

Management of Invasive Bladder Cancer: The case for integration, regionalization, and subspecialization

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No Disclosures



CUA 2019

Potential Conflict of Interest Disclosure

I have no conflict of interest to disclose.



Invasive Bladder Cancer

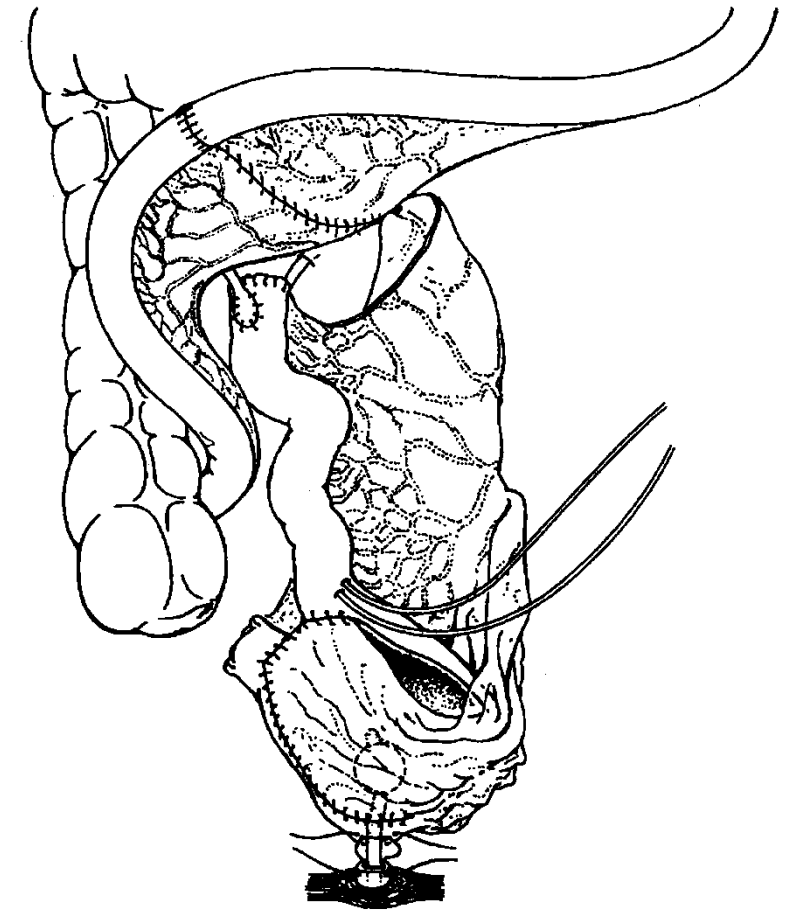
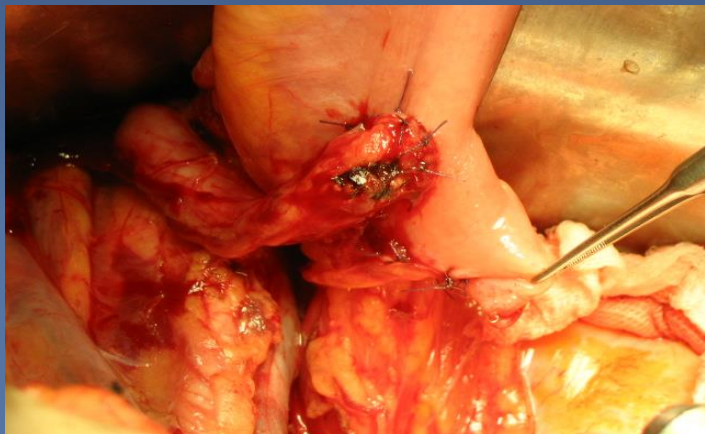
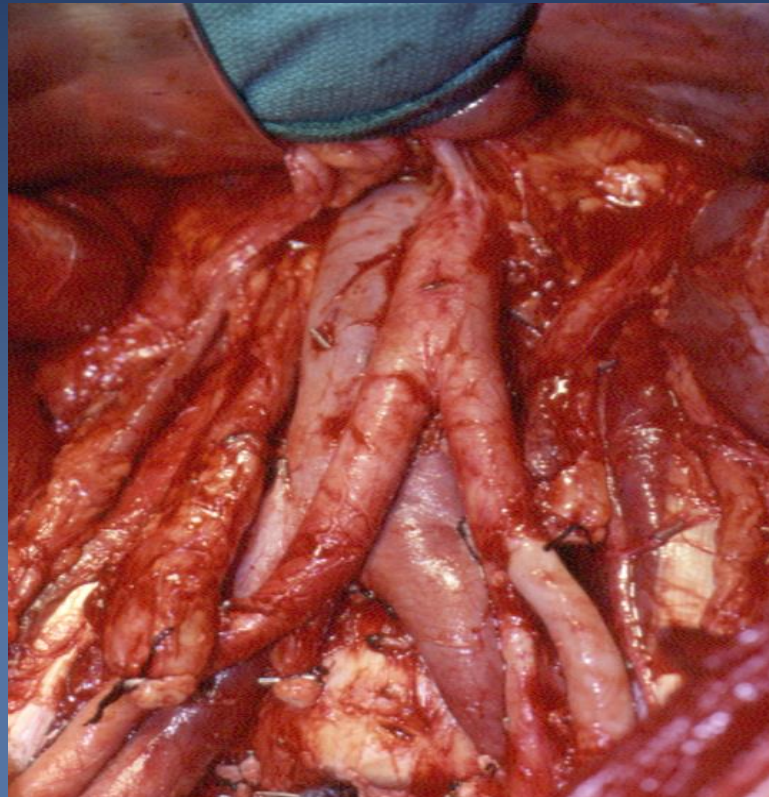
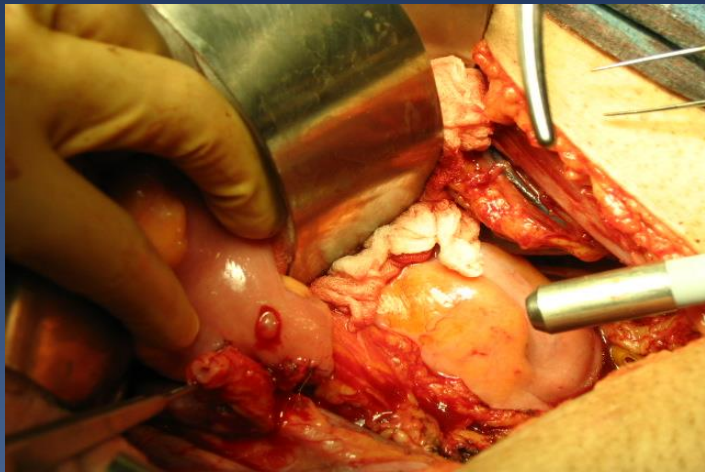
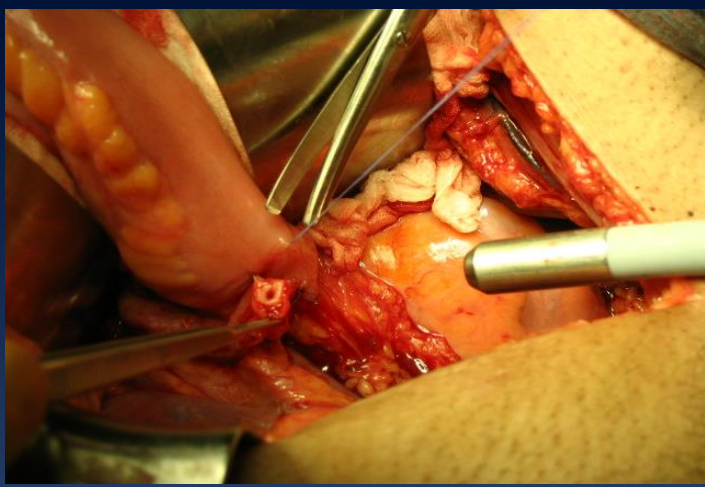
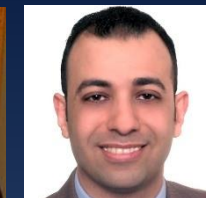


