

The uptake of active surveillance for the management of prostate cancer: A population-based analysis

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Appendices

Appendix 1. Ontario Health Insurance Plan (OHIP) physician billing claims used to identify prostate cancer-related management

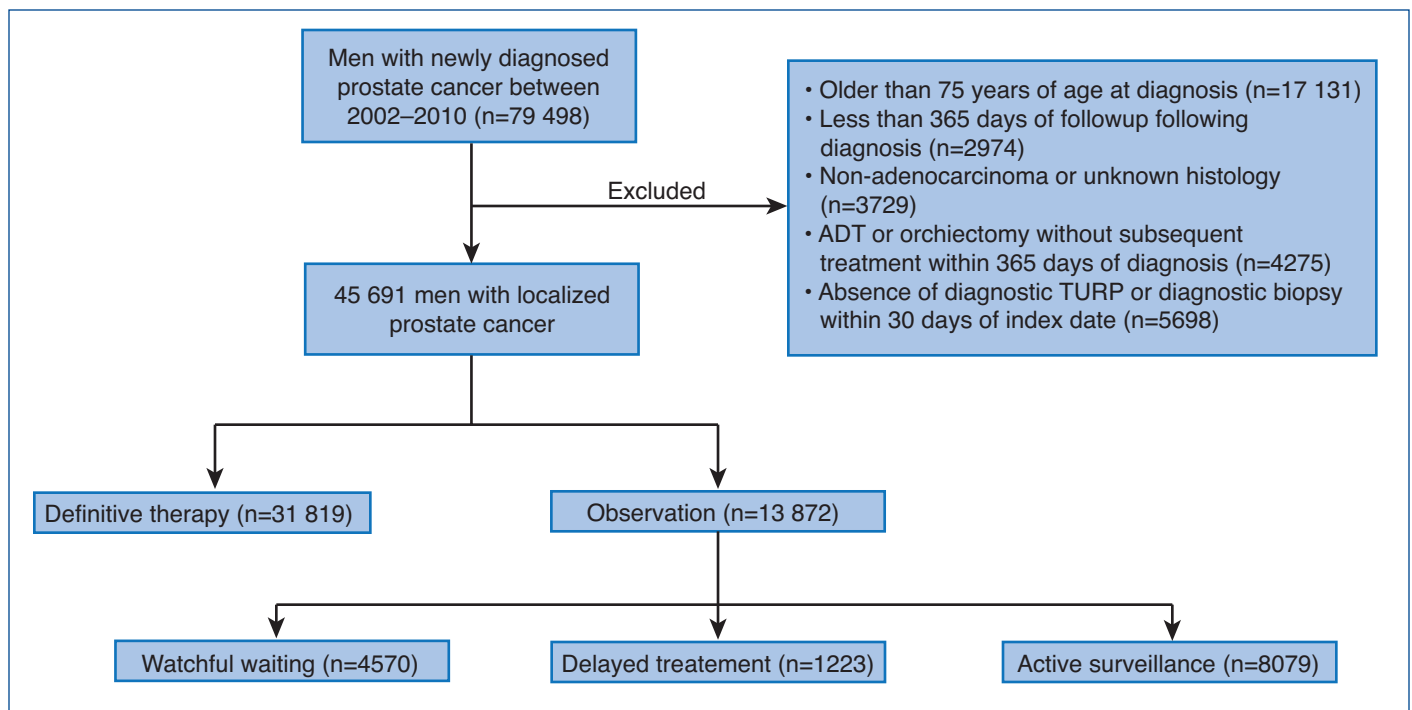
Billing claims - code	Fee code: OHIP definition
Androgen-deprivation therapy	G342: implantation of hormone pellets
Orchiectomy	S589: orchiectomy; S598: radical orchiectomy
Biopsy	Z712: biopsy, needle; Z713 biopsy, needle with drainage of abscess; S644: biopsy, perineal; E780: cystoscopy with needle biopsy of prostate
Transurethral resection of the prostate	S654: transurethral resection of prostate for residual tissue; S655: transurethral resection of prostate
Radical prostatectomy	S645: perineal prostatectomy; S646: perineal prostatectomy with vesiculectomy; S651: radical retropubic prostatectomy; S653: laparoscopic radical prostatectomy;
Pelvic lymph node dissection	S652: staging pelvic lymph node dissection for prostate cancer
Brachytherapy	S640: stereotactic prostate brachytherapy; X322: radium (sealed sources) treatment planning dosage; X323: radium (sealed sources) Intracavit. applic. - 1st applic.; X324: radium (sealed sources) - Interstitial; X325: radium (sealed sources) Applic. plaque/mould; X334: radium (sealed sources) Intracavit. applic. - rep. applic.
Radiotherapy	X310: simple treatment planning; X311: intermediate treatment planning; X312: complex treatment planning; X313: full 3D treatment preparation
Urologist visits	A355: consultation; A935: special surgical consultation; A356: repeat consultation; A353: specific assessment; A354: partial assessment; C355: in-patient consultation; C935: in-patient special surgical consultation; C356: in-patient repeat consultation; C353: in-patient specific assessment; C354: in-patient partial assessment; C352: in-patient subsequent visits – first five weeks; C357: in-patient subsequent visits – sixth to thirteenth week; C359: in-patient subsequent visit – after thirteenth week
Radio-oncologist visits	A340: medical specific re-assessment; A341: complex medical specific re-assessment; A343: medical specific assessment; A345: consultation; A346: repeat consultation; A348: partial assessment; A745: limited consultation; C340: in-patient medical specific re-assessment; C341: in-patient complex medical specific re-assessment; C343: in-patient medical specific assessment; C345: in-patient consultation; C346: in-patient repeat consultation; C348: in-patient partial assessment; C745: in-patient limited consultation

