Evaluating the impact of the recommendations of the Canadian Common Drug Review on provincial health technology assessment decisions

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Evaluating alignment between Canadian Common Drug Review recommendations and provincial health technology assessment decisions: an exploratory study

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Interpretation: The findings of the study show agreement between the Common Drug Review recommendations and provincial listing decisions, which appears greater compared with previous study results. This could be due to provinces becoming more reliant on the Common Drug Review over time and may also indicate that the Common Drug Review continues to improve and develop to meet payers' needs. However, the fact that the provinces are able to come to different decisions on the basis of the Common Drug Review recommendations, illustrates the flexibility of the process.

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As with many sources of health technology assessment reviews, the Common Drug Review has been subjected to criticism. In 2011, a study reported the agreement for reimbursement recommendations and listing decisions between the Common Drug Review and three provinces to be "no better than random chance" [5]. However, these

findings contradict those of an earlier study [6]. No studies have subsequently been published comparing post-2009 Common Drug Review recommendations with provincial listing decisions, creating a gap in the existing body of knowledge. This recent comparison is more relevant to the current health technology assessment environment and helps to identify whether the Common Drug Review is creating more standardised coverage for medicines across Canada [7]. More recent research may provide further evidence to support or oppose Morgan and colleagues [8] who argued that multiple provincial decision makers reduce the impact of the Common Drug Review. Similarly, Hollis [9] predicted that, without a national Canadian formulary, the Common Drug Review would only slightly improve the standardisation of medicines coverage across provinces. Therefore, the aim of this study was to compare the non-mandatory reimbursement recommendations from the Common Drug Review process with the final listing decisions from provincial drug plans to demonstrate its impact.

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We subsequently searched the websites for the provincial payers/agencies for the latest listing decision of the same medicine-indication combinations identified from the Common Drug Review up to 1January 2015. Each health technology assessment recommendation or provincial drug plan listing decision was recorded by proprietary drug name and indication and categorised as either a positive or negative recommendation/ reimbursement decision. We then compared the Common Drug Review recommendation for each medicine with the medicine listing from each of the four provincial payers/agencies and subsequently calculated the percentage of listings that agreed with the Common Drug Review recommendations.

Statistical analysis

We compared the Common Drug Review recommendations with payer listing decisions to identify the total number that were aligned. As these differed between provinces, reporting the total number of those aligned could be misleading and therefore we calculated the percentage agreement between jurisdiction pairs to report the proportion of concordant recommendations. We also calculated the Kappa coefficient as it

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Results

The Common Drug Review recommendations and provincial listing decisions were compared by categorising reimbursement recommendations/decisions as either positive or negative, where a recommendation to reimburse the medicine including any restrictions was considered a positive recommendation and a recommendation to not reimburse was considered negative. We identified 174 medicine-indication pairs in CADTH Common Drug Review reports issued from January 2009 to January 2015 and 110 medicine-indication pairs that met the inclusion criteria of an initial submission (Appendix 2). However, when a resubmission had also been issued with a Common Drug Review recommendation by January 2015, the latest recommendation was considered.

An overview of the Common Drug Review and provincial recommendations for the 110 medicine-indication pairs reveals that Alberta Health reviewed the fewest number of medicines (n=95), followed by Quebec with 102, Ontario reviewed 104 and British Columbia reviewed 106 (Figure 1). The largest proportion of negative/not recommended medicine-indication pairs was issued by the Common Drug Review (47.3%). The proportion of negative recommendations issued by the three Common Drug Review

participating provinces ranged from 31.7% (Ontario Drug Benefit Plan) to 45.3% (British Columbia Pharmacare) (Table 1; Figure 1). Quebec, which is not a Common Drug Review participant, had the lowest proportion of negative recommendations (30.4%). When comparing the proportion of provincial listing decisions aligned with the Common Drug Review recommendations; the percentage agreement ranged from 74.5% with Quebec, 78.8% with Ontario, 78.9% with Alberta and 81.1% with British Columbia (Table 2).

