Canadian cost data associated with treating overactive bladder is lacking

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Abstract

Introduction: Cost-effectiveness analysis forms an integral part of the approval process for new medical treatments in Canada, including drug and non-drug technologies. This study's primary objective was to identify peer-reviewed studies that report Canadian-specific cost data for treating overactive bladder (OAB) based on the Canadian Urological Association (CUA) guidelines. A secondary objective was to identify studies that report cost data from other healthcare jurisdictions that could be generalizable to the Canadian context.
Methods: We conducted a systematic review of the published peer-reviewed literature. We included studies from Organization for Economic Cooperation and Development countries, excluding the U.S., published in English since January 2009.
Results: From 165 abstracts identified in our initial search, 18 studies were ultimately included for analysis. This included one Canadian-based study reporting costs in Canadian dollars, all related to second-line treatments. The other studies were primarily from Europe, reporting costs in Euros or U.K. pounds. There were no studies reporting costs for first-line treatments. Gaps in costs for select second-line and third-line treatments recommended by the CUA were also identified.

Conclusions: Canadian-specific cost data for OAB treatments published in the peer-reviewed literature is limited to a single study reporting costs for only a few second-line treatments sourced from a single province over 10 years ago. Cost data from other healthcare jurisdictions are available, but the generalizability of costs associated with third-line treatments is questionable.

Introduction

Idiopathic overactive bladder (OAB) is a chronic condition involving the perceived or real urge to urinate, that is not determined to be caused by neurologic, hormonal or metabolic disruption1. In general, OAB involves abnormal contractions of the detrusor muscle during the normally relaxed storage phase of micturition, which causes bladder urgency and frequent voiding2. There are several pathophysiologies for OAB: lifestyle, pelvic floor muscular weakness, incorrect function of urinary system, and comorbidities with pre-existing health conditions3.

The Canadian Urologic Association (CUA) has established treatment guidelines for OAB that include several lines of treatment varying in terms of their intensity4. First line treatments include behavioural modifications and lifestyle treatments, second line treatments involve the use of pharmaceutical drugs, and third line treatments involve interventional procedures. For those with severe symptoms refractory to these treatments, alternatives are suggested, including indwelling catheters, augmentation cystoplasty, and urinary diversion.

It is important to understand how these treatments are review, approved, and recommended in Canada for inclusion in drug formularies or lists of medically insured benefits. Understanding these processes and the information upon which these decisions are made can help shape an agenda for future research in the development of new treatments for OAB.

For new pharmaceuticals, there is a centralized process for reviewing and recommending new drugs for federal, provincial, and territorial drug plans5. This process is undertaken largely by The Canadian Agency for Drugs and Technologies in Health (CADTH)6. For non-drug technologies (NDTs), the process is more decentralized, with each province – and in some cases health authorities or hospitals – having their own unique list of organizations/boards/committees responsible for reviewing and recommending new NDTs7. For example, in Alberta, new NDTs for surgery are conducted by the Evidence Decision Support Program (EDSP) within the province's single health region, Alberta Health Services8.

Regardless of whether it is a new pharmaceutical or NDT, evidence syntheses, also referred to as health technology assessments (HTA), largely inform decisions with respect to recommending a new treatment9. HTAs weigh the clinical effectiveness and safety of the new treatment against its costs9. HTAs will often compare the cost-effectiveness of new treatments relative to older treatments. For example, CADTH reviewed the clinical- and cost-effectiveness of intravesical botulinum toxin to treat OAB compared to lifestyle modifications, bladder

retraining, use of anticholinergic drugs, and placebo10. Rarely do these agencies collect primary data for themselves. For the most part, data regarding clinical benefits, harms, and costs are synthesized from published peer-reviewed studies.

The studies from which cost data are sourced for HTA can have a great deal of influence on the interpretation of a new treatment's cost-effectiveness. CADTH prefers that the cost data be sourced from the jurisdiction in which the new treatment is being considered11. For example, if a new treatment is being considered for Canada, then ideally the cost data would come from Canada. If these data do not exist, CADTH recommends using data sourced from a closely generalizable jurisdiction, and preferrable a single jurisdiction for all costs.

