

Low-Molecular-Weight Heparins

FINAL PHARMACOEPIDEMIOLOGY REPORT

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Conflict of Interest Statement

Muhammad Mamdani was a member of an advisory board for Hoffman La Roche, Pfizer, Novartis, GlaxoSmithKline and Eli Lilly Canada. Tara Gomes, Muhammad Mamdani, and David Juurlink have received grant funding from the Ministry of Health and Long-term Care. No other study members report any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock options, expert testimony, grants or patents received or pending, or royalties) that may present a potential conflict of interest in the Low-Molecular-Weight Heparin (LMWH) Drug Class Review.

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Executive Summary

National and Provincial Trends in Low-Molecular-Weight Heparin (LMWH) Use

Quarterly dispensing of prescriptions for anticoagulant medications in Canada has increased by 42.9% over the past 4 years. A total of \$116.1 million was spent on all anticoagulant medications nationally in the second quarter (Q2) of 2015, an increase of 249% from Q4 2009 (\$33.3 million). This increase was largely driven by the increased use and costs of direct-acting oral anticoagulants (DOACs), which comprised 40% of the total prescription market share (N=2.1 million prescriptions) but accounted for 65% of the total costs (\$74.9 million of \$116.1 million) in Q2 2015. Low-molecular-weight heparin (LMWH) accounted for 4.5% (95,366 prescriptions) of all anticoagulant prescriptions in Canada in Q2 2015 and 26.9% (\$31.2million) of total costs. In the same time period, the number of prescriptions dispensed and costs for LMWH increased by 30.6% and 65.8%, respectively (from 73,020 prescriptions dispensed at a cost of \$18.8 million in Q4 2009 to 95,366 prescriptions dispensed at a cost of \$31.2 million in Q2 2015). Among all LMWH medications dispensed nationally in Q2 2015, over half (53.3%) were for dalteparin, followed by enoxaparin (28.5%). Increased utilization of LMWH may be due to an aging population, expansion of indications, and improved adherence to practice guidelines.

There was a wide variation in the rate of prescriptions dispensed for publicly-funded LMWH medications between provinces in Canada (range in Q2 2015: 0.8 [PEI] to 12.6 (Quebec) prescriptions dispensed per 1,000 eligible population). In Q2 2015, the rate of publicly-funded LMWH medication use in Ontario was similar to the national average (6 prescriptions per 1,000 eligible population compared to the national average of 5 prescriptions per 1,000 eligible population). Ontario exhibited the second lowest rate of non-publicly funded LMWH medication use (0.7 prescriptions per 1,000 eligible population compared to the national average of 1.2 prescriptions per 1,000 eligible population).

In 2014, approximately \$61.2 million was spent on publicly-funded LMWH prescriptions in the studied provinces in Canada, with 63.8% of costs (\$39.1 million) attributed to users aged 65 and older. Ontario had the highest overall costs (\$33.7 million) compared to other studied provinces in Canada in 2014. Dalteparin was the most commonly dispensed publicly-funded LMWH medication in most provinces in 2014, except for New Brunswick and Newfoundland and Labrador where enoxaparin was the most commonly dispensed and Saskatchewan where tinzaparin was the most commonly dispensed. The rate of publicly-funded LMWH medication users and prescriptions dispensed was lowest in Prince Edward Island (0.8 users and 1.1 prescriptions dispensed per 1,000 active drug plan beneficiaries) and highest in Alberta (16.9 users and 31.9 prescriptions dispensed per 1,000 active drug plan beneficiaries) in 2014 among provinces compared. Ontario had the third highest rate of LMWH use (8.4 users and 24.9 prescriptions dispensed per 1,000 active drug beneficiaries) in 2014.

Use of LMWH in Ontario

Similar to national trends, the number of prescriptions dispensed for LMWH has increased 15.2% in Ontario, from 21,480 prescriptions dispensed in Q4 2009 to 24,747 prescriptions dispensed in Q2 2015. Costs have increased by 47.7% over the study period in Ontario, from

\$6.5 million in Q4 2009 to \$9.9 million in Q2 2015. At the beginning of the study period in Q4-2009, dalteparin accounted for over half (58.9%; 12,866 of 21,840 prescriptions) of all LMWH prescriptions dispensed in Ontario. By the end of the study period in Q2-2015, this decreased to 47.8% (11,839 of 24,747 prescriptions).

Characteristics of Publicly-Funded LMWH Users and Patterns of Prescribing in Ontario

Ontario has seen a 142.9% increase in the number of publicly-funded users of LMWH over 10 years, from 10,121 users in 2004 to 24,584 users in 2014. Dalteparin has remained the LMWH with the most users but has seen a decrease in its market share from 62.2% (6,300 users) in 2004 to 43.9% (10,791 users) in 2014.

There were 127,333 new users of LMWHs in Ontario between 2002 and 2012. The majority of users (87.6%; N=111,507) were 65 years of age or older when they received their first prescription. Approximately three-quarters (75.2%; N=95,704) had been hospitalized at least once in the year prior to receiving their first LMWH prescription and 39% of users (N=49,631) had received a warfarin prescription in the 120 days prior to their first LMWH prescription. One-third of new-users (32%; N=40,690) received their initial prescription from a general practitioner.

Use of Limited Use Codes for LMWH Prescription Claims in Ontario

Limited Use (LU) code 186 and 188, indicative of DVT, was used most frequently regardless of the medical indication determined by physician diagnosis codes or hospitalization/emergency department information. The exception was for individuals with an indication for pregnancy or lactation, in which case the appropriate LU code (LU 187) was used most often (52.9%; N=146 of 276 identified as pregnant or lactating). The median time to discontinuation across all indications was 30 days or less. The longest median time to discontinuation was found in users with cancer and DVT (30 days (IQR=7 to 149 days)) and pregnant or lactating users (30 days (IQR=12 to 101 days)). Shorter periods of continuous use were found with other indications and ranged from 8 to 16 days.

Cost of LMWH in Ontario

The overall cost for LMWHs obtained through the OPDP program in 2014 was \$33,660,440. Average costs for dalteparin and enoxaparin were calculated for each LU code. These average costs were used to calculate the total cost if access to only dalteparin or enoxaparin was available, where indicated for use. The total cost savings by using enoxaparin when possible is estimated to be \$10,684,793 per year, a 32% savings (from \$33,660,440 to \$22,975,647). Whereas, switching to dalteparin is estimated to increase costs by \$7,787,299 to \$41,447,740. These results should be interpreted with caution as there may be variation in dosing, duration, and indications of use. Future analysis should control for these factors and include all LMWHs.

Overall Conclusion

Use of LMWH continues to grow both nationally and in Ontario. Over the last 5 years there has been a slight change in the use of LMWH medications. Dalteparin remains the most

utilized LMWH across Ontario but has seen a decrease in market share as use of enoxaparin and tinzaparin has increased. The large majority of provincially funded LMWH prescriptions are reimbursed using LU codes but our evidence suggests that the LU codes do not often align with patient indication. Instead, LU codes for DVT are commonly used for all indications. With a growing elderly population, extended life-expectancy, and the expansion of indications we anticipate continued growth in cost and use of this drug class.

Introduction

In Canada, there are currently five Low-Molecular-Weight heparins (LMWHs) that are used as anticoagulants for a variety of indications (dalteparin, enoxaparin, nadroparin, and tinzaparin). There is also fondaparinux, which is a synthetic heparin-like compound and will be grouped in the LMWH category for this review. LMWHs are available as subcutaneous injections that are used in both the inpatient and outpatient setting. LMWHs were approved by Health Canada in the last 25 years and differ in their public plan listings on provincial formularies across Canada. Detailed information on public plan listings is provided in **Appendix A**.

The objectives of this report are:

1. To present national and provincial utilization trends in use of anticoagulants and LMWHs among adults in Canada, by drug dispensed and by payer.
2. To present cross provincial comparisons of the trends in use of LMWH among adults in public drug programs across Canada using population-adjusted rates of use.
3. To examine trends in use of LMWH funded through the OPDP.
4. To describe characteristics of patients prescribed provincially-funded LMWH in Ontario.
5. To investigate the duration of publicly-funded LMWH use among users in Ontario.
6. To report the number of accepted submissions and explore the accuracy of Limited Use (LU) codes for publicly-funded LMWH in Ontario.
7. To explore the budget impact of varying LMWH utilization.

IMS Geographic Prescription Monitor (GPM¹²)

IMS Geographic Prescription Monitor (GPM¹²) is a premium source of sales intelligence on retail prescription activity in Canada. Data is obtained from a representative sample of 65% of all Canadian pharmacies and is projected monthly by province or customized geography. Projections incorporate the number of pharmacies in a given area, the distance between IMS-captured and uncaptured pharmacies, and the size of the pharmacies. Projections are representative of provincial and national sales volumes. Data available through IMS Geographic Prescription Monitor (GPM¹²) includes prescription volumes dispensed, and are stratified by payer type (e.g. public drug plan, private drug plan, cash, Non-Insured Health Benefits). Data from IMS Geographic Prescription Monitor (GPM¹²) is available from the fourth quarter of 2009 to the second quarter of 2015.

Canadian Institute for Health Information NPDUIS

The National Prescription Drug Utilization Information System (NPDUIS) was developed by the Canadian Institute for Health Information (CIHI) to provide pan-Canadian information on public drug programs. NPDUIS data can be used to obtain estimates of populations eligible for provincial drug coverage in Alberta, British Columbia (BC), Saskatchewan, Manitoba, New

Brunswick, Nova Scotia, Newfoundland and Labrador and Labrador and Prince Edward Island (PEI). Data from NPDUIS is available from calendar year 2000 to 2014. Data is only available as of 2002 for Nova Scotia, 2005 for PEI, 2006 for BC and 2009 for Newfoundland and Labrador and Labrador.

Administrative Databases in Ontario

These datasets were linked using unique, encoded identifiers and analyzed at the Institute for Clinical Evaluative Sciences (ICES).

Ontario Drug Benefit Database

The Ontario Drug Benefit (ODB) database contains individual-level claims data for all prescription drugs dispensed to Ontario residents eligible for public drug funding. Eligibility criteria include unemployment, disability, high prescription drug costs relative to net household income, receipt of home care services, residence in a long-term care facility, or age 65 years or older. This database is of high quality, with an error rate of <1% and can be linked to other health administrative databases to obtain patient demographic information¹. We analyzed data from the ODB between January 2001 and March 2015.

Other Health Administrative Databases

We used data from the Ontario Registered Persons Database (RPDB), Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD) and National Ambulatory Care Reporting System (CIHI-NACRS) database, Ontario Health Insurance Plan (OHIP) database, mother-baby linked database, Ontario Cancer Registry (OCR) database and the ICES Physician Database (IPDB) to obtain patient vital statistics, describe health care use, and other patient comorbidities and characteristics.

Methods

All analyses were approved by the Research Ethics Board of Sunnybrook Health Sciences Centre, Toronto, Ontario.

National and Provincial Trends in LMWH Use

We used data from IMS Geographic Prescription Monitor (GPM¹²) to examine overall trends in the prescribing volumes of LMWH among all individuals, at both national and provincial levels. We examined the number of prescriptions dispensed for anticoagulants between October 1 2009 and June 30 2015. Analyses were stratified by drug, drug class, province and coverage (private, public, cash, Non-Insured Health Benefits) and by LMWH. Publicly funded prescriptions were those paid for through public drug programs or Non-Insured Health Benefits; non-publicly funded prescriptions were those paid for through private insurance plans or cash payments. All cross-provincial analyses compared population-adjusted rates.