Kappa coefficients were calculated for inter-rater reliability between the Common Drug Review and the four provincial payers/agencies. British Columbia (k=0.622 (95% CI, 0.473 to 0.771)) demonstrated substantial levels of agreement with the Common Drug Review. Alberta (k=0.578 (95% CI, 0.415 to 0.741)), Ontario (k=0.562 (95% CI, 0.407 to 0.717)) and Quebec (k=0.474 (95% CI, 0.309 to 0.639)) all scored moderate agreement with the Common Drug Review recommendations [17-18].

Interpretation

Main findings

Reimbursement recommendations issued by the Common Drug Review for 110 medicine-indication pairs from January 2009 to January 2015 compared with a previous study shows a greater agreement with the Common Drug Review recommendations (Table 2). This model has the potential to be of value in other regions with multiple payers, such as Europe. Currently, the European Medicines Agency provides a centralised marketing authorisation for all member states, but the reimbursement and

decision-making processes remain the responsibility of each country [1]. The Common Drug Review model could be implemented in Europe if a centralised body evaluated new medicines to inform reimbursement recommendations for European payers even if the final reimbursement decision remained the responsibility of the individual jurisdictions [1].

Explanation and comparison with other studies

The Common Drug Review participating drug plans are generally congruent with the Common Drug Review, but price negotiations and other factors can impact the final decision. Manufacturers and provincial payers often negotiate price with product listing agreements, but there is wide variation between provinces primarily due to their population size [19]. Price negotiations are a key cause of lack of congruity between Ontario and the Common Drug Review, as Ontario has the largest population and thus the greatest negotiating power and research has also shown Ontario to have the greatest proportion of medicines funded with product listing agreements [20]. The review process in Alberta only allows manufacturers to negotiate a product listing agreement after the formal review decision on the initial price is determined [21]. The Common Drug Review recommendations framework has evolved over time. In November 2012, a recommendations framework was made publicly available and included a category of “List with criteria and/or conditions” that may include a condition for a lower price to lead to a greater likelihood of a positive listing recommendation and accommodate the price negotiations post- Common Drug Review[22]. In addition, the

recommendations framework included a separate category of “Do not list at submitted price” that has been used in cases in which the drug under review demonstrated a comparable clinical benefit to its comparator(s). Prior to November 2012, the “Do not list at submitted price” was used as a subcategory of the “Do not list” category. The Common Drug Review does not evaluate budget impact analyses and affordability and there is no explicit willingness to pay thresholds [22]. Prior to April 2015, product listing agreements could not be negotiated in Quebec before a medicine had been included in the list of medicines approved for reimbursement [23]. In addition, the Quebec pricing policy also ensures that Quebec shall not pay more than the lowest negotiated price in Canada[24]. The pan-Canadian Pharmaceutical Alliance was established in 2010 and aims to combine the purchasing power of participating provinces (excluding Nunavut) for negotiating prices of medicines reviewed by the Common Drug Review or the pan-Canadian Oncology Drug Review[25]. The pan-Canadian Pharmaceutical Alliance could lead to more consistent reimbursement decisions across Canada, while the participating provinces will still have varying budgets and the prices negotiated by the pan-Canadian Pharmaceutical Alliance may still be more affordable for wealthier provinces.

The results of this study expand previous work and provide valuable insights when compared with those of previous studies with similar methodology. Gamble et al.[6] calculated agreement between the Common Drug Review and 11 public drug plans for all Common Drug Review recommendations issued from inception to May 2009 using the binomial categories ‘listed’ and ‘not listed’. The comparison of the percentage

agreements and kappa coefficients that were calculated for this study also used binomial classifications and a comparison of study results demonstrates that provincial payers have a greater agreement with the Common Drug Review recommendations (Table 2). Gamble et al. [6] identified Ontario as the province with the lowest percentage agreement (64.2%) and kappa coefficient (k=0.28) with the Common Drug Review. However, this more recent data set calculated the Common Drug Review and Ontario percentage agreement to be 78.8% and the kappa coefficient doubled to k=0.562 (Table 2). Therefore, these results show that recent Common Drug Review recommendations are in more agreement with Ontario's listing decisions. The kappa coefficients from this study also suggest that there is now greater provincial alignment for listing decisions by comparison with the results of a study conducted prior to the inception of Common Drug Review [26]. Other studies have evaluated agreement between provincial listing decisions, but are difficult to compare with this study due to differing methodologies. Anis et al.[26] calculated kappa coefficients for provincial listing decisions using binomial categories for the 10 provinces by directly comparing provinces as there was no Common Drug Review at the time of the study and produced kappa coefficients ranging from k=0.06 to k=0.39 for Alberta, British Columbia, Ontario and Quebec. The results from MacDonald and Potvin (2004) are also difficult to compare as they utilised 'full' and 'restricted' as the two categories for comparison [27]. Morgan et al. also used different reimbursement categories and did not limit their comparison only to new medicines issued a reimbursement recommendation from the Common Drug Review [28]. Attaran *et al*. [5] also calculated percentage agreements using a multinomial