The purpose of this study is to identify peer-reviewed studies that include cost data for OAB treatments. Our primary aim is to identify published studies that report Canadian-specific cost data. If no such studies can be identified, our secondary aim is to identify studies that report cost data from other healthcare jurisdictions that could be generalizable to the Canadian context. The results from this study will help reveal the shortcomings in our current knowledge of OAB treatment costs, areas that are in need of future research and reporting, and the ultimate improvement of HTAs for future urologic treatments for OAB.

Methods

We conducted a systematic review of the published peer-reviewed literature regarding the costs associated with treating OAB. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)12, and a completed PRISMA checklist was provided with the submission of this manuscript.

Search strategy

We focused our literature search on studies reporting data from OECD (Organization for Economic Cooperation and Development) countries, excluding the United States. Given the United States' unique health care system, we did not think that costs from this jurisdiction would be generalizable to the Canadian context, thus not relevant for future HTAs. A trained medical librarian assisted in developing the search strategy for Ovid Medline and Embase databases. The list of keywords used, and an example of the search strategy, is included as Appendix 1. The search was executed between August and September 2020. The search was limited to studies that were published in English since January 2009. This date restriction was used to limit the search to more current estimate of costs associated with contemporary OAB treatment and management plans. The last day of the literature searching was September 9, 2020.

The search results were uploaded and reviewed using Covidence13. Two reviewers (DV and CB) independently screened the abstracts resulting from the searches. Abstracts were included for full text review if they listed monetary costs associated with OAB for patients aged 18 years or older. Abstracts were excluded if they: 1) focused on neurogenic detrusor overactivity (NDO); 2) primarily reported cost data from the U.S.; or 3) were editorials, commentaries, review articles, letters, conference transcripts, posters. If the eligibility could not

be determined by from the abstract, the reviewers aired on the side of caution and included it for full text review. Discrepancies were compared and resolved by a third reviewer (RTC). Because the search was looking for initial input costs, there was low chance for bias affecting the observations. However, the sources of all costs were noted, when available, to help identify the chance of bias.

Data summary

DV and CB abstracted the data from the articles that met the inclusion and exclusion criteria. Two Microsoft Excel spread sheet were used, one to collect study details (jurisdiction, methods, intervention(s), sample size, etc.) and another to collect costs. Costs associated with treating OAB were recorded exactly as found in original studies. Where costs were presented as existing within a range of two numbers, the average value of the high and low values was used. The dosage or unit of analysis were also recorded.

To allow informative cost comparison between different years and countries, all costs were converted into January 1, 2020 Canadian dollars. These rates were calculated upon historic exchange and inflation rates of the original costs. If only the year of the costs were given and no date specified, the costs were then converted to the January 1st rate of that calendar year. Where costs covered a two-year range, the earlier year was selected for the calculation of costs. The online historical currency converters fx-rate.net 14, freecurrencyrates.com 15 and the Bank of Canada historical Canadian inflation converter 16 were used for the conversion of currencies.

We summarized the results by lines of treatment recommended in the CUA guidelines on OAB. These results first identify those studies that report Canadian costs, then costs from other jurisdictions. When different studies report costs from the same source, we report data from only the most recent study.

Results

The search strategy yielded 165 abstracts, from which 63 were selected for full-text review. Primary reasons for exclusion included: no cost data reported or not reported for a specific treatment (e.g., reported as general antimuscarinics drugs), U.S.-based studies, not reporting costs in a comparable unit (e.g., for an unspecified “cycle” of treatment), focused on NDO, and reviews/ commentaries. A total of 18 unique studies met the criteria for inclusion in our analysis. Figure 1 provides the PRISMA flow chart.

Study Characteristics

Table 1 provides the details of the 18 studies included in the analysis. The majority (n = 12; 67%) were published between 2009 and 2014. There was one study that included data from Canada. The remaining studies came from the United Kingdom (U.K.) (n = 7; 39%), Spain (n = 5; 28%), and Italy (n = 3; 17%). Similarly, there was one study that reported costs in Canadian Dollars. The others reported costs in Euros (n = 10; 56%), British Pounds (n = 6; 33%), and Japanese Yen (n = 1; 6%).