Population Adjustment

Provincial population estimates were obtained from Statistics Canada for each quarter from 2009 to 2015 and used to standardize overall utilization rates (per 1,000 population) of LMWH dispensed across the provinces. Because all individuals (both those eligible for public drug

programs and non-beneficiaries) might pay for LMWH out of pocket, measures of non-provincially funded use were adjusted using overall provincial population estimates from Statistics Canada.

Cross-Provincial Comparisons of Publicly-Funded LMWH Use

We used claims data from NPDUIS and ODB to examine trends in the number and rate of provincially funded users of LMWH at the provincial level between January 2004 and December 2014. We examined the number and rate of users in 2014. Analyses were stratified by province, drug, and age (<65 and 65+). Provincially funded prescriptions were those paid for through public drug programs. All cross-provincial analyses compared population-adjusted rates (per 1,000 active beneficiaries), using the number of active drug beneficiaries in each provincial drug program. Data was not available for Quebec or the territories.

Characteristics of Provincially-Funded LMWH Users in Ontario between 2002-2012

We used claims data from ODB to perform additional analyses of use of LMWH among new users in Ontario, stratifying by drug, between January 1st 2002 and December 31st 2012. These analyses examined demographic and clinical characteristics of users who were prescribed a LMWH medication in Ontario.

Patterns of Use and Accuracy of Limited Use Codes among LMWH Users in Ontario

We established a cohort of adults who were new users of LMWH between January 1, 2002 and December 31, 2012 to examine the duration of LMWH therapy in Ontario. A new user was defined as having no prescription for a LMWH in the past year. We followed each individual forward from the time of their first prescription until they discontinued any LMWH, died, had 2 years of follow-up, or reached the end of the study period (December 31, 2014). Accuracy to the LU criteria were explored by comparing the LU code used for the initial prescription claim to the medical indication determined by physician diagnosis codes or hospitalization/emergency department (ED) information. Discontinuation was defined on the basis of no subsequent prescription for a LMWH within 1.5 times the day's supply of the previous prescription (with a minimum 10 day grace period), which is consistent with previously published studies.¹⁻⁴ The length of therapy was compared to the recommended length of therapy based on the LU code associated with the index drug claim.

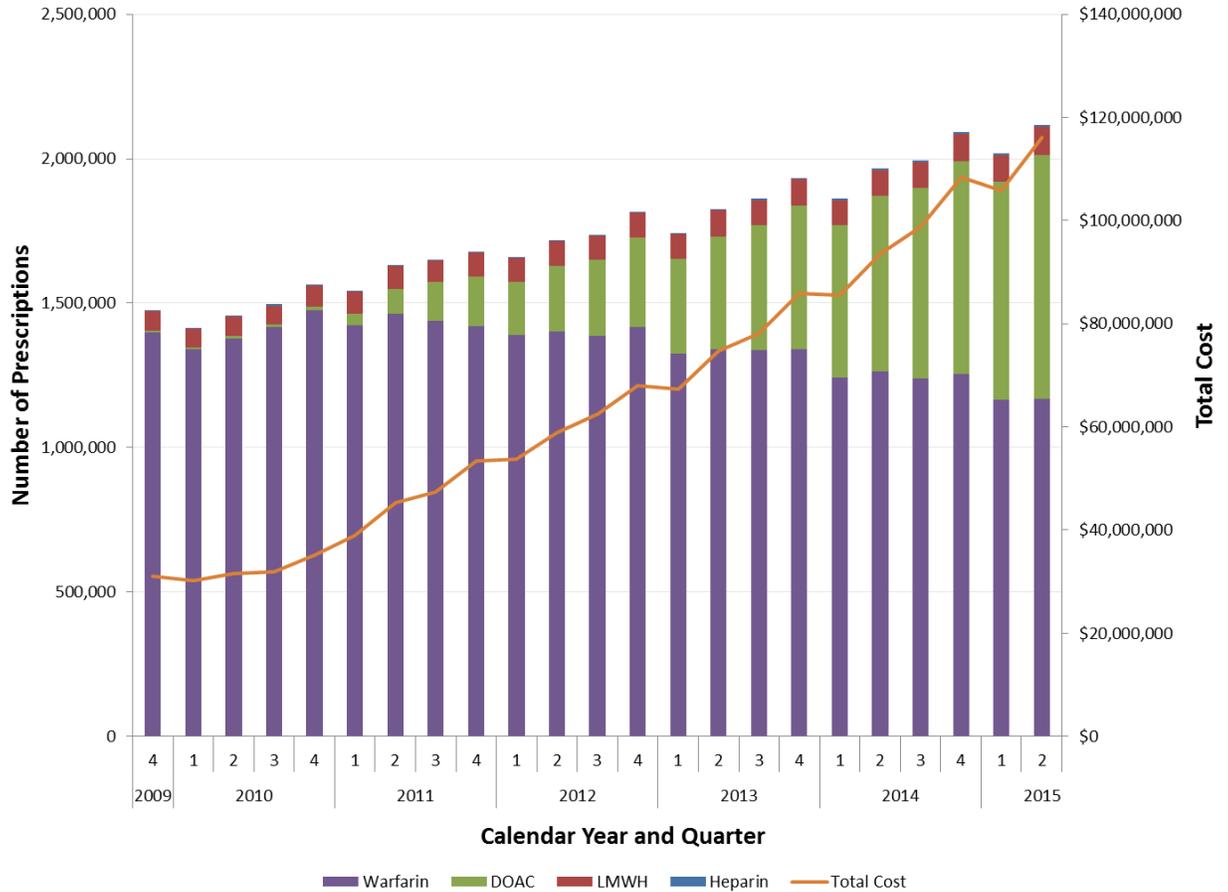
Cost and Budget Impact of LMWH in Ontario

We established a cohort of adults who were users of LMWH between January 1, 2014 and December 31, 2014 to examine the cost of therapy by indication using the LU code on the LMWH prescription. We reported the total spent on publicly funded LMWH in Ontario in 2014. Average cost per user was calculated for dalteparin and enoxaparin for each LU code and was used to calculate the total cost if access to only dalteparin or enoxaparin was available. Note for indications where dalteparin or enoxaparin are not indicated for use these averages remained the same.

Exhibits and Findings

National Trends in Use of LMWH

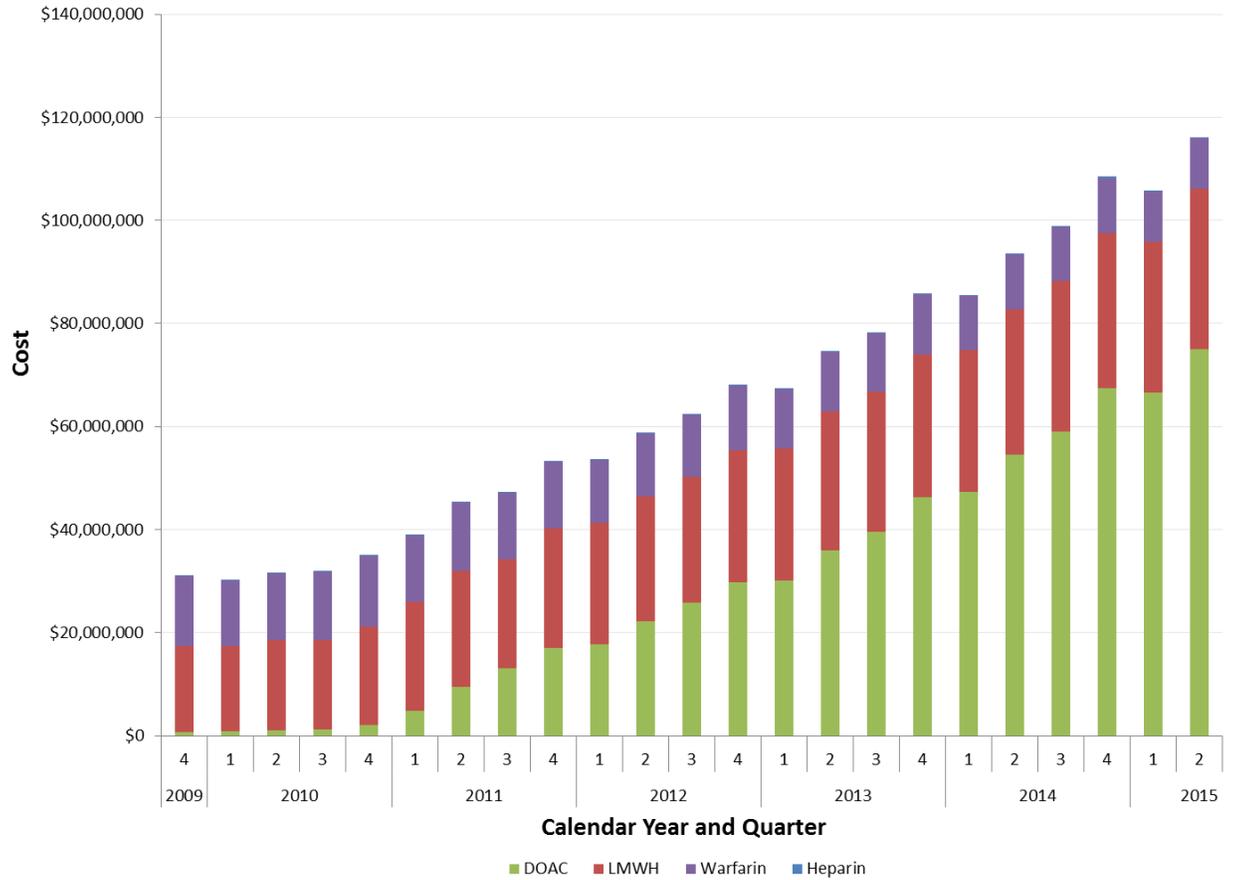
Exhibit 1: Total number of prescriptions and total cost of anticoagulants dispensed to all individuals in Canada, by drug class and quarter



Data Source: IMS GPM¹²

The number of anticoagulant prescriptions dispensed has increased by 43% across Canada and costs have increased 249% in the same time period. LMWH accounted for only 4.5% of all anticoagulant prescriptions in Canada.