classification category, which have been criticised due to the difficulty of accurately comparing restrictions [29].

Limitations

At the time of data collection, the recommendations listed on the Common Drug Review and provincial websites met the inclusion criteria of the study. However, the Common Drug Review and provincial drug plans continue to update their reports and formularies, so these results provide an insight into the health technology assessment landscape and reimbursement recommendations for a defined point in time and adds to the ongoing body of research. As there are 18 public drug plans that participate in the Common Drug Review process, reviewing only three Common Drug Review participating provincial plans and Quebec is a limitation for this research. The evolution of the CDR recommendations framework and the different categories of recommendations over time may pose some challenge in comparing the agreement between recommendations and provincial decisions in some cases. Each Common Drug Review participating drug plan has varying resources available for reviewing new medicines in the context of the local population and therefore the results of this study may not be generalizable to all 18 participating drug plans. Future studies can build on this research by evaluating the concordance of all Common Drug Review participating federal, provincial and territorial drug plans.

Conclusions and implications for practice and future research

The provincial listing decisions and Common Drug Review recommendations demonstrated moderate to substantial agreement, providing evidence that the Common Drug Review is aligned with provincial listing decisions and therefore provides value for participating plans. It could be argued that these observed scores of alignment could be the result of provinces becoming more reliant on the Common Drug Review over time and that the Common Drug Review continues to improve and develop to meet payers' needs. However, the fact that the provinces are able to come to different decisions on the basis of Common Drug Review recommendations, illustrates the flexibility of the process. This enables provincial payers to incorporate local context and make drug funding or listing decisions that are appropriate for public plans with varying budgets and patient populations. European countries are much more heterogeneous than Canadian provinces, but the Common Drug Review does provide an example of a centralized review process that generates evidence to support the common requirements of participating plans with the added flexibility of incorporating evidence and budget impact that is context specific. It is envisaged that the outcome of this study could have implications for other regions with a centralised regulatory authority and a fragmented payer environment, such as Europe.

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Ministry of Health and Long-term care) and the Institut national d'excellence en santé et en services sociaux for their invaluable contribution. The authors would also like to acknowledge the contribution of Ms Patricia Connelly for her thorough and thoughtful editorial assistance.

Competing interests

Since production of this manuscript, Nicola Allen has become employed by ICON plc, Global Pricing and Market Access, London, UK. Chander Sehgal was a director of CADTH Common Drug Review from April 2011 to July 2016.

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Figure legends

Figure 1. Overview of medicine recommendations issued from January 2009 to May 2013 by the Common Drug Review with provincial payers and listing decisions

Tables

Table 1. Proportion of medicine-indication pair recommendations by binomial categories

Table 2. Comparison of percentage agreement and kappa coefficients for Common Drug Review and Provincial payers with previous study

Appendix

Appendix 1: STROBE checklist

Appendix 2: Medicine-indication pairs

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Interpretation

Main findings

Reimbursement recommendations issued by the Common Drug Review for 110 medicine-indication pairs from January 2009 to January 2015 compared with a previous study shows a greater agreement with the Common Drug Review recommendations (Table 2). This model has the potential to be of value in other regions with multiple payers, such as Europe. Currently, the European Medicines Agency provides a centralised marketing authorisation for all member states, but the reimbursement and

decision-making processes remain the responsibility of each country [1]. The Common Drug Review model could be implemented in Europe if a centralised body evaluated new medicines to inform reimbursement recommendations for European payers even if the final reimbursement decision remained the responsibility of the individual jurisdictions [1].