The majority of included studies (n = 13; 72%) reported cost data related to the use of pharmaceutical drugs. Cost data related to the use of Botulinum toxin A were reported in 6 (33%) studies, although one (study ID #12) did not report a dosage unit and was therefore excluded for this particular treatment. Four (22%) studies reported cost data related to sacral neuromodulation.

First-line treatment

The CUA guidelines recommends behavioural therapy (i.e., bladder training and pelvic floor muscle therapy) and lifestyle changes (i.e., fluid and caffeine intake, diet management, weight loss) as first line treatments for OAB. Our search did not identify any studies reporting costs associated with these treatments, either from Canada or from any other jurisdiction.

Second-line treatment

As second line treatments, the CUA guidelines recommends antimuscarinics (i.e., oxybutynin, immediate release, extended release, transdermal; tolterodine, immediate release, extended release; darifenacin; solifenacin; propiverine; fesoterodine) and beta-3 adrenoceptor agonist (i.e., mirabegron). The costs associated with second line treatments extracted from the included studies are provided in Table 2. There were no studies that reported costs related to propiverine.

There were 4 (22%) studies that reported costs for oxybutynin. A single study reported Canadian costs in 2010 dollars, $0.20 for 5 mg of immediate release ($0.23 in 2020 terms). The remaining studies were all based in the U.K. and reported costs in the U.K. Pound taken from the British National Formulary. The most recent, from 2015, included costs for both 5 mg of immediate and extended release ($0.14 and $0.90 in 2020 Canadian dollars, respectively).

There were 9 (50%) studies that reported costs for tolterodine. Again, one study reported Canadian costs in 2010 dollars ($2.13 in 2020 terms). Four (22%) studies reported costs in Euros from six different countries, between 2006 and 2012 (range: $1.51 - $4.39 in 2020 Canadian dollars). Four (22%) studies reported costs in U.K. Pound, the most recent from 2015 ($1.80 and $0.18 in 2020 Canadian dollars for extended and immediate release, respectively). One study reported costs in 2016 Japanese Yen ($2.32 in 2020 Canadian dollars).

Two (11%) studies reported costs for darifenacin. Both reported costs in U.K. Pound, the most recent in 2015 ($1.85 in 2020 Canadian dollars for 15 mg and $1.78 in 2020 Canadian dollars for 7.5 mg). There were no studies reporting Canadian costs.

There were 9 (50%) studies that reported costs for solifenacin. One study reported Canadian costs in 2010 dollars ($1.92 in 2020 terms). Four (22%) studies reported costs in U.K. Pound, the most recent in 2015 ($2.35 in 2020 Canadian dollars and $1.80 in 2020 Canadian dollars for 10 mg and 5 mg, respectively). Four (22%) studies reported Euros from seven different countries, the most recent 2012 (range: $2.20 - $4.07 in 2020 Canadian dollars).

There were 5 (28%) studies that reported fesoterodine. Two (11%) of these reported costs in U.K. Pound, the most recent from 2015 ($1.80 in 2020 Canadian dollars). Three (17%)

reported costs in Euros from 2 different countries, the most recent in 2015 (range: $2.10 - $3.81 in 2020 Canadian dollars). There were no studies reporting Canadian costs.

Three (17%) studies reported costs related to mirabegron. Two (11%) of these reported costs in U.K. Pound, the most recent from 2015 ($1.90 in 2020 Canadian dollars). One study, from Spain, reported costs in 2015 Euros ($2.13 in 2020 Canadian dollars). One reported 2016 Japanese Yen ($2.44 in 2020 Canadian dollars). There were no studies reporting Canadian costs.

Third-line treatment

For third line treatments, the CUA guidelines recommends OnabotulinumtoxinA, peripheral tibial nerve stimulation (PTNS), and sacral neuromodulation (SNM). The costs associated with third line treatments extracted from the included studies are provided in Table 3. There were no studies that reported Canadian costs, nor were there any studies reporting costs associated with PTNS.

The heterogeneity with which these treatments were described in the respective studies makes it a difficulty to directly compare them across countries. For example, most studies reported costs for a generic "procedure", without a full description of what was included in that category. Consequently, the costs, particularly for SNM, vary widely.