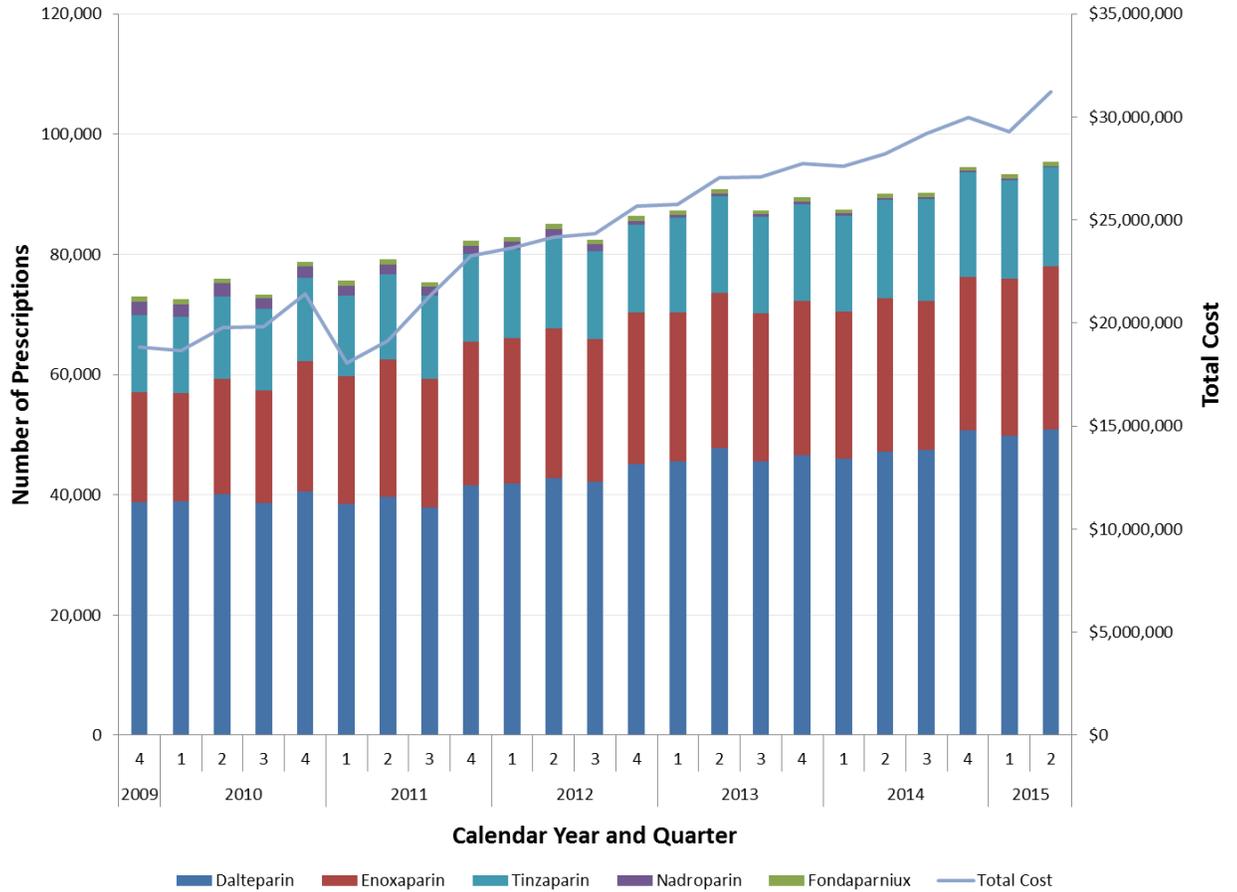
Exhibit 2: Total cost of anticoagulants dispensed to all individuals in Canada, by drug class and quarter



Data Source: IMS GPM¹²

Increases in quarterly anticoagulant prescription costs were largely driven by the introduction of direct-acting oral anticoagulants (DOAC) onto the Canadian market. LMWH costs have increased but at a lower rate.

Exhibit 3: Total number of prescriptions and total cost of LMWH dispensed to all individuals in Canada, by drug and quarter



Data Source: IMS GPM¹²

Over half (53.3%) of all LMWH prescriptions dispensed in Canada were for dalteparin. Enoxaparin (28.5%) and tinzaparin (17.2%) accounted for the majority of the other LMWH prescriptions across Canada.

Summary of Findings for Exhibit 1, Exhibit 2 and Exhibit 3

- The number of prescriptions dispensed for anticoagulant medications in Canada increased by 42.9% over the past 6 years, from 1.5 million prescriptions (Q4-2009) to 2.1 million prescriptions (Q2-2015).
- Among all anticoagulant prescriptions dispensed (2.1 million prescriptions) in Q2-2015 over half (55.3%, 1.2 million prescriptions) were for warfarin, followed by DOACs (39.9%; 844,330 prescriptions), LMWH (4.5%, 95,366 prescriptions) and heparin (0.3%, 6,079 prescriptions).
- A total of \$116.1 million was spent on all anticoagulant medications nationally in Q2-2015, an increase of 249% from Q4-2009 (\$33.3 million). This increase was largely driven by the costs of DOACs, which comprised 40% (844,430 prescriptions) of the total prescription market share (n=2.1 million prescriptions) but accounted for 65% (\$74.9 million) of the total costs (\$116.1 million).
- Between Q4-2009 and Q2-2015, the number of prescriptions dispensed and costs for LMWH have also increased by 30.6% and 65.8%, respectively (from 73,020 prescriptions dispensed at a cost of \$18.8 million to 95,366 prescriptions dispensed at a cost of \$31.2 million).
- Increased utilization of LMWH may be due to an aging population, expansion of indications, and improved adherence to practice guidelines.
- Among all LMWH medications dispensed in Q2-2015, over half (53.3%, 50,855 prescriptions) were for dalteparin, followed by enoxaparin (28.5%; 27,202 prescriptions), tinzaparin (17.2%, 16,403 prescriptions), fondaparinux (0.7%; 667 prescriptions), and nadroparin (0.3%, 239 prescriptions).
- In Q2-2015, dalteparin accounted for over half (56.3%; \$17.6 million) of all LMWH medication costs, followed by enoxaparin (28.9%; 7.4 million), tinzaparin (19.1%; \$6.0 million), fondaparinux (0.6%; \$185,047) and nadroparin (0.2%; \$51,667).
- There was a 16% decrease in overall costs during Q1-2011 which may be due to

Cross Provincial Trends in Use of LMWH

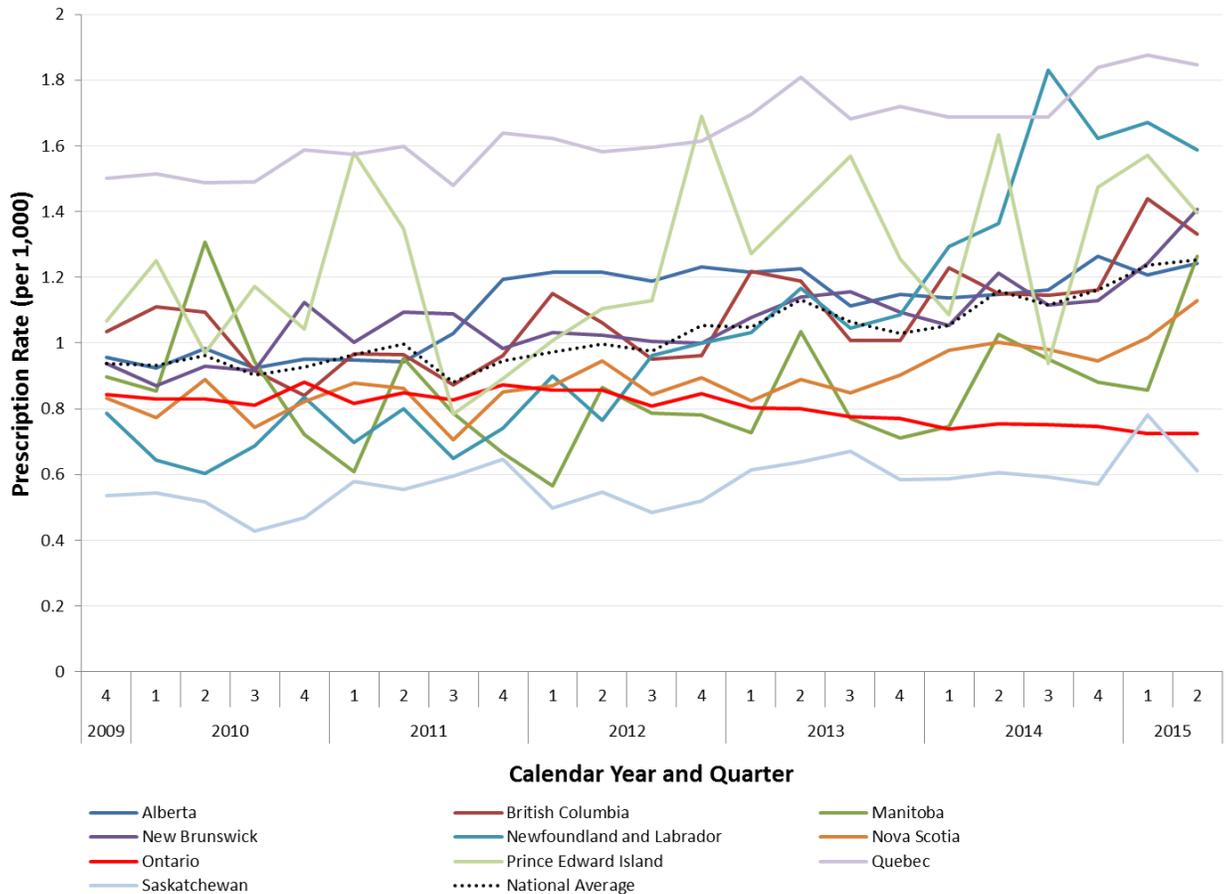
Methodological Note:

Non-publicly funded use represents use outside of provincial drug plans. This includes prescriptions paid by:

- Private drug insurance
- Cash
- Non-Insured Health Benefits

Provincial plan listings for LMWH vary across provinces by drug. More detailed information on provincial plan listings is provided in Appendix A.

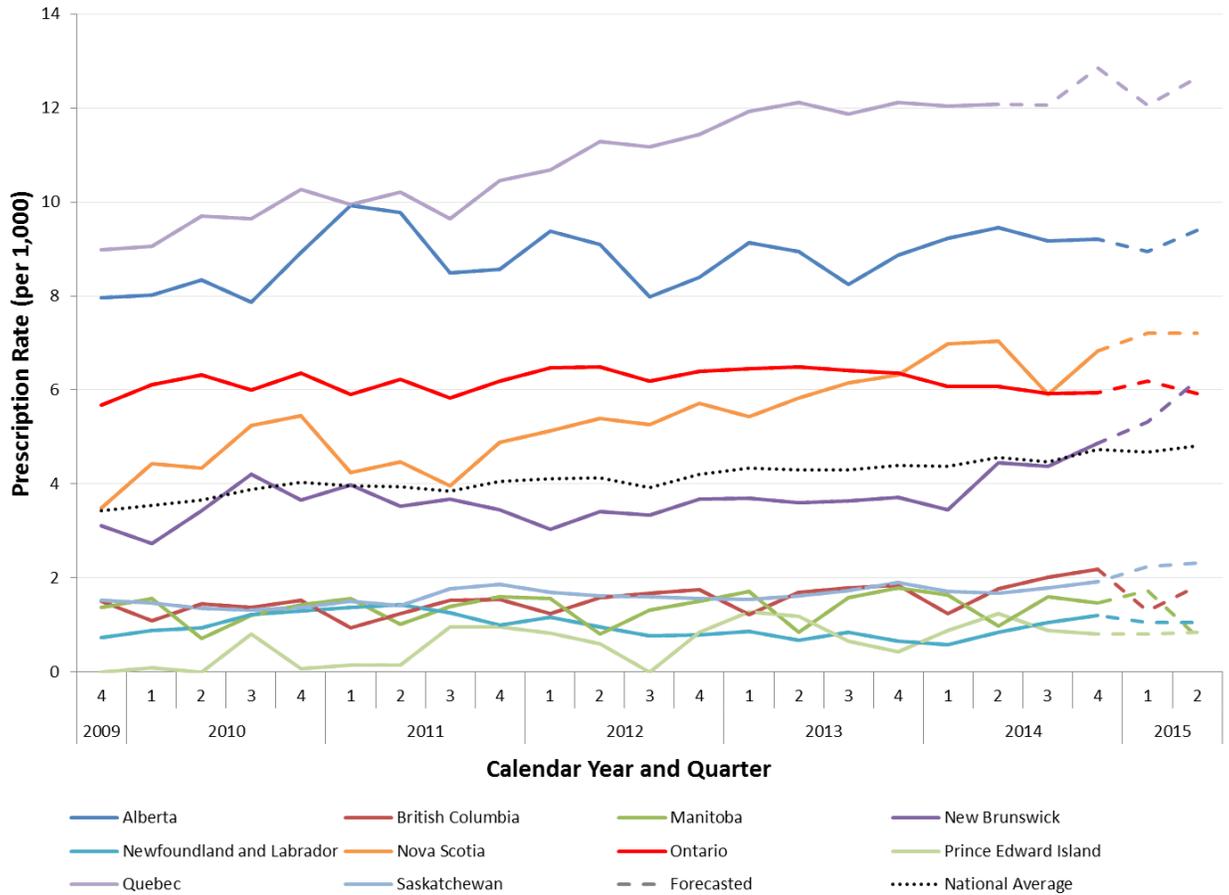
Exhibit 4: Population-adjusted rate of non-publicly-funded prescriptions for LMWH dispensed in Canada, by province and quarter



Data Source: IMS GPM¹²

Ontario exhibited the second lowest rate of non-publicly funded LMWH drug prescribing in Canada (0.7 per 1,000 eligible population in Q2-2015).

