.W., 2007. Editorial: The new era of mixed methods. J. Mixed Methods Res. 1, 3–7.
Teo, K.K., Ounpuu, S., Hawken, S., Pandey, M., Valentin, V., Hunt, D., et al., 2006. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. Lancet 368 (9536), 647–658.
Tubiana, S., Blotière, P.-O., Hoen, B., Lesclous, P., Millot, S., Rudant, J., . . . , Duval, X., 2017. Dental procedures, antibiotic prophylaxis, and endocarditis among people with prosthetic heart valves: nationwide population based cohort and a case-crossover study. BMJ 358, j3776.
Tuckett, A.G., 2005. Part II. Rigour in qualitative research: complexities and solutions: Anthony G Tuckett outlines the strategies and operational techniques he used to attain rigour in a qualitative research study through relying on Guba and Lincoln's trustworthiness criterion. Research strategies such as use of personal journals, audio recording and transcript auditing, and operational techniques including triangulation strategies and peer review, are examined. Nurse Researcher 13, 29–42.
Vaismoradi, M., Turunen, H., Bondas, T., 2013. Content analysis and thematic analysis: implications for conducting a qualitative descriptive study. Nurs. Health Sci. 15, 398–405.
Vass, C., Gray, E., Payne, K., 2016. Discrete choice experiments of pharmacy services: a systematic review. Int. J. Clin. Pharm. 38, 620–630.
Watson, M.C., Skelton, J.R., Bond, C.M., Croft, P., Wiskin, C.M., Grimshaw, J.M., Mollison, J., 2004. Simulated patients in the community pharmacy setting – Using simulated patients to measure practice in the community pharmacy setting. Pharm. World Sci. 26, 32–37.
Watson, M., Norris, P., Granas, A., 2006. A systematic review of the use of simulated patients and pharmacy practice research. Int. J. Pharm. Pract. 14, 83–93.
Wei, L., Ratnayake, L., Phillips, G., Mcguigan, C.C., Morant, S.V., Flynn, R.W., . . . , Macdonald, T.M., 2017. Acid-suppression medications and bacterial gastroenteritis: a population-based cohort study. Br. J. Clin. Pharmacol. 83 (6), 1298–1308.
Woods, A., Cashin, A., Stockhausen, L., 2016. Communities of practice and the construction of the professional identities of nurse educators: a review of the literature. Nurse Educ. Today 37, 164–169.
Wu, E.B., Sung, J.J.Y., 2003. Haemorrhagic-fever-like changes and normal chest radiograph in a doctor with SARS. Lancet 361 (9368), 1520–1521.
Xu, T., De Almeida Neto, A.C., Moles, R.J., 2012. A systematic review of simulated-patient methods used in community pharmacy to assess the provision of non-prescription medicines. Int. J. Pharm. Pract. 20, 307–319.
Yardley, L., 2000. Dilemmas in qualitative health research. Psychol. Health 15, 215–228.
Yin, R.K., 2014. Case Study Research: Design and Methods. Sage Publications.

Further Reading

Baxter, P., Jack, S., 2008. Qualitative case study methodology: study design and implementation for novice researchers. Qual. Rep. 13, 544–559.
Boyatzis, R.E., 1998. Transforming Qualitative Information: Thematic Analysis and Code Development. Sage.
Bryman, A., 2015. Social Research Methods. Oxford University Press.
Easton, K.L., Mccomish, J.F., Greenberg, R., 2000. Avoiding common pitfalls in qualitative data collection and transcription. Qual. Health Res. 10, 703–707.
Eisner, E.W., 2017. The Enlightened Eye: Qualitative Inquiry and the Enhancement of Educational Practice. Teachers College Press.
Gibbs, A., 2012. Focus groups and group interviews. Research Methods and Methodologies in Education. Thousand Oaks pp. 186–192.
Grodstein, F., Manson, J.E., Stampfer, M.J., 2001. Postmenopausal hormone use and secondary prevention of coronary events in the nurses' health study. a prospective, observational study. Ann. Intern. Med. 135, 1–8.
Halcomb, E.J., Davidson, P.M., 2006. Is verbatim transcription of interview data always necessary? Appl. Nurs. Res. 19, 38–42.
Hanson, J.L., Balmer, D.F., Giardino, A.P., 2011. Qualitative research methods for medical educators. Acad. Pediatr. 11, 375–386.

Jonsson, P., Jakobsson, A., Hensing, G., Linde, M., Moore, C.D., Hedenrud, T., 2013. Holding on to the indispensable medication—a grounded theory on medication use from the perspective of persons with medication overuse headache. J. Headache Pain 14 (1), 43.
Kruijtbosch, M., Göttgens-Jansen, W., Floor-Schreudering, A., Van Leeuwen, E., Bouvy, M.L., 2018. Moral dilemmas of community pharmacists: a narrative study. Int. J. Clin. Pharm. 40, 74–83.
Landier, W., Hughes, C.B., Calvillo, E.R., Anderson, N.L.R., Briseño-Toomey, D., Dominguez, L., Martinez, A.M., Hanby, C., Bhatia, S., 2011. A grounded theory of the process of adherence to oral chemotherapy in Hispanic and Caucasian children and adolescents with acute lymphoblastic leukemia. J. Pediatr. Oncol. Nurs. 28, 203–223.
Lecompte, M.D., Goetz, J.P., 1982. Problems of reliability and validity in ethnographic research. Rev. Educ. Res. 52, 31–60.
Maclean, L.M., Meyer, M., Estable, A., 2004. Improving accuracy of transcripts in qualitative research. Qual. Health Res. 14, 113–123.
Morgan, D.L., 1997. Focus Groups as Qualitative Research. Sage.
Morse, J.M., 1998. The Contracted Relationship: Ensuring Protection of Anonymity and Confidentiality. Sage Publications Sage CA, Thousand Oaks, CA.
Myers, G., 2004. Matters of Opinion: Talking about Public Issues. Cambridge University Press.
Nisbet, J., Watt, J., 1984. Case Study, Chapter 5 in Bell, K., et al. Conducting Small-Scale Investigations in Educational Management.
Nunkoosing, K., 2005. The problems with interviews. Qual. Health Res. 15, 698–706.
Pearce, R., 2014. Learning How to Lead through Engagement with Enquiry Based Learning as a Threshold Process: A Study of How Post-graduate Certificate in Education Healthcare Professional Students Learn to Lead. University of Birmingham.
Ping, W.L., 2008. Data analysis in health-related qualitative research. Singapore Med. J. 49, 435–1435.
Polit, D.F., Beck, C.T., 2013. Essentials of Nursing Research: Appraising Evidence for Nursing Practice. Lippincott Williams & Wilkins.
Rivas, C., Sohanpal, R., Macneill, V., Steed, L., Edwards, E., Antao, L., . . . , Walton, R., 2017. Determining counselling communication strategies associated with successful quits in the National Health Service community pharmacy Stop Smoking programme in East London: a focused ethnography using recorded consultations. BMJ Open 7 (10), e015664.
Rubin, H.J., Rubin, I.S., 2012. Qualitative Interviewing: The Art of Hearing Data. Sage.
Ryan, K., Patel, N., Lau, W.M., Abu-Elmagd, H., Stretch, G., Pinney, H., 2018. Pharmacists in general practice: a qualitative interview case study of stakeholders' experiences in a West London GP federation. BMC Health Serv. Res. 18, 234.
Santiago-Delefosse, M., Gavin, A., Bruchez, C., Roux, P., Stephen, S.L., 2016. Quality of qualitative research in the health sciences: analysis of the common criteria present in 58 assessment guidelines by expert users. Soc. Sci. Med. 148, 142–151.
Shiyanbola, O.O., Brown, C.M., Ward, E.C., 2018. "I did not want to take that medicine": African-Americans' reasons for diabetes medication nonadherence and perceived solutions for enhancing adherence. Patient Prefer. Adherence 12, 409.
Shoemaker, S.J., Ramalho, D.E., Oliveira, D., 2008. Understanding the meaning of medications for patients: the medication experience. Pharm. World Sci. 30 (1), 86–91.
Silverman, D., 2013. Doing Qualitative Research: A Practical Handbook. SAGE Publications Limited.
Sim, J., 1986. Informed consent: ethical implications for physiotherapy. Physiotherapy 72, 584–587.
Skukauskaite, A., 2012. Transparency in Transcribing: Making Visible Theoretical Bases Impacting Knowledge Construction from Open-Ended Interview Records.
Sofaer, S., 1999. Qualitative methods: what are they and why use them? Health Serv. Res. 34, 1101.
Tobin, G.A., Begley, C.M., 2004. Methodological rigour within a qualitative framework. J. Adv. Nurs. 48, 388–396.
Todd, A., Holmes, H., Pearson, S., Hughes, C., Andrew, I., Baker, L., Husband, A., 2016. I don't think I'd be frightened if the statins went': a phenomenological qualitative study exploring medicines use in palliative care patients, carers and healthcare professionals. BMC Palliat Care 15, 13.

Quantitative Methods in Pharmacy Practice Research

Rabia Hussain*, **Mohamed Azmi Hassali***, **Zaheer-Ud-Din Babar**†, *School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia; †Department of Pharmacy, University of Huddersfield, Queensgate, Huddersfield, United Kingdom

© 2019 Elsevier Inc. All rights reserved.

Background

Research methods are specific procedures, techniques, and strategies that can be employed to analyze and interpret data (Merriam, 2002; Bodgan and Biklen, 2007). The three research methods, that is, quantitative, qualitative, and mixed methods serve to a different set of epistemological and ontological perspectives (Morrison, 2000; Creswell and Creswell, 2017). The selection of a particular research method is based on its capability to provide answers to a specific research problem (Polit and Beck, 2008; LoBiondo-Wood et al., 2013). In quantitative research methods, a researcher designs a research framework, analyzes, and quantifies the relationship between the variables (Polit and Beck, 2004; Creswell and Clark, 2007).

Pharmacy and Research Methods

Pharmacy profession has experienced a significant progress in terms of health-care delivery. To play the role effectively, a pharmacist has to be well equipped with the knowledge and skills to evaluate quality and outcome of treatment; however, this can only be done by considering both qualitative and quantitative research techniques (Azhar et al., 2009).

But looking into the long history of quantitative methods, researchers, especially the pharmacists, are more familiar with the quantitative research than the qualitative research (Smith, 2010b). Quantitative research deals with the findings that can be observed and quantified by involving subject of interests. This also includes people and events to establish a relationship between variables by applying statistical techniques (Leedy, 1993; Couchman and Dawson, 1995).

In this paper, we will elaborate various quantitative methods that can be employed in pharmacy practice research.

Types of Quantitative Research Methods

Quantitative research methods employed in pharmacy practice include nonexperimental research and experimental research methods (Austin and Sutton, 2018) (**Fig. 1**).

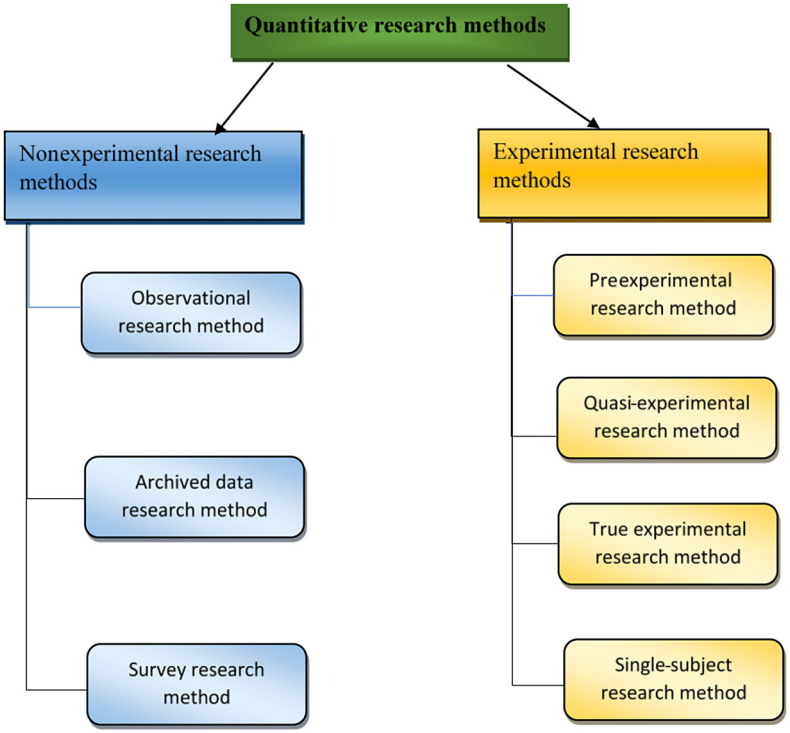

Figure 1 Quantitative research methods.

Nonexperimental Research Methods

Nonexperimental research or descriptive research method involves methodology that measures the variables in their true form without changing the study variables (Belli, 2009).

It is meant to describe a single or multivariables and a possible link between them. In this research method, researchers collect data to generate a hypothesis rather than other methods where a hypothesis is first generated and then tested. Nonexperimental research or descriptive research method selects subjects on the basis of the characteristics that meet the criteria to be included in a research study, for example, knowledge, attitudes, or health status (Dulock, 1993).

Nonexperimental research methods can be classified into the following three main categories (**Fig. 1**):

1. Observational research method
2. Archived data research method
3. Survey research method

Observational Research Method

In observational research method, a researcher observes subjects as samples and collects data for a certain period of time, but this is done without interacting with the environment they are living or working in; neither the researcher initiates any situation nor does the researcher manipulate any behavior (Smith, 1998; Austin and Sutton, 2018). In some cases, a researcher directly observes behaviors, attitude, practices, and events instead of depending upon the information provided by the participants, known as nonparticipant observation.

The researcher then analyzes the information to get numeric frequencies to establish a relationship between the observed data.

Sometimes, a researcher may visit a community pharmacy and act as a patient, observing and recording information for further analysis (Green and Norris, 2015). Madden et al. (1997) named these subjects as surrogate patients, mystery shoppers, or undercover care-seekers. In this scenario, the researcher directly observes and interprets findings, and relates and applies these to pharmacy practice setting.

Observational research method in pharmacy practice research also relies on the reported behavior and attitudes of people involved in a particular study setting (Green and Norris, 2015). Observational research methods are based on either nonparticipant observation or participant observation. However, for quantitative studies, we rely more on nonparticipant observation method where the researcher selects the site of the study and then designs a data collection tool. This method is used to explore, for instance,

services at a particular pharmacy by vising it to observe patient experience or visiting an outpatient clinic without involving the patients or healthcare providers. This technique may help in finding out more about experiences in a healthcare setting (Green et al., 2013; Austin and Sutton, 2018).

Limitations of Observational Research Method

In observational research, there is a little or no involvement from the participants, and things happen naturally in a flow, making the study more reliable.

Availability of resources can be a limitation in observation methods, as the researcher or an observer needs to travel and be present at the site of data collection. In this context, the study population and the study site could be an area of concern, especially in the settings when there are limited resources. The identity of study participants should be kept confidential in observational research, because otherwise, it may raise serious concern for the validity of the observational study (Smith, 1998).

Archived Data Research Method

Another nonexperimental method to collect data is by analyzing previously available datasets. This enables the researchers to analyze and interpret relationship between the variables of interest. Analysis of dataset is a popular method to look for possible research answers related to the use of medicines, medication safety, and rational prescribing (Green and Norris, 2015).

The following categories are described later.

Collecting Data from Administrative Datasets

Administrative datasets include information on prescribing or funding (Green and Norris, 2015). These can be available in the form of surveys, health insurance claims, electronic financial transactions for health insurance claims, computer-based patient records (CPRs), and disease registries (Lohr and Donaldson, 1994). Datasets also help in the prediction of trends. Sushmita et al. (2015) used machine learning algorithms to predict the cost of health care from data based on the public surveys and found a significant relationship between these variables.

Some administrative databases may have data on prescription medicine use, but normally they do not have data for nonprescription or over-the-counter medicines, as this happened in the case of over-the-counter sale of statins in the United Kingdom (Stewart et al., 2007).

In Canada medicines are funded on the basis of State policy; Ontario is the only state where elderly patients are fully covered by this scheme. Thus, most medicine use data and research outputs from Ontario are related to elderly population (Foster et al., 2013; Piszczek et al., 2014). This shows that the results based on a particular dataset or only on prescription medicine use may be biased, and thus it will be difficult to generalize the findings (Green and Norris, 2015).

Secondary Analysis of Primary Data

The already available data can be reanalyzed as some datasets may remain underanalyzed. Systematic reviews and meta-analysis are some examples of reanalysis of published and unpublished data, and this may help in finding the trends over rational medicine prescribing and medicine use (Green and Norris, 2015).

Survey Research Method

Survey research methods are widely used in health services research, and they employ standardized questionnaires to systematically collect data about a certain population regarding their attitudes, behaviors, and practices (Austin and Sutton, 2018). Survey research helps to describe the characteristics of a specific population and to present their opinion, attitudes, and practices (Creswell, 2005).

In pharmacy practice, these can be related to the assessment of beliefs, knowledge, attitudes, and experiences about medicine use, adherence, or other health-related topics both from patients and practitioners perspective (Green and Norris, 2015). To assess the perceptions of the general practitioners on access to medicines issues in New Zealand, Babar et al. (2015) conducted a questionnaire-based survey. The findings suggested that the GPs have the opinion that the medicines are sufficiently available to treat the conditions they saw in their daily practice. However, the majority of the GPs felt that New Zealand is slower to fund new medicines (Babar et al., 2015). Surveys are also used to assess services at the community pharmacies as shown in a survey-based study in Jordan (El-Dahiyat et al., 2019).

Survey is an excellent tool for the measurement of a wide-ranging population datasets, including traits, preferences, beliefs, and other information (Jones et al., 2013). This method is convenient and cost-effective as compared to experimental research or the case study research method (Mertler, 2016).

There are two main types of surveys: cross-sectional and longitudinal surveys.

A cross-sectional survey gives the evaluation of similar characteristics and differences among several samples of a population, and this is done at one point in time (Christensen et al., 2014c). Longitudinal survey involves the consideration of a single population during different times. This requires the administration of surveys at several points in time describing change, stability, or trends over a specified period of time (Dulock, 1993; Christensen et al., 2014c).

Method of Data Collection for Surveys

The use of questionnaire in data collection is a very useful tool. However, the results from the questionnaires can only be valid if they are constructed precisely and are consistent and clear. The method is cheap and quick, but the risk of bias cannot be ruled out in this method (Mathers et al., 2007; Austin and Sutton, 2018).

In postal surveys, the questionnaires are sent in hard copy to the targeted individuals requesting them to return the mail before a specified date. The process can be expensive, but the researcher gains access to a wider range of population. However, this also has some disadvantages, including the lack of encouragement in the absence of a face-to-face interaction resulting in a lower response rate (Christensen et al., 2014c; Austin and Sutton, 2018).

Telephone surveys are more expensive as they require individual administration to the participants. In these surveys, each survey question needs to be read by the researcher or the other supporting staff, requiring more time and resources (Christensen et al., 2014c; Austin and Sutton, 2018).

The technological advancement has led to the development of electronic surveys that are time- and cost-efficient (Mertler, 2002). Such surveys are delivered to the potential participants by sending them email messages or a link to the survey web page (Christensen et al., 2014c; Austin and Sutton, 2018).

Mentioned hereunder are the links for several websites that can be helpful in developing these surveys:

Kwik Surveys (www.kwiksurveys.com) (Kwik Surveys, 2019)
Question Pro (www.questionpro.com) (Question Pro, 2019)
So Go Survey (www.sogosurvey.com) (So Go Survey, 2019)
SurveyMonkey (www.surveymonkey.com) (Survey Monkey, 2019)

The limitations of this method include: filling the online survey, inactive email address of the participants, and failure to deliver email to multiple participants (Carbonaro and Bainbridge, 2000; Mertler, 2002).

Bias in Survey

There are several factors that contribute to bias in a survey methodology. The types of biases that can have an impact on the outcomes of the survey are discussed below (Bhattacherjee, 2012).

Sampling bias

Sampling bias is rampant in telephone surveys, where the respondents are selected and contacted from a random sample of publicly available telephone numbers. This systematically excludes people who do not have a mobile phone, landline numbers, or are unable to take the call when the survey is conducted. This also leads to disproportionate representation in the survey sample of—respondents with listed phone numbers; people who stay at home; elderly, disabled, or unemployed. Similarly, young people and students have more chances to be contacted through online surveys as they use technology and Internet more than other groups of population, thus systematically excluding people with no access to Internet.

In questionnaire surveys, there is a tendency to exclude uneducated and children as they are unable to read and write. Such bias in sampling compromises the generalizability of the results (Bhattacherjee, 2012).

Recall bias

Willingness to respond to a survey question is influenced by memory and motivation of the respondents as many survey questions draw from the past experiences (Green and Norris, 2015). It means that if a respondent cannot recall the information, the response would not be accurate. The problem of recall bias can be overcome by asking the respondents about the incidents rather than asking them about their emotions or behaviors (Bhattacherjee, 2012).

Social desirability bias

This bias arises when the respondents are asked about their views on negative opinions about their surroundings, thus making them uncomfortable to answer in a truthful manner. Many participants try to avoid responding to negative opinions or a question regarding their workplace, family, or friends.

In such situation, they usually try to spin the truth with not-so-true response as, otherwise, it may disturb their social desirability (Green and Norris, 2015).

These biases in a survey disturb the validity of the survey outcomes. The problem can be tackled by opting for an in-depth interview, as this can identify inconsistency in the answers (Bhattacherjee, 2012).

Experimental Research Methods

In experimental research methods, the researcher establishes different situations or treatments as variables and studies their effects on the participants (Hopkins, 2008). Researcher can control and manipulate variables and can study the cause and effect relationship for each variable (Christensen et al., 2014b). These are also known as intervention-based studies as they involve more than just observing the phenomenon (Hopkins, 2008).

The general requirements for the experimental research studies are as follows:

- A randomly selected or a randomly assigned group of participants to be included in a comparison group (which can either be an experimental group or a control group) except quasi-experimental design where the randomization of sample is not possible.
- An independent variable (a treatment, a cause, or an experiment variable) applied to the experimental group.
- A dependent variable commonly known as criterion variable (also known as posttest or effect variable) is identically measured in all groups in a study (Mertler, 2016).

Random selection of the study population and random assignment of these individuals to both experimental and control group are mandatory requirements for an experimental research method. This ultimately helps to maintain the equivalence between two groups, and also helps to control the factors that may interfere with the results of the study (Smith, 2010b).

Experimental research methods can be further categorized into the following four categories (Mertler, 2016) (**Fig. 1**):

1. Pre-experimental research method
2. Quasi-experimental research method
3. True experimental research method
4. Single-subject research method

Experimental methods can also be categorized into two main groups: single variable design and factorial design. Single variable design involves manipulation of one independent variable, whereas factorial design is comprised of two or more variables, in which at least one independent variable is manipulated (Mertler, 2016).

Pre-experimental Research Method

The method is called one-shot case study, and it is used to get the preliminary data regarding a problem. Preexperimental research method involves the inclusion of a single group of population that undergoes treatment and is also posttested. This research method does not control extraneous or unrelated variables; hence, it is not a preferred choice for a study research (Christensen et al., 2014b).

There is another type of preexperimental research method that is posttest only, that is, no pretest is done before exposure of treatment. Another method is pretest–posttest design, which is similar to the single group posttest design, but prior to the exposure of treatment, a pretest is done (Gay et al., 2009; Smith, 2010b). Pretest and posttest scores are evaluated to see if there is any change in the response. In this case, the researcher will be able to find out the difference in the response and its possible explanation (Smith, 2010b; Leedy and Ormrod, 2013).

Limitations

The method does not have any control over unrelated variables, hence making researcher unable to conclude definitive cause and effect relationship between variables (Leedy and Ormrod, 2013; Christensen et al., 2014b).

Quasi-experimental Research Method

Quasi-experimental research methods are considered as the closest form of true experiments, but they do not involve the random selection of the participants, and this ultimately weakens the ability to control extraneous factors (Christensen et al., 2014a). However, like other experimental research methods, quasi-experimental research seeks a causal relationship between an intervention and its outcome, and ultimately they provide further rationale for more exploratory trial involving robust research system (Krass, 2016).

Thus, in pharmacy practice, quasi-experimental method helps in the assessment of an intervention over a certain period of time. In a study at the University of Michigan Medical Center, it was observed that the medication-related discrepancies were resolved by the involvement of pharmacist in a hospital discharge program (Walker et al., 2009). Another pharmacist-led intervention study in six hospitals in Hawaii showed a significant reduction in the cost of hospitalization of elderly patients (Pellegrin et al., 2017).

Quasi-experimental research is a preferred choice in the cases where it is not feasible to randomize participants to a treatment or intervention group due to logistical or ethical reasons (Krass, 2016).

Limitations

The design is very useful in cases where random assignments of participants are not possible (Christensen et al., 2014a). However, the design lacks the random assignment of participants to the treatment groups. This ultimately results in an increased risk of bias in the study (Thompson and Panacek, 2006).

True Experimental Research Method

The method involves the random selection of participants to the assigned treatment conditions (Gay et al., 2009). In such design, participants are randomly assigned to the control and experimental group, and the study design is commonly known as randomized controlled trial. Such research design is a preferred choice in pharmacy practice research, and it helps in evaluating the impact of new health-care service or intervention (Smith, 2010b).

In control group, no active treatment is given or sometimes a standard value is used that does not affect the value of the independent variable. But, in an experimental group or a treatment group, participants receive a treatment or an intervention that can alter the value of an independent variable resulting in an impact or an effect (Christensen et al., 2014b). The involvement of at least one comparison group is an important feature in this study design (Mertler, 2016).

In a research method, where the participants are not aware of the identity of treatment or intervention is known as single blind controlled trial. In a double blind controlled trial, both researchers and participants have no information regarding who is receiving a treatment or an intervention (Hopkins, 2008; Christensen et al., 2014b). The randomization of participants helps to control the risk factors, which may emerge as a threat to the validity of data (Fraenkel et al., 2011).

Limitations

The major strength of a truly experimental research method is its ability to clearly draw a cause and effect relationship in a study. However, true experimental methods require stringent requirements to not risk the validity of the data (Mertler, 2016).

Single-Subject Research Method

Most of the experimental studies require group of participants, whereas in single-subject research design, the studies can be conducted on an individual case basis (Smith, 2010a). Single-subject research design is preferably used to study the time course, effect of a treatment, or an intervention on a single patient, and is mostly employed in primary care research-based studies (Janosky, 2005).

In the single-subject case studies, the outcome from dependent variables is measured and recorded for individual participants during different times and at different levels of intervention (Lobo et al., 2017). The performance of a subject is evaluated both in a nontreatment and treatment phase (Gay et al., 2009). The nontreatment phase can be regarded as phase A, while the treatment phase can be marked as phase B (Janosky, 2005). There are various types of single-subject design, one of which is called the A-B design. In single-subject research, initial measurement of variables (A) is taken, and then a treatment (B) is given to the subject and a change is observed to see the treatment effect (Janosky, 2005).

Another design is reverse design or commonly known as A-B-A (measurement-treatment-measurement). This design is comprised of baseline measurements (first phase) followed by treatment (second phase) and finally the removal or withdrawal of treatment (third phase). However, it is required that the researcher should accurately measure the behavior change before and after applying the treatment. This can be repeated many times (Hopkins, 2008). On the removal of the treatment, if condition reverses, it means that the treatment has some positive effect on the subject (Price et al., 2015). A study by Freeman et al. (2010) employed an A-B-A research method to determine the core stability training in eight patients with multiple sclerosis. The researcher maintained the baseline level for 4 weeks, followed by 8 weeks of intervention then was a withdrawal after 4 weeks resulting into patient's improved walking (Freeman et al., 2010).

Limitations

A major limitation of single-subject research method is that some interventions cannot be withdrawn or reversed (Mertler, 2016; Lobo et al., 2017). Also, this research design lacks the generalizability in terms of its outcome and is only focused to study the effectiveness of treatment on a single participant. This is effective to measure an impact and study behavior modifications in one single individual. However, a possibility of an alternative explanation for a certain behavior in an individual cannot be ruled out (Janosky, 2005; Mertler, 2016).

Validation of a Research Method

Validity of a research method refers to the value, truth, and originality one can place on the study findings. Validity of research is the degree to which one can say that the research outcomes are accurate and generalizable. Factors affecting internal and external validity should be controlled; otherwise, it may jeopardize the reliability of results and the conclusion of the study (Green and Norris, 2015; Mertler, 2016).

In order to measure the external validity of the quantitative research methods, it is important that the accurate data from the appropriate subjects must be collected in the right setting. The specifications of a target population must be clearly described, and the selected subjects must represent the population under study (Smith, 2010a; Austin and Sutton, 2018). The instruments used (equipment, questionnaires, or interviews that measure physiological or psychosocial variables) should be standardized. Before employing newly developed instruments into a research study, the same should be pilot tested (Dulock, 1993).

Conclusion

There are many different quantitative approaches, which give the freedom to the researcher to choose the appropriate methodology. However, it is important to understand that every design has it's own set of limitation, and this is vital to consider when choosing a research method in the pharmacy practice research.

References

Austin, Z., Sutton, J., 2018. Research Methods in Pharmacy Practice Research. Elsevier, Canada.

Azhar, S., Hassali, M.A., Ibrahim, M.I.M., Ahmad, M., Masood, I., Shafie, A.A., 2009. The role of pharmacists in developing countries: the current scenario in Pakistan. Hum. Resour. Health 7, 54.

Babar, Z.U.D., Lessing, C., Stewart, J., Sheridan, J., 2015. Evaluating general practitioners' opinions on issues concerning access to medicines in New Zealand. J. Pharm. Health Serv. Res. 6, 145–154.

Belli, G., 2009. Nonexperimental quantitative research. In: Lapan, S.D., Quartaroli, M.T. (Eds.), Research Essentials: An Introduction to Designs and Practices. Jossey-Bass, San Francisco, CA.

Bhattacherjee, A., 2012. Social Science Research: Principles, Methods, and Practices. University of South Florida, Tampa, FL.

Bodgan, R., Biklen, S., 2007. Qualitative Research for Education: An Introduction to Theory & Methods. Pearson, New York.

Carbonaro, M., Bainbridge, J., 2000. Design and development of a process for web-based survey research. Alberta J. Educ. Res. 46, 392–394.

Christensen, L.B., Johnson, B., Turner, L.A., 2014a. Creating a Quasi-Experimental Design. Research Methods, Design, and Analysis, twelfth ed. Pearson Education Limited, England.

Christensen, L.B., Johnson, B., Turner, L.A., 2014b. Creating the Appropriate Research Design. Research Methods, Design, and Analysis, twelfth ed. Pearson Education Limited, England.

Christensen, L.B., Johnson, B., Turner, L.A., 2014c. The Survey as Non-Experimental Research. Research Methods, Design, and Analysis, twelfth ed. Pearson Education Limited, England.

Couchman, W, Dawson, J., 1995. Nursing and Healthcare: A Practical Guide. Balliere Tindall in Association with the Royal College of Nursing, London.

Creswell, J.W., 2005. Educational Research: Planning, Conducting, and Evaluating Quantitative and Qualitative Research. Merrill, Upper Saddle River, NJ.

Creswell, J.W., Clark, V.L.P., 2007. Designing and Conducting Mixed Methods Research. Sage Publications, Thousand Oakes, CA.

Creswell, J.W., Creswell, J.D., 2017. Research Design: Qualitative, Quantitative, and Mixed Methods Approaches. Sage Publications, Los Angeles, CA.

Dulock, H.L., 1993. Research design: descriptive research. J. Pediatr. Oncol. Nurs. 10, 154–157.

El-Dahiyat, F., Curley, L.E., Babar, Z.U.D., 2019. A survey study to measure the practice of patient counselling and other community pharmacy services in Jordan. J. Pharm. Health. Serv. Res. 10, 133–139.

Foster, P., Mamdani, M., Juurlink, D., Shah, B., Paterson, J., Gomes, T., 2013. Trends in selection and timing of first-line pharmacotherapy in older patients with Type 2 diabetes diagnosed between 1994 and 2006. Diabet. Med. 30, 1209–1213.

Fraenkel, J.R., Wallen, N.E., Hyun, H.H., 2011. How to Design and Evaluate Research in Education. McGraw-Hill Humanities/Social Sciences/Languages, New York.

Freeman, J., Gear, M., Pauli, A., Cowan, P., Finnigan, C., Hunter, H., Mobberley, C., Nock, A., Sims, R., Thain, J., 2010. The effect of core stability training on balance and mobility in ambulant individuals with multiple sclerosis: a multi-centre series of single case studies. Mult. Scler. J. 16, 1377–1384.

Gay, L.R., Mills, G.E., Airasian, P.W., 2009. Educational Research: Competencies for Analysis and Applications, Student Value Edition. Merrill, Upper Saddle River, NJ.

Green, J., Norris, P., 2015. Quantitative methods in pharmacy practice research. In: Babar, Z. (Ed.), Pharmacy Practice Research Methods. Springer, New Zealand.

Green, J.A., Brown, K., Burgess, J., Chong, D., Pewhairangi, K., 2013. Indigenous and immigrant populations' use and experience of community pharmacies in New Zealand. J. Immigr. Minor. Health 15, 78–84.

Hopkins, W.G., 2008. Quantitative Research Design. SPORTSCIENCE, Dunedin, New Zealand. Available from: http://sportsci.org/jour/0001/wghdesign.html.

Janosky, J., 2005. Use of the single subject design for practice based primary care research. Postgrad. Med. J. 81, 549–551.

Jones, T., Baxter, M., Khanduja, V., 2013. A quick guide to survey research. Ann. R. Coll. Surg. Engl. 95, 5–7.

Krass, I., 2016. Quasi experimental designs in pharmacist intervention research. Int. J. Clin. Pharm. 38, 647–654.

Kwik Surveys, 2019. United Kingdom. Available from: https://kwiksurveys.com/#!/.

Leedy, P., Ormrod, J., 2013. The nature and tools of research. In: Practical Research: Planning and Design, Pearson Education, Inc., Harlow, pp. 1–26.

Leedy, P.D., 1993. Practical Research: Planning and Design. Prentice Hall, Upper Saddle River, NJ.

LoBiondo-Wood, G., Haber, J., Berry, C., Yost, J., 2013. Study Guide for Nursing Research—E-Book: Methods and Critical Appraisal for Evidence-Based Practice. Elsevier Health Sciences, St. Louis, Missouri.

Lobo, M.A., Moeyaert, M., Baraldi Cunha, A., Babik, I., 2017. Single-case design, analysis, and quality assessment for intervention research. J. Neurol. Phys. Ther. 41, 187–197.

Lohr, K.N., Donaldson, M.S., 1994. Health Data in the Information Age: Use, Disclosure, and Privacy. National Academies Press, Washington, DC.

Madden, J.M., Quick, J.D., Ross-Degnan, D., Kafle, K.K., 1997. Undercover careseekers: simulated clients in the study of health provider behavior in developing countries. Soc. Sci. Med. 45, 1465–1482.

Mathers, N., Fox, N., Hunn, A., 2007. Surveys and Questionnaires. Sheffield, Trent RDSU.

Merriam, S.B., 2002. Qualitative Research in Practice: Examples for Discussion and Analysis. Jossey-Bass Inc. Pub, San Francisco, CA.

Mertler, C., 2002. Demonstrating the potential for web-based survey methodology with a case study. Am. Secondary Educ. 30, 49–61.

Mertler, C.A., 2016. Action Research: Improving Schools and Empowering Educators. Sage Publications, Thousand Oaks, California.

Morrison, K., 2000. Research Methods in Education. Taylor & Francis, New York.

Pellegrin, K.L., Krenk, L., Oakes, S.J., Ciarleglio, A., Lynn, J., Mcinnis, T., Bairos, A.W., Gomez, L., Mccrary, M.B., Hanlon, A.L., 2017. Reductions in medication-related hospitalizations in older adults with medication management by hospital and community pharmacists: a quasi-experimental study. J. Am. Geriatr. Soc. 65, 212–219.

Piszczek, J., Mamdani, M., Antoniou, T., Juurlink, D.N., Gomes, T., 2014. The impact of drug reimbursement policy on rates of testosterone replacement therapy among older men. PLoS One 9, e98003.

Polit, D.F., Beck, C.T., 2004. Essentials of Nursing Research: Appraising Evidence for Nursing Practice. Lippincott Williams & Wilkins, Philadelphia, PA.

Polit, D.F., Beck, C.T., 2008. Nursing Research: Generating and Assessing Evidence for Nursing Practice. Lippincott Williams & Wilkins, Philadelphia, PA.

Price, P.C., Chiang, I.-C.A., Jhangiani, R., 2015. Research methods in psychology, BCcampus, BC Open Textbook Project.

Question Pro, 2019. Available from: https://www.questionpro.com/.

Smith, F., 1998. Health services research methods in pharmacy: focus groups and observation studies. Int. J. Pharm. Pract. 6, 229–242.

Smith, F., 2010a. Conducting Your Pharmacy Practice Research Project. Pharmaceutical Press, London.

Smith, F., 2010b. Conducting Your Pharmacy Practice Research Project: A Step-by-Step Approach. Pharmaceutical press, London.

So Go Survey, 2019. Virginia. Available from: https://www.sogosurvey.com/create-online-survey/?gclid=CjwKCAjw85zdBRB6EiwAov3RihS5GKTvbqUnFDBrFlmAhFCaPrrqfF0R-UwJObE9scJgAQYR9Y-f3BoCBikQAvD_BwE.

Stewart, D., John, D., Cunningham, S., Mccaig, D., Hansford, D., 2007. A comparison of community pharmacists' views of over-the-counter omeprazole and simvastatin. Pharmacoepidemiol. Drug Saf. 16, 1290–1297.

Survey Monkey, 2019. Available from: https://www.surveymonkey.com/.

Sushmita, S., Newman, S., Marquardt, J., Ram, P., Prasad, V., Cock, M.D., Teredesai, A., 2015. Population cost prediction on public healthcare datasets. Proceedings of the 5th International Conference on Digital Health 2015, ACM, pp. 87–94.

Thompson, C.B., Panacek, E.A., 2006. Research study designs: experimental and quasi-experimental. Air Med. J. 25, 242–246.

Walker, P.C., Bernstein, S.J., Jones, J.N.T., Piersma, J., Kim, H.-W., Regal, R.E., Kuhn, L., Flanders, S.A., 2009. Impact of a pharmacist-facilitated hospital discharge program: a quasi-experimental study. Arch. Intern. Med. 169, 2003–2010.

Qualitative Methods in Pharmacy Practice Research

Helena Herrera, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, UK

© 2019 Elsevier Inc. All rights reserved.

Introduction

Until recently, much of the health and pharmacy practice research undertaken focused on what were considered good rigorous practices, based on the measurement and collection of numerical data that would be able to quantify phenomena or test hypotheses (Smith, 2002). This was the result of the widespread acceptance of the scientific method as the cornerstone of science and the way by which reality could be appropriately researched (Crotty, 2003). The scientific method was built on the belief that measurement was at the center of discovery, and that the designing and execution of the right experiments or observations would lead to the advancement of knowledge (Popper, 1959/2002). This view of what would constitute good research has been increasingly challenged in recent times due to its limitations in arriving at understanding of many aspects of healthcare and the provision of services. This would be the case in studies involving human participants, who could be patients, professionals, students, educators, or other stakeholders, which need to deal with the subjectivity which is associated with human behavior (Bowling, 2014). As a result of this, it is now accepted that the world and society may not operate according to general laws, and therefore measurement may not always be possible, with the testing of hypotheses or the quantifying of variables being unable to provide complete answers to certain research questions (Robson and McCartan, 2015).

Qualitative research has presented itself as a practical solution to this problem, providing a whole new range of approaches to data analysis and methodologies for data collection that can enable the investigation of issues that could not be explored in such depth before (Patton, 2015). It has particularly succeeded on studying the perceptions of those involved in healthcare, also looking at experiences and the way that individuals and groups communicate and relate to the world, being also very useful in educational research (Austin and Sutton, 2018). This shift from focusing in measurement and prediction, to exploration and understanding can be considered to constitute a paradigm shift, affecting the way science is understood, with this no longer seen as objective and invariable (Kuhn, 1970). This is a very important point to consider for those engaging in qualitative research, which need to embrace that they will be managing more than one possible interpretation of reality, and questions which may be answered in more than one way (Denzin and Lincoln, 2017).

A range of research traditions within the qualitative paradigm have been proposed to exist in order to guide those navigating through all the possibilities that these approaches and methodologies can offer (Poth and Creswell, 2013). These have been named and categorized by authors in different ways, and can appear at times artificial and confusing (Tesh, 1990). In the following sections, key aspects to consider when undertaking and understanding this type of work have been presented without focusing on these

research traditions. This is with the purpose of avoiding confusion and helping investigators and practitioners gain the knowledge they would need to undertake, report, and critique these studies. For this reason, building on accepted terminology and classifications, this chapter would aim to prepare for *real world research* (Robson and McCartan, 2015), and for solving relevant problems in a way which is methodologically sound. On these lines it must be noted that it will focus on using qualitative data in ways which are consistent with the principles of qualitative research. Some of the approaches can be thought to be part of the quantitative rather than the qualitative paradigm, or sit in between, and they have been covered in this chapter as the results that they can arrive to can be very useful in qualitative pharmacy practice studies. It must be remembered that qualitative data is something different than nominal data; qualitative data involves information provided through the use of language on a phenomenon, while nominal data can be a value or variable which is expressed in words (Denzin and Lincoln, 2017).

There are many options to choose from when using qualitative methods in pharmacy practice research (Austin and Sutton, 2018). It is advisable to read this chapter in its entirety before using its content to inform any choices, as the subtle differences in these approaches and methodologies can sometimes only become apparent when comparing one another. The degree of interpretation and depth of analysis required by a specific study can be particularly difficult to judge by individuals with more limited experience in this field. It is therefore encouraged that familiarity with the whole qualitative paradigm is achieved before engaging in data collection and analysis, as this will ensure that rigorous practices continue to guide researchers in this area. For this purpose, understanding the different approaches to finding meanings in the data is essential, and should be achieved prior to making decisions with regard to how this data should be collected and handled.

Choosing an Appropriate Qualitative Method

The most important aspect of qualitative research and managing qualitative data is the central role which language plays to convey messages and provide meanings, which are shared by human participants, and after analysis will lead to answers to the research questions under investigation (Smith et al., 2009). The approach selected to finding meanings will therefore determine the results which will be obtained, and it is useful to consider analysis prior to making decisions about how the data will be collected (Silverman, 2016). For example, if further understanding was required on how patients make sense of being diagnosed with a terminal illness, meanings sought would be of greater depth than those involved in finding out what service users thought of having to pay car park charges when visiting a hospital. The following sections outline what aspects of the different approaches to finding meanings in the data need to be considered before choosing one based on the depth of analysis, degree of interpretation required, and the main implications of using these.

The first consideration to make when engaging on finding meanings in qualitative data would be whether descriptive or latent meanings are sought (Smith et al., 2009). This is the fundamental distinction between finding meanings by analyzing concepts and finding meanings by analyzing themes. A concept would represent an idea which is defined and described by the terminology used to relate to it, having a near literal meaning. In contrast, a theme would relate to a latent meaning found in the data after a process of interpretation, where language does not explicitly present an idea (Braun and Clarke, 2008). For example, when researching community pharmacists' role satisfaction, it could be possible to come across the following a statement from a participant in a group discussion: "Oh, yes, I like admin work." This data could include the concept "admin work," as it is explicitly quoted, and also the theme "dislike of admin work," depending on what was meant by the participant when making this statement.

The following sections explain this in more detail, providing an overview of the different approaches for finding meanings by analyzing concepts and themes, defining what these approaches are, when they would be most useful, and providing examples to illustrate how they can be applied.

Finding Meanings by Analyzing Concepts

As it has been explained before, approaches to finding meanings by analyzing concepts are not based on interpretation (Smith et al., 2009). However, it would be very difficult to argue that they do not involve some degree of subjectivity (Robson and McCartan, 2015). They aim to arrive at categorizations where there is no overlap, and in some cases, there is even a degree of quantifying taking place. When investigators aim to find meanings by analyzing concepts, the purpose is to arrive at results that could be accepted as some definitive answer to the research question (Hsiu-Fang and Shannon, 2005).

These approaches do not entirely belong within the qualitative paradigm, and are included in this chapter because they rely on qualitative data (Poth and Creswell, 2013). For some of these there are prescriptive ways of undertaking analysis, with others embedding a number of different practices (Poth and Creswell, 2013). Analyzing concepts enables researchers in pharmacy practice to ascertain, and sometimes quantify, key meanings, which is often done to inform policy and to make judgments with regard to health interventions (Smith, 2002). They can be very useful in providing specific answers to general problems, where there are larger amounts of data and limited depth in the analysis is required (Robson and McCartan, 2015).

When finding meanings by analyzing concepts, the process can be deductive or inductive, by which specific meaning are searched for in the data, or in contrast, emerge from it and are not anticipated (Silverman, 2016). For example, in a deductive approach to investigating factors that influence the choice of community pharmacy, the data may be searched for the presence of specific concepts which have been chosen prior to starting analysis (often by reviewing the literature or because these have been judged as important). These could be convenience, waiting times, services offered, and friendliness of the staff, with the analysis

focusing on whether these are present in the data and what importance participants attributed to them. In contrast, in an inductive approach, the process would involve to look for factors which emerge from the data, without any preconceptions on what these would be (Ritchie et al., 2013). As such, it could emerge that availability of parking spaces, allowing to pre-order prescriptions on-line or having a members of staff which speak additional languages are the factors present in a specific dataset. In this way, finding meanings by analyzing concepts would be useful to check interpretations, to some extent quantify and explain phenomena, and sometimes proposing hypothesis or theories for further testing (Austin and Sutton, 2018). While the more limited degree of interpretation that they require and the set steps prescribed for some of them may make them appear as more accessible and easier to use (Hsiu-Fang and Shannon, 2005), they require an amount of skills and experience which can be as large as those needed to effectively find meanings in the data by analyzing themes. They should therefore only be chosen when they would be best suited to answer the research question under investigation.

Content Analysis

Content analysis would be the most basic way of manipulating qualitative data, and is often concerned with how frequently a concept, or single unit of meaning (which could include more than one word), is present in the data. In content analysis, concepts are identified, categorized, and often counted (Hsiu-Fang and Shannon, 2005). For example, "teamwork" would be a concept often sought when undertaking analysis of job applications in order to identify, for the purpose of recruitment, what could suitable candidates for a role which involves working with others. Content analysis can be undertaken in any way which ensures that concepts are identified and grouped consistently under pertinent categories (Ritchie and Spencer, 1994). As per the example given, it can provide quicker answers to specific questions, but it is of limited used within pharmacy practice research, as there are other approaches which can deal with the greater complexities which are often present in this type of work (Smith, 2002). Sometimes authors have used the term content analysis to refer to thematic analysis (Braun and Clarke, 2008), and care must be exercised when accessing the literature, as both are very different approaches, which may be suitable in very different situations.

Framework Analysis

Framework analysis is a defined approach to finding meanings by analyzing concepts, which is carried out following set steps proposed by the authors (Ritchie and Spencer, 1994). In this approach, meanings are sought in order to construct a framework which provides an overall description of a phenomenon, dealing with a greater degree of complexity than content analysis, while looking at key concepts present in the data and how they relate to each other (Ritchie et al., 2013). For example, framework analysis could be very useful to study barriers and drivers affecting the success of a childhood obesity intervention implemented across a number of schools. Using framework analysis, concepts within the dataset can be indexed, and presented in a simple but effective model (Ritchie and Spencer, 1994). While it may not enable to investigate aspects in great deal of detail, or including additional meanings to those which are in the majority, it can be useful when answers are needed to specific questions within large datasets. Framework analysis is successfully used in policy making and larger scale studies involving qualitative data (Gale et al., 2013).

Delphi Technique

The Delphi technique involves a process by which the views of a group of individuals on a specific subject are gathered with the purpose of establishing what issues are important and determine a hierarchy of how these would relate to each other (Keeney and McKenna, 2010). This is done following steps which aim to arrive at consensus among the individuals in the group on the degree of importance of these different issues. It is a structured approach to arrive at which concepts are more pertinent to the research question under investigation. By arriving at those which are more representative, it would be expected that predictions could be made (Salkin, 2010). Delphi technique often involves a face-to-face data collection event where there are two rounds of questions, for which answers are provided, with these being ordered by the group and a hierarchy arrived at. All suggestions are then passed unedited and unattributed to all group members, who are asked to re-rank suggestions, drawing up a priority list from members' rankings (Skulmoski et al., 2007).

The Delphi technique can be useful when agreement is sought from a group of informants or experts on an aspect for which there is little or no evidence, there would be a variety of factors to consider, and it is necessary to narrow these down to those which would be most important (Skulmoski et al., 2007). For example, in order to identify which would be the attributes which define professionalism in practicing pharmacists in order to inform the development of a suitable education and training initiative, this could be a useful approach.

Grounded Theory

Grounded theory is a well-defined and prescriptive approach to finding meanings in qualitative data where a theory is constructed at the end of the process (Poth and Creswell, 2013). Grounded theory can be useful in large datasets when the purpose is to arrive at a model which would aim to describe and explain relationships within the phenomenon under investigation (Bowling, 2014). This approach could sit well within the quantitative paradigm if it were not based on the analysis of qualitative data. It follows a set of defined steps with the purpose of standardizing the analysis and avoiding the need for interpretation. The two main approaches to undertaking grounded theory (Glaser and Strauss, 1967; Strauss and Corbin, 1997) are covered in a different chapter of this book.

Finding Meanings by Analyzing Themes

In contrast to those included in the previous sections, approaches for finding meanings by analyzing themes are based on varying degrees of interpretation (Braun and Clarke, 2008). Their way of manipulating data leads to categories that overlap, and no quantifying takes place, nor becomes necessary. In these, interpretation is aimed for and put at the center of analysis (Smith et al., 2009). These approaches enable qualitative data to be fully understood and analyzed following the fundamental principles which guide the qualitative paradigm. When finding meanings by analyzing themes, there is no single prescribed way of how analysis should happen, with authors making suggesting rather than proposing set methodologies or steps (Robson and McCartan, 2015). Analyzing themes enables researchers in pharmacy practice to ascertain, sometimes unveil, but never quantify, meanings within the data which can often be hidden. These are used to understand how individuals perceive service provision or a certain aspect of reality (Smith, 2002). They can be very powerful in providing insights and answers to research questions which involve personal views and accounts, experiences, and how these are felt by those being researched (Crotty, 2003).

Approaches to finding meanings by analyzing themes are language centered, but they are also concerned with the context in which the language frames meanings (Polgar and Thomas, 2013). They see this as a tool for communication, not merely for the transmission of information, and these approaches are built on the assumption that how things are talked about matters, in addition to what it is said (Smith et al., 2009). Researchers must be careful therefore when using these approaches to avoiding fragmenting the phenomena being study, and ensure that there is clarity with regard to how themes have been developed to ensure transparency and rigor of the practices followed. When finding meanings by analyzing themes, the approach should always be inductive, by which themes emerge from the data, rather than investigators looking for the presence or frequencies of certain themes (Patton, 2015). In this way, these approaches would be useful for studies which aim to build interpretations, explain phenomena, and sometimes propose hypothesis for further testing (Smith, 2012).

Thematic Analysis

Thematic analysis would be a versatile approach to finding meanings in qualitative data for pharmacy practice and health research in general (Bowling, 2014). This is due to its flexibility, lack of assumptions on what constitutes knowledge, and its ability to provide ways to find meanings which allow a degree of interpretation that can be adapted to the nature of the research question and the aims of the study. It focuses on finding patterns of commonality, which are not always obvious in the data, and for which clear practical ways have been proposed (Braun and Clarke, 2008). Thematic analysis is undertaken by facilitating that themes emerge from the data, rather than being imposed by looking for specific concepts. In order for this to happen, research questions are left deliberately loose, and a process of induction and iteration, by which researchers go through a dataset many times, is used until meanings are found (Patton, 2015).

Thematic analysis would be best suited for real life problems which require an investigation which does not need to be entirely focused at the outset, is able to deal with complexities and individuality on how a situation is perceived, while aiming to gather common themes that can illustrate key aspects of a phenomenon (Braun and Clarke, 2008). For example, it can be very useful at assessing views on services or educational interventions, where there is limited knowledge about what are the perceptions of the relevant stakeholders.

Discourse Analysis

Discourse analysis is concerned with looking at the ways that things are talked about. It aims to reveal socio-psychological aspects that intentionally or accidentally are hidden in language (Robson and McCartan, 2015). It is similar to thematic analysis, but can be considered to have added layers of interpretation. This is because discourse analysis builds on the assumption that individuals talk about things choosing certain language which on itself frames reality and would add to the meaning of the message that it gives. It aims to reveal characteristics beyond looking at a text structure and meaning (Hodges et al., 2008).

Discourse analysis can be useful to gather meanings on aspects where the choice of language is as important as the choice of content, and when there are potential relationships of power between stakeholders and non-explicit agendas guiding communication (Ritchie et al., 2013). For example, it could be useful to study the nature of discussions between pharmacists and patients about their non-adherence to prescribed medication.

Interpretive Phenomenological Analysis

Interpretive phenomenological analysis (IPA) is a very in-depth approach to finding meanings by analyzing themes, where data analysis is centered on aspects of a *lived experience*. It has been relatively recently introduced in the social sciences (Smith et al., 2009), and is being used in patient-centered healthcare research due to its powerful ways of helping to understand how an individual perceive and make sense of health and care. IPA studies involve a very close examination of the accounts of a small number of participants. This is so in order to obtain the richest meanings in the data through a thorough and complex analysis. More advanced IPA study designs may include participants which provide different perspectives of the same lived experience as a result of belonging to different groups (for example, patients and people who care for these) or they may follow these for some length of time (Brocki and Wearden, 2006).

IPA requires an insightful and skillful interpretation through a process of reflection, where researchers must make sense of how participants make sense of the lived experience under research in a process of double hermeneutic analysis (Smith, Flowers and Larkin, 2009). It would therefore be suitable for studies for which very little is known, which need to deal with the complex aspects of

interpreting human nature and human experience (Silverman, 2016). For example, it would be very useful in order to understand the experience of caring for a terminally ill patient at home, or processes such as how transgender patients' experiences in their journey through care.

Collecting Qualitative Data and Reporting Results

The previous section has described how to find meanings in qualitative data in order to provide answers to research questions which are relevant to pharmacy practice. It is necessary to understand how analysis is going to take place within an investigation in order to make decisions about how to collect and manage the data (King and Horrocks, 2010). This section provides guidance on how to do so, covering sampling and recruitment, and including specific aspects to consider with regard to ethical issues and reporting results in these types of studies.

While some of the approaches for finding meanings would be incompatible with some of the methods for gathering data, for example, Delphi technique would be incompatible with reflective diaries, when the practicalities enable the collection of the data needed to be done by a specific method, investigators can decide how to pair the approach to analysis with the method for data collection (Polgar and Thomas, 2013). There will be occasions where data can be obtained using more than one method, but in others there may be one which is more adequate to arrive at meanings of type sought (Austin and Sutton, 2018). The aim at all times should be to obtain data which is of the most possible quality, as any compromises made here will have an impact on the study; analyzing data which has not been collected well is much more difficult to do, as its focus can easily deviate from what was the original research question set for investigation (Bowling, 2014).

Sampling and Recruitment of Participants

Sampling of participants in qualitative research is different than that in other types of enquiry, as it allows the intentional selection of specific individuals by virtue of the investigators deciding that they present a specific characteristic or characteristics which makes their inclusion in the study adequate. This is generally done through purposive sampling, where the sample frame includes potential participants which are chosen for a reason, rather than these being selected at random (Patton, 2015). For example, in a study looking at the transition into higher education of pharmacy students which have undertaken their previous education in a country other than where they register to complete their pharmacy degree, the selection of students within a course at random would not be appropriate. Those individuals which are suitable can be identified as having the characteristics sought after and subsequently invited to take part in the study. In those occasions where the characteristic which is sought in individuals to be included in the study is rare, or there is no sampling frame available, snowball sampling can be of used (Salkin, 2010). In this, potential participants and those taking part in the investigation are asked to identify further participants, which can subsequently be invited. The use of purposive or snowball sampling should not be seen as a limitation of the study, as if this is done well, it will increase richness in the data being collected and lead to more meaningful and complete results (Denzin and Lincoln, 2017).

In terms of recruitment for studies which involve the collection of qualitative data, this is often driven by the practicalities of sampling participants. It could be the case that the entirety of a group available with the specific feature or involvement in the phenomenon under research is invited, for example, having being subject to an intervention or experience an innovative service or educational program (Smith, 2002). When there are potentially large numbers of individuals for which this may be the case, accessing previous literature can be very useful to identify how purposive sampling could better take place (Austin and Sutton, 2018). Alternatively, additional practicalities for accessing participants can be used to inform recruitment strategies, always remembering that gathering quality data rather than convenience should be guiding sampling and recruitment. It must be noted that, particularly in approaches to finding meanings by analyzing concepts, sometimes sampling and recruitment of participants is not necessary, as there may be suitable secondary data already available for analysis (Ando et al., 2014).

Gathering and Preparing Qualitative Data

As in any investigation, the process of gathering and preparing data is central to qualitative research. However, unlike in other designs, in this case data collection is often an iterative process which is informed by data analysis, with results obtained feeding into how further data collection is undertaken (Braun and Clarke, 2008). This process can be flexible and allows to aim for investigating issues which may have not been anticipated but rather emerge from the data. As a result of this, piloting data collection tools is not undertaken in the same way as it would be if following a quantitative design, as it is possible to refocus how the data is collected as part of the process of gathering it (Ando et al., 2014). For example, when researching patients' health choices within individuals of a certain ethnicity, there may be a specific aspect which features as more important to some participants, which is in tension with which the literature shows to be the case for other groups, and therefore worth investigating. Once this is identified, subsequent participants can be asked widely about their choices, but also more specifically about this emerging theme. When sampling and recruiting participants to a study, it is important to consider any ethical issues that can be encountered, as there may be instances where sensitive or confidential information is involved in an investigation, or data which relates to patients and their care (Wingfield and Badcott, 2007). Ethical issues are covered in a further section of this chapter, where their implications and how to avoid key issues are explained.

Generally, qualitative research data in pharmacy practice will be obtained from documents, observations, or discussions, by being written, observed, or shared (Smith, 2002). Irrespectively of how this data is gathered, it will generally be presented or prepared as a written text which will subsequently be analyzed, either by finding concepts or themes which are present. This is not to say that data could not be accessed in other prepared formats, such as audio-recordings or pictures, which although much less common, may suit certain investigations (Austin and Sutton, 2018). The following sections will outline key practical considerations when gathering and preparing qualitative data depending on how this is obtained, in order to ensure that key aspects are not overlooked.

Collecting Data Which Is Observed

The collection of data which is observed, or participant observation, is a method widely used in other disciplines, such as psychology, in order to research behavior (Patton, 2015). In pharmacy practice it can be useful to explore how processes are undertaken and in which ways these could become more efficient, to identify learning needs and to investigate aspects of service provision which are overlooked by those involved with it. Participant observation can encounter challenges in ensuring that it is carried out with the consent of all of those which would be involved and in a way that is still able to capture real practices and behaviors, not influenced by the presence of the investigators (DeWalt, 2001). This method has great potential of growth within pharmacy practice, although currently it still encounters barriers as a result of the need to deal with issues of confidentiality, rigor of the observation and any bias introduced by the presence of the investigators (Bryman, 2015).

Data which is observed is generally collected through field notes, data collection forms or audit tools aiming to capture the aspects of reality that are being investigated (Polgar and Thomas, 2013). In any case, researchers need to be vigilant to identify conducts and trends relevant to the research question. Unlike the gathering of data by other means, participant observation often relies on collecting data in a process as it happens in real time, with no opportunity to go back to the phenomenon to check or expand on incomplete information. There may be situations where it could be possible to video-record the process which is being investigated, although when this is the case, the potential for more complete data which can be revisited at a later data may be over outweighed by the introduction of additional bias as a result of participants changing their behavior due to not only being observed, but also recorded (DeWalt, 2001).

Participant observation can be very useful in educational research, when the aim is to look at how students learn or apply some learning (Austin and Sutton, 2018). For example, it would be a good choice in order to collect data to look at inter-professional working involving students of different disciplines, and how they relate to each other when undertaking practical work.

Collecting Data Which Is Written

As mentioned earlier in this section, most of the qualitative research undertaken in pharmacy practice leads to a dataset which is converted into a written text (Smith, 2002). This section will cover the collection of data which is originated in a written format, rather than gathered in a different way to then be prepared as a written text. Written texts of any type can be subject to qualitative data analysis, and what types of texts may be suitable, if at all, to answer a research question will depend on what the question is and what meanings are sought in the data (Bryman, 2015). As explained in the previous sections, the information that could be found in written texts could be explicit, and often documents are used in this way to find meanings by analyzing concepts (Hsiu-Fang and Shannon, 2005). In some cases, investigators may be looking for information within the data of certain texts which is not explicit, in which case it would be useful to look for meanings by analyzing themes (Ryan and Bernard, 2003). For example, discourse analysis could be undertaken on written information provided to the general public on a certain aspect of healthcare, looking at how language constructs aim to influence healthcare behaviors as part of the promotion of public health.

There are two types of texts which can be particularly useful in health research: documents and reflective journals (Bowling, 2014). Documents which can be subject to analysis would include written processes, policies, lay literature, and medical documents. Reflective diaries offer an additional and powerful tool for collecting data which is written, and unlike documents constructed for a different purpose, reflective diaries are often designed and set up for gathering data to describe a specific experience (Robson and McCartan, 2015). They can be very useful to enable participants to develop a view on a particular aspect over time, or make sense of a change of identity, and they can be paper based or undertaken on-line. Reflective diaries require participants to be able to articulate their thoughts and reflections in writing, and are well suited for educational research (Polgar and Thomas, 2013).

Collecting Data Which Is Shared

The collection of data which is shared by participants can be considered the most common way of gathering qualitative data for pharmacy practice research. This is the case as this enables a focused investigation, where researchers remain in some control over participants' contributions, while allowing the necessary flexibility to follow ideas which were not anticipated but are relevant to the research question (Austin and Sutton, 2018). There are two main ways of collecting data which is shared by participants: one-to-one and group interviews, with the latter also being called focus groups (Bloor et al., 2000).

One-to-one interviews are very popular in qualitative research in general, as they would suit most investigations to some extent, the practicalities involved in carrying these out being less than those involved in other ways of collecting data, and they also perceived as being less intrusive than other methods such as participant observation (King and Horrocks, 2010). They enable the gathering of relevant data in great deal of depth, considering individualities and issues which are important for the specific participant from which the data is gathered (Robson and McCartan, 2015). In pharmacy practice research, one-to-one interviews

will generally be semi-structured, following an interview guide with set open questions which may also include scenarios or pictures to facilitate discussion (Smith, 2002). This interview schedule is designed to be used flexibly, and the questions that it contains often become more focused as the interview progresses in order to gather more general thoughts first, to then narrow these down to those aspects which are more closely related to the investigation (Austin and Sutton, 2018). In some cases, one-to-one interviews can go into more depth looking at life stories and including un-structured descriptions and accounts of life events (Smith et al., 2009). These are less used within pharmacy practice research, although they can lead to very powerful interpretations of specific aspects that can be presented as case studies. One-to-one interviews as always better carried out face-to-face, and this way of communication would almost inevitably lead to richer data. However, it would sometimes be adequate or necessary to undertake one-to-one interviews by telephone or video-conference, in which case practical aspects such as privacy and ensuring matters discussed are sufficiently covered should be considered to minimize any potential impact of the lack of face-to-face contact (Robson and McCartan, 2015).

Group interviews, or focus groups, are another way of collecting data which is shared by participants and are increasingly popular in pharmacy practice and healthcare research (Barbour, 2018). Group interviews generally involve 6–8 participants discussing a topic following an interview schedule with the direction of a moderator. While they do not provide the opportunity to arrive at the depth of exploration that one-to-one interviews may do, they allow for issues to be discussed as a group, and the different perspectives of the different people to be explored and developed (Polgar and Thomas, 2013). Group interviews can include individuals with similar or different backgrounds and a variety of stakeholders that can be similarly or differently affected by the issue under investigation, depending on the focus of the study. They can be very useful in research questions that look at processes or services which involve different stakeholders, and discussions where a range of perspectives can be beneficial (Smith, 2002). As many services and educational experiences are provided in this way, the use of group discussions would be very suitable to research these, as they would enable inclusion of different types of individuals that would be affected by the experience or phenomenon being researched. While group discussions are generally guided by a semi-structured interview schedule, they can also be based around the discussion of scenarios in the same way as one-to-one interviews (Krueger and Casey, 2014).

Both in the case of one-to-one and group interviews, the content of these discussions is generally audio recorded with permission from the participants (King and Horrocks, 2010). These recordings are transcribed verbatim to arrive at a written account which contains the narrative produced on the discussion. The process of transcribing the content of one-to-one or group interviews is very time consuming, but facilitates data analysis enormously as it enables easy access to the entirety of the dataset, assisting in the complex process of finding meanings (Barbour, 2018).

Ethical Issues

Qualitative research in pharmacy practice will inevitable involve human participants or data which relates to some aspect of human behavior. Even in situations where there are no specific individuals associated with information or data, for example, in some forms of documentary analysis, how the research may impact on research participants, researchers and society, is very important (Wiles, 2012). The two key aspects to consider to ensure that qualitative research is undertaken ethically mirror those involved in professional practice. These are confidentiality and consent (Wingfield and Badcott, 2007), which are very closely linked to each other. They are particularly relevant as this type of research can easily involve sensitive issues, vulnerable participants, and data which have been shared under certain assumptions (Austin and Sutton, 2018).

Qualitative research data is generally anonymized very early on in the analysis, if it included any participants' details, and while information can sometimes be held that can lead to linking specific meanings to a named person, this is not normally accessed and can be easily kept secure (King and Horrocks, 2010). Research participants may have agreed for the data they have provided and the information that enable linking it to individuals to be kept for a lengthy period of time, and even to be re-analyzed or contrasted with data from future studies (Wiles, 2012). However, there are two specific circumstances where care must be exercised. Firstly, when reporting this data, as while specific meanings may not be attributed to individual participants, it would be impossible to ensure that, due to its context or other details provided, a participant could not ultimately be identified (Smith, 2002). Another instance which can compromise anonymity is the collection of data through group discussions, where despite that it could be requested that all the participants keep the contents of any discussion private, there is no way to warrantee that this will be the case (Bowling, 2014).

An additional consideration would particularly apply to approaches for finding meanings by analyzing themes. In the more interpretive forms of this, there could be very powerful processes where individuals are making sense of reality, with meanings emerging during the research process which were not anticipated by investigators or participants (Smith et al., 2009). While constructing and sharing these meanings, participants may become aware of interpretations of their own reality which they did not have before (Crotty, 2003). This may mean that, for example, that an interview on a topic which could present itself as being relatively safe to discuss, can bring up unanticipated and sensitive issues. At the same time, investigators may find that very personal views and experiences are shared with them, which could have an effect on how they relate to the person being researched. It is therefore important that participants and investigators understand completely what is involved in a study, have time to reflect and understand this information, and in the case of those being researched, feel that they can withdraw participation at any time (Wiles, 2012). Provided that all the aspects described here with regard to confidentiality are adequately explained to participants, consent needs to extend as well to ensure that they understand practicalities, who is undertaking the study, how is funded, and ensuring that participants do not feel pressured to take part (Salkin, 2010).

Reporting and Writing up Results

Qualitative research in pharmacy practice can be undertaken for a variety of purposes, and while its design and results will have to be reported, this may be done differently depending on the nature of the research question, the approach to analysis and the type of data collected in the project (Silverman, 2016). Studies that aim to find meanings by analyzing concepts may follow prescriptive ways for presenting results provided by the authors, or arrive at a specific output at the end of the research process such as a framework or a theory (Glaser and Strauss, 1967; Ritchie and Spencer, 1994). Those where meanings are found by analyzing themes often combine results and discussion, to construct a narrative which tells a story and describes, explains and illustrates with relevant quotes from the participants, the given interpretation of the phenomenon under research (Smith, 2002). This section would focus on the reporting of these types of studies.

In the more interpretive types of research, where meanings are found by analyzing themes, difficulties can be encountered in constructing the narrative which will present the results and in making judgments with regard to how the story that this narrative provides should be told (Patton, 2015); researchers may unnecessarily be trying to arrive at a final interpretation, when this is conceptually unnecessary (Smith et al., 2009). The narrative presenting the results, and the quotes which are chosen to illustrate these, should be driven by the research question and what it is trying to answer, rather than how frequently a theme appears in the data and other similar measures which belong to the quantitative paradigm (Braun and Clarke, 2008). In this way, it is arriving at a useful and informative story what researchers should strive to do. While quotes can be perceived to provide validity checks of the researcher interpretation, they should instead enrich and illustrate this, building on the assumption that, if the analysis has been performed well, this interpretation truly describes aspects of the phenomenon under investigation (Robson and McCartan, 2015). When providing the quotes, these can be introduced with the participant number, transcript number, or similar, so there is an element of context provided within this story.

Any report from a pharmacy practice study involving qualitative data, as with any type of research, should contain an overview of previous literature (Smith, 2002). This will include not only that which is relevant to provide an introduction to what is being investigated, but also some background which relates to how this was researched and the characteristics of what was studied that led to the use of the selected approach to finding meanings and method for gathering data (Ritchie et al., 2013). For example, in a study looking at organizational factors affecting pharmacists' role satisfaction within a big pharmacy chain, previous literature would show that the phenomenon can be complex enough to need meanings to be sought by analyzing themes. The fact that pharmacists often work in isolation from each other, staff members work under their supervision and most organizational factors are under the control of their line managers need to be provided as a context to show that the investigation would better involve one-to-one rather than group interviews. After providing a clear account of what previous literature exists on the subject and any relevant context that informs the reader of background to the methods selected, the methodology followed to undertake the study will have to be reported with great deal of clarity, to demonstrate that this has been rigorous and the gathering, preparation, and analysis of the data are robust and trustworthy (Robson and McCartan, 2015). While in some types of studies it would not be appropriate to claim that there is a unique interpretation of what is being researched, it is always necessary to be transparent on how the given interpretation has been arrived at (Braun and Clarke, 2008). Otherwise the research runs the risk of being considered under-developed and with limited credibility on the results that it has arrived at. Particular attention will have to be paid to report how the meanings have been found, and if a tradition has been followed, whether any modifications to the way that is described by the authors has taken place, referencing these appropriately (Robson and McCartan, 2015).

Writing up a study involving qualitative research data can be a much lengthier process than initially anticipated, as further refining of the results arrived at can take place as part of the writing process. Researchers involved in reporting these type of studies are encouraged to start writing up results at the nearest opportunity, as this can take as long as the very time consuming process of finding meanings in the data (Salkin, 2010).

Final Considerations and Steps to Go Further

Investigators have been concerned with obtaining knowledge and what is its nature since research began to shape the way that we find out more about the world (Bowling, 2014). As explained at the beginning of this chapter, in the scientific method, which underpins quantitative research, knowledge can be considered to be factual, unique, and accessible (Popper, 1959/2002). In contrast, the qualitative paradigm is built on the assumption that knowledge is socially constructed, and only real as beliefs in individuals, with a changing nature and no longer valid by the time is identified (Patton, 2015). These two paradigms do not have to be in tension, nor the approaches described here or the traditions defined by other authors (Poth and Creswell, 2013). Researchers need to make methodological choices that suit the investigations they are undertaking and to be responsive to what it is being researched. A pluralistic approach, where barriers are limited and enquiry is led by the need to provide practical solutions to real world problems, rather than underlying assumptions about the world and knowledge could be favored (Frost et al., 2010). More experienced researchers can even go further to undertake dual analysis, looking at the same data from different perspectives, finding meanings by analyzing concepts, themes or both in different ways in order to maximize what it can tell about what it is investigated (Ryan and Bernard, 2003). The webpages included in the list of relevant websites at the end of this chapter provide more in-depth explanations, examples, and aspects to reflect on which can guide researchers wanting to further their expertise on this field. For this purpose, it can also be useful to revisit previous sections of this chapter that can

provide additional useful information on a second read, once further development of understanding of these approaches and techniques has taken place.

In the same way that early generations of researchers pushed the boundaries of accepted practices by using innovative techniques (Paley and Lilford, 2011), those starting to look at questions for which no easy methodological choices exist should continue to make this field to evolve. In this respect, some terms such as data saturation, triangulation, and mixed-methods are in decreased use, as a result of further understanding of what these methodologies are about (Teddlie and Tashakkori, 2008). Research in pharmacy practice should be guided by the needs of patients, practitioners, and service provision, and change to ensure it is able to provide answers to questions to better meet these needs.

Glossary

Analysis: Process by which research data is manipulated in order to present it in a way that makes the results more accessible to the reader.
Concept: A unit of meaning which contains an idea which is defined and described by the terminology used to relate to it, having a near literal meaning.
Data saturation: The arrival at a point in the research process where the collection of additional qualitative data to answer a specific research question is thought to no longer arrive at finding additional meanings.
Deduction: Process by which pre-specified meanings are sought in research data.
Epistemology: The branch of philosophy which studies the nature of knowledge.
Framework: An ordered presentation of results which has some structure. It aims to provide some explanation of a phenomenon but is less developed than a theory.
Hermeneutics: Method for understanding aspects of a phenomenon based on interpreting how these are perceived by individuals who relate to them closely, generally by having experienced them.
Induction: Process by which meanings emerge from research data, without being pre-specified or anticipated.
Iteration: The recurrent process of looking at meanings to frame understanding of a phenomenon, which will then determine the way by which further meanings continue to be sought.
Meanings: In the context of this chapter, meanings are concepts and themes, both of which are understood as aspects of a phenomenon.
Nominal data: Data which relates to properties, which can provide a measure of an attribute without including any numerical values.
Paradigm: A model, which could be based on beliefs about the world and what is knowledge, which underpins explanations about reality, and how this can be studied.
Phenomenon: An occurrence that can be observed and researched. This is often what a research question in qualitative research aims to describe.
Phenomenology: The philosophical study of the structures of experience and consciousness.
Philosophy: The study of the fundamental problems concerning existence, knowledge, values, reason, mind, and language.
Research tradition: An accepted overarching and distinct set of assumptions about the world and knowledge, and how this would be best understood and researched.
Scientific method: An approach to investigation based on measurement and the collection of data to test pre-formulated hypotheses and build theories.
Theme: An idea which has been extracted from a latent meaning found in data after a process of interpretation, and which has not been explicitly shared by research participants.
Theory: An ordered and structured presentation of results which aims to explain phenomena. A theory would be further developed than a framework.
Triangulation: The use of one or more methods of data collection with the purpose of corroborating or arriving to a more complete description of a phenomenon.

References

Ando, H., Cousins, R., Young, C., 2014. Achieving saturation in thematic analysis: development and refinement of a codebook. Compr. Psychol. 3, 3–4.
Austin, Z., Sutton, J., 2018. Research Methods in Pharmacy Practice: Methods and Application Made Easy. Elsevier, Oxford.
Barbour, R., 2018. Doing Focus Groups, 2nd ed.. SAGE Publications, Thousand Oaks.
Bloor, M., Frankland, J., Stewart, K., 2000. Focus Groups in Social Research. SAGE Publications, Thousand Oaks.
Bowling, A., 2014. Research Methods in Health, 4th ed.. McGraw-Hill, Maidenhead.
Braun, V., Clarke, V., 2008. Using thematic analysis in psychology. Qual. Res. Psychol. 3 (2), 77–101.
Brocki, J., Wearden, A.J., 2006. A critical evaluation of the use of interpretative phenomenological analysis (IPA) in health psychology. Psychol. Health 21, 87–108.
Bryman, A., 2015. Social Research Methods, 5th ed.. Oxford University Press, Oxford.
Crotty, M., 2003. The Foundations of Social Research, 2nd ed.. SAGE Publications, Thousand Oaks.
Denzin, N., Lincoln, Y., 2017. The SAGE Handbook of Qualitative Research. SAGE Publications, Thousand Oaks.

DeWalt, K., 2001. Participant Observation: A Guide for Fieldworkers, 2nd ed.. Altamira Press, Lanham.
Frost, N., Nolas, S.M., Brooks-Gordon, B., et al., 2010. Pluralism in qualitative research: the impact of different researchers and qualitative approaches on the analysis of qualitative data. Qual. Res. 10 (4), 441–460.
Gale, N., Heath, G., Cameron, E., et al., 2013. Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med. Res. Methodol. 13, 117.
Glaser, B., Strauss, A., 1967. The Discovery of Grounded Theory: Strategies for Qualitative Research. Routledge, New York.
Hodges, B.D., Kuper, A., Reeves, S., 2008. Discourse analysis. Br. Med. J. 337, a879.
Hsiu-Fang, H., Shannon, S.E., 2005. Three approaches to qualitative content analysis. Qual. Health Res. 9, 1277–1288.
Keeney, S., McKenna, H., 2010. The Delphi Technique in Nursing and Health Research. John Wiley and Sons, Oxford.
King, N., Horrocks, C., 2010. Interviews in Qualitative Research. SAGE Publications, London.
Krueger, R., Casey, M., 2014. Focus Groups: A Practical Guide for Applied Research, 5th ed.. SAGE Publications, Thousand Oaks.
Kuhn, T.S., 1970. The Structure of Scientific Revolutions. The University of Chicago Press, Chicago.
Paley, J., Lilford, R., 2011. Qualitative methods: an alternative view. Br. Med. J. 342, d424.
Patton, M.Q., 2015. Qualitative Research and Evaluation Methods: Integrating Theory and Practice, 4th ed.. SAGE Publications, Thousand Oaks.
Polgar, S., Thomas, S., 2013. Introduction to Research in the Social Sciences. Elsevier, Edinburgh.
Popper, K.R., 1959/2002. The Logic of Scientific Discovery. Routledge, London.
Poth, C., Creswell, J.W., 2013. Qualitative Inquiry and Research Design: Choosing Among Five Approaches, 3rd ed.. SAGE Publications, Thousand Oaks.
Ritchie, J., Spencer, L., 1994. Qualitative data analysis for applied policy research. In: Real World Research: A Resource for Social Scientist and Practitioner-Researchers, 4th ed.. John Wiley and Sons, Oxford.
Ritchie, J., Lewis, J., Nicholls, C.M., et al., 2013. Qualitative Research Practice. SAGE Publications, Thousand Oaks.
Robson, C., McCartan, K., 2015. Real World Research: a Resource for Social Scientist and Practitioner-Researchers, fourth edn.. John Wiley & Sons, Oxford.
Ryan, G., Bernard, H.R., 2003. Techniques to identify themes. Field Methods 15 (1), 85–109.
Salkin, N., 2010. Encyclopedia of Research Design. SAGE Publications, Thousand Oaks.
Silverman, D., 2016. Qualitative Research. SAGE Publications, London.
Skulmoski, G., Hartman, F., Krahn, J., 2007. The Delphi method for graduate research. J. Inform. Technol. Educ. 6, 2–21.
Smith, F., 2002. Research Methods in Pharmacy Practice. Pharmaceutical Press, London.
Smith, J.A., Flowers, P., Larkin, M., 2009. Interpretative Phenomenological Analysis. SAGE Publications, Thousand Oaks.
Strauss, A., Corbin, J., 1997. Grounded Theory in Practice. SAGE Publications, Thousand Oaks.
Teddlie, C., Tashakkori, A., 2008. Foundations of Mixed Methods Research: Integrating Quantitative and Qualitative Approaches in the Social and Behavioral Sciences. SAGE Publications, Thousand Oaks.
Tesh, R., 1990. Qualitative Research: Analysis Types and Software Tools. Routledge, New York.
Wiles, R., 2012. What Are Qualitative Research Ethics? Bloomsbury Academic, London.
Wingfield, J., Badcott, D., 2007. Pharmacy Ethics and Decision Making. Pharmaceutical Press, London.

List of Relevant Websites

British Psychological Society [Internet]. Available from: http://beta.bps.org.uk/ [cited 2017 Nov 27].
Interpretive Phenomenological Analysis [Internet]. Available from: http://www.ipa.bbk.ac.uk/ [cited 2017 Nov 27].
British Society for Phenomenology [Internet]. Available from: http://www.britishphenomenology.org.uk/ [cited 2017 Nov 27].

Meta-Synthesis of Qualitative Research in Pharmacy Practice

Fatima Tauqeer*, Zikria Saleem†, Zaheer-Ud-Din Babar‡, *Institute of Health and Society, University of Oslo, Oslo, Norway; †University College of Pharmacy, University of the Punjab, Lahore, Pakistan; ‡University of Huddersfield, Huddersfield, United Kingdom

© 2019 Elsevier Inc. All rights reserved.

Introduction

Qualitative research in health care is a relatively new phenomenon and has gained a lot of attention in the past two decades (Shuval et al., 2011). It intends to synthesize views, experiences, behaviors, and opinions of a wide variety of pharmacy-oriented stakeholders, which may include pharmacists, patients, and other health-care providers (Tonna and Edwards, 2013). It provides a valuable snapshot on why people do what they do and focuses on extracting underlying reasons, factors, and attitudes in doing so (Austin and Sutton, 2014; Yin, 2016). A variety of methods to conduct a qualitative study in pharmacy practice have been adopted such as interviews, focus group discussions, participant observations, contextual inquiry, and document analysis (Kaae and Traulsen, 2015; Tonna and Edwards, 2013). The study sample is chosen in such a way as to bring out distinctive experiences and opinions, which may or may not include a general pattern or theme (Yin, 2016). The syntheses of a number of qualitative studies generate new evidence-based knowledge for potential use in pharmacy practice and health-related policy formation (Tong et al., 2012).

What Is Meta-Synthesis of Qualitative Research?

Much like a systematic review, a systematic approach to identify, sum up, and synthesise novel knowledge from multiple qualitative studies on a chosen topic of interest is called meta-synthesis (Barnett-Page and Thomas, 2009). According to Walsh and Down, it is a process that assembles findings from a collection of different yet interconnected qualitative studies with an "interpretive, rather than aggregating, intent" (Walsh and Downe, 2005) and as Margarete Sandelowski describes, "are more than the sum of parts, in that they offer novel interpretations of findings" (Thorne et al., 2004). The process uses a systematic style to infer readily accessible and understandable themes from studies about the topic of inquiry, to enable knowledge development (Barnett-Page and Thomas, 2009; Thorne et al., 2004).

The process of meta-synthesis goes one step ahead of systematic literature review and traditional narrative review (Britten et al., 2002). It involves translation and comparison of interpretations gathered from the selected studies into one another to synthesise new knowledge and possibly to introduce "conceptual innovation." This conceptual development through systematic charting of the concepts extracted from the available data distinguishes meta-synthesis from other methods of literature review (Britten et al., 2002). It enhances the power of available qualitative data by generating theories that can be further explored and investigated (Britten et al., 2002; Sandelowski, 2007). However, the analysis and interpretations, otherwise known as third-order interpretations, depends mainly on the "judgment and insights of the reviewers" (Noblit and Hare, 1988; Thomas and Harden, 2008). Hence, an interdisciplinary team can further improve the quality of a meta-synthesis (Lachal et al., 2017).

Several scholars have illustrated the process of meta-synthesis. Thorne explains meta-synthesis as a process that,

> "demands exploitation of variations and complexities within the data set toward an integrative conclusion that extends beyond the scope of what would have been achievable within the temporal, spatial, or epistemological confines of individual studies or programs of research" (Thorne, 2008).

Barroso explains it as a method that "refers to both an interpretive product and the analytic processes, by which the findings of studies are aggregated, integrated, summarized, or otherwise put together" (Julie et al., 2003). Meta-synthesis is an umbrella term and has been used interchangeably with meta-ethnography and qualitative meta-analysis many times (Finfgeld, 2003).

A classic explanation of meta-synthesis by Schreiber states,

> "it is the bringing together and breaking down of findings, examining them, discovering the essential features, and, in some way, combining phenomena into a transformed whole" (Schreiber et al., 1997).

Types of Meta-Synthesis

There is no definite rule to perform meta-synthesis. It can be done in a number of different ways, and each technique has a name as proposed by Schreiber (Schreiber et al., 1997) and explained by Finfgeld (Finfgeld, 2003). These approaches overlap in many instances and can go hand in hand (Finfgeld-Connett, 2010). A brief description of the types of meta-synthesis is as follows:

1. Theory building, for example, grounded formal theory or meta-study
2. Theory explication
3. Descriptive meta-synthesis or meta-summary
4. Meta-ethnography

Theory building is the approach of meta-synthesis that involves building either a formal theory using "Grounded formal theory" or creating a new theoretical interpretation using "meta-study" method based on findings found from the qualitative studies included in the process (Finfgeld, 2003). Theory explication reconceptualizes an original concept. It involves a deconstruction, followed by a reconstruction and finally synthesis of the findings around a single concept. In descriptive meta-synthesis, original findings are evaluated comprehensively (Finfgeld, 2003).

Meta-Synthesis of Qualitative Research in Pharmacy Practice

The aim of meta-synthesis in pharmacy practice qualitative research is to combine, understand, and synthesize findings from the present pool of empirical qualitative studies around a phenomenon and then to generate a comprehensive understanding of that phenomenon (Sandelowski, 2007). It has been applied expansively in health-related research and has branched out into the field of pharmacy practice. A well-executed qualitative pharmacy practice meta-synthesis has the potential to develop new knowledge and understandings. This also has the capability to help make evidence-informed policy decisions and value-added clinical choices (Finfgeld-Connett, 2010; Mohammed et al., 2016b).

The approach of meta-synthesis is in its infancy in pharmacy practice qualitative research and here are a few examples of qualitative meta-synthesis.

Examples of Meta-Synthesis in Pharmacy Practice

Illustrated examples of meta-synthesis in pharmacy practice research (2005 till 2018)

Categories	*Examples*	*Synthesis*
Pharmacy services	Qualitative meta-synthesis of barriers and facilitators that influence the implementation of community pharmacy services: perspectives of patients, nurses, and general medical practitioners (Hossain et al., 2017)	Three-stage method for thematic synthesis described by Thomas and Harden (2008)
Meaning of medications for patients	Understanding the meaning of medications for patients: The medication experience (Shoemaker and Ramalho de Oliveira, 2008)	Analytic technique, "free imaginative variation" to determine the essential, structural themes
Perceptions and experiences of taking oral medicines	Perceptions and experiences of taking oral medications for the treatment of Type 2 diabetes mellitus: a systematic review and meta-synthesis of qualitative studies (McSharry et al., 2016)	Meta-ethnography model described by Noblit and Hare (1988)
Accessibility and affordability of medicines	Trans-Pacific Partnership Agreement and Its Impact on Accessibility and Affordability of Medicines—a meta-synthesis (Yap et al., 2017)	Meta-synthesis—thematic analysis
Migraine patients' perspectives regarding migraine treatment	Meta-synthesis on migraine management (Minen et al., 2018)	Meta-synthesis—thematic analysis
Medication-related burden and patients' lived experience with medicines	Medication-related burden and patients' lived experience with medicine: a systematic review and meta-synthesis of qualitative studies (Mohammed et al., 2016a)	Meta-ethnography methods and a comparative thematic analysis
Patients' experiences and perceptions of receiving benzodiazepines and Z-drugs	A systematic review and meta-synthesis of patients' experiences and perceptions of seeking and using benzodiazepines and Z-Drugs: toward safer prescribing (Sirdifield et al., 2017)	Thematic synthesis

Step-by-Step Guide to Meta-Synthesize Qualitative Literature in Pharmacy Practice

There are a number of recommended guidelines to synthesize new and overarching knowledge from the existing qualitative studies (Lachal et al., 2017; Noblit and Hare, 1988; Tong et al., 2012; Walsh and Downe, 2005). These guidelines coincide in many respects and have differences as well; however, none are binding or all-encompassing. Based on our literature review, some of these guidelines assume an "aggregate" approach toward meta-synthesis, while most incline toward "interpretative" style. A multidisciplinary meta-synthesizing team is deemed important "to assess rigor and develop richer and more complex understandings" of the data (Lachal et al., 2017). The team can choose one author's guidelines or may combine two or more depending on the nature of their review and the intended approach.

The earliest work on meta-synthesis is done by Noblit and Hare, who recommended seven steps to perform a meta-ethnographic synthesis: *getting started:* the initial stage where the meta-synthesizers build an interest in their research topic; *deciding what is relevant to the initial interest:* the stage where relevant qualitative studies are sought and included; *reading the studies*: to read the included studies in-depth; *determining how the studies are related*: creating a list of relevant concepts and chunks from all the studies and establishing a relationship among them; *translating the studies into one another*: the stage in which all the extracted concepts and chunks are compared and contrasted; *synthesising translations*: bringing together all the concepts and chunks in one new piece; and *expressing the synthesis*: as a written paper or in the form of a video (Noblit and Hare, 1988). Later, Walsh and Down illustrated five stages of meta-synthesis, which include framing the scope of the meta-synthesis, locating relevant papers, framing the inclusion criteria, appraising the studies, and finally analyzing and synthesizing (Walsh and Downe, 2005).

Tong advanced the concept of standardizing the process of qualitative synthesis as a whole by composing the ENTREQ (The Enhancing transparency in reporting the synthesis of qualitative research) checklist, which provides an all-encompassing framework to report the key steps in qualitative syntheses (Tong et al., 2012). This 21-item checklist gives a very broad sense of planning and executing a synthesis and covers five general domains: introduction, methods and methodology, literature search and selection, appraisal, and synthesis of findings (Tong et al., 2012).

After reviewing a set of seminal academic work on meta-synthesis, the following step-by-step guide provides comprehensive information for reviewers who intend to design and conduct a meta-synthesis.

Step 1 Frame a Clear Research Question/Objective

A clear and focused research question or objective should be established before diving into the process of meta-synthesis. One rational approach to frame the research objective is to have a preliminary review of the available qualitative literature. Therefore, a preliminary literature search on the topic of interest is required to ensure that enough data are available to meet the merit of a meta-synthesis. The team aiming to write a meta-synthesis should be clear about "What" and "Why" of their research objective.

In one example, the research question in a qualitative meta-synthesis was to pinpoint barriers and facilitators to implement community pharmacy services in Australia from the available literature (Hossain et al., 2017). Just like a systematic review of primary studies, they conducted a systematic search in three databases, namely, PubMed, Scopus, and Informit, to find studies that explored patients', general practitioners', and nurses', perceptions about community pharmacy services in Australia.

Step 2 Strategize the Search

The next step is to establish a strategy to systematically search for the required literature. However, there is no clear consensus on the need to follow some sort of methodical search strategy, and this is one way where a meta-synthesis differs from systematic review (Britten et al., 2002; Tong et al., 2012). Furthermore, for a meta-synthesis, there is no set requirement on the number of studies to include (Thomas and Harden, 2008). The process of data inclusion can terminate once saturation is achieved.

The search strategy includes a set of rules to find and select studies starting off by identifying the databases that are relevant to the research objective. Commonly used databases include PubMed, EMBASE, Web of Science, CINAHL, COCHRANE, SCOPUS, and ProQuest. Search terms or queries are developed based on the target topic. These search terms or queries can be developed using a number of search tools such as PICO, PICOS, and SPIDER (Alison et al., 2012; Curtin University, 2018).

PICOS and SPIDER are intended for qualitative and mixed methods evidence synthesis. Whatever search tool or concept is preferred, it results in a list of relevant key words or search terms. The PICO tool (Curtin University, 2018) is the most comprehensive one and focuses on the *Population, Intervention, Comparison and Outcomes*. It is intended for quantitative evidence synthesis but has been descrambled to suit qualitative setting as *Population, Interest and Context* (Curtin University, 2018). The PICOS tool focuses on the *Population, Intervention, Comparison, Outcomes and the Study design* of an article. The SPIDER tool, developed by Cooke et al. focuses on *Sample, Phenomenon of Interest, Design, Evaluation and Research type* (Alison et al., 2012). It narrows down the initial number of articles due to its high specificity (Methley et al., 2014). Methley recommends SPIDER for researchers achieving systematic narrative reviews of qualitative literature but finds it less effective than PICO (Methley et al., 2014). To translate the research topic more effectively into search queries, Boolean operators OR, AND, and NOT can be used with the search terms.

The search strategy may also include the following filters:

1. Original qualitative studies: Would you include only qualitative studies or mixed-methods too?
2. Language: Would you include studies published in English only?
3. Time span: What would be the time span, e.g., from 2000 to 2018, to search studies?

One way of reporting the search strategy clearly is by using the PRISMA tool. Although meant for systematic reviews and meta-analyses, it is a comprehensive tool to enhance the quality of search strategy (Moher et al., 2009).

The search strategy of a meta-synthesis on women's experiences of their pregnancy and postpartum image used PICO tool—Population (pregnan* OR postnatal OR postpartum OR prenatal OR antenatal OR *gravida* OR *parou) and Outcome (appearance OR body image OR body dissatisfaction). In addition, the researchers observed PRISMA guidelines to report their methods (Hodgkinson et al., 2014).

Step 3 Define and Refine an Inclusion Criterion

Once an initial list of studies has been finalized, the meta-synthesis panel will review all the studies to filter the ones that meet the inclusion criteria. In general, a study may be included based on the following information:

1. Relevance to the research objective
2. Relevance to the design methodology predefined by the meta-synthesis panel
3. Published in a peer-reviewed journal

At first, the screening process includes reading the titles and abstracts of all articles to evaluate if they align with the research objectives. Later, the preferred literature is refined by reading full text articles. Another recommended manual practice is to adopt the "pearl-growing" technique, which is to hand-search the reference lists and selectively choose additional research articles from the included literature (Schlosser et al., 2006). This way citations are thoroughly screened to assess their eligibility to be included in the meta-synthesis.

An optional yet valuable step is to do a quality appraisal of included studies. Most researchers have found it useful (Atkins et al., 2008; Tong et al., 2012; Uhrenfeldt et al., 2013). It could be performed by using any quality assessment tool from a plethora of options such as Critical appraisal skills program (2017), The Joanna Briggs Institute Reviewers' Manual (2015), checklist designed by Atkins et al. (2008), etc. An assessment of the quality of the selected studies can make a difference in the overall quality of the meta-synthesis. Before selecting a study for review, the reviewers can check its trustworthiness and rigor, i.e., Are the findings credible? or How valid is the data? (Sullivan and Sargeant, 2011).

Levack and his team explored the use of meta-synthesis to inform discussion on the selection of outcome measures for evaluation of services provided to adults with traumatic brain injury using several databases. They included studies comprising adult participants between 1965 and 30 June 2009. The search strategy was based on text–words and Medical Subject Headings terms intended to detect studies that talked about the key components of topic (Levack et al., 2010):

1. patients with TBI—search terms "exp Craniocerebral trauma/," "exp Cerebrovascular Trauma/," "brain injury," as a text–word, etc.,
2. study methodology of interest—search terms such as "exp Qualitative Research/," "qualitative" as a text–word, "grounded theory" as a text–word, etc., and
3. phenomena of interest, e.g., text–words concerning the concepts of experience, outcome and recovery

Step 4 Synthesize New Knowledge

This phase is the essence of a meta-synthesis. After finalizing the studies to be included, the meta-synthesis team can read the studies together with extracting relevant codes and themes. Later, all the codes and themes are organized together to look for similarities and differences and can be grouped under major themes or concepts. These themes are then further discussed and refined.

1. **Reading and analyzing to generate analytical themes**
   The reading phase is the nucleus as all the subsequent steps are dependent on this step. Effective reading might involve: R = recording, E = extracting, A = appraising, D = describing (Lachal et al., 2017). Careful reading of each study is essential to familiarize oneself with the original content and with the prominent findings across all the studies (Noblit and Hare, 1988). These findings are in the form of either interpreted data, original quotes, documents, or notes. In addition, formal details about each study, which may include study context, location, methodology and data analysis, should be recorded and presented in the final report (Lachal et al., 2017). During and after this phase, each member of the panel should start extracting codes and themes they find relevant to their research objective or theoretical framework. For the management of qualitative data, NVivo, a computer software, is a recommended tool (Mohammed et al., 2016b). Data extraction and management could be done by other ways too, for instance, using a methodological framework that entails categorizing extracted data in a tabular form or in groups or in the form of a grid (Britten et al., 2002) and then codifying that data for themes and concepts related to the topic under study (Graneheim and Lundman, 2004).

In principle, data analysis, that is, coding and/or thematizing, can be performed simultaneouly on both forms of the data, that is, informant quotes (findings/results) and authors' interpretations (dicussion). At this stage, initial extracted themes or concepts should be clustered in one place, be it NVivo or a simple Excel sheet, to have an idea about the available data. This would help in translating the studies into one another. One way of doing the analysis is using Noblit and Hare's ethnographic approach to begin with identifying the first-order constructs. These are key findings or codes identified by the reviewers from the original quotations in the studies. This should be followed by identifying the second-order constructs, which are extracted key findings or codes from the interpretations done by the authors in the discussion section of the studies (Noblit and Hare, 1988). The reviewers generate their third-order constructs, which are the final product of a meta-ethnography, based on the first- and second-order constructs (Thomas and Harden, 2008) translated across all the studies. These synthesized third-order constructs open on to the synthesis of new knowledge that might take the form of a succinct conceptual "line of argument" that goes "beyond the content of the original studies" (Thomas and Harden, 2008), and/or a new model or theory (Atkins et al., 2008; Lachal et al., 2017).

Data analysis can also be performed by following the six phases of thematic analysis described by Braun and Clarke: (1) familiarization with the data; (2) coding; (3) searching for themes; (4) reviewing themes; (5) defining and naming themes, and; (6) writing up (Braun and Clarke, 2006). In addition, Thomas and Harden describe thematic synthesis in three steps (Thomas and Harden, 2008). The first step is coding of findings of studies "line-by-line" and to group the codes based on similarities and differences between them. This step complements Noblit and Hare's recommendation to translate studies into one another, that is, themes from one study are compared with themes from another, through a repetitive comparison of similarities and differences across studies. The second step is the development of "descriptive themes" to describe the cluster of codes and/or concepts. Third, the generation of "analytical themes" where comprehensions of the reviewers are included that act to a specific review question and/or a theoretical framework. (Thomas and Harden, 2008). The analytical process in meta-synthesis works by an initial deconstruction of "what is known" and "how it is known" (Paterson et al., 2001). It includes extracting, aggregating, interpreting, and finally synthesizing the analytical themes from primary qualitative studies (Sandelowski, 2007).

Conceptually, analytical themes seem very much like third-order interpretations; however, according to Thomas and Harden, they differ based on the types of review questions. Analytical themes are constructed by comparing and contrasting the descriptive themes with a specific review question. In contrast, third-order interpretations build on the data to attend to a comprehensive or emerging review question (Thomas and Harden, 2008).

At this stage, the meta-synthesis team has developed key overall concepts or translations across studies, which are synthesized to grow into overall new interpretations or understandings (Britten et al., 2002; Noblit and Hare, 1988). The SAGE encyclopaedia of Qualitative Research Methods elaborates on this step as:

> "the meta-synthesist's task is not simply to determine a best fit, but rather to transform the data set that exists, with all of its inherent strengths and limitations, into a new conceptualization with the capacity of integrating the entire body of qualitatively derived knowledge about the phenomenon" (Given, 2008).

In one example, the reviewers adopted thematic synthesis to synthesize new insights about suicidal youths' care in the field of psychiatry. They developed their third-order interpretations to recommend a more conceptual line-of-argument or conclusion stating that "the violence of the message of a suicidal act and the fears associated with death lead to incomprehension and interfere with the capacity for empathy of both family members and professionals" (Lachal et al., 2017).

2. **Going back and forth to confirm analytical themes**

With codes, core themes as structured data sets or constructs, and analytical themes in place, clarification is done next through in-depth examination and analysis. Both Braun and Clarke and Thomas (Braun and Clarke, 2006; Thomas and Harden, 2008) emphasize that thematic analysis is an iterative process—moving back and forth between the stages is recommended as part of reconsidering original data. The analytical themes now require team work to redetermine the analysis with frequent discussions on the extracted common themes and on the emerging themes or concepts by recurrent returns to the original data.

A meta-synthesis on perceptions and experiences of taking oral medications for the treatment of Type 2 diabetes mellitus by McSharry et al. translated the included studies by identifying one paper and adding it to the first row of the translation table. Subsequent papers were added to this translation table in chronological order of publication. Later, they assessed the relationships, variances, and contradictions across studies to develop twelve overall translations. Three third-order constructs, such as (1) medication for diabetes: a necessary evil, (2) the passive patient as active experimenter, and (3) taking oral medication for Type 2 diabetes: a unique context, were established (McSharry et al., 2016).

3. **Framing the syntheses output**

After interpreting, reinterpreting, and analyzing the formulated theories and concepts across the studies, the final meta-synthesis report should generate a synthesis of new knowledge, understandings, and interpretations that go beyond a compilation of the primary studies. This new knowledge could be a new model of evidence, a critical framework, or a new theoretical insight (Tong et al., 2012). **Fig. 1** illustrates the process of meta-synthesis.

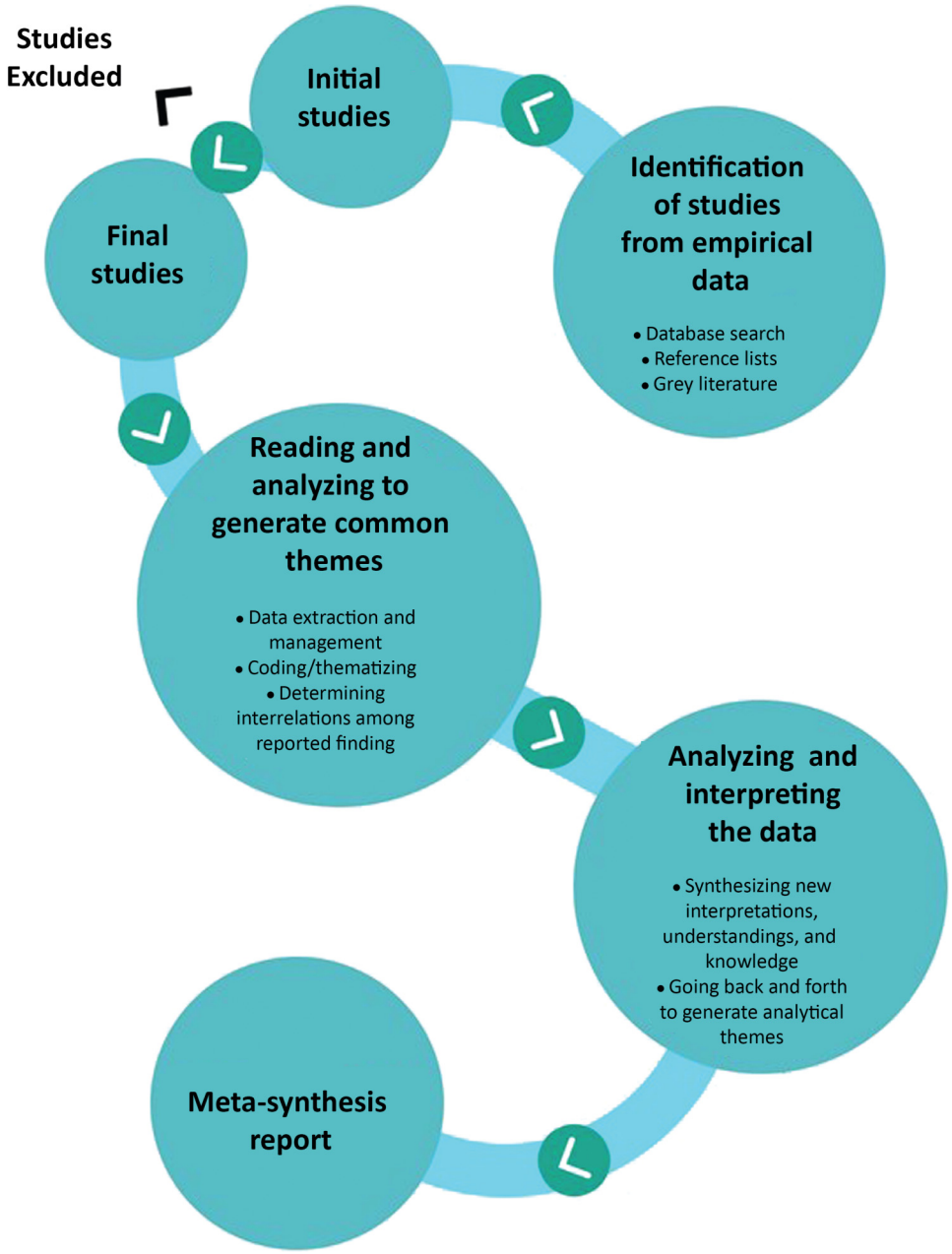

Figure 1 The step-by-step process to prepare a meta-synthesis report.

Conclusion

This chapter summarizes the key stages to conduct a meta-synthesis illustrating examples from the qualitative literature. Meta-synthesis is an important approach in qualitative research, and this aims to aggregate, interpret, and present previous findings to synthesise new knowledge for a wide range of health-related stakeholders. It is a rigorous way of fusing several qualitative findings to generate new knowledge for potential application in pharmacy and clinical practice, and to inform policy.

Acknowledgment

We would like to offer our special thanks to Kirsten Myhr (MSciPharm, MPH) for her comments and language editing on an earlier version of the manuscript.

References

Alison, C., Debbie, S., Andrew, B., 2012. Beyond PICO: the SPIDER tool for qualitative evidence synthesis. Qual. Health Res. 22, 1435–1443.

Atkins, S., Lewin, S., Smith, H., Engel, M., Fretheim, A., Volmink, J., 2008. Conducting a meta-ethnography of qualitative literature: lessons learnt. BMC Med. Res. Methodol. 8, 21.

Austin, Z., Sutton, J., 2014. Qualitative research: getting started. Can. J. Hosp. Pharm. 67, 436–440.

Barnett-Page, E., Thomas, J., 2009. Methods for the synthesis of qualitative research: a critical review. BMC Med. Res. Methodol. 9, 59.

Braun, V., Clarke, V., 2006. Using thematic analysis in psychology. Qual. Res. Psychol. 3, 77–101.

Britten, N., Campbell, R., Pope, C., Donovan, J., Morgan, M., Pill, R., 2002. Using meta ethnography to synthesise qualitative research: a worked example. J. Health Serv. Res. Policy 7, 209–215.

Curtin University, 2018. Allied Health Honours Research Design: PICO/PICo? [Online]. Library. Available from: http://libguides.library.curtin.edu.au/c.php?g=202429&p=1332736.

Finfgeld, D.L., 2003. Metasynthesis: the state of the art—so far. Qual. Health Res. 13, 893–904.

Finfgeld-Connett, D., 2010. Generalizability and transferability of meta-synthesis research findings. J. Adv. Nurs. 66, 246–254.

Given, L. 2008. The SAGE Encyclopedia of Qualitative Research Methods. Thousand Oaks, California.

Graneheim, U.H., Lundman, B., 2004. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Edu. Today 24, 105–112.

Hodgkinson, E.L., Smith, D.M., Wittkowski, A., 2014. Women's experiences of their pregnancy and postpartum body image: a systematic review and meta-synthesis. BMC Pregn. Childbirth 14, 330.

Hossain, L.N., Fernandez-Llimos, F., Luckett, T., Moullin, J.C., Durks, D., Franco-Trigo, L., Benrimoj, S.I., Sabater-Hernández, D., 2017. Qualitative meta-synthesis of barriers and facilitators that influence the implementation of community pharmacy services: perspectives of patients, nurses and general medical practitioners. BMJ Open 7.

Julie, B., Claudia, J.G., Margarete, S., Janet, M., Patricia, F.P., Linda, J.C., 2003. The challenges of searching for and retrieving qualitative studies. West. J. Nurs. Res. 25, 153–178.

Kaae, S., Traulsen, J.M., 2015. Qualitative methods in pharmacy practice research. In: Babar, Z.-U.-D. (Ed.), Pharmacy Practice Research Methods. Springer, Cham.

Lachal, J., Revah-Levy, A., Orri, M., Moro, M.R., 2017. Metasynthesis: an original method to synthesize qualitative literature in psychiatry. Front Psychiatry 8.

Levack, W.M.M., Kayes, N.M., Fadyl, J.K., 2010. Experience of recovery and outcome following traumatic brain injury: a metasynthesis of qualitative research. Disabil. Rehabil. 32, 986–999.

McSharry, J., McGowan, L., Farmer, A.J., French, D.P., 2016. Perceptions and experiences of taking oral medications for the treatment of Type 2 diabetes mellitus: a systematic review and meta-synthesis of qualitative studies. Diab. Med. 33, 1330–1338.

Methley, A.M., Campbell, S., Chew-Graham, C., Mcnally, R., Cheraghi-Sohi, S., 2014. PICO, PICOS and SPIDER: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. BMC Health Serv. Res. 14, 579.

Minen, M.T., Anglin, C., Boubour, A., Squires, A., Herrmann, L., 2018. Meta-synthesis on migraine management. Headache J. Head Face Pain 58, 22–44.

Mohammed, M.A., Moles, R.J., Chen, T.F., 2016a. Medication-related burden and patients' lived experience with medicine: a systematic review and metasynthesis of qualitative studies. BMJ Open 6.

Mohammed, M.A., Moles, R.J., Chen, T.F., 2016b. Meta-synthesis of qualitative research: the challenges and opportunities. Int. J. Clin. Pharm. 38, 695–704.

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 6.

Noblit, G.W., Hare, R.D., 1988. Meta-Ethnography: Synthesizing Qualitative Studies. Sage Publications, Newbury Park, CA.

Paterson, B., Thorne, S., Canam, C., Jillings, C., 2001. Meta-Study of Qualitative Health Research. SAGE, Thousand Oaks, CA.

Sandelowski M, B.J., 2007. Handbook for Synthesizing Qualitative Research. Springer.

Schlosser, R.W., Wendt, O., Bhavnani, S., Nail-Chiwetalu, B., 2006. Use of information-seeking strategies for developing systematic reviews and engaging in evidence-based practice: the application of traditional and comprehensive Pearl Growing: a review. Int. J. Lang. Commun. Dis. 41, 567–582.

Schreiber, R., Crooks, D., Stern, P., Morse, J., 1997. Completing a Qualitative Project: Details and Dialogue. Sage, Newcastle upon Tyne.

Shoemaker, S.J., Ramalho de Oliveira, D., 2008. Understanding the meaning of medications for patients: the medication experience. Pharm. World Sci. 30, 86–91.

Shuval, K., Harker, K., Roudsari, B., Groce, N.E., Mills, B., Siddiqi, Z., Shachak, A., 2011. Is qualitative research second class science? A quantitative longitudinal examination of qualitative research in medical journals. PLoS One 6, e16937.

Sirdifield, C., Chipchase, S.Y., Owen, S., Siriwardena, A.N., 2017. A systematic review and meta-synthesis of patients' experiences and perceptions of seeking and using benzodiazepines and z-drugs: towards safer prescribing. Patient–Patient-Centered Out. Res. 10, 1–15.

Smith, F., 1998. Health services research methods in pharmacy: qualitative interviews. Int. J. Pharm. Pract. 6, 97–108.

Sullivan, G.M., Sargeant, J., 2011. Qualities of qualitative research: part I. J. Grad. Med. Educ. 3, 449–452.

Thomas, J., Harden, A., 2008. Methods for the thematic synthesis of qualitative research in systematic reviews. BMC Med. Res. Methodol. 8, 45.

Thorne, S., Jensen, L., Kearney, M.H., Noblit, G., Sandelowski, M., 2004. Qualitative metasynthesis: reflections on methodological orientation and ideological agenda. Qual. Health Res. 14, 1342–1365.

Thorne, S.E., 2008. The SAGE Encyclopedia of Qualitative Research Methods. SAGE, Thousand Oaks, CA.

Tong, A., Flemming, K., Mcinnes, E., Oliver, S., Craig, J., 2012. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC Med. Res. Methodol. 12, 181.

Tonna, A.P., Edwards, R.M., 2013. Is there a place for qualitative research methods in pharmacy practice? Eur. J. Hosp. Pharm. Sci. Pract. 20, 97–99.

Uhrenfeldt, L., Aagaard, H., Hall, E.O.C., Fegran, L., Ludvigsen, M.S., Meyer, G., 2013. A qualitative meta-synthesis of patients' experiences of intra- and inter-hospital transitions. J. Adv. Nursing 69, 1678–1690.

Walsh, D., Downe, S., 2005. Meta-synthesis method for qualitative research: a literature review. J. Adv. Nurs. 50, 204–211.

Yap, Y.Y., Wong, C.P., Lee, K.S., Ming, L.C., Khan, T.M., 2017. Trans-pacific partnership agreement and its impact on accessibility and affordability of medicines: a meta-synthesis. Therap. Innov. Regul. Sci. 51, 446–459.

Yin, R.K., 2016. Qualitative Research From Start to Finish. Guilford Press, New York.

Mixed Methods Research in Pharmacy Practice: Basics and Beyond

Sara Ramzan*, Muhammad Abdul Hadi†, Zaheer-Ud-Din Babar*, *University of Huddersfield, Huddersfield, United Kingdom; †University of Birmingham, Birmingham, United Kingdom

© 2019 Elsevier Inc. All rights reserved.

Introduction

The role of pharmacists has become more patient oriented in the past couple of decades. Pharmacists are now involved in direct patient care and play a crucial role in ensuring safe and effective use of medicines in both community and hospital settings (Dhanani et al., 2017). In this context, pharmacy practice research is critically important to generate evidence to support and identify weaknesses, if any, for improvement of pharmacy services within health care systems (Bissell and Traulsen, 2005). Although, mixed methods is not a new methodology, it has become more popular in the last decade as it brings together strengths of both qualitative and quantitative approaches (Creswell and Plano Clark, 2018; Johnson et al., 2007; Pelto, 2015). Mixed methods research offers an alternative methodology to researchers who seek to answer complex research questions requiring both qualitative and quantitative approaches within a single study (Creswell and Plano Clark, 2018). Furthermore, it allows researcher to choose and mix methods from both qualitative and quantitative methodologies best suited to answer the research question.

In this chapter a range of topics related to mixed methods methodology have been discussed including typologies of mixed methods methodology, methods of integration of qualitative and quantitative strands within a mixed methods study, challenges in undertaking these studies, how to evaluate quality of these studies and examples of research questions that can be answered by mixed methods studies. These examples have been taken from the recent pharmacy practice literature.

What is Mixed Methods Research?

Mixed methods is often referred to as the *third methodological movement* (Teddlie and Tashakkori, 2009; Venkatesh et al., 2013). Although, mixed methods studies have both qualitative and quantitative components but how and when these strands should be combined is still a hotly debated area among methodologists (Tashakorri, 2007). Various terminologies have been used in the literature to describe mixed methods research including "integrated," "hybrid," "mixed research," "mixed methodology," "mixed methodology research," "combined," "multimethod," and "methodological triangulation" (Bryman, 2007; Driscoll et al., 2007; Johnson et al., 2007; Morse, 1991). Johnson et al. (2007) analyzed definitions of mixed methods provided by a number of "leaders" in the field. After analyzing these definitions, they defined mixed methods research as a type of research *"in which a researcher or team of researchers combines elements of qualitative and quantitative research approaches (e.g., use of qualitative and quantitative viewpoints, data collection, analysis, inference techniques) for the broad purposes of breadth and depth of understanding and corroboration."* (p. 123).

This definition was extended with a definition of the research type:

> "A mixed methods study would involve mixing within a single study; a mixed method program would involve mixing within a program of research and the mixing might occur across a closely related set of studies" (p. 123).

Figure 1 Knowledge cycle illustrating phases in the planning of mixed methods research design in pharmacy practice.
Source: Adapted from Creswell and Plano Clark (2018).

Tashakkori and Creswell's (2007) defined mixed methods research in the first editorial of *Journal of Mixed Methods Research* as *"research in which the investigator collects and analyses data, integrates the findings, and draws inferences using both qualitative and quantitative approaches or methods in a single study or program of inquiry"* (p. 4).

The key message from these definitions is that the mixed methods designs should be not used as a "tool" to collect two different datasets but there should be purposeful integration between qualitative and quantitative datasets to comprehensively answer the research question.

Planning of Mixed Methods Research

Several frameworks have been developed to guide on how to conduct and evaluate mixed methods research (Creswell et al., 2011; Tashakkori and Teddlie, 2010; Wisdom et al., 2012). In this chapter, we have adapted and modified framework developed by Creswell and colleagues (Creswell and Plano Clark, 2018) to illustrate the planning of a mixed methods research design (**Fig. 1**). In the first phase, the researcher would be driven by their curiosity regarding a theme or issue within the health-care setting. According to King et al. (1994), intellectual stimuli are the "purest" drive for conducting research (King et al., 1994). If the researchers decide to pursue this curiosity, they will have to formulate objectives and research questions which require a mixed methods approach. The rationale for using a mixed methods research design should always be justified and should result in more valuable and comprehensive findings than using a single method (Creswell and Plano Clark, 2018).

After formulating a strong research question/objective, a suitable methodological approach must be considered. The selection of appropriate mixed methods research study design in pharmacy practice must always be guided by the research question (Hadi et al., 2013a). There are a few questions which researchers need to ask themselves to establish if a mixed method approach is suitable for the planned study; Do the posed questions have quantitative and qualitative elements? How will the quantitative and qualitative methods be prioritized? In which sequence will they be conducted? And how and when will the integration of data take place? (Creswell and Plano Clark, 2018; Liamputtong, 2013). The sample size, data collection, data analysis must be planned for both qualitative and quantitative phases, and ethical approval should be obtained, if necessary. It is also critically important to consider and plan the integration and interpretation of the data. All these steps should be clearly and transparently reported in a manner that other researchers can replicate the methods. Authors must reflect on the findings of the study and explain how the use of mixed methods has helped to answer the original research question.

Mixed Methods Research Designs: How to Use Them?

Choosing between mixed methods designs is challenging (Creswell and Plano Clark, 2018; Leech and Onwuegbuzie, 2009). It is recommended for new researchers to familiarize themselves with established mixed methods research designs and choose a suitable

mixed methods design based on the research question (Bryman, 2007; Driscoll et al., 2007). Although, mixed methods research is a flexible methodology, it is important that the study design is justifiable and the pros and cons of all available study designs are weighed carefully (Creswell and Plano Clark, 2018).

Several typologies and classifications of mixed methods research exist in the literature (Greene et al., 1989; Leech and Onwuegbuzie, 2009; Teddlie and Tashakkori, 2009). We need to consider how each component will be integrated when the data have been collected. The following four guiding questions can help researcher to choose best mixed methods design for their research study (Creswell and Plano Clark, 2018):

- First, the researcher should decide the level of interaction between qualitative and quantitative strands. Will the qualitative and quantitative strands be kept independent or interactive?
- Secondly, the researcher must decide on the timing of data collection of both qualitative and quantitative strands. Quantitative and qualitative data can be collected sequentially or concurrently.
- Thirdly, the researcher needs to consider weighing of each component in mixed-methods design. Will the quantitative or qualitative component be given priority in answering the research question, or will they be weighed equally?
- Lastly, the researcher must decide the timing of integration of two datasets, as this can happen at different phases of the research (i.e., during data collection, data interpretation, etc.).

The four commonly used typologies used in mixed methods research are described below together with an example of their application from published pharmacy practice literature.

The Exploratory Sequential Design

In this design, the research is conducted in two sequential phases. This qualitative component is conducted first and is given more weighing in answering the research question. The quantitative component is used to generate generalizable data from the qualitative phase (Hadi et al., 2013a; Morse, 1991; Teddlie and Tashakkori, 2009; Wittenberg, 2000).

Fisher et al. (2018) conducted a mixed methods study to gain understanding of pharmacist independent prescribers' knowledge, perception and beliefs about departmental infrastructure, pharmacy and multidisciplinary team support, attitudes and behavioral determinants associated with prescribing. The study was conducted across 14 health care boards in Scotland. The qualitative data, gathered through focus groups and semistructured interviews of pharmacist independent prescribers, informed the design of a structured questionnaire (online cross-sectional survey) used to assess knowledge, perception, attitudes, and beliefs toward prescribing. Using mixed methods as methodological approach in this study allowed not only generalizable results but also provided broader insight to which organizational culture changes are required to influence prescribing.

The Explanatory Sequential Design

This design also consists of two phases. The quantitative component is conducted first and is given preference in answering the research question. In the first phase, quantitative data are collected and analyzed. In the second phase qualitative data are collected. This method is suitable when the qualitative component is needed to explain and clarify findings from the quantitative component (Hadi et al., 2013a; Morse, 1991; Teddlie and Tashakkori, 2009; Wittenberg, 2000).

Stewart et al. (2018) used an explanatory mixed methods research design to explore behavioral determinants related to error reporting among health care professionals. In the first phase behavioral determinants were identified through a cross-sectional survey. The authors reported that medication error reporting was associated with issues related to emotions and belief of consequences. Although, all health care professionals included in the sample had these issues, however, these were more common among younger health care professionals. In the second phase of the study, focus group interviews were conducted to develop an in-depth understanding of the survey findings. The data from the two components were triangulated at the completion of study to get a broader understanding of medication error reporting.

The Convergent Parallel Design

In convergent parallel design, the quantitative and qualitative components are undertaken at the same time. Each component is carried out independently but at the same time (i.e., each dataset is collected, analyzed and then findings are integrated during the interpretation phase). The study design allows to triangulate findings from the two components in order to understand the research question. For this reason, the study design is also referred to as "current triangulation," "simultaneous triangulation," and "parallel study design" (Hadi et al., 2013a; Morse, 1991; Teddlie and Tashakkori, 2009; Wittenberg, 2000).

El-Jardali et al. (2017) used a convergent parallel mixed methods research design to investigate the attitudes of community pharmacists and their practices in relation to the implementation of the generic drug substitution policy in Lebanon. The two components in the study were given equal priority. The quantitative component (self-administered questionnaires) was followed by the qualitative component (semistructured interviews). The aim of both components was to document experiences while implementing this new policy. In the quantitative phase, respondent's attitudes toward generic substitution and outcomes of the new generic drug substitution policy were measured. The semistructured interviews supplemented the quantitative findings by

expanding on the participants' experiences by exploring perceived barriers and facilitators. The data collection was carried out separately, but the findings were interpreted and reported together.

The Embedded Design

In the embedded design, one component act as a principal method and the other component is used as a "supportive method." Depending on the study objectives, both qualitative and quantitative components can act as the principal method. The data can either be collected concurrently or sequentially. The research design is suited when the researcher intends to use different methodologies for different research questions within the same study (Hadi et al., 2013a; Morse, 1991; Teddlie and Tashakkori, 2009; Wittenberg, 2000).

Hadi et al. (2013b, 2016a,b) conducted a mixed methods study to evaluate nurse pharmacist managed pain clinic. The quantitative component evaluated the impact of clinic on patient reported outcomes (e.g., pain intensity, physical functioning, and quality of life) and qualitative component explored patients' experiences of the clinic. This research design allowed the authors to answer different research question within a single study by using different methods. Quantitative method was given priority in answering the research question and the qualitative component (semistructured interviews) were used as supportive method which generated data associated with the quality and effectiveness of the service and interaction with the nurse and pharmacist.

Literature Review: Mixed Methods Studies in Pharmacy Practice

To develop a broader picture of how mixed methods research designs have been used in recent pharmacy practice literature, a scoping literature review was undertaken. We searched PubMed for studies describing or evaluating the roles of pharmacist and pharmacy interventions using mixed methods design in the past five years (1 June 2013–31 May 2018). During our search we used the keywords: "Pharmacy practice," "pharmacy," "pharmacist," "mixed methods," "pharmacy interventions," "public health pharmacy," "health system pharmacy," "health pharmacist," "medicine use," and "Health care." The search was restricted to only include full-text research articles only published in English language. Fifty-three articles were identified for full-text review. The final sample included 35 relevant articles after duplicates were removed (date of search; 8 August 2018). The included studies were conducted in UK (15)), USA (3), Qatar (2), Uganda (1), Guatemala (1), Ghana (1), Iraq (1), Australia (2), Korea (1), India (2), Lebanon (1), Thailand (1), Canada (1), Brazil (1), Netherlands (1), and Switzerland (1). This highlights that mixed methods approach has gained popularity among pharmacy practice researchers across the world. The studies were conducted in community pharmacies, primary care settings, hospitals and clinics. Mixed methods studies investigated pharmacy services, physicians' attitudes and perception, medicine use, and education and knowledge of patients.

In the literature review, all the studies were labeled as mixed methods studies, however only one-fourth of the studies described and justified the application of the mixed methods design.

There were few examples of multimethods research inappropriately labeled as mixed methods. As mixed methods has evolved over time, we believe that the mixing of quantitative and qualitative methods should only be labeled as mixed methods research. Labeling multiple methods of collecting qualitative or quantitative data only as mixed methods research design is inappropriate and should be discouraged.

The quantitative component in included studies mostly consisted of surveys. There were more variations in the use of the qualitative component which included interviews, focus groups, observations, and document analysis. Only four of the included studies described how the quality of the collected data was assessed. The description of the integration between quantitative and qualitative components was found to be very shallow in most studies. Scarce details and unclear reporting of a study does not only make it hard for the reader to understand the intend of the study but also makes it low quality research.

Approaches of Integration of Findings in Mixed Methods Research

As previously mentioned, mixed methods research does not only involve mere collection quantitative and qualitative data. Without meaningful integration, the true purpose of undertaking mixed methods study would not be fulfilled. The integration of data starts as early as at the planning stage of the research (e.g., study design and methodological approach). In the early days of mixed methods research, Jick and colleagues acknowledged the method's ability to draw on the strengths of individual qualitative and quantitative methods used in the study (Jick, 1979).

Hammersley (1996) proposed the following three methods for integration of qualitative and quantitative data: triangulation, facilitation, and complementarity. There must be a clear reflection from the beginning of the study on how one approach will be supporting the other (Venkatesh et al., 2013). The literature describes triangulation as a method to study a research question using multiple methods (Fetters et al., 2013; O'Cathain et al., 2010). The literature classifies triangulation into four categories: methodological triangulation, theory triangulation, data triangulation, and investigator triangulation (Denzin, 2009). There are limitations with regard to a step-by-step guidance on how to perform triangulation of results in health care studies (Jick, 1979; Östlund et al., 2011). Farmer and colleagues have developed a triangulation protocol which can help increase transparency in the conducted research regardless of the used typology (Farmer et al., 2006). In terms of triangulation the researcher must consider three aspects of

the research methods: First, explore the research process itself (e.g., did the applied methods answer the posed research question). Second, look for incongruity in the used method; are the findings the same or do they contradict each other? Finally, look at how the methods complement each other; which results are gained from each method (Farmer et al., 2006)? O'Cathain et al. emphasizes the importance of making an informed decision about the weighing of the used dataset (O'Cathain et al., 2010). Currently, these decisions are likely to be subjectively assessed. If there is no consensus approach on how to order triangulated datasets, these decisions are left to the researcher. Farmer et al. (2006) described that these decisions should be based on the contribution each method brings toward answering the research question (Farmer et al., 2006). One method can be used to validate the findings from the other method. Quantitative data can, for example, be used to explain findings from qualitative data (Fetters et al., 2013).

Quality in Mixed Methods Research

It is commonly agreed that health services research should be reported transparently (Creswell and Tashakkori, 2007; O'Cathain et al., 2008b; Wisdom et al., 2012). The literature reports on various methods for evaluating the quality of quantitative and qualitative methods on their own. During our review of pharmacy practice literature, we found that there is a lack of definition of the mixed methods research. There are currently several definitions of "mixed methods" (Creswell et al., 2004; Johnson et al., 2007) and it is important to justify and describe the adapted definitions, so the reader can make an informed judgment of the quality of the study.

There is a lack of consensus in the description of quality of a mixed method study. This is also being observed in other areas of health serviced research (Hadi and Closs, 2016b; O'Cathain et al., 2008b). One reason for this trend could be that there is a lack of consensus guidelines on how to evaluate mixed methods research designs. Currently there are no rules on how to evaluate mixed methods research. However, there are several mixed methods guidelines and frameworks proposed in the literature (Hadi et al., 2014a; Leech and Onwuegbuzie, 2010; NIH, 2018). The mentioned guidelines and frameworks have a common goal to improve reporting quality. The key elements in the guidelines are to: justify the used methods approach, describe the mixed methods design (priority, purpose, sequencing, and stage of integration), describe the used methods (sample size, data collection, and analysis), describe how, when, and where integration has occurred and identify limitations related to the applied research design. Adhering to these guidelines and frameworks as well as to individual standards for the quantitative and qualitative components is recommended. In terms of integration of data and how will disagreements between two components be dealt with. It is important to emphasize that it should be described how these disagreements will be resolved to allow the reader to asses quality of the study (Curry et al., 2013; O'Cathain et al., 2010).

To summaries, different disciplines uses different typologies within mixed methods research design (Tashakkori and Teddlie, 2010). There are no rigorous rules on how to validate mixed methods research designs, and hence it is up to the individual researcher to choose an appropriate method to evaluate their study design.

What are the Challenges in Using Mixed Methods Research

Mixed methods is as challenging as any other method, expertise in multiple areas is required due to the use of quantitative and qualitative methods in the same study.

Conducting mixed methods research is time consuming and expensive, hence the researcher must consider if they have the necessary time and resources to carry out mixed methods research (Ivankova et al., 2006). The researcher also needs to consider, whether one has the necessary skills to conduct mixed methods research. In the past, the tendency has been toward studies being carried out by researchers who either possess quantitative or qualitative skills. This trend has changed toward research projects being carried out in research teams utilizing the individual researcher's strengths across disciplines (Hadi et al., 2014a,b; O'Cathain et al., 2008a). A lead investigator with research experience with quantitative and qualitative methodologies can act as in an important bridge in the mixed methods research team. There is currently no standard systematic way to conduct a mixed methods study. A well-considered rationale for the approach may help ease this process (Hadi et al., 2014a). Bryman suggests that it is not easy to make sense of one's findings the mixed methods research designs may need to be reconsidered (Bryman, 2007). Lastly, there is the question of reaching a wider audience. Policymakers and practitioners need multiple forms of evidence to document and inform a research problem. Pioneers in the application of mixed methods in pharmacy practice have reported that it has been challenging to report on mixed methods without compromising on the transparency of the design due to the journals word limit of original articles (Hadi et al., 2014a,b; Wisdom et al., 2012).

Application of Mixed Methods Methodology in a Program of Inquiry

Until now, the focus of this chapter has been on the use and application of mixed methods research within a single study (fixed mixed methods designs), however, mixed methods approaches (emergent mixed methods designs) can be used within a program of enquiry. Emergent mixed methods arise to resolve quires and address issues that develop during the process of conducting research (Creswell, 2018). To illustrate this we will use an example of health services evaluation of a chronic pain service. As part of these

services the pharmacist conducted medication reviews and offered medication related advice to ensure safe and effective use of medicines. The nurse educated patients about pain, clarified misconceptions, managed treatment expectations, and promoted self-management of chronic pain. The original focus of the research at the beginning of protocol development was to evaluate a community-based nurse-pharmacist managed pain clinic using a mixed methods design (Hadi et al., 2013b, 2016a). However, during extensive literature review and the course of the study, following additional questions arose:

1. Is pharmacist-led medication review effective in the management of chronic pain in adult patients?
2. What is the magnitude and extent of the impact of chronic pain on patients' quality of life in relation to other long-term conditions?
3. What are the barriers to effective pain management encountered by patients with chronic pain in primary care?

Subsequently, a pragmatic approach was adopted to answer these questions. For the first question, a systematic review and metaanalysis was conducted to evaluate the effectiveness of pharmacist-led medication review in chronic pain management (Hadi et al., 2013b, 2014b). The metaanalysis found that patients in pharmacist-led medication review group had significant reduction in pain intensity, improvement in physical functioning and patient satisfaction compared to the control group. For the second and third questions, the qualitative interview guide was expanded and additional questions were asked to explore the impact of chronic pain on patients' lives and barriers to effective management of chronic pain in primary care, in addition to originally proposed questions aiming to explore patients' experiences of nurse-pharmacist managed pain clinic. In order to truly understand the impact of chronic pain of patients' lives, a mixed methods approach was adopted (convergent parallel design) (Hadi et al., 2018). Published data on quality of life from two different datasets, the Third Oxford and Lifestyles Survey and Welsh Health Survey, were also extracted and a secondary analysis was undertaken to allow comparison of QoL of chronic pain patients with that of the general population and patients with long-term conditions. The authors found that patients with chronic pain had significantly poorer quality of life compared to patients with other long-term conditions (Hadi et al., 2018). Qualitative themes emerged from data analysis reflected the diversity in the nature of impact of chronic pain on patients' lives. For the third question, qualitative-only approach was used and qualitative data were analyzed with an aim to develop themes based on the barriers encountered by patients with chronic pain in primary care (Hadi et al., 2017). This example demonstrates the use of emergent mixed methods design in pharmaceutical health services research. It should be noted here that the selection of choosing an appropriate method was guided by research question. Quantitative-only and qualitative-only and mixed methods approaches were used as appropriate during the program of enquiry. The emergent mixed methods design gave authors the flexibility to choose the best method to answer the research question.

Conclusion

A mixed methods approach is suitable when the use of two methods is likely to enhance our understanding enhance the knowledge in a specific research question as compared to using a monomethod approach. It is essential to choose an appropriate typology for the mixed methods research approach and this should be guided by the individual research question. Rigor in mixed methods research should be ensured by adhering to quality principles of the quantitative and qualitative components as well as mixed methods research guidelines and frameworks. Both humanist and financial resources should be carefully considered before embarking on a mixed methods study. New mixed methods researchers should choose fixed mixed methods approach and should consider collaborating with an experienced researcher early during the designing phase of the study.

References

Bissell, P., Traulsen, J.M., 2005. Sociology and Pharmacy Practice. Pharmaceutical Press, London.
Bryman, A., 2007. Barriers to integrating quantitative and qualitative research. J. Mixed Methods Res. 1 (1), 8–22.
Creswell, J.W., Plano Clark, V.L., 2018. Designing and Conducting Mixed Methods Research, 3rd ed. (International student) SAGE, Los Angeles.
Creswell, J.W., Tashakkori, A., 2007. Editorial: Developing publishable mixed methods manuscripts. J. Mixed Methods Res. 1 (2), 107–111.
Creswell, J.W., Fetters, M.D., Ivankova, N.V., 2004. Designing a mixed methods study in primary care. Ann. Fam. Med. 2 (1), 7–12.
Creswell, J.W., Klassen, A.C., Plano Clark, V.L., Smith, K.C., 2011. Best Practices for Mixed Methods Research in the Health Sciences. Retrieved from: https://obssr.od.nih.gov/wp-content/uploads/2016/02/Best_Practices_for_Mixed_Methods_Research.pdf.
Curry, L.A., Krumholz, H.M., O'Cathain, A., Plano Clark, V.L., Cherlin, E., Bradley, E.H., 2013. Mixed methods in biomedical and health services research. Circ. Cardiovasc. Qual. Outcomes 6 (1), 119–123.
Denzin, N.K., 2009. The Research Act: A Theoretical Introduction to Sociological Methods. Aldine Transaction, London; Somerset, NJ.
Dhanani, T.C., Mantovani, E.H., Turner, J.R., 2017. Clinical pharmacists' opportunities to reduce inappropriate prescription of QT-prolonging medications: calls to action. Int. J. Pharm. Pract. 25 (2), 176–179.
Driscoll, D.L., Appiah-Yeboah, A., Salib, P., Rupert, D.J., 2007. Merging qualitative and quantitative data in mixed methods research: how to and why not. Ecol. Environ. Anthropol. 3 (1), 19–27.
El-Jardali, F., Fadlallah, R., Morsi, R.Z., Hemadi, N., Al-Gibbawi, M., Haj, M., Khalil, S., Saklawi, Y., Jamal, D., Akl, E.A., 2017. Pharmacists' views and reported practices in relation to a new generic drug substitution policy in Lebanon: a mixed methods study. Implement. Sci. 12 (1), 23.
Farmer, T., Robinson, K., Elliott, S.J., Eyles, J., 2006. Developing and implementing a triangulation protocol for qualitative health research. Qual. Health Res. 16 (3), 377–394.
Fetters, M.D., Curry, L.A., Creswell, J.W., 2013. Achieving integration in mixed methods designs—principles and practices. Health Serv. Res. 48 (6pt2), 2134–2156.

Fisher, J., Kinnear, M., Reid, F., Souter, C., Stewart, D., 2018. What supports hospital pharmacist prescribing in Scotland?—A mixed methods, exploratory sequential study. Res. Social Adm. Pharm. 14 (5), 488–497.
Greene, J.C., Caracelli, V.J., Graham, W.F., 1989. Toward a conceptual framework for mixed-method evaluation designs. Educ. Eval. Policy Anal. 11 (3), 255–274.
Hadi, M.A., Alldred, D.P., Closs, S.J., Briggs, M., 2013a. Mixed-methods research in pharmacy practice: basics and beyond (part 1). Int. J. Pharm. Pract. 21 (5), 341–345.
Hadi, M.A., Alldred, D.P., Closs, S.J., Marczewski, K., Briggs, M., 2013b. A mixed-methods evaluation of a nurse-pharmacist-managed pain clinic: design, rationale and limitations. Can. Pharm. J. 146 (4), 197–201.
Hadi, M.A., Alldred, D.P., Closs, S.J., Briggs, M., 2014a. Mixed-methods research in pharmacy practice: recommendations for quality reporting. Part 2. Int. J. Pharm. Pract. 22 (1), 96–100.
Hadi, M.A., Alldred, D.P., Briggs, M., Munyombwe, T., Closs, S.J., 2014b. Effectiveness of pharmacist-led medication review in chronic pain management: systematic review and meta-analysis. Clin. J. Pain 30 (11.), 1006–1014.
Hadi, M.A., Alldred, D.P., Briggs, M., Marczewski, K., Closs, S.J., 2016a. Effectiveness of a community based nurse-pharmacist managed pain clinic: a mixed-methods study. Int. J. Nurs. Stud. 53, 219–227.
Hadi, M.A., Closs, S.J., 2016b. Applications of mixed-methods methodology in clinical pharmacy research. Int. J. Clin. Pharm. 38 (3), 635–640.
Hadi, M.A., Alldred, D.P., Briggs, M., Marczewski, K., Closs, S.J., 2017. Treated as a number, not treated as a person': a qualitative exploration of the perceived barriers to effective pain management of patients with chronic pain. BMJ Open 7, e016454.
Hadi, M.A., McHugh, G.A., José, S., 2018. Impact of chronic pain on patients' quality of life: a comparative mixed-methods study. J. Patient Exp., doi:10.1177/2374373518786013.
Hammersley, M., 1996. The relationship between qualitative and quantitative research: paradigm loyalty versus methodological eclecticism. In: Richardson, J.T.E. (Ed.), Handbook of Qualitative Research Methods for Psychology and the Social Sciences. British Psychological Society, Leicester.
Ivankova, N.V., Creswell, J.W., Stick, S.L., 2006. Using mixed-methods sequential explanatory design: from theory to practice. Field Methods 18 (1), 3–20.
Jick, T.D., 1979. Mixing qualitative and quantitative methods: triangulation in action. Adm. Sci. Q. 24 (4), 602–611.
Johnson, R.B., Onwuegbuzie, A.J., Turner, L.A., 2007. Toward a definition of mixed methods research. J. Mixed Methods Res. 1 (2), 112–133.
King, G., Keohane, R.O., Verba, S., 1994. Designing Social Inquiry: Scientific Inference in Qualitative Research. Princeton University Press, Princeton, NJ.
Leech, N.L., Onwuegbuzie, A.J., 2009. A typology of mixed methods research designs. Qual. Quant. 43 (2), 265–275.
Leech, N.L., Onwuegbuzie, A.J., 2010. Guidelines for conducting and reporting mixed research in the field of counseling and beyond. J. Couns. Dev. 88 (1), 61–69.
Liamputtong, P., 2013. Research methods in health: foundations to evidence-based practice, Second ed. Oxford University Press, South Melbourne, Victoria.
Morse, J.M., 1991. Approaches to qualitative-quantitative methodological triangulation. Nurs. Res. 40 (2), 120–123.
NIH, 2018. Best Practices for Mixed Methods Research in the Health Sciences. Retrieved from NIH Office of Behavioral and Social Sciences: https://www.obssr.od.nih.gov/wp-content/uploads/2018/01/Best-Practices-for-Mixed-Methods-Research-in-the-Health-Sciences-2018-01-25.pdf.
O'Cathain, A., Murphy, E., Nicholl, J., 2010. Three techniques for integrating data in mixed methods studies. BMJ 341 (7783), 1147–1150.
O'Cathain, A., Murphy, E., Nicholl, J., 2008a. Multidisciplinary, interdisciplinary, or dysfunctional? Team working in mixed-methods research. Qual. Health Res. 18 (11), 1574–1585.
O'Cathain, A., Murphy, E., Nicholl, J., 2008b. The quality of mixed methods studies in health services research. J. Health Serv. Res. Policy 13 (2), 92–98.
Östlund, U., Kidd, L., Wengström, Y., Rowa-Dewar, N., 2011. Combining qualitative and quantitative research within mixed method research designs: a methodological review. Int. J. Nurs. Stud. 48 (3), 369.
Pelto, P.J., 2015. What is so new about mixed methods? Qual. Health Res. 25 (6), 734–745.
Stewart, D., Thomas, B., MacLure, K., Wilbur, K., Wilby, K., Pallivalapila, A., Dijkstra, A., Ryan, C., El Kassem, W., Awaisu, A., McLay, J.S., Singh, R., Al Hail, M., 2018. Exploring facilitators and barriers to medication error reporting among healthcare professionals in Qatar using the theoretical domains framework: a mixed-methods approach. PLOS One 13 (10), e0204987.
Tashakkori, A., Teddlie, C., 2010. Sage Handbook of Mixed Methods in Social & Behavioral Research, 2nd ed. SAGE, London; Los Angeles, CA.
Tashakorri, A., Creswell, J.W., 2007. The new era of mixed methods. J. Mixed Methods Res. 1 (1), 3.
Teddlie, C., Tashakkori, A., 2009. Foundations of Mixed Methods Research: Integrating Quantitative and Qualitative Approaches in the Social and Behavioral Sciences. SAGE, London; Los Angeles, CA.
Venkatesh, V., Brown, S.A., Bala, H., 2013. Bridging the qualitative-quantitative divide: guidelines for conducting mixed methods research in information systems. MIS Q. 37 (1), 21.
Wisdom, J.P., Cavaleri, M.A., Onwuegbuzie, A.J., Green, C.A., 2012. Methodological reporting in qualitative, quantitative, and mixed methods health services research articles. Health Serv. Res. 47 (2), 721–745.
Wittenberg, R., 2000. *Abbas Tashakkori* und *Charles Teddlie*: Mixed methodology. Combining qualitative and quantitative approaches. Applied social research method series, volume 46: Thousand Oaks/London/New Delhi: Sage 1998. XI und 183 Seiten. ISBN 0-7619-0071-3 (pbk). Preis: $ 21,95. KZfSS Kölner Zeitschrift für Soziologie und Sozialpsychologie 52 (1), 180–183.

Publication Bias

Rabia Hussain*, Mohamed Azmi Hassali*, Mahendra Patel†, Zaheer-Ud-Din Babar†, *Universiti Sains Malaysia, Penang, Malaysia; †University of Huddersfield, Huddersfield, United Kingdom

© 2019 Elsevier Inc. All rights reserved.

Background

The "dictionary of epidemiology" defines publication bias as "an editorial predilection for publishing particular findings, e.g., positive results, which leads to the failure of authors to submit negative findings for publication (Last et al., 2001)." The term "Publication Bias" was first defined by Begg in 1985 as studies in which the observed efficacy of the treatment is much more likely to be reported than those in which the observed efficacy is average or poor (Begg, 1985). Publication bias is the biased projection of researchers, reviewers, and editors to submit and publish studies based on usually positive findings (Dickersin, 1990). Publication

bias also occurs when the chance of getting publishing a paper depends on the outcome of the findings (Brown et al., 2017). It means that the statistically insignificant results, studies of small magnitude or findings contradicting prior theories or findings from other studies will be less likely to be published (Harrison et al., 2017; Dickersin and Min, 1993).

Publication bias can also be explained as results having statistical significance, have a likelihood to be published faster, multiple times, publishing in high impact journals and to be cited more often. In this regard, the evidence based on "non-significant results" in systematic reviews cannot be ignored and hence it is as much important as the evidence contributed by significant results (Rodrigues, 2013).

Role of Publication Bias in Evidence-Based Clinical Decision Making

Publication bias has not only influenced the education and psychology related research, but it has also greatly affected the medical literature too. The main consequence of this bias would be exaggerated claims of treatment effects or presence of risk-factors related to published work. These could be misleading in many ways including management of patients or health related policy making (Easterbrook et al., 1991). Meta-analysis and systematic review-based syntheses of published research is in high demand to support the evidence-based decision making policy. But, research with unfavorable results is less likely to be published and hence contributes to bias in the selection of the studies for meta-analyses or systematic reviews (Dickersin, 1990; Dickersin and Min, 1993; Easterbrook et al., 1991). As unpublished studies and studies are marked as grey literature and they are not easily accessible (Mueller et al., 2013). So, the effect estimates on the basis of such publications might be overestimating the effect size than what actually exists (Song et al., 2000; Easterbrook et al., 1991). It also compromises the quality of the systematic reviews and meta-analysis, which are only based on published literature (Easterbrook et al., 1991). Systematic reviews and meta-analyses are considered as the most powerful analytical tool, thus claimed to have an impact on the current and future research trends (Easterbrook et al., 1991; Crawford et al., 2010).

Easterbrook et al. performed a literature search for 1982–89 and found that two-thirds of meta-analyses are based on the studies, which were more biased prone especially more toward publication bias. The study further suggested that non-randomized trials with small sample size should be used cautiously, specifically when to be included in a systematic review or meta-analysis or otherwise (Easterbrook et al., 1991). This can be further explained as the field of medicine relies on multiple studies based on small sample size (Ioannidis, 2005). So, if the effects of a medicine are demonstrated as combination of both positive and negative outcomes, so, only the studies with positive results will be published. In this context, the researcher and practitioner will think that the medicine or a treatment is beneficial, while this is not the case in actual sense (Paulson et al., 2011). Paulson et al. evaluated abstracts submitted at the 2006 Center for International Blood and Marrow Transplant Research (CIBMTR)/American Society for Blood and Marrow Transplantation (ASBMT) "tandem" meeting. They found that only 43% of the abstracts were later published as complete papers. Another interesting finding came out from the study that the results with the positive findings were published in high impact journals, while unstated or negative studies were published in low impact factor journals (Paulson et al., 2011).

Similarly clinical trials-based medical decisions are based on the public reporting of such clinical trials (Craig et al., 2001; Hagdrup et al., 1998).

Due to the failure of an intervention, the results of a clinical trial remain unpublished especially if the intervention is found to be harmful, so chances are that considering these studies may have greater harm to the patients (Parekh-Bhurke et al., 2011). Therefore, selective publication of clinical trials and their associated outcome can mislead due to unrealistic estimation of drug effect (Kyzas et al., 2005; Whittington et al., 2004). In this regard, Turner et al. conducted a systematic review of literature on 12 antidepressants agents and compared them with the reviews from Food and Drug Administration involving 12564 patients in trials (Turner et al., 2008). They compared the trials' outcomes and effect size of the treatment from published data and the data obtained from the FDA. The published literature showed that 94% of the conducted trials were positive comparable to the 51% derived from the FDA (Turner et al., 2008). Thus, a non-representative selection of the data in a systematic review may decrease the validity and usefulness of practice and policy based on such studies, hence it is important for clinicians, health policy makers, and researchers to understand the concept of publication bias before considering such evidence (Parekh-Bhurke et al., 2011).

History of Publication Bias

The decision of what should be or what should not be published is solely a personal decision and to some extent influenced by the trends, however, science does not dictate any formal guidelines on what should be included in a publication (Dickersin, 1990). Robert Boyle was the first scientist to bring the necessary details of the experiments into the publication. This initiative of sharing research findings with peers led to a new type of reporting that described the errors and difficulties, one can encounter doing the experiment. Thus, between 1600 and 1800s, the scientific reporting not only presented the "positive" but also the "negative" results. In 1661, Boyle being concerned about the publication practices in the field of science expressed his concerns over this issue and said that the scientists are being compelled not to publish the experiments but to bring out something "big" (Dickersin, 1990).

Awareness of publication bias began in 1956 when the editor of the *Journal of Abnormal Social Psychology* indicated that negative studies were less likely to be published in his journal (Thornton and Lee, 2000). In 1959, it was found that very few negative results were reported in four psychological journals, a finding strongly suggesting publication bias (Sterling, 1959). Since 1979, the number

of references relevant to publication bias has increased (Boisen, 1979). In 1979 Rosenthal used another term "file-drawer problem" to describe the lack of publication of completed studies (Song et al., 2013).

Types

Publication bias does not only include the urge to publish positive results, but it also includes various other reasons which can be listed as different types of bias influencing the publication.

Here are different types of publication bias:

Multiple Publication Bias

Depending upon the nature and outcome of the study, studies that get chance to publish in more than one place might get more weightage for readership and more likely to be included in a meta-analysis (Egger and Smith, 1998; Higgins and Green, 2011).

Time Lag Bias

Time lag bias indicates that some studies take long time to get published especially those with the undesired or no positive outcome. Contrary to this, studies with positive results or attention drawing findings are published much faster (Hopewell et al., 2007). For example, one study assessing efficacy trials of HIV treatments concluded that the time from study enrollment to publication was significantly longer for negative trials than that for positive trials (Ioannidis, 1998).

Location Bias

It is related to the publication of research findings in journals, which are indexed in different databases and then perhaps comparing them with the outcomes of the study (Pittler et al., 2000; Vickers et al., 1998).

Citation Bias

Citation bias is based on the selection of the study that a researcher wants to cite from other studies or sources (Christensen-Szalanski and Beach, 1984).

Language Bias

The choice of publication in a particular language, ignoring those studies which are not in your native language (Egger et al., 1997).

Outcome Reporting Bias

It is based upon the publication of selective research findings depicting positive outcome of the study (Chan et al., 2004).

Confirmatory Bias

When one's beliefs and experiences are supported by some studies and they emphasize certain studies to build a support and ignore others though relevant, this type of bias is known as confirmatory bias and it is most evident in clinical research (Mahoney, 1977).

Funding Bias

Sometimes the funders may withhold the results with negative outcomes and do not disclose them to the public. It has been observed that independent studies have less significant or favorable results than the funded studies (Lexchin, 2012).

Factors Contributing Toward Publication Bias

Several factors contributing toward publication bias are described as below:

Design and Implementation of Study

The role of design or execution of single studies is a factor contributing toward publication bias as sample size and method of data reporting greatly influences the phenomenon (Thornton and Lee, 2000). Besides, the belief and expectation of the investigator also play an important role in publication bias (Angell, 1989). A small sample size lacks the power thus fails to prove the statistical

importance of an effect under study and hence fails to get published (Thornton and Lee, 2000). Contrary to this, large studies have a good chance to answer many questions as the author has to dig in the information deeply to obtain positive results even if the data is showing negative outcomes. This means that the chances to get significant results will increase with the detailed analysis of further subgroups (Angell, 1989; Thornton and Lee, 2000). Publication bias also arises if the data recording is inadequate. Although the difference between data produced and published is rare, but some researchers may tamper the data and this data tempering remains unnoticed during peer-review and even during the replication (Engler et al., 1987; Felson, 1992)

Publication Bias due to Unpublished Studies

Sometimes findings from a study do not seem to impart much for the promotion of a certain theory or a policy, for which the study was meant for. Certain results seem less interesting to be published and less appraised by the editors and reviewers. Due to these reasons, researchers find it inconvenient to publish certain research findings (Brown et al., 2017).

Publication bias may also occur when researcher has a lack of interest in publication or want to submit the research to a specific journal for the publication. For instance, if a study is based on a large sample size, researchers are keen to publish their research, regardless of the outcome of the study (Thornton and Lee, 2000).

Publication Bias due to Rejection of Journals

The *British Medical Journal* states that "negative results have never made riveting reading" (Dickersin, 1990). Some readers and editors strongly discourage negative outcome-based studies as thinking that only positive outcome studies improve the clinical practice. While negative studies are not published, however in some cases it has been found that even the studies with negative outcomes are better planned and conducted than positive outcome studies (Dickersin, 1990).

A study explored process of peer review by assigning manuscripts with positive, negative, no and mixed results to 75 journal reviewers. Reviewers gave minor revisions on studies with positive outcomes and gave major revisions and rejections to the negative studies (Mahoney, 1977).

Sponsorship

Sponsorship is another important factor which cannot be ignored while evaluating factors of publication bias. Sometimes funders decide whether a study would be published or otherwise, considering that, if a pharmaceutical product shows null effects, the manufacturers usually discourage the publication of the results (Thornton and Lee, 2000; Lexchin, 2012). A study revealed that up to 89% of studies funded by the pharmaceutical industry ended up in favoring a new therapy, while only 61% favored the therapy, if the studies are funded by other sources (Begg and Berlin, 1988).

Methods of Detecting and Correcting for Publication Bias

To address problem of publication bias, is as crucial as to promote good scientific knowledge (Brown et al., 2017). Hence, several methods have been developed to identify and minimize such bias (Song et al., 2010).

A Health Technology Assessment (HTA) report published in 2000, highlighted the issues in publication bias. The report included 193 systematic reviews published in 1996 (Song et al., 2000). It was found in the report that not only the literature search was inadequate in some reviews, but also the publication bias was not taken into account while conducting those reviews (Landis and Koch, 1977). Another shortcoming of this review was the lack of representation of the sample studies (Landis and Koch, 1977). Besides, it was found in HTA report that the issue of publication bias was largely being overlooked, as a small number of reviews actually used any methods to identify, avoid, or counter publication bias (Song et al., 2000).

To evaluate whether the practices have changed an assessment of systematic reviews published in 2006 was compared to the systematic review done in 1996. It has been observed that there has been a remarkable increase in the consideration of measures to identify and decrease publication bias in a decade (Parekh-Bhurke et al., 2011).

To detect publication bias in a systematic review or a meta-analysis, several measures have been suggested (Song et al., 2010) as below:

Unpublished Data and Publication Bias

If relevant studies are missed or are available as gray literature or in languages other than English, risk of bias is present. Hence, to overcome the issue an in-depth literature search should be done while conducting a systematic review and multiple electronic databases should be searched, as many journals are not listed in certain databases. These strategies help to avoid chances of bias (McDonald et al., 1999). An in-depth literature search related to non-bibliographical sources will also help to overcome publication bias. This include searching for conference abstracts, scientific reports from companies, reports from government and regulatory bodies, study registries, scientific data from personal research group, which are otherwise not available in standard databases (Lefebvre et al., 2009).

Graphical and Statistical Methods

To assess the publication bias different methods are used including both graphical and statistical methods. Graphical assessment includes funnel plots which were first used in the educational research (Richard et al., 1984). To detect publication bias in systematic reviews, most common methods employed were, Begg's test, Egger's test, and funnel plots. Similarly, in 1996, the Fail-N safe method was used in some reviews, however it is being much less likely to be used in recent reviews (7% vs. 1%, respectively) (Song et al., 2010).

Funnel Plot

Funnel plot is the simplest and easiest method to detect publication bias. A funnel graph is a simple graph between sample size of the component studies and summary outcome measures or effect size, assuming that all studies will assume the similar effect (Richard et al., 1984). It is plotted by taking effect size on *X* axis and variance or sample size on *Y* axis (Borenstein et al., 2009).

To do so, the point estimate from studies under consideration is plotted against the standard error or the sample size. The studies having highest precise values usually appear high on the *y* axis in a cluster fashion (Borenstein et al., 2009). Plot of studies having little or no publication bias appears more like an inverted funnel. Small studies appear arranged in a symmetrical manner on both sides of the larger studies which are located at the apex of the funnel plot (Torgerson, 2006).

However, in case of publication bias, usually one side (mostly the left side) of the funnel is missing indicating negative or null studies (Borenstein et al., 2009). On the other side, it can also be recognized as deterioration of the central part of funnel, suggesting that publications with statistically significant results are published while those without significant results are not. Therefore, it is necessary to consider the funnel plots before and during finalizing the systematic review (Torgerson, 2006).

Funnel plot asymmetry may not always reflect accurate publication bias, and there may be other factors contributing toward asymmetry, therefore, if the results from funnel plots are interpreted inappropriately, it could lead to misleading conclusions (Lau et al., 2006; Ioannidis and Trikalinos, 2007; Sterne et al., 2008). In some cases, due to small and methodologically weak studies, an irregular funnel plot appears, producing biased estimates of effect and this appear as positive. In reality, however this should appear as null or negative result otherwise (Torgerson, 2006).

Sterne et al. has listed four reasons that may possibly contribute toward an asymmetry in funnel plots. These include bias in publication, poor study design, irregularity in data, and heterogeneity (Sterne et al., 2000).

Fail-Safe N Test

To check whether a systematic review has a publication bias, one can use Fail-safe N test to detect publication bias (Rosenthal, 1979).

This test determines the number of missing studies averaging a *z* value of zero to make the combined effect size of zero (Rosenthal, 1979). This would reduce the summary effect to non-significance or would show the overall probability of Type 1 error to a stated level of significance, such as $P = 0.05$ (Rosenthal, 1978, 1979). Rosenthal (1979) suggested that to make *P*-value insignificant, it is important to know that how many missing studies would be needed to retrieve and to be added in the analysis, considering the mean effect of the missing studies as zero. In case, if only a few studies such as five or ten are required, to cancel the effect, then the true effect will be zero, while, in case if a large number of studies are needed to cancel the effect, such as 20,000 studies, hence it will be safe to assume that there is no publication bias in this case (Rosenthal, 1979). Rosenthal (1979) also identified the presumed location of missing studies as File drawer and Harris Cooper (Begg and Mazumdar, 1994) suggested that to nullify the effect, the number of missing studies to be incorporated to an analysis should be called the Fail-safe N (Begg and Mazumdar, 1994).

Fail-safe N test has certain limitations, that it does not emphasize on the substantive significance (real world relevance), rather its more oriented toward the statistical significance (Miller, 2008; Borenstein et al., 2009). For instance, it focuses on questions such as how many hidden studies should be added to make the effect statistically insignificant instead of looking into the answer that how many hidden studies are required to reduce the effect where it no more remains of substantive importance (Borenstein et al., 2009). This test relies on the *P*-values based test of significance, but with recent development in statistics, first the summary effect is calculated and then the *P*-value for this effect is computed. As the *P*-values are computed by using different approaches, testing different null hypotheses means that *P*-vales are not the same. Hence, the approach is not recommended in cases where effect size is priority (Borenstein et al., 2009).

Orwin's Fail-Safe N

Orwin (1983) developed a variant to Rosenthal's method, as the later allowed to determine that how many missing studies could bring the overall effect to a specified level, rather to bring it to a zero value (Orwin, 1983). Thus allowing the researcher to select the value with smallest effect is important as one can calculate that how many studies will be needed to bring the summary effect below the specified point (Borenstein et al., 2009). This method also helps the researcher to label the mean effect in missing studies as non-zero value and allow to compute a model for a series of other distributions and missing studies (Begg and Mazumdar, 1994).

Duval and Tweedie's Trim and Fill

The Trim and Fill method is used to estimate the number of studies missing from a meta-analysis that may result from the suppression of the most extreme results on one side of the funnel plot. The method does not validate the outcome or the overall effect but it helps in the determination of particular form of publication bias (Duval and Tweedie, 2000b, 2000a).

Trim and Fill method re-computes the effect size by removing the extremely small studies from the positive side of the funnel plot, thus making the funnel plot, more like a symmetric as of the new effect size. This trimming yield adjusts effect size, reduces the variance effect, and produces a confidence interval of too narrow value. Hence, the algorithm adds back the studies to the analysis and produces a mirror image for each, making the variance correct but no impact on point estimate (Borenstein et al., 2009; Duval and Tweedie, 2000a, 2000b).

The advantage of the above-mentioned approach is that it helps in the estimation of unbiased effect size. Besides, the computer programs based on Trim and Fill method are able to create a funnel plot comprised of both the observed and the imputed studies (to replace the missing data) (Borenstein et al., 2009). Hence, one can easily observe that how the effect size shifts when studies are added to the plot (Borenstein et al., 2009).

Limitations of this method includes that Trim and Fill method largely depends on the assumptions that why studies are missing. Also, the algorithm for detecting an asymmetry can be influenced if one or two studies are not-uniform (Borenstein et al., 2009).

Comparison of Published and Unpublished Data

Another method to detect publication bias is to compare the results from both published and unpublished studies evaluating the same research question. If a single meta-analysis includes both published and unpublished studies, the difference in results can indicate the presence and extent of publication bias.

In an example, published results of selective serotonin reuptake inhibitors showed favorable risk benefit profile for childhood depression, however the unpublished data on citalopram, paroxetine, and sertraline clearly indicate the associated risk of these medicines and their impact on children and youngsters (Whittington et al., 2004). However, the true estimates of unpublished results are difficult to predict, as to obtain data from such unpublished studies is a big challenge for the researchers (Song et al., 2013).

Analyzing Larger Studies Only

Another strategy to deal with publication bias is limiting the analysis to only larger studies (Borenstein et al., 2009). If it is assumed that the publication bias is majorly associated with smaller studies, then considering only larger studies would overcome the problem in theory. A strategy is to illustrate all possible thresholds by drawing a cumulative meta-analysis. This is developed by running one study at a time, then perhaps adding a second study, third, and so on (Borenstein et al., 2009).

Similar to this is a cumulative forest plot. In the forest plot the first row shows the effect expressed by one study, the second rows show effect based on two studies, and so on.

A potentially useful strategy is to illustrate all possible thresholds by drawing a cumulative meta-analysis (Borenstein et al., 2009). In order to examine the effect of different threshold for study size, the studies are arranged in the sequence of largest to smallest or being most precise to least precise.

Then a cumulative meta-analysis is performed with the addition of each study. If the point estimate has no effect upon the addition of smaller studies and if it has stabilized with the addition of larger studies, it can be assumed that smaller studies are not contributing toward any bias. Contrary to this if point estimate upon the addition of smaller studies shows a shift then there is a definite need to find out the reason for this shift (Borenstein et al., 2009).

Technological Aids in the Detection of Publication Bias

A number of computer-based programs are available to help in the detection of publication bias in meta-analysis. These include Comprehensive Meta Analysis (CMA), RevMan Analyses, Stata, and MetaWin (Borenstein, 2005).

Comprehensive Meta Analysis (Version 2.0)

Comprehensive Meta Analysis (CMA) is considered as the unique program for carrying out meta-analysis. The software was developed with the collaboration of experts from medicine, social sciences, and epidemiology (Meta-analysis.com, 2006). The program has an ability to execute all tests for the detection of publication bias including funnel plot, forest plot, rank correlation test, Trim and Fill, Egger's test, and other related tests (Borenstein et al., 2005). CMA accepts data in around 100 formats, the most utilized of which are number of events occurring in a single group and sample size. It can also execute the data if data input is in the format of means and standard deviations, correlations, point estimates, and confidence intervals (Borenstein, 2005).

Review Manager (Version 4.2)

Review Manager is a special software provided to researchers by the Cochrane Collaboration, meant for the reviews to be included in Cochrane library (Cochrane, 2014). The statistical procedure of the software is based on a module called RevMan Analyses, previously known as MetaView (Borenstein, 2005). RevMan will only execute data in the format of point estimate and standard error. It also accepts data in the form of number of events and sample size in each group, means and standard deviation (Borenstein, 2005).

Stata (Version 8.2)

Stata is a general software based on statistical package, which is not routinely used for meta-analysis (Stata.com, 2018). However, with some modifications in the running of this program (by using certain macros), Stata can create funnel plot, forest plot, compute

Egger's test, Trim and Fill test, rank correlation test (Sterne et al., 2009). It will accept data in the format of point estimate and standard error, point estimate and confidence interval, number of events and sample size, and means and standard deviations in each group (Borenstein, 2005).

MetaWin (Version 2.0)

MetaWin is another program for meta-analysis. It is mostly utilized in the field of ecology but due to its generalizability, it can be used in many other fields. It is capable to create funnel plot, forest plot, to compute the fail-safe N test, rank correlation, and other tests (Borenstein, 2005). MetaWin will only process the data if it is available in the format of number of events and sample size, means and standard deviation, correlations. It will also analyze the data if data is formatted as point estimate and variance (Rosenburg et al., 2000).

Tackling Publication Bias

There are many strategies which can help minimizing publication bias:

Trial Registries

If the researcher add registries in their search strategies and the results are accessible, this can help in the reduction of publication bias (Parekh-Bhurke et al., 2011). Because once the trial is registered, regardless of the outcome whether negative or positive or insignificant, the trial needs to be published (Parekh-Bhurke et al., 2011).

In 2004, an initiative was taken by the International Committee of Medical Journal Editors, which made it mandatory to register the trial and it needs to be available to the public at no cost (De Angelis et al., 2005). In 2005, the World Health Organization has initiated efforts to set International standards for clinical trial registration (Gülmezoglu et al., 2005). The British Medical Journal has also asked for trial registration and devised a modified-criteria for the registration of trials (Abbasi, 2004). These policies have resulted in the numbers of trial registration and been effective in reducing the risk of publication bias (Laine et al., 2007).

Data Availability

Sharing of the data and making it public would reduce the chances of publication bias. However, the availability of data and issues related to its privacy are challenging. A number of data repositories are available, where data can be saved with no or minimal cost. In addition to this, challenges related to data privacy and its transparency can be overcome by arranging the data in such a way that the data linking with participants cannot be possible (Brown et al., 2017).

Mandating Publication

Another approach to tackle the publication bias is to have the mandatory publication of research studies (Carroll et al., 2017). Some institution has made it mandatory to publish the research funded through them and one such initiative is Wellcome Open Research (2018). Another option is to publish in the journals, where authors can upload the paper even before the peer review, for instance F1000 research open platform, where authors upload the manuscript before the actual review of the study (F1000 Research, 2018).

Open Access Journals

Sometimes scientifically valid results remain unpublished due to limited readership, editors' decision making and due to limited space in journals. Therefore online, open access journals improve the readability and reduce publication bias. Therefore the studies which might get delay in publication due to being less attractive to the high impact print based journals can be published in online, open access journals, without wasting too much time on the process of rejection and submission (Brown et al., 2017). The electronic publishing has more advantages as compared to conventional publishing as electronic publish is not bound to follow the limits as the traditional printed journal has to do (Berlin, 1992)

Peer Review Process and Publication Bias

Peer review serves as the source to improve quality checks to published articles, but delay in publication or preference of a reviewer or even journal's choice to publish a certain study result in publication bias (Brown et al., 2017). Thus, change in the traditional review process may decrease the chance of publication bias.

Some journals have the policy that the editor of the original journal, which has originally rejected the article may suggest an alternative journal, thus decreasing time between submissions and peer-review process. Another option is "registered reports"; this is a two tier process, in which the outcome is independent of the review process (Chambers, 2013). An article is published based on the proposed hypotheses, methodology and predesigned analysis and it is published once the data is collected, interpreted and results

are finalized. Thus publication in such journals is based on the methodology and perhaps not on the outcome of the results (Brown et al., 2017).

Editorial Policy

An editorial policy can also be helpful to eliminate the publication bias (Thornton and Lee, 2000). This can be done only if the journal editors and reviewers could focus on reviewing high standards in conducting research, as well as excluding key factors influencing publication bias. They can look or may ask for the proof of registration of a trial, confirmation of randomization or any other factor that may contribute toward publication bias (Begg and Berlin, 1988; Chalmers et al., 1990).

Conclusion

The publication bias has significantly influenced the scientific research. It can be in various forms; however, it deteriorates the quality of published research thus resulting in the waste of resources and leading to poor patient health outcomes. There is a need to employ data quality assurance techniques before publishing scientific results as this may undermine the quality of evidence-based decision making in health research.

References

Abbasi, K., 2004. Compulsory registration of clinical trials. BMJ 329, 637–638.
Angell, M., 1989. Negative studies. N. Engl. J. Med. 464–466, doi: 10.1056/nejm198908173210708.
Begg, C.B., 1985. A measure to aid in the interpretation of published clinical trials. Stat. Med. 4, 1–9.
Begg, C.B., Berlin, J.A., 1988. Publication bias: a problem in interpreting medical data. J. R. Stat. Soc. Ser. A (Stat. Soc.) 419–463.
Begg, C.B., Mazumdar, M., 1994. Operating characteristics of a rank correlation test for publication bias. Biometrics 1088–1101.
Berlin, JA., 1992. Will publication bias vanish in the age of online journals? Online J. Curr. Clin. Trials 1 (1).
Boisen, E., 1979. Testicular size and shape of 47, XYY and 47, XXY men in a double-blind, double-matched population survey. Am. J. Human Genet. 31, 697.
Borenstein, M., 2005. Software for publication bias. In: Rothstein, H.R., Sutton, A., Borenstein, M. (Eds.), Publication Bias in Meta-analysis: Prevention, Assessment and Adjustments. John Wiley & Sons Ltd, Chichester, England.
Borenstein, M., Hedges, L., Higgins, J., Rothstein, H., 2005. Comprehensive Meta-Analysis 2.0. Biostat, Englewood, NJ.
Borenstein, M., Hedges, L.V., Higgins, J., Rothstein, H.R., 2009. Publication biasIn: Introduction to Meta-Analysis, John Wiley & Sons, Ltd, Chichester, pp. 277–292.
Brown, A.W., Mehta, T.S., Allison, D.B., 2017. Publication bias in science: what is it, why is it problematic, and how can it be addressed? In: The Oxford Handbook of the Science of Science Communication, Oxford University Press, New York, USA, pp. 93–101.
Carroll, H.A., Toumpakari, Z., Johnson, L., Betts, J.A., 2017. The perceived feasibility of methods to reduce publication bias. PLOS One 12, e0186472.
Chalmers, T.C., Frank, C.S., Reitman, D., 1990. Minimizing the three stages of publication bias. JAMA 263, 1392–1395.
Chambers, C.D., 2013. Registered reports: a new publishing initiative at Cortex. Cortex 49, 609–610.
Chan, A.-W., Hróbjartsson, A., Haahr, M.T., Gøtzsche, P.C., Altman, D.G., 2004. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. JAMA 291, 2457–2465.
Christensen-Szalanski, J.J., Beach, L.R., 1984. The citation bias: fad and fashion in the judgment and decision literature. Am. Psychol. 39, 75.
Cochrane, 2014. Review Manager (RevMan), 5.3 ed. The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen.
Craig, J.C., Irwig, L.M., Stockler, M.R., 2001. Evidence-based medicine: useful tools for decision making. Med. J. Aust. 174, 248–253.
Crawford, J.M., Briggs, C.L., Engeland, C.G., 2010. Publication bias and its implications for evidence-based clinical decision making. J. Dent. Educ. 74, 593–600.
De Angelis, C.D., Drazen, J.M., Frizelle, F.A., Haug, C., Hoey, J., Horton, R., Kotzin, S., Laine, C., Marusic, A., Overbeke, A.J.P., 2005. Is this clinical trial fully registered?—A statement from the International Committee of Medical Journal Editors. Mass Medical Soc.
Dickersin, K., 1990. The existence of publication bias and risk factors for its occurrence. JAMA 263, 1385–1389.
Dickersin, K., Min, Y.I., 1993. Publication bias: the problem that won't go away. Ann. N. Y. Acad. Sci. 703, 135–148.
Duval, S., Tweedie, R., 2000a. A nonparametric "Trim and Fill" method of accounting for publication bias in meta-analysis. J. Am. Stat. Assoc. 95, 89–98.
Duval, S., Tweedie, R., 2000b. Trim and Fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 56, 455–463.
Easterbrook, P.J., Gopalan, R., Berlin, J., Matthews, D.R., 1991. Publication bias in clinical research. Lancet 337, 867–872.
Egger, M., Smith, G.D., 1998. Bias in location and selection of studies. BMJ 316, 61.
Egger, M., Zellweger-Zähner, T., Schneider, M., Junker, C., Lengeler, C., Antes, G., 1997. Language bias in randomised controlled trials published in English and German. Lancet 350, 326–329.
Engler, R.L., Covell, J.W., Friedman, P.J., Kitcher, P.S., Peters, R.M., 1987. Misrepresentation and responsibility in medical research. N. Engl. J. Med. 317, 1383–1389.
Felson, D.T., 1992. Bias in meta-analytic research. J. Clin. Epidemiol. 45, 885–892.
Gülmezoglu, A.M., Pang, T., Horton, R., Dickersin, K., 2005. WHO facilitates international collaboration in setting standards for clinical trial registration. Lancet 365, 1829–1831.
Hagdrup, N., Falshaw, M., Gray, R.W., Carter, Y., 1998. All members of primary care team are aware of importance of evidence based medicine. BMJ 317, 282.
Harrison, J.S., Banks, G.C., Pollack, J.M., O'Boyle, E.H., Short, J., 2017. Publication bias in strategic management research. J. Manag. 43, 400–425.
Higgins, J., Green, S., 2011. Cochrane Handbook for Systematic Reviews of Interventions. Cochrane.
Hopewell, S., Clarke, M.J., Stewart, L., Tierney, J., 2007. Time to publication for results of clinical trials. Cochrane Database Syst. Rev. 18 (2).
Ioannidis, J.P., 1998. Effect of the statistical significance of results on the time to completion and publication of randomized efficacy trials. JAMA 279, 281–286.
Ioannidis, J.P., 2005. Why most published research findings are false. PLoS Med. 2, e124.
Ioannidis, J.P., Trikalinos, T.A., 2007. The appropriateness of asymmetry tests for publication bias in meta-analyses: a large survey. Can. Med. Assoc. J. 176, 1091–1096.
Kyzas, P.A., Loizou, K.T., Ioannidis, J.P., 2005. Selective reporting biases in cancer prognostic factor studies. J. Natl. Cancer Inst. 97, 1043–1055.
Laine, C., Horton, R., Deangelis, C.D., Drazen, J.M., Frizelle, F.A., Godlee, F., Haug, C., Hébert, P.C., Kotzin, S., Marusic, A., 2007. Clinical trial registration—looking back and moving ahead. Mass Medical Soc.
Landis, J.R., Koch, G.G., 1977. The measurement of observer agreement for categorical data. Biometrics 159–174.
Last, J.M., Abramson, J.H., Freidman, G.D., 2001. A Dictionary of Epidemiology. Oxford University Press, New York.

Lau, J., Ioannidis, J.P., Terrin, N., Schmid, C.H., Olkin, I., 2006. Evidence based medicine: the case of the misleading funnel plot. BMJ 333, 597.
Lefebvre, C., Manheimer, E., Glanville, J., Higgins, J., Green, S., 2009. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0. 2.
Lexchin, J., 2012. Sponsorship bias in clinical research. Int. J. Risk Saf. Med. 24, 233–242.
Mahoney, M.J., 1977. Publication prejudices: an experimental study of confirmatory bias in the peer review system. Cogn. Ther. Res. 1, 161–175.
Mcdonald, S., Taylor, L., Adams, C., 1999. Searching the right database. A comparison of four databases for psychiatry journals. Health Inform. Libr. J. 16, 151–156.
Miller, J.E., 2008. Interpreting the substantive significance of multivariable regression coefficients. In: Proceedings of the American Statistical Association, Denver, CO, USA., pp. 3–7.
Mueller, K.F., Meerpohl, J.J., Briel, M., Antes, G., Von Elm, E., Lang, B., Gloy, V., Motschall, E., Schwarzer, G., Bassler, D., 2013. Detecting, quantifying and adjusting for publication bias in meta-analyses: protocol of a systematic review on methods. Syst. Rev. 2, 60.
Orwin, R.G., 1983. A fail-safe N for effect size in meta-analysis. J. Educ. Stat. 8, 157–159.
Parekh-Bhurke, S., Kwok, C.S., Pang, C., Hooper, L., Loke, Y.K., Ryder, J.J., Sutton, A.J., Hing, C.B., Harvey, I., Song, F., 2011. Uptake of methods to deal with publication bias in systematic reviews has increased over time, but there is still much scope for improvement. J. Clin. Epidemiol. 64, 349–357.
Paulson, K., Saeed, M., Mills, J., Cuvelier, G.D., Kumar, R., Raymond, C., Robinson, T., Szwajcer, D., Wall, D., Seftel, M.D., 2011. Publication bias is present in blood and marrow transplantation: an analysis of abstracts at an international meeting. Blood 118 (25), 6698–6701.
Pittler, M., Abbot, N., Harkness, E., Ernst, E., 2000. Location bias in controlled clinical trials of complementary/alternative therapies. J. Clin. Epidemiol. 53, 485–489.
Richard, J., Richard, J., Pillemer, D.B., 1984. Summing up. Harvard University Press, Cambridge, MA.
Rodrigues, V., 2013. Publication and reporting biases and how they impact publication of research. *Editage Insights (29-10-2013)*.
Rosenburg, M., Adams, D., Gurevitch, J., 2000. MetaWin. Statistical Software for Meta-Analysis, Version 2. Sinauer Associates, Sunderland, MA.
Rosenthal, R, 1978. Combining results of independent studies. Psychol. Bull. 85, 185.
Rosenthal, R., 1979. The file drawer problem and tolerance for null results. Psychol. Bull. 86, 638.
Song, F., Eastwood, A., Gilbody, S., Duley, L., Sutton, A., 2000. Publication and related biases: a review. Health Technol. Assess. 4.
Song, F., Hooper, L., Loke, Y., 2013. Publication bias: what is it? How do we measure it? How do we avoid it?. Open Access J. Clin. Trials 2013, 71–81.
Song, F., Parekh, S., Hooper, L., Loke, Y.K., Ryder, J., Sutton, A.J., Hing, C., Kwok, C.S., Pang, C., Harvey, I., 2010. Dissemination and publication of research findings: an updated review of related biases. Health Technol. Assess. 14, 1–193.
Sterling, T.D., 1959. Publication decisions and their possible effects on inferences drawn from tests of significance—or vice versa. J. Am. Stat. Assoc. 54, 30–34.
Sterne, J., Harris, R., Harbord, R., Steichen, T., 2009. Community-Contributed Packages for Meta-Analysis in Stata [Online]. StataCorp LLC. Available: https://www.stata.com/support/faqs/statistics/meta-analysis/.
Sterne, J.A., Egger, M., Moher, D., 2008. Addressing reporting biasesIn: Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series, pp. 297–333.
Sterne, J.A., Gavaghan, D., Egger, M., 2000. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. J. Clin. Epidemiol. 53, 1119–1129.
Thornton, A., Lee, P., 2000. Publication bias in meta-analysis: its causes and consequences. J. Clin. Epidemiol. 53, 207–216.
Torgerson, C.J., 2006. Publication bias: the achilles' heel of systematic reviews? Br. J. Educ. Stud. 54, 89–102.
Turner, E.H., Matthews, A.M., Linardatos, E., Tell, R.A., Rosenthal, R., 2008. Selective publication of antidepressant trials and its influence on apparent efficacy. N. Engl. J. Med. 358, 252–260.
Vickers, A., Goyal, N., Harland, R., Rees, R., 1998. Do certain countries produce only positive results? A systematic review of controlled trials. Control. Clin. Trials 19, 159–166.
Whittington, C.J., Kendall, T., Fonagy, P., Cottrell, D., Cotgrove, A., Boddington, E., 2004. Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data. Lancet 363, 1341–1345.

List of Relevant Websites

F1000 Research, 2018. F1000 Research-Open for Science [Online]. Available: https://f1000research.com/.

Meta-analysis.com, 2006. Comprehensive Meta Analysis [Online]. Biostat, New Jersey, USA. Available: https://www.meta-analysis.com/.

Stata.com, 2018. Stata: Software for Statistics and Data Science [Online]. StataCorp LLC. Available: https://www.stata.com/.

Wellcome Open Research, 2018. Wellcome Open Research [Online]. F1000, United Kingdom. Available: https://wellcomeopenresearch.org/.

Further Reading

Kirkham, J.J., et al., 2010. The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews. BMJ 340, c365.
Sterne, J.A.C., 2011. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 343, d4002.
Rothstein, H.R., Sutton, A.J., Borenstein, M., 2005. Publication Bias in Meta-analysis: Prevention, Assessment and Adjustments. John Wiley & Sons, Ltd, Chichester, UK.

Discrete Choice Experiment

Dalia M. Dawoud, Cairo University, Giza, Egypt

© 2019 Elsevier Inc. All rights reserved.

Introduction

Methods for eliciting people's preferences for choosing products and services have evolved over the time. Opinion polls and traditional satisfaction surveys have been the most commonly used methods. However, more rigorous methods used in marketing and psychology research started to attract considerable attention from the pharmacy practice research community.

Preferences, in general, can be either "revealed" in the choices people make in real-life situations or "stated" by the individual when asked about them in surveys. Revealed preferences are considered the most informative for understanding the real decisions made by individuals. However, there are methodological problems that hinder the feasibility of measuring revealed preferences, particularly in the context of preferences for pharmaceutical products and services that are still in development and not currently available in the market. Hence, measuring stated preferences is more widely used in this context and is generally considered an acceptable alternative (Quaife et al., 2018).

Stated preference methods, on the other hand, involve asking people to state how they would behave, or what they would prefer, based on a hypothetical scenario (Louviere et al., 2000). Several methods exist for assessing stated preferences. These can be classified into either choice-based; where individuals are asked to make choices between alternatives with different attributes (i.e., characteristics), or nonchoice-based methods; where only one option is given and the respondent is asked to rate her/his preference for this option (Carson and Louviere, 2011). **Fig. 1** provides a taxonomy of stated preference elicitation techniques.

Choice-based methods are, generally, preferred for eliciting stated preferences as these can give more granular information regarding the trade-offs that people are willing to make between different attributes of a product or service (e.g., people may be willing to accept higher risk in return for improved outcomes and/or reduced costs). They also reflect real-life situations, where people are faced by choices and trade-offs to make in their everyday life. The most widely used of these choice-based methods is the conjoint analysis, best-worst scaling, and discrete choice experiments (DCEs) (Elliott and Payne, 2005). In this chapter, we discuss DCE as a promising methodology that has many applications in pharmacy practice research.

Discrete Choice Experiment

Definition

DCE is a survey-based quantitative technique for eliciting individuals' preferences. The method involves asking individuals to choose between alternatives, where each is described by a number of attributes and their levels (Mangham et al., 2009). These attributes are the characteristics of the intervention of interest and can relate to its outcomes (e.g., the probability of conceiving for a fertility treatment) or the processes involved in delivering the intervention (e.g., waiting time for or the location of a service).

The choices are usually presented to respondents in the form of choice sets. Respondents are asked to indicate their preference between a discrete set of two (or more) alternatives; using the attributes and levels to describe these alternatives (Amaya-Amaya et al., 2008). The responses are used to determine the attributes that significantly influence individual preferences as well as their relative importance (Mangham et al., 2009).

Fig. 2 presents a hypothetical example of a choice set from a DCE illustrating its basic elements.

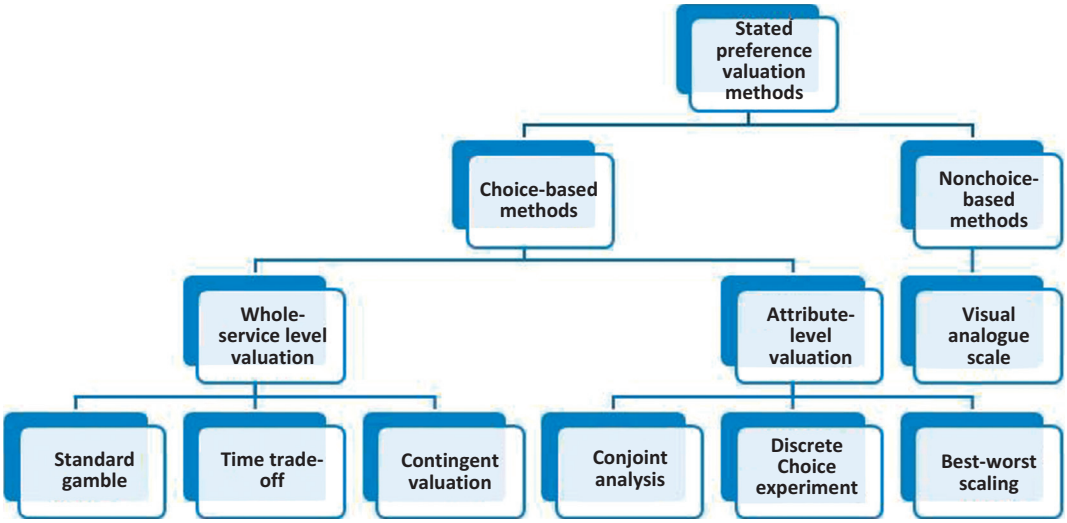

Figure 1 Stated preference valuation methods.

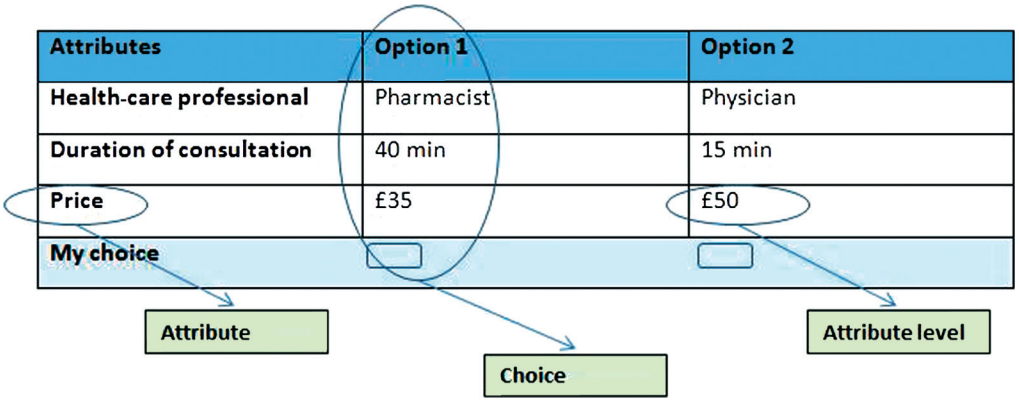

Figure 2 A hypothetical example of DCE choice set with illustration of its elements.

The DCE technique is particularly useful in the absence of revealed preference data; for example:

- if the product or service in question is still under development,
- if there is no variation in the available product or service, and
- if there is value for individuals who are not currently using the product or service in question (e.g., if the individual would have preference for a service to be available for potential use in the future).

Theoretical Foundation of Discrete Choice Experiments

DCE has its foundations in economic theories, namely, random utility theory (Hall et al., 2004b) and Lancaster's theory (Lancaster, 1966). The former is based on two main assumptions: "economic rationality" and "utility maximization." These refer to assuming that individuals make rational choices (economic rationality), and in doing so, they choose the alternative that yields the highest individual benefit (utility) for them (utility maximization). Lancaster's theory argues that utility generated for the individual by an alternative is assumed to depend on the utilities associated with its composing attributes and attribute levels (Lancaster, 1966).

As Mangham et al. (2009) explain:

If $\boldsymbol{Y_{iq}}$ is the utility of individual q for the ith alternative, then

$$Y_{iq} = X_i\beta_i + \varepsilon_{iq}$$

where

$\boldsymbol{X_i}$ is a vector of attributes for the ith alternative, $\boldsymbol{\beta_i}$ is a set of weights that establish the relative contribution of each attribute to the utility associated with the ith alternative, $\boldsymbol{\varepsilon_{iq}}$ is the residual capturing the unobserved variation in the characteristics of different options and any measurement errors.

Design and Administration of Discrete Choice Experiments

As an experimental technique, undertaking a DCE involves a number of steps. It starts with design, followed by data collection, analysis, and interpretation. The ultimate aim of the experiment is to examine the effect of the intervention's attributes at their different levels on respondents' preferences for/valuation of the intervention. Thus, the attributes are considered as the independent variables, which can take two or more values (levels) each and the preference for/valuation of the intervention as the dependent variable.

However, before embarking on undertaking a DCE, it is important to make a decision about the target population. This means deciding whose preferences should be elicited. Eliciting the preferences of current service users is usually the main aim of a DCE, but it is also important to consider the views of future users to inform service/product development. Furthermore, in health care, eliciting the views of the service providers such as doctors, nurses, and pharmacists would be important to allow comparisons with the views and preferences of the service/product users.

The following are the main steps involved in undertaking a DCE.

1. *Choosing the attributes*

   The first step in designing a DCE is the choice of the attributes that can be used to describe the product or service of interest. These attributes can be qualitative (e.g., who delivers an immunization service) or quantitative (e.g., the number of follow-up visits required) (Hensher et al., 2005; Ryan et al., 2001). Mangham et al. (2009) consider reviewing the published and gray literature, such as policy documents, to be the best starting point for identifying relevant attributes (Mangham et al., 2009). However, they argue that primary data collection might still be needed to improve the face validity of the DCE by ensuring that it reflects the study setting. This usually takes a qualitative research approach (e.g., face-to-face interviews or focus groups) and requires input from stakeholders and decision makers who will be using the results of the DCE in informing the design and/or delivery of the product/intervention.

   It is also important to ensure that there is no overlap between the attributes, which is referred to as inter-attribute correlation, as this makes it difficult to establish the effect of each attribute in isolation. The chosen attributes should also represent both the benefits and risks of the product or intervention in question in order to give a comprehensive description and ensure that the respondent is aware of both aspects when making a choice (Ryan et al., 2001). This is particularly important when a trade-off is required between benefits and harms, for example, where increased efficacy through using higher doses of a drug means more side effects. Including both risks and benefits of pharmaceutical products allows the estimation of benefit–risk assessment (BRA) models and calculating the maximum acceptable risk (MAR) that respondents are willing to take (Seston et al., 2007a).

   Including a cost attribute has an added benefit, as it allows estimating the monetary value placed by the respondents on each of the attributes included in the DCE (Morris et al., 2007). When a cost attribute is included; the willingness to pay (WTP) for a favorable change in the level of each of the other attributes can also be calculated. This is presented as the marginal rate of substitution (MRS), which is a measure of the trade-offs that the respondent (consumer, patient, or health-care professional) is willing to make, and is calculated by dividing the coefficient for this attribute by the coefficient for the cost attribute (i.e., $\beta_{\text{attribute}}/\beta_{\text{cost}}$) (Morris et al., 2007). This trade-off vs cost can, alternatively, be represented as the willingness to accept (WTA), which is the amount of money respondents believe compensates for an unfavorable change in the attribute. A drawback of including a cost attribute arises in health systems where the intervention will be free at the point of service, where the respondents may not provide credible answers (Guttmann et al., 2009). More detailed discussion of the applications of WTP calculations in pharmacoeconomic evaluations using cost–benefit analyses can be found elsewhere (Drummond et al., 1987).

   It has to be noted that it is not possible to include every single attribute or characteristic of the service/product in question in the DCE. This is why deciding the number of attributes to include in a DCE is another important aspect of its design. In practice, most DCEs will include fewer than 10 attributes so that all of them can be considered by the respondents when making their choice; with some arguing that a maximum of 7 should be considered (DeShazo and Fermo, 2002). The rationale behind this is that the more the attributes, the greater the cognitive burden of completing the DCE. So, to avoid the risk of low response rate, it is advisable to limit the number of attributes to a recommended maximum of 7–10 (DeShazo and Fermo, 2002).

2. *Assigning levels to the chosen attributes*

   The nature of the attribute, qualitative or quantitative, will dictate the nature of the levels to be used. For example, an attribute may be related to who delivers the service in question, and in this case, the levels listed will be those professionals that are likely to provide the service (e.g., for an immunization service, this could include pharmacist, nurse, or doctor). Quantitative attributes, such as the frequency of administration of a new drug and cost, will be given numerical levels.

   The chosen levels should reflect the range that the respondents might experience or expect to experience if the product or service is a new one (e.g., a new treatment being developed), so that a comprehensive description of the intervention in question is given (Lancsar and Louviere, 2008). Additionally, the chosen levels for the quantitative variables should be evenly spaced and cover a wide range to avoid respondents' not making a choice because of the similarity of the levels. This also allows more accurate estimation of the effect of these quantitative attributes (Lancsar and Louviere, 2008).

   A specific issue relating to defining levels for risk attributes (e.g., percentage probability of side effects) is the difficulty that some respondents may have in understanding probabilities. Hence, effort should be made to ensure that the descriptions are clear and communicated in a way easy to understand (Peters et al., 2006).

Similar to the number of attributes, the number of levels should be kept to a minimum to avoid cognitive overload and difficulty making choices for the respondent. Piloting can then show whether a change to the chosen attributes and levels is required (Mangham et al., 2009).

3. *Designing the choice sets*

   Each DCE consists of a number of choices made of the same number of attributes. The total possible number of choices in the experiment will be based on the total number of attributes and levels in a full factorial design. Considering a DCE that includes 5 attributes, each with 3 levels, then, the total number of possible choices is 243 (3^5). However, this is likely to result in an unmanageable number of choices to be presented to the respondents. As a general rule, it has been reported that respondents can manage between 9 and 16 pairwise choices before they get tired or bored of the experiment (Hanley et al., 2007).

   Hence, approaches have been developed to allow reducing the number of choice sets in a DCE. These include linear and nonlinear methods. The classical linear method uses fractional factorial design and orthogonal arrays to create the choice set, while nonlinear methods utilize Bayesian optimal designs.

   The linear fractional factorial design uses a principle of maintaining orthogonality. This means that each attribute independently affects the overall preference for the service and its utility. The task of reducing the number of choice sets is facilitated by the use of programs such as SPSS Statistics Software (IBM®). These can provide scenarios that describe the level to assign to each of the attributes. However, the full and fractional factorial designs may result in DCE parameters that do not fit the linear models.

   A Bayesian design, on the other hand, maximizes precision of estimated parameters for a given number of choice questions by incorporating *a priori* information about the sign and value of parameters (Reed Johnson et al., 2013). The *a priori* information can be obtained by undertaking pilot studies (Hifinger et al., 2017b). Bayesian optimal designs can be generated algorithmically by using JMP statistical software (SAS Institute Inc.).

   Creating the choice sets then follows, by combining the scenarios in sets of two or more. Two methods are usually quoted as the most commonly used approaches to undertake this task: constant comparison and random pairing (Phillips et al., 2002). In the former, one scenario is kept constant and paired against the remaining scenarios to create the choice sets. This is usually a scenario that describes the status-quo or the existing service. In the latter, the scenarios are randomly paired to create the required number of choice sets.

   Additionally, decisions concerning various presentation options, including whether and how to include the opt-out option and how to frame and depict the attribute levels should be made. The inclusion of a nonchoice option is considered to represent the real-world context. However, these nonchoice responses do not provide any information on how individuals trade-off the attribute levels presented to them. Labeling the choices, e.g., by mentioning the product name, is not generally preferred as it usually introduces selection bias and reduces respondents' attention to the attribute levels (de Bekker-Grob et al., 2010).

   Checks can be incorporated to assess internal validity by examining whether the respondents understand what is required. Two approaches are reported in the literature to do this, namely, dominance and consistency (Janssen et al., 2017). Dominance works by including a choice that includes a dominant scenario, which is better than the alternative in all attributes. If the respondent understands the task, then he/she should be choosing the dominant option. On the other hand, consistency works by repeating a choice set to check if the respondent will have consistency in his/her choice by choosing the same scenario in both instances (Janssen et al., 2017).

4. *Designing the DCE questionnaire*

   Designing the DCE questionnaire is a very important step that affects its validity and usefulness. The choice sets created form the basis of the DCE questionnaire. However, it is important to provide enough context to the task, and this is why the questionnaire usually starts by a detailed introduction to the task and what is required.

   Taking into account the level of respondents' understanding and ensuring they know what is required and how to complete the task will ensure collecting useful data. This is usually achieved by providing enough explanation and examples. Thus, it might be essential to provide the questionnaire in more than one language and more than one format (Mangham et al., 2009).

   Additionally, in populations with lower levels of literacy, the use of diagrams and pictures can be particularly useful. Another design decision that has to be made is about the order of presenting the choice sets, which can affect the choices respondents make. It is good practice to collect data on socioeconomic indicators as this allows analysis of the impact of individual characteristics on the choices made (Mangham et al., 2009).

   Sample size calculation is an important consideration at the stage of designing the DCE. Formal calculations of sample size need to take into account the heterogeneity in preferences and any planned subgroup analysis (de Bekker-Grob et al., 2015). A commonly used method for calculating sample size in DCEs is the Rule of Thumb calculation described by Orme (Orme, 1998, 2010). It has been reported that the precision of DCEs rapidly decreases at sample sizes less than 150 (Reed Johnson et al., 2013).

5. *Pretesting/piloting*

   Piloting is an essential step before the administration of the DCE. The pilot exercise should be used primarily to ensure that respondents properly understand the questions and the tasks they are asked to complete. For example, respondents can be asked to mark every question or answer category that they did not understand and provide suggestions for improvement. This is particularly relevant when working with different languages and or/cultures (Hall et al., 2004a).

   During piloting, it is also possible to check whether respondents consider the range of attributes and levels included in the DCE to be appropriate and to invite them to suggest changes to existing attributes or their levels, addition of new attributes or levels or omission of attributes or levels. This can be done in different formats, including the use of face-to-face interviews or focus groups.

It can also take the form of a ranking exercise in which the respondents are asked to rank the attributes according to their importance (Mangham et al., 2009).

If a sufficiently large sample is included in the pilot DCE, it is possible to quantitatively analyze the data to get some information about the significance of the included attributes and any interaction between them. This information is very valuable in informing the analysis of the final DCE. Additionally, the quantitative information from the analysis of pilot DCE data can be used to finalize the decisions regarding the appropriate attributes and levels that can be included in the analysis of the final DCE. Piloting also ensures that the range of socio-economic and other information requested from respondents in the final DCE are appropriate. Moreover, sample size calculations can be based on the pilot data to ensure that significant differences for each attribute can be detected (Bliemer and Rose, 2009).

6. *Administration*

Once the design of the DCE is finalized, based on the outcomes of the piloting stage, and the sampling frame is agreed; administration and data collection for the main study can be initiated. The DCE can either be self- or interviewer administered. Self-administered questionnaires can be administered by post, phone, or online, while Interviewer-administered DCEs are usually completed face-to-face or over the phone (Ryan, 2004).

Postal and online surveys may not always be feasible particularly in settings with lower levels of literacy. Additionally, they usually have low response rates. Thus, having trained interviewers administering the DCE is usually the preferred method as it can ensure that respondents will be given the required directions to facilitate completing the task. However, this is usually more costly.

Analysis and Interpretation

Analysis of DCE data is based on the use of statistical regression models, which have a categorical dependent variable that is either dichotomous or polychotomous (Hauber et al., 2016). These models include probit, logit, and multinominal logit. Panel data estimation techniques are usually required in the analysis of DCE data as respondents are asked to consider multiple choice pairs, which means independence of the error terms cannot be assumed (Hauber et al., 2016).

In DCEs where two choices without an opt-out option are presented to a respondent, either random effects logit or random effects probit are usually considered most appropriate. On the other hand, if the respondent is asked to choose from more than two options, or two options plus an opt-out, then the data can usually be analyzed using multinomial models (Hauber et al., 2016).

Generally, a positive significant coefficient, β, means that the respective attribute levels significantly increase overall preference (utility). This is usually expected for favorable attributes such as treatment efficacy. A negative significant coefficient, β, in contrast means that the respective attribute level decreases the overall preference. This is expected to be seen for attributes representing side effects or costs of services or treatments.

The analysis of DCE data also involves the quantification of the trade-offs made by the respondents. For example, in benefit–risk assessment studies of pharmaceutical products, MAR for each risk attribute is usually presented. MAR is defined as the maximum level of each risk criterion, which participants are willing to accept in order to increase 1 unit level of efficacy. It is equal to the ratios between benefit and risk coefficients (i.e., $\beta_{\text{benefit}}/\beta_{\text{risk}}$) (Vass and Payne, 2017). Similarly, as explained earlier, it is possible to calculate the WTP and the WTA in DCE studies that include a cost attribute, which represent the monetary trade-offs that participants are willing to make.(Drummond et al., 1987).

DCE is also useful in understanding the estimation of differences between subgroups and identifying the individual characteristics that have significant effect on individual preferences. This is usually done by including interaction terms into the analysis model with a priori determined variables of interest (Hauber et al., 2016).

Applications in Pharmacy Practice Research

DCE is a relatively new research method when it comes to its use in pharmacy practice research. However, its use in healthcare research in general predates its use in pharmacy research. A scoping search of the literature conducted in MEDLINE in May 2018, using the free text terms Discrete Choice Experiment* AND Pharm* to identify some examples of applications of DCE in pharmacy research, returned 61 records. Of these, 41 primary research studies, (Albada and Triemstra, 2009; Ashcroft et al., 2006; Bansback et al., 2016; Boonen et al., 2011; Boonen et al., 2009; Byun et al., 2016a; Byun et al., 2016b; Cheung et al., 2018; Cristina et al., 2002; de Vries et al., 2015; Diaby et al., 2011; Feehan et al., 2017; Gerard et al., 2012; Grindrod et al., 2010; Haac et al., 2017; Hifinger et al., 2017a; Hifinger et al., 2017b; Hong et al., 2011; Kawaguchi et al., 2014; Laba et al., 2013; Laba et al., 2012; Mantovani et al., 2005; Munger et al., 2017; Naik-Panvelkar et al., 2012a; Naik-Panvelkar et al., 2012b; Ngorsuraches et al., 2015; Ngorsuraches and Thongkeaw, 2015; Park et al., 2012; Porteous et al., 2016; Porteous et al., 2006; Rennie et al., 2012; Rockers et al., 2012; Scalone et al., 2009; Scott et al., 2007; Seston et al., 2007a, 2007b; Tinelli et al., 2009; Wang et al., 2011; Wanishayakorn et al., 2016; Wellman and Vidican, 2008; Whitty et al., 2015) and 3 systematic reviews (Katherine and Rachel, 2005; Pradnya et al., 2013; Vass et al., 2017) were considered relevant.

The identified systematic reviews (n = 3) were all focused on studies of pharmaceutical services (Katherine and Rachel, 2005; Pradnya et al., 2013; Vass et al., 2016). The primary research studies dated back to 2002, with the number published annually up to 2017 ranging from 1 to 7.

Most of the primary research studies focused on examining aspects of pharmaceutical services (n = 23), while the remainder focused on pharmaceutical products (n = 18). The studies were either conducted in a single country (n = 39) or were multinational (n = 2). The single country studies were conducted in the United Kingdom (n = 8), the United States (n = 7), the Netherlands (n = 6), Australia (n = 5), Korea (n = 3), Thailand (n = 3), Italy (n = 2), and one each in Canada, Cote d'Ivoire, Japan, New Zealand, and Uganda. Of the two multinational studies, one was conducted in the United Kingdom, Hungary, and Romania, and the second was conducted across 12 European countries.

Studies of Pharmaceutical Services

The most recent systematic review of DCEs in pharmacy has included 17 studies (Vass et al., 2016). These covered studies published up to 2012. Since then, six more studies were identified that were considered to be good examples of using DCEs to assess preferences to pharmaceutical services, taking the total to 23 studies (Albada and Triemstra, 2009; Boonen et al., 2011; Boonen et al., 2009; Cristina et al., 2002; Feehan et al., 2017; Gerard et al., 2012; Grindrod et al., 2010; Hong et al., 2011; Kawaguchi et al., 2014; Munger et al., 2017; Naik-Panvelkar et al., 2012a; Naik-Panvelkar et al., 2012b; Porteous et al., 2016; Porteous et al., 2006; Rennie et al., 2012; Rockers et al., 2012; Scalone et al., 2009; Scott et al., 2007; Seston et al., 2007b; Tinelli et al., 2009; Wang et al., 2011; Wellman and Vidican, 2008; Whitty et al., 2015).

The main interventions/services assessed in these studies included pharmacist prescribing, medicines management and other specialist services, electronic prescribing, pharmacist counseling, community pharmacy service models, community pharmacy-based services for chronic conditions, and management of minor ailments.

The sampling frames in these studies included single, mainly patients or health-care professionals, or multiple populations. The number of respondents ranged from 80 to 9252; with response rates ranging from 10% to 99%. Similar to studies of pharmaceutical products; studies that used face-to-face and online administration seemed to achieve higher response rates. In the majority of the studies, mailed survey was the method used for the administration of the DCEs, followed by online/web administration, which was used in the most recent studies.

The approaches used for choosing the attributes and levels were primarily literature reviews with expert input. Few studies reported the use of some form of formal qualitative research methods and, where used, reporting quality was generally low. The number of attributes included in the scenarios ranged from 3 to 11, with the majority including 6 or more attributes. The number of levels for each attribute ranged from 2 to 7. This is likely to be due to the complex nature of the pharmaceutical services interventions compared to pharmaceutical products, which necessitates the use of large number of attributes to allow accurate description of the intervention. The attributes were generally study specific. Examples include who delivers the service, length of consultations, waiting time, the cost or copayments, and workload.

Similar to studies of pharmaceutical products, the most commonly used DCE design was the fractional factorial design, though Bayesian approaches featured in a few studies. The analysis approach used in the majority of the studies utilized the multinomial logit model.

Studies of Pharmaceutical Products

Studies of pharmaceutical products (n = 18) focused on assessing patients' and/or health-care professionals' preferences for the characteristics of these drug products (e.g., timing, frequency, and route of administration), the benefit–risk trade-offs they make, their WTP for and adherence to these products) (Ashcroft et al., 2006; Bansback et al., 2016; Byun et al., 2016a; Byun et al., 2016b; Cheung et al., 2018; de Vries et al., 2015; Haac et al., 2017; Laba et al., 2013; Laba et al., 2012; Mantovani et al., 2005; Park et al., 2012; Seston et al., 2007a; Wanishayakorn et al., 2016; Diaby et al., 2011; Hifinger et al., 2017a; Hifinger et al., 2017b; Ngorsuraches et al., 2015; Ngorsuraches and Thongkeaw, 2015). These studies are useful in informing the development of pharmaceutical products and ensuring their acceptability to the consumer/patient and prescriber.

The pharmaceutical products covered in these studies included drugs for psoriasis, hemophilia, osteoarthritis, rheumatoid arthritis, renal cell carcinoma, breast cancer, diabetes, venous thromboembolism (VTE) prophylaxis, insomnia, and hypercholesterolemia, as well as human papilloma virus (HPV) vaccination. Two studies focused on examining the public's preferences for the characteristics of prescribed medications; in general, to assess their impact on adherence (Laba et al., 2012, 2013) while another study examined prescribers' preferences for these characteristics to assess their impact on formulary inclusion and reimbursement decisions (Diaby et al., 2011).

The sampling frames in these studies included patients, carers, consumers/general public, health-care professionals (physicians, nurses, and pharmacists). Some studies included both patients/consumers and health-care professionals to compare between the preferences of these groups (Mantovani, 2005; Park, 2012; Byun, 2016; Wanishayakorn, 2016). The number of respondents in the included studies ranged from 126 to 2663, with a response rate ranging from 10% to 100%. The majority of the DCEs were administered using postal or online surveys. Face-to-face interviews were used mainly with patients. The higher response rate appeared to be associated with face-to-face administration of the DCE.

The most common approach used for choosing the attributes and levels was using literature reviews and expert input, with only one study reporting the use of formal qualitative research methods (Wanishayakorn et al., 2016). The number of attributes included in the scenarios ranged from 4 to 8. These were primarily related to treatment efficacy, side-effect, route, and frequency of administration and cost. The cost attributes were included in 9 studies and facilitated the calculation of WTP for favorable

changes in the included attributes. The number of levels ranged from 2 to 4 and included combination of qualitative and quantitative descriptors.

The most commonly used DCE design was the fractional factorial design, although other design approaches including Bayesian design were also utilized. The analysis approach used in the majority of the studies was the multinomial conditional logit modeling.

An example of a DCE study is provided in Box 1.

Box 1

Example

Study:
Haac et al. (2017)

Title
Patient preferences for venous thromboembolism (VTE) prophylaxis after injury: a discrete choice experiment

Objective
To elicit patient preferences towards route of administration, complications, and costs of prophylaxis options for VTE after injury

Country
USA

Population
Adult orthopedic trauma patients who have survived a VTE event

DCE design:

1. *Choosing the attributes:*
   Seven attributes were chosen based on literature review, patient interviews, expert consultation, and retrospective review of patient outcomes
   The attributes are route of administration, cost, possible side effects, risk of major bleeding, risk of VTE requiring therapeutic anticoagulation for 6 months, risk of requiring reoperation, and risk of death due to pulmonary embolism (PE).
2. *Assigning levels to the chosen attributes:*
   Two attributes were qualitative: Route of administration (oral tablet, subcutaneous injection) and possible side effects (none, bruising on leg, stomach pain). Five attributes were quantitative. Risk attributes were presented as *n* per 1000.
3. *Designing the choice sets*
   Forty choice sets were developed, using Bayesian D-optimal optimal design with using JMP statistical soft-ware (SAS Institute Inc.) and randomly divided into 4 groups of 10 choice sets each. Two hypothetical medications were compared in each choice set.
4. *Designing the DCE*
   The questionnaire included questions covering the respondents' demographics including age, sex, race, type of injury, income, health insurance, and days on prophylaxis. Sample size calculation was completed using the Rule of Thumb calculation (Orme, 1998).
5. *Pretesting/piloting*
   No piloting or retesting was reported.
6. *Administration*
   The survey was self-administered face-to-face in the presence of a member of the research team. Demographic data were also collected in the survey.

Analysis:

- A multinomial logit model with effect coding was used in the analysis to calculate the marginal utility, willingness to pay (WTP), and acceptable trade-off estimates for 1% reduction in VTE complication or side effects. Preference heterogeneity based on respondent characteristics was also assessed by adding interaction terms.

Results:

- Reducing the risk of death due to PE was the most strongly preferred attribute, with a marginal utility of 4.57 ($P < 0.0001$) followed by preference for reducing the risk of VTE requiring therapeutic anticoagulation (0.25; $P < 0.0001$).
- Oral administration was also preferred (marginal utility 0.16; $P < 0.0001$); however; possible medication side effects such as stomach pain or bruising were not a significant attribute ($P > 0.1$).
- The highest WTP was for 1% absolute risk reduction in PE was $1686.9. Respondents also were willing to pay $117.45 to receive prophylaxis via the oral route.
- To change preference from oral to subcutaneous route, an absolute reduction in the risk of death due to PE of only 0.07% is required, while the absolute VTE risk reduction required for this change was 1.27%.
- Subgroup analysis assessing the heterogeneity of respondents' preferences showed that some covariates significantly affected preference for the oral route. These were being female, white, or having lower extremity injury.

Conclusion
The study demonstrated that orthopedic trauma patients preferred the oral route for VTE prophylaxis administration, when all other attributes were equal. However, reducing the risk of death due to PE was the most influential factor when making a decision about medication choice.

Summary

From this quick snapshot of the literature, it was possible to see that the use of DCE in pharmacy practice research has been growing steadily. Many topics have been suitable areas for this new research method. Studies that used DCE assessed preferences of different populations groups (patients, carers, general public, health-care professionals, and decision makers) to a range of interventions (pharmaceutical products and services) with the results directly impacting on policy making, clinical practice, and product development. This goes to show the potential for this technique to exponentially grow as a research method in pharmacy practice research over the coming years. It is important for pharmacy practice researchers to equip themselves with the knowledge of the basics and applications of this research method in order to make the best use of DCE to advance pharmacy practice and science.

Glossary

Attributes Characteristics of the intervention of interest. These could be quantitative or qualitative and are described using levels.
Best-worst scaling A survey-based method for assessing stated preferences where respondents are asked to select their most preferred and least preferred option out of a number of options.
Conjoint analysis A survey-based method used in market research that helps determine how people value different attributes of a product or service.
Discrete choice experiment A survey-based method underpinned by economic theory that allows the systematic quantification of respondents' preferences for the different characteristics (attributes) of a good or service, the balance between these different attributes and the relative value of each attribute.
Levels The values that the attributes describing a good or service can take.
Stated preferences The preferred options for individuals as stated by them when asked to choose their preferred option from a series of hypothetical scenarios.

References

Albada, A., Triemstra, M., 2009. Patients' priorities for ambulatory hospital care centres. A survey and discrete choice experiment among elderly and chronically ill patients of a Dutch hospital. Health Expect 12, 92–105.

Amaya-Amaya, M., Gerard, K., Ryan, M., 2008. Using Discrete Choice Experiments to Value Health and Health Care. In: Ryan, M., Gerard, K., Amaya-Amaya, M. (Eds.), The Economics of Non-Market Goods and Resources. 1st ed. Springer, Netherlands.

Ashcroft, D.M., Seston, E., Griffiths, C.E., 2006. Trade-offs between the benefits and risks of drug treatment for psoriasis: a discrete choice experiment with U.K. dermatologists. Br. J. Dermatol. 155, 1236–1241.

Bansback, N., Harrison, M., Marra, C., 2016. Does introducing imprecision around probabilities for benefit and harm influence the way people value treatments? Med. Decis. Making 36, 490–502.

Bliemer, M.C., Rose, J.M., 2009. Efficiency and sample size requirements for stated choice experiments.

Boonen, L.H., Donkers, B., Schut, F.T., 2011. Channeling consumers to preferred providers and the impact of status quo bias: does type of provider matter? Health Serv. Res. 46, 510–530.

Boonen, L.H., Schut, F.T., Donkers, B., Koolman, X., 2009. Which preferred providers are really preferred? Effectiveness of insurers' channeling incentives on pharmacy choice. Int. J. Health Care Finance Econ. 9, 347–366.

Byun, J.H., Kwon, S.H., Ha, J.H., Lee, E.K., 2016a. A benefit-risk assessment model for statins using multicriteria decision analysis based on a discrete choice experiment in Korean patients. Ther Clin. Risk Manag. 12, 965–974.

Byun, J.H., Kwon, S.H., Lee, J.E., Cheon, J.E., Jang, E.J., Lee, E.K., 2016b. Comparison of benefit-risk preferences of patients and physicians regarding cyclooxygenase-2 inhibitors using discrete choice experiments. Patient Prefer Adherence 10, 641–650.

Carson, R.T., Louviere, J.J., 2011. A common nomenclature for stated preference elicitation approaches. Environ. Resour. Econ. 49, 539–559.

Cheung, J.M.Y., Bartlett, D.J., Armour, C.L., Saini, B., Laba, T.L., 2018. Patient preferences for managing insomnia: a discrete choice experiment. Patient.

Cristina, U., Angela, B., Mandy, R., Terry, P., Christine, B., Roma, R., 2002. Using discrete choice experiments to evaluate alternative electronic prescribing systems. Int. J. Pharm. Prac. 10, 191–200.

de Bekker-Grob, E.W., Donkers, B., Jonker, M.F., Stolk, E.A., 2015. Sample size requirements for discrete-choice experiments in healthcare: a practical guide. The Patient 8, 373–384.

de Bekker-Grob, E.W., Hol, L., Donkers, B., Van Dam, L., Habbema, J.D., Van Leerdam, M.E., Kuipers, E.J., Essink-Bot, M.L., Steyerberg, E.W., 2010. Labeled versus unlabeled discrete choice experiments in health economics: an application to colorectal cancer screening. Value Health 13, 315–323.

de Vries, S.T., de Vries, F.M., Dekker, T., Haaijer-Ruskamp, F.M., de Zeeuw, D., Ranchor, A.V., Denig, P., 2015. The role of patients' age on their preferences for choosing additional blood pressure-lowering drugs: a discrete choice experiment in patients with diabetes. PLoS ONE 10, e0139755.

DeShazo, J.R., Fermo, G., 2002. Designing choice sets for stated preference methods: the effects of complexity on choice consistency. J. Environ. Econ. Manage. 44, 123–143.

Diaby, V., Die Kakou, H., Lachaine, J., 2011. Eliciting preferences for reimbursed drugs selection criteria in Cote d'Ivoire. Patient 4, 125–131.

Drummond, M.F., Stoddart, G.L., Torrance, G.W., 1987. Methods for the Economic Evaluation of Health Care Programmes. Oxford University Press.

Elliott, R., Payne, K., 2005. Valuing Preferences. In: Essentials of Economic Evaluation in Healthcare, 1st ed. Pharmaceutical Press, London.

Feehan, M., Walsh, M., Godin, J., Sundwall, D., Munger, M.A., 2017. Patient preferences for healthcare delivery through community pharmacy settings in the USA: A discrete choice study. J. Clin. Pharm. Ther. 42, 738–749.

Gerard, K., Tinelli, M., Latter, S., Blenkinsopp, A., Smith, A., 2012. Valuing the extended role of prescribing pharmacist in general practice: results from a discrete choice experiment. Value Health 15, 699–707.

Grindrod, K.A., Marra, C.A., Colley, L., Tsuyuki, R.T., Lynd, L.D., 2010. Pharmacists' preferences for providing patient-centered services: a discrete choice experiment to guide health policy. Ann. Pharmacother. 44, 1554–1564.

Guttmann, R., Castle, R., Fiebig, D., 2009. Use of Discrete Choice Experiments in Health Economics: An Update of the Literature. CHERE, University of Technology, Sydney.
Haac, B.E., O'hara, N.N., Mullins, C.D., Stein, D.M., Manson, T.T., Johal, H., Castillo, R., O'toole, R.V., Slobogean, G.P., 2017. Patient preferences for venous thromboembolism prophylaxis after injury: a discrete choice experiment. BMJ Open 7, e016676.
Hall, J., Viney, R., Haas, M., Louviere, J., 2004a. Using stated preference discrete choice modeling to evaluate health care programs. J. Business Res. 57, 1026–1032.
Hall, J., Viney, R., Haas, M., Louviere, J., 2004b. Using stated preference discrete choice modelling to evaluate health care programs. J. Business Res. 57, 1026–1032.
Hanley, N., Shogren, J., White, B., 2007. Environmental Economics: In Theory & Practice, Second Edition. Palgrave Macmillan.
Hauber, A.B., González, J.M., Groothuis-Oudshoorn, C.G.M., Prior, T., Marshall, D.A., Cunningham, C., Ijzerman, M.J., Bridges, J.F.P., 2016. Statistical methods for the analysis of discrete choice experiments: a report of the ISPOR Conjoint Analysis Good Research Practices Task Force. Value Health 19, 300–315.
Hensher, D.A., Rose, J.M., Greene, W.H., 2005. Applied Choice Analysis: A Primer. Cambridge University Press.
Hifinger, M., Hiligsmann, M., Ramiro, S., Watson, V., Berghea, F., Pentek, M., Keat, A., Severens, J.L., Fautrel, B., Boonen, A., 2017a. Influence of disease activity on RA treatment choices in countries with restricted access to expensive, innovative drugs: a discrete choice experiment among rheumatologists. RMD Open 3, e000453.
Hifinger, M., Hiligsmann, M., Ramiro, S., Watson, V., Severens, J.L., Fautrel, B., Uhlig, T., Van Vollenhoven, R., Jacques, P., Detert, J., Canas, D.A., Silva, J., Scire, C.A., Berghea, F., Carmona, L., Pentek, M., Keat, A., Boonen, A., 2017b. Economic considerations and patients' preferences affect treatment selection for patients with rheumatoid arthritis: a discrete choice experiment among European rheumatologists. Ann. Rheum. Dis. 76, 126–132.
Hong, S.H., Liu, J., Wang, J., Brown, L., White-Means, S., 2011. Conjoint analysis of patient preferences on Medicare medication therapy management. J. Am. Pharm. Assoc. (2003) 51, 378–387.
Janssen, E.M., Marshall, D.A., Hauber, A.B., Bridges, J.F.P., 2017. Improving the quality of discrete-choice experiments in health: how can we assess validity and reliability? Expert Rev. Pharmacoecon. Outcomes Res. 17, 531–542.
Katherine, P., Rachel, E., 2005. Using discrete choice experiments to value preferences for pharmacy services. Int. J. Pharm. Prac. 13, 9–20.
Kawaguchi, T., Azuma, K., Yamaguchi, T., Iwase, S., Matsunaga, T., Yamada, K., Miyamatsu, H., Takeuchi, H., Kohno, N., Akashi, T., Unezaki, S., 2014. Preferences for pharmacist counselling in patients with breast cancer: a discrete choice experiment. Biol. Pharm. Bull. 37, 1795–1802.
Laba, T.L., Brien, J.A., Fransen, M., Jan, S., 2013. Patient preferences for adherence to treatment for osteoarthritis: the MEdication Decisions in Osteoarthritis Study (MEDOS). BMC Musculoskelet. Disord. 14, 160.
Laba, T.L., Brien, J.A., Jan, S., 2012. Understanding rational non-adherence to medications. A discrete choice experiment in a community sample in Australia. BMC Fam. Pract. 13, 61.
Lancaster, K.J., 1966. A new approach to consumer theory. J. Polit. Econ. 74, 132–157.
Lancsar, E., Louviere, J., 2008. Conducting discrete choice experiments to inform healthcare decision making: a user's guide. Pharmacoeconomics 26, 661–677.
Louviere, J., Hensher, D., Swait, J., 2000. Stated Choice Methods: Analysis and Application. Cambridge University Press.
Mangham, L.J., Hanson, K., Mcpake, B., 2009. How to do (or not to do) . . . Designing a discrete choice experiment for application in a low-income country. Health Policy Plan. 24, 151–158.
Mantovani, L.G., Monzini, M.S., Mannucci, P.M., Scalone, L., Villa, M., Gringeri, A., 2005. Differences between patients', physicians' and pharmacists' preferences for treatment products in haemophilia: a discrete choice experiment. Haemophilia 11, 589–597.
Morris, S., Devlin, N., Parkin, D., 2007. Economic Analysis in Health Care. John Wiley & Sons.
Munger, M.A., Walsh, M., Godin, J., Feehan, M., 2017. Pharmacist's demand for optimal primary care service delivery in a community pharmacy: The OPTiPharm Study. Ann. Pharmacother. 51, 1069–1076.
Naik-Panvelkar, P., Armour, C., Rose, J., Saini, B., 2012a. Patients' value of asthma services in Australian pharmacies: the way ahead for asthma care. J. Asthma 49, 310–316.
Naik-Panvelkar, P., Armour, C., Rose, J.M., Saini, B., 2012b. Patient preferences for community pharmacy asthma services: a discrete choice experiment. Pharmacoeconomics 30, 961–976.
Ngorsuraches, S., Nawanukool, K., Petcharamanee, K., Poopantrakool, U., 2015. Parents' preferences and willingness-to-pay for human papilloma virus vaccines in Thailand. J. Pharm. Policy Pract. 8, 20.
Ngorsuraches, S., Thongkeaw, K., 2015. Patients' preferences and willingness-to-pay for postmenopausal hormone receptor-positive, HER2-negative advanced breast cancer treatments after failure of standard treatments. Springerplus 4, 674.
Orme, B. 1998. Sample size issues for conjoint analysis studies. Sequim: Sawtooth Software Technical Paper.
Orme, B.K., 2010. Getting Started with Conjoint Analysis: Strategies for Product Design and Pricing Research, Research Publishers.
Park, M.H., Jo, C., Bae, E.Y., Lee, E.K., 2012. A comparison of preferences of targeted therapy for metastatic renal cell carcinoma between the patient group and health care professional group in South Korea. Value Health 15, 933–939.
Peters, E., Vastfjall, D., Slovic, P., Mertz, C.K., Mazzocco, K., Dickert, S., 2006. Numeracy and decision making. Psychol. Sci. 17, 407–413.
Phillips, K.A., Maddala, T., Johnson, F.R., 2002. Measuring preferences for health care interventions using conjoint analysis: an application to HIV testing. Health Serv. Res. 37, 1681–1705.
Porteous, T., Ryan, M., Bond, C., Watson, M., Watson, V., 2016. Managing minor ailments; the public's preferences for attributes of community pharmacies. a discrete choice experiment. PLoS One 11, e0152257.
Porteous, T., Ryan, M., Bond, C.M., Hannaford, P., 2006. Preferences for self-care or professional advice for minor illness: a discrete choice experiment. Br. J. Gen. Pract. 56, 911–917.
Pradnya, N.P., Carol, A., Bandana, S., 2013. Discrete choice experiments in pharmacy: a review of the literature. Int. J. Pharm. Prac. 21, 3–19.
Quaife, M., Terris-Prestholt, F., Di Tanna, G.L., Vickerman, P., 2018. How well do discrete choice experiments predict health choices? A systematic review and meta-analysis of external validity. Eur. J. Health Econ.
Reed Johnson, F., Lancsar, E., Marshall, D., Kilambi, V., Muhlbacher, A., Regier, D.A., Bresnahan, B.W., Kanninen, B., Bridges, J.F., 2013. Constructing experimental designs for discrete-choice experiments: report of the ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force. Value Health 16, 3–13.
Rennie, L., Porteous, T., Ryan, M., 2012. Preferences for managing symptoms of differing severity: a discrete choice experiment. Value Health 15, 1069–1076.
Rockers, P.C., Jaskiewicz, W., Wurts, L., Kruk, M.E., Mgomella, G.S., Ntalazi, F., Tulenko, K., 2012. Preferences for working in rural clinics among trainee health professionals in Uganda: a discrete choice experiment. BMC Health Serv. Res. 12, 212.
Ryan, M., 2004. Discrete choice experiments in health care. BMJ 328, 360–361.
Ryan, M., Bate, A., Eastmond, C., Ludbrook, A., 2001. Use of discrete choice experiments to elicit preferences. Quality Health Care 10, i55–i60.
Scalone, L., Mantovani, L.G., Borghetti, F., Von Mackensen, S., Gringeri, A., 2009. Patients', physicians', and pharmacists' preferences towards coagulation factor concentrates to treat haemophilia with inhibitors: results from the COHIBA Study. Haemophilia 15, 473–486.
Scott, A., Bond, C., Inch, J., Grant, A., 2007. Preferences of community pharmacists for extended roles in primary care: a survey and discrete choice experiment. Pharmacoeconomics 25, 783–792.
Seston, E.M., Ashcroft, D.M., Griffiths, C.E., 2007a. Balancing the benefits and risks of drug treatment: a stated-preference, discrete choice experiment with patients with psoriasis. Arch. Dermatol. 143, 1175–1179.
Seston, E.M., Elliott, R.A., Noyce, P.R., Payne, K., 2007b. Women's preferences for the provision of emergency hormonal contraception services. Pharm. World Sci. 29, 183–189.
Tinelli, M., Ryan, M., Bond, C., 2009. Patients' preferences for an increased pharmacist role in the management of drug therapy. Int. J. Pharm. Pract. 17, 275–282.
Vass, C., Gray, E., Payne, K., 2016. Discrete choice experiments of pharmacy services: a systematic review. Int. J. Clin. Pharm. 38, 620–630.
Wang, J., Hong, S.H., Meng, S., Brown, L.M., 2011. Pharmacists' acceptable levels of compensation for MTM services: a conjoint analysis. Res. Social Adm. Pharm. 7, 383–395.
Wanishayakorn, T., Sornlertlumvanich, K., Ngorsuraches, S., 2016. Benefit-risk assessment of HMG-CoA reductase inhibitors (statins): a discrete choice experiment. BMJ Open 6, e009387.

Wellman, G.S., Vidican, C., 2008. Pilot study of a hierarchical Bayes method for utility estimation in a choice-based conjoint analysis of prescription benefit plans including medication therapy management services. Res. Social Adm. Pharm. 4, 218–230.
Whitty, J.A., Kendall, E., Sav, A., Kelly, F., Mcmillan, S.S., King, M.A., Wheeler, A.J., 2015. Preferences for the delivery of community pharmacy services to help manage chronic conditions. Res. Social Adm. Pharm. 11, 197–215.

Further Reading

Bech, M., Gyrd-Hansen, D., 2005. Effects coding in discrete choice experiments. Health Econ. 14, 1079–1083.
de Bekker-Grob, E.W., Ryan, M., Gerard, K., 2012. Discrete choice experiments in health economics: a review of the literature. Health Econ. 21, 145–172.
Janssen, E.M., Hauber, A.B., Bridges, J.F., 2018. Conducting a discrete-choice experiment study following recommendations for good research practices: an application for eliciting patient preferences for diabetes treatments. Value Health 21, 59–68.
Lakdawalla, D.N., Doshi, J.A., Garrison, L.P., Phelps, C.E., Basu, A., Danzon, P.M., 2018. Defining elements of value in health care—a health economics approach: an ISPOR Special Task Force report [3]. Value Health 21, 131–139.
Mangham, Lindsay J., Hanson, Kara, Mcpake, Barbara, 2009. How to do (or not to do) . . . Designing a discrete choice experiment for application in a low-income country. Health Policy Plann. 24, 151–158.
Ryan, M., Gerard, K., Amaya-Amaya, M. (Eds.), 2008. Using Discrete Choice Experiments to Value Health and Health Care. Springer.
Tockhorn-Heidenreich, A., Ryan, M., Hernández, R., 2017. Discrete Choice Experiments. In: Facey, K., Ploug Hansen, H., Single, A. (Eds.), Patient Involvement in Health Technology Assessment. Adis, Singapore.
Vanniyasingam, T., Daly, C., Jin, X., Zhang, Y., Foster, G., Cunningham, C., Thabane, L., 2018. Investigating the impact of design characteristics on statistical efficiency within discrete choice experiments: a systematic survey. Contemp. Clin. Trials Comm. 10, 17–28.
Vass, C., Rigby, D., Payne, K., 2017. The role of qualitative research methods in discrete choice experiments: a systematic review and survey of authors. Med. Decis. Making 37, 298–313.
Vass, C.M., Payne, K., 2017. Using discrete choice experiments to inform the benefit-risk assessment of medicines: are we ready yet? PharmacoEcon 35, 859–866.
Viney, R., Lancsar, E., Louviere, J., 2002. Discrete choice experiments to measure consumer preferences for health and healthcare. Expert Rev. Pharm. Out 2, 319–326.
Viney, R., Savage, E., Louviere, J., 2005. Empirical investigation of experimental design properties of discrete choice experiments in health care. Health Econ. 14, 349–362.

List of Relevant Web Pages

Discrete Choice Experiment (DCE) [online], 2016. York; York Health Economics Consortium; 2016. http://www.yhec.co.uk/glossary/discrete-choice-experiment-dce/.
Boomer G. Introduction to Experimental Design for Discrete-Choice Models. http://www.statwizards.com/sites/default/files/files/introduction_to_experimental_design_for_discrete-choice_models.pdf.

Quality of Qualitative Research

Muhammad Abdul Hadi*, Theo Ansong†, Josie Solomon†, *School of Pharmacy, Institute of Clinical Sciences, University of Birmingham, Birmingham, United Kingdom; †Leicester School of Pharmacy, University of Lincoln, Lincoln, United Kingdom

© 2019 Elsevier Inc. All rights reserved.

Chapter Overview

This chapter focuses on, perhaps, the most debated issue among research methodologists-quality assurance of qualitative research. Unlike existing literature, which either focuses on the process-oriented approach or the output-oriented approach, this chapter provides a comprehensive review of both approaches. This chapter begins with an introduction section, which provides an overview of the issue of quality in qualitative research. The first half of the chapter focuses on process-oriented approach and various strategies/tools that can be used to ensure quality. The second half focuses on output-oriented approach and highlights advantages and disadvantages of the two most commonly used checklists developed to improve quality of reporting of qualitative research. The chapter has been divided in various subsections to improve the readability and flow.

Introduction

Like any other research methodology, quality is of critical importance in qualitative research and this is to ensure that the qualitative research is credible and dependable. The reasons that make issue of quality in qualitative research complicated are multifaceted. These include: the diversity in research methods available under the umbrella term of qualitative research methodology; multiplicity of viewpoints available in literature on the issue of "quality" and lack of clear and explicit guidance in simple language understandable to health-care researchers undertaking qualitative research, and the very nature of health-care researchers-who are fundamentally trained with "quantitative" mindset, often find it difficult to transit to "qualitative" mindset and truly embrace the philosophy of qualitative research. Furthermore, health-care researchers have "borrowed" qualitative research methods from social science disciplines, and therefore, the understanding of what constitutes a good qualitative research may vary across these disciplines.

Reynolds et al. (2011) reviewed literature debating various issues related to quality assurance of qualitative research and found two dominant, yet contrasting, approaches to quality assurance in qualitative research, process-oriented approach and

output-oriented approach. The process-oriented approach, epistemologically linked to interpretive/constructionist approach, is based on the internal set of values or principles of "best practices" inherent to qualitative research. The authors identified six principles of process-oriented approach: reflexivity in terms of researcher's epistemological position, assumptions, and practice; detailed description of decisions made, and assumptions supported; comprehensiveness of approach to research question; responsibility toward decision making throughout the research process; adherence to good ethical practices; and a methodical approach in designing and conducting the study (Reynolds et al., 2011). On the other hand, output-oriented approach is drawn from positivist or post-positivist paradigm. It advocates the use of certain techniques, often in the form checklists, and demonstrating their use is considered an indicator of quality.

In this chapter, we will discuss the issue of quality in qualitative research based on these two narratives proposed by Reynolds et al. (2011).

Process-Oriented Approach: Practices to Ensure Rigour and Trustworthiness

Given the theoretical and philosophical differences between qualitative and quantitative methodologies, applying the same quality criteria of validity and reliability across both research methodologies is unjustified. Therefore, instead of using quantitative terms such as reliability, internal validity, objectivity, and generalizability; the use of alternative qualitative equivalent terminologies such as dependability, credibility, conformability, and transferability, respectively, is advocated to describe rigor and trustworthiness in qualitative research (Lincoln and Guba, 1985; Noble and Smith, 2015).

Methodologists have developed several strategies to ensure trustworthiness of qualitative research. It is not expected that the researcher would engage with all these strategies in a single study as it will not be always either practical or possible to engage with of all them. However, it has been recommended that at least two of these strategies should be used in a particular qualitative study (Creswell, 2006). A brief description of commonly used strategies is given below.

Triangulation

Triangulation aims to reduce bias typically associated with single data source and/or method by using at least two different but related data sources, data collection methods, or researchers. It is frequently used to ensure credibility and conformability of qualitative studies (Creswell, 2006) as it helps researchers to ascertain the validity of the interpretations derived from different data sources. For example, a researcher who is interested to understand barriers to medication adherence among patients with long-term conditions may consider interviewing both patients and their health-care providers. The researcher then draws themes after analyzing and integrating data from both datasets.

Self-Description/Reflexivity

Self-description also referred as self-reflection is perhaps the most important tool not only to acknowledge but also to reduce researcher bias. Self-description allows qualitative researchers to explain their epistemological position, personal beliefs in relation to the research topic, field experiences, and previous research and/or professional training and how these things might have influenced the research findings (Hammersley and Atkinson, 1995; Long and Johnson, 2000). To recognize and disclose any personal bias, it has been suggested that the qualitative researchers should make field notes and maintain a reflective journal (Long and Johnson, 2000). Self-reflection ensures credibility and conformability of research findings.

Member Checking

Member checking, also known as respondent validation, is considered in the literature as the single most important method to ensure a study's credibility (Lincoln and Guba, 1985). Member checking involves checking of various, but not all, steps of data collection, analysis, and interpretation by the study participants from whom the data were originally collected (Long and Johnson, 2000). For example, a researcher using member checking technique may take themes emerged from the analysis of focus group interviews back to the participants of a particular focus group and discuss if the themes resonate their experiences/views. Member checking can ensure dependability and credibility of qualitative research. However, member checks should not be used as a verification strategy to judge the "truth" in data analysis. Researchers should also be very careful in accommodating respondent's views as this method can alter researcher's interpretation and may make findings descriptive.

Prolonged Engagement

Given the nature of qualitative research, establishing rapport with respondents and gaining their trust are critical to obtain in-depth information from the respondents. Prolonged engagement with respondents and community aims to do that and will help researcher to study the research topic more comprehensively (Creswell, 2006). Prolonged engagement may promote the credibility of a qualitative study. Typically used in ethnography, prolonged engagement involves spending sufficient time in the field observing different social, political, and economic constructs of a culture/society, engaging with diverse group of people, and developing

relationships with members of the culture with an aim to understand and appreciate the culture, social setting, or phenomenon of interest beyond personal preconceptions (Creswell, 2006).

Audit Trail

Audit tail involves providing detailed description of all the steps (data collection, analysis, and interpretation) and decisions made during the course of the study. This will facilitate readers to make their own personal judgments about the rigor, trustworthiness, and worth of a study (Sandelowski, 1986).

Peer Debriefing

Peer debriefing is another commonly used technique in qualitative research. In peer-debriefings, the researcher holds regular meetings with a peer throughout the research process and discusses the research methodology, data analysis, and interpretations (Lincoln and Guba, 1985). Ideally, a typical peer is someone who is not directly involved in the research and is an experienced qualitative researcher who can not only stimulate critical thinking but also can ask questions about the researcher's interpretations. Research supervisors/mentors can act as "peers" for their research students. Presenting research findings to interested groups and at conferences can also provide alternative forms of peer debriefing. Peer debriefing is also known as "analytic triangulation" (Nguyen, 2008).

Thick Description

Thick description refers to providing detailed description about settings, inclusion/exclusion criteria, sample characteristics, and data collection and analysis methods. This will enable the readers to evaluate the extent to which authors' conclusions are transferable to other external settings and different populations. Thick description is the most important tool to ensure external validity (transferability) of qualitative research (Long and Johnson, 2000). It also promotes study credibility as well.

Output-Oriented Approach: Quality of Reporting of Qualitative Research

Increasing numbers of qualitative research are being published by journals as a contribution to understanding of decisions and behaviors not only of patients but also of the health-care professionals involved in their care (Morse, 2015). The increased acceptance and publication of qualitative research is a reflection of the wide variety of qualitative methodologies and the maturity of the associated methods (Sidhu et al., 2017). In spite of this expansion, qualitative research is still viewed negatively by some journal editors as it was noted in an editors' meeting of the *British Medical* Journal. The editors argued in favor to effectively restrict publication of research aligned to the qualitative research philosophy (Greenhalgh et al., 2016; Loder et al., 2016).

Sidhu et al. (2017) argued that the current negative views about qualitative research may be overcome by ensuring that authors adhere to acceptable reporting standards. In particular, they mentioned that in addition to appropriately framing the research question in relation to existing evidence base, it is also important to make due consideration to the contribution of the research to clinical practice through the research process and the completeness and clarity of how this is being reported within the criteria imposed by relevant medical journals (Sidhu et al., 2017).

Significance of Quality of Reporting to Stakeholders

It has been highlighted that incomplete or unclear write-up reporting of qualitative research can largely contribute to rejection of papers. This, in turn, leads to the lack of dissemination of new knowledge and insights that could influence practice (Blignault and Ritchie, 2009). In addition, poorly designed studies make it difficult for users to assess the research findings and may lead to adoption and incorrect changes to health-care practice (Tong et al., 2007). It is important for authors to present clear and transparent research so that the readers can understand the process of research and how credible the findings are for adoption. Moher et al. (2014a,b) asserted that researchers have an ethical responsibility to provide a clear and accurate report of their research.

Appropriate and clear reporting of the research process and its outcome contributes to the establishment of rigor and credibility of qualitative research through demonstration of transparency (Malterud, 2001). Transparency of the research process and its findings is necessary to help stakeholders make appropriate judgments about how to identify and use the new knowledge.

Reporting Guidelines

The problem of incomplete reporting of qualitative research has led to the development of criteria, which guide authors while preparing and submitting qualitative papers. Simera et al. (2010) while writing about Enhancing the Quality and Transparency of Health Research Network (EQUATOR) described reporting guidelines as minimum set of required items (in the form of a checklist or flow diagram). These items provide advice on how to report research methods, results, and issues, which may contribute to bias in research.

The development of appropriate and relevant reporting guidelines is important for several reasons:

1. Availability of reporting guidelines enable authors to provide the necessary information required by journal editors.
2. Knowledge of established guidelines enables these to be taken account during the planning and execution of the research study.
3. Reviewers have the benefit of a uniform set of standards for comparability of submitted manuscripts.
4. There is improved appraisal of qualitative evidence synthesis due to the enhanced quality of reports available.
5. The guidelines can help peer reviewers to assess manuscripts for suitability and quality.
6. Editors can refer to existing reporting standards or develop specific guidelines, which contributes to accuracy, clarity, and transparency in the reporting of the qualitative research.
7. Meeting reporting standards will provide confidence to users of research such as health-care professionals, and it will enable them to adopt these findings into practice.
8. Stringent reporting standards provide the research community with assurance that qualitative research has appropriate scientific rigor.

Reporting Guidelines: Do They Improve Quality?

The development and promotion of reporting guidelines by editors and researchers is widely advocated. This may be a recognition that reporting guidelines are proving effective in improving the transparency and rigour in the way the design and procedures of research are communicated. A Cochrane review of the impact of the CONSORT statement indicates that the adoption of reporting guidelines contributed modestly to improvement in transparency of reporting (Turner et al., 2012). Many believe that the development and promotion of reporting guidelines for qualitative research will follow a similar pattern (The Equator Network).

Altman and Moher (2014) described a growing recognition that the adoption of reporting guidelines is effective in communication of research methods and findings. It is therefore important that researchers are encouraged to adopt reporting guidelines appropriate to their type of study as it would help improve transparency in research. In this regard, editors have an important role to play by demanding full and transparent reporting (Altman and Simera, 2010).

Concerns about the existence of checklists for reporting guidelines have been raised in that they may appear overly prescriptive thereby promoting overuse. There is a risk that without a broader understanding of the qualitative research design and data analysis, the unique contribution of qualitative research to health services research may be compromised (Barbour, 2001).

Mcleroy et al. (2016) make it clear that the primary purpose of reporting guidelines is to help readers to understand the published research by enhancing transparency. They are not intended to define how the research itself is conducted, nor are they meant to be used to evaluate the quality of the study per se. Smith et al. (2018) also states that the most appropriate reporting guidelines must be selected based on the relevant qualitative methodology guiding the study.

Common Reporting Guidelines for Qualitative Research

Guidelines for conduct and reporting of quantitative research have long existed to improve quality and allow understanding of various aspects of the respective research types. In recent years, there has been a proliferation of reporting different kinds of guidelines for qualitative research studies. However, the Consolidated Criteria for Reporting Qualitative Research (COREQ) developed by Tong et al. (2007) and Standards for Reporting Qualitative Research (SRQR) (O'Brien et al., 2014) are two key guidelines widely adopted for evaluating the quality of reporting of qualitative research. Consolidated Criteria for Reporting Qualitative Research (COREQ) is a set of reporting guidelines consisting of 30 items, which is meant to enhance comprehensiveness of reporting of interviews and focus group studies. SRQR, on the other hand, is a 21-item framework, which was developed through the input of international experts to act as standards for accurate reporting of a variety of qualitative studies.

Another widely used reporting guideline is the Enhancing Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ) (Tong et al., 2012). The ENTREQ statement (framework) consists of 21 items grouped into five domains (Introduction, Methods and Methodology, Literature Search and Selection, Appraisal, and Synthesis of Findings). ENTREQ is useful to students and researchers on how to conduct and assess the synthesis of multiple qualitative health research studies (Tong et al., 2012). Notably, the framework has not undergone a Delphi exercise, a fundamental step in guideline development. This means that it has only fulfilled the first criterion for guideline development (Flemming et al., 2018). Users are advised to be mindful of this limitation.

There are other reporting guidelines for qualitative research studies that have been developed for specific health-care areas and other forms of interventions. The Enhancing the Quality and Transparency of Health Research (Equator) Network is an international initiative that seeks to promote accurate reporting of research through wider use of reporting guidelines thereby enhancing the value of research (*The Equator Network*). The EQUATOR website has a compilation of reporting guidelines for qualitative and other types and forms of research. In addition, it disseminates regular online newsletters highlighting new reporting guidelines and organizes workshops and courses to support the adoption and use of the resources listed on its website (Simera et al., 2010).

In addition to the above, specific guidelines have been developed by respective journals to ensure standardization of qualitative research manuscripts for peer review and publication. For example, The American Pharmaceutical Education journal (Anderson, 2010) has developed criteria to be used by authors for reporting their research. On the other hand, some journals and publications such as Biomed Central, BMJ, and Journal of Advanced Nursing advised authors to follow acceptable reporting guidelines for the respective type of study (e.g., COREQ, SRQR) as recommended by repositories such as the EQUATOR network.

Consolidated Criteria for Reporting Qualitative Research

COREQ is a 32-item checklist developed by Tong et al. (2007) for evaluating the comprehensiveness of reporting of qualitative studies. It does not purport to set standards for conducting qualitative research and it is mainly focussed on studies reporting focus groups and interviews. The development of COREQ is based on a systematic literature review and identifying items published within other tools and checklists for qualitative research studies.

Development of the COREQ Checklist

The authors searched electronic databases (CINAHL, MEDLINE), Cochrane, and Campbell protocols, including author and reviewer guidelines of major medical journals and reference lists of relevant publications for guidelines and checklists used to evaluate qualitative studies. After excluding duplicate checklists, criteria for assessing and reporting qualitative studies from each of the studies were extracted to give a comprehensive list of 72 items from 22 checklists (Tong et al., 2007). The items were grouped into three domains with duplicates removed and a descriptor was attached to each item to promote clarity (**Table 1**). Two new items: "identifying the authors who conducted the interviews or focus group" and "presence of nonparticipants" were considered relevant for reporting qualitative research by consensus and therefore included to make a final list of 32 items.

Uses and Benefits of COREQ

COREQ offers the following benefits:

1. COREQ can be used by editors and reviewers in the assessment of qualitative research manuscripts prior to publication.
2. It can be used to evaluate the validity and transferability of the findings from qualitative research reports.
3. It can be used as a form of standardization for researchers undertaking qualitative evidence synthesis and systematic reviews.
4. The popular application of COREQ as indicated by recommendations of journal editors and other members of the research community despite the absence of specific empirical validation gives an indication that it serves as a useful tool for comprehensive and accurate reporting of qualitative studies. Subsequently, there has been an increase in number of papers published in the BMJ and BioMed Central group journals by adhering to these guidelines.
5. The authors of COREQ suggest that although it was developed based on interviews and focus groups, it may still be used for other qualitative research methods.

Limitations of COREQ

1. The development of COREQ was based on interviews and focus groups, and therefore, its value may be more limited when used for other qualitative methodologies.
2. The absence of Delphi studies or consensus meetings in the development of COREQ appears to have limited its rate of adoption and acceptability.
3. The tool has not been validated to provide an empirical confirmation that it is likely to improve the quality of reporting of qualitative studies. However, the authors contend that the effect is likely to be similar to when other guidelines such as CONSORT was introduced and has subsequently been found to have improved the quality of reporting of the specific study type (Moher et al., 2001).
4. The slow development of extensions to the COREQ tool may arise from the absence of empirical validation and a lack of international consensus on uniform criteria for qualitative research.

Standards for Reporting Qualitative Research

SRQR is a 21-item checklist (**Table 2**) of clear reporting standards which is aimed at improving the transparency of all aspects of qualitative research (O'Brien et al., 2014). It was formulated through a systematic approach of rigorous synthesis of previously published guidelines followed by expert recommendations. Key elements of each item are defined and explained by the authors including providing examples from published articles (O'Brien et al., 2014).

Development of the Standards

The authors of SRQR identified previously proposed recommendations by systematically reviewing PubMed, Web of Science, and Google and by reviewing the reference list of the retrieved sources. A comprehensive list of items that were potentially important in reporting qualitative research was initially generated, which was then refined to a shorter list by identifying core concepts and combining related items.

The shorter list was then compared with the original sources to check for missing concepts and then appropriate explanatory definitions were included. The resulting prefinal list was reviewed by five experienced qualitative researchers for omitted or redundant items and to suggest improvement in clarity and relevance. Following the expert review, a final set of reporting standards was created by consolidating some items and making amendments to the wording of some labels and definitions (O'Brien et al., 2014).

Table 1 Domains and items in the COREQ list

	Details of item	*Guide questions/Descriptions*
Domain 1—research team and reflexivity		
Personal characteristics		
1.	Interviewer/Facilitator	Which author(s) conducted the interview or focus group?
2.	Credentials	What were the researcher's credentials? For example, PhD, MD.
3.	Occupation	What was their occupation at the time of the study?
4.	Gender	Was the researcher male or female?
5.	Experience and training	What experience or training did the researcher have?
Relationship with Participants		
6.	Relationship established	Was a relationship established prior to study commencement?
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? For example, personal goals, reason for doing the research.
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? For example, bias, assumptions, reasons, and interests in the research.
Domain 2—study design		
Theoretical framework		
9.	Methodological orientation and theory	What methodological orientation was stated to underpin the study? For example, grounded theory, discourse analysis, ethnography, phenomenology, content analysis.
Participant selection		
10.	Sampling	How were participants selected? For example, purposive, convenience, consecutive, snowball.
11.	Method of approach	How were participants approached? For example, face to face, telephone, mail, email.
12.	Sample size	How many participants were in the study?
13.	Nonparticipation	How many people refused to participate or dropped out? Reasons?
Setting		
14.	Setting of data collection	Where was the data collected? For example, home, clinic, workplace.
15.	Presence of nonparticipants	Was anyone else present beside the participants and researchers?
16.	Description of sample	What are the important characteristics of the sample? For example, demographic data, date.
Data collection		
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?
18.	Repeat interviews	Were repeat interviews carried out? If yes, how many?
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data?
20.	Field notes	Were field notes made during and/or after the interview or focus group?
21.	Duration	What was the duration of the interviews or focus group?
22.	Data saturation	Was data saturation discussed?
23.	Transcripts returned	Were transcripts returned to participants for comments or corrections?
Domain 3—analysis and findings		
Data analysis		
24.	Number of data coders	How many data coders coded the data?
25.	Description of the coding tree	Did authors provide a description of the coding tree?
26.	Derivation of themes	Were themes identified in advance or derived from the data?
27.	Software	What software, if applicable, was used to manage the data?
28.	Participant checking	Did participants provide feedback on the findings?
Reporting		
29.	Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? For example, participant number.
30.	Data and findings consistent	Was there consistency between the data presented and the findings?
31.	Clarity of major themes	Were major themes clearly presented in the findings?
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?

Source: Adapted from Tong, A., Sainsbury, P., Craig, J., 2007. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int. J. Qual. Health Care, 19 (6), 349-357.

Table 2 Standards for reporting qualitative research (SRQR)[a]

	Topic	*Item*
Title and abstract		
S1	Title	Concise description of the nature and topic of the study, identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory), or data collection methods (e.g., interview, focus group) are recommended.
S2	Abstract	Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions
Introduction		
S3	Problem formulation	Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement
S4	Purpose or research question	Purpose of the study and specific objectives or questions
Methods		
S5	Qualitative approach and research paradigm	Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale[b]
S6	Researcher characteristics and reflexivity	Researchers' characteristics that may influence the research, including personal attributes, qualifications/ experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability
S7	Context	Setting/site and salient contextual factors; rationale[b]
S8	Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale[b]
S9	Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues
S10	Data collection methods	Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale[b]
S11	Data collection instruments and technologies	Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study
S12	Units of study	Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)
S13	Data processing	Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/deidentification of excerpts
S14	Data analysis	Process by which inferences, themes, etc., was identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale[b]
S15	Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale[b]
Results/findings		
S16	Synthesis and interpretation	Main findings (e.g., interpretations, inferences, and themes) might include development of a theory or model or integration with prior research or theory
S17	Links to empirical data	Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings
Discussion		
S18	Integration with prior work, implications, transferability, and contribution(s) to the field	Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field
S19	Limitations	Trustworthiness and limitations of findings
Other		
S20	Conflicts of interest	Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed
S21	Funding	Sources of funding and other support; role of funders in data collection, interpretation, and reporting

[a]The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

[b]The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available; the assumptions and limitations implicit in those choices; and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Source: Adapted from O'Brien, B., et al., 2014. Standards for Reporting Qualitative Research: A Synthesis of Recommendations. Acad. Med. 89 (9), 1245-1251.

Uses and Benefits of SRQR

1. The twenty one standards provide users with a framework and recommendations for comprehensive reporting of qualitative studies.
2. The standards can assist users during preparation of their manuscripts to meet requirements of editors and other reviewers for complete reporting of qualitative research.
3. Journal editors, funding organizations, and other members of the research community may find SRQR useful in relation to standardization of clarity and completeness of reporting of qualitative research studies.
4. The authors identified items with broad relevance in an attempt to cover the wide range of qualitative approaches and methodologies.
5. The framework is robust because it is based on previously published criteria, critical review by experts, and wide-ranging experience and perspectives among its authors.
6. Descriptions and examples of how the framework can be used have been supplied by the authors to enable researchers to use these standards.
7. A checklist for reporting standards such as SRQR can help advance qualitative research methodologies by enhancing transparency in the research process and its findings.

Limitations of SRQR

1. The authors of SRQR advise that it may be inappropriate to use the framework to assess the quality of research methods and findings. This follows from the deliberate avoidance of recommendations that define methodological rigour during the development of the framework.
2. The diverse range of qualitative research approaches may lead some users to be critical of the suitability of a consolidated framework for evaluating different types of qualitative studies. This could limit its usefulness among a section of the research community.

Conclusion

In conclusion, both process- and output-oriented approaches should be considered while designing, conducting, and reporting qualitative research. For novice researchers, engaging with literature of appropriate quality, getting formal training in undertaking qualitative research, and working with a senior qualitative researcher can facilitate good quality qualitative research. No single checklist is applicable to all forms of qualitative research. Checklist gives reporting so transparency in order to enable the quality of the research, but a high score intensified does not necessarily indicate high quality research, nor would getting a lower score necessarily indicate poor quality research. Engagement with reporting checklists in early stages of designing qualitative studies can help researchers ensure quality in qualitative work.

References

Altman, D.G., Simera, I., 2010. Responsible reporting of health research studies: transparent, complete, accurate and timely. J. Antimicrob. Chemother. 65 (1), 1–3.
Anderson, C., 2010. Presenting and evaluating qualitative research. Am. J. Pharmaceut. Educ. 74 (8), 141.
Barbour, R.S., 2001. Checklists for improving rigour in qualitative research: a case of the tail wagging the dog? BMJ 322 (7294), 1115–1117.
Blignault, I., Ritchie, I., 2009. Revealing the wood and the trees: reporting qualitative research. Health Promot. J. Aust. 20 (2), 140–145.
Creswell, J.W., 2006. Qualitative Inquiry and Research Design: Choosing Among Five Approaches, 2nd edition. Sage, Thousand Oaks, CA.
Flemming, K., et al., 2018. Cochrane Qualitative and Implementation Methods Group guidance series-paper 6: reporting guidelines for qualitative, implementation, and process evaluation evidence syntheses. J. Clin. Epidemiol. 97, 79–85.
Greenhalgh, T., et al., 2016. An open letter to The BMJ editors on qualitative research. BMJ 352, i563.
Hammersley, M., Atkinson, P., 1995. Ethnography: Principles in Practice, 2nd edition. Routledge, London.
Loder, E., et al., 2016. Qualitative research and The BMJ. BMJ 352, pi641.
Long, T., Johnson, M., 2000. Rigour, reliability and validity in qualitative research. Clin. Effective Nurs. 4, 30–37.
Lincoln, Y.S., Guba, E.G., 1985. Naturalistic Inquiry. Sage, Beverly Hills, CA.
Malterud, K., 2001. Qualitative research: standards, challenges, and guidelines. The Lancet 358 (9280), 483–488.
Mcleroy, K.R., et al., 2016. Scientific reporting: raising the standards. Health Educ. Behav. 43 (5), 501–508.
Moher, D., et al., 2014a. Importance of Transparent Reporting of Health Research. In: Guidelines for Reporting Health Research: A User's Manual. John Wiley & Sons, Ltd, Oxford, UK, pp. 1–13.
Moher, D., et al., 2001. Use of the CONSORT statement and quality of reports of randomized trials: a comparative before-and-after evaluation. JAMA 285 (15), 1992–1995.
Moher, D., et al., 2014b. Reducing waste from incomplete or unusable reports of biomedical research. Lancet 383 (9913), 267–276.
Morse, J.M., 2015. Qualitative health research: one quarter of a century. Qual. Health Res. 25 (1), 3–4.
Nguyen, T.S.T., Peer debriefing. The Sage Encyclopedia of Qualitative Research Methods. 2008. Available from: http://srmo.sagepub.com/view/sage-encyc-qualitative-research-methods/n312.xml.
Noble, H., Smith, J., 2015. Issues of validity and reliability in qualitative research. Evid. Based Nurs. 18, 34–35.
O'Brien, B., et al., 2014. Standards for reporting qualitative research: a synthesis of recommendations. Acad. Med. 89 (9), 1245–1251.

Reynolds, J., Kizito, J., Ezumah, N., Mangesho, P., Allen, E., Chandler, C., 2011. Quality assurance of qualitative research: a review of the discourse. Health Res. Policy Syst. 9, 43.
Sandelowski, M., 1986. The problem of rigor in feminist research. Adv. Nurs. Sci. 8, 27–37.
Sidhu, K., Jones, R., Stevenson, F., 2017. Publishing qualitative research in medical journals. Br. J. Gen. Pract. 67 (658), 229–230.
Simera, I., et al., 2010. Transparent and accurate reporting increases reliability, utility, and impact of your research: reporting guidelines and the EQUATOR Network. BMC Med. 8 (1), 24.
Smith, G.D., et al., 2018. The position of reporting guidelines in qualitative nursing research. J. Clin. Nurs. 27 (5-6), 889–891.
The Equator Network, 2001. Available from: http://www.equator-network.org.
Tong, A., et al., 2012. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. BMC Med. Res. Methodol. 12 (1), 181.
Tong, A., Sainsbury, P., Craig, J., 2007. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int. J. Qual. Health Care 19 (6), 349–357.
Turner, L., et al., 2012. Does use of the CONSORT Statement impact the completeness of reporting of randomised controlled trials published in medical journals? A Cochrane review. Syst. Rev. 1, 60.

Further Reading

Morse, J.M., et al., 2002. Verification strategies for establishing reliability and validity in qualitative research. Int. J. Qual. Methods 1, 13–22.

Clinical Pharmacists as Principal Investigators in Clinical Trials

Sheraz Ali[*,§], **Dimitrios Karakitsos**[†,‡], [*]Institute of Biomedicine, University of Eastern Finland, Kuopio, Finland; [†]University of Southern California, Los Angeles, CA, United States; [‡]King Saud Medical City, Ministry of Health, Riyadh, Kingdom of Saudi Arabia; [§]Ministry of Health, Riyadh, Kingdom of Saudi Arabia

© 2019 Elsevier Inc. All rights reserved.

Introduction

Clinical research is a multidisciplinary endeavor that follows a collaborative approach to promote advances in health care (VanWormer et al., 2012). The extent to which clinical trials are conducted is a reflection of the level of advancement that exists within a health care system. Clinical trials are conducted on human volunteers in a prospective manner to ascertain the effectiveness and safety of investigational products, such as drugs and devices; clinical trials data eventually serve to optimize patient care. Clinical trials are typically conducted in four phases [**Table 1**] (U.S. National Library of Medicine, 2018). Randomized controlled trials are the gold standard in the spectrum of clinical research; they ascertain the effects of interventions and possess a higher place in the hierarchy of evidence (Burns et al., 2011). Clinical trials are usually conducted by collaborative efforts of the principal investigator (PI) or investigator, subinvestigator, pharmacist, physician/dentist, research nurse, clinical research coordinator and clinical research associate or monitor. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice Guidelines (ICH-GCP) defined an investigator as "a person responsible for the conduct of the clinical trial at a trial site." If a trial involves several individuals at a study site, one individual is designated as a PI and will therefore be the responsible team leader (ICH, 2016).

It is imperative for the research team to maintain the credibility of clinical trials by protecting the rights, safety and well-being of the study volunteers (ICH, 2016). After the adoption of the Kefauver Harris Amendment in 1962 by US Food and Drug Administration (US FDA), pharmaceutical sponsors are required to submit both efficacy and safety data of drugs to obtain regulatory approvals (Kay et al., 2018). This major development was a result of human tragedy that occurred due to the use of thalidomide in pregnant women, which, in turn, prompted the US FDA to amend the Federal Food, Drug, and Cosmetic Act. The American Society of Health-System Pharmacists (ASHP) highlights the role of pharmacists in the management of investigations and approving drugs in a clinical trial and/or a routine clinical care setting. Moreover, their presence in a clinical research team is crucial for executing successful research projects (ASHP, 2016; Kay et al., 2018).

The ICH-GCP, the American College of Clinical Pharmacy (ACCP), and the research guidelines issued by the ASHP uphold the participation of trained and experienced pharmacists as PIs in clinical trials. The provision of educational sessions and monitoring of investigational drugs are deemed core components of drug trials, whereas pharmacists are also best suited to perform these functions (ASHP, 2016; Kay et al., 2018).

The credit of conducting the first ever controlled clinical trial of the modern era is given to physician Dr. James Lind. This clinical trial was conducted in 1747 to ascertain the cure of scurvy (Bhatt, 2010).

Ethics in Clinical Trials

There have been several cases of unethical practices when patients' rights, safety and well-being were not taken into consideration by physicians, eventually resulting in the reporting of fatalities. For example, the Tuskegee syphilis study (1932–72), Nazi medical experiments (1939–45), and the thalidomide tragedy (1960s) are well-known historical events in clinical research. In addition, the

Table 1 Phases of clinical trials

Phase	*Objective*	*Questions*	*Typical number of subjects*
I (or first-in-man studies)	Safety	Evaluated parameters: Dose, frequency, route, pharmacokinetics and pharmacodynamics	20–100
II	Efficacy and safety	To assess efficacy and define therapeutic dose range and dosing regimen. Further information on safety, pharmacokinetics and pharmacodynamics	50–300
III	Confirmation of efficacy and safety	To assess treatment outcomes and compare investigational drug with an approved treatment or placebo	100–1000
IV	Post marketing surveillance, effectiveness of drug, and impact on quality of life	To evaluate long-term effects of drugs (efficacy, safety, and side effects) in a large number of population and explore new indications	1000

aforementioned incidents prompted the emergence of ethical principles that were included in the Nuremberg Code, the Belmont Report, and the Declaration of Helsinki.

The ICH-GCP remains a vital document for conducting clinical trials. Several regulatory authorities, including the European Medicines Agency and the FDA, endorse the GCP as a unified document for conducting ethically and scientifically sound clinical trials. These guidelines are followed for designing, conducting, recording and reporting clinical trials involving human volunteers. The first version of the ICH harmonized guideline, E6 (R1), was released in 1996, and its amended version, E6 (R2), was recently released in November 2016 (ICH, 2016). Sponsors have a mandate to select the study investigators by assessing the statement of investigators, Form FDA 1572, which is utilized to acquire qualification and experience details. Form FDA 1572 is only required for studying investigational new drugs; this form is not employed for investigational device studies where a signed investigator agreement is collected (FDA, 2010). Investigators are permitted to initiate clinical trials (phases I–IV) after the submission of Form FDA 1572, and approval is at the discretion of the study sponsors. However, the requirement of this form is specifically for studies that are conducted under the US Investigational New Drug Application (IND); this form is also mandatory when an IND study is conducted outside the territory of the US, while foreign clinical studies are typically not conducted under an IND. Furthermore, postmarketing and observational studies are exempted from the requirement of Form FDA 1572. Investigators comply with the GCP and other requirements of regulatory authorities that are crucial for promoting the subject's safety and successful execution of clinical trials. The selection of a clinical pharmacist as a PI is subject to the inclusion of a doctor (or dentist, when appropriate) as a subinvestigator (FDA, 2010).

Health care professionals should familiarize themselves with principles and guidelines such as the ICH-GCP, the Nuremberg Code, the Belmont Report, and the Declaration of Helsinki. These ethical considerations are of paramount importance in clinical trials to develop safe and effective medications. As of December 2017, more than 250,000 clinical studies are registered on ClinicalTrials.gov, which is recognized as the oldest and largest registry of clinical trials managed by the National Library of Medicine at the National Institutes of Health in the US Notably, 41% of the clinical studies are registered under the map of the US (U.S. National Library of Medicine, 2017).

Roles and Responsibilities of the PI in Clinical Trials

The existence of the PI is a driving force behind the successful execution of clinical trials as per the defined standards and regulations. The diligence of the PI promotes the rights, safety, and well-being of the study subjects. Likewise, investigations involving human subjects are collaborative activities, and the role of the PI as a team leader is inevitable in this regard (Baer et al., 2011; Katz et al., 2011).

PIs must perform several functions, including extensive clinical research documentation, and abide by policies and regulations after the initiation of a trial at the study site. A well-acquainted PI transfers knowledge in an effective way to the entire staff involved in clinical investigations while cultivating a proactive team mind-set and optimizing communication. Moreover, a PI ensures that clinical trial personnel are aware of their responsibilities and comply with the study protocol, hence generating high-quality clinical data. It is a prerequisite for PIs to demonstrate the training and experience required for a clinical program prior to their selection, which is crucial to perform responsibilities in a diligent manner (ICH, 2016). PIs are given adequate time by the sponsor to review the study documents such as the protocol and the investigator's brochure; the investigator's brochure is a document that contains clinical and nonclinical data on the Investigational Medicinal Product (IMP) (ICH, 2016). The following are the core responsibilities of the PI in clinical trials (ICH, 2016; Kay et al., 2018):

- Organizing GCP training

It is a common practice for the study sponsors to provide GCP training to personnel involved in clinical trials. GCP training is conducted either through the specific web portal of the trial, CDs, training sessions and/or workshops.

- Seeking IRB approval

Clinical trials are commenced at the study site after IRB approval. A PI is responsible for submitting all the required documents to the IRB. If the selected PI is a member of the IRB, then he or she will not participate in the decision process or voting. However, any information pertinent to the clinical trial can be provided by the PI to the IRB (ICH, 2016). The PI is also responsible for submitting progress reports to the IRB annually or frequently (when requested); these reports are also submitted to the study sponsor.

- Clinical trial's study file for the PI

Table 2 shows the sections and content of a PI study file provided by the sponsor for conducting a randomized, double-blind placebo-controlled trial. This table is merely used for the guidance of novice PIs and is based on previous experience in multinational clinical trials sponsored by Novartis Oncology, F. Hoffmann-La Roche AG and the London School of Hygiene and Topical Medicine. Section 8 of the ICH-GCP also discusses the essential documents that are used before, during and after the conduct of clinical trials. Data collection should follow previously established guidelines. The concept of ALCOAC (Attributable, Legible, Contemporaneous, Original, Accurate, and Complete) is followed for maintaining high standards in clinical research documentation. ALCOAC is also specified in the joined version of the ICH-GCP under the section entitled "Records and Reports" (ICH, 2016). The US FDA initially introduced the ALCOA concept, which later evolved into ALCOAC (Bargaje, 2011). There is a common saying in clinical trials, "if it wasn't documented, it wasn't done." During audits and inspections, a lack of ALCOAC

Table 2 PI study file index for clinical trials

Section	*Contents*
Inside cover	• Laminated protocol summary • Protocol • CD containing training presentations, data forms and guidance, patient and representative information sheet, consent form, adverse event form, screening log, randomization log, delegation log • Guidance for trial materials • Materials order form • Participating sites—trial website address is included for updated list
Contacts	• Contact information
Protocol	• Trial protocol version submitted to local ethics committee • Master copy of patient/representative information sheets and consent form for hospital/study site • Master copy of brief information leaflet and wall poster for the family • Protocol amendments
Training materials	• DVD training film • Trial overview • Manual of Operating procedures • Power point presentations on CD in front cover • ICH-GCP guidelines summary. website address is also provided for complete ICH-GCP guidelines • GCP training and test guidance • Further training materials on secure collaborator's intranet
Trial drug guidance and information	• Drug administration guidance • Investigator brochure • Summary of product characteristics
Consent procedure	• Consent procedure overview • Guidance for completing the consent form
Data handling	• How to complete the data entry form • How to submit data online • How to send data by upload, email and fax • Guidance on protocol violations and deviations, data discrepancies, data queries and corrections • Serious data discrepancy form sample • Protocol breach form sample
Adverse events	• Adverse events reporting guidance • How to complete AE form • Unblinding forms • AE/SAE forms—also on CD • Notification of SAE/SUSAR by trial coordinating center • Reports from PI to local ethics committee

(*Continued*)

Table 2 PI study file index for clinical trials (*cont'd*)

Section	*Contents*
Ethics	• Copy of application submitted • Correspondence with ethics committee • Ethics committee approval • Approvals of protocol amendments
Regulatory	• National regulatory approval • Approvals of protocol amendments
Other approvals and indemnity	• Indemnity • Other approvals
Agreements	• PI agreement • Other agreements
Trial monitoring	• Site visit log • Guidance on monitoring procedures • Site monitoring report sample • Consent monitoring report sample • Central monitoring report sample • Completed site monitoring reports (consent monitoring, central monitoring, site visits) • Audit and inspection reports • Close out report
Trial drugs documentation	• DAL guidance • DAL forms • Drug receipts/shipping document
Patient information sheets and consent forms	• Spare information sheets for patient and their representative—also in treatment boxes and on CD • Spare consent forms—also in treatment boxes and on CD • Alert cards and contact labels • Brief information leaflets for family • Professional legal representative log • Sample label sheet • Sample ward transfer sheet • Sample waiver label
Patient entry	• Screening log • Randomisation log • Spare entry forms—also in treatment boxes and on CD • Example letter to personal doctor • Sample transfer pack
Completed forms	• Original consent forms • Completed adverse event forms • Completed protocol breach forms
Correspondence	• Correspondence on data queries/resolutions • General correspondence, printed emails
Site responsibilities, training logs and certificates	• Delegation of responsibilities/signature log • Training logs • Site training reports • Hospital information sheet • CV template • CV of principal investigator • CVs of trial team members who have been delegated responsibilities • GCP and other training certificates
Reports	• Reports to ethics committee • Reports to regulatory authority • Final and other trial reports • Publication(s) • Log of patients who have requested the study results

DAL, Drug Accountability Log; *GCP*, Good Clinical Practice; *CD*, Compact Disk; *DVD*, Digital Optical Disk; *AE*, Adverse event; *SAE*, Serious Adverse Event; *CV*, Curriculum Vitae.

attributes in source documents is a common finding (Bargaje, 2011); PIs and other team members should follow the concept of ALCOAC during the course of a clinical trial.

- Risk Assessment Form for Investigational Medicinal Product

An IMP is defined as "a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorization but used or assembled (formulated or packaged) in a way different from the authorized form, or when used for an unauthorized indication, or to gain further information about the authorized form" (Directive 2001/20/EC, 2001).

The IMP Risk Assessment Form is filled out by the PI in collaboration with the clinical trials pharmacist and lead research nurse. Risk is assessed by the study sponsor, and risk level is usually categorized into three levels: (1) low, (2) medium, and (3) high. The study sponsor does not release the IMP before the receipt of this form. The purpose of the IMP Risk Assessment Form is to solicit information pertinent to the IMP storage facility, the policy of the IMP at the study site, locked cabinet/cupboard and its location, other drugs to be stored in the same cabinet/cupboard, labels (For Clinical Trial Use Only and Packs May Contain Placebo) on cabinet/cupboard, monitoring frequency of the IMP stock/drug accountability log/randomization log, and the name and role of a person responsible for monitoring the IMP stock.

- Signing/endorsing treatment box receipt

The PI is required to sign the box receipt form after receiving the shipment of the IMP and check that the packs have been received in good condition; this form is sent to the sponsor either by fax or email.

- Consenting process

Informed consent is collected by the PI from all study subjects prior to their inclusion in the clinical trial, and in particular cases, from the subject's legal representatives, depending on the nature of the population involved (ICH, 2016). The consenting process is done without coercing, and study subjects have the right to withdraw from the study at any time (ICH, 2016).

- Randomization procedures and reporting of unblinding

A PI should abide by the randomization procedures specified in the study protocol and ensure that the breaking of code follows the standard procedures. Moreover, PIs also document and inform the study sponsor regarding unbinding issues that arise either accidently or due to the occurrence of serious adverse events (ICH, 2016).

- Drug accountability log

As per the ICH-GCP, the PI is accountable for the management of the IMP at the study site. A prepopulated form is sent to the PI by the study sponsor with each drug box. The PI records the usage of all treatment packs and destroys any partly used packs or any packs that are damaged and cannot be used for randomization. The drug accountability form is sent to the sponsor either by fax or email after ensuring that all packs have been used/destroyed, or when requested.

- Delegation of trial-related duties

The PI maintains a list of all qualified research personnel that were assigned any trial-related duties by the PI. A PI also ensures that the trial team has adequate knowledge regarding their role in the clinical trial and is aware of the protocol and investigational products (ICH, 2016).

- Safety reporting

Serious adverse events/serious adverse drug reactions and unexpected adverse drug reactions are reported by the PI to the sponsor and applicable authorities (regulatory authority and ethical committee) following the reporting timelines specified in the study protocol (ICH, 2016).

- Retention of trial records

After the completion of a clinical trial, the PI/study institution is informed by the study sponsor to retain all trial-related documents for a specific time period; destroying documents is carried out after the written notification of sponsors to the PI/study institution (ICH, 2016).

Clinical Pharmacists in Clinical Research

Direct patient care is defined as "a practice which involves the pharmacist's direct observation of the patient and his/her contributions to the selection, modification, and monitoring of patient-specific drug therapy; this is often accomplished within an interprofessional team or through collaborative practice with another health care provider" (Carter, 2016). As per the ACCP, residency training and board certifications are indispensable for direct patient care. According to the ACCP, clinical pharmacists are pharmacy professionals concerned with the science and practice of rational drug therapy (ACCP, 2008). From 2003 to 2014, there was a fivefold increase in the total number of board certified clinical pharmacists in the US alone (Carter, 2016).

The action of clinical pharmacists before, during and after prescribing a drug influences the outcomes of drug therapy, thus improving patient care. The before the prescription role is pertinent to their participation in clinical trials, representation in ethical review boards and regulatory bodies, and preparation of drug therapy guidelines. The during the prescription role is related to their influence on the prescribers at the time of prescribing medications, while the after the prescription role includes medication reconciliation, patient counseling, medication compliance, and drug monitoring (Bhatt, 2014).

Clinical pharmacy professionals are uniquely qualified in therapeutics and provide comprehensive medication management to patients and health care professionals (Kaboli et al., 2006). Safety evaluation is a fundamental component of the entire drug development process, and it is crucial to monitor patient safety during clinical trials (Yao et al., 2013). There are several cases in which high-profile approved drugs were withdrawn from the market due to safety concerns. The presence of clinical pharmacists at the bedside improves the quality, safety and efficiency of care (Kaboli et al., 2006). Clinical pharmacists play an integral role in the routine care of hospitalized patients by promoting the rational use of drugs and patient safety. Previous reports found an inverse relationship between the rates of medication errors and the number of clinical pharmacists per occupied bed (Bahrani et al., 2014; Kaboli et al., 2006; Kuo et al., 2013). Clinical trials are conducted on a target population with a specific medical condition. Likewise, findings of 49 systematic reviews reported that the clinical pharmacists exerted a positive impact on the outcomes of patients with a specific disease (Rotta et al., 2015). Physicians also acknowledge the impact of clinical pharmacists on patient health outcomes (Tegegn et al., 2018).

The following are the activities of clinical pharmacists in a health care setting: assessment of current medication management, clinical review, therapeutic drug monitoring, provision of drug information to health care professionals and patients/caregivers, drug use evaluation, and conducting clinical research (ACCP, 2014). Clinical pharmacists have profoundly improved patients' outcomes by improving patients' knowledge regarding diseases, increasing patients' compliance to their prescribed therapy, and reducing the incidence of adverse events, hospitalizations and admission rates (Jacobi, 2016). Clinical pharmacists can also eliminate insecurities surrounding their profession by performing clinical interventions, participating in outreach programs, establishing professional relationships with other health care professionals and publishing scientific articles by executing clinical trials. Interventions by clinical pharmacists proved to be an effective practice to reduce treatment cost in health care and clinical research settings (ACCP, 2000b; Dalton and Byrne, 2017). Counseling the patient is one of the clinical pharmacist's interventions that tends to improve patient adherence and compliance with the treatment protocol (Martinez et al., 2017). Clinical pharmacists also assist in identifying eligible study subjects, thus increasing the research capacity and revenues of the study site (Smith et al., 2010). Pharmacists must be involved in all aspects of clinical research, from preclinical investigations to clinical studies (Koshman and Blais, 2011).

Prior to 1983, pharmacists were mostly involved in traditional pharmacy practice, and they could not obtain ample opportunities to lead drug trials for pharmaceutical companies; their roles were mainly supportive in clinical trials. In addition, research activities were confined to the university level and were common among undergraduate pharmacy students. The evolution of the pharmacy profession from the dispensing of medications to direct patient care has profoundly increased the importance of pharmacists among other health care providers. This paradigm shift also provided opportunities for clinical pharmacists in clinical research. Pharmacists are an integral part of the clinical research team, and their role is crucial for quality assurance and executing successful clinical trials (Gamboa et al., 2011; Ise et al., 2017). The process of maintaining data integrity is crucial in clinical research (ICH, 2016; Kay et al., 2018). Clinical pharmacists are required to maintain the highest standards of integrity and honesty, which is one of the core elements of their competencies put forward by the ACCP in a publication entitled "ACCP Clinical Pharmacist Competencies." Clinical pharmacists should serve as role models/leaders for other health care professionals and uphold the standards of professionalism (Saseen et al., 2017). Pharmaceutical aspects of clinical research are better managed by clinical pharmacists, thus ensuring the rights, safety and well-being of human subjects (Gamboa et al., 2011). Likewise, an increasing number of clinical trials requires the inclusion of qualified and trained clinical pharmacists (Gamboa et al., 2011). A clinical pharmacist's expertise that is pertinent to the pharmaceutical aspects of the drugs warrants them to advise patients on the correct use of investigational drugs. Consequently, clinical outcomes of the clinical trials can be improved by the presence of clinical pharmacists on a clinical research team (Kay et al., 2018; Luisetto, 2016). The Royal Pharmaceutical Society and Pharmacy Research UK (PRUK) play an important role in promoting pharmacist-initiated research studies (Crilly et al., 2017). PRUK also introduced a mentoring scheme for novice clinical researchers. The PRUK Mentoring scheme is intended for clinical pharmacy professionals who want to develop their professional capacity within clinical research and are seeking advice, guidance or support from experienced clinical pharmacy scientists (Crilly et al., 2017). The PRUK mentoring scheme provides guidance to clinical pharmacy professionals working in the UK and abroad. Time and resources are the major limitations of today's pharmacy research. The ACCP report underlined a scarcity of clinical pharmacy scientists or pharmaceutical research mentors, which has been one of the barriers for clinical pharmacists to pursue research projects (Parker et al., 2013). The other most common barrier is research funding, which remains problematic for pharmacist-initiated studies (Crilly et al., 2017; Parker et al., 2013).

The role of clinical pharmacists as PIs was first discussed in 2000 by the ACCP in a commentary article (ACCP, 2000a). Moreover, the National Institute of Health (NIH), a US government entity for the promotion of biomedical and public health research, also substantiated the role of clinically oriented pharmacists as trial investigators in a special conference on pharmacy research held from December 13–14, 2006 in Maryland, US (Figg et al., 2008). Previously, pharmaceutical companies used to show reluctance in the selection of pharmacists as PIs in clinical trials and promoted them in only pharmacokinetic studies (ACCP, 2000a). This is evident from a fivefold increase in the selection of US physicians as PIs from 1990 to 2010, particularly for industry-sponsored clinical trials.

Consequently, pharmaceutical companies retain more control of clinical trial data, which raises issues pertinent to conflict of interest and publication bias (Fisher and Kalbaugh, 2012).

A retrospective analysis revealed that a large number of pharmacists published clinical research studies in major peer-reviewed scientific journals in 1993 and 2003 (Touchette et al., 2008). The US FDA explicitly clarified their policy in 1983, 1989, and 1990, based on a query pertaining to the role of clinical pharmacists as PIs in clinical trials (ACCP, 2000a). The FDA's response document was later used as an educational tool by clinical pharmacists to educate pharmaceutical sponsors, which eventually proved to be an effective activity for acquiring PI status. Following these developments, a large number of clinical pharmacists supervised clinical trials as PIs (ACCP, 2000a). As per the ICH-GCP guidelines and Form FDA 1572, a PI should be qualified by education, training and experience; merely having a pharmacy or medical degree is not enough to serve as a PI in clinical trials (ICH, 2016). The ICH-GCP clause 4.3 explicitly states the role of physicians in the provision of medical care for trial subjects in case of any adverse events and as a decision maker in medical conditions; these guidelines do not reflect the mandatory appointment of a physician as a PI in clinical studies. The general section of Form FDA 1572 also states that the selection of a physician as a PI is not mandatory according to regulations. The US Code of Federal Regulations contains 50 titles of different sections; title 21 (21CFR 312.53), which represents "Food and Drugs," also confirms these statements regarding the eligibility of PIs. Clinical pharmacists must acquire required training, credentials and clinical experience, which are the determinants in the selection of PIs by pharmaceutical sponsors. An ideal approach is to start participating in clinical trials either as a research coordinator, clinical research associate or monitor, or subinvestigator, which will eventually pave the way for junior pharmacy professionals to acquire experience alongside an experienced clinical research professional. Mentorship and nurturing from experienced clinical researchers are also crucial for enhancing the competency of novice investigators (Ward et al., 2017). The study sponsor intends to give preference to health care professionals who demonstrate relevant experience in a population group that will be selected for the proposed clinical trial (ACCP, 2000a). There are plenty of opportunities in a health care setting or hospital where pharmaceutical companies conduct their drug trials, whereas clinical pharmacists' direct interactions with patients and physicians ease their way into the clinical research field. Consistent with this notion, an interprofessional collaboration of clinical pharmacy professionals for improving patient outcomes makes them ideal candidates for multidisciplinary clinical research. In contrast, pharmacists working in a community pharmacy setting are deprived of these opportunities due to a prerequisite of conducting drug trials in an ideal environment with basic necessities, which, in turn, facilitates the recruitment of human volunteers following the ICH-GCP guidelines.

Currently, clinical trials are being carried out under the supervision of clinical pharmacists in conjunction with a qualified physician. Likewise, there is no formal hindrance by research foundations, the pharmaceutical sector or government entities for the selection of clinically oriented pharmacists as PIs. Since the 2000 publication of the ACCP commentary regarding the role of clinical pharmacists as PIs, there has been a surge in the number of clinical trials supervised by clinical pharmacists; this surge includes both industry-sponsored and clinical pharmacist-initiated trials (Burton et al., 2010). Professionals with a PharmD degree have been successful in acquiring financial grants from different stakeholders, particularly the NIH, and executing research projects as PIs. An unwavering support from the employers of pharmacists is also a key determinant in the professional transition of novice pharmacy scientists to a veteran study investigator (Burton et al., 2010). However, clinical pharmacists in developing countries are still facing impediments to building their reputation as a PI. In the UK, 237 pharmacists were registered with the clinical trial network of the Royal Pharmaceutical Society (Malson, 2015). There are no recent statistics regarding the total number of clinical trials being carried out under the supervision of clinical pharmacists; ClinicalTrials.gov provided a hit of 523 clinical trials performed by clinical pharmacists in 2009 (Burton et al., 2010). Despite the associated prestige, the role of a clinical pharmacist as a PI has yet to be explored.

The ACCP's Position Statement for Clinical Pharmacists Working as PIs (ACCP, 2000a; ACCP, 2014)

The ACCP believes that clinical pharmacists, as PIs, are crucial for the management of successful clinical trials. Furthermore, clinical pharmacists, as PIs, play a vital role in administrative (institutional approvals and IRB logistics) and operational (physical and human resources) plans. The PI should assess the feasibility of conducting a clinical trial in his/her institution before participating in a trial. PIs are required to assess whether the study contract or investigator's agreement are acceptable to the study institution, thus avoiding issues and delays in the conduct of a clinical trial. The handling of financial contracts and the distribution of study expenses to the PI vary by institution, which needs to be figured out during the initial correspondence with the sponsors.

PIs should also determine the meeting frequency of the IRB and their requirements for conducting clinical trials; it is prudent for PIs to familiarize themselves with the review process of the IRB.

PIs are also required to locate a specific area where a clinical trial will be conducted and assess the available resources that are crucial for conducting clinical trials. PIs should also confirm a secure place for record keeping; trial documents are usually retained for a specific period of time after the completion of a clinical trial in the study institution. PIs should also determine the total number of members that will be required for clinical trials, such as coinvestigators, study coordinators and research fellows.

Recommended Education and Training for Clinical Pharmacists to Work as PIs

The dearth of clinical pharmacy scientists in universities and the industry sector prompted the ACCP to recommend necessary education and training for preparing future leaders in clinical research. Due to the establishment of a large number of pharmacy colleges, academic institutions have faced a shortage of skillful clinical research faculty for pharmacy students, whereas experienced clinical researchers are indispensable for pharmacy institutions. There is a huge demand for clinical pharmacy scientists in clinical

trials, and professionals with pharmacy backgrounds have the potential to contribute to clinical research after acquiring the necessary skills and education. Phase 1 clinical trials are conducted to assess clinical pharmacology, and other phases are designed to ascertain the efficacy and safety of investigational drugs. Pharmacists have strong knowledge on pharmacology and therapeutics, which gives them an edge to enhance the quality of clinical trials. Graduate programs in clinical pharmaceutical sciences open doors for clinical pharmacists to work with experienced PIs. Globally, a doctoral degree or PhD in clinical pharmaceutical sciences is offered by several pharmacy institutions; this degree is particularly for candidates interested in clinical research (Dowling et al., 2009). In 2009, an editorial published by the ACCP in favor of PhDs for preparing future generations of clinical pharmaceutical scientists exerted a substantial impact on the clinical research environment (Parker et al., 2013). The shortage of clinical pharmacy scientists in clinical research enterprises can also be reduced by increasing awareness among students to pursue PharmD/PhD combined degree programs. However, PharmD graduates without a PhD degree have also demonstrated their expertise in the field of clinical research, but their number is quite limited.

Clinical Research Training Programs for Clinical Pharmacists

A 2-year post-PharmD fellowship of a minimum of 3000 h is offered by the ACCP for enhancing research skills and conducting clinical trials as an independent investigator. This fellowship aids PharmD graduates in developing skills for different aspects of research, such as the formulation of a hypothesis, study design, protocol preparation, research grant writing, data collection, study management, interpretation of study results, scientific writing, and publication. It is preferred to acquire residency training or practical experience prior to the initiation of the ACCP fellowship. PharmD graduates receive clinical research education and training from experienced investigators who serve as preceptors throughout the fellowship program. The selection of preceptors is based on their qualifications, earlier experience as PIs in clinical trials, scientific publications in peer-reviewed journals and clinical research collaborations with other researchers. The participants of this fellowship are required to conduct at least one research project or participate in multiple clinical research studies, thus providing hands on experience in clinical research that is imperative to manage a study independently (ACCP, 2016).

Other Clinical Research Training Programs

The National Institute of Health (NIH) also provides funding for several research programs. The NIH Clinical Center provides clinical research training to students, residents/fellows, and mid-career professionals, thus preparing the next generation of clinical research scientists (NIH, 2017). The Office of Clinical Research Training and Medical Education at the NIH Clinical Center also provides distance learning courses, and the theme is "Core Curriculum in Clinical Research." The following three courses are provided under this theme: (1) ethical and regulatory aspects of clinical research, (2) introduction to the principles and practice of clinical research, and (3) principles of clinical research. It is the best opportunity for pharmacy students and professionals not residing in the US and those who have difficulty attending in-house programs due to professional commitments. The NIH Office of Extramural Research also offers a free web-based training course, "Protecting Human Research Participants," for health care professionals. This certification is usually requested by the Institutional Review Board or ethical committee of health care institutions before grating an approval for research projects that involve human subjects. Although not mandatory, it remains an important certification for protecting the rights, safety and well-being of human subjects. Moreover, this course consists of seven modules that take approximately 3 h to complete.

Mid-career clinical pharmacy professionals with at least 7 years of clinical research experience may join a program entitled "Sabbatical in Clinical Research Management"; participants of this program work with NIH experts. This program is not intended for novice clinical research scientists; they should consider the NIH clinical research curriculum for appropriate programs. The Clinical Research Training On-Line Course for PIs is a free web-based course that provides an ideal opportunity for clinical pharmacists and other health care professionals willing to work as a PI in clinical trials. This web-based course is mandatory for all NIH intramural PIs and is recognized as an essential standard in terms of education and training (NIH, 2017).

Clinical pharmacists should acquaint themselves with the GCP guidelines, as they also contain informative sections such as the glossary of all technical words that are used in the process of conducting clinical trials and the list of essential documents for the conduct of a clinical trial, thus serving as a strong foundation. The compliance of the PI, study sponsor and study monitor is ascertained by the evaluation of the essential documents specified in the GCP document. In addition, the validity of the clinical trial conduct and the clinical trial's data integrity also depends on the essential documents.

The core activities of clinical pharmacists in clinical trials are: (1) dispensing medications, (2) managing investigational medicinal products, (3) coordinating clinical studies, (4) providing drug information to health care professionals and patients, (5) reconciling medication, (6) representing pharmacists in a research committee to provide expertise on drug use, and (7) overseeing clinical trials as PIs or subinvestigators (Brown et al., 2017; Kay et al., 2018). Research pharmacists maintain a pharmacy file that is provided by the study sponsor for their clinical trials prior to the initiation of the subject recruitment process. **Table 3** shows the sections and content of a pharmacy file provided by the sponsor for conducting a randomized, double-blind placebo-controlled trial; the pharmacy file is managed by a clinical trial pharmacist. This table is only for the guidance of clinical pharmacists and is based on my earlier experience in multinational clinical trials. Clinical pharmacists also contribute to the development of research protocols, particularly in providing expertise for the management of drugs, which is one of the basic elements in pharmacy practice. Likewise, they also contribute to the preparation of drug information and safety tools, thus ensuring the appropriate use of investigational drugs in a clinical trial setting (Brown et al., 2017). The presence of clinical pharmacists in a trial setting is paramount for assessing protocol adherence (Shehab and Tamer, 2004). Pharmacists exert a

Table 3 Pharmacy file index for clinical trials

Section	*Contents*
General	• Safety alert • Contact information • Information for pharmacy; study drug hazard sheet • CD containing training presentations
Drug accountability	• Complete IMP management risk assessment form • Pharmacy tracking log • Drug accountability log—sample copy • QP release certificates • Drug receipts/shipping documents
Unblinding	• Unblinding guidance for pharmacies • Unblinding request form × 1
Adverse events	• Adverse events reporting guidance • SAE/SUSAR forms • Notification of SAE/SUSARs by CTU
Ethics	• Local ethics approval • National ethics approval • National regulatory approval • Approvals of protocol amendments
Trial monitoring	• Pharmacy visit signature log • Pharmacy IMP monitoring log
Correspondence	• Correspondence, emails
Protocol	• Laminated protocol summary • Protocol • Protocol amendments • Manual of operating procedures
Drug information	• Drug administration and storage guidance • Drug accountability at site—work procedure • MAIMP (packing) • MAIMP (placebo) • Summary of product characteristics • Investigator's Brochure

QP, Qualified Person; *CTU*, Clinical Trial Unit; *SAE*, Serious Adverse Event; *SUSARs*, Suspected Unexpected Serious Adverse Drug Reaction; *IMP*, Investigational Medicinal Product; *MAIMP*, Manufacturer's Authorisation for Investigational Medicinal Products.

significant impact on the quality of clinical research by improving protocol compliance due to reconciling medication, reducing the occurrence of drug-related deviations, and decreasing medication discrepancies, which eventually improve patient care in a clinical trial setting (Redic et al., 2017). Pharmacists also effectively enhance the drug-related aspects (dosage, indications, drug–drug interactions, contraindications, and adverse drug events) of clinical trials, thus strengthening the backbone of drug trials. Drug-related issues exert a significant impact on patient outcomes; clinical pharmacists are experts and are skillful in tackling the aforementioned issues (ACCP, 2000b).

The safety practices of investigational drugs have not been standardized, unlike commercially available or approved medications (Cruz and Brown, 2015). The majority of research pharmacists have consistently raised serious concerns pertinent to the safety practices of investigational drugs during the conduction of clinical trials (Brown et al., 2017). Safety concerns related to naming, labeling, packaging and storage, are also highlighted by the Institute for Safe Medication Practices (ISMP). In addition, the ISMP recommended Institutional Review Boards (IRBs) to include pharmacists for the review of all investigation drug protocols, thus mitigating safety concerns of investigational drugs (Cruz and Brown, 2015). These concerns are not new to clinical research and were also addressed in a survey during the 1980s. Cruz and Brown (2015) also addressed safety concerns of investigational drugs in the findings of a national survey; these findings were based on more than 80% of pharmacists who had safety concerns (Cruz and Brown, 2015). The ICH-GCP requires all investigators to acquire thorough knowledge regarding the investigational drugs and ensure correct use of drugs, whereas clinical pharmacists are also deemed to be the best choice to qualify for PIs owing to their pharmacy qualification and training. Moreover, investigational drugs are also managed by pharmacists during clinical trials, requiring them to ensure drug use as per the approved protocol. The management and control of investigational drugs is crucial for executing successful

clinical trials, and clinical pharmacists are deemed to be the ideal choice in a clinical research team for effectively handling these matters. Pharmacists have a vital role in the receiving, handling, safe keeping, dispensing, safe disposal, and return of investigational drugs (Brown et al., 2017). According to the Joint Commission, the safe management of investigational drugs is essential in all accredited hospitals and is solely a responsibility of a pharmacy. In addition, pharmacists place auxiliary labels containing expiry and lot number details during the dispensing of these drugs, thus ensuring safe use during clinical trials. These measures reduce medication errors and promote subject safety (Brown et al., 2017). Thirty-nine percent of prescription orders for hospitalized populations have been reported to cause medication errors (Franklin et al., 2005). Prescribing errors can be minimized by employing pharmacists to review and verify prescription orders; moreover, they can provide expertise on therapeutic drug monitoring (Brown et al., 2017; Cohen and Sanborn, 2008). Clinical trial pharmacists ensure that the transportation of an investigational drug follows all standard protocols specified in the sponsor documents and promptly notify the former in case of any divergence from this process. Therefore, the inclusion of pharmacists in clinical trials is crucial in promoting medication safety and producing high-quality data (Brown et al., 2017).

The Role of Clinical Pharmacist in Improving Adherence Issues in Clinical Trials

The act of following instructions or directions given by health care professionals or research personnel during routine clinical care and clinical trials is termed adherence (Robiner, 2005). Fear of investigational drug's side effects, polypharmacy, dose frequency, and lengthy duration of treatment eventually lead to a higher incidence of poor medication adherence, thus making it difficult to evaluate the clinical efficacy of an investigational drug. Furthermore, prevalent nonadherence in clinical trials makes it difficult to ascertain the long-term effects of drugs (Kvarnström et al., 2018). It is prudent that additional efforts be directed toward maintaining medication adherence to generate a high-quality clinical trial data. The existing literature reports subjects' poor adherence or compliance to investigational drugs during clinical trials (Martinez et al., 2017). Another study revealed a 40% decline in adherence during clinical trials over a period of 1 year (Blaschke et al., 2012). Clinical setting, drug–drug interactions, side effects, comorbidities, psychological issues, and communication problems are recognized as possible causes that lead to poor adherence (Robiner, 2005). Poor adherence profoundly affects treatment goals and increases drug resistance, thus affecting morbidity and mortality rates (Martinez et al., 2017). Moreover, it exerts a negative impact on the quality of clinical trial data and prolongs study duration, which eventually inflates trial expenditures. The research team may not obtain a satisfactory response from interventional drugs due to nonadherence; hence, statistical power is tampered. Adherence for taking long-term medications in clinical trials was found to be 59%, while it was 78% for short-term medications (Robiner, 2005). Bouwman et al. (2017) reported that 50% of patients do not adhere to the treatment protocol. Such statistics advocate for a need to enhance adherence during the conduction of clinical trials (Martinez et al., 2017). The rapport between trial participants and caregivers is correlated with adherence and retention rates (Robiner, 2005). The positive effect of the pharmacist-trial participant relationship on the medication adherence of diabetes patients was also documented (Chung et al., 2014; Jin et al., 2008). Pharmacists' expertise in drugs plays a vital role in decreasing poor adherence rates and the success of clinical trials. Consistent with this notion, pharmacists are also able to respond to drug-related queries over the course of a clinical trial in a timely manner (Martinez et al., 2017). Pharmacists keep the dispensing record of investigational drugs, which gives them an edge to scrutinize the patient's adherence to medication regimens (Kay et al., 2018). A systematic review of 38 clinical studies showed improvement in medication adherence and treatment outcomes mainly due to clinical pharmacists' interventions (Tan et al., 2014).

The Importance of Integrating Clinical Pharmacists in Clinical Trials

A randomized controlled trial in the UK found that pharmacist counseling is crucial to decreasing cardiovascular risk and medication-related issues in patients with diabetes. Participants in an intervention group showed lower levels of hemoglobin A_{1c} compared to the control group. Moreover, participants in the intervention group showed significant improvement in their quality of life (Ali et al., 2012). Likewise, a prospective randomized controlled trial in Malaysia demonstrated a decline (9.6%–8.2%) in hemoglobin $A_{1c,}$ and medication adherence in an intervention group was also significantly improved due to pharmacists' consultations (Chung et al., 2014). Failure of drugs due to the clinical trials or failure of clinical trials due to the drugs are the two important notions in an experimental setting. Pharmacists are drug information experts with specialized training in drug therapy, and their role in clinical trials is paramount. Their counseling and rapport with study subjects improves the accuracy of outcomes (Martinez et al., 2017).

A prospective, cluster randomized, controlled clinical trial in the US showed that drug therapy recommendations by clinical pharmacists resulted in a significant improvement in the control of blood pressure (Carter et al., 2009; Weber et al., 2010). Similarly, evaluations of drug regimens and the provision of recommendations to patients and physicians reduced inappropriate prescribing and safety issues (Hanlon et al., 1996).

Enhancing Medication-Related Aspects of Clinical Trials by Integrating Clinical Pharmacists

The study protocol is a mainstay for clinical trials, whereas deviation from the protocol can be managed by the principal investigator. In addition, the protocol contains all trial-related information, including the management of investigational medications (Kay