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

1 January 2020 to 31 December 2020

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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
OPCRD	Optimum Patient Care Research Database
OPRI	Observational and Pragmatic Research International Ltd
PRO	Patient-reported outcomes
RCT	Randomised clinical trial
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 what a year it has been. We hope that you and your families have stayed safe during these difficult times and, like us, are looking forward to a life where we can live with Covid rather than being dominated by it.

It is inevitable that, during such times, research has to take a back seat. This is particularly true for an organisation where most of the research is respiratory in origin. Despite this, we have still received a good number of protocols for review, recognising the ADEPT Committee's ability to work remotely and to provide a quick response to applications. Our turnaround times have remained excellent – mean duration of 11 days – which reflects the quality of the team we have working together around the Globe, despite the limitations raised by Covid.

One reflection that we have is that, after attending a few virtual meetings where the benefits of real-life research have been discussed, there seems to be increasing acceptance of a need for more than the classical randomised clinical trial to assess the effectiveness of an intervention. We feel that the future of real-world research, post Covid, will be very positive.

We hope you enjoy reading the 2020 report and that you remain part of the REG family in the years to come.

Stay safe and well, and we look forward to a time when we can all meet in person again.

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 2020 to 31 December 2020.

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. The process 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 a 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 EHR-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 2020 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, Associate Clinical Director Norfolk Community Health & Care, Chair Norfolk & Waveney Respiratory Working Group. Todor (Ted) Popov, Professor at the University Hospital Sv. Ivan Rilski in Sofia, Bulgaria, has been ADEPT Chair since January 1, 2019. 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 2020 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 review, communicates Committee decisions to applicants and invoices and processes application submissions, as appropriate.

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

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, 2020

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.

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 2021.

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

During the 2020 reporting period, ADEPT reviewed 20 protocols, of which 18 were for new studies and 2 amendments to prior protocol submission. The Committee approved all protocols submitted for review in 2020.

3.1 2020 ADEPT applications by research database

Half of all study protocols submitted for ADEPT review in 2020 (n= 10) involved use of the OPCRD. The other ten protocols involved use of the ISAR and OPCRD DARTNet databases (20% each) and of the OPC Australia and Delphi databases (10% each) (**Table 2**). Compared with 2019, a lower proportion of 2020 protocols proposed use of the OPCRD (50% versus 84%).

Table 2. ADEPT applications in 2020 by research database of interest

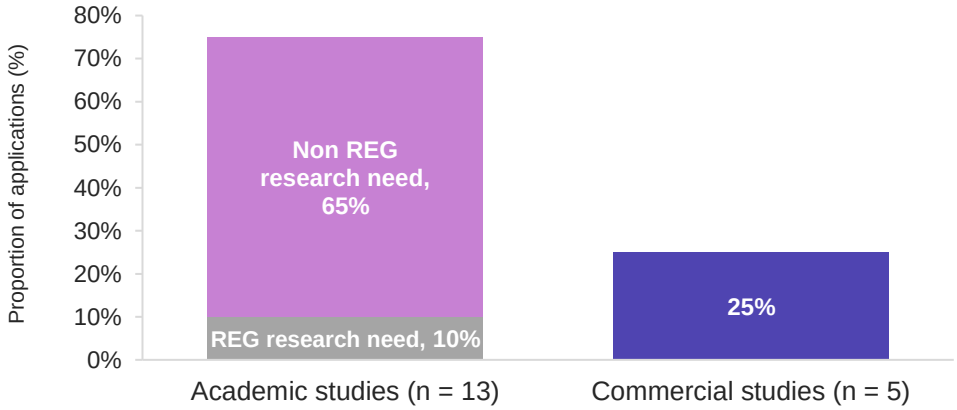
Database	Distribution of applications, N (%)	
	2020 (N = 20)	2019 (N = 19)
OPCRD	10 (50)	16 (84)
ISAR	4 (20)	3 (16)
OPC DARTNet	4 (20)	0 (0)

OPC Australia	**1 (10)**	**0 (0)**
Delphi	**1 (10)**	**0 (0)**

3.2 Research protocol funding

A breakdown of the commercial/academic profile of research protocols submitted for ADEPT approval in 2020 is presented in **Figure 1a** and a comparison of the commercial/academic profile of 2020 versus 2019 applications is detailed in **Figure 1b**.