Exhibit 5: Population-adjusted rate of publicly-funded prescriptions for LMWH dispensed in Canada, by province and quarter



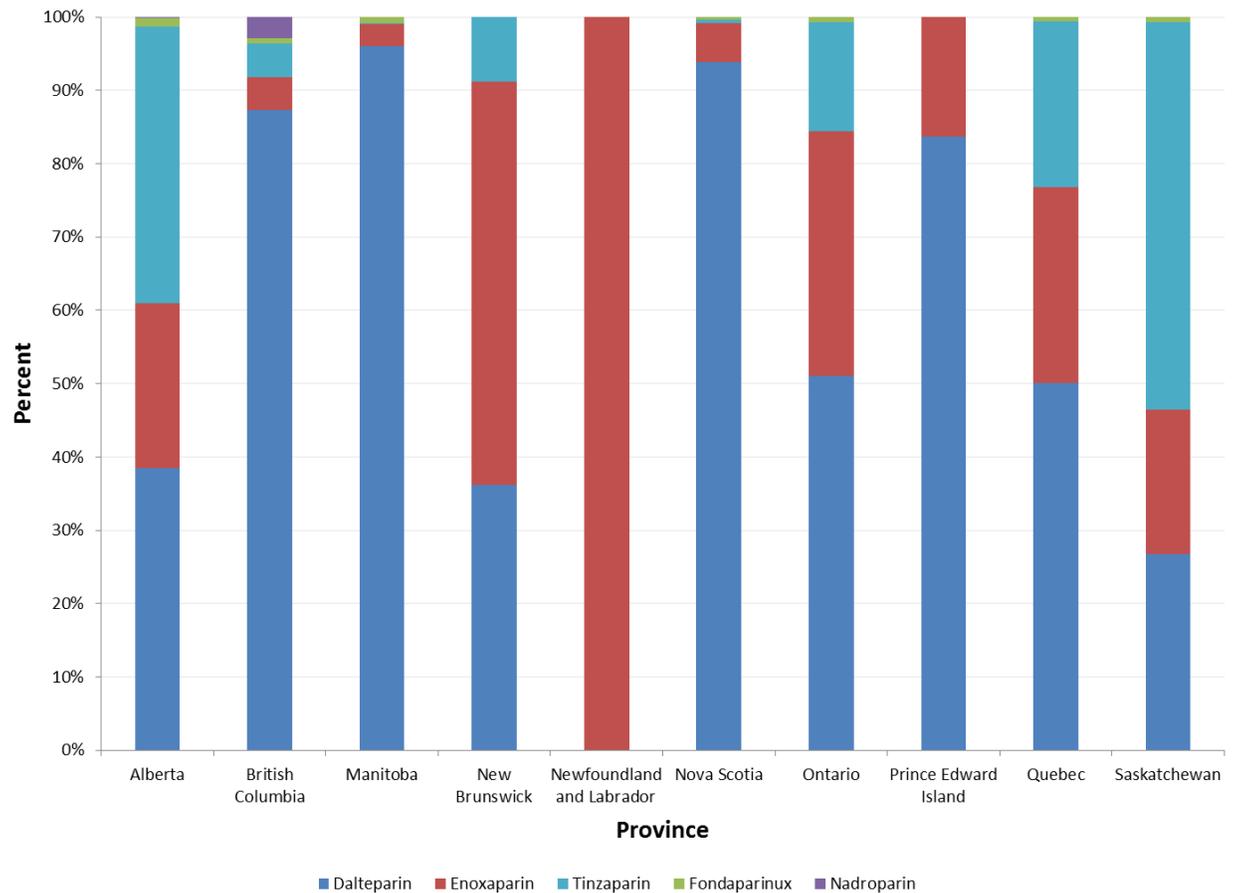
Data Source: IMS GPM¹²

The rate of publicly-funded LMWH use varied widely across Canada, and ranged from 0.8 per 1,000 in PEI to 12.6 per 1000 in Quebec in Q2 2015. The rate of publicly-funded LMWH use in Ontario (6 per 1,000 eligible population) was comparable to the national average (5 per 1,000 eligible population).

Summary of Findings for Exhibit 4 and Exhibit 5

- There was a wide variation in the rate of publicly funded LMWH prescriptions dispensed across provinces in Canada (range in Q2-2015: 0.8 [PEI] to 12.6 [Quebec] prescriptions dispensed per 1,000 eligible population).
- In Q2-2015, the rate of publicly-funded LMWH prescriptions dispensed in Ontario was similar to the national average (6 prescriptions per 1,000 eligible population compared to the national average of 5 prescriptions per 1,000 eligible population).
- A higher number of prescriptions for publicly-funded LMWH products were noted in Quebec, Alberta, Nova Scotia, New Brunswick, and Ontario (Q2-2015: 13, 9, 7, 6, 6 prescriptions per 1,000 eligible population, respectively) which is likely due to the unrestricted access to these products.
- Overall, less cross-provincial variations were noted among non-publicly funded LMWH prescriptions dispensed (range in Q2-2015: 0.6 [Saskatchewan] to 1.8 [Quebec] prescriptions dispensed per 1,000 eligible population).
- Ontario had the second lowest rate of non-publicly funded LMWH prescriptions dispensed (0.7 prescriptions per 1,000 eligible population compared to the national average of 1.2 prescriptions per 1,000 eligible population).

Exhibit 6: Market share of publicly-funded LMWH by province and medication in Canada, in 2014



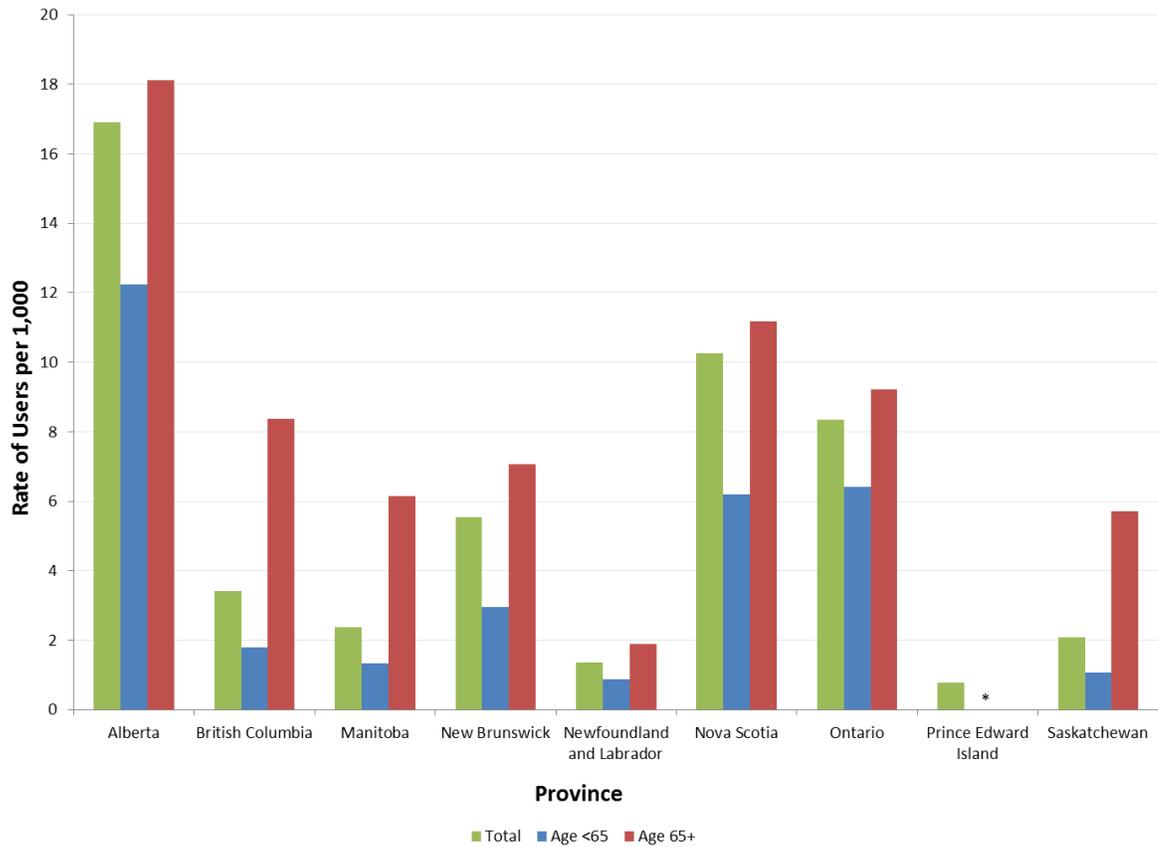
Data Source: IMS GPM¹²

Dalteparin was the most commonly prescribed publicly-funded LMWH in 2014 in all provinces, except in New Brunswick and Newfoundland and Labrador (where enoxaparin is most common) and Saskatchewan (where tinzaparin is most common)

Summary of Findings for Exhibit 6

- Dalteparin was the most commonly dispensed publicly-funded LMWH medication in Alberta (38.2%, n=6,511), British Columbia (87.3%; n=11,593), Manitoba (96.0%, n=3,043), Nova Scotia (93.8%; n=3,113), Ontario (51.1%; n=29,691), PEI (83.6%; n=92) and Quebec (50.1%; n=52,698) in 2014.
- Enoxaparin was the most commonly dispensed publicly-funded LMWH medication in New Brunswick (55.1%; n=938) and the only medication dispensed in Newfoundland and Labrador (100%; n=316). This is despite all drugs being listed as general benefit in New Brunswick and as a restricted benefit in Newfoundland and Labrador (excluding fondaparinux, which is not listed).

Exhibit 7: Rate of publicly-funded LMWH medication users by province and age in Canada, in 2014



In accordance with the CIHI privacy policy, in cases where the number of beneficiaries () is less than 5 (but greater than 0), this number, along with other associated data element, have been suppressed to ensure confidentiality. Data Source: CIHI NPDUIS and ICES.

The rate of publicly-funded LMWH medication users is higher among those aged 65 and older across all studied provinces in Canada in 2014. Higher rates of LMWH use are observed among those aged less than 65 in Alberta, Ontario, and Nova Scotia compared to other provinces.