Discussion

This study aimed to understand the availability of Canadian cost data for OAB treatment. In the absence of data from Canada, we sought to identify the most recently published cost data from healthcare jurisdictions that are generalizable to the Canadian context. Using the CUA guidelines for the management of OAB, we characterized treatments by first, second, and third lines.

A single Canadian study reporting treatments – all related to second line – in Canadian dollars was identified. This study was published over a decade ago and is based on data sourced from a single province, Ontario. Moreover, these costs were all related to antimuscarinics, specifically oxybutynin, tolterodine, and solifenacin. There were no published cost data related to beta-3 adrenoceptor agonist. Nor did we find any published Canadian cost data related to first- or third-line treatments.

The results from our study demonstrate the deficiencies in our understanding of Canadian-specific costs for OAB treatments. These deficiencies limit the ability to conduct HTAs because cost-effectiveness analyses of new and old treatments require accurate cost data. This impairs the introduction of new treatments for OAB to provincial drug formularies or the NDTs that are covered by provincial health insurance programs. Ultimately, this reduces the choice of OAB treatments for clinicians and their patients.

Canadian agencies conducting HTAs, like CADTH, are willing to consider cost data from other jurisdictions, provided that they are generalizable to the Canadian context. The results from this study demonstrate that there are several studies reporting OAB treatment cost data from a number of countries with publicly-funded healthcare systems, mostly from Europe. Although,

even here we have identify gaps in the published research. Most notably, that there are no cost data published for first line treatments.

For second line treatments, the most recently published cost data are from 2015, all sourced from the U.K. There are costs data published for all second line treatments recommended by the CUA, save for propiverine. The dosages reported are aligned with those recommended by the CUA, so the use of these data in cost-effectiveness research should be straightforward.

For third line treatments, cost data from 2014 for onabotulinumtoxinA have been published from several European countries. For SNS, the most recent data comes from the U.K. in 2012. There were no studies for PTNS with useable cost data. The applicability of these data to the Canadian context is not as simple as it is for second line treatment, which is strictly comprised of the cost of the drug. Third line treatments can include physician fees for procedures, disposables, hospital recovery, specialized nursing costs, revisions, etc. These may not be translatable to the Canadian context.

This study demonstrates the need for more rigorous Canadian-specific research into OAB treatments that reports cost data from reliable sources. These studies need not come from clinical trials, but come from "real world" data taken from administrative data maintained by provincial health authorities17. In Canada, both Ontario and Alberta collect microcosting data that would provide the granularity for reporting treatment costs, particularly as they relate to third line treatments18,19. The field of urology should take it upon itself to develop a research agenda that would systematically address the gaps in Canadian-specific cost gaps identified through this study.

There are several limitations to this study that should be noted. First, the search was limited to publications that were written in English. We are aware of work by le Institut national d'excellence en santé et en services sociaux that has reported the costs associated with mirabegron and OnabotulinumtoxinA.20,21 However, these works are not formally published in peer-reviewed journals and are written in French, and therefore fall out of the scope of this systematic review. There may be French studies from Quebec that were excluded. Second, our search strategy did not include grey literature. This was intentional as we wanted to maintain a manageable number of studies for review and limit the chance for bias in our results from costs data that may not have been peer-reviewed. Finally, we limited the results to only those treatments recommended by the CUA. We identified cost data for other treatments (e.g., trospium) but refrained from reporting them to keep within the boundaries of the CUA's own evidence-based evaluation.

Conclusions

Canadian-specific cost data for OAB treatments published in the peer-reviewed literature is limited. What is available is for second line treatment, sourced from a single province, and dated. Cost data from other healthcare jurisdictions similar to the Canadian context is available, but the

applicability of costs associated with third line treatments is questionable. A systematic and coordinated effort is needed to fill the gaps in our cost knowledge in order to facilitate HTAs for future OAB treatments.

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Figures and Tables

Fig. 1. PRISMA flow diagram of records identified, included, and excluded.

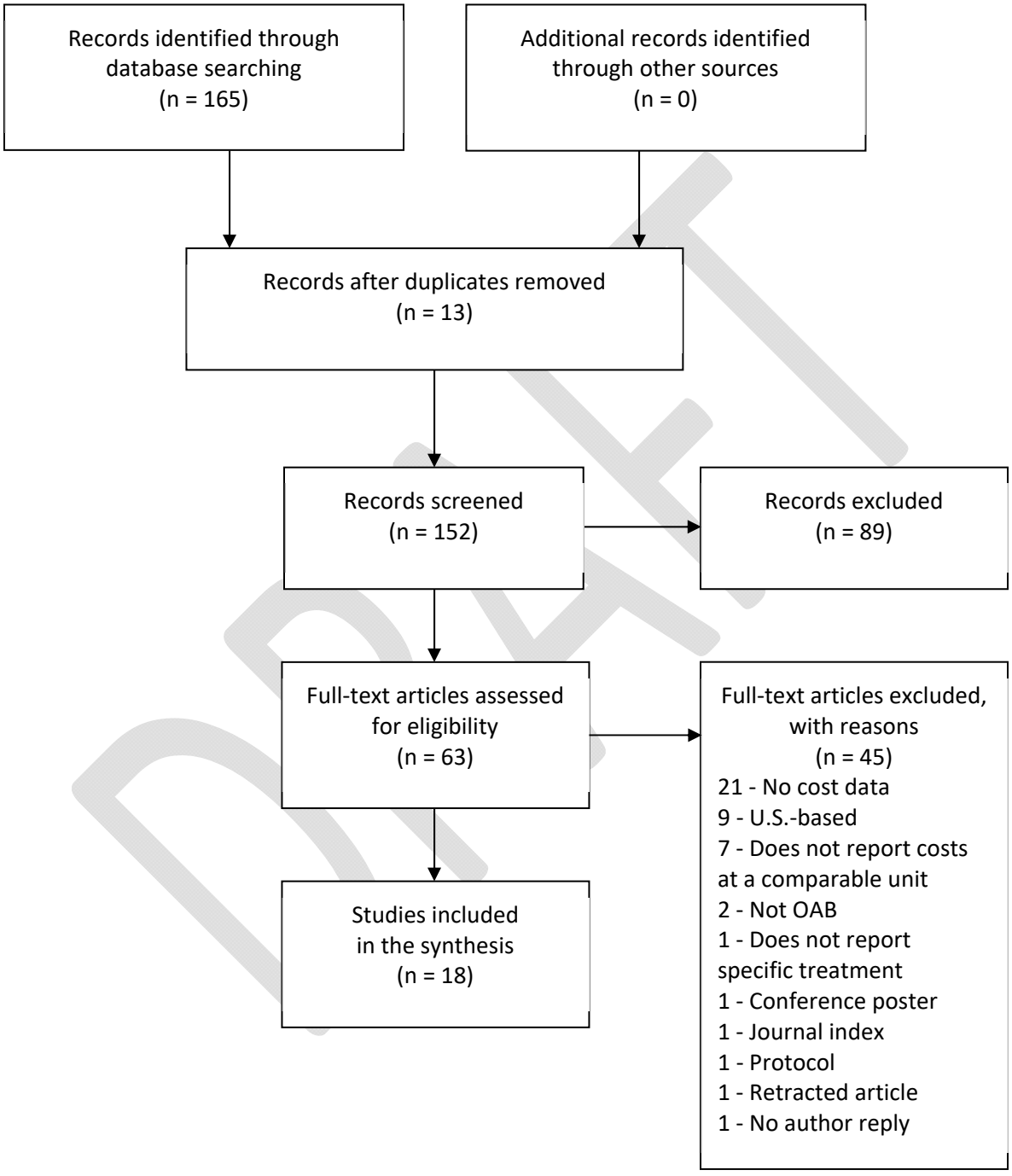

Table 1. Details on studies selected for full-text review					
Study ID (reference)	**Publication year**	**Country / countries**	**Currency**	**Price year**	**Included treatments**
1 (22)	2009	U.K.	British Pound	2004	Solifenacin
2 (23)	2009	Italy	Euro	2009	Solifenacin, tolterodine
3 (24)	2009	Denmark, Finland, Norway, Sweden	Euro	2006	Solifenacin, tolterodine
4 (25)	2010	Canada	Canadian Dollars	2009	Oxybutynin, solifenacin
5 (26)	2010	The Netherlands	Euro	2012	Botulinum toxin A, sacral neuromodulation
6 (27)	2011	Spain	Euro	2008	Botulinum toxin A, sacral neuromodulation
7 (28)	2011	Spain	Euro	2010	Fesoterodine, solifenacin, tolterodine
8 (29)	2012	U.K.	British Pound	2010	Tamsulosin, tolterodine
9 (30)	2013	U.K.	British Pound	2010	Oxybutynin, solifenacin, tolterodine
10 (31)	2014	Germany	Euro	2012	Solifenacin, trospium
11 (32)	2014	Finland, Spain	Euro	2012	Fesoterodine, tolterodine
12 (33)	2014	Italy	Euro	2011	Botulinum toxin A, sacral neuromodulation
13 (34)	2015	U.K.	British Pound	2012	Botulinum toxin A*, darifenacin, fesoterodine, mirabegron, oxybutynin, solifenacin, tolterodine, trospium
14 (35)	2015	U.K.	British Pound	2012	Botulinum toxin A, sacral neuromodulation
15 (36)	2016	France, Germany, Italy, Spain, U.K.	Euro	2014	Botulinum toxin A
16 (37)	2016	Spain	Euro	2011	Fesoterodine, mirabegron
17 (38)	2017	U.K.	British Pound	2015	Darifenacin, flavoxate, fesoterodine, mirabegron, oxybutynin, solifenacin, tolterodine, trospium
18 (39)	2018	Japan	Japanese Yen	2016	Mirabegron, tolterodine

Table 2. Most recent costs reported for second-line overactive bladder treatments, by jurisdiction

Treatment	Study ID	Country	Original currency	Dosage unit	Source	Reported cost	Converted cost (CAN 2020)
Oxybutine	4	Canada	Canadian Dollars - 2010	5 mg (IR)	Ontario Drug Benefit Formulary (2009)	0.20	0.23
	17	U.K.	U.K. Pound - 2015	5 mg (ER)	British National formulary (2016)	0.46	0.90
	17	U.K.	U.K. Pound - 2015	5 mg (IR)	British National formulary (2016)	0.07	0.14
Tolterodine	4	Canada	Canadian Dollars - 2010	4 mg	Ontario Drug Benefit Formulary (2009)	1.82	2.13
	2	Italy	Euro - 2007	4 mg	Italian National Formulary (2007)	2.34	4.39
	3	Sweden	Euro - 2006	4 mg (SR)	Not referenced	1.48	2.54
	3	Norway	Euro - 2006	4 mg (SR)	Not referenced	1.42	2.44
	3	Denmark	Euro - 2006	4 mg (SR)	Not referenced	1.77	3.04
	11	Finland	Euro - 2012	4 mg (ER)	Not referenced	1.42	2.08
	11	Spain	Euro - 2012	4 mg (ER)	Not referenced	1.03	1.51
	17	U.K.	U.K. Pound - 2015	4 mg (ER)	British National formulary (2016)	0.92	1.80
	17	U.K.	U.K. Pound - 2015	4 mg (IR)	British National formulary (2016)	0.09	0.18

	18	Japan	Japanese Yen - 2016	4 mg	Not referenced	190.00	2.32
Darifenacin	13	U.K.	U.K. Pound - 2012	15 mg	British National Formulary (2012)	0.92	1.85
	17	U.K.	U.K. Pound - 2015	7.5 mg	British National formulary (2016)	0.91	1.78
Solifenacin	4	Canada	Canadian Dollars - 2010	5 mg	Astellas Pharma Canada Inc.	1.64	1.92
	2	Italy	Euro - 2007	5 mg	Italian National Formulary (2007)	2.17	4.07
	3	Sweden	Euro - 2006	5 mg	Not referenced	1.36	2.34
	3	Sweden	Euro - 2006	10 mg	Not referenced	1.65	2.83
	3	Norway	Euro - 2006	5 mg	Not referenced	1.28	2.20
	3	Norway	Euro - 2006	10 mg	Not referenced	1.51	2.59
	3	Finland	Euro - 2006	5 mg	Not referenced	1.79	3.07
	3	Finland	Euro - 2006	10 mg	Not referenced	1.64	2.82
	3	Denmark	Euro - 2006	5 mg	Not referenced	1.46	2.51
	3	Denmark	Euro - 2006	10 mg	Not referenced	1.82	3.13
	7	Spain	Euro - 2010	5 mg	Portalfarma; General Council of Provincial Pharmacy Chambers (2009)	1.67	2.95
	7	Spain	Euro - 2010	10 mg	Portalfarma; General Council of Provincial Pharmacy Chambers (2009)	2.67	4.72
	10	Germany	Euro - 2012	5 mg	Data from various German sickness funds	1.66	2.43
	10	Germany	Euro - 2012	10 mg	Data from various German sickness funds	1.97	2.89
	17	U.K.	U.K. Pound - 2015	5 mg	British National formulary (2016)	0.92	1.80
	17	U.K.	U.K. Pound - 2015	10 mg	British National formulary (2016)	1.20	2.35
Fesoterodine	11	Finland	Euro - 2012	4 mg	Not referenced	1.43	2.10
	11	Finland	Euro - 2012	8 mg	Not referenced	1.57	2.30
	16	Spain	Euro - 2015	4 mg	Portalfarma; General Council of Provincial Pharmacy Chambers (2015)	1.60	2.44

	16	Spain	Euro - 2015	8 mg	Portalfarma; General Council of Provincial Pharmacy Chambers (2015)	2.50	3.81
	17	U.K.	U.K. Pound - 2015	4/8 mg	British National formulary (2016)	0.92	1.80
Mirabegron	16	Spain	Euro - 2015	50 mg	Portalfarma; General Council of Provincial Pharmacy Chambers (2015)	1.40	2.13
	17	U.K.	U.K. Pound - 2015	50 mg	British National formulary (2016)	0.97	1.90
	18	Japan	Japanese Yen - 2016	50 mg	Not referenced	200.00	2.44

Table 3. Most recent costs reported for third-line overactive bladder treatments by jurisdiction

Treatment	Study ID	Country	Original currency	Explanation	Dosage/ unit	Source	Reported Cost	Converted cost (CAN 2020)
Onabotulinumtoxin A	5	The Netherlands	Euro - 2008	Pre procedure	Per event	Healthcare Institute Netherlands	290.00	508.78
	5	The Netherlands	Euro - 2008	Procedure (including 200 U injection)	Per event	Healthcare Institute Netherlands	1564.00	2743.88
	6	Spain	Euro - 2008	Pre procedure	Per event	e-Salud database; Spanish Ministry of Health	572.00	1003.52
	6	Spain	Euro - 2008	Procedure	Per event	e-Salud database; Spanish Ministry of Health	1192.00	2091.24
	12	Italy	Euro - 2011	Pre procedure	Per event	Not referenced	217.07	328.69
	12	Italy	Euro - 2011	Procedure (including 100 U injection)	100 U	Not referenced	1654.99	2505.99
	15	France	Euro - 2014	Injection	100 U	Allergan Ltd (2015)	216.10	340.75
	15	France	Euro - 2014	Procedure	Inpatient	Allergan Ltd (2014)	2169.28	3420.52
	15	France	Euro - 2014	Procedure	Day-case	Referentiel de couts MCO. ScanSante, 2012	754.00	1188.91
	15	France	Euro - 2014	Procedure	Outpatient	Study	213.00	335.86
	15	Germany	Euro - 2014	Injection	100 U	Allergan Ltd (2015)	406.87	641.55
	15	Germany	Euro - 2014	Procedure	Inpatient	Allergan Ltd (2015)	2700.00	4257.36