Figure 1a. Commercial / academic profile of ADEPT-approved protocols, 2020

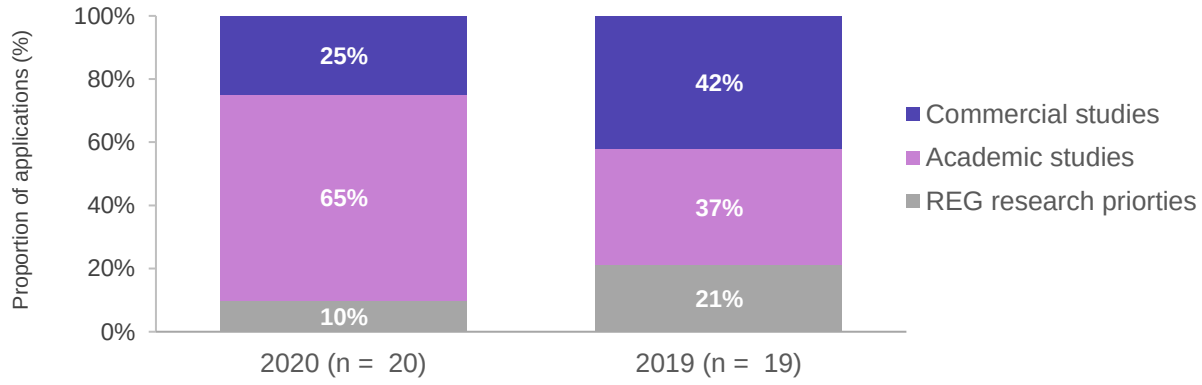


The majority (75%, n = 15) of the research protocols approved by ADEPT in 2020 were for academic research, including 2 (10%) applications for studies responding to REG-identified research priorities.[2] The academic research protocols approved in 2020 were submitted by: the Asthma UK Centre for Applied Research (AUKCAR; n = 4), the Observational and Pragmatic Research Institute (OPRI, n = 3),[3] the Respiratory Effectiveness Group (n = 2), the Centre for Public Health, Belfast (n = 1), and OPC Global (n = 5). Over the same period, ADEPT approved protocols for commercial research funded by AstraZeneca, Chiesi, GlaxoSmithKline and Sanofi Genzyme.

Compared with research protocols reviewed/approved by ADEPT in 2019, a smaller proportion of 2020 protocols were for commercial studies (25% vs 42%) and a smaller proportion were responses to REG-identified research needs (10% vs 21%) (**Figure 1b**).