Appendix 2. Description of covariates used in the multilevel mixed models			
Variables	Definition	Type of variable	Categories
Individual-level characteristics			
Age, years	Age at index year	Categorical	Less than 55 years 55–65 years 66–75 years
Index year	Year of diagnosis	Categorical	Year 2002–2004 Year 2005–2007 Year 2008–2010
Income quintile	Neighborhood average income quintile	Categorical	1–5, with 1 representing the lowest income quintile and 5 the highest
ADG score	ADG summary score	Continuous	Per 1-unit increment
Area of residency	Primary area of residency	Categorical	Urban Rural
Physician-level characteristics			
Type of primary physician	Specialty of primary caregiver	Categorical	Urologist Radiation oncologist
Physician volume, consultation/year	Annual new PCa-related consultation volume during study period - physician	Categorical	First quartile (<37 case/year) Second quartile (37–58 case/year) Third quartile (58–94 case/year) Fourth quartile (≥94 case/year)
Institution-level characteristics			
Type of centre	Main treating institution during first year	Categorical	Non cancer centre Cancer centre
Institution volume, consultation/year	Annual new PCa-related consultation volume during study period - institution	Continuous	First quartile (<81 case/year) Second quartile (81–165 case/year) Third quartile (165–358 case/year) Fourth quartile (≥358 case/year)

ADG: Aggregated Diagnosis Groups; PCa: prostate cancer.

Appendix 3. Definitions of the three sensitivity analyses used to identify men managed by active surveillance	
Sensitivity analysis	Definition
Primary definition	Men who underwent repeat biopsies following diagnosis with or without a definitive treatment thereafter.
Sensitivity analysis #1	Men who underwent repeat biopsies following diagnosis with or without a definitive treatment thereafter as well as men who did not undergo a repeat biopsy but underwent definitive treatments more than 12 months after diagnosis.
Sensitivity analysis #2	Men who underwent repeat biopsies following diagnosis with or without definitive treatments thereafter as well as men who did not undergo a repeat biopsy but were treated more than 2 years after diagnosis.
Sensitivity analysis #3	Men who underwent repeat biopsies following diagnosis with or without definitive treatments thereafter, men who did not undergo a repeat biopsy but were treated more than 12 months after diagnosis as well as healthy young men who were not treated nor had a repeat biopsy following diagnosis. The latter group was defined as individuals younger than 65 years of age with an ADG score in the lowest tertile.

ADG: Aggregated Diagnosis Groups.



Appendix 4. Study flow diagram. ADT: androgen-deprivation therapy; TURP: transurethral resection of the prostate.

