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Original Research

Analysis of Trends in Insulin Utilization and Spending Across Canada From 2010 to 2015

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Key Messages

- Long-acting and rapid-acting insulin dispensing rates are increasing across Canada, while dispensing rates for all other insulin types are decreasing.
- Public payers with lower utilization of long-acting insulin products resulted in lower overall spending.

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ABSTRACT

Objectives: To describe insulin utilization and spending across Canada and investigate how interprovincial variations in long-acting insulin uptake impact provincial spending.
Methods: We conducted a cross-sectional time-series analysis of insulin products dispensed nationally from January 1, 2010, to December 31, 2015, using data from IQVIA (Durham, North Carolina, United States). Analysis was stratified according to insulin type, payer and province. We report annual numbers for national insulin dispensing and spending and provincial numbers for publicly funded long-acting insulin dispensing and spending rates that are standardized by public drug beneficiary enrolment and diabetes prevalence. We report the percent of change of an annual provincial cost-to-utilization index of total insulin spending to total insulin dispensing between 2010 and 2015.
Results: Between 2010 and 2015, total insulin utilization increased 21% (4.4 million to 5.3 million prescriptions), and total insulin costs increased 54% ($345 million to $530 million) nationally. The national dispensing rate of long-acting insulin (+96%) and rapid-acting insulin (+38%) increased, while the national dispensing rate for intermediate-acting (–23%), short-acting (–37%) and premixed (–28%) insulins declined. Large interprovincial variation was observed for the rate of long-acting insulin uptake (range, Alberta, +1,505%; British Columbia, +27%) and the rate of long-acting insulin spending (Alberta, +2,177%; British Columbia, +44%) between 2010 and 2015 after standardization. Provinces with higher rates of long-acting insulin uptake experienced faster increases in their cost-to-utilization index (Alberta, +78%; British Columbia, +24%).
Conclusions: Overall, the rate of uptake of long-acting insulins has increased nationally. Uptake varies widely among provinces and is likely to be associated with differential cost increases across public payers in Canada.

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RÉSUMÉ

Objectifs : Nous décrivons l'utilisation de l'insuline et les dépenses qui y sont liées au Canada, et examinons dans quelle mesure les variations interprovinciales de l'utilisation de l'insuline à action prolongée se répercutent sur les dépenses provinciales.
Méthodes : Nous avons réalisé une analyse de données en coupe transversale et sur séries temporelles des produits d'insuline offerts à l'échelle nationale du 1er janvier 2010 au 31 décembre 2015 à partir des données de l'IQVIA (Durham, Caroline du Nord, États-Unis). L'analyse a été stratifiée selon le type d'insuline, le payeur et la province. Nous présentons les taux annuels de délivrance de l'insuline et des dépenses qui y sont associées à l'échelle nationale et les taux annuels de délivrance d'insuline à action prolongée et des dépenses financées par les fonds publics à l'échelle provinciale, qui sont standardisés par l'inscription des bénéficiaires au régime public d'assurance-médicaments et la prévalence du diabète. Nous présentons le pourcentage de variation de l'indice provincial annuel coût-utilisation des dépenses totales en insuline par rapport à la délivrance totale d'insuline entre 2010 et 2015.
Résultats : Entre 2010 et 2015, l'utilisation totale d'insuline a augmenté de 21 % (de 4,4 millions à 5,3 millions d'ordonnances) et les coûts totaux en insuline ont augmenté de 54 % (de 345 M$ à 530 M$) à l'échelle nationale. Les taux de délivrance à l'échelle nationale de l'insuline à action prolongée (+96 %) et de l'insuline à action rapide (+38 %) ont augmenté, alors que les taux de délivrance à l'échelle nationale de l'insuline à action intermédiaire (–23 %), à courte durée d'action (–37 %) et prémélangée (– 28 %) ont diminué. Nous avons observé une grande variation interprovinciale du taux d'utilisation de l'insuline à action prolongée (étendue, Alberta, +1,505 %; Colombie-Britannique, +27 %) et du taux de dépenses en insuline à action prolongée (Alberta, +2,177 %; Colombie-Britannique, +44 %) entre 2010 et 2015 après la standardisation. Les provinces qui ont des taux plus élevés d'utilisation de l'insuline à action prolongée ont subi des augmentations plus rapides de leur indice coût-utilisation (Alberta, +78 %; Colombie-Britannique, +24 %).
Conclusions : Dans l'ensemble, le taux d'utilisation des insulines à action prolongée a augmenté à l'échelle nationale. La grande variation de l'utilisation entre les provinces est vraisemblablement associée aux différences dans l'augmentation des coûts au sein de tous les payeurs publics du Canada.