Figure 1b. ADEPT-approved protocols by commercial/academic profile, 2020 vs 2019

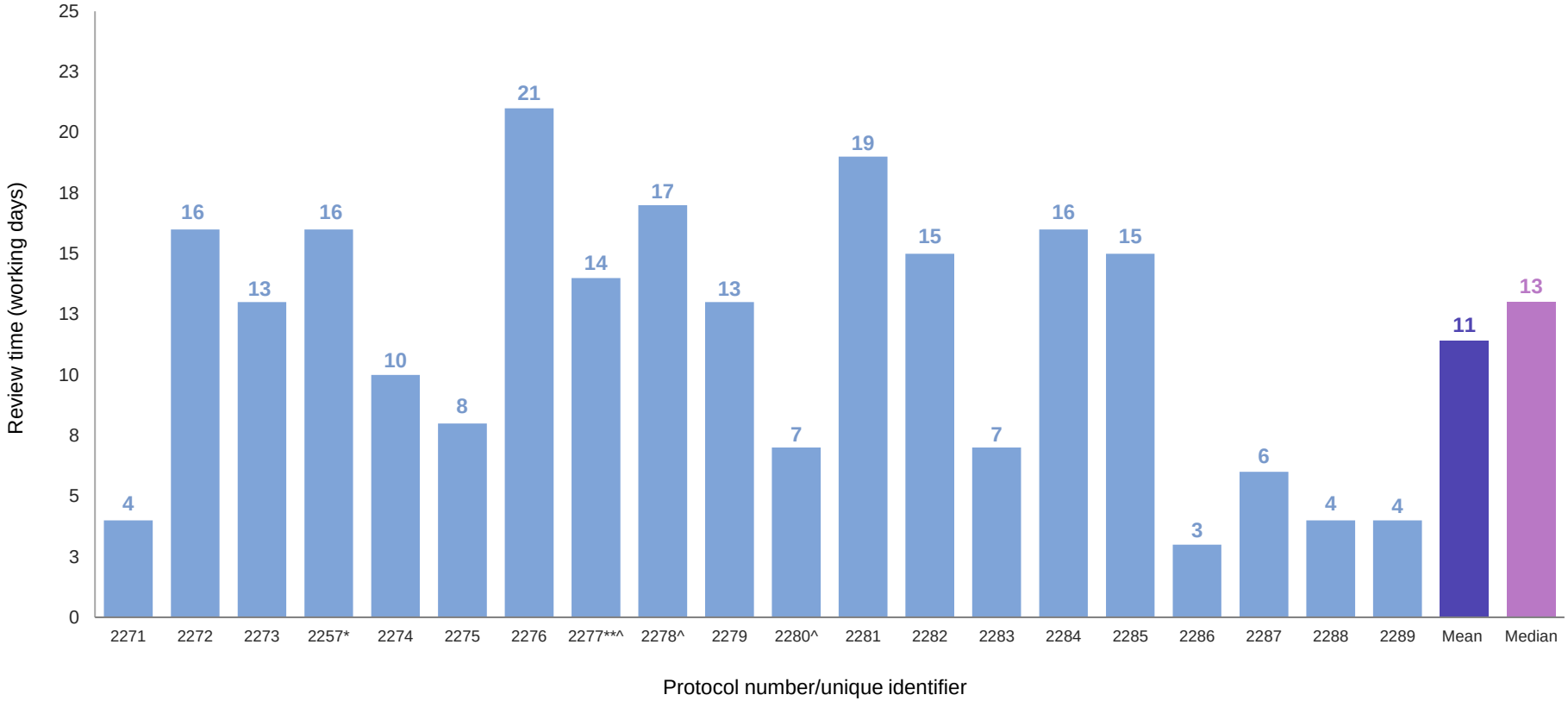
[2] Protocols outlining research that is responding to an REG-identified research priority may be commercially or academically funded, but the research will be non-commercial. All REG research priorities relate to scientific evidence gaps or clinical needs identified by the expert respiratory collaborator group.
[3] OPRI UK, n = 1; OPRI, n = 2


Proportion of applications (%)
100%
80%
60%
40%
20%
0%
25%
65%
10%
42%
37%
21%
2020 (n = 20)
2019 (n = 19)
Commercial studies
Academic studies
REG research priorties

3.3 Protocol turnaround time: submission to approval

The average duration of ADEPT review in 2020 was broadly in keeping with the Committee's 15 working day target: mean duration of 11 working days; median (range) duration of 13 (3–21) working days (**Figure 2a**).