Exhibit 8: Number and rate of publicly-funded LMWH medication users by province, age and LMWH medication, in Canada, in 2014

Province	Total Rate of Users per 1,000	Total Number of Prescriptions	Total Cost of LMWH		Drug				
			Total Cost for <65	Total Cost for 65+	Enoxaparin	Tinzaparin	Nadroparin	Fondaparinux	Dalteparin
					Rate of Users per 1,000				
Alberta	16.9	17,285	\$2,153,389	\$7,442,679	4.2	4.5	*	0.2	8.4
British Columbia	3.4	24,401	\$4,524,199	\$5,033,235	0.2	0.2	0.1	0.0	2.9
Manitoba	2.4	6,610	\$1,798,128	\$1,386,709	0.1	0.0	0.0	0.0	2.3
New Brunswick	5.5	1,632	\$214,405	\$557,908	3.2	0.3	0.0	0.0	2.1
Newfoundland and Labrador	1.4	356	\$80,713	\$70,768	1.3	*	0.0	0.0	*
Nova Scotia	10.3	3,261	\$310,497	\$1,093,539	0.5	*	0.0	*	9.8
Ontario	8.4	72,240	\$11,705,219	\$21,955,222	3.5	1.1	0.0	0.3	3.8
Prince Edward Island	0.8	36	\$648	\$8,928	0.4	0.0	0.0	0.0	0.4
Saskatchewan	2.1	4,377	\$1,378,740	\$1,515,665	0.5	1.0	0.0	0.0	0.6

In accordance with the CIHI privacy policy, in cases where the number of beneficiaries() is less than 5 (but greater than 0), this number, along with other associated data element, have been suppressed to ensure confidentiality. Data Source: CIHI NPDUIS and ICES

Alberta had the highest rate of publicly-funded LMWH medication users in Canada in 2014. Dalteparin had the highest rate of users in all provinces except New Brunswick and Newfoundland.

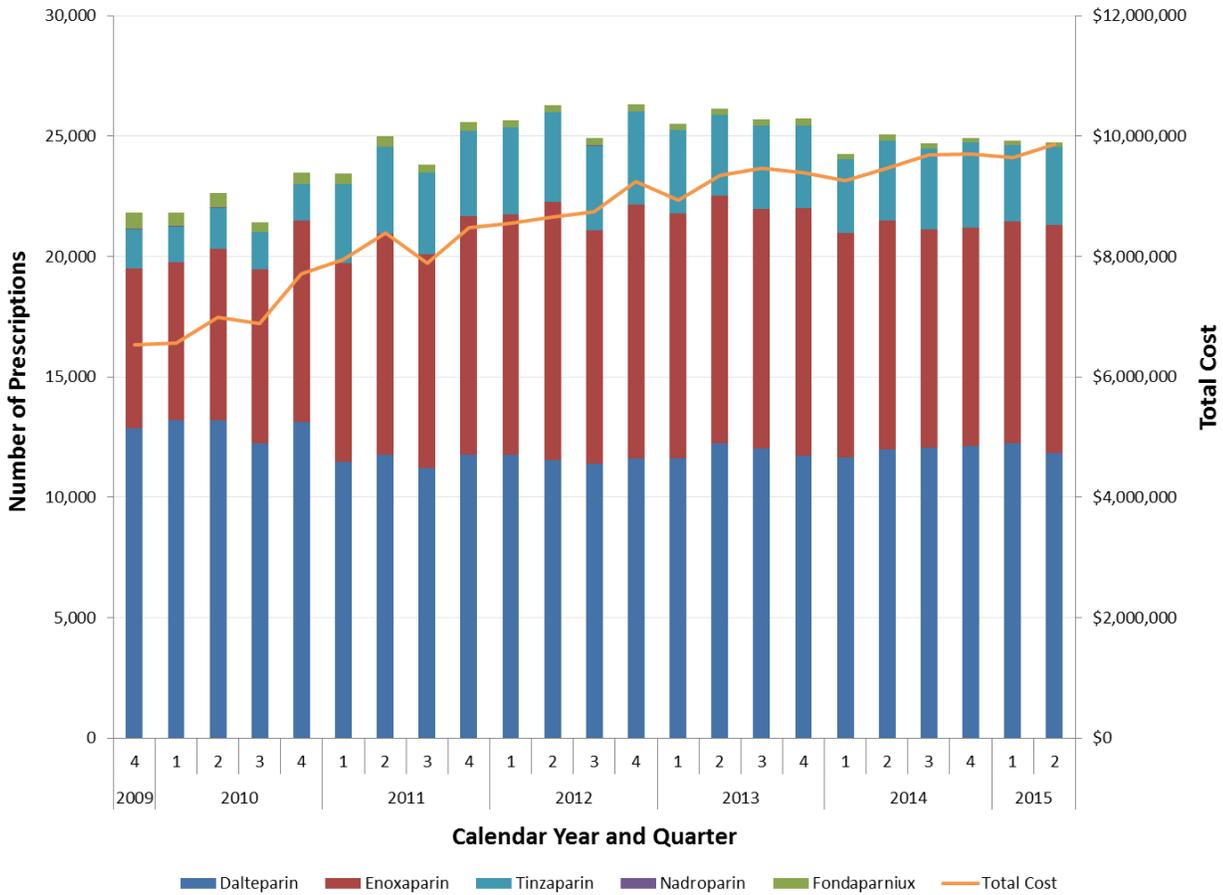
Summary of Findings for Exhibit 7 and Exhibit 8

- In 2014, approximately \$61.2 million was spent on publicly-funded LMWH prescriptions dispensed in the studied provinces in Canada, with 63.8% of costs (\$39.1 million) attributed to users aged 65 and older.
- Nova Scotia and Alberta had the highest rate of publicly-funded dalteparin users (9.8 users and 8.4 users per 1,000 active drug plan beneficiaries, respectively), which was more than double the rate of dalteparin users found in other provinces across Canada (2.9 users per 1,000 active drug plan beneficiaries).
- Alberta, Ontario and New Brunswick had the highest rate of publicly-funded enoxaparin users (4.2, 3.5 and 3.2 users per 1,000 active drug beneficiaries, respectively) which was largely greater than the rate of enoxaparin users found in other provinces across Canada (0.3 users per 1,000 active drug plan beneficiaries).
- Alberta has the highest rate of publicly-funded tinzaparin users (4.5 users per 1,000 active drug beneficiaries) compared to minimal use in other provinces.
- Along with Alberta, Nova Scotia and Ontario having the highest rate of LMWH users (16.9, 10.3, 8.4 users per 1,000 active drug plan beneficiaries, respectively), these provinces also had higher rates of use among individuals aged less than 65 (12.2, 6.2 6.4 users per 1,000 active drug plan beneficiaries, respectively) compared to other studied provinces.

Note: No data available for Quebec.

Trends in Use of LMWH in Ontario

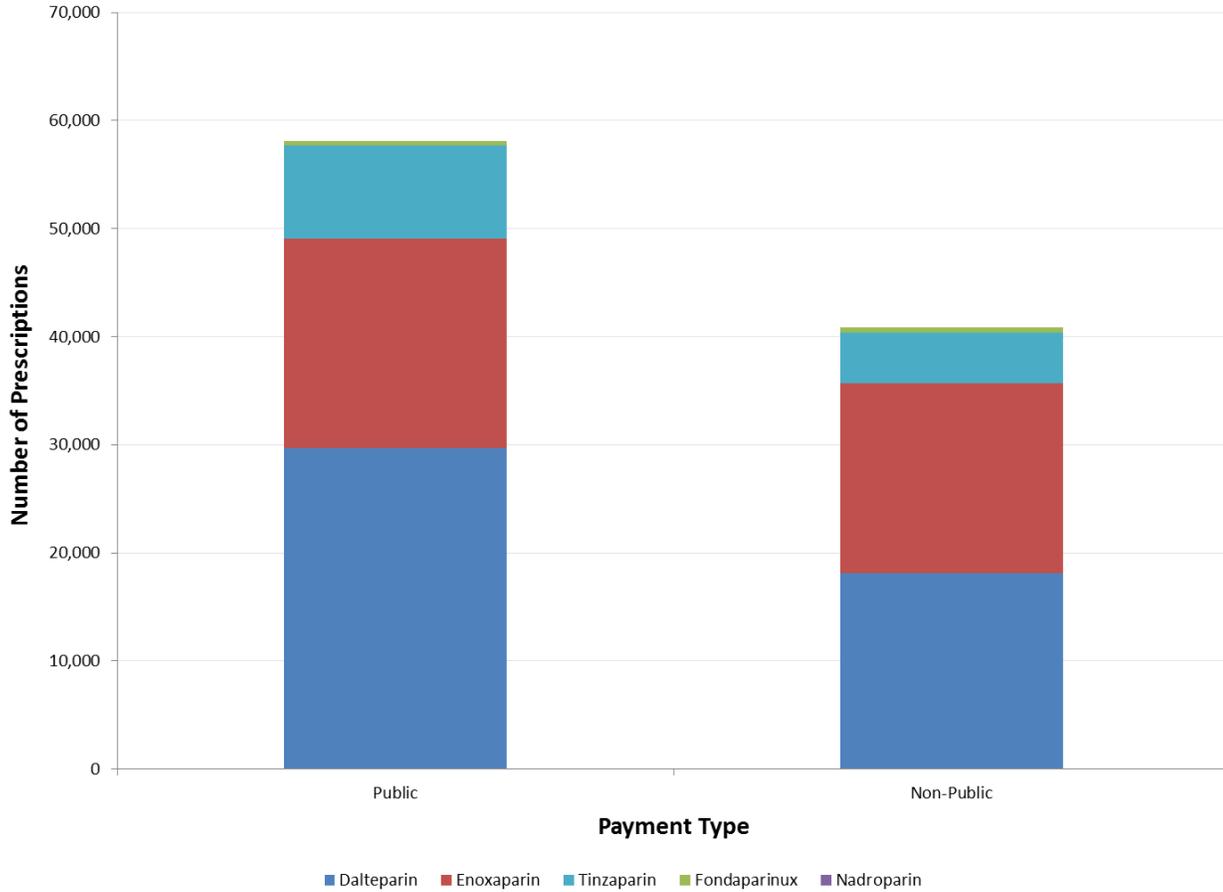
Exhibit 9: Total number of prescriptions and cost of LMWH dispensed in Ontario, by drug and quarter



Data Source: IMS GPM¹²

Utilization and costs of LMWH medications in Ontario have increased by 15% and 48% over the study period, respectively.

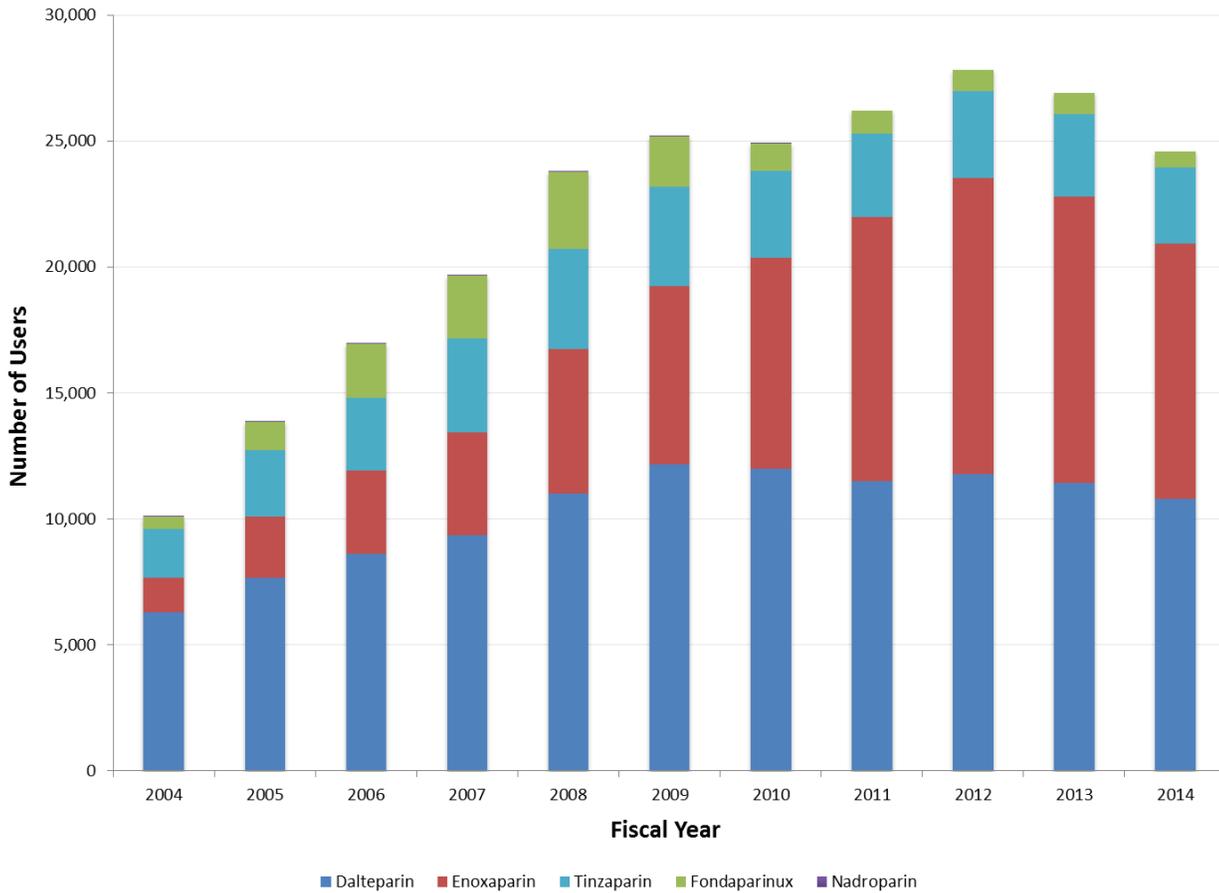
Exhibit 10: Total number of LMWH prescriptions dispensed in Ontario, by drug and payer in 2014