Appendix 5. Type of management according to year of diagnosis (expectant therapy vs. upfront definitive treatment)

Year of diagnosis	Expectant therapy n (%)	Definitive treatment n (%)	Total per year n (%)
2002	968 (24)	3044 (76)	4012 (9)
2003	1057 (26)	2952 (74)	4009 (9)
2004	1212 (27)	3321 (73)	4533 (10)
2005	1382 (29)	3403 (71)	4785 (11)
2006	1650 (31)	3716 (69)	5366 (12)
2007	1812 (31)	3974 (69)	5786 (13)
2008	1816 (33)	3773 (68)	5589 (12)
2009	2011 (34)	3835 (66)	5846 (13)
2010	1964 (34)	3701 (66)	5765 (13)
Total	13 872 (30)	31 819 (70)	45 691 (100)

Cochrane-Armitage test for trend p value <0.001.

Appendix 6. Individual, physician, and institution-level effects on the uptake of active surveillance (multivariable non-linear mixed model adjusted for physician and institution-level clustering)					
Individuals: 45 691 Physicians: 424 Institutions: 215	Model 1 (null model)	Model 2 (plus individual-level char.)	Model 3 (plus physicians- level char.)	Model 4 (plus institution- level char.)	Model 5 (Full model)
-2 log likelihood	32148	30169	32233	32258	31656
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Individual-level characteristics					
Age (years old)					
Less than 55		REF			REF
55–65		1.17 (1.07–1.28)			1.18 (1.08–1.29)
66–75		1.55 (1.41–1.70)			1.56 (1.42–1.72)
Index year					
2002–2004		REF			REF
2005–2007		1.54 (1.54–1.81)			1.66 (1.54–1.80)
2008–2010		1.89 (1.89–2.23)			2.04 (1.88–2.22)
Neighbourhood income quintile					
First quintile (lowest)		REF			REF
Second quintile		1.04 (0.94–1.14)			1.04 (0.94–1.15)
Third quintile		0.98 (0.89–1.09)			0.98 (0.89–1.09)
Fourth quintile		1.03 (0.94–1.15)			1.04 (0.94–1.14)
Fifth quintile (highest)		1.16 (1.06–1.29)			1.17 (1.06–1.28)
ADG score, per 1-unit increase rural		1.00 (0.997–1.003)			1.00 (0.998–1.003)
Rural living		REF			REF
Urban living		1.28 (1.16–1.42)			1.28 (1.16–1.42)
Physician-level characteristics					
Type of primary physician					
Radiation oncologist			REF		REF
Urologist			2.10 (1.61–2.73)		2.26 (1.73–2.97)
Annual volume					
First quartile (lowest)			REF		REF
Second quartile			0.95 (0.70–1.28)		0.95 (0.70–1.28)
Third quartile			0.97 (0.67–1.39)		0.98 (0.68–1.40)
Fourth quartile (highest)			1.28 (0.85–1.91)		1.31 (0.87–1.96)
Institution-level characteristics					
Type of centre					
Non-cancer centre				REF	REF
Cancer centre				0.95 (0.68–1.33)	1.13 (0.80–1.60)
Institution volume					
First quartile (lowest)				REF	REF
Second quartile				0.68 (0.32–1.48)	0.60 (0.28–1.26)
Third quartile				0.71 (0.28–1.80)	0.87 (0.24–1.50)
Fourth quartile (highest)				0.94 (0.22–4.01)	1.13 (0.25–4.29)
Level 2 (physician) variance	1.13	1.15	0.95	1.13	0.95
Level 3 (institution) variance	2.51	2.46	2.46	2.48	2.40
Intra-class correlation, physician	16%	17%	14%	16%	14%
Intra-class correlation, institution	36%	36%	37%	36%	36%

ADG: Aggregated Diagnosis Groups; CI: confidence interval; OR: odds ratio.