Introduction

Diabetes was estimated to affect 3.4 million Canadians in 2015 (approximately 9.3% of Canadians) and is projected to grow 44% by 2025, costing $16.9 billion annually by 2020 in both direct and indirect costs (1,2). Insulin is an essential management strategy for many Canadians living with diabetes; regimens are diverse and are individualized based on patients' characteristics, patients' preferences, diabetes type, disease severity and cost considerations.

Insulin is available in multiple formulations that vary by onset, half-life and clinical use. Older formulations of insulins include short-acting, intermediate-acting and premixed analogues. Two newer formulation categories, long-acting and rapid-acting analogues, have been introduced to the market in the past 2 decades; rapid-acting insulin, lispro, was first approved in 1996, and long-acting insulin, glargine, was first approved in 2004 (3). Newer long-acting analogues have gained popularity as the long-acting insulin of choice because of their longer half-life, convenient once-daily dosing and lower incidence of nocturnal hypoglycemia than intermediate-acting (NPH) insulins (4). Similarly, rapid-acting analogues are newer counterparts of the short-acting (regular) insulins and are considered superior due to the improvements in metabolic control (5).

All provincial public drug plans have coverage for insulin but vary in their coverage for the differing formulations. Specifically, most provinces fund newer insulin products; however, 7 of the 10 provinces require prior authorization before reimbursement for the more expensive long-acting insulins (Supplementary Table S1) (6–12). Because of the variation in reimbursement for insulins and recent shifts in practice, we aimed to describe the utilization and spending trends of insulin in Canada across time and to investigate how uptake of long-acting insulins impacted overall public spending across provinces. Our research offers a baseline assessment of utilization and cost, which is a stepping stone in estimating cost-effectiveness in an increasingly resource-stressed environment.

Methods

Study design

We conducted a cross-sectional time-series analysis describing the trends in Canadian insulin prescription dispensing and spending between January 1, 2010, and December 31, 2015, using data from IQVIA (Durham, North Carolina, United States) Geographic Prescription Monitor (GPM). Insulins were categorized by type—rapid-acting, short-acting, intermediate-acting, long-acting or premixed analogues—on the basis of the Diabetes Canada (formerly the Canadian Diabetes Association) guide (Supplementary Table S2) (13).

Data source

The source of information supporting IQVIA GPM is the IQVIA retail prescription database, which contains prescription transactions from Canadian drug stores for all dispensed branded and generic products. At the national level, more than 79% of total prescriptions dispensed are captured by a panel composed of approximately 6,000 pharmacies. The monthly estimates are created using IQVIA's patented geospatial projection methodology. These projections are representative of drug utilization and cost at the provincial and national levels. At the provincial level, the sampling error can reach slightly higher levels, although it will not exceed 5% to 10% in the vast majority of cases (14). The cost supplied includes drug costs, markups and dispensing fees. This data source is regularly used for research purposes (15,16).

Analysis

To examine national trends in dispensing and spending, we report the unadjusted monthly numbers of total insulins dispensed between 2010 and 2015 and the unadjusted monthly numbers of prescriptions dispensed, stratified by insulin type (long-acting, intermediate-acting, premixed, rapid-acting and short-acting insulins). Unadjusted monthly cost was also stratified by payment methods (private,

provincial public, noninsured health benefits [NIHB] and cash) during the same time period. NIHB is a federal plan that covers registered First Nations and Inuit persons for medical items not listed on provincial formularies. NIHB does not come directly from the provincial budget, so it was excluded in the analysis of publicly funded medications. The numbers reported represent unadjusted actual spending. Because of the short duration of the study period and the slow rate of change in drug prices in Canada, we did not adjust for inflation (17).

