Chronic Obstructive Pulmonary Disease in Canadian Primary Care: A CPCSSN Study

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a significant source of morbidity and mortality in Canada. Although, it is primarily managed within primary care there is little Canadian evidence on the prevalence or management of COPD in this setting.

Methods: Electronic Medical Record data was obtained from the Canadian Primary Care Sentinel Surveillance Network (CPCSSN) at the end of 2012. Validated case finding algorithms were used to identify COPD cases. Descriptive statistics and multivariate modeling analyses were used to calculate the prevalence of COPD, its association with key demographic factors and co-morbidities and patterns of medication prescribing.

Results: Observed prevalence of COPD is 4.0%, representing a population prevalence of 3.4% using age-sex standardization. Co-morbidity was the common with prevalence ratios ranging from 1.12 for presence of a single co-morbid condition to 1.9 for 4 or more co-morbid conditions. Anticholinergic agents(63%) , short(48%) and long acting(38%) beta agonists and inhaled corticosteroids(41%) were the most commonly used medications.

Interpretation: The prevalence of physician diagnosed COPD in Canadian primary care practices identified by the CPCSSN algorithms is similar to that reported in other practice-based studies at approximately 3-4%. Most patients have co-morbid conditions and are on multiple medications. This suggests early milder disease is often not diagnosed. Compared to other data sources EMR data has the potential to provide more specific estimates without compromising sensitivity and to also provide more complete information on treatment practices.

Background:

Chronic Obstructive Pulmonary Disease (COPD) is a significant source of morbidity and mortality in Canada and globally. Estimates place the worldwide prevalence at 9-10% from physiological based studies and 3-8% from studies based on physician or patient reported diagnosis or symptoms.[1,2] Globally, it is rated as the 5th leading cause of death, and 9th in contributions to Disability Adjusted Life Years lost.[3,4] A recent systematic review of COPD epidemiology worldwide identified 12 Canadian studies which produced prevalence estimates that ranged from 3-12% depending on the method used.[5] Canadian data from a study using spirometry to screen a population based sample suggest a rate of about 10%.[6] There is limited data on COPD either alone or in combination with other chronic diseases from primary care settings.

In other countries, the limited reports on COPD prevalence in primary care settings show marked variation depending on the method of identification of illness. A UK study based on electronic records in the Computerized Patient Records Database (CPRD) found the prevalence of physician diagnosed COPD to be less than 1% for women and only 1.35% for men.[7] Another UK practice based research network study that invited subjects participating in a postal survey to come for spirometry if they had either symptoms or a smoking history found a much higher prevalence (4.1% overall, 9.6% in patients over 40).[8] A recent Spanish study using data from electronic medical records found a physician diagnosed prevalence of 3.2%, 90% of whom were also found to have at least one co-morbid condition.[9]

Our current understanding of the extent of COPD in Canada and its impact on health and health systems is not based on primary care data, but is based on data from large population health surveys or from administrative data.. However, COPD is primarily managed within the primary care sector. The Canadian Primary Care Sentinel Surveillance Network (CPCSSN) was established in 2008 to bring together practice based research networks using diverse electronic medical record systems to generate data on chronic disease in Canadian primary care settings. COPD is one of the eight common chronic conditions targeted by CPCSSN. This study was undertaken to (1) explore the prevalence of COPD,(2) the degree of co-morbidity with respect to the other conditions for which CPCSSN has validated algorithms and (3) common patterns of treatment of COPD by Canadian primary care physicians.

Methods:

Data sources and study population:

CPCSSN is a national network of practice based research networks whose member primary care practices use various electronic medical records. Its overall architecture and approach have been described in detail elsewhere.[10,11] This study used CPCSSN data extracted on Dec 31, 2012. At the time there were 444 physicians in 10 networks covering 8 provinces of Canada using 12 different EMRs. Case finding algorithms have been established for eight chronic diseases including COPD and

validated against chart abstraction and physician identification of cases.[12,13,14] For COPD the CPCSSN algorithms have a sensitivity of 82% and specificity of 97%.[13] This study population has been shown elsewhere to be reasonably representative of the primary care population in Canada.[15] We estimated the prevalence using the denominator described by Griever et. al. as it approximates the general population while the 24 -month contact group. approximates those attending the practice.[16]

