PULMONARY PERSPECTIVE

The Projected Epidemic of Chronic Obstructive Pulmonary Disease Hospitalizations over the Next 15 Years
A Population-based Perspective

Amir Khakban[1,2], Don D. Sin[2,3,4], J. Mark FitzGerald[2,4,5], Bruce M. McManus[2,3,6,7], Raymond Ng[2,3,7,8], Zsuzsanna Hollander[2,3,7], and Mohsen Sadatsafavi[1,2,4,5]

[1]Collaboration for Outcomes Research and Evaluation, Faculty of Pharmaceutical Sciences, [4]Department of Medicine (Respiratory Division), [5]Centre for Clinical Epidemiology and Evaluation, [6]Department of Pathology and Laboratory Medicine, [7]Centre of Excellence for Prevention of Organ Failure (PROOF), and [8]Department of Computer Sciences, University of British Columbia, Vancouver, British Columbia, Canada; [2]Institute for Heart and Lung Health, Vancouver, British Columbia, Canada; and [3]Centre for Heart Lung Innovation, St Paul's Hospital, Vancouver, British Columbia, Canada

Chronic obstructive pulmonary disease (COPD) is a major source of morbidity, mortality, and costs in the Western world (1). In the United States, for example, COPD is responsible for $72 billion/yr in direct healthcare expenditures (2). The biggest driver of these healthcare costs is hospitalization. Unlike many other major causes of hospitalization, hospitalizations related to COPD continue to increase despite falling rates in cigarette smoking. It is projected that within 5 years, COPD hospitalizations will exceed those of ischemic heart disease, which is the current number one cause of medical hospitalization in the United States (Figure 1) (3). In countries such as Canada, which have older demographics than the United States, COPD has already surpassed ischemic heart disease as the leading cause of hospitalization (4). Cigarette smoking is the single most important modifiable risk factor for COPD (5), but it has been postulated that population aging may counterbalance the beneficial effects of diminishing smoking rates on the burden of COPD in many countries (6).

What Will the Future Burden of COPD Look Like over the Next 15 Years?

Predicting the future burden of diseases has been the subject of many studies (7–10). Such predictions play a critical role in policy making and resource allocation. They can help estimate the required future capacity (e.g., number of hospital beds) and the return on investments in strategies aimed at coping with the changing burden of diseases. There have been several previous studies on the future burden of COPD (10–14). For the most part, previous studies have used simulation techniques for projections by explicitly modeling the trends of known risk factors and their relation with the occurrence of the disease of interest. A recent systematic review identified 22 studies that provided model-based estimates of the future burden of COPD (15). However, when longitudinal data on the burden of a disease are available, it is possible to "learn" the pattern of growth and to extrapolate it to predict the future (16). An advantage of such data-driven forecasting techniques over model-based predictions is that they do not require specification of the complex interplay of multiple risk factors, some of which are not yet identified. Instead, they work based on the assumption that the effects of all risk factors have been captured on the observed trends (e.g., incidence and prevalence). Extrapolating such trends implies incorporating the effect of all known and unknown risk factors, assuming that no disruptive changes in risk factor trends or disease management will occur during the projection period. It is also possible to combine the elements of model-based and data-driven approaches. Reliable projection of trends for important risk factors can be combined with data-driven extrapolations within subgroups defined by levels of such risk factors to enable more robust predictions. In many countries, for instance, very robust projections of population growth and aging based on national census data are available, which can be combined with data-driven projections of disease incidence and prevalence within age groups to enable accurate projection of future trends.

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Correspondence and requests for reprints should be addressed to Don D. Sin, M.D., M.P.H., St. Paul's Hospital, 1081 Burrard Street, Vancouver, British Columbia, V6Z 1Y6, Canada. E-mail: don.sin@hli.ubc.ca