Data Source: IMS GPM¹²

Approximately 60% of LMWH prescriptions dispensed in Ontario were paid for by public payers in 2014. Dalteparin was the most commonly dispensed LMWH medication for both public and private payers.

Exhibit 11: Number of publicly-funded LMWH medication users in Ontario by drug, 2004 to 2014



Data Source: IMS GPM¹²

The number of publicly-funded LMWH users in Ontario has sharply increased over the study period. The market share of dalteparin has dropped from 62.2% of all publicly-funded LMWH users in 2004 to 43.9% in 2014.

Summary of Findings for Exhibit 9, Exhibit 10, and Exhibit 11

- Similar to national trends, the number of prescriptions dispensed for LMWH has increased 15.2% in Ontario, from 21,480 prescriptions dispensed in Q4-2009 to 24,747 prescriptions dispensed in Q2-2015. Costs have increased by 47.7% over the study period in Ontario, from \$6.5 million in Q4-2009 to \$9.9 million in Q2-2015.
- Dalteparin was the most commonly dispensed LMWH in Ontario but the overall market share has decreased over time. At the beginning of the study period in Q4-2009, dalteparin accounted for over half (58.9%; 12,866 of 21,840 prescriptions) of all LMWH prescriptions dispensed in Ontario. By the end of the study period in Q2-2015, this decreased to 47.8% (11,839 of 24,747 prescriptions).
- Over a 10-year study period, Ontario has seen a 142.9% increase in the number of publicly-funded users of LMWH in Ontario from 10,121 users in 2004 to 24,584 users in 2014.
- Beginning in 2004, dalteparin's market share in the public drug program has reduced from 62.2% (6,300 users) to 43.9% (10,791 users) in 2014. In the same time period the proportion of users of Enoxaparin has increased from 13.3% (1,354 users) to 41.2% (10,140 users).
- The decrease in dalteparin use is likely due to the increased use of enoxaparin (38.3%; 9,471 prescriptions) and tinzaparin (13.1%; 3,241 prescriptions).
- In 2015, almost 60% (58.7%; 58,099 prescriptions) of LMWH prescriptions dispensed in Ontario were paid for by public payers.
- Private and public payers had similar distributions of LMWH use. Dalteparin was the most commonly dispensed LMWH in 2014 for both public (51.1%; 29,691 prescriptions) and private (44.5%; 18,149 prescriptions) payers. Enoxaparin was the second most dispensed LMWH (public: 33.3%; 19,360 prescriptions, private: 43.1%; 17,578 prescriptions). There was little use of fondaparinux (<1%) and no use of nadroparin in 2014.

Characteristics of Provincially-Funded New LMWH Users in Ontario Between 2002-2012

Exhibit 12: Characteristics of provincially-funded LMWH Users in Ontario between 2002-2012

Characteristics of new provincially-funded users of LMWH medications in Ontario	
	Overall
Number of new users	N=127,333
Age category	
<65	15,826 (12.4%)
65+	111,507 (87.6%)
Sex - Male	54,483 (42.8%)
Residence in LTC	21,416 (16.8%)
Location of residence	
Rural	20,151 (15.8%)
Urban	107,092 (84.1%)
Income quintile	
1	26,922 (21.1%)
2	26,284 (20.6%)
3	24,725 (19.4%)
4	24,602 (19.3%)
5	24,308 (19.1%)
Prescriber of initial prescriptions	
Hematology	11,946 (9.4%)
Oncology	3,661 (2.9%)
Internal medicine	7,947 (6.2%)
Cardiology	4,315 (3.4%)
Orthopedic surgery	18,789 (14.8%)
General practitioner	40,690 (32.0%)
Missing	26,416 (20.7%)
Other	13,569 (10.7%)
Index LMWH drug prescribed	
Dalteparin	62,133 (48.8%)
Enoxaparin	35,952 (28.2%)
Fondaparinux	10,634 (8.4%)
Nadroparin	264 (0.2%)
Tinzaparin	18,350 (14.4%)
Comorbidities	
Charlson comorbidity index	
No hospitalization	21,791 (17.1%)

Characteristics of new provincially-funded users of LMWH medications in Ontario	
0	43,089 (33.8%)
1	20,253 (15.9%)
2+	42,200 (33.1%)
Number of unique medications in last year	
Median (IQR)	10 (6-15)
Past medication use (past 120 days)	
Warfarin	49,631 (39.0%)
DOACs (rivaroxaban, dabigatran, apixaban)	464 (0.4%)
Aspirin	5,775 (4.5%)
Clopidogrel	5,761 (4.5%)
Other antiplatelets	1,336 (1.0%)
Physician office visits within the last year	
Median (IQR)	13 (8-20)
Hospitalizations within the last year	
Number with 1 or more hospitalizations	95,704 (75.2%)
Emergency visits within the last year	
Median (IQR)	1 (0-3)
0	38,313 (30.1%)
1	35,558 (27.9%)
2-4	40,980 (32.2%)
5+	12,482 (9.8%)

Data Source: ICES

Summary of Findings for Exhibit 12

- There were 127,333 new users of provincially-funded LMWH medications in Ontario between calendar years 2002 to 2012.
- The majority of new users (87.6%; n=111,507) were 65 years of age or older when they received their first prescription.
- About half (47.3%; n=60,227) of new users received their initial prescription from a specialist.
- Approximately three-quarters (75.2%; n=95,704) of new users had been hospitalized at least once in the year prior to receiving their first LMWH prescription and approximately one-third of users (33.1%; n=42,200) had a Charlson comorbidity score of 2 or higher.
- Thirty nine percent of users (n=49,631) had received a warfarin prescription in the 120 days prior to their first LMWH prescription.

Use of Limited Use Codes and the Exceptional Access Program for LMWH Prescription Claims in Ontario

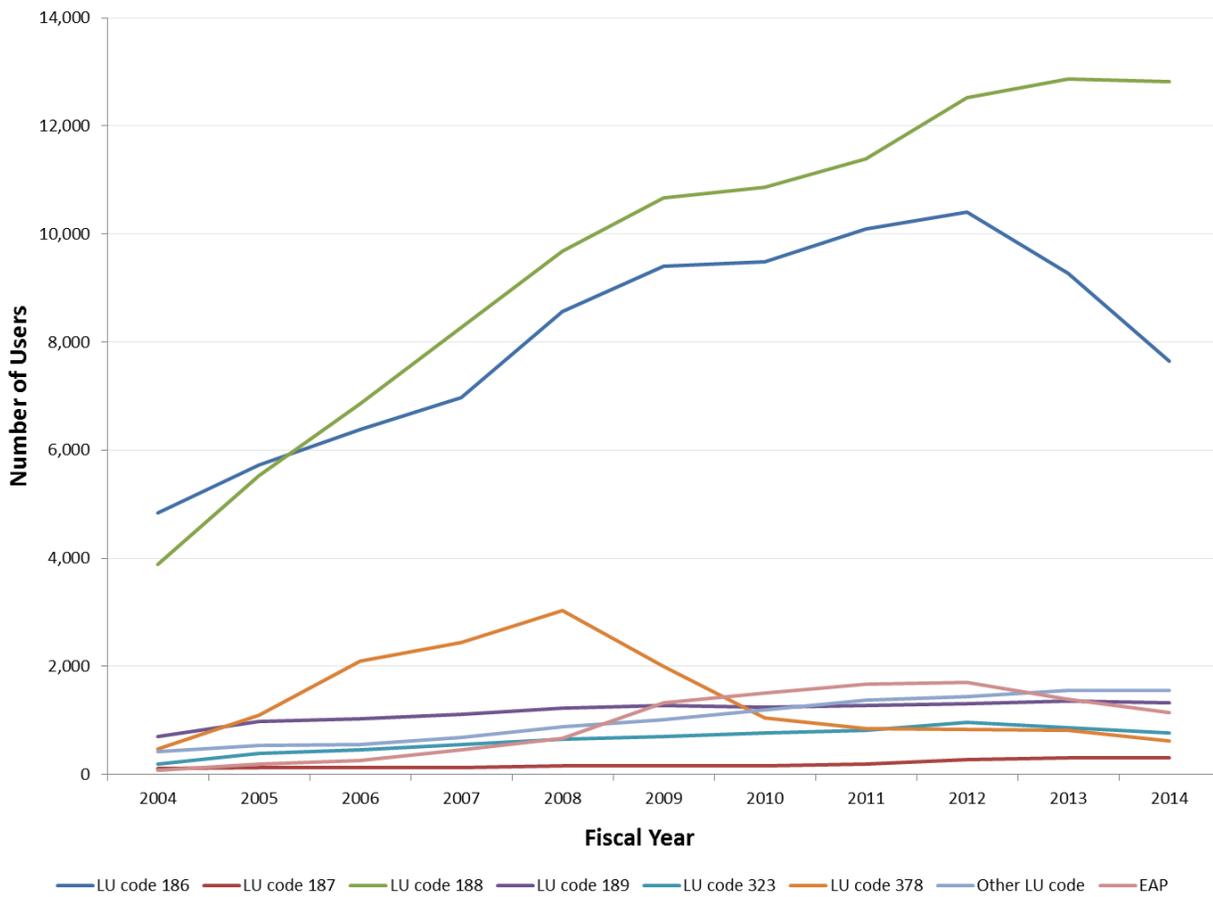
Methodological Note:

LMWH medications are reimbursed through the Ontario Public Drug Program as Limited Use (LU) and through the Exceptional Access Program (EAP) based on the indication for use. The limited use indications are given unique LU codes that include:

- 186 – Deep venous thrombosis (DVT)
- 187 – Pregnant or lactating females
- 188 – DVT in patients whom treatment with warfarin is not well tolerated
- 189 – DVT in patients who have failed treatment with warfarin
- 323 – Pulmonary embolism (PE)
- 378 – Post-operative prophylaxis of venous thromboembolic events in patients undergoing orthopedic surgery of the lower limbs
- 901 and 979 – Other codes not specific to LMWH

Note: Prescription claims through EAP will have no LU code. Details of the various EAP reimbursed indications can be found in the Environmental Scan report.