Figure 2a. ADEPT review times from protocol submission to approval in 2020



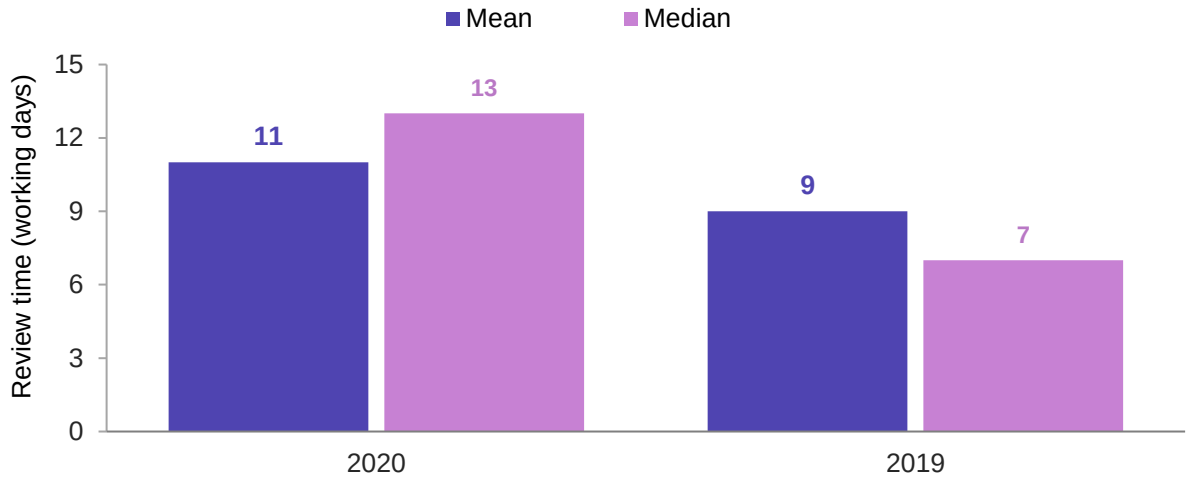
*Submitted for protocol amendment.

**Addition to previously approved protocol.

^During the year, IT complications resulted in delayed receipt and processing of 3 protocols (#2277, #2278 and #2280). If the IT delay is included in the overall review time, the total review time was 33 (vs 14) working days for protocol 2277, 46 (vs 17) working days for protocol 2278, and 49 (vs 7) working days for protocol 2280.

Overall, average ADEPT review duration in 2020 was slightly longer than in 2019: mean (median) review duration of 11 (13) working days compared with 9 (7) working days in 2019 (**Figure 2b**).

Figure 2b. Average review times for protocols approved by ADEPT in 2020 versus 2019



3.4 Areas of research interest

Of the 20 protocols approved by ADEPT in 2020, the majority 80% (n = 16) were for respiratory studies. The remaining 20% of approved protocols covered a range of topics, including neurology (1 protocol) and genetic diseases (1 protocol) (**Figure 3a**).

The majority representation of respiratory research in protocols submitted for ADEPT review in 2020 mirrored the predominance of respiratory research protocols approved by ADEPT in 2019 (80% in 2020 vs 84% in 2019) (**Figure 3b**).