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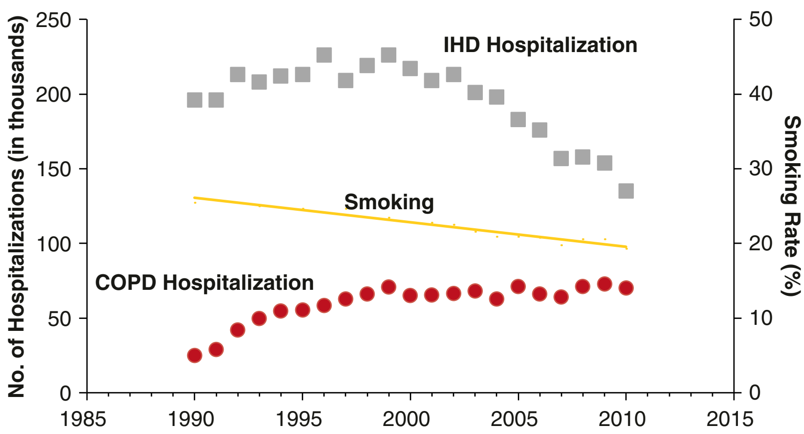

Figure 1. Hospitalizations for chronic obstructive pulmonary disease (COPD) and ischemic heart disease (IHD) as primary or secondary diagnoses and cigarette smoking rates in the United States between 1990 and 2010 (Data from Reference 3).

In this Perspective, we use such an approach based on projections of population growth and aging in concert with time series forecasting technique for COPD-related outcomes to predict the future burden of COPD in British Columbia, a Canadian province with a population of 4.7 million as of 2015 (17). This is a case study to illustrate the pending epidemic of COPD hospitalizations in North America and most other industrialized nations, where there is already a high prevalence of COPD and where there will be significant aging of the population over the next 15 years. British Columbia is an exemplary jurisdiction for predicting the future trends in COPD hospitalizations, because all hospitalizations and healthcare resource utilizations occur within a publicly funded healthcare system and are accurately captured in the provincial administrative databases. These databases are known to be of high quality, with very few missing or erroneous records (18), creating a unique source of data to estimate the burden of COPD at the population level. It is projected that British Columbia's population will reach 5.6 million in 2030, and the proportion of individuals 65 years of age and older will increase from 17.5 to 24.0% during this time period (19).

Combining Projections of Population Growth and Aging with a Time-Series Forecasting Model to Predict the Future Burden of COPD

Data-driven Period: 2001 to 2010

We used British Columbia's administrative health databases from 2001 to 2010 for the data-driven phase of this study. All inferences, opinions, and conclusions drawn in this research are those of the authors and do not reflect the opinions or policies of the Data Steward(s). Details of the data elements are provided in the online supplement. We have previously reported on the economic burden of COPD in British Columbia from 2001 to 2010 using these data (20). In brief, we created a cohort of patients with COPD by applying a validated case definition (21) and selected up to two individuals without COPD (i.e., control subjects) from the general population and matched them to COPD cases with respect to sex, birth year, local health area, and socioeconomic status. This was performed to create a comparison group for calculation of excess burden of patients with COPD with individuals without COPD.

The quantities that were estimated were the quarterly incidence and annual prevalence of COPD as well as annual excess all-cause mortality and annual excess all-cause hospitalizations in patients with COPD. Estimates were derived separately within each sex and age (35–54, 55–64, 65–74, 75+ yr) group. Excess all-cause mortality (defined as the difference between the overall mortality rate between the COPD and comparison group), instead of COPD-specific mortality, was estimated because of the high prevalence of comorbidity in patients with COPD and the difficulty in accurately ascertaining the cause of death in the presence of multiple morbidities (22). Similarly, we evaluated the excess burden of hospitalization (defined as difference in total length of stay between the COPD and comparison groups) to capture the burden of COPD and all comorbid conditions (21).

As a secondary outcome, we estimated COPD-related hospitalization as the sum of length of stay of all inpatient episodes in which the primary or secondary reason for hospitalization was COPD.

Projection of the Burden to 2030

We used an autoregressive integrated moving average (ARIMA) model to extrapolate the estimated burden within each sex and age group (23). Among many time-series techniques for projections, ARIMA is generally considered to be one of the most robust methods, which is particularly suitable in incorporating periodical patterns such as the seasonality incidence of disease (24, 25). The main variables for time-series extrapolation were the quarterly incidence and excess mortality rates, whose projections were performed separately within each sex and age group. Projection of total number of patients was performed in an iterative fashion using the following equation:

$$
\begin{aligned}
N_{\text{sex,age}}(t+1) &= 0.9 \times N_{\text{sex,age}}(t) \\
&\quad + \text{incidence}_{\text{sex,age}}(t+1) \\
&\quad - \text{mortality}_{\text{sex,age}}(t+1) \\
&\quad + 0.1 \times N_{\text{sex,age}-1}(t),
\end{aligned}
$$