Explanation and comparison with other studies

The Common Drug Review participating drug plans are generally congruent with the Common Drug Review, but price negotiations and other factors can impact the final decision. Manufacturers and provincial payers often negotiate price with product listing agreements, but there is wide variation between provinces primarily due to their population size [19]. Price negotiations are a key cause of lack of congruity between Ontario and the Common Drug Review, as Ontario has the largest population and thus the greatest negotiating power and research has also shown Ontario to have the greatest proportion of medicines funded with product listing agreements [20]. The review process in Alberta only allows manufacturers to negotiate a product listing agreement after the formal review decision on the initial price is determined [21]. The Common Drug Review recommendations framework has evolved over time. In November 2012, a recommendations framework was made publicly available and included a category of “List with criteria and/or conditions” that may include a condition for a lower price to lead to a greater likelihood of a positive listing recommendation and accommodate the price negotiations post- Common Drug Review[22]. In addition, the

recommendations framework included a separate category of “Do not list at submitted price” that has been used in cases in which the drug under review demonstrated a comparable clinical benefit to its comparator(s). Prior to November 2012, the “Do not list at submitted price” was used as a subcategory of the “Do not list” category. The Common Drug Review does not evaluate budget impact analyses and affordability and there is no explicit willingness to pay thresholds [22]. Prior to April 2015, product listing agreements could not be negotiated in Quebec before a medicine had been included in the list of medicines approved for reimbursement [23]. In addition, the Quebec pricing policy also ensures that Quebec shall not pay more than the lowest negotiated price in Canada[24]. The pan-Canadian Pharmaceutical Alliance was established in 2010 and aims to combine the purchasing power of participating provinces (excluding Nunavut) for negotiating prices of medicines reviewed by the Common Drug Review or the pan-Canadian Oncology Drug Review[25]. The pan-Canadian Pharmaceutical Alliance could lead to more consistent reimbursement decisions across Canada, while the participating provinces will still have varying budgets and the prices negotiated by the pan-Canadian Pharmaceutical Alliance may still be more affordable for wealthier provinces.

The results of this study expand previous work and provide valuable insights when compared with those of previous studies with similar methodology. Gamble et al.[6] calculated agreement between the Common Drug Review and 11 public drug plans for all Common Drug Review recommendations issued from inception to May 2009 using the binomial categories ‘listed’ and ‘not listed’. The comparison of the percentage

agreements and kappa coefficients that were calculated for this study also used binomial classifications and a comparison of study results demonstrates that provincial payers have a greater agreement with the Common Drug Review recommendations (Table 2). Gamble et al. [6] identified Ontario as the province with the lowest percentage agreement (64.2%) and kappa coefficient (k=0.28) with the Common Drug Review. However, this more recent data set calculated the Common Drug Review and Ontario percentage agreement to be 78.8% and the kappa coefficient doubled to k=0.562 (Table 2). Therefore, these results show that recent Common Drug Review recommendations are in more agreement with Ontario's listing decisions. The kappa coefficients from this study also suggest that there is now greater provincial alignment for listing decisions by comparison with the results of a study conducted prior to the inception of Common Drug Review [26]. Other studies have evaluated agreement between provincial listing decisions, but are difficult to compare with this study due to differing methodologies. Anis et al.[26] calculated kappa coefficients for provincial listing decisions using binomial categories for the 10 provinces by directly comparing provinces as there was no Common Drug Review at the time of the study and produced kappa coefficients ranging from k=0.06 to k=0.39 for Alberta, British Columbia, Ontario and Quebec. The results from MacDonald and Potvin (2004) are also difficult to compare as they utilised 'full' and 'restricted' as the two categories for comparison [27]. Morgan et al. also used different reimbursement categories and did not limit their comparison only to new medicines issued a reimbursement recommendation from the Common Drug Review [28]. Attaran *et al*. [5] also calculated percentage agreements using a multinomial

classification category, which have been criticised due to the difficulty of accurately comparing restrictions [29].