Figure 3a. Protocols approved by ADEPT in 2020 by therapy area

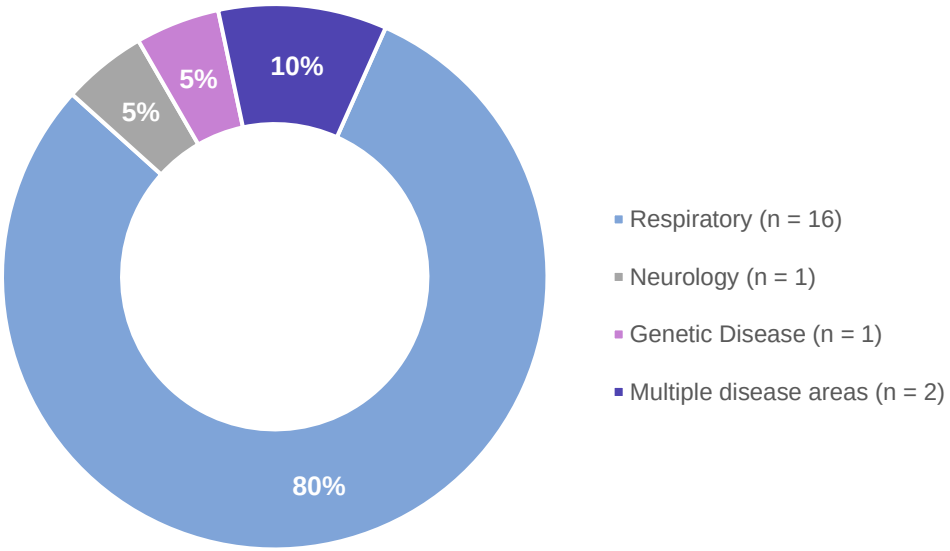
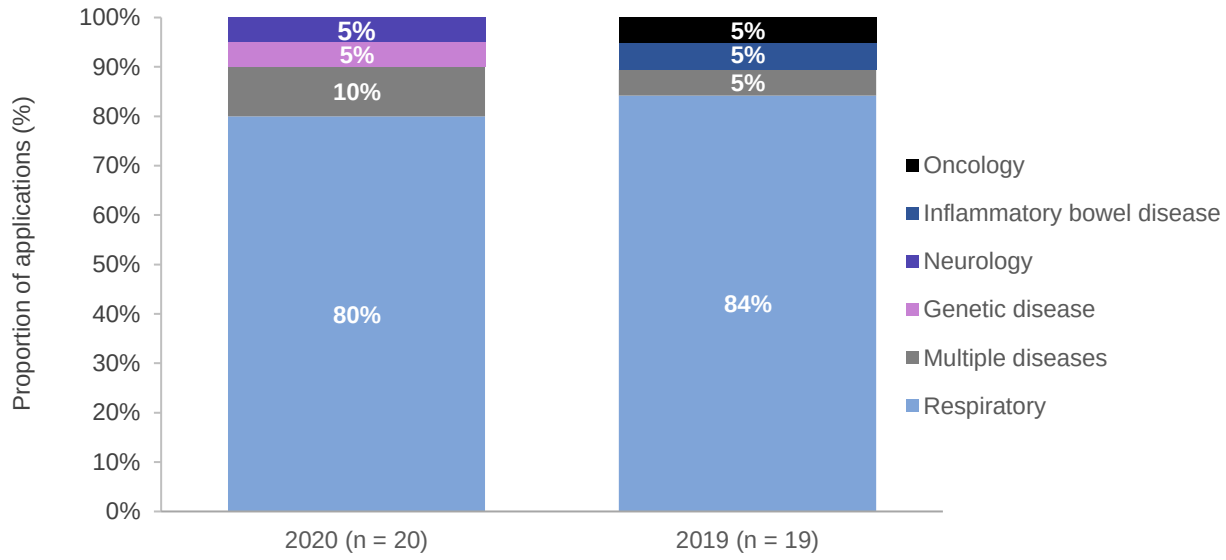
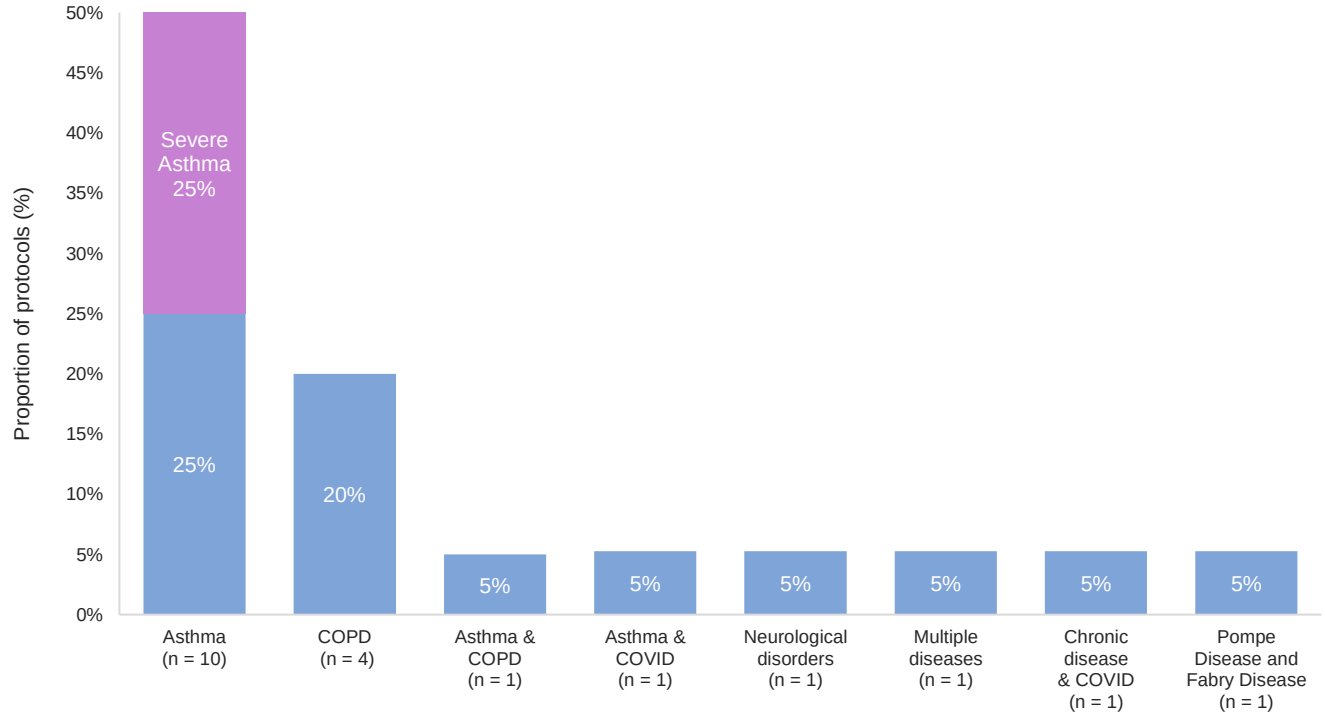


Figure 3b. Protocols approved by ADEPT in 2020 by therapy area, 2020 vs 2019



When considered at a disease-specific level, asthma featured in 60% of protocols: 50% (n = 10) asthma or severe asthma only; 5% (n = 1) asthma and COPD, and 5% (n = 1) asthma and COVID. Chronic Obstructive Pulmonary Disease was the focus of 25% (n = 5) of protocols: 20% COPD only; 5% (n = 1) asthma and COPD. Research involving neurological disorders and the genetic conditions (Pompe Disease and Fabry Disease) accounted for another 10% of protocols (n = 1 each) (**Figures 3c**).

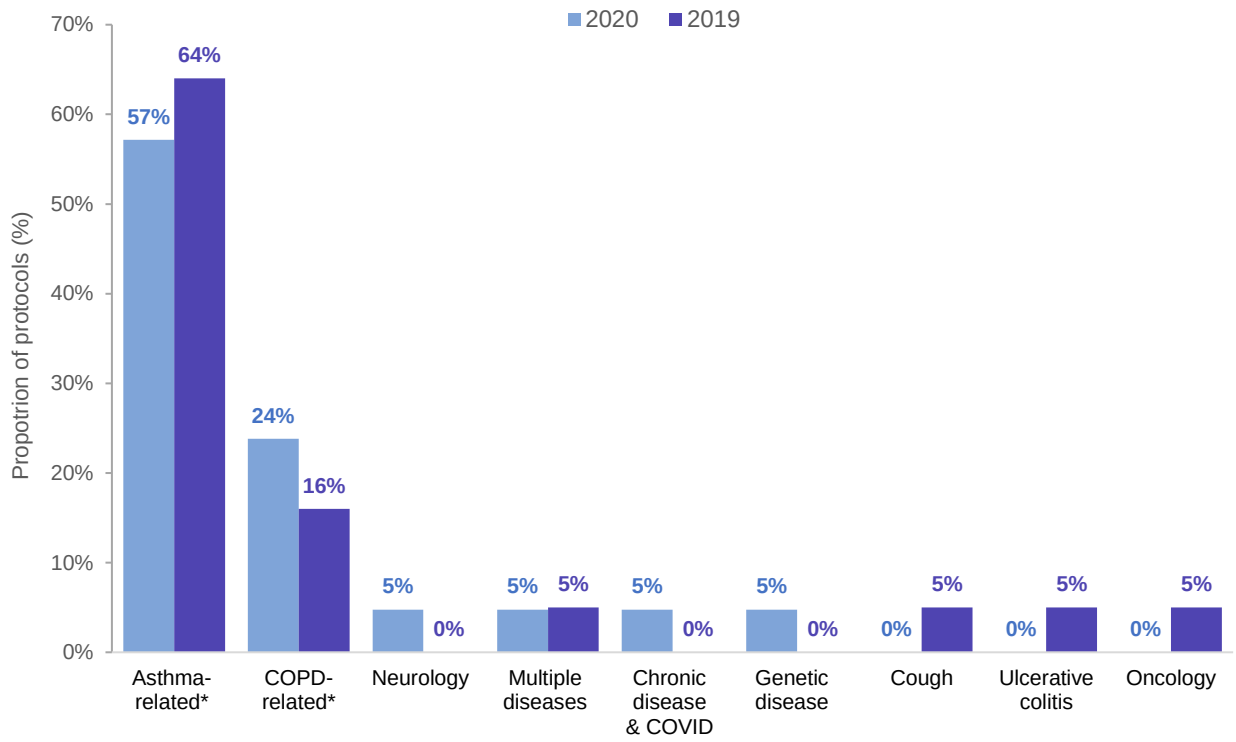
Figure 3c. ADEPT-approved protocols by disease, 2020



COPD, chronic obstructive pulmonary disease; COVID, coronavirus disease

The distribution of approved protocols by focus disease was broadly similar in 2020 and 2019 with asthma-related studies being most common followed by COPD studies (**Figure 3d**).

Figure 3d. ADEPT-approved protocols by disease, 2020 vs 2019



*One approved protocol in 2020 related to both asthma and COPD and so contributes to both the asthma- and COPD-related categories for 2020. A denominator of 21 has been used for all 2020 percentages.

COPD, chronic obstructive pulmonary disease; COVID, coronavirus disease; IBD, irritable bowel disease

The protocols approved by ADEPT in 2020 covered a range of different research topics and study designs, from epidemiology and disease characterisation to phenotyping, predictive modelling, comparative effectiveness and post-marketing surveillance studies (**Figures 3e**).

The nature of the studies and research topics covered by protocols approved by ADEPT in 2020 was not dissimilar to that of protocols approved by the committee in 2019 (**Figure 3f**).

Figure 3e. ADEPT-approved protocols by research topic, 2020

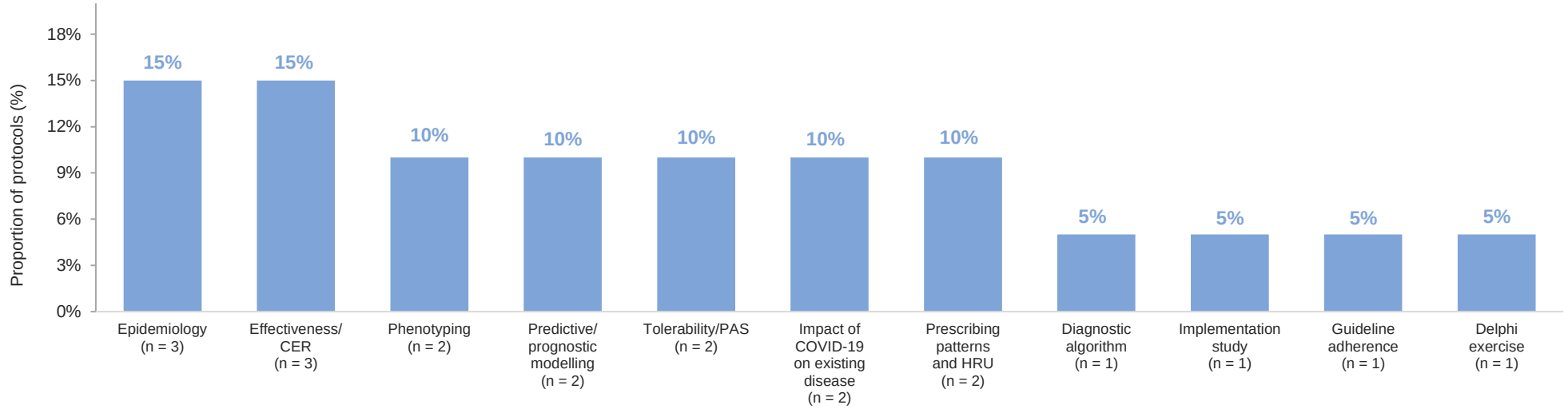
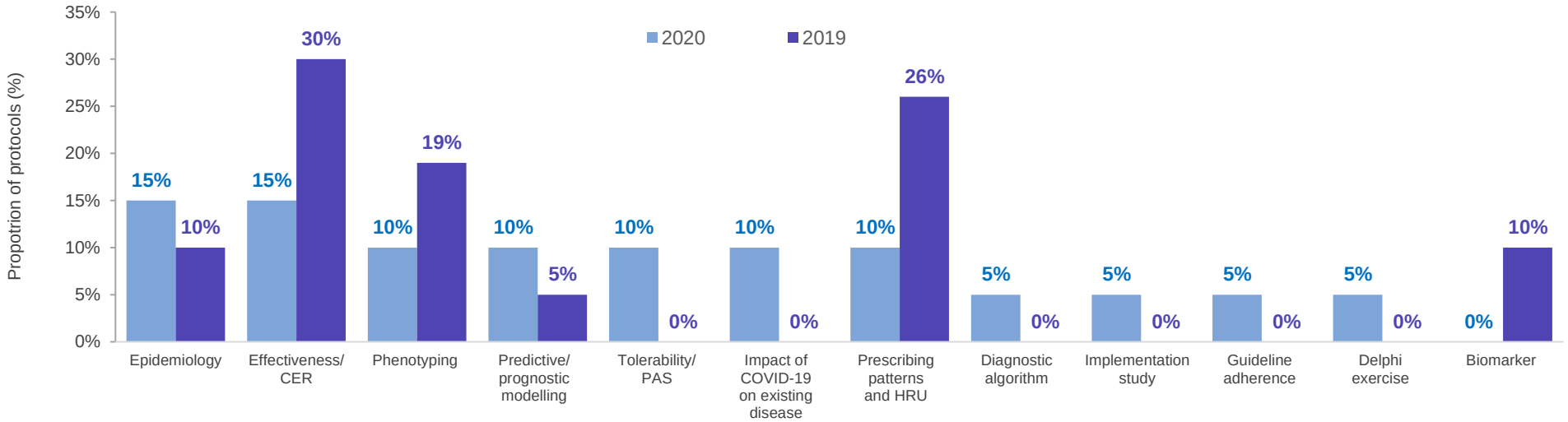


Figure 3f. ADEPT-approved protocols by research topic, 2019



CER, comparative effectiveness research; HRU, healthcare resource utilisation; PAS, post-marketing authorization study

3.5 Overview

This is the second annual report of the ADEPT Committee. It summarises the work of the Committee in 2020 and the scope of that work in comparison to activities in 2019.

During the 2020 reporting period, the Committee received and approved 20 research protocols, 18 new submissions and 2 protocol resubmissions/amendments.

The mean (median) duration of protocol review in 2020 was 11 (13) working days, which compares with mean (median) times of 9 (7) working days for 19 protocols in 2019. Although the average review times in 2020 were slightly longer than in 2019, they remained within the Committee's 15-working-day target despite the significant impact of COVID-19 during the period.

The majority of protocols approved by ADEPT in 2020 were for academic studies (75%). Respiratory medicine was the therapy area of greatest research interest in both 2020 and 2019 (focus of 80% and 84% of protocols, respectively). Asthma continued to be the most commonly researched condition in 2020, featured in 57% of protocols in 2020 and 64% in 2019. In 2020 non-respiratory study protocols featured studies of genetic and neurological conditions; in 2019 non-respiratory research topics included ulcerative colitis and oncology.

Protocols submitted in 2020 covered a diverse range of research topics and study designs, as was the case in 2019. In both years, submissions featured epidemiology, phenotyping, prognostic modelling, effectiveness and tolerability studies, but 2 protocols approved by ADEPT in 2020 were for studies relating to the impact of COVID-19 on pre-existing chronic conditions.

Appendix 1. ADEPT Committee Members, 2020

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