The high cost and growing popularity of long-acting insulins led us to conduct further analysis of long-acting insulin prescriptions stratified by province to assess the burden placed on public plans. We report annual publicly funded long-acting insulin dispensing and costs adjusted by beneficiary enrolment and provincial prevalence of diabetes from 2010 to 2015, and the percentage of change was calculated based on unrounded numbers (18,19). Data about diabetes prevalence, obtained from Statistics Canada, describe the self-reported cases of diabetes from 2010 to 2015 and were population-adjusted using Quarter 4 population census data for the respective provinces and years as the denominator (18,20,21). Beneficiary enrolment data were obtained from the National Prescription Drug Utilization Information System developed by the Canadian Institute for Health Information (19).

To contextualize the relationship between interprovincial variations in cost and insulin utilization, we report an annual cost-to-utilization ratio comparing the total public spending on insulins to the total number of all insulin prescriptions dispensed annually through public plans. The cost-to-utilization ratio represents a rough estimate of the average cost per prescription. Percentage of change in the index was calculated for the period between 2010 and 2015. Correlation analysis was conducted between the percentage of change in provincial publicly funded long-acting insulin utilization (adjusted by diabetes prevalence and population) annually from 2010 to 2015 and the percentage of change in the cost-to-utilization ratio over this same period using the Pearson product-moment correlation. We defined a coefficient of >0.5 as a strong correlation and a coefficient of <0.3 as a small correlation. We used descriptive statistics, and all analyses were completed in Python 3.5.2 (Python Software Foundation, Wilmington, Delaware, United States) using the Python Data Analysis Library (pandas) 0.19.2 as well as Microsoft Office Excel 2016 (22–24).

Results

Overall national trends in insulin utilization and costs

A total of 29,185,307 insulin prescriptions were dispensed in Canada between January 1, 2010, and December 31, 2015 (Figure 1). In 2015, 5.28 million insulin prescriptions were dispensed, resulting in a total cost of $530,046,826 nationally. In 2015, public payment of all insulins comprised 52% of all insulin spending (a 61% increase from 2010 to 2015, from $172,274,256 to $277,453,745); private payment comprised 37% (a 61% increase from 2010 to 2015, from $120,873,809 to $194,753,205); cash comprised 8% (a 2% decrease from 2010 to 2015; range, $46,014,136 to $45,000,312); and NIHB comprised 2% (a 114% increase from 2010 to 2015; range, $6,012,405 to $12,839,564) (Figure 1).

Dispensing of all insulin products increased 21% from 2010 to 2015 (4,366,148 prescriptions to 5,281,919 prescriptions), while spending on all insulin products increased 54% ($345,187,257 to $530,050,672) in the same period (Figure 1). During this time period, dispensing of long-acting insulin increased 96% (1,025,764 prescriptions to 2,011,118 prescriptions), and dispensing of rapid-acting insulins increased 38% (1,281,112 prescriptions to 1,762,032 prescriptions) (Figure 2). In contrast, dispensing decreased by 23%