Limitations

At the time of data collection, the recommendations listed on the Common Drug Review and provincial websites met the inclusion criteria of the study. However, the Common Drug Review and provincial drug plans continue to update their reports and formularies, so these results provide an insight into the health technology assessment landscape and reimbursement recommendations for a defined point in time and adds to the ongoing body of research. As there are 18 public drug plans that participate in the Common Drug Review process, reviewing only three Common Drug Review participating provincial plans and Quebec is a limitation for this research. The evolution of the CDR recommendations framework and the different categories of recommendations over time may pose some challenge in comparing the agreement between recommendations and provincial decisions in some cases. Each Common Drug Review participating drug plan has varying resources available for reviewing new medicines in the context of the local population and therefore the results of this study may not be generalizable to all 18 participating drug plans. Future studies can build on this research by evaluating the concordance of all Common Drug Review participating federal, provincial and territorial drug plans.

Conclusions and implications for practice and future research

The provincial listing decisions and Common Drug Review recommendations demonstrated moderate to substantial agreement, providing evidence that the Common Drug Review is aligned with provincial listing decisions and therefore provides value for participating plans. It could be argued that these observed scores of alignment could be the result of provinces becoming more reliant on the Common Drug Review over time and that the Common Drug Review continues to improve and develop to meet payers' needs. However, the fact that the provinces are able to come to different decisions on the basis of Common Drug Review recommendations, illustrates the flexibility of the process. This enables provincial payers to incorporate local context and make drug funding or listing decisions that are appropriate for public plans with varying budgets and patient populations. European countries are much more heterogeneous than Canadian provinces, but the Common Drug Review does provide an example of a centralized review process that generates evidence to support the common requirements of participating plans with the added flexibility of incorporating evidence and budget impact that is context specific. It is envisaged that the outcome of this study could have implications for other regions with a centralised regulatory authority and a fragmented payer environment, such as Europe.

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Competing interests

Since production of this manuscript, Nicola Allen has become employed by ICON plc, Global Pricing and Market Access, London, UK. Chander Sehgal was a director of CADTH Common Drug Review from April 2011 to July 2016.

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Figure legends

Figure 1. Overview of medicine recommendations issued from January 2009 to May 2013 by the Common Drug Review with provincial payers and listing decisions

Tables

Table 1. Proportion of medicine-indication pair recommendations by binomial categories

Table 2. Comparison of percentage agreement and kappa coefficients for Common Drug Review and Provincial payers with previous study

Appendix

Appendix 1: STROBE checklist

Appendix 2: Medicine-indication pairs

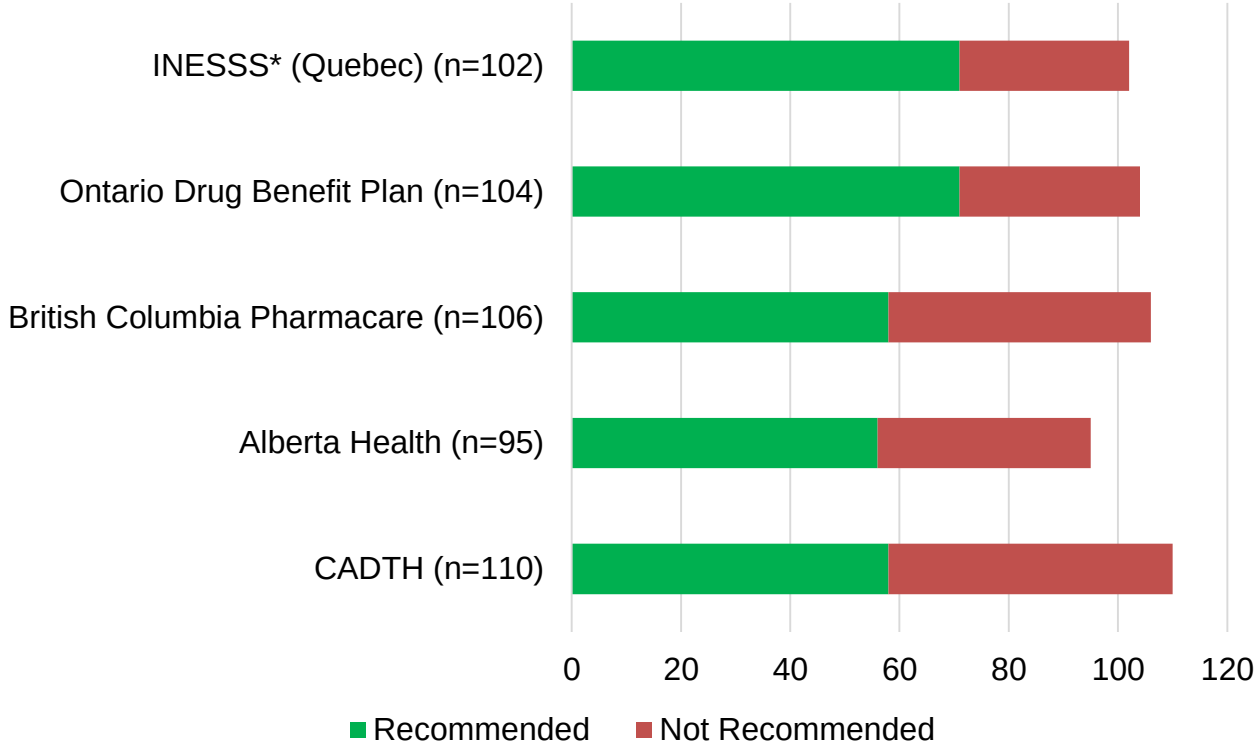
Table 1: Proportion of medicine-indication pair recommendations