Exhibit 13: Number of publicly-funded LMWH users by limited use code on prescription in Ontario, between fiscal year 2004 and 2014

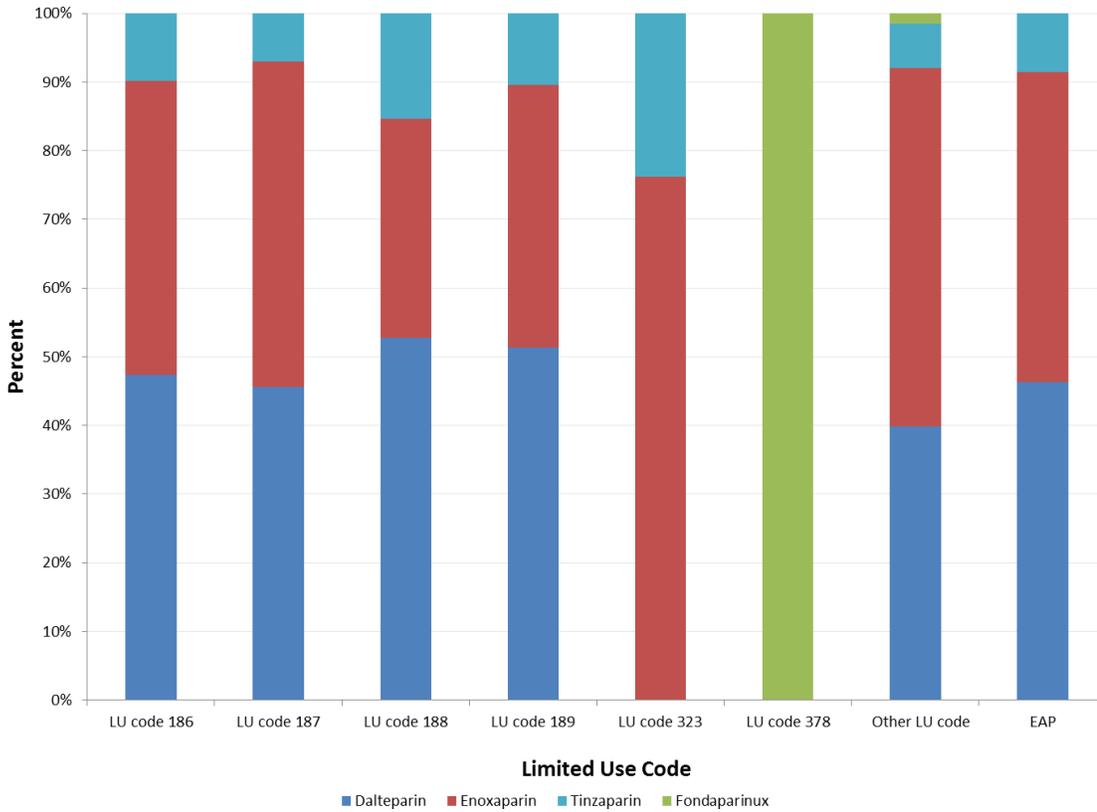


Data Source: ICES

** Note: Claims with no LU code were assumed to be EAP

Limited Use (LU) code 188 and code 186 accounted for the majority of codes used for publicly-funded LMWH users in Ontario from 2004 to 2014. Both codes are indicative of DVT.

Exhibit 14: Market share of publicly-funded LMWH medications by Limited Use code in the ODB Formulary in fiscal year 2014



Data Source: ICES

** Note: Claims with no LU code were assumed to be EAP.

Dalteparin, enoxaparin and tinzaparin are prescribed similarly for most approved limited use (LU) indications. The exception is pulmonary embolism (LU 323) where enoxaparin is prescribed most frequently and post-operative prophylaxis (LU 378) where fondaparinux is the only reimbursed drug.

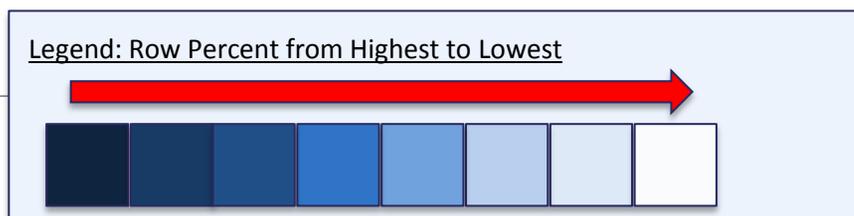
Exhibit 15: Medical Indications for LMWH use among new-users in Ontario, overall and by Limited Use (LU) code on prescription, 2002-2012

	Limited Use code on prescription								
	Overall (N)	LU code 186	LU code 187	LU code 188	LU code 189	LU code 323	LU code 378	Other	EAP**
Total Number of New Users	127,333	51,736 (40.6%)	405 (0.3%)	44,465 (34.9%)	5,049 (4.0%)	3,300 (2.6%)	10,441 (8.2%)	6,622 (5.2%)	5,315 (4.2%)
Medical Indication									
Surgery without DVT	24,929	8,085 (32.4%)	31 (0.1%)	6,591 (26.4%)	773 (3.1%)	189 (0.8%)	6,371 (25.6%)	301 (1.2%)	2,588 (10.4%)
Surgery with DVT	3,423	634 (18.5%)	≤5*	2,572 (75.1%)	48 (1.4%)	16-20*	83 (2.4%)	42 (1.2%)	22 (0.6%)
DVT with no past warfarin use	6,430	3,804 (59.2%)	10 (0.2%)	1,982 (30.8%)	206 (3.2%)	28 (0.4%)	95 (1.5%)	287 (4.5%)	18 (0.3%)
DVT with past warfarin use	12,397	9,719 (78.4%)	23 (0.2%)	1,635 (13.2%)	405 (3.3%)	106 (0.9%)	36 (0.3%)	231 (1.9%)	242 (2.0%)
PE	3,646	1,749 (48.0%)	16 (0.4%)	578 (15.9%)	108 (3.0%)	1,109 (30.4%)	18 (0.5%)	58 (1.6%)	10-15*
Suspected DVT	737	479 (65.0%)	≤5*	103 (14.0%)	45-50*	16 (2.2%)	20-25*	65 (8.8%)	6-10*
Cancer without DVT	25,410	7,759 (30.5%)	39 (0.2%)	11,907 (46.9%)	1,120 (4.4%)	895 (3.5%)	1,624 (6.4%)	1,198 (4.7%)	868 (3.4%)
Cancer with DVT	13,712	5,951 (43.4%)	24 (0.2%)	6,584 (48.0%)	568 (4.1%)	250 (1.8%)	49 (0.4%)	215 (1.6%)	71 (0.5%)
Pregnant or lactating females	276	74 (26.8%)	146 (52.9%)	35 (12.7%)	≤5*	14 (5.1%)	≤5*	0	≤5*
No indication	36,291	13,482 (37.1%)	101 (0.3%)	12,478 (34.4%)	1,774 (4.9%)	675 (1.9%)	2,136 (5.9%)	4,164 (11.5%)	1,481 (4.1%)

Data source: ICES

Note: %s are row percent. Column totals do not add up to 100% due to exclusion of those with a DVT/PE with no DVT/PE LU code.

*Note: In accordance with the ICES privacy policy, in cases where the number of total users is less than 6, this number has been suppressed to ensure confidentiality. In cases where there is only one record being suppressed, another record has been suppressed (by providing ranges) as well in order to avoid residual disclosure issues. Data Source: ICES ** Note: Claims with no LU code were assumed to be EAP.



Summary of Findings for Exhibit 13, Exhibit 14 and Exhibit 15

- The LU codes 188 and 186 (both indicative of DVT) accounted for the majority of LU codes used for publicly funded LMWH new users in Ontario from FY 2004 to 2014 (48.9% and 29.2% of people treated with LMWH in FY 2014).
- For most LU codes, the relative market share of LMWH medications is similar, with approximately 50% of prescribing for dalteparin, 30-40% for enoxaparin and 10-20% for tinzaparin.
- Exceptions to this include:
 - Pulmonary embolism (LU Code 323): approximately three-quarters (76.2%, N=1,233) of LMWH prescriptions with this LU code were for enoxaparin. The remaining 24.8% (n=386) of prescriptions were for tinzaparin.
 - Post-operative prophylaxis of VTE events in patients undergoing orthopedic surgery of the lower limbs (LU Code 378): The only medication approved for this indication is fondaparinux, and therefore all dispensed LMWH medications (N=1,129 prescriptions) were for this drug.
- LU code 186 or 188 was recorded most frequently on LMWH prescriptions regardless of the actual indication. The exception was for individuals who were pregnant or lactating, in which case LU code 187, the correct LU code, was used most often (52.9%; n=146 of 276 identified as pregnant or lactating).
- In patients with surgery and no concurrent diagnosis for DVT, only 25.6% (n=6,371) were identified under the correct LU code 378. Higher proportions were identified under LU code 186 (32.4%; n=8,085) and LU code 188 (26.4%; n=6,591). In contrast, among patients undergoing surgery with a concurrent diagnosis of DVT, the majority were identified under LU 188 (75.1%; n=2,572).
- In patients with cancer (which does not have an associated LU code), LU code 188 (47.3%) and 186 (37.0%) were used most frequently.

Exhibit 16: Duration of LMWH therapy and number of individuals exceeding the LU authorization criteria duration limit, by medical indication, 2002-2012

Medical indication	Number of new users	Median time to discontinuation (days (IQR))	N(%) duration exceeding 3 weeks	N(%) duration exceeding 1 year
Surgery without DVT	N=24,929	10 (9-20)	2,678 (10.7%)	0 (0.0%)
Surgery with DVT	N=3,423	10 (10-14)	563 (16.4%)	0 (0.0%)
DVT with no past warfarin use	N=6,430	12 (7-30)	2,097 (32.6%)	89 (1.4%)
DVT with past warfarin use	N=12,397	7 (5-10)	1,023 (8.3%)	50 (0.4%)
PE	N=3,646	8 (5-17)	723 (19.8%)	35 (1.0%)
Other	N=82	10 (5-20)	17 (20.7%)	0 (0.0%)
Suspected DVT	N=737	8 (5-15)	118 (16.0%)	≤5*
Cancer without DVT	N=25,410	16 (8-62)	10,015 (39.4%)	787 (3.1%)
Cancer with DVT	N=13,712	30 (7-149)	6,973 (50.9%)	601 (4.4%)
Pregnant or lactating females	N=276	30 (12-100.5)	174 (63.0%)	≤5*
No indication	N=36,291	10 (6-18)	6,289 (17.3%)	124(0.3%)

Note*: In accordance with the ICES privacy policy, in cases where the number of total users is less than 6, this number has been suppressed to ensure confidentiality. In cases where there is only one record being suppressed, another record has been suppressed (by providing ranges) as well in order to avoid residual disclosure issues. Data Source: ICES

Summary of Findings for Exhibit 16

- The median time to discontinuation across all LMWH users was 30 days or less, though this differed by medical indication.
- Users identified with cancer had a high median duration of use. Those with cancer and DVT used LMWHs for a median of 30 days (IQR=7 to 149 days), 50.9% (n=6,973 of 13,712) of these users were receiving therapy for more than 3 weeks, and 4.4% (n=601 of 13,712) were on therapy for more than 1 year.
- Users that had undergone surgery were on LMWHs for a median of 10 days and no users exceeded use for more than 1 year.
- Among users identified with DVT and no past warfarin use, the median time to discontinuation was 12 days (IQR=7 to 30 days) and 32.6% (n=2,097 of 6,430) continued therapy for more than 3 weeks. In contrast, of those identified with DVT and past warfarin use, the median time to discontinuation was 7 days (IQR=5 to 10 days) and only 8.3% (n=1,023 of 12,397) continued use for more than 3 weeks.
- Users with PE used LMWHs for a median of 8 days (IQR=5 to 17 days) and 19.8% (n=723 of 3,646) continued use for more than 3 weeks. Similarly, those with suspected DVT used LMWHs for a median of 8 days (IQR=5-15 days) and 16% (n=118 of 737) used LMWHs for more than 3 weeks.