where sex and age refer to sex groups and age groups of interest, and t refers to calendar year. age − 1 refers to the immediately younger age group; for the youngest age group, $N_{\text{sex,age}-1}(t) = 0$. This equation incorporates the dynamic factors that can affect the prevalence of COPD, including the existing patients with COPD who remain alive and within the same age group within the year-long period, those who develop COPD, those with COPD who die, and those who transition from the younger to the older age groups. We assumed that patients with COPD are uniformly distributed across the 10-year age bands; as such, the annual transition rate of individuals from the younger to older age group at the end of each year was set to 10% (thus the appearance of 0.1 and 0.9 in the above equation). Incidence and mortality terms in the above equation were the product of their respective projected rates from the ARIMA model and the projected population size within the subgroup. We used Statistics Canada's projected population growth estimations within sex and age groups for the province from 2011 to 2030 (26).

The projection of excess hospital bed–days and COPD-related hospitalizations was made by multiplying the projected total number of patients in each group by the corresponding average length of stay or the annual probability of admission due to COPD during the observation period. Approximate 95% confidence intervals (CIs) around the projections were generated by combining ARIMA-based CIs for incidence and mortality (the lower bound of the projection was based on the lower bound of incidence and higher bound of mortality, and vice versa). All statistical analyses were performed in SAS enterprise (Version 6.1; Cary, NC).

Observed and Projected COPD Incidence

In 2010, the annual incidence rate of COPD was 0.53%. Across age and sex groups, this value varied from 0.15 to 1.79%, with older age groups having higher rates. There was no statistically significant difference in the incidence of COPD between men and women in younger age groups, but in those who were 75 years of age or older, the incidence rate was 30% higher for men than women ($P < 0.001$). The model predicted relatively constant incidence rates over the study period (*see* Figures E1 and E2 in the online supplement).

Observed and Predicted Excess Mortality

In general, the excess mortality rate decreased during the observation time, and our model predicted continued reductions in mortality to 2030 (Figure E4). For older patients, particularly those older than 64 years, there was a robust and steady trend in the reduction of mortality. For instance, the model predicted that mortality would drop in total by 1.4% for the 65- to 74-year-old group and 3.8% for patients 75 years of age and older during the period of 2011 to 2030. Observed and predicted quarterly mortality rates are provided in Figures E4–E6.

Observed and Predicted Number of Diagnosed COPD Cases

The top panels of Figure 2 provide the observed and predicted number of subjects diagnosed with COPD. During the observation period, the number of patients diagnosed with COPD increased from 59,091 in 2001 to 98,368 in 2010. This number will increase to 250,074 in 2030, representing a 155% increase during this period and an annual growth rate of 4.8%. The increase in the number of cases will be particularly striking in the older age groups. By 2030, 55% of the patients with COPD will be 75 years and older (*see* Figure E7 for detailed breakdown based on age and sex).

Observed and Predicted Excess and COPD-related Hospital Days

In 2010, the COPD cohort spent a total of 236,066 extra days in the hospital compared with the comparison group, with an average of 2.4 extra days per patient-year. Among this, 45% were directly related to COPD. The observed and projected all-cause and COPD-related excess inpatient days stratified by sex and age groups are shown in the bottom panels of Figure 3. Excess inpatient days will reach 667,497 days in 2030, which is 182% higher than the

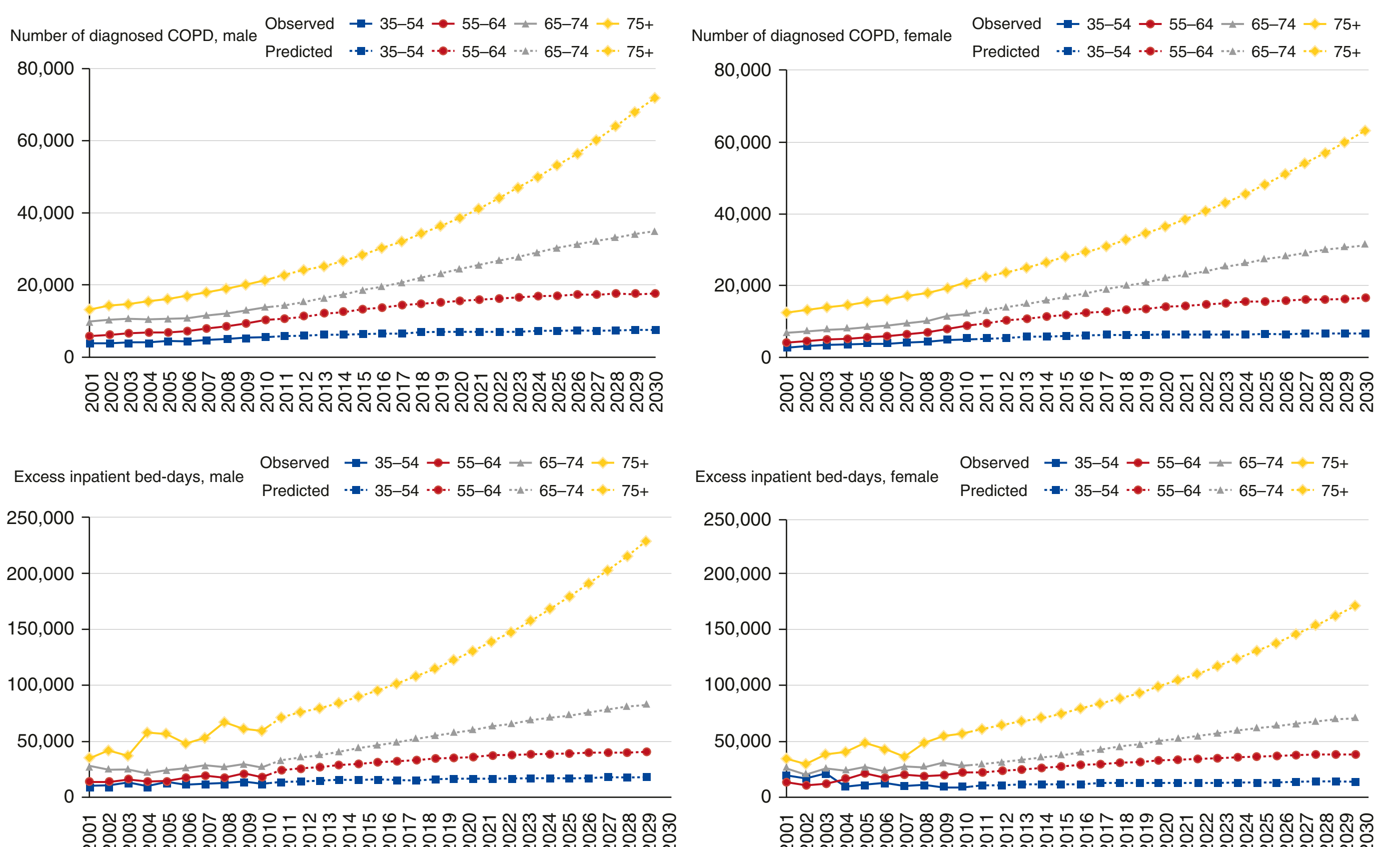

Figure 2. Number of diagnosed chronic obstructive pulmonary disease (COPD) cases (*top panels*) and annual excess bed-days (*bottom panels*) by sex and age groups. The ranges 35–54, 55–64, 65–74, and 74+ are age groups, in years.

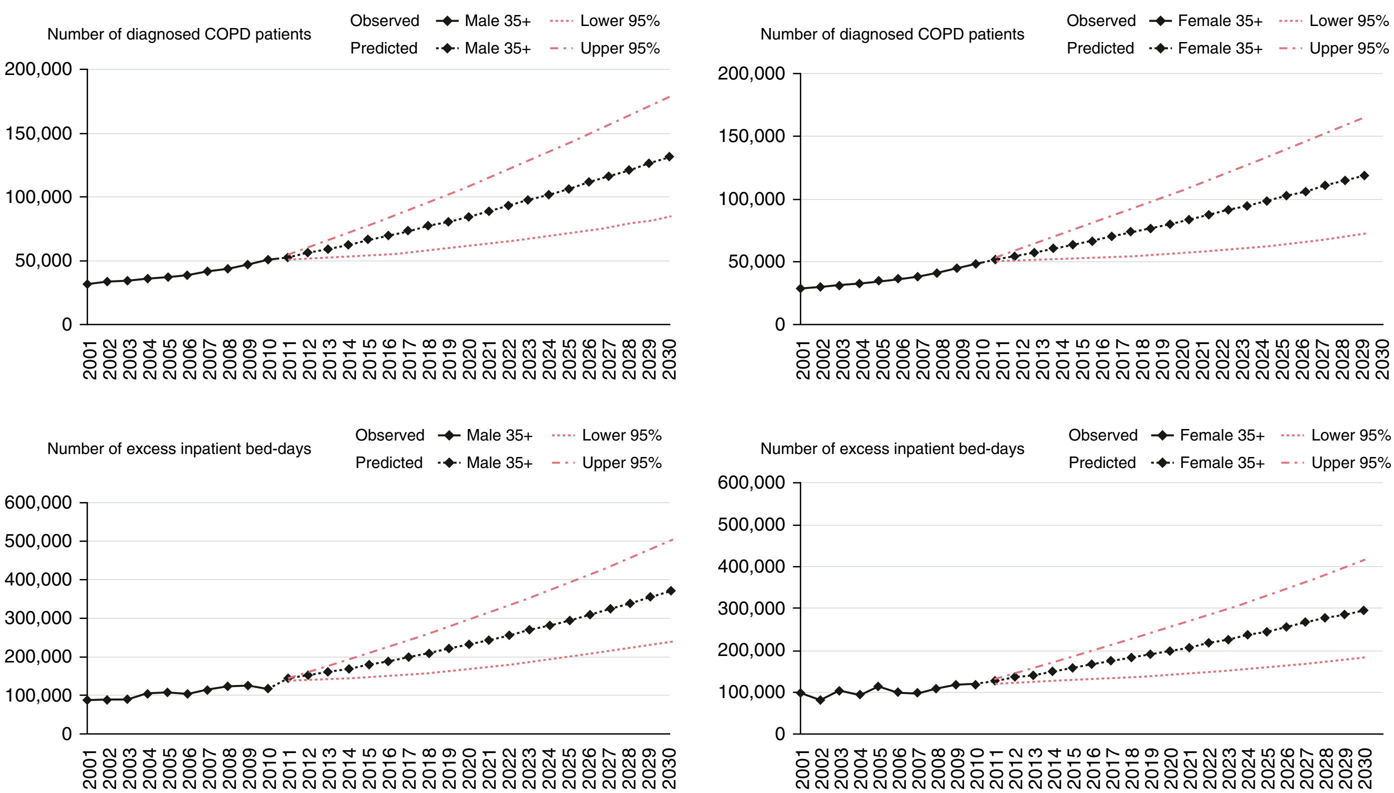

Figure 3. Total number of diagnosed chronic obstructive pulmonary disease (COPD) cases (*top panels*) and annual excess number of inpatient bed-days (*bottom panels*) by sex with confidence limits. 35+ indicates age, in years.

value for 2010. In 2030, patients older than 75 years of age will be responsible for 60% of the excess inpatient days; 83% of the excess inpatient days will belong to those 65 years or older in 2030.

Figures E8 and E9 show the total inpatient days for patients with COPD in which COPD is the primary or secondary reason for hospitalization. COPD-related inpatient days will increase by 210% between 2010 and 2030. In 2030, they reach a value of 326,260, 92% of which will be contributed by patients 65 years or older.

Uncertainty and Sensitivity Analyses

The finite sample of the study and follow-up time means the projections made in this study are subject to uncertainty. Figures E7–E9 provide approximate 95% CIs for the projected number of patients with COPD and the excess and COPD-related burden of inpatient care (annual number of hospital bed–days). Although within subgroups, especially the younger ones, uncertainty was high due to small sample sizes, the population-level projections remained relatively robust. For example, in 2030 the 95% confidence bounds around the increases in the total number of hospital bed–days were 420,500 to 916,500, representing an increment of 79 to 290% of current values (Figure 3, *bottom panel*). The 95% CIs for the total number of patients diagnosed with COPD were 59 to 251% (Figure 3, *top panel*), and for the relative increase in COPD-specific number of inpatient bed–days they were 98 to 316%.

Figures E10–E14 provide results of sensitivity analyses on important components affecting the projections. In a sensitivity analysis that kept the future mortality rate constant and equal to the rate in 2010, the projected growth in the number of patients by 2030 was 125%. This represents a drop in the number of patients with COPD in 2030 from the main estimation (from 250,074 to 223,632). In this analysis, the projected excess hospitalization in 2030 was 590,000 inpatient days, representing a growth of 150% in burden of inpatient care of COPD from 2010. It also predicted a 165% growth for COPD-related inpatient days by 2030 from 2010. In another sensitivity analysis, we imposed a steady decline in the projected incidence of COPD for all age groups, corresponding to a 20% reduction in incidence in the next 15 years. We still observed an increase of 151% in the burden of inpatient care in 2030 compared with 2010.

Coping with the Future of COPD

We found that over the next 15 years, the incidence of COPD will remain constant or slightly decrease across sex and age groups; however, the total number of cases and the burden of inpatient care will substantially increase. This mainly reflects the influence of projected demographic changes on the burden of COPD, especially population aging. Although total population growth rate is predicted to be less than 25% between 2010 and 2030, the total number of patients diagnosed with COPD will increase by 155% in this period. We predict that by 2030, the burden of inpatient care will increase by 182% from 2010 (to 667,000 inpatient-days). COPD-related hospitalization will increase by 210% in this period. Patients with COPD who are 65 years and older will drive most of the increases over the next 15 years. Despite uncertainties in the trends, the plausible ranges of predictions were all consistent with a substantial increase in the future burden.

Similarly, projections remained consistent in a series of sensitivity analyses.

Our projections for the future burden of COPD on the basis of the observed patterns indicate that the demographic changes, including population growth and aging, will escalate the already high burden of COPD. Although we have used data and statistics from a Canadian province, the factors underlying this increase in burden are likely to be present in other similar populations. For example, the proportion of individuals older than 65 years of age will surge from 16.2 to 23.6% in Canada and from 14.5 to 20% in the United States (27) between 2015 and 2030, respectively. Therefore, the relative rates of growth reported in this work can be applied to all these other jurisdictions where the population is aging.

The increase is especially striking for hospital-based care, which already is responsible for the greatest share of the direct costs of COPD (20); the predicted trend in inpatient care *per se* is likely to significantly impact healthcare systems. Unless major novel new interventions are implemented to address the burden of COPD, the healthcare, policy, and research community should brace for this rapidly escalating burden. Although preventive strategies against chronic diseases are likely to be the most efficient ones in the long term, it is unlikely that any such strategy would result in significant improvements in the burden of COPD over the next 15 years. This is because of the prolonged period of time it takes for a chronic disease like COPD to develop and for preventive strategies to diffuse into the healthcare market and to show their effects on downstream outcomes, such as hospitalizations due to COPD. Even preventive strategies with immediate action cannot plausibly counter the effect of aging. This is clear in the sensitivity analysis that modeled a 20% reduction in the incidence of COPD in the next 15 years, which showed that the future burden would still be substantial. As such, acute and disruptive policies and therapeutic interventions aimed at reducing the burden of COPD need to be developed and adopted urgently. Any disease-management strategies that can efficiently manage and alleviate COPD burden in the community can potentially be associated with a significant return on investment. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