Appendix 7. Comparison of the fixed effects estimates (full models) modelling the uptake of active surveillance using each of the different definitions

	Main definition	Sensitivity analysis #1 [†]	Sensitivity analysis #2* [*]	Sensitivity analysis #3 [†]
-2 log likelihood	31656	35230	33648	37911
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Individual-level characteristics				
Age (years old)				
Less than 55	REF	REF	REF	REF
55–65	1.18 (1.08–1.29)	1.13 (1.04–1.24)	1.13 (1.04–1.24)	1.18 (1.09–1.28)
65–75	1.56 (1.42–1.72)	1.56 (1.43–1.71)	1.56 (1.43–1.71)	1.36 (1.26–1.48)
Index year				
2002–2004	REF	REF	REF	REF
2005–2007	1.66 (1.54–1.80)	1.48 (1.37–1.59)	1.59 (1.48–1.72)	1.52 (1.42–1.63)
2008–2010	2.04 (1.88–2.22)	1.83 (1.69–1.98)	1.89 (1.75–2.04)	1.86 (1.73–2.00)
Neighbourhood income quintile				
First quintile (lowest)	REF	REF	REF	REF
Second quintile	1.04 (0.94–1.15)	1.04 (0.94–1.15)	1.04 (0.94–1.15)	1.01 (0.92–1.11)
Third quintile	0.98 (0.89–1.09)	0.99 (0.90–1.10)	1.00 (0.90–1.10)	0.95 (0.86–1.04)
Fourth quintile	1.04 (0.94–1.14)	1.07 (0.97–1.17)	1.06 (0.96–1.16)	1.00 (0.92–1.10)
Fifth quintile (highest)	1.17 (1.06–1.28)	1.20 (1.09–1.32)	1.17 (1.07–1.29)	1.11 (1.02–1.21)
ACG score, per 1-unit increase rural	1.00 (0.998–1.003)	1.002 (0.999–1.004)	1.001 (0.998–1.004)	0.997 (0.995–1.00)
Rural living	REF	REF	REF	REF
Urban living	1.28 (1.16–1.42)	1.33 (1.21–1.47)	1.28 (1.17–1.29)	1.23 (1.13–1.34)
Physician-level characteristics				
Type of primary physician				
Radiation oncologist	REF	REF	REF	REF
Urologist	2.26 (1.73–2.97)	2.46 (1.80–3.36)	2.10 (1.61–2.73)	2.16 (1.69–2.77)
Annual volume				
First quartile (lowest)	REF	REF	REF	REF
Second quartile	0.95 (0.70–1.28)	0.96 (0.72–1.28)	0.90 (0.67–1.20)	1.00 (0.76–1.32)
Third quartile	0.98 (0.68–1.40)	0.89 (0.63–1.26)	0.91 (0.64–1.29)	0.85 (0.61–1.19)
Fourth quartile (highest)	1.31 (0.87–1.96)	1.16 (0.78–1.71)	1.16 (0.79–1.72)	1.10 (0.75–1.59)
Institution-level characteristics				
Type of centre				
Non-cancer centre	REF	REF	REF	REF
Cancer centre	1.13 (0.80–1.60)	0.66 (0.19–2.29)	1.16 (0.84–1.62)	1.32 (0.97–1.80)
Institution volume				
First quartile (lowest)	REF	REF	REF	REF
Second quartile	0.60 (0.28–1.26)	0.73 (0.34–1.58)	0.56 (0.28–1.13)	0.50 (0.23–1.06)
Third quartile	0.87 (0.24–1.50)	0.77 (0.30–1.96)	0.61 (0.26–1.44)	0.42 (0.17–2.71)
Fourth quartile (highest)	1.13 (0.25–4.29)	0.99 (0.21–4.68)	1.29 (0.34–4.82)	0.65 (0.16–1.80)
Level 2 (physician) variance	0.95	0.91	0.91	0.84
Level 3 (institution) variance	2.40	2.48	2.04	2.45
Intra-class correlation, physician	14%	14%	15%	13%
Intra-class correlation, institution	36%	37%	33%	37%

[†]Active surveillance defined as a repeat biopsy or delayed treatment (12 months after diagnosis); *active surveillance defined as a repeat biopsy or delayed treatment (24 months after diagnosis); [†]active surveillance defined as a repeat biopsy, delayed treatment (12 months after diagnosis) or no repeat biopsy and no treatment in a young and healthy patient. ADG: Aggregated Diagnosis Groups; CI: confidence interval; OR: odds ratio.