Exhibit 17: Duration of LMWH therapy and number of individuals exceeding the LU authorization criteria, by LU code, 2002-2012

LU code on prescription	Number of new users	Median time to discontinuation (days (IQR))	N(%) exceeding the approved duration of use	Approved duration of use
Deep venous thrombosis (DVT) (LU code 186)	N=51,736	10 (6-18)	7,451 (14.4%)	3 weeks
Pregnant or lactating females (LU code 187)	N=405	17 (7-58)	≤5 (1.2%)	1 year
DVT in patients whom treatment with warfarin is not tolerated (LU code 188)	N=44,465	15 (9-45)	1,235 (2.8%)	1 year
DVT in patients who have failed treatment with warfarin (LU code 189)	N=5,049	14 (6-30)	128 (2.5%)	1 year
Pulmonary embolism (LU code 323)	N=3,300	10 (6-21)	777 (23.5%)	3 weeks
Post-operative prophylaxis of venous thromboembolic events in patients undergoing orthopedic surgery of the lower limbs (LU code 378)	N=10,441	9 (9-9)	1,759 (16.8%)	9 days
Other LU code (LU code 901 and 979)	N=6,622	14 (10-30)	NA	NA
Exceptional Access Program (No LU Code)	N=5,315	10 (7-15)	NA	NA

Note: In accordance with the ICES privacy policy, in cases where the number of total users is less than 6, this number has been suppressed to ensure confidentiality. In cases where there is only one record being suppressed, another record has been suppressed (by providing ranges) as well in order to avoid residual disclosure issues. Data Source: ICES*

Duration on LMWH therapy was short, with median time to discontinuation ranging between 9 days (post-operative prophylaxis) and 17 days (pregnant or lactating females).

Summary of Findings for Exhibit 17

- In general, the median duration on LMWH was short, ranging between 9 days (post-operative prophylaxis of VTE) and 17 days (pregnant or lactating women).
- Among the LU codes that provide approval for 1 year, it was rare for people to exceed this approved duration of use (range 1.2% to 2.8%)
- Among LU codes with approval durations of 3 weeks, use exceeding the approved duration was more common:
 - Approximately one-quarter (23.5%; N=777) of those with a code for PE (LU code 323) exceeded 3 weeks duration of use
 - 14.4% (N=7,451) of those with a code for DVT (LU 186) exceeded 3 weeks duration of use
- LMWH is approved for 9 days for VTE prophylaxis post-operatively. Among these patients, the vast majority received exactly 9 days of therapy (median, IQR: 9, 9-9).

Exhibit 18: Summary of EAP applications for LMWHs between April 1, 2014 and March 31, 2015

Medication	Total EAP request volume	EAP approval rate	TRS* request volume (% total volume)	TRS request approval rate	Non-TRS** request approval rate
Dalteparin	2,045	1,944 (95%)	1,142 (56%)	98.8%	90%
Enoxaparin	1,022	999 (98%)	982 (96%)	99.7%	47%
Tinzaparin	167	156 (93%)	144 (86%)	99.3%	60%
Fondaparinux	10	≤5	n/a (not TRS eligible)	n/a	≤50%
Nadroparin	None	n/a	n/a	n/a	n/a

*TRS=Telephone request service **non-TRS = Fax (and very rarely mail or email)

Note*: In accordance with the ICES privacy policy, in cases where the number of total users is less than 6, this number has been suppressed to ensure confidentiality. In cases where there is only one record being suppressed, another record has been suppressed (by providing ranges) as well in order to avoid residual disclosure issues. Data Source: EAP Submissions

The majority of EAP applications for LMWH are approved, with the majority approved through the telephone request service.

Summary of Findings for Exhibit 18

- The majority of EAP requests for LMWH are approved (95.6%, 3,102 of 3,244), and approximately 70% (2,268 of 3,244) of requests are made through the telephone request service.
- Approval type and rate differs by LMWH drug:
 - 95% of dalteparin requests are approved, with just over half (56%) being made through the TRS.
 - Over 90% of requests for enoxaparin (98%) and tinzaparin (93%) are approved, with almost all being approved through the TRS (96% and 86%, respectively).
 - Fondaparinux is rarely requested through EAP, and among those requests, less than half were approved.
 - Applications made outside of the TRS are less likely to be approved (range 47% to 90% depending on LMWH drug).

Cost of Publicly-Funded LMWH in Ontario

Exhibit 19: ODB LMWH total costs and simulated budget impact in 2014

		Overall		LU code 186	LU code 187	LU code 188	LU code 189	LU code 323	LU code 378	EAP**	Other LU code
Year		Total cost	Total Cost Saving	Total cost							
2014	Total with all Drugs	\$ 33,660,440	--	\$5,109,003	\$493,571	\$24,152,338	\$2,403,203	\$711,006	\$85,848	\$304,932	\$400,536
2014	Total using cost/user for dalteparin	\$ 41,447,740	-\$7,787,299	\$6,512,514	\$538,401	\$29,450,698	\$3,366,434	\$711,006	\$85,848	\$346,915	\$435,921
2014	Total using cost/user for enoxaparin	\$ 22,975,647	\$10,684,793	\$3,440,707	\$ 471,211	\$16,480,617	\$1,256,152	\$627,7108	\$85,848	\$241,900	\$371,499

Data Source: ICES ** Note: Claims with no LU code were assumed to be EAP.

Summary of Findings for Exhibit 19

- The overall cost for LMWHs obtained through the Ontario Public Drug Program in 2014 was \$33,660,440.
- The total cost savings by using enoxaparin when possible is estimated to be \$10,684,793 per year, a 32% savings.
- Switching to dalteparin where possible would increase costs by \$7,787,299 to \$41,447,740
- These results should be interpreted with caution as there may be variation in dosing, duration, and indications of use. Future analysis should control for these factors and include all LMWHs.

Health Equity

Stratified analyses suggest that there is not a major equity issue in access to LMWH by sex. Given the passive nature of the restricted listing of these products on the Ontario public drug formulary, rates of use among those eligible for drug coverage in Ontario are among the highest in Canada. This suggests that there are no considerable barriers to access of these products.

Limitations

Several limitations to the availability of data warrant discussion:

1. No data is available for the territories, and therefore all analyses are restricted to inter-provincial comparisons.
2. IMS Geographic Prescription Monitor (GPM¹²) does not collect patient-level data, and therefore information on privately funded prescriptions is only available at the prescription and unit (e.g. tablet) level.
3. There is no data available for publicly paid prescriptions in Quebec from CIHI NPDUIS. Therefore, we were unable to make comparisons between publicly-funded rates in Ontario and in Quebec.
4. Data on the number of active beneficiaries eligible for public drug coverage was estimated based on active prescriptions in each quarter and annually. Therefore, these may slightly underestimate the true size of the public beneficiary population; however, this does reflect the number of active beneficiaries (e.g. those filling at least one prescription over a given year) each year.
5. All data presented are based on prescriptions filled. We are unable to confirm whether a patient actually took the medication.
6. Some codes used to flag diagnosis have not been validated and are likely underestimating diagnosis rates. There was a substantial portion of patients with an unknown indication that could not be accurately examined for accuracy of LU codes and length of therapy.

Generalizability

Some analyses were restricted to individuals aged 66 and older. Therefore some of these findings might not be generalizable to a younger population.

Overall Conclusion

Use of LMWH continues to grow both nationally and in Ontario. Over the last 5 years there has been a slight change in the use of LMWH medications. Dalteparin remains the most utilized LMWH across Ontario but has seen a decrease in the market share as use of enoxaparin and tinzaparin has increased. The large majority of provincially funded LMWH prescriptions are reimbursed using Limited Use (LU) Codes but our evidence suggests that the LU Codes do not often align with patient indication. Instead, LU codes indicating DVT are commonly used for all medical indications. With a growing elderly population, extended life-expectancy, and the expansion of indications we anticipate continued growth in cost and use of this drug class.

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Appendix

Appendix A: Listing of Low-Molecular Weight Heparins (LMWH) across Jurisdictions in Canada

Drug	Brand/ generic name	BC	AB	SK	MB	ON	QC	NB	NS	PEI	NL	YK	NIHB/ NU/ NW
Dalteparin	Fragmin	Res	FB	Res	Res	Pas/ Res	FB	FB	FB	Res	Res	Res	FB
Enoxaparin	Lovenox	Res	FB	Res	Res	Pas/ Res	FB	FB	FB	Res	Res	Res	FB
Nadroparin	Fraxiparine	Res	FB	Res	Res	Pas/ Res	FB	FB	No	No	No	Res	FB
Tinzaparin	Innohep	Res	FB	Res	Res	Pas/ Res	FB	FB	FB	Res	Res	Res	FB
Fondaparinux	Arixtra	No	FB	No	No	Pas/ Res	FB	No	No	No	No	Res	No
	Generic	No	FB	No	No	Pas/ Res	FB	No	No	No	No	Res	No

Appendix B: Summary of Exceptional Access Program approvals and rejections by indication and drug between April 1, 2014 and March 31, 2015

Indication	Approved	Rejected
Dalteparin		
Antiphospholipid syndrome	<5*	0
Arrhythmia-Atrial Fibrillation	0	<5*
Artificial Aortic Valve	<5*	0
Deep Vein Thrombosis (DVT) Prophylaxis	945	<5*
Deep Vein Thrombosis (DVT) Treatment	<5*	<5*
Extended treatment of symptomatic VTE in cancer patients	0	<5*
Pulmonary Embolism	<5*	<5*
Recurrent thrombosis despite warfarin use	0	<5*
Stroke/TIA-Secondary Prophylaxis	<5*	0
Suspected PE with concurrent IPF	0	<5*
Thromboembolic Disease- Prophylaxis	0	<5*
Thromboprophylaxis- Peri Operative (Bridging)	270	0
Thromboprophylaxis- Post Operative	129	0
Venous Thromboembolism (VTE) Prophylaxis	439	<5*
Venous Thromboembolism (VTE) Treatment	8	<5*
Indication unknown (not tagged)	147	0
Enoxaparin		
Infants- Compassionate Review	7	0
Deep Vein Thrombosis (DVT) Prophylaxis	448	<5*
Pulmonary Embolism	<5*	<5*
Thromboprophylaxis- Peri Operative (Bridging)	401	<5*
Thromboprophylaxis- Post-Operative	0	<5*
Venous Thromboembolism (VTE) Prophylaxis	<5*	<5*
Indication unknown	145	0
Tinzaparin		
Thromboprophylaxis	0	<5*
Deep Vein Thrombosis (DVT) Prophylaxis	8	<5*
Thromboprophylaxis-Peri Operative (Bridging)	126	0
Venous Thromboembolism (VTE) Prophylaxis	0	<5*
Indication Unknown	22	<5*
Fondaparinux		
Treatment/ prophylaxis of VTE in patients with HIT	<5*	0
Other	<5*	<5*

Note: This includes both telephone and written submissions. This does not include claims that were re-directed to use LU codes or requests for more information.

Note*: In accordance with the ICES privacy policy, in cases where the number of total users is less than 6, this number has been suppressed to ensure confidentiality. Data Source: EAP Submission