References

1. Ehteshami-Afshar S, FitzGerald JM, Doyle-Waters MM, Sadatsafavi M. The global economic burden of asthma and chronic obstructive pulmonary disease. *Int J Tuberc Lung Dis* 2016;20:11–23.
2. Ford ES, Murphy LB, Khavjou O, Giles WH, Holt JB, Croft JB. Total and state-specific medical and absenteeism costs of COPD among adults aged ⩾ 18 years in the United States for 2010 and projections through 2020. *Chest* 2015;147:31–45.
3. Centers for Disease Control and Prevention. Health data interactive [updated 2016 Jul 22; accessed 2016 Jul 1]. Available from: http://www.cdc.gov/nchs/hdi/index.htm
4. Benady S. The human and economic burden of COPD: a leading cause of hospital admission in Canada; 2010 [accessed 2016 Dec 29]. Available from: http://www.respiratoryguidelines.ca/sites/all/files/CTS_COPD_report.pdf
5. Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007;370:765–773.
6. Reid JL, Hammond D, Rynard VL, Burkhalter R. Tobacco use in Canada: patterns and trends, 2015 Edition. Waterloo, ON: Propel Centre for Population Health Impact, University of Waterloo; 2015.
7. Denton FT, Spencer BG. Chronic health conditions: changing prevalence in an aging population and some implications for the delivery of health care services. *Can J Aging* 2010;29:11–21.
8. Reinhardt UE. Does the aging of the population really drive the demand for health care? *Health Aff (Millwood)* 2003;22:27–39.
9. Lehnert T, Heider D, Leicht H, Heinrich S, Corrieri S, Luppa M, Riedel-Heller S, König HH. Review: health care utilization and costs of elderly persons with multiple chronic conditions. *Med Care Res Rev* 2011;68:387–420.
10. Feenstra TL, van Genugten ML, Hoogenveen RT, Wouters EF, Rutten-van Mölken MP. The impact of aging and smoking on the future burden of chronic obstructive pulmonary disease: a model analysis in the Netherlands. *Am J Respir Crit Care Med* 2001;164:590–596.
11. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, Schmid V, Buist S. Chronic obstructive pulmonary disease: current burden and future projections. *Eur Respir J* 2006;27:397–412.
12. Hoogendoorn M, Rutten-van Mölken MP, Hoogenveen RT, van Genugten MLL, Buist AS, Wouters EFM, Feenstra TL. A dynamic population model of disease progression in COPD. *Eur Respir J* 2005;26:223–233.
13. Peabody JW, Schau B, Lopez-Vidriero M, Vestbo J, Wade S, Iqbal A. COPD: a prevalence estimation model. *Respirology* 2005;10:594–602.
14. Pichon-Riviere A, Augustovski F, Bardach A, Colantonio L; Latinclen Tobacco Research Group. Development and validation of a microsimulation economic model to evaluate the disease burden associated with smoking and the cost-effectiveness of tobacco control interventions in Latin America. *Value Health* 2011;14:S51–S59.
15. McLean S, Barbour V, Wild S, Simpson C, Sheikh A. Models for estimating projections for disease prevalence and burden: a systematic review focusing on chronic obstructive pulmonary disease. *J Health Serv Res Policy* 2015;20:246–253.
16. To T, Stanojevic S, Feldman R, Moineddin R, Atenafu EG, Guan J, Gershon AS; RESPONSE Team. Is asthma a vanishing disease? A study to forecast the burden of asthma in 2022. *BMC Public Health* 2013;13:254.
17. Statistics Canada. Population by sex and age group, by province and territory. 2016 [accessed 2016 Mar 17]. Available from: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/demo31a-eng.htm
18. Williams J, Adger W. Inventory of studies on the accuracy of Canadian health administrative databases. Toronto: Institute for Clinical Evaluative Sciences; 1996.
19. BC Stats. Population projections, British Columbia [accessed 2016 Apr 27]. Available from: http://www.bcstats.gov.bc.ca/StatisticsBySubject/Demography/PopulationProjections.aspx
20. Khakban A, Sin DD, FitzGerald JM, Ng R, Zafari Z, McManus B, Hollander Z, Marra CA, Sadatsafavi M. Ten-year trends in direct costs of COPD: a population-based study. *Chest* 2015;148:640–646.
21. Bedouch P, Sadatsafavi M, Marra CA, FitzGerald JM, Lynd LD. Trends in asthma-related direct medical costs from 2002 to 2007 in British Columbia, Canada: a population based-cohort study. *Plos One* 2012;7:e50949.
22. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD: role of comorbidities. *Eur Respir J* 2006;28:1245–1257.
23. Rosychuk RJ, Youngson E, Rowe BH. Presentations to emergency departments for COPD: a time series analysis. *Can Respir J* 2016;2016:e1382434.
24. Permanasari AE, Rambli DRA, Dominic PDD. Performance of univariate forecasting on seasonal diseases: the case of tuberculosis. *Adv Exp Med Biol* 2011;696:171–179.
25. Ríos M, García JM, Sánchez JA, Pérez D. A statistical analysis of the seasonality in pulmonary tuberculosis. *Eur J Epidemiol* 2000;16:483–488.
26. Statistics Canada. Population projections for Canada, provinces and territories. 2016 [accessed 2016 Mar 17]. Available from: http://www.statcan.gc.ca/pub/91-520-x/2010001/tablesectlist-listetableauxsect-eng.htm
27. United States Census Bureau. 2014 National population projections [created 2012 Jul 6; accessed 2016 Apr 27]. Available from: https://www.census.gov/population/projections/data/national/2014/summarytables.html