	15	Germany	Euro - 2014	Procedure	Day-case	Allergan Ltd (2015)	850.00	1340.28
	15	Germany	Euro - 2014	Procedure	Outpatient	Allergan Ltd (2015)	109.00	171.87
	15	Italy	Euro - 2014	Injection	100 U	Allergan Ltd (2015)	214.54	338.29
	15	Italy	Euro - 2014	Procedure	Inpatient	Italia. Decreto Ministriale (2013)	1075.00	1695.06
	15	Italy	Euro - 2014	Procedure	Day-case	Allergan Ltd (2015)	404.66	638.07
	15	Italy	Euro - 2014	Procedure	Outpatient	Allergan Ltd (2014)	406.66	641.22
	15	Spain	Euro - 2014	Injection	100 U	Allergan Ltd (2015)	205.03	323.29
	15	Spain	Euro - 2014	Procedure	Inpatient	Ministerio de Sanidad, Servicios Sociales e Igualdad (2013-2014)	875.31	1380.19
	15	Spain	Euro - 2014	Procedure	Day-case	Study	162.97	256.97
	15	Spain	Euro - 2014	Procedure	Outpatient	Allergan Ltd (2015)	162.97	256.97
	15	U.K.	Euro - 2014	Injection	100 U	Allergan Ltd (2015)	195.16	307.73
	15	U.K.	Euro - 2014	Procedure	Inpatient	Payment by results in the NHS: Tariff for 2013-14	545.62	860.33
	15	U.K.	Euro - 2014	Procedure	Day-case	Payment by results in the NHS: Tariff for 2013-14	275.33	434.14
	15	U.K.	Euro - 2014	Procedure	Outpatient	Payment by results in the NHS: Tariff for 2013-14	275.33	434.14
Sacral neuromodulation	5	The Netherlands	Euro - 2008	Pre procedure	Per event	Healthcare Institute Netherlands	278.00	487.72

	5	The Netherlands	Euro - 2008	First-stage tined lead procedure	Per event	Healthcare Institute Netherlands	3445.00	6043.91
	5	The Netherlands	Euro - 2008	Second-stage tined lead procedure	Per event	Healthcare Institute Netherlands	9150.00	16 052.76
	5	The Netherlands	Euro - 2008	Surgical revision	Per event	Healthcare Institute Netherlands	2590.00	4543.90
	5	The Netherlands	Euro - 2008	Surgical removal	Per event	Healthcare Institute Netherlands	11 448.00	20 084.37
	6	Spain	Euro - 2008	Test pre-procedure	Per event	Medtronic	558.00	978.96
	6	Spain	Euro - 2008	Test	Per event	Medtronic	2781.00	4878.99
	6	Spain	Euro - 2008	Procedure	Per event	Medtronic	9734.00	17 077.33
	12	Italy	Euro - 2011	Test pre-procedure	Per event	Not referenced	213.65	323.51
	12	Italy	Euro - 2011	Test and implanted devices	Per event	Not referenced	5622.35	8513.36
	12	Italy	Euro - 2011	Implantation pre-procedure costs	Per event	Not referenced	104.59	158.37
	12	Italy	Euro - 2011	Implantation including implanted devices	Per event	Not referenced	9433.34	14 283.96
	12	Italy	Euro - 2011	Lead repositioning for migration or decreased clinical response including implanted devices	Per event	Not referenced	5873.03	8892.94
	12	Italy	Euro - 2011	Lead replacement for breaking including implanted devices	Per event	Not referenced	5684.37	8607.27
	12	Italy	Euro - 2011	Generator repositioning	Per event	Not referenced	2674.69	4050.02

	12	Italy	Euro - 2011	Lead explantation	Per event	Not referenced	724.55	1097.11
	14	U.K.	Pound - 2012	Physician visit follow up	Per Visit	National tariff information workbook (2014-2015)	319.00	563.00
	14	U.K.	Pound - 2012	Removal of temporary electrodes	Per event	Study	1166.00	2,057.87
	14	U.K.	Pound - 2012	First-stage implant	Per event	Study	8641.00	15 250.50
	14	U.K.	Pound - 2012	Battery replacement	Per event	Study	6623.00	11688.93
	14	U.K.	Pound - 2012	Device explant	Per event	Study, OPCS classification of interventions and procedures	923.00	1629.00
	14	U.K.	Pound - 2012	Surgical revision	Per event	Study, Department of Health: NHS reference costs	592.00	1044.82

Appendix 1

EMBASE Classic <2009 to present> Search date: 9 June 2020

Number	Searches	June 9 Results
1	Urinary Bladder, Overactive/	4482
2	exp "Costs and Cost Analysis"/	347462
3	1 and 2	143
4	limit 3 to yr="2009 -Current"	55
5	limit 4 to english language	53

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