HTA agencies and payers	Positive recommendation (±95% CI)	Negative recommendation (±95% CI)
CADTH (n=110)	52.7% (43.5%; 61.8%)	47.3% (38.2%; 56.5%)
Alberta Health (n=95)	58.9% (48.9%; 68.3%)	41.1% (31.7%; 51.1%)
British Columbia Pharmacare (n=106)	54.7% (45.2%; 63.9%)	45.3% (36.1%; 54.8%)
Ontario Drug Benefit Plan (n=104)	68.3% (58.8%; 76.4%)	31.7% (23.6%; 41.2%)
INESSS* (Quebec) (n=102)	69.6% (58.8%; 76.4%)	30.4% (21.9%; 39.2%)

*Institut national d'excellence en santé et en services sociaux (INESSS)

Table 2: Comparison of percentage agreement and kappa coefficients for the Common Drug Review recommendations and provincial payers with previous study

	Alberta	British Columbia	Ontario	Quebec
Percentage agreement from (Gamble, 2011)	86.8%	67.9%	77.8%	71.7%
Percentage agreement from this study	78.9%	81.1%	78.8%	74.5%
Kappa coefficients from (Gamble, 2011)	0.73	0.33	0.28	0.45
Kappa coefficients from this study	0.578	0.622	0.562	0.474



*Institut national d'excellence en santé et en services sociaux

Appendix 1: Checklist of recommendations for reporting of observational studies using the STROBE guidelines

Section/Topic	Item No	Recommendation	Reported
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	Introduction
Methods			
Study design	4	Present key elements of study design early in the paper	Methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	Not Applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods
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	Methods
Bias	9	Describe any efforts to address potential sources of bias	Methods

Study size	10	Explain how the study size was arrived at	Methods, based on number of CDR reviews within eligibility criteria
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Methods
		(*b*) Describe any methods used to examine subgroups and interactions	Not Applicable
		(*c*) Explain how missing data were addressed	Not Applicable
		(*d*) If applicable, explain how loss to follow-up was addressed	Not Applicable
		(*e*) Describe any sensitivity analyses	Not Applicable
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	Methods
		(b) Give reasons for non-participation at each stage	Not Applicable
		(c) Consider use of a flow diagram	Not Applicable
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Appendix
		(b) Indicate number of participants with missing data for each variable of interest	Not Applicable

		(c) Summarise follow-up time (eg, average and total amount)	Not Applicable
Outcome data	15	Report numbers of outcome events or summary measures over time	Results
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	Results
		(*b*) Report category boundaries when continuous variables were categorized	Not Applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not Applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not Applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Limitations
Generalisability	21	Discuss the generalisability (external validity) of the study results	Limitations
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	Competing Interests