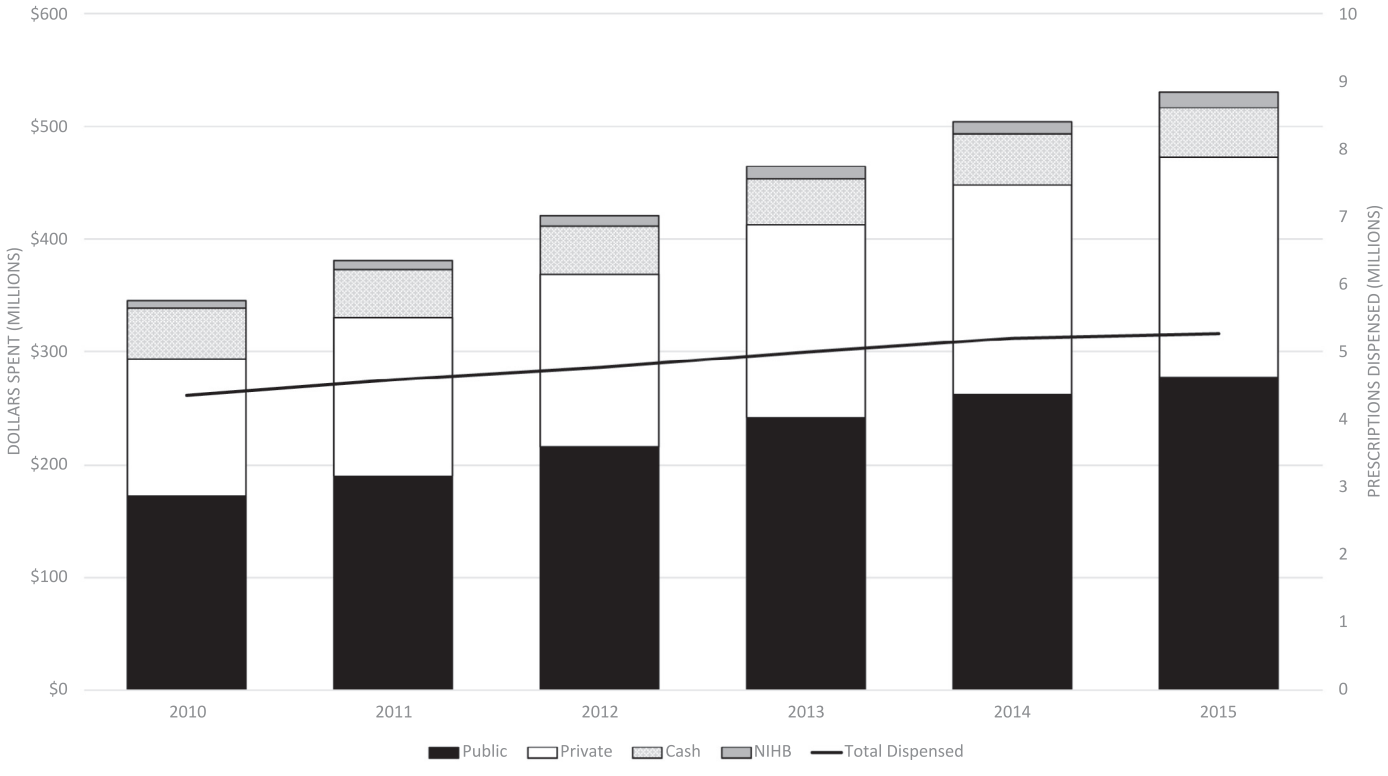

Figure 1. National trends in insulin spending by payment type and total national insulin dispensing. Annual spending numbers are reported in Canadian dollars from 2010 to 2015 and are categorized by method of payment for the prescription. Black, public payer; white, private payer; grey-checkered, cash; grey, noninsured health benefits (NIHB); solid line, total insulin prescriptions dispensed.