Statistical analysis

We used a combination of descriptive statistics and multivariate modeling for data analysis using SAS statistical software version 9.3.[17] We first calculated the prevalence rates for COPD, classified by an appropriate age group and gender. As COPD is primarily a disease of older adults we limit our reporting here to adults 40 years of age or older. We also calculated age-sex standardized prevalence rates according to Canadian national age-sex distribution (Census 2011).[18] We then looked at the prevalence ratios by three risk factors: rural postal code of clinic (second digit of the postal code being zero), BMI categories (underweight: BMI<18, normal: 18≤BMI<25, overweight: 25≤BMI<30 and obese≥30), and smoking (never, past, current). Three separate log-binomial regression analyses were carried out to calculate prevalence ratios, each controlling for age and sex of the study population. Along with prevalence ratios (PRs), the corresponding 95% confidence intervals (CI) and p-values were also reported. We then analyzed the presence of each of the other CPCSSN comorbid conditions, adjusting for age and sex, using the same log-binomial approach and then expressing the results in terms of prevalence ratios, 95% CI and p-values. In addition, we looked at the cumulative proportion of patients diagnosed with one or more of the other CPCSSN conditions, with respect to the absence and presence of the index condition in question. Also, we calculated the average number of comorbid conditions by age group. Finally we investigated the medication data by analysing the pattern of medication use by those who were diagnosed with COPD. In this report, medication use for a particular medication means that there is at least one prescription for that medication somewhere in the patient's electronic medical record.

Results:

Table 1/Figure 1 presents the age-sex distribution of our sample population and the prevalence of COPD. The overall observed prevalence is 4.0%, which represents a prevalence of 3.4% using standard age-sex standardization or 3.2% using the CPCSSN general population denominator. Diagnosis of COPD was associated with rural location (PR=1.22 95% CI 1.17-1.28), current (PR=7.09 95% CI 7.3-8.5) and past (PR=3.25 95% CI=3.01-3.51) smoking, and weight category other than normal (Underweight PR=1.35 95% CI 1.1.21-1.50; Overweight PR=0.90 95% CI .85-.96; Obese PR=1.17 95% CI 1.10-1.23).

Information on co-morbidity with other CPCSSN conditions is presented in Tables 2 and 3, and Figure 2. Table 2 presents the prevalence ratios for the presence of

the other chronic diseases identified by CPCSSN for patients with a CPCSSN diagnosis of COPD in comparison to those who do not have COPD. Patients with COPD are more likely to receive a CPCSSN diagnosis of every other condition except Parkinsonism. Table 3 reports both the prevalence of co-morbidity with one or more other CPCSSN condition for COPD patients and the prevalence ratios for multimorbidity in COPD patients as compared to other CPCSSN patients who have at least one chronic disease. Of all COPD patients, 76.7% had one or more other chronic conditions and 3.2% had 4 or more other conditions. Prevalence ratios for co-morbidity were all greater than one, ranging from 1.12 for presence of a single co-morbid condition to 1.9 for 4 or more co-morbid conditions. Figure 2 shows the mean number of co-morbid conditions and the prevalence ratios by age and sex for COPD patients compared to other chronic disease patients. Co-morbidity is higher for COPD for all age groups with the prevalence ratio being highest in the younger age groups and diminishing with increasing age.

Tables 4 and 5 present information on prescribed medications for treatment of COPD. Table 4 provides the prevalence of prescriptions for various therapeutic agents by class and drug. Table 5 presents data on patterns of drugs prescribed. Table 5a presents data on the numbers of drug classes used and table 5b provides additional detail on the class combinations.

Interpretation:

Prevalence In this study the estimated prevalence of COPD overall for adults over 40 in primary care practices was 3.4% using age-sex standardization. This is similar to the rate (3.2%) reported by Garcia-Olmos et al. in a recent EMR based study in primary care practices in Spain.[9] It is lower than rates of 9-10% expected based on population based studies using physiologic measures.[2,6,19] This difference is in keeping with past studies finding COPD to be underdiagnosed or misdiagnosed quite frequently. Frank et al (2006) found that less than half of patients with GOLD categories 2-4 lung disease by spirometry had a diagnosis of COPD recorded in their primary care medical records.[20] Prevalence rates based on administrative data may be biased in the opposite direction. Lacasse et al. conducted a large validation of COPD as recorded in administrative data from Quebec and found a diagnosis of COPD as the principal diagnosis for hospital discharges to have a PPV of only 50.4% in identifying "true cases" as assessed by specialist physician review of hospital records.[21] Gerhsorn et al. (2009) also validated their administrative data definition of COPD against a chart review and found a sensitivity of 85% and specificity of 78.4 % for the most inclusive definition, which was subsequently adopted by this group, as more restricted definitions had poor sensitivity.[22] In comparison the CPCSSN case finding algorithm for COPD has a sensitivity of 82% while retaining a high specificity of 97%.[13] This may explain in part the significant differences between the rates observed in our data and the prevalence of almost 12% in adults over age 35 reported most recently by this research group.[23,24] The true prevalence is likely found between these levels. A recent study by Muggah et al (2013) also showed poor agreement between data from a large population health survey and the administrative data definition used in Ontario (kappa =.29, prevalence 11.1% HA

data, 5.6% self-reported).[25] These large gaps highlight the issues raised by Manuel et al and Green et al on the importance of looking closely at the biases inherent in data sources when interpreting the results of even well designed studies and surveillance systems that exploit our ability to access data that is generated during the provision of health care services.[26,27] In our findings, the prevalence is similar for men and women in younger age categories, but significantly higher among men for all age groups over age 60. This may be related to historical differences in smoking rates in addition to other factors.

Co-morbidities Levels of co-morbidity were very high, with 76.7% of COPD patients having at least one additional CPCSSN identified condition. Real rates of co-morbidity are likely even higher as CPCSSN currently only flags a limited number of conditions. Co-morbidity for COPD patients was significantly higher than that experienced by other chronic disease patients, particularly for those who are younger. This is consistent with the limited number of prior studies of this issue that also found most COPD patients had other co-morbid chronic conditions.[2,28] For example, in the Spanish study that also used EMR data as a source and which included a much more comprehensive list of conditions, 90% of COPD patients had at least one co-morbid condition.[9] The higher prevalence ratio for co-morbidities in the younger age groups would be consistent with the notion of distinct COPD "phenotypes" in which younger patients with more severe disease are one distinct type.[29] This is particularly important for our conceptualization of COPD as an illness. It seldom occurs alone and should prompt a thorough assessment for the presence of other chronic conditions.

Medications The current Canadian guidelines for management of COPD recommend anticholinergic medications or long acting beta agonists, either alone or in combination, for patients with persistent symptoms .The addition of Inhaled corticosteroids-long-acting beta agonists combination to long acting anticholinergic (ie. triple therapy) should ideally be reserved for patients with moderate to severe airway obstruction who are prone to exacerbations. In selected patients who have persistent breathlessness despite optimal inhaled bronchodilators a trial of oral theophyllines might be considered. Oral anti-inflammatory agents (eg roflumilast) may be appropriate in selected patients with a chronic bronchitis phenotype who are prone to exacerbations and who have more advanced disease.[30] Short acting beta agonists are recommended as an adjunctive symptom relieving medication in all patients on anticholinergics who still have symptoms. In keeping with guidelines, anticholinergics were also most likely to be used alone but some patients were prescribed ICS alone raising the question of an asthma pattern of treatment or even diagnosis,some patients in the younger age groups having a mixed picture of asthma and COPD A relatively small proportion of patients on ICS (10%) and SABAs (7%) were found to be on these agents alone, which would not be concordant with current COPD guidelines but would fit nicely with asthma guidelines. Most patients were on 2 or more classes of medications suggesting that they were GOLD class 2-4 rather than those with early , and less detected, disease.

Limitations:

One significant limitation in our approach to using EMR data is that some information may not be accessible to the automated extraction processes used by CPCSSN (ie. such as image files, scanned reports such as pulmonary function tests or radiology reports, free text fields. In addition, CPCSSN is a voluntary network of primary care providers in Canadian primary care practices and thus may not be fully representative of the full range of patients and providers. However, the overall age sex distribution of the network's patients is comparable to national averages and adjustment measures have been used to account for this when estimating prevalence.[15] With respect to the reporting of co-morbidities CPCSSN currently only has validated algorithms for 8 conditions, so reporting is limited to these at the present time. Finally we are relying on physician diagnosis for COPD, which may or may not include spirometry for confirmation.

Conclusions:

The prevalence of physician diagnosed COPD in Canadian primary care practices identified by the CPCSSN algorithms is similar to that reported in other practice-based studies at approximately 3-4%. When compared to rates of about 10% suggested by population-based samples tested by spirometry, this suggests that underdiagnosis remains a significant issue. Targeted spirometry screening for smokers at risk of COPD is one strategy that could be considered to improve this. Compared to other data sources such as administrative databases or population based surveys, EMR data has the potential to provide more specific estimates without compromising sensitivity and to also provide more complete information on treatment practices. Co-morbidity is extremely common, with most patients having at least one additional condition. Medication prescribing patterns are roughly aligned with current guidelines, but a more detailed analysis of medication combinations would be required to adequately assess this fully.

Acknowledgements: The Canadian Primary Care Sentinel Surveillance Network is a committee of the College of Family Physicians of Canada and is funded through a contribution agreement with the Public Health Agency of Canada. The conclusions and opinions expressed in this article are those of the authors and not necessarily of the CFPC or PHAC. This article is written by the authors on behalf of the CPCSSN network and its members. We would like to thank Rachel Morkem and the Centre for Studies in Primary Care staff for their assistance with the organization and support of the writing group.

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19. *Reference to BOLD study or other– Denis or Andrew to provide* Note International overall paper would be best, Canadian results already cited. Different citation that ref #6

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Table 1. Prevalence of COPD by patient age and sex

Age group	Male		Female		All	
	%	n	%	n	%	n
18-29	0.0	17110	0.0	25626	0.0	42736
30-39	0.3	14516	0.3	23839	0.3	38355
40-49	1.4	17508	1.3	24836	1.4	42344
50-59	3.2	20562	3.3	26812	3.3	47374
60-69	7.0	17208	6.2	20798	6.6	38006
70-79	12.1	10446	10.6	13316	11.3	23762
80+	18.1	6832	12.8	10937	14.8	17769
All ages	4.5	104182	3.7	146164	4.0	250346
Aged 40 years and older	6.3	72556	5.5	96699	5.9	169255
Aged 50 years and older	7.9	55048	6.9	71863	7.4	126911

Note: Age-standardized prevalence for patients 18 years and older = 3.4%, and patients 40 years and older = 5.3% and patients 50 years and older = 6.9%.

Figure 1. Prevalence of COPD for patients 40 years and older

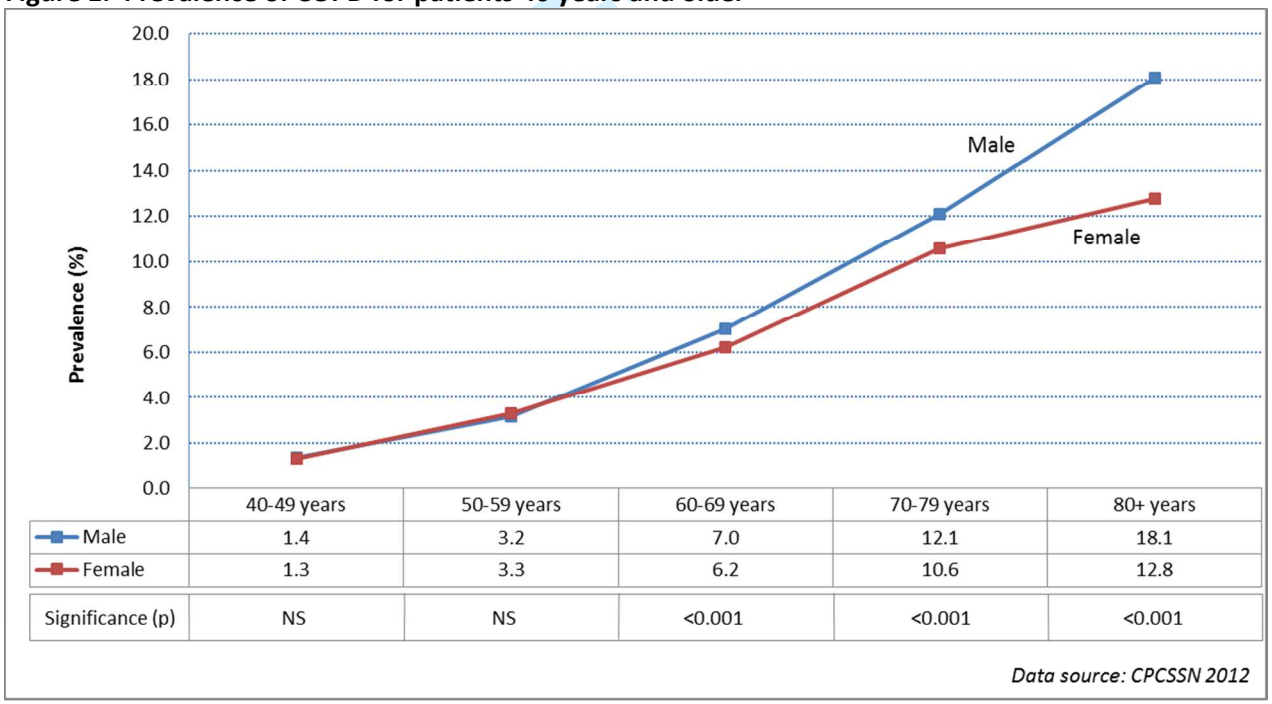

Table 2. Comorbidity – age and sex adjusted prevalence ratio: A log-binomial approach

Comorbidity	Parameter Estimates			p
	Prev. Ratio	Lower 95% CI	Upper 95% CI	
Hypertension**	1.09	1.067	1.111	<0.001
Diabetes**	1.30	1.249	1.345	<0.001
Depression**	1.68	1.625	1.744	<0.001
Osteoarthritis**	1.19	1.152	1.229	<0.001
Dementia*	1.11	1.026	1.191	0.008
Epilepsy**	1.68	1.428	1.981	<0.001
Parkinsonism	0.90	0.730	1.109	0.321

Modeled the probability of each of the comorbid conditions, for which the predictor is COPD (yes/no), along with age and sex. Interpretation: People with COPD are 1.09 times as likely to be hypertensive as people without COPD, and so on.

* p <0.01, ** p<0.001.

Table 3. Comorbidity: COPD vs. other conditions

Comorbidity	Percent		Poisson Model: Parameter Estimates (n=250,346)			
	COPD=Yes N (%)	COPD=No N (%)	Prev. Ratio	Lower 95% CI	Upper 95% CI	p
COPD alone	2338 (23.3)	--	--	--	--	--
1 or more other conditions	7705 (76.7)	68297 (66.2)	1.12	1.102	1.129	<0.001
2 or more other conditions	4156 (41.4)	34896 (33.8)	1.31	1.274	1.343	<0.001
3 or more other conditions	1436 (14.3)	8597 (8.3)	1.61	1.528	1.703	<0.001
4 or more other conditions	319 (3.2)	1450 (1.4)	1.90	1.674	2.147	<0.001

Note: # of patients with COPD=10,043;
# of patients without COPD but with at least one of the other CPCSSN conditions=103,193

Models included the predictor COPD (yes/no), along with age and sex.
Interpretation: Patients with COPD are 1.12 times as likely to have one or more other chronic conditions as those without COPD, and so on.

Figure 2. COPD Status vs. Mean Numbers of Other Comorbid Conditions, by Age

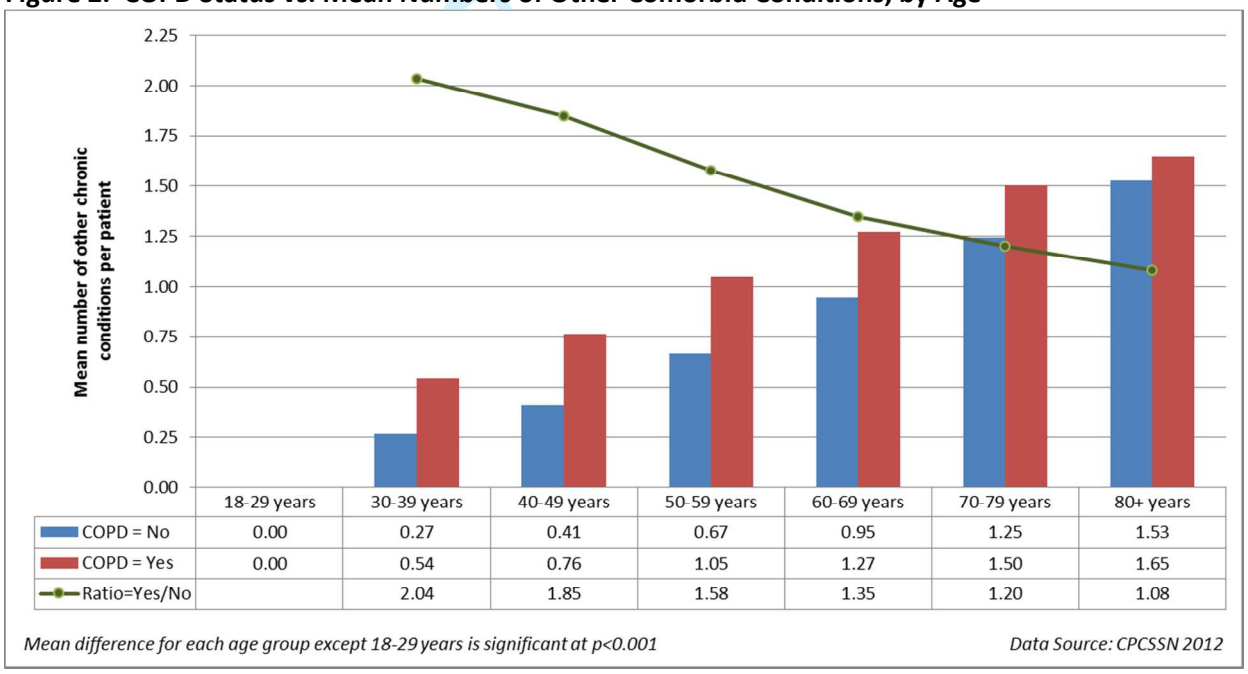

Table 4. Use of medications by patients with COPD

Drug class	% (N=10,043)	Drugs	% (N)
Anticholinergics (ANTI)	63.0	IPRATROPIUM	53.3 (6323)
		TIOTROPIUM	58.9 (6323)
Inhaled Corticosteroids (ICS)	40.6	BECLOMETASONE	2.0 (4080)
		BUDESONIDE	22.7 (4080)
		CICLESONIDE	10.8 (4080)
		FLUTICASONE	55.5 (4080)
		MOMETASONE	35.3(4080)
Short Acting Beta Agonists (SABA)	48.1	SALBUTAMOL	96.4 (4829)
		TERBUTALINE	5.8 (4829)
Long Acting Beta Agonists (LABA)	38.2	FENOTEROL	0.2 (3838)
		FORMOTEROL	41.2 (3838)
		SALMETEROL	70.0 (3838)
Theophyllines (THEO)	1.7	AMINOPHYLLINE	4.0 (172)
		CHOLINE	1.7 (172)
		THEOPHYLLINE	96.0 (172)
Other COPD meds (OCM)	4.9	CROMOGLICIC	12.7 (487)
		MONTELUKAST	80.3 (487)
		OMALIZUMAB	0.2 (487)
		ROFLUMILAST	7.6 (487)
		ZAFIRLUKAST	2.5 (487)

Table 5a. Use of multiple classes of medication

# of other classes	%	N
0 other class	16.8	1687*
1 other class	20.8	2090
2 other classes	26.3	2643
3 other classes	23.2	2329
4+ other classes	12.9	1294
Total	100.0	10043

* Of 1687 COPD patients, 1372 (or 81.3%) were on non-COPD meds and 315 (or 18.7%) were not taking any meds.

Table 5b. Use of multiple classes of medication

# of classes	ANTI (N=6323)	ICS (N=4080)	LABA (N=3838)	SABA (N=4829)	THEO (N=172)	OCM (N=487)
Alone	16.4	10.1	7.3	7.2	2.3	2.7
1 or more other classes	83.6	89.9	92.7	92.8	97.7	97.3
2 or more other classes	53.2	60.6	70.3	66.9	93.6	87.7
3 or more other classes	19.9	28.5	32.2	25.7	83.1	66.1

STROBE Statement—checklist of items that should be included in reports of observational studies

We have reviewed the checklist for observational studies and feel all of the issues have been addressed in the paper.

	Item No	Recommendation
YTitle and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

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Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
		Case-control study—Report numbers in each exposure category, or summary measures of exposure
		Cross-sectional study—Report numbers of outcome events or summary measures
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.