Figure 9. Passage of the ureteral stents and cystostomy tube before complete closure of the pouch.

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Quality in Surgical Oncology: Invasive Bladder Cancer

- **Disease-specific surgical indicators**

- Adherence to guidelines

- Lymph node counts

- Margins of resection

- Functional outcomes

- Recurrence rates

- Disease-specific survival

- **General surgical oncology indicators**

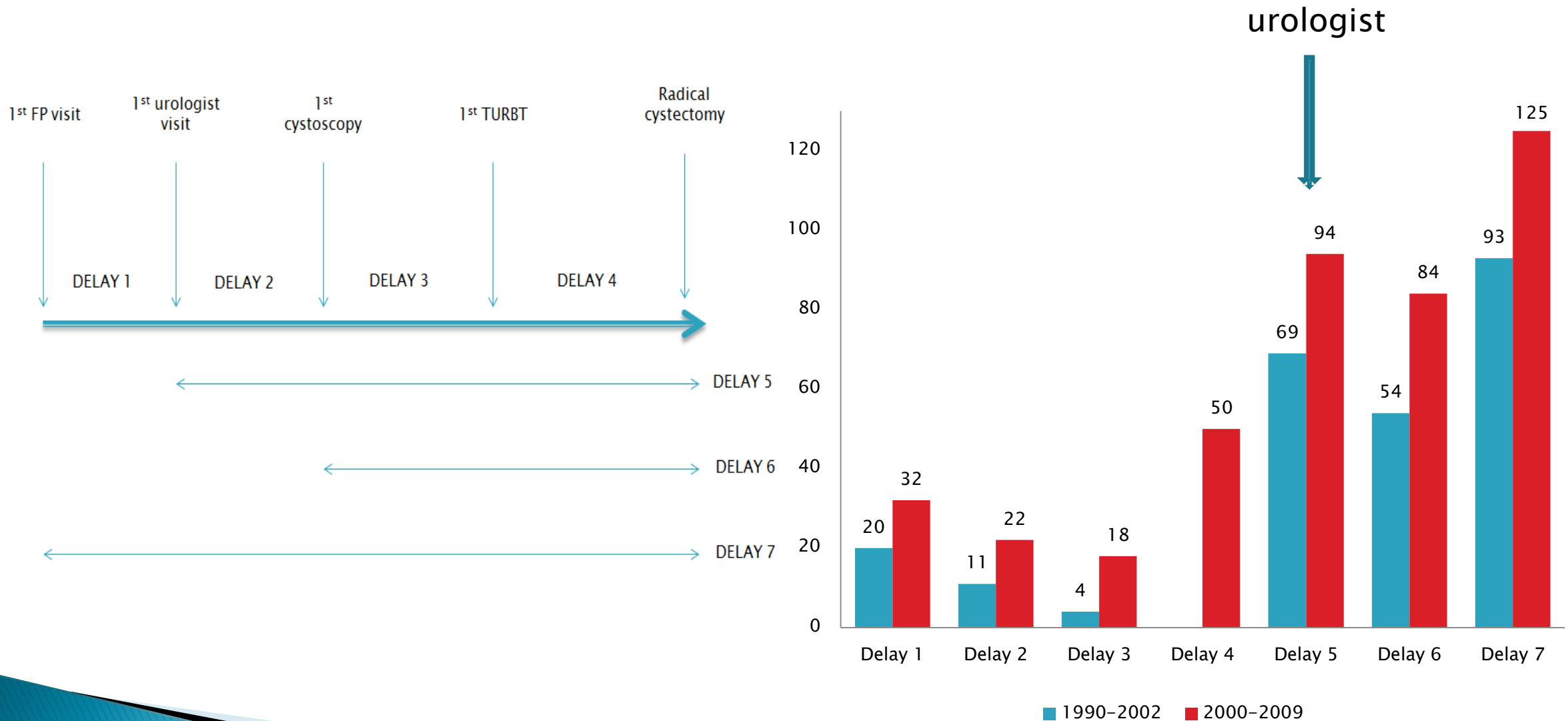
- Access – wait-times

- Complications, re-hospitalization, transfusion

- Post-operative mortality

- Cost

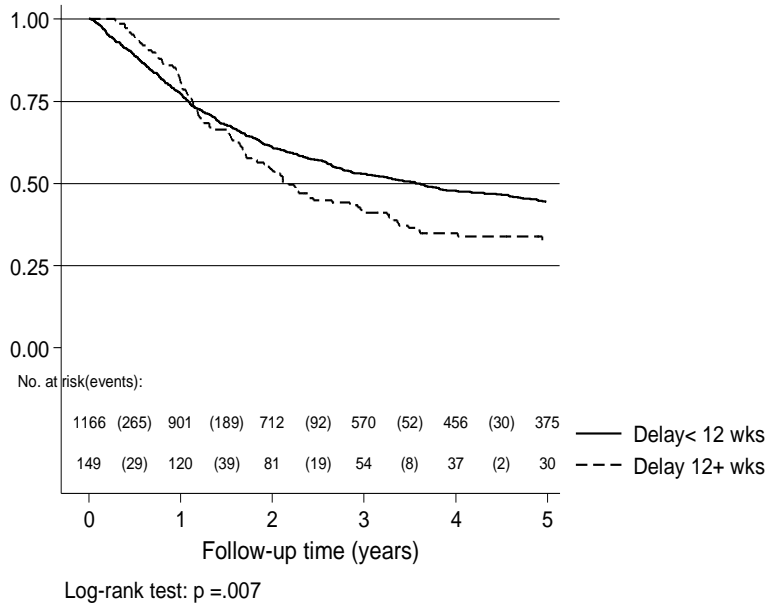
Delays to Surgery in Quebec



1990-2009 data from: Fahmy Aprikian et al.
Can Urol Assoc J. 2008 Apr;2(2):102-8.

Delays and Overall Survival

- 6- Survival analyses: Kaplan-Meier plot of overall survival by delay 4.



Aprikian et al, J Urol 2006

Bladder surgery wait time unsafe: study

CHARLIE FIDELMAN
GAZETTE HEALTH REPORTER

Quebec bladder cancer patients are dying unnecessarily because of increasing delays in treatment, a leading urologist said yesterday.

The death rate among patients stuck waiting 12 weