Anonymised Data Ethics Protocols & Transparency Committee (ADEPT) Annual Report

1 January 2019 to 31 December 2019

CONTENTS

Glossary

ADEPT	Anonymisation Data Ethics Protocols & Transparency Committee
AUKCAR	Asthma UK Centre for Applied Research
COPD	Chronic obstructive pulmonary disease
EHR	Electronic health records
HES	Hospital episode statistics
HRU	Healthcare resource utilisation
IBD	Inflammatory bowel disease
iHARP	International helping asthma in real-life patients
ISAR	International Severe Asthma Registry
MREC	Medical Research Ethics Committee
NIHR	National Institute for Health Research
OPC	Optimum Patient Care Ltd
OPRI	Observational and Pragmatic Research International Ltd
PRO	Patient-reported outcomes
REG	Respiratory Effectiveness Group
SOP	Standard operating procedure
UK	United Kingdom

Foreword from the Chair & Vice Chair of ADEPT

Another year has gone by and REG has been increasingly busy supporting and encouraging innovative real-life research. As might be expected for an Ethics Committee within the Respiratory Effectiveness Group, the majority of protocols submitted to ADEPT for approval in 2019 pertained to airway diseases. However, the value of real-life data for informing decisions about patient care was also recognised in other disciplines, specifically cancer and gastroenterology.

Real-life research is no longer perceived as a 'poor relation' to randomised controlled trials (RCTs). Evidence from real-world studies is increasingly recognised by guideline committees and practising clinicians as an important adjunct to RCT data for informing routine care management decisions. This is clearly demonstrated by the large number of studies submitted for ADEPT review and also undertaken by REG in 2019.

ADEPT remains an important part of the REG research process and its oversight not only ensures the safety of patients, but also supports researchers in the development of robust study protocols and by ensuring the presence of a study team with sufficient experience to deliver planned research. ADEPT oversight also makes sure that proposed studies align with the principles of the REG. In the submitted protocols, ADEPT looks for topics that are often missed by conventional research programmes, for studies designed to evaluate the effectiveness of novel clinical options or assessment methods, and for opportunities to support new researchers on their journey to publication.

You will read in the report that ADEPT's average turnaround time for a protocol is 9 days. This is an outstanding achievement, but it also presents practical workload challenges. We are grateful for the sterling service that the current Committee has provided, but are mindful that new members and the continuing involvement and enthusiasm of existing members is required to maintain current standards and efficiencies.

We hope you enjoy reading the 2019 ADEPT Annual Report. If you are reading it as a current committee member, we thank you for your efforts and contributions and hope you will remain an active member in 2020 and that you will input to the planned review of ADEPT processes in the coming year. If you have colleagues with an interest and expertise in real-life research, we encourage you to invite them to join REG and, thereafter, ADEPT.

If you're reading the report as an REG collaborator with an interest in joining ADEPT, or as a non-collaborator with an interest in getting involved, we'd be happy to hear from you – please contact: enquiries@regresearchnetwork.org

That's all from us – read on and feel free to feed back!

Professor Todor A. Popov, MD (BG)
ADEPT Chair

Daryl Freeman, MBChB FRCGP
ADEPT Vice Chair

1. Introduction

The Respiratory Effectiveness Group (REG) is an international research and advocacy group led by clinical academics with expertise in respiratory medicine and real-world research. REG initiatives target unmet needs in routine clinical care and the group provides leadership in real-world evidence generation through collaborative working, knowledge sharing and demonstration of quality research in practice.

The Anonymised Data Ethics and Transparency Committee (ADEPT) is an independent body commissioned by the REG to assess the feasibility and scientific merit of real-world research studies and to provide expert critique, as appropriate (see **Section 2**).

This ADEPT Annual Report outlines the Committee's role and operating procedures, and summarises its activities over the period 1 January 2019 to 31 December 2019.

2. Governance and Review of Research Applications

2.1 Role of ADEPT

2.1.1 Database governance

ADEPT is an independent body of experts and regulators commissioned by the REG to quality appraise research protocols involving the use of electronic health records (EHRs) and clinical databases, such as:

- The Optimum Patient Care Research Database (OPCRD, https://opcrd.co.uk)
- The International Severe Asthma Registry (ISAR, http://isaregistries.org)
- The Implementing Helping Asthma in Real Patients Database (iHARP, https://opcrd.co.uk/international-helping-asthma-in-real-life-patients-iharp/)
- Hospital Episode Statistics (HES, https://digital.nhs.uk/data-and-information/data-tools-and-services/data-services/hospital-episode-statistics)

The ADEPT review process involves an evaluation of a proposed study's clinical relevance and quality of design, as well as an assessment of its practical feasibility using the intended database. It does not constitute formal medical research ethics committee (MREC) approval. All ADEPT-approved protocols remain subject to local / institutional MREC approval requirements, as appropriate for the outlined research.

In addition to applications for formal protocol approval, ADEPT is also open to requests for expert guidance on the optimum design of studies intending to use EHRs and clinical databases. Requests for such expert input must be made prior to submission of related study protocols to relevant ethical bodies.

2.1.2 Terms of reference

ADEPT approval is contingent on the submitted protocol meeting (as a minimum) the following quality standards – the proposed research must:

- Ensure practice and patient confidentiality will be maintained throughout the study
- Address a well-defined research hypothesis or address clear research question

- Propose the use of a data source (e.g. EHRs or a clinical database) adequate for the intended research
- Outline methods appropriate for the proposed research
- Demonstrate scientific rigor in the study design and approach
- Have previously secured (or will prior to commencement) all necessary ethical approvals
- Involve a team with experience in (or supported by experts) in real-life research

2.2 Membership

ADEPT is a committee made up of independent clinical experts and scientists with expertise in statistics, epidemiological experience and/or HER-based research, and of lay members.

2.2.1 Member appointment

ADEPT membership is voluntary, but limited to expert or lay collaborators of the REG. Self-appointment from a body of pre-identified experts in real-world research, such as REG, not only ensures the expertise of the Members, but also a broad range of specialisms within the Committee so that protocols can be aligned by topic to the most appropriate reviewer.

2.2.2 Membership over the reporting period

Throughout the 2019 calendar year covered by this report, there were 21 ADEPT members, including the Chair. The full list of is detailed in
Appendix 1. ADEPT Committee Members

Between 2014–2016, ADEPT was Chaired Dr Daryl Freeman, Clinical Director of the East of England Strategic Clinical Network (Respiratory Clinical Director NHS England – Midlands & East). On 1 January 2019, Todor (Ted) Popov, Professor at the University Hospital Sv. Ivan Rilski in Sofia, Bulgaria, became ADEPT Chair. Dr Freeman took up the position of Vice Chair where she provides ongoing support to the Chair, including cover during periods of Chair absence or on occasions of conflict of interest.

2.3. Committee working

During the 2019 reporting period, all protocols submitted for ADEPT review were processed virtually. Committee members received no renumeration for their review of ADEPT applications; all applications were reviewed on an honorary basis.

Application processing and review was facilitated by the very efficient ADEPT Secretariat and conducted by the Committee in accordance with the ADEPT SOP, as summarised in
Section
2.8 Review of research protocols of this report.

2.4 ADEPT Secretariat

The ADEPT Secretariat is made up of REG employees who provide administrative support to the Committee.[1] The Secretariat forwards ADEPT applications for Chair and Committee

[1] Address: ADEPT Secretariat, ESpace North, 181 Wisbech Road, Littleport, ELY, Cambridgeshire, CB6 1RA

review, communicates Committee decisions to applicants and invoices and processes application submissions, as appropriate.

2.5 Application channels

Researchers applying for ADEPT review must submit their research protocols and supporting materials for the Chair and Committee's attention. Applications can be submitted to the Secretariat by email (to application@adeptcommittee.com) or via an web-based submission form on the REG website (https://www.regresearchnetwork.org/adept).

In 2019, the online application infrastructure was supported by Smartsheet content management software (Smartsheet Inc, https://www.smartsheet.com).

2.6 Application fees

The REG charges a processing fee for all ADEPT applications. The fee is intended to cover administrative cost of the ADEPT Secretariat and Committee.

The fee level is set by the nature of the research (e.g. commercial or academic) and profile of the applicant (e.g. academic, REG supporter or non-supporter), with discounts offered for applications submitted by REG supporters or pertaining to academic studies.

The ADEPT fee is waived for any research application responding to an REG-identified research priority. Invoices are issued following by the ADEPT Secretariat following their confirmation of a complete submission.

Table 1. ADEPT fees, 2019

Applicant type		**Fee**
Commercial	**Non REG supporter**	£1500
	REG supporter	£750
Academic		£350

2.7 Application requirements

ADEPT applicants must complete and provide the following documents:

- Covering letter on headed paper
- ADEPT application form
- Research protocol
- Chief Investigator CV

The ADEPT Secretariat assesses each submission for completeness. Once it has been confirmed that all necessary documentation has been provided, the Secretariat confirms receipt by issuing a formal email to the corresponding applicant. The confirmation of receipt email includes the protocol's assigned "ADEPT number" and any relevant information relating to the dates of meeting(s) at which the protocol will be discussed.

The Secretariat then blinds the submission (through removal of identifying names and institution details) and releases the application to the ADEPT Chair for onward processing.

2.8 Review of research protocols

ADEPT applications can be reviewed and adjudicated by the Chair alone (under Chairperson's actions), or can be circulated for wider Committee review.

The scope of the proposed study informs the Chair's decision to process the application under Chairperson's actions, or to involve specific experts from the Committee.

2.8.1 Chairperson's actions

To be eligible for Chairperson's actions (i.e. "fast-track review") a study protocol must relate to a descriptive characterisation study, or to a retrospective analysis of a historical dataset.

Submissions whose scope meets any of the following criteria must be reviewed by at least one ADEPT member, in addition to the Chair:

- Forward-looking / prospective studies involving an *a priori* defined follow-up (within the historical dataset) after a defined index date
- Comparative effectiveness evaluations
- Studies requiring statistical matching

The Chair can circulate any application for wider ADEPT review, at their discretion.

2.8.2 Committee / Chairperson's Decision

ADEPT can 'Approve' a study protocol, or return any of the following decisions:

- Conditionally approved
- Resubmit with amendments
- Reject

If a protocol is not deemed eligible for ADEPT approval, it can be resubmitted if the applicant(s) feel it is possible to revise the protocol to address the Committee's concerns.

All phases of the ADEPT review process are overseen and signed-off by the Chair.

2.9. ADEPT contributions to research

2.9.1 Publications

ADEPT has supported the real-world research efforts of a wide range of expert researchers (clinical, commercial, academic, public health workers) from around the world. Research protocols reviewed by ADEPT have led to an extensive number of publications in MEDLINE®-listed, peer review journals, particular within the field of Respiratory Medicine.

ADEPT-approved studies have helped to address important questions relating to routine care management practises, real-world (comparative) effectiveness, real-world tolerability of interventions, natural history of disease, prognostic and predictive risk markers and opportunities for early intervention to reduce disease burden. Examples of ADEP-approved research publications include:

Natural history and disease characterisation:

- Krishnan JA, Nibber A, Chisholm A, et al. Prevalence and Characteristics of Asthma–Chronic Obstructive Pulmonary Disease Overlap in Routine Primary Care Practices. *Annals ATS* 2019;16:1143–50.
- Jones RC, Price D, Ryan D, et al. Opportunities to diagnose chronic obstructive pulmonary disease in routine care in the UK: a retrospective study of a clinical cohort. The Lancet Respiratory Medicine. 2014 Apr 1;2(4):267-76.
  (A collaboration with the Department of Health in England in response to the national COPD and Asthma strategy[2])

Disease management characterisation:

- Launders N, Ryan D, Winchester CC, et al. Management Of Community-Acquired Pneumonia: An Observational Study In UK Primary Care. *Pragmat Obs Res*. 2019;10:53–65

Future risk prediction:

- Blakey JD, Price DB, Pizzichini E, et al. Identifying risk of future asthma attacks using UK medical record data: a respiratory effectiveness group initiative. *JACI In Prac* 2017;5:1015–24
- Kerkhof M, Sonnappa S, Postma DS, et al. Blood eosinophil count and exacerbation risk in patients with COPD. *Eur Resp J*. 2017;50:1700761

Comparative effectiveness research:

- Grigg J, Nibber A, Paton JY, et al. Matched cohort study of therapeutic strategies to prevent preschool wheezing/asthma attacks. *J Asthma Allergy* 2018;11:309–21
- Barnes N, Price D, Colice G, et al. Asthma control with extrafine-particle hydrofluoroalkane-beclometasone vs. large-particle chlorofluorocarbon-beclometasone: a real-world observational study. *Clin Exp Allergy* 2011;41:1521–32

REG publications originating from ADEPT-approved protocols can be found on the REG website: https://www.regresearchnetwork.org/publications

2.9.2 Acknowledgement

All authors of publications resulting from ADEPT-approved protocols are requested to include a statement acknowledging *a priori* protocol approval by ADEPT (citing their ADEPT reference number) when publishing their work.

2.10 Future governance

The ADEPT governance structure and standard operating procedures (SOP) outlined in this report will be subject to review and revision in 2020.

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[2] Department of Health and Social Care. *An outcomes strategy for people with chronic obstructive pulmonary disease (COPD) and asthma in England*. 18 July 2011. Available at: https://www.gov.uk/government/publications/an-outcomes-strategy-for-people-with-chronic-obstructive-pulmonary-disease-copd-and-asthma-in-england (accessed 25 January 2020)

Central aspects of the review will be:

1) Consideration of the feasibility of a fully online application process including data validation and protocol anonymisation to automate the Secretariat's submission assessment
2) Characterisation of the Committee Members' areas of expertise, current tenure and on-going commitment, formal documentation of declaration of interests and identification of opportunities to attraction new members.

3. Activities and Outputs

3.1 Total ADEPT applications in 2019

During the 2019 reporting period, ADEPT reviewed 19 applications: 18 new research protocols and one revised protocol (originally submitted in 2016).

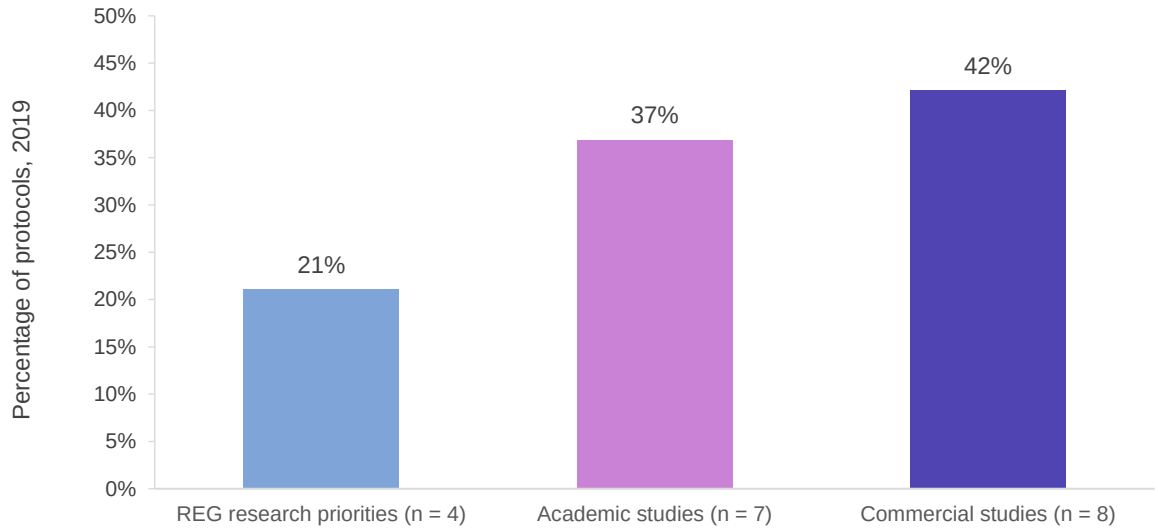
The majority of research protocols (84%, n = 16) involved the use of the OPCRD. All others (16%, n = 3), outlined research intending to use the ISAR database.

All 19 protocols submitted for ADEPT review during the reporting period were approved; none were rejected or returned for revision.

3.2 Commercial versus academic profile of research protocols

A breakdown of the approved protocols by source of research funding (academic / commercial, REG research priority[3]) is detailed in **Figure 1**.

Figure 1. Commercial / academic profile of ADEPT-approved protocols, 2019



[3] Protocols outlining research that is responding to an REG-identified research priority may be commercially or academically funded, but the research will be non-commercial. All REG research priorities relate to scientific evidence gaps or clinical needs identified by the expert respiratory collaborator group.

More than half (58%, n = 11) of the research protocols approved by ADEPT in 2019 were for non-commercial research, including four applications for studies responding to REG-identified research priorities.

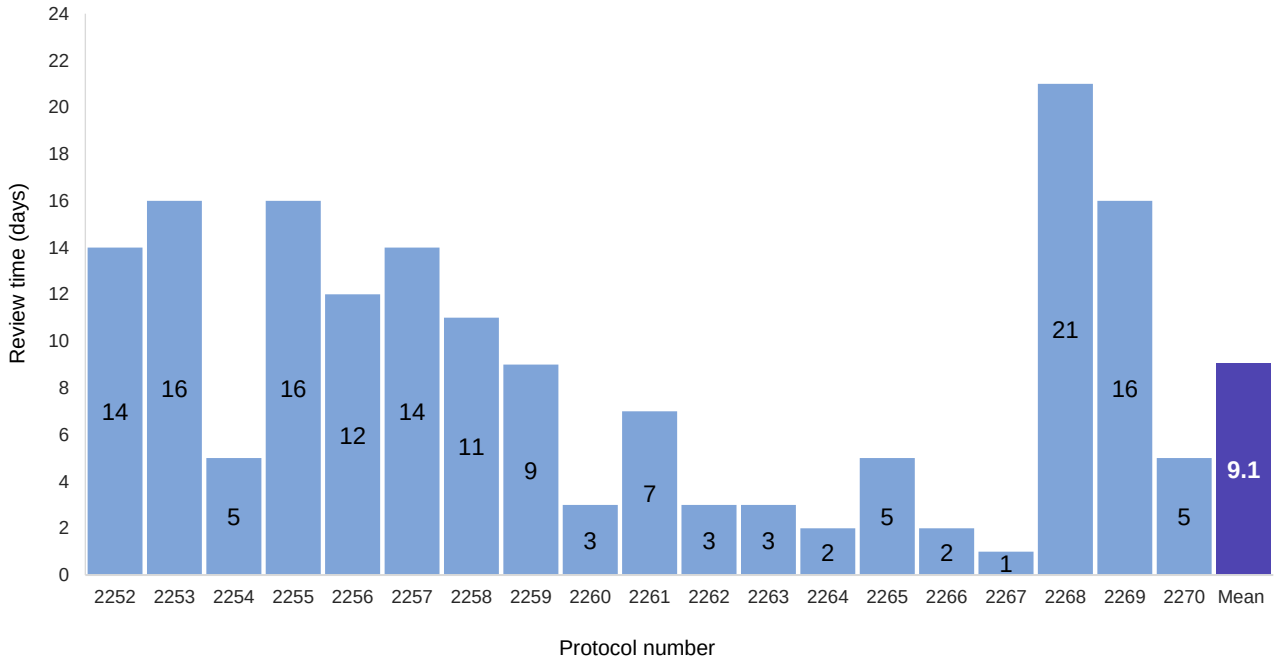
In 2019, ADEPT reviewed protocols for non-commercial research submitted by: the National Institute for Health Research- (NIHR-) funded Asthma UK Centre for Applied Research (AUKCAR; 3 applications); the REG (3 applications); the social enterprise, OPC Ltd (OPC; 1 application), and from joint OPC–partner collaborations (4 applications).

Over the same period, ADEPT reviewed protocols for commercial research projects from: AstraZeneca (alone and in partnership with OPC Global), Janssen-Cilag Limited, Chiesi, Mylan, Observational and Pragmatic Research International Ltd (OPRI) and Harvey Walsh.

3.3 Protocol turnaround time: submission to approval

ADEPT aims to review all protocols within 15 working days of receipt. In 2019, the mean (range) time from protocol submission to approval by the Committee was: 9.1 (1–21) days (**Figure 2**).

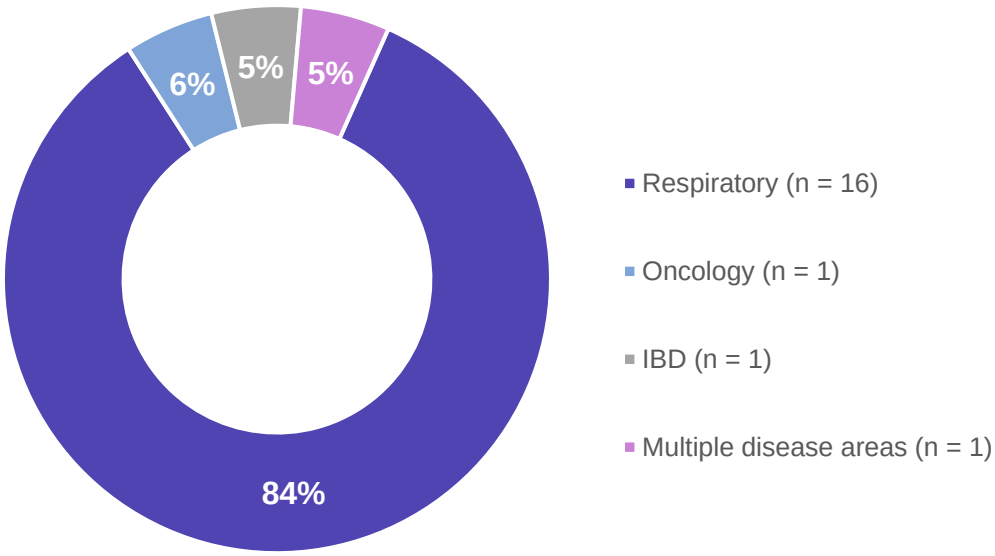
Figure 2. ADEPT review times (days) from protocol submission to approval in 2019



3.4 Areas of research interest

Of the 19 research protocols approved by ADEPT in 2019, the majority 84% (n = 16) were for respiratory-related research. The remaining 16% of approved protocols related to oncology (n = 1), inflammatory bowel disease (IBD, n = 1) or multiple disease areas (n = 1) (**Figure 3**).

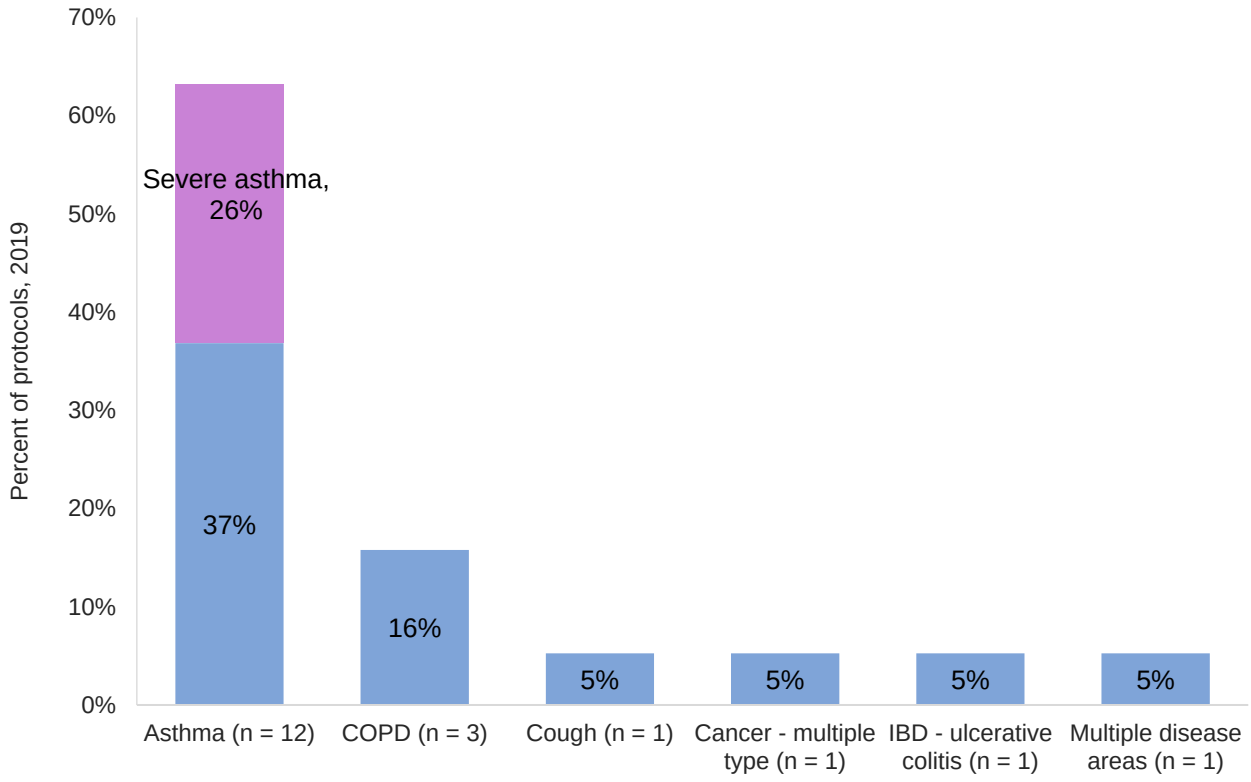
Figure 3. ADEPT-approved protocols by research speciality, 2019



IBD, inflammatory bowel disease

When considered at the disease level, almost two-thirds (63%) of the approved protocols were for asthma-related research; 26% relating to severe asthma, specifically (**Figure 4**).

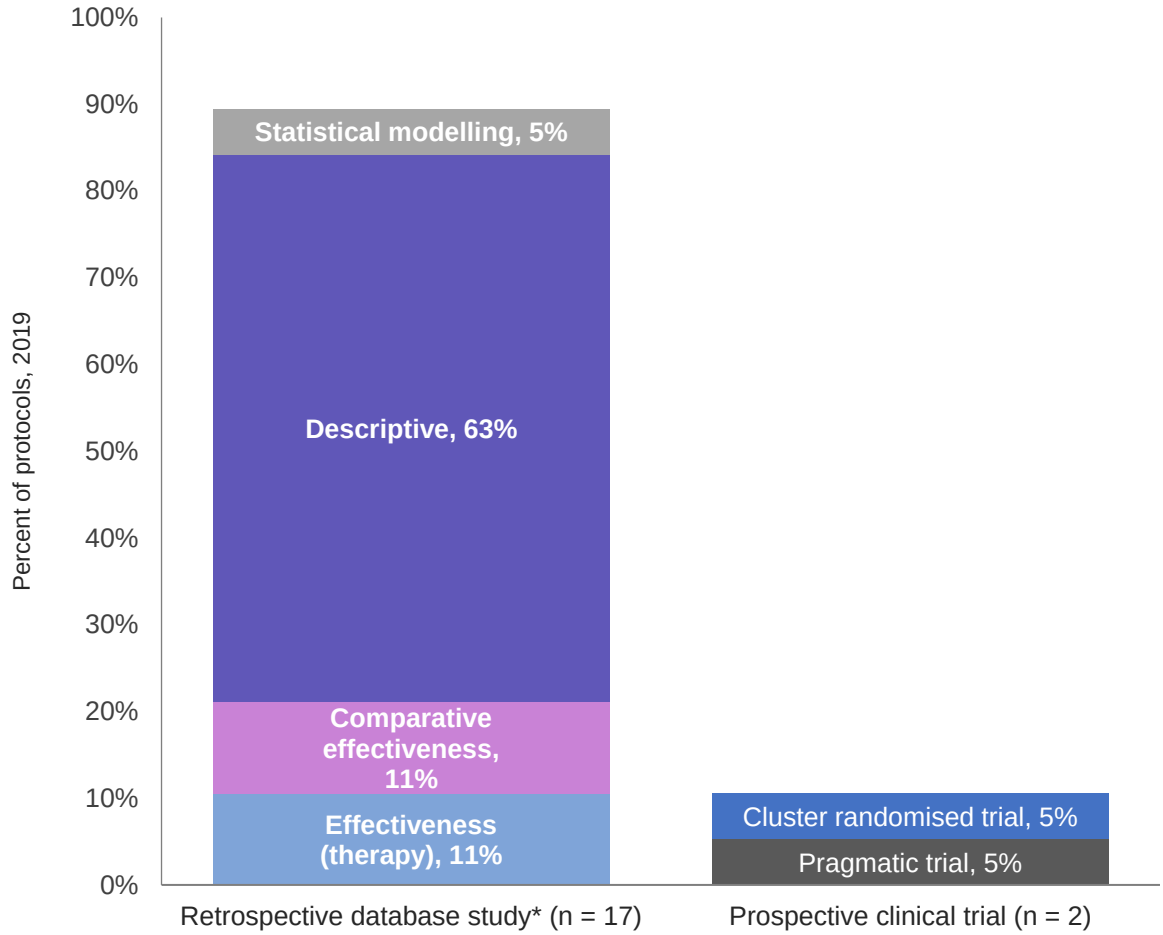
Figure 4. ADEPT-approved protocols by disease, 2019



COPD, chronic obstructive pulmonary disease; IBD, inflammatory bowel disease

Of the 19 protocols submitted for ADEPT review in 2019, 10% (n = 2) involved a prospective clinical trial design. All others (90%, n = 17) proposed retrospective analyses of the OPCRD or ISAR databases (**Figure 5**).

Figure 5. ADEPT-approved protocols by study design, 2019

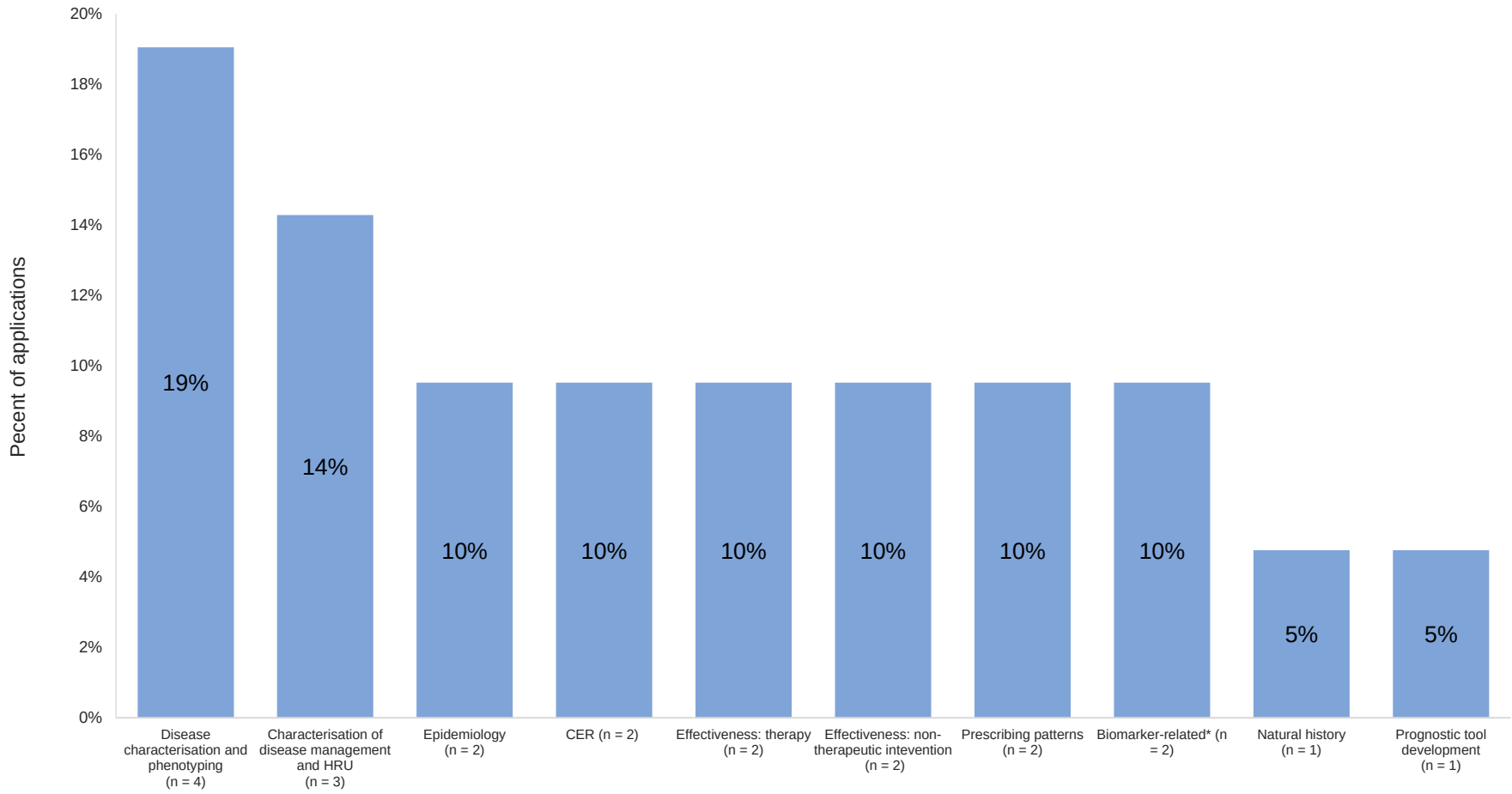


*EHRs from routine care clinical databases (OPCRD) or disease registries (ISAR)

The protocols approved by ADEPT in 2019 covered a broad range of research interests (**Figure 6**). The most common research focus was disease characterisation and phenotyping (19%, n = 4), followed by characterisation of disease management and healthcare resource utilisation (HRU; 14%, n = 3).

Other types of approved research related to epidemiology (10%, n = 3), comparative effectiveness (10%, n = 2) or effectiveness research (20%, n = 4), routine care prescribing patterns (10%, n = 2), biomarker characterisation or validation (10%, n = 2), prognostic tool development or natural history characterisation (5%, n = 1, each).

Figure 5. ADEPT-approved protocols by research topic, 2019



*Biomarker characterisation and/or validation.
Two applications (related to both characterisation of a disease and its management) have been included twice.
CER, comparative effectiveness research; HRU, healthcare resource utilisation

3.5 Overview

This is the first formal ADEPT annual report and will serve not only as a summary of the Committee's activities in 2019, but also as a baseline against which to measure future ADEPT activities.

During the 2019 calendar-year reporting period, ADEPT received and approved 19 research protocols, with a mean review time of 9.1 working days. The rapid turnaround achieved, exceeded the Committee's 15-working-day review target.

More than half (58%) of all protocols submitted for ADEPT review during the period were for non-commercial studies. The majority of protocols (84%) were for respiratory studies. Asthma was the condition of greatest research interest and accounting for 63% of all protocols; severe asthma accounted for more than one-quarter (26%) of approved protocols. Other disease areas of interest included oncology and IBD (ulcerative colitis).

ADEPT-approved protocols covered a range of research types, most commonly relating to disease characterisation and phenotyping (19%), or characterisation of routine care disease management and HRU (14%). The majority of research protocols involved a retrospective study design (90%); only two protocols involved prospective data collection as part of a pragmatic or cluster randomised trial.

Appendix 1. ADEPT Committee Members, 2019

ADEPT Chair

Todor (Ted) Popov, Professor at the University Hospital Sv. Ivan Rilski in Sofia, Bulgaria

Prof. Popov has pursued a career in the field of Allergy & Asthma at the Medical University in Sofia, Bulgaria for approximately 30 years. His main research interests include allergology, pulmonology and clinical immunology, and have led to his authorship of nearly 200 articles. In addition to his role as ADEPT Chair, he is a board member of a number of medical journals and societies; he is former President of the Union of the Bulgarian Medical Societies; Former President of INTERASMA, and Former Vice President of the European Academy of Allergology and Clinical Immunology.

Prof. Popov has been a member of the REG since it was founded in 2013.

ADEPT Vice Chair

Daryl Freeman, (MD) Associate Clinical Director Norfolk & Waveney UK

Dr Freeman is an Associate Clinical Director for Norfolk Community Health & Care, which involves a clinical role (working across community hospitals in Norfolk) and working with the Integrated Care System across Norfolk & Waveney to improve hospital care. She also serves as the Chair of the Norfolk & Waveney Right Care Respiratory Working Group which aims to standardise & prioritise respiratory care across all providers in Norfolk. She is current Chair of the Service Development Committee for the Primary Care Respiratory Society, and former Clinical Director for NHS England Respiratory Strategic Clinical Network.

Her non-respiratory interests include equestrian trauma – which combines her love of horses (she owns 3) with a desire to keep her acute medical skills up to date.

Dr Freeman has been a member of the REG since it was founded in 2013.

Members

Bernardino Alcazar, Pneumologist at the Hospital de Alta Resolución de Loja, and Assistant Professor in the Department of Medicine at the University of Granada, Granada, Spain

Aji Barot, VP Pharma (EMA), Medisafe® Meication Management Platform, London, UK

John Blakey, Adjunct Associate Professor Curtin University and Senior Medical Practitioner in Respiratory Medicine, Sir Charles Gairdner Hospital, Perth, Australia

George Christoff, Professor, Faculty of Public Health, Department of Health Technology Assessment, Medical University, Sofia, Bulgaria

Alexandra Dima, Senior Research Fellow, Health Services and Performance Research (HESPER) Claude Bernard University Lyon 1, Lyon, France

Mark FitzGerald, Professor and Director, Centre for Heart and Lung Health, The Lung Centre, Vancouver, BC, Canada

Elizabeth Kern, Professor of Medicine, Division of Medical, Behavioral & Community Health National Jewish Health, Denver, CO, USA

Fabrizio Luppi, Associate Professor, Respiratory Disease Department, Universita degli Studi di Milano-Bicocca, Milan, Italy

Andrew McIvor, Professor, Division of Respirology, Department of Medicine, Firestone Institute of Respiratory Health, St. Joseph's Healthcare, MacMaster University, Hamilton, Ontario, Canada

Jenni Quint, Reader in Respiratory Epidemiology in Respiratory Epidemiology, Occupational Medicine and Public Health at the National Heart and Lung Institute and Honorary Consultant Physician in Respiratory Medicine at Royal Brompton Hospital, London

Nicolas Roche, Professor of Respiratory Medicine, University Paris Descartes, Respiratory and Intensive Care Medicine department, Hôtel-Dieu Hospital, Paris, Franc

Miguel Roman-Rodríguez, Research Director, Instituto de Investigación de Palma de Mallorca, Mallorca, Spain

Richard Russell, (MD) Department of Respiratory Medicine, University of Oxford, Oxford, UK

Patrick Souverein, Assistant Professor of Pharmacoepidemiology, Division of Pharmacopathology and Pharmacotherapy, Utrecht University, Utrecht, The Netherlands

Jens Søndergaard, Head of Department, Research Unit for General Practice, University of Southern Denmark, Odense, Denmark

Mihaela Stefan, Associate Director of the Institute for Healthcare Delivery and Population Science and Associate Professor of Medicine at University of Massachusetts Medical School-Baystate, Baystate Medical Center, Springfield, MA, USA

Omar Usmani, Reader in Respiratory Medicine and Consultant Physician at the National Heart and Lung Institute (NHLI), Imperial College London & Royal Brompton Hospital (RBH), London, UK

Job van Boven, Assistant Professor, Universitair Medisch Centrum, Groningen, Groningen, The Netherland

Andrew Wilson, Clinical Professor, Norwich Medical School, University of East Anglia, Norfolk, England, UK