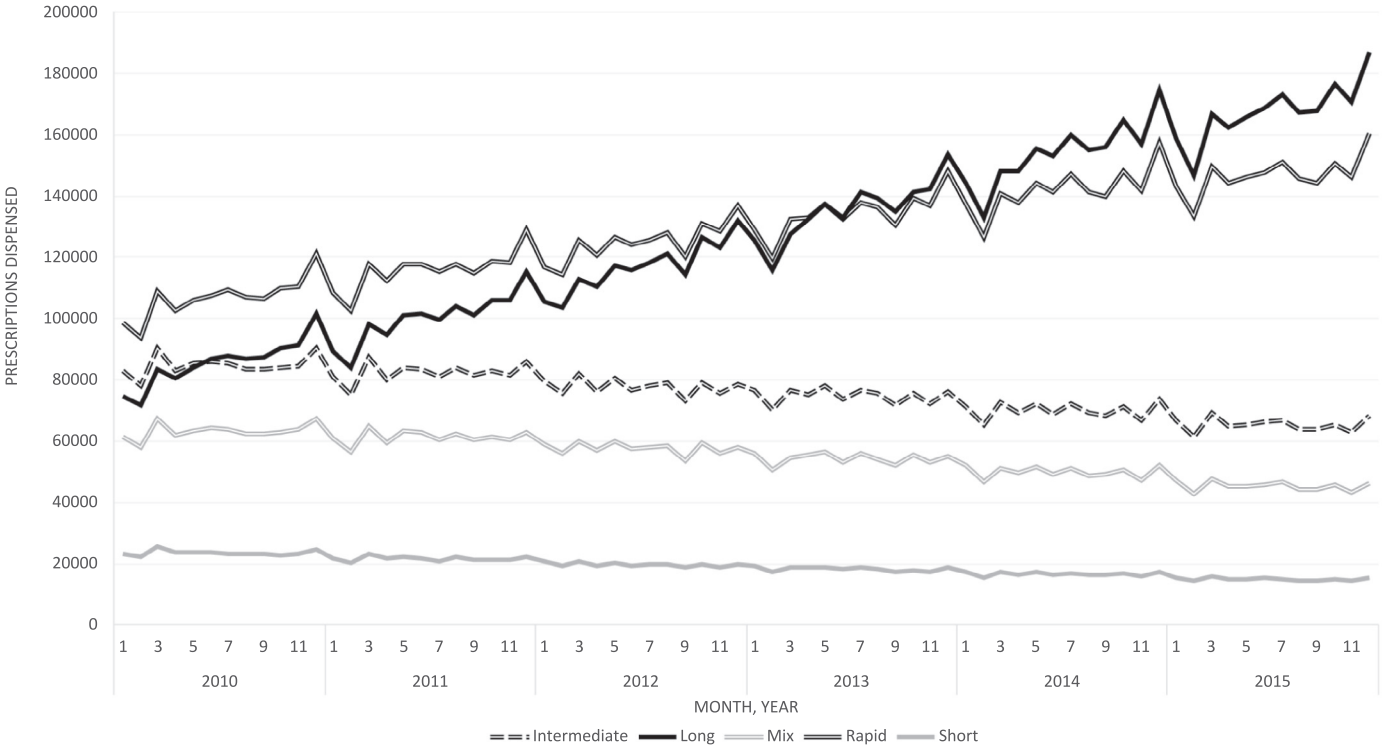

Figure 2. National trends in dispensing by insulin type. Monthly numbers of prescriptions dispensed are reported for 2010 to 2015. Double dashed black line, intermediate-acting insulin; solid black line, long-acting insulin; double grey line, premixed insulin; double black line, rapid-acting insulin; solid grey line, short-acting insulin.

for intermediate-acting insulins (1,016,448 prescriptions to 785,071 prescriptions), by 37% for short-acting insulins (282,981 prescriptions to 179,612 prescriptions) and by 28% for premixed insulins (759,843 prescriptions to 544,086 prescriptions) (Figure 2).

Interprovincial variation in publicly funded long-acting insulin utilization and cost

The dispensing rate of publicly funded long-acting insulins increased in all provinces between 2010 and 2015 but varied widely among provinces. After adjusting for diabetes prevalence and beneficiary enrolment, the province with the largest percentage of change in long-acting insulin uptake between 2010 and 2015 was Alberta (a 1,505% increase, from 0.28 to 4.55 prescriptions per person), whereas the province with the lowest percentage of change in uptake was British Columbia (a 27% increase from 0.56 to 0.71 prescriptions per person) (Figure 3A). The province with the lowest overall dispensing rate for publicly funded long-acting insulins in 2015 was Newfoundland and Labrador (165% increase; range, 0.07 to 0.18 prescriptions per person between 2010 and 2015) (Figure 3A).

Total spending on insulin products varied widely among provinces. Between 2010 and 2015, annual public spending increased 36% nationally for all insulins (from $411.97 to $561.00 per person) after adjusting for diabetes prevalence and drug beneficiary enrolment. Alberta experienced the highest increase in total public spending on all insulin products between 2010 and 2015 (127%; from $552.79 to $1,257.31 per person), as well as the fastest uptake and spending on publicly funded long-acting insulin in the same period (2,177%; from $33.71 to $767.40 per person) (Figure 3B). British Columbia had the lowest increase in public spending on long-acting products (44%; from $70.09 to $100.62 per person) and had the second lowest increase in total public spending on insulin (–4%, from $210.81 to $202.71 per person) (Figure 3B). An analysis completed without adjusting for diabetes prevalence revealed similar results.

Overall, provinces with higher uptakes of long-acting insulins experienced faster increases in total insulin spending (Table 1). Provinces with the greatest change in their cost-to-utilization ratio (a measure of average cost per prescription) also had higher dispensing rates of long-acting insulins. Between 2010 and 2015, Alberta experienced the greatest change in its cost-to-utilization index for total insulin spending to total insulin dispensing (a 78% increase, from $70.5 to $125.70 per prescription) (Table 1). A correlation analysis revealed that the Pearson correlation coefficient between the percentage of change in long-acting insulin uptake and the percentage of change in the cost-to-utilization ratio was 0.83 (R-squared: 0.69, p=0.001, 95% confidence interval 0.47 to 0.96), which represents a strong correlation between the 2 variables.

Discussion

Our study found that overall spending and utilization of insulin has increased across Canada. Specifically, the use of long- and rapid-acting insulins increased, while the use of other insulin types decreased. The majority of insulin was publicly funded, but utilization and spending were found to vary across provinces. Although wide interprovincial variations were observed, the extent to which provinces dispensed long-acting insulin was consistent with increased public costs.

We found that between 2010 and 2015, the dispensing of long-acting insulins increased 96% nationally. Despite the decreasing use of most other insulin types, total insulin spending increased 54% over the same period. This increase in long-acting insulin dispensing and insulin spending is consistent with utilization trends observed in other jurisdictions (25,26). This is not surprising because the cost per unit of long-acting insulins is approximately 2 to 3 times the cost of intermediate-acting insulins, while the cost for rapid-acting analogues, which also increased in use during this period, is similar to the cost of short-acting insulins (8,27–29). A consensus

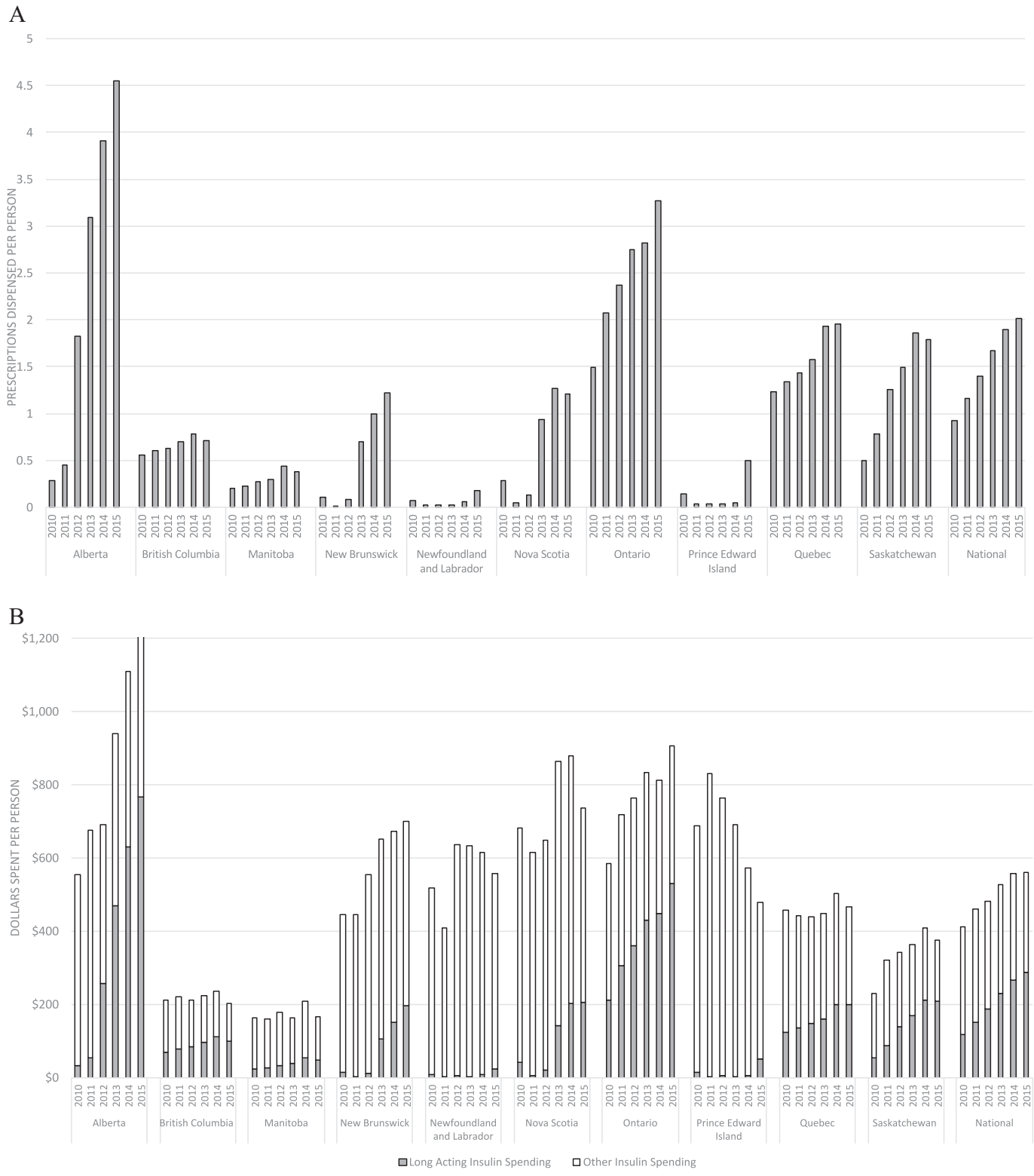

Figure 3. Publicly funded long-acting insulin prescriptions: dispensing and spending rates by province and time. A, Annual dispensing rate is reported for each province from 2010 to 2015. Dispensing rate is adjusted by public drug beneficiary enrolment in each province and by self-reported cases of diabetes. B, Annual public spending rate is reported for each province from 2010 to 2015 in Canadian dollars. Spending rate is adjusted by public drug beneficiary enrolment in each province and by self-reported cases of diabetes. Grey bars, spending on long-acting insulins; white bars, spending on all insulin products.

has not been reached on the cost-effectiveness of insulin analogues (30–33). Several landmark trials have shown evidence that intensive glucose control and early utilization of long-acting insulins may modestly reduce microvascular complications (34,35). However, it is unclear whether the increase in long-acting insulin use is the result of earlier initiation of insulin therapy or to the replacement of intermediate-acting insulin counterparts. Future research should explore the trends in initiation of insulin therapy in Canada.

Table 1
Annual provincial cost-to-utilization index

	2010	2011	2012	2013	2014	2015	Percentage of change* (cost-to-utilization index)	Percentage of change* (public long-acting insulin dispensed)
Alberta	70.48	74.14	91.75	106.25	117.39	125.74	78%	1,505%
British Columbia	77.26	81.01	85.39	90.27	94.08	95.91	24%	27%
Manitoba	65.35	68.41	71.81	76.07	79.71	82.29	26%	87%
New Brunswick	70.86	72.70	76.10	84.57	93.22	100.52	42%	1,055%
Newfoundland and Labrador	61.56	63.18	69.78	74.77	76.67	78.92	28%	165%
Nova Scotia	68.72	70.52	73.35	81.86	88.27	92.94	35%	325%
Ontario	100.64	109.06	116.10	122.85	128.32	132.44	32%	119%
Prince Edward Island	52.24	54.26	55.57	56.95	56.76	58.02	11%	254%
Quebec	56.58	58.11	61.18	61.10	63.90	65.90	16%	59%
Saskatchewan	59.39	62.32	70.09	76.59	81.45	86.04	45%	260%
National	75.77	80.34	86.21	90.40	95.56	99.55	31%	117%

Notes: Index depicts the annual total publicly funded insulin spending in dollars and the total publicly funded insulin-dispensing ratio from 2010 to 2015. Percentage of change is calculated from 2010 to 2015.

* Pearson correlation coefficient: 0.83 (df: 9, R-squared: 0.69; p value: 0.001, 95% CI 0.47 to 0.96).

Our study also observed significant interprovincial variations in the rate of publicly funded long-acting insulins. In general, we observed that provinces with greater utilization of long-acting insulins tended to have higher overall insulin spending. Alberta, Ontario and Saskatchewan are the only 3 provinces that listed long-acting insulins as a general benefit status during our study period (13,27–29). In the other provinces, physicians must document a failed trial of an intermediate-acting insulin due to an allergy or inability to achieve glycemic control without an adverse reaction and must receive prior approval before funding is granted (6–12). Despite this restriction, several Maritime provinces have also experienced rapid growth in long-acting insulin uptake, suggesting that formulary restriction may not play a major role in limiting long-acting insulin uptake. This may be the result of patient-level factors, such as age and comorbidities, which may impact the rate of overall insulin prescribing, and a higher susceptibility to adverse events due to comorbidities, such as declining renal function, polypharmacy and hospitalizations (36–38). Many provinces have added Basaglar, a biosimilar alternative to glargine, to the formulary since 2017. Future work should explore the impact of the addition of biosimilars to overall uptake and spending. Prince Edward Island was the only province to experience a decrease in total insulin spending, despite its increasing usage of long-acting insulins. This change is likely to be due to the change in their provincial reimbursement policy in 2014, which switched the provincial plan from primary to secondary payer during the coordination of benefits with private payers, thus allowing them to decrease overall reimbursement for each prescription (39).

There are several limitations to our study that warrant discussion. IQVIA does not provide patient-level data, so we were unable to determine the number of insulin units filled for each user. The numbers reported represent the number of insulin prescriptions, but multiple vials or cartridges of insulin may be filled for each prescription. Because of the lack of clinical information, such as associated indications and patient information (e.g. age, sex), we were also unable to determine the appropriateness of the prescriptions or the exact insulin regimens, nor were we able to discern whether the increases in the use of long-acting insulins is due to a replacement of other insulin types or to an earlier initiation of diabetes management. We were unable to adjust for age among provinces, which could impact the overall utilization of insulin drugs; however, we did adjust for the number of people diagnosed with diabetes according to Statistics Canada data. We also restricted provincial analysis to publicly reimbursed dispensing data due to the transparency of the enrolment and formulary listing, thus limiting the private-payer variables that could skew the analysis. Last, our database includes only prescription insulin items, and we are unable to account for over-the-counter sales because no published statistics are available.

Conclusions

Insulin is an essential glycemic management strategy for many Canadians; however, we observed considerable variation in the dispensing patterns and spending trends among provinces between 2010 and 2015. Our findings demonstrate that public payers with lower utilization of long-acting insulin products tend to have lower overall spending on insulin products. Formulary restriction did not have any apparent effect on publicly funded long-acting insulin uptake; however, further studies are needed to investigate this observation. This brings into question the value of increased spending and whether these trends in utilization translate into clinical benefits. Further research should examine patient-level clinical factors associated with dispensing to better understand the observed provincial variations as well as the potential clinical impact of these observations.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Diabetes* at https://www.canadianjournalofdiabetes.com.

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Author Disclosures

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Nordisk, and Pfizer, all outside of the submitted work. The remaining authors declare no potential conflicts of interest.

Author Contributions

All authors were involved in the design, interpretation of results, writing, conceptualization of recommendations and revision of the manuscript (YX, MT, TG, MMM, DNJ, SMC); YX and MT were involved in the implementation of the study; MT is the guarantor of the content of the manuscript, including the data and analysis.

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Supplementary Material

Supplementary Table S1
Summary of provincial coverage status for insulin products

	Rapid-acting	Short-acting	Intermediate-acting	Long-acting	Premixed
Alberta	Listed	Listed	Listed	Listed	Listed
British Columbia	Partial reimbursement	Listed	Listed	Restricted	Listed
Manitoba	Listed	Listed	Listed	Restricted*	Listed
New Brunswick	Listed	Listed	Listed	Restricted*	Listed
Newfoundland and Labrador	Listed	Listed	Listed	Restricted*	Listed
Nova Scotia	Listed	Listed	Listed	Restricted*	Listed
Ontario	Listed	Listed	Listed	Listed	Listed
Prince Edward Island	Listed	Listed	Listed	Restricted*	Listed
Quebec	Listed	Listed	Listed	Restricted*	Listed
Saskatchewan	Listed	Listed	Listed	Listed	Listed

Listed, can be prescribed by any doctor; costs are covered by drug plan; *partial reimbursement,* patient must pay the difference in cost; *restricted,* available only to those who meet eligibility criteria and receive prior approval.
Notes: Coverage status during the study period, 2010 to 2015. Please refer to the formulary listings for diabetes medication in Canada from Diabetes Canada for the most current listings.
* Basaglar was added as a listed drug in 2017.

Supplementary Table S2
List of drugs included in each category

Long-acting
Lantus (Glargine)
Levemir (Detemir)
Toujeo (Glargine)
Basaglar
Hypurin NPH
Mix
Novolin GE 10/90
Novolin GE 40/60
Novolin GE 20/80
Novolin GE 30/70
Humulin 30/70
Novolin GE 50/50
Humalog Mix 25
Humalog Mix 50
Rapid-acting
Apidra (Glulisine)
Novorapid (Aspart)
Humalog (Lispro)
Intermediate-acting
Novolin GE NPH
Humulin N
Short-acting
Hypurin R
Novolin GE Toronto
Humulin R
Insulin-Toronto