Appendix 2

Generic name	Proprietary name	Indication
aclidinium bromide	Tudorza Genuair	Chronic obstructive pulmonary disease (COPD)
aflibercept	Eylea	Macular degeneration, age-related
alendronate sodium / cholecalciferol	Fosavance 70/5600	Osteoporosis
alitretinoin	Toctino	Eczema
apixaban	Eliquis	Prevention of venous thromboembolic events (VTE)
aripiprazole	Abilify Maintena	Schizophrenia
aripiprazole	Abilify	Schizophrenia and related psychotic disorders
asenapine	Saphris	Bipolar I disorder
asenapine	Saphris	Schizophrenia
azelaic acid	Finacea	Rosacea
azilsartan medoxomil	Edarbi	Hypertension, essential
azilsartan medoxomil + chlorthalidone	Edarbyclor	Hypertension, essential
aztreonam for inhalation solution	Cayston	Cystic fibrosis (CF) with chronic pulmonary pseudomonas aeruginosa infections
belimumab	Benlysta	Systemic lupus erythematosus
brinzolamide and timolol maleate suspension	Azarga	Glaucoma and ocular hypertension
calcitriol	Silkis	Psoriasis, mild to moderate plaque
canakinumab	Ilaris	Cryopyrin-associated periodic syndrome (CAPS)
certolizumab pegol	Cimzia	Arthritis, rheumatoid
clostridium botulinum neurotoxin type a, free from complexing proteins	Xeomin	Blepharospasm
clostridium botulinum neurotoxin type a, free from complexing proteins	Xeomin	Cervical dystonia
clostridium botulinum neurotoxin type a, free from complexing proteins	Xeomin	Spasticity, post-stroke
colesevelam hydrochloride	Lodalis	Hypercholesterolemia
collagenase clostridium histolyticum	Xiaflex	Dupuytren's contracture with a palpable cord

cyclosporine	Restasis ophthalmic emulsion	Dry eye disease, moderate to moderately severe
dabigatran etexilate	Pradaxa	Thromboembolism (venous), prevention
denosumab	Prolia	Osteoporosis, postmenopausal women
desvenlafaxine succinate	Pristiq	Depressive, major disorder (MDD)
dexamethasone intravitreal implant	Ozurdex	Macular oedema following central retinal vein occlusion
dienogest	Visanne	Pain (pelvic) associated with endometriosis
doxycycline monohydrate	Apprilon	Rosacea treatment
dronedarone hydrochloride	Multaq	Atrial fibrillation
eculizumab	Soliris	Paroxysmal nocturnal hemoglobinuria (PNH)
eltrombopag olamine	Revolade	Thrombocytopenic purpura chronic immune (idiopathic)
elvitegravir / cobicistat / emtricitabine / tenofovir disoproxil fumarate	Stribild	HIV-1 infection
emtricitabine / rilpivirine / tenofovir disoproxil fumarate	COMPLERA	HIV-1 infection in antiretroviral treatment-naïve adults
eplerenone	Inspra	Post myocardial infarction
everolimus	Afinitor	Renal angiomyolipoma associated with tuberous sclerosis complex (TSC)
exenatide	Byetta	Diabetes mellitus, Type 2
fampridine	Fampyra	Multiple sclerosis, improve walking disability
febuxostat	Uloric	Gout
fentanyl citrate	Abstral	Pain, cancer (breakthrough
fesoterodine fumarate	Toviaz	Bladder, overactive
fidaxomicin	Dificid	Clostridium difficile infection
fingolimod	Gilenya	Multiple sclerosis
fluticasone furoate /vilanterol	Breo Ellipta	Chronic obstructive pulmonary disease (COPD)
glycopyrronium bromide	Seebri	Chronic obstructive pulmonary disease (COPD), maintenance

		bronchodilator treatment
golimumab	Simponi	Arthritis, rheumatoid
golimumab	Simponi	Arthritis, psoriatic
golimumab	Simponi	Ankylosing spondylitis
grass pollen allergen extract	Oralair	Allergic rhinitis (grass pollen)
guanfacine hydrochloride	Intuniv XR	Attention-deficit/hyperactivity disorder (ADHD)
hydromorphone hydrochloride	Jurnista	Pain, chronic (moderate to severe)
indacaterol	Onbrez	Chronic obstructive pulmonary disease (COPD), maintenance bronchodilator treatment
indacaterol/glycopyrronium	Ultibro Breezhaler	Chronic obstructive pulmonary disease (COPD)
infliximab	Inflectra	Ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, rheumatoid arthritis
ingenol mebutate	Picato	Keratosis, actinic
insulin glulisine	Apidra	Diabetes, mellitus (Type 1 & 2)
interferon beta 1a	Rebif	Clinically isolated syndrome
lacosamide	Vimpat	Epilepsy, partial onset seizures (POS)
levodopa / carbidopa	Duodopa	Parkinson's disease
linagliptin	Trajenta	Diabetes mellitus, Type 2
linagliptin-metformin	Jentadueto	Diabetes mellitus (Type 2)
liraglutide	Victoza	Diabetes mellitus, Type 2, dual therapy
lisdexamfetamine dimesylate	Vyvanse	Attention deficit hyperactivity disorder
loteprednol etabonate	Lotemax	Post-operative inflammation following cataract surgery
lurasidone	Latuda	Schizophrenia
methylnaltrexone bromide	Relistor	Constipation, opioid-induced
mirabegron	Myrbetriq	Bladder, overactive

mometasone furoate	ASMANEX	Asthma, (bronchial) prophylactic management of steroid responsive
mometasone furoate and formoterol	Zenhale (inhalation aerosol)	Asthma maintenance (adults, children 12 or older)
nebivolol	Bystolic	hypertension essential
olmesartan medoxomil	Olmetec	Hypertension
olmesartan medoxomil + hydrochlorothiazide	Olmetec Plus	Hypertension
onabotulinumtoxina	Botox	Neurogenic detrusor overactivity
oxybutynin chloride gel	GELNIQUE	Bladder, overactive
paliperidone palmitate	Invega Sustenna	Schizophrenia
palonosetron hydrochloride	Aloxi (capsule)	Nausea and vomiting (chemotherapy induced) prevention
palonosetron hydrochloride	Aloxi (injection)	Nausea and vomiting (chemotherapy induced) prevention
pirfenidone	Esbriet	Pulmonary fibrosis (idiopathic, mild to moderate)
plerixafor	Mozobil	Hematopoietic stem cell mobilizer in non-Hodgkin's lymphoma and multiple myeloma
prasugrel hydrochloride	Effient	Acute coronary syndrome (ACS)
prucalopride	Resotran	Constipation, chronic
ranibizumab injection	Lucentis	Macular oedema, secondary to retinal vein occlusion, (branch retinal vein occlusion)
remicade	Infliximab	Ulcerative colitis
rilpivirine	Edurant	HIV (treatment - naive adult)
riociguat	Adempas	Pulmonary hypertension, chronic thromboembolic
rivaroxaban	Xarelto	Thromboembolic events (venous), pulmonary embolism

roflumilast	Daxas	Chronic obstructive pulmonary disease (COPD)
romiplostim	Nplate	Chronic immune (idiopathic) thrombocytopenic purpura (ITP)
rotigotine	Neupro	Parkinson's disease
rufinamide	Banzel	Lennox-Gastaut syndrome; adjunctive treatment of seizures
sapropterin dihydrochloride	Kuvan	Phenylketonuria (PKU).
saxagliptin	onglyza	Diabetes mellitus (Type 2)
saxagliptin + metformin	Komboglyze	Diabetes mellitus, Type 2
silodosin	RAPAFLO	Prostatic hyperplasia, benign
sitagliptin phosphate monohydrate / metformin hydrochloride	Janumet	Diabetes mellitus (Type 2)
sofosbuvir	Sovaldi	Hepatitis C, chronic
somatropin	Genotropin	Growth hormone deficiency, adult
somatropin	Genotropin	Growth hormone deficiency, paediatric
somatropin	Genotropin	Turner syndrome
stiripentol	Diacomit	Dravet syndrome
tadalafil	Adcirca	Pulmonary arterial hypertension
tapentadol	Nucynta CR	Pain, moderate to moderately severe
telaprevir	Incivek	Hepatitis C infection (genotype 1), chronic (treatment experienced)
telmisartan / amlodipine	Twynsta	Hypertension, essential
ticagrelor	Brilinta	Thrombotic events in acute coronary syndromes, prevention
tocilizumab	Actemra	Arthritis, rheumatoid
tolvaptan	Samsca	Hyponatremia, non-hypovolemic
ustekinumab	Stelara	Psoriasis
velaglucerase alfa	VPRIV	Gaucher disease
zolpidem tartrate	Sublinox	Insomnia, short-term treatment