ORIGINAL RESEARCH

Advancing the Patient EXperience (APEX) in COPD Registry: Study Design and Strengths

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The Advancing the Patient Experience (APEX) in Chronic Obstructive Pulmonary Disease (COPD) registry (https://www.apexcopd.org/) is the first primary care health system-based COPD registry in the United States. While its ultimate goal is to improve the care of patients diagnosed with COPD, the registry is also designed to describe real-life experiences of people with COPD, track key outcomes longitudinally, and assess the effectiveness of interventions. It will retrospectively and prospectively collect information from 3000 patients enrolled in 5 health care organizations. Information will be obtained from electronic health records, and from extended annual and brief questionnaires completed by patients before clinic visits. Core variables to be collected into the APEX COPD registry were agreed on by Delphi consensus and fall into 3 domains: demographics, COPD monitoring, and treatment. Main strengths of the registry include: 1) its size and scope (in terms of patient numbers, geographic spread and use of multiple information sources including patient-reported information); 2) collection of variables which are clinically relevant and practical to collect within primary care; 3) use of electronic data capture systems to ensure high-quality data and minimization of data-entry requirements; 4) inclusion of clinical, database development, management and communication experts; 5) regular sharing of key findings, both at international/national congresses and in peer-reviewed publications; and 6) a robust organizational structure to ensure continuance of the registry, and that research outputs are ethical, relevant and continue to bring value to both patients and physicians. (J Am Board Fam Med 2021;34:22–31.)

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Introduction

In 2001, the Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Lung Disease (GOLD) was first published, marking a new generation of evidence-based recommendations.[1] These recommendations were designed to

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improve on existing chronic obstructive pulmonary disease (COPD) management strategies, and to be a core resource for the care of people with COPD globally. The most recent update of the GOLD strategy document outlines criteria for COPD diagnosis (including spirometry), provides evidence-based guidance on COPD treatment according to symptom burden and exacerbation risk, and highlights the importance of correct inhaler technique and regular technique assessment.[2] Despite this well-outlined management strategy, COPD remains under- and misdiagnosed,[3–5] with significant underuse of spirometry to confirm the COPD diagnosis.[6,7]

A series of campaigns to increase awareness of COPD and best clinical practice in primary care have been conducted.[6,8,9] Appropriately, the focus has been on primary care in recognition of the fact that, within the United States, 80% of patients diagnosed with COPD are managed by their family physician or general internist.[10] Despite these efforts, many US family physicians and other primary care clinicians are unfamiliar with recent advances in COPD management and updates to the GOLD strategy document.[7] Making a diagnosis of COPD based on clinical findings alone is not uncommon. Prescribed treatments are not always aligned with COPD management strategy recommendations.[11,12] Furthermore, adherence to treatment is low, in terms of taking medication and using inhalers correctly, both of which negatively impact treatment outcomes.[13] Each of these factors has cost, effectiveness, and safety implications. For example, a survey including 784 US-based primary care physicians showed highly varied treatment preferences for COPD, and a strong preference for inhaled corticosteroid use, regardless of exacerbation history or knowledge of low lung function, in contravention of GOLD recommendations.[2,11] Furthermore, poor adherence to COPD medications has been associated with reduced effectiveness and poor outcomes, including mortality.[14]

Concerned about the growing prevalence of COPD, members of the Congressional COPD Caucus; the National Institutes of Health's National Heart, Lung, and Blood Institute; National Heart and Lung Institute; Centers for Disease Control and Prevention; and many COPD community and health care professional stakeholders collaborated to formulate The COPD National Action Plan (Plan).[15] The Plan outlines 5 goals to improve the management of COPD, including a focus on patient empowerment and improvement of disease prevention diagnosis and treatment. The Plan also encourages collection, analysis, and dissemination of public health data, highlights the need to continue research and to translate national recommendations into research and public health care actions.[15] The use of newer technologies such as electronic health records (EHRs) and patient reported information/patient reported outcomes (PRI/PRO) data collection, and incorporation of these data, into a registry may be one way to support implementation of the National Action Plan.

Registries are well-established tools to observe the course of disease, understand the impact of treatment variations and outcomes, and examine factors that can influence prognosis.[16] Key features that should be included in a registry have been summarized by Nelson and colleagues (Table 1).[17] Registries can be particularly suited to tracking the natural progression of COPD, where progression is slow, and trends can be easily hidden. Registries are also useful to describe care patterns, disparities in care delivery, and to assess effectiveness, safety, and quality of care.[16] The main

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Table 1. Key Features of Registry-Based Learning Systems

Feature	Delivered by APEX COPD registry
Social network of patients and families encouraged to engage in the patient's healthcare and supported by tools that enable them to track their health outcomes and support self-care	The APEX COPD registry provides rapid feedback of data to both patients and physicians to encourage engagement, support shared decision making, and facilitate self-management by enabling patients to track their disease over time.
Collaborative network of clinical teams that can provide care and who engage in a system providing longitudinal and comparative data	The APEX COPD registry comprises a collaborative network of primary care physicians, nurses, physician assistants, specialists, research scientists, and database experts to collect longitudinal, comparative, clinically relevant, and individual-level data.
Sharing of power and responsibility among patients, clinicians, and scientists for designing, governing and evaluating services to improve and research	The APEX COPD registry is overseen by 5 governing bodies to ensure collection of clinically relevant data, and ethically-sound research.
Digital collection and use of both clinical and patient-reported outcomes to guide care and as a basis for improvement, research, and public health policy	The APEX COPD registry collects data digitally from EHR and from patients in the form of on-line questionnaires and during the office visit.
Demonstration of measurable improvement in individual and public health outcomes through improved adherence to current evidence and rigorous trials of new approaches	The APEX COPD registry will track all relevant variables longitudinally to assess improvement in individual and public health outcomes.
Dissemination and translation of ideas and findings through publication in peer-reviewed journals, presentations and meetings, and outreach to patients, clinicians, researchers, and health policy analysts	The APEX COPD registry incorporates a team of communication specialists to ensure timely dissemination of research both at scientific/medical congresses and in peer-reviewed publications.

APEX, Advancing the Patient Experience; COPD, chronic obstructive pulmonary disease; EHR, electronic health record.
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advantages of prospective, observational patient registries are the inclusion of "real-world" patients, with enhanced generalizability, and the ability to examine clinical questions for which a randomized controlled trial (RCT) is either impractical or unethical.[16,18] Registries also have the potential to improve diagnostics and may be used as a rich source of data to inform treatment algorithms or clinical decision support systems. Although a few COPD registries and patient cohorts already exist (eg, COPDGene and the COPD Foundation Patient-Powered Research Network Registry),[19,20] none are based in primary care.

A well-designed registry can provide benefits for all key stakeholders involved in COPD management.[16] Physicians promptly receive a real-world picture of disease presentation, treatment practices, and outcomes in a large number of patients. Adherence to evidence-based recommendations can be assessed. Patients and patient advocacy organizations benefit from an increased understanding of the natural history of disease and the impact of treatment. Payers can obtain detailed information on the cost effectiveness of procedures, devices, or pharmaceuticals in a large number of patients.[16] Unfortunately, few registries have realized their full potential. Data flow back to participating centers is frequently delayed; many registries rely on manual data entry, which is costly

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Table 2. APEX COPD Registry Core and Research Projects

Description
Delphi consensus of core variables to capture in the APEX COPD registry
Demographic and clinical baseline characteristics of COPD patients based in US primary care
Variation in demographic and clinical characteristics of COPD patients managed in US primary care
Treatment patterns of COPD patients managed in US primary care

APEX, Advancing the Patient Experience; COPD, chronic obstructive pulmonary disease.

and prone to error; and patients usually do not have access to their own data, or have the opportunity to add data outside the structure of the patient-physician/clinician consultation.[17]

In answer to the call to action of the COPD National Action Plan,[15] the Advancing the Patient Experience (APEX) COPD registry (https://www.apexcopd.org/) will provide a mechanism to standardize and store data on COPD patients seen in primary care in the United States. It will integrate clinically relevant data from existing sources (ie, EHRs) and from patients themselves (through use of questionnaires and information obtained during the office visit) to answer key research questions relating to COPD in primary care. The primary objectives of the APEX COPD registry are to describe and characterize the primary care COPD population in the United States; to compare the effectiveness (both clinical and cost) and safety of current COPD treatments; and to understand predictors of response to available COPD treatment options. Current APEX COPD registry research projects closely align with these aims and are summarized in Table 2. Secondary objectives of the registry are numerous reflecting the scope of this initiative and its potential not only to improve both family physician awareness and management of COPD, but also to answer key research questions relevant to physicians treating COPD patients in every day clinical practice (Table 3). The aim of this article is to describe the APEX COPD registry study design and to summarize its strengths.

Study Design of the APEX COPD Registry

Registry Design

This registry is a US-based, primary care registry, supported by a multinational and multi-organizational team of experts. It has been designed to be an observational, primary care initiative which will retrospectively and prospectively collect EHR COPD variables (from December 2008 through December 2022), supplemented with PRI/PRO data and information gathered from COPD patients during primary care visits. Due to the real-life nature of the

Table 3. Secondary Objectives of the APEX COPD Registry Initiative

Improve quality of care, and primary care patient outcomes through structured COPD support and increased understanding of COPD management
Understand the clinical phenotypes of COPD that predict response to or appropriateness of inhaled treatments
Understand the current burden and minimize side effects of steroid exposure through use of appropriate treatments
Support the development of effective and efficient diagnostic routines and therapeutic principles
Assess the level of classification differences as defined by comparing clinician-diagnosed COPD at baseline against established guidelines' diagnostic criteria
Describe disease management patterns such as treatment changes over time (eg, step up, step down, and switches), as well as the reasons for changes and the effect of these changes on disease progression
Assess the impact of inhaler technique, inhaler type and lung function on disease management and severity (eg, exacerbations and CAT scores)
Describe factors associated with treatment choice at baseline and describe disease progression
Describe risk factors (eg, age, sex, smoking, BMI, occupation, family history, presence of comorbidities, socioeconomic status, quality of care, lung function, exacerbations) associated with disease progression, PROs, and healthcare utilization
Assess the occurrence of exacerbations and other conditions, including URTIs and seasonal variations
Assess biomarker data and estimate their predictive value for disease diagnosis, pheno- and endo-type characterization, response to treatment and disease progression
Identify patients who may be eligible for participation in future research studies

APEX, Advancing the Patient Experience; BMI, body mass index; CAT, COPD assessment test; COPD, chronic obstructive pulmonary disease; PRI/PRO, patient-reported information & outcomes; URTI, upper respiratory tract infection.

registry, the routine clinical care of patients will continue to be provided in accordance with the patient and his/her health care professionals at the mutually agreeable utilization level. It is estimated that patients with prior COPD diagnoses will have at least 1 clinic visit per year. Central ethics (Institutional Review Board) approval has been obtained from the American Academy of Family Physicians for most sites (Institutional Review Board reference number 19-349). One site has its own ethics approval boards. Secondary ethics approval will also be sought where sites require their own ethics approval board. The study is registered with ENCePP (study reference number EUPAS29401; http://www.encepp.eu/encepp/viewResource.htm?id=29348).

Patient Population

Three thousand patients with COPD will be enrolled into the registry, identified using health care system EHR data. Patients will be recruited from participating primary care sites in accordance with local regulatory/ethical requirements. Patients will be eligible to participate if they have a diagnostic code for COPD (or a COPD monitoring review code), including chronic bronchitis, emphysema, α1-antitrypsin deficiency and mixed COPD/asthma, before, or at, the enrolment consultation, and were aged ≥ 35 years at the time of COPD diagnosis. Registry activities include clarifying COPD diagnoses to further understand current diagnostic approaches in US primary care. Patients will be excluded if they are currently participating in a COPD drug therapy clinical trial at time of enrolment, have a life expectancy < 12 months from date of enrolment, have had an active cancer diagnosis in the past 3 years (excluding nonmelanoma skin cancer), and/or are receiving hospice care. Informed consent will be obtained from patients via an online portal to allow data sharing for ethically approved research purposes as well as recruitment for future studies.

Sites

Clinic sites within 5 or more health care organizations (HCOs) will be recruited (Figure 1). Current participating sites (HCOs) are located in Texas (Bandera Family Health Center), Ohio (Metro Health System), Colorado (Miramont Family Medicine), New York (Urban Family Practice), and North Carolina (Wilmington Health System). Participating sites will provide access to a limited EHR data set through a data use agreement of all patients with COPD who do not specifically opt out of the project. During the registry consent process, some patients may opt out of all data sharing. The data in the registry will be populated directly from EHRs with supplementary point of care data populated by primary care clinicians (eg, physicians, nurse practitioners and physician assistants working in primary care) during routine clinical care. These clinicians will be provided with an information pack outlining the APEX COPD initiative, including an overview of the information patients may bring to visits, operational and technical support for data entry (if required).

Data Collection and Management

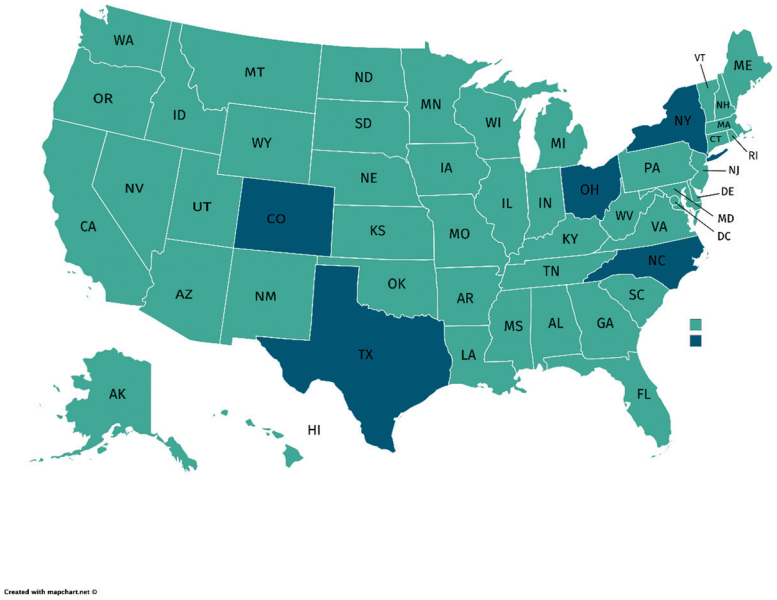
Data Collection

The APEX COPD registry will contain information obtained from multiple sources including additional information on assessment (eg, data from EHRs, patients, and clinicians at time of visits). The EHR data look-back period will be up to 10 years from December 1, 2018 for clinic visits, observations (eg, social history), measurements (eg, blood pressure, laboratory values), and procedures (eg, spirometry, surgeries). Medications and conditions (eg, diagnoses) will not be limited in their look-back period but extend back as far as EHRs exist at each site for patients included in the registry. PRI/PRO data will be provided via patient surveys (ie, baseline, annual and preclinic visit questionnaires). These data will be updated after, and potentially during, each encounter and supplemented by clinician-reported data collected for visit activities not recorded in the EHR (eg, inhaler technique observation).

Variables Collected

Basic demographic and diagnostic variables collected in the APEX COPD registry were developed by Delphi consensus.[21] These are subdivided into 3 main areas: demographics, disease monitoring, and treatment variables. Specific data to be collected includes information on diagnosis, COPD exacerbations, symptom burden, lung function, quality of life, comorbidities, smoking status/history, treatment specifics (including side-effects), inhaler management (for example, inhaler satisfaction, and patient education/self-management (Appendix Table 1).[21] Much of this information is extracted from existing EHRs, but some must be manually entered (eg, point of care variables; see Appendix Table 1). Additional variables used to assess COPD control (eg, use of rescue medication, physical activity and sputum color)[22] and lung

Figure 1. US states (blue) in which sites have been identified for inclusion in Advancing the Patient Experience in chronic obstructive pulmonary disease.



function were added to the registry after the Delphi exercise. These additional variables were agreed by consensus of the whole steering committee.

Research Database

High data quality standards will be maintained, and processes will be utilized to ensure that the data are as accurate as possible when presented for analysis. Data quality will be enhanced through a series of programmed data quality checks that automatically detect out of range or anomalous data. All modifications to data will be recorded in an audit log. EHR data will be extracted remotely by the DARTNet Institute (a nonprofit organization that hosts data sets of health information for quality improvement and research). Data will be standardized using the Observational Medical Outcomes Partnership common data model (v6), which allows for the analysis of data from disparate sources by transforming the data into a standard format and representation. The data will then be cleaned, quality checked, and deposited into a database on a biennial basis. PRI/PRO data will be collected into the Patient Engaged Electronic Reporting System (PEERS), a Health Insurance Portability and Accountability ACT (HIPAA) 1996–compliant, Internet-based study management system; and paired with patient-level EHR data. To preserve confidentiality, all individuals will be assigned a

Figure 2. Operational overview of the Advancing the Patient Experience (APEX) in chronic obstructive pulmonary disease (COPD) initiative. Abbreviation: EHR, electronic health record.

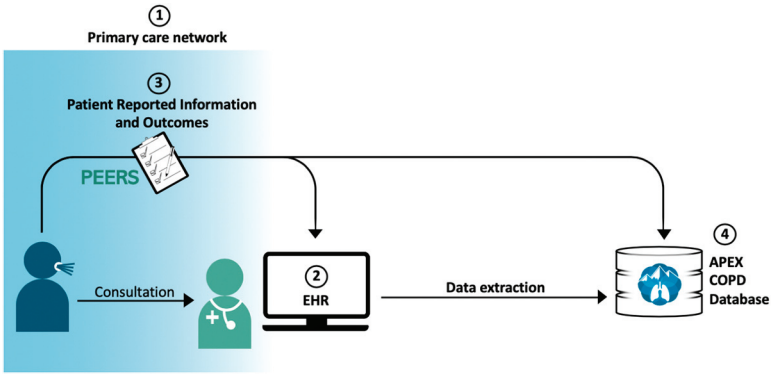
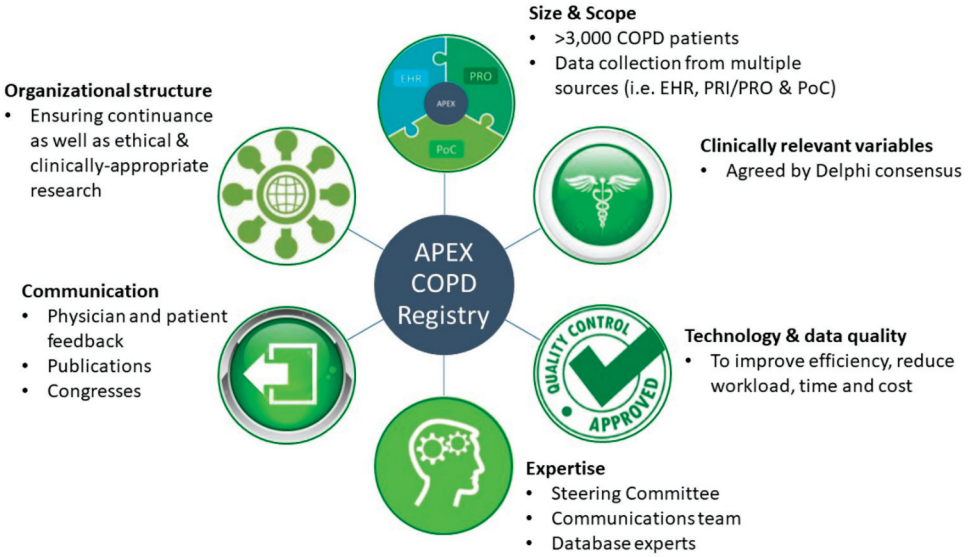


Figure 3. Key strengths of the Advancing the Patient Experience (APEX) in chronic obstructive pulmonary disease (COPD) initiative. Abbreviations: EHR, electronic health record; PoC, point of care; PRI/PRO, patient reported information/patient reported outcomes.



unique Registry ID using a 1-way hashing algorithm before being stored in the database. The APEX COPD database will be hosted in the United States on an Amazon Web Service (AWS) firewall-firewall-protected server. This server will be part of the HIPAA 1996–compliant DARTNet server environment maintained by AWS. Optimum Patient Care Global (OPC) will act as data custodians, but each site/patient will continue to own the patient-level data they contribute to the APEX COPD database.

Research

APEX COPD has a collaborative consensus voting system in place for the selection of research projects. Funded research proposals will be voted on annually by the APEX COPD Steering Committee. Each committee member has 1 vote. Voting is anonymous with a simple majority required for research project selection. All research projects will be approved by the US Steering Committee, the US Independent Review Board and the Anonymised Data Ethics & Protocol Transparency (ADEPT) Committee. APEX COPD registry research proposals are summarized in Table 2.

How It All Links Together: The Operational Delivery Model

The APEX COPD registry incorporates 4 key and inter-related components (Figure 2). The primary care network includes a network of engaged clinicians and their patients diagnosed with COPD. The registry is fed by data obtained from existing EHRs and supplemented with PRI/PRO data (obtained via online questionnaires) and patient information gathered during office visits. All this information is gathered and extracted to the APEX COPD database. A clinical decision support system may be developed as an exploratory feature of the initiative in the future. This will provide current and evidence-based information support to primary care clinicians regarding treatment, monitoring, and care of COPD patients in primary care.

Strengths of the APEX COPD Registry

The strengths of the APEX COPD initiative and how it will improve management of COPD in primary care settings are summarized in Figure 3.

Size and Scope

This registry plans to capture information from 3000 COPD patients, from clinic sites within 4 to 5 HCOs, with wide geographic coverage throughout the United States (Figure 1). The scope of the initiative is broad, integrating information from multiple sources (ideally both EHR- and patient derived) to provide a snapshot of the COPD population managed in primary care in the United States; as

well as the capability to conduct longitudinal analyses to examine the impact of appropriate COPD variables on disease prognosis, progression, and treatment outcomes (Table 1). The APEX COPD initiative, therefore, has the potential to improve primary care awareness of COPD and its management, and to answer key research questions, with the ultimate goal of improving care for patients diagnosed with COPD.

Clinically Relevant Variables

APEX COPD registry variables have been developed by consensus of the APEX COPD Delphi panel (Appendix Table 2). These variables will be integrated predominantly from existing EHRs (n = 115 variables), but will also include up to 34 PRI/PRO variables and 5 variables collected from patients during office visits: forced expiratory volume in 1 second (forced vital capacity, moderate and severe exacerbations, and inhaler technique [Table 1; Appendix Table 1]).[21] A balance was achieved between collecting the minimum information needed to effectively study the diagnosis and management of COPD, while also ensuring a comprehensive description of COPD patients managed in real-life clinical practice in the United States. Variable selection was also driven by practicality of collection by primary care clinicians, and the need to be clinically relevant and useful to physicians, other clinicians, and patients.

Technology and Data Quality

The true value of any registry is measured in terms of the quality of data it collects. Data provided for research will be analyzed as a limited data set at the individual patient level rather than the aggregate level. This offers the potential to explore clinically relevant and previously unanswered research questions, compared with the limited options possible with aggregate data.[23] Electronic data capture systems will be used to capture data directly from EHR systems, which will improve efficiency, reduce workload, time, and cost, as well as enhance the quality of data collected, while minimizing data entry burden (Table 1).

Clinical and Scientific Expertise

Broad clinical expertise is integrated into each layer of the APEX COPD initiative. First, the APEX COPD Steering Committee consists of 14 experts in primary and specialist care from the United States and internationally (5 family physicians, 3 pulmonologists, and 6 respiratory researchers) with approximately 70% of members based in the United States (Appendix Table 2). These individuals are all experts in the field of COPD evidenced by their 1) publication history; 2) participation in the development and/or management of severe COPD registries, epidemiologic databases, and scientific congress committees and/or; 3) experience as a medical provider with interest in advancing COPD management in clinical practice. Second, primary care clinics involved in data acquisition will include experienced primary care doctors, nurse practitioners, and physician assistants. Lastly, the APEX COPD initiative includes an experienced communications team and partners with experts in database management and registry delivery (DARTNet Institute, Aurora, Colorado; Table 1).

Communication

The APEX COPD initiative plans to provide written feedback to both physicians and patients for use during clinic visits. Patients will receive feedback on meeting goals, health status, smoking and prevention, an inhaler satisfaction rating, and an annual treatment and hospitalization tracker. Physicians will receive feedback on patients' health test results (eg, GOLD category, COPD Assessment Test score) and information on smoking status, treatment adherence, and inhaler technique. The aim is to encourage patient empowerment, shared decision making, and improve physician-patient communication. APEX COPD registry research findings will also be regularly disseminated in peer-reviewed journals and at both national and international medical/scientific congresses (Table 1).

Organizational Structure

APEX COPD is overseen by 5 governing bodies: 1) OPC Global, 2) the Respiratory Effectiveness Group, 3) the ADEPT Committee, 4) the AAFP, and 5) the APEX Steering Committee. Their purpose is to safeguard the continuance of the registry into the future and to ensure that APEX COPD registry research is ethical, clinically appropriate, and continues to bring genuine value to patients and physicians (Table 1). The roles and responsibilities of each of these 5 governing bodies is provided in the Appendix.

Limitations and Advantages of Registry Data

Certain limitations of registry data should be acknowledged. First, due to their design, registry data may possess lower internal validity than data collected prospectively in RCTs, limiting the extent to which they can support causal relationships. However, to counterbalance this limitation, the APEX COPD registry includes information from real-world patients receiving care they and their health care professionals direct, thus providing generalizable data not available from tightly controlled clinical trials with multiple exclusion criteria and limited enrolment settings. Second, the large volume of data collected by registries also creates the potential for many analyses with selective reporting. With the APEX COPD registry, this will be mitigated by a priori agreement of research protocols. A database is only as good as the data it collects, so a system to validate and verify data integrity (such as that employed by APEX COPD) is essential to ensure database utility.[24] Lastly, although much of the information used to populate the APEX in COPD registry is extracted digitally from EHRs, some manual data entry is required both from healthcare professionals (HCPs) and patients, in the form of point of care and questionnaire variables, respectively. Minimization of the number of manual entry variables (n = 5) and use of shortened online patient questionnaires will reduce this burden. Administrative burden is also reduced as the Ethics Committees at each of the 5 sites have approved these questionnaires for implementation as part of clinical care. They do not require research consent. Furthermore, the APEX COPD registry will also supplement EHR data with information routinely recorded, such as inhaler technique education.[25] Registry data may be collected prospectively and retrospectively using data that are routinely collected with opportunities to obtain more data, more quickly, over a long period of time, and at a lower cost than RCTs.[25]

Conclusions

The APEX COPD registry is the first health-system based primary care COPD registry in the United States, and closely aligns with the key features of a registry-based learning system.[17] It will encourage patient engagement in care and shared decision making, use a collaborative network of clinical teams to provide longitudinal and comparative real-world care and outcomes data, conduct clinically relevant and ethical research, collect information from both physicians and patients, and is committed to dissemination of its findings to key stakeholders involved in the management of COPD in primary care. The APEX COPD registry will continue to evolve to best serve the needs of those living with and caring for people with COPD.

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To see this article online, please go to: http://jabfm.org/content/34/1/22.full.

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Appendix

Patients: Rules of Exclusion

Patients found to have 1 or more exclusion criteria after they have consented for the study will be left in the study as there is no intervention and they are at no increased medical risk to continue. This decision was made in recognition of the fact that documentation concerning hospice care and cancer treatments may not always be available in primary care electronic health record (EHR).

Primary Care Clinic Number

The current primary care clinic (PCC) sizes range from 1200 to 1900 patients. Each PCC is estimated to include 102 patients with chronic obstructive pulmonary disease (COPD; based on 1500 patients per PCC and a 6.8% COPD prevalence), of which 60% (ie, 61 patients) are predicted to be included in the Advancing Patient Experience (APEX) in COPD registry. Therefore, 50 participating primary care clinicians will be required to enroll 3000 COPD patients over a 4-year period. At least 50% of recruited patients will have a minimum of 2 years of prospective data and the majority at least 1 year.

Patient Recruitment

Multiple methods will be used to recruit patients and minimize attrition rates. The registry will focus on recruitment through information provided to patients in the PCC office, supplemented with invitational/opt out letter directing people to the study website where they can self consent. Follow-up phone calls (by DARTNet staff) for patients signing an interest card in the PCC office will also be used.

Data Collection

Patient reported information/patient reported outcomes (PRI/PROs) to be collected will pertain to any data the patient has access to and can accurately relay via online survey. Questionnaires will be collected using Patient Engaged Electronic Reporting System and will be compatible with multiple devices to maximize ease of data collection. Patients will be sent 3 reminder messages 48 hours apart as a reminder to complete questionnaires.

Three PRI/PRO questionnaires will be used.

1. Baseline questionnaire to include a broad set of questions including historical information related to exposures that increase the risk of COPD, family history, COPD control, quality of life, and medication preferences.
2. Annual questionnaire to update baseline information which can change over time such as exacerbations, quality of life and medication preference.
3. Short pre-clinic visit questionnaire designed to focus on data of use for clinical assessment; to be completed at least 30 days from any previous data collection.

APEX COPD Organizational Structure and Responsibilities

Optimum Patient Care

Optimum Patient Care (OPC) Global specializes in delivering medical research and services to improve the diagnosis, treatment, and care of chronic diseases within primary care. OPC has a proven track record in delivering primary care research, clinic support services, customized data sets for academic research as IG-compliant data extractions and delivering global registry projects. It acts as data custodians of the APEX COPD database, but each site/patient continues to own patient-level data contributed.

Respiratory Effectiveness Group

The Respiratory Effectiveness Group (REG) is a not-for-profit investigator-led academic initiative comprising over 420 respiratory/allergy experts globally collaborating on delivering independent, academic real-life and comparative effectiveness research in respiratory medicine. The REG initiative focuses on establishing best practice methodologies and standards, with the objective of raising the quality and profile of real-life research for all stakeholders including patients, clinicians, industry, and guideline/regulatory bodies. REG provides ethical and scientific review of APEX in COPD research study proposals.

Anonymised Data Ethics & Protocol Transparency Committee

The Anonymised Data Ethics & Protocol Transparency (ADEPT) committee is an independent body of experts commissioned by REG to govern the standard of research conducted on internationally renowned databases. It comprises scientists with statistical and epidemiologic experience, members with specific database related expertise, and independent clinical experts. Its function within the APEX COPD registry is to provide ethical governance and approval of study protocols requiring the APEX COPD registry data.

American Academy of Family Physicians

The American Academy of Family Physicians is one of the largest medical organizations in the United States, with 134,600 members in 50 states. Its aim is to promote and maintain high-quality standards for family doctors who are providing continuing comprehensive health care to the public. American Academy of Family Physicians provides ethical approval of APEX in COPD registry research projects and is represented on the APEX COPD Steering Committee.

APEX COPD Steering Committee

The regulation of the registry is under the jurisdiction of the APEX COPD steering committee. The steering committee determines the scientific and research merits of any research proposal that accesses and/or uses anonymous data from the registry.

DARTNet Institute

DI is a not-for-profit 501(c)3 research institute and collaborative of US practice–based research networks. DI coordinates and supports research, quality improvement and safety activities across partner research networks through the aggregation, analysis, and standardization of EHR data, and are working to build a national collection of EHR data, claims data and PRI/PRO data. DI is a recognized Patient Safety Organization (PSO) and has significant registry experience. DI is running the APEX COPD registry in the US, including handling all practice recruitment, PRO data collection, EHR data standardization, clinical decision support development and delivery and obtaining regulatory approvals. DI is an active partner with OPC in all phases of the project.

Appendix Reference

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Appendix Table 1. APEX COPD Registry Variables Agreed by Delphi Consensus

Category	Sub-Category	Variable
EHR Variables (n = 115)		
Demographics		Height (In)
		Weight (lb)
		Biological sex
		Age (yrs)
		BMI
		Race
Disease monitoring	COPD diagnosis	COPD
		Chronic bronchitis
		Emphysema
		AATD
	Differential diagnosis	Asthma
	Respiratory infection	Number pneumonia infections in past 2 years
		Number of other RTI in past 2 years
	Exacerbations*	No. moderate exacerbations in past year
		No. severe exacerbations in past year
	Symptoms	Wheezing
	Physiological measurements	Predicted FEV1 (auto-calculated)
		FEV1 pre-bronchodilator
		FEV1 post-bronchodilator
		FEV1 (pre-bronchodilator)/Predicted FEV1 (auto-calculated)
		Predicted FVC (auto-calculated)
		FVC pre-bronchodilator
		FVC post-bronchodilator
		FVC (pre-bronchodilator)/Predicted FVC (auto-calculated)
		Predicted FEV1/FVC ratio (auto-calculated)
		FEV1/FVC pre-bronchodilator (auto-calculated)
		FEV1/FVC post-bronchodilator (auto-calculated)
		Reversibility (%)
		PIF
		Pulse oximetry (spO2, %)
		Full blood count
		Blood eosinophil count
		Chest Radiograph
		CT scan
		Systolic BP (mm Hg)
		Diastolic BP (mm Hg)
		6-minute walking test (ft)
	GOLD categorization	GOLD 1 to 4 (auto-calculated)
		GOLD A-D (auto-calculated)
	Differential diagnosis (predicting asthma)	Allergy
		Rhinitis
		Nasal polyps
		Eczema
		Sinusitis
		Ankle edema

Continued

Appendix Table 1. Continued

Category	Sub-Category	Variable
EHR Variables (n = 115)		
	Differential diagnosis (predicting heart failure)	Echo cardiogram
		Elevated B-type natriuretic peptide
	Differential diagnosis (predicting lung cancer)	Weight loss
		Hemoptysis
	Other diff. diagnosis	Pneumonia
	Co-morbidities (cardiovascular)	Angina pectoris/Heart disease/CHD
		Heart failure
		Stroke
		Hypertensive disease
	Co-morbidities (pulmonary)	Lung cancer
		Obstructive sleep apnea
		Hypoxemia
	Co-morbidities (endocrinological)	Diabetes mellitus
		Osteoporosis
		Osteoarthritis
		Metabolic syndrome
	Co-morbidities (mental)	Depression
		Anxiety
	Co-morbidities (other)	GERD
		Anemia
Treatment	Bronchodilators	SABA
		LABA
		SAMA
		LAMA
	Steroids	ICS
		OCS
	Combinations	SABA/SAMA
		LABA/LAMA
		ICS/LAMA
		ICS/LABA
		ICS/LAMA/LABA
	Co-morbidity treatments	Heart failure
		Diabetes
		Osteoporosis
		Asthma
	Other treatments	Antibiotics
		Macrolides
		PDE inhibitors
		Methylxanthines (eg, theophylline)
		LTRA
		Diuretics
		Mucolytics
	Smoking	Smoking status
		How many years has patient smoked?
		Pack years
	Vaccinations	Influenza
		Pneumococcal (both)
	Smoking cessation	Smoking cessation advice given
		Referral to stop-smoking clinic/advisor

Continued

Appendix Table 1. Continued

Category	Sub-Category	Variable
EHR Variables (n = 115)		
		Nicotine replacement therapy
		Drug therapy (eg, bupropion)
	Surgery	Bullectomy
		Lung Volume Reduction Surgery (LVRS)
		Lung volume reduction coil
		Endobronchial Valve (EBV)
		Lung transplant
		Chest wall vibration
	Specialist referral	Palliative care
		Physiotherapist
		Occupational therapist
		Speech therapist
		Clinical psychiatrist
		Clinical psychologist
		Dietitian
		Exercise physiologist
		Chest physician
	Other therapies	Pulmonary rehabilitation (PR)
		Oxygen therapy
		Home nebuliser
		Ventilatory support
PRI/PRO variables (n = 34)		
Disease monitoring	Differential diagnosis	Asthma
	Respiratory infections	No. of pneumonia infections in past 2 years
		No. of other RTI in past 2 years
	Exacerbations*	No. of moderate exacerbations in past year
		No. of severe exacerbations in past year
	Health status (QoL)	Modified MRC Dyspnea Scale
		COPD Assessment Test
	Risk factors	Childhood respiratory infections
		Occupational exposure
		Tobacco exposure
		Age of onset of respiratory symptoms yrs)
		Family history of COPD
	Co-morbidities (mental)	Depression
		Anxiety
Treatment	Inhaler management	Spacer with MDI
		Inhaler technique training
		Inhaler use/adherence
		Test of Adherence to Inhalers (TAI) questionnaire
		Inhaler satisfaction
	Treatment side effects	Oral
		Physiological
	Smoking	Smoking status
		Date ceased smoking (if applicable)
		How many cigarettes smoked per day?

Continued

Appendix Table 1. Continued

Category	Sub-Category	Variable
EHR Variables (n = 115)		
		How many years has patient smoked?
		Uses e-cigarette?
	Vaccinations	Influenza
	Smoking cessation	Desire to quit smoking
		Tried to quit in the past
		Smoking cessation advice given
	Education & self- management	COPD education
		COPD self-management plan
		Patient's use of COPD self-management plan
	Other therapies	Pulmonary rehabilitation
PoC Variables (n = 5)		
Disease monitoring	Exacerbations*	No. of moderate exacerbations in past year
		No. severe exacerbations in past year
	Physiological measures	FEV1 post-bronchodilator
		FVC post-bronchodilator
Treatment	Inhaler management	Inhaler technique assessment

Modified from Edwards et al, 2020[1].
*COPD exacerbations were defined as an explicit exacerbation (coded in a patient EMR), OR a COPD code (which included COPD, chronic bronchitis and emphysema) alongside an antibiotic and/or OCS prescription, OR an acute bronchitis, LRTI, influenza, asthma, bronchiectasis or general lower respiratory condition code alongside an OCS and/or antibiotic prescription.
AATD, Alpha-1 antitrypsin deficiency; Atb, antibiotic; BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; COPD, Chronic Obstructive Pulmonary Disease; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; GERD, gastroesophageal reflux disease; GOLD, Global initiative for chronic Obstructive Lung Disease; ICS, inhaled corticosteroid; LABA, long-acting $\beta 2$-agoinist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; MDI, metered dose inhaler; MRC, Medical Research Council; OCS, oral corticosteroid; PDE, phosphodiesterase; PIF, peak inspiratory flow rate; RTI, respiratory tract infection; SABA, short-acting $\beta 2$-agonist; SAMA, short-acting muscarinic antagonist; CT scan, computerized tomography scan.

Appendix Table 2. APEX COPD Steering Committee Members and Delphi Panel

David B. Price, FRCGP	Research, primary care	UK/Singapore
Barbara P. Yawn, MD, MSc, MSPH, FAAFP	Research, primary care	USA
Janwillem W.H. Kocks, MD, PhD	Research, primary care	Netherlands
Wilson D. Pace, MD	Research, primary care	USA
Ku-Lang Chang, MD, FAAFP, MRO	Primary care	USA
Chester Fox, MD, FAAFP	Primary care	USA
Barry Make, MD	Specialist	USA
Alan Kaplan, MD, CCFP(EM), FCFP	Primary care, specialist	Canada
Neil Skolnik, MD	Primary care	USA
MeiLan K. Han, MD, MSc	Specialist	USA
Alvaro Aranda, MD	Specialist	Puerto Rico
Gokul Gopalan, MD, MPH	Research	USA
Asif Shaikh, MD, MPH	Research	USA
Cathy D. Mahle, PhD, MBA	Research	USA

APEX, Advancing the Patient Experience; COPD, chronic obstructive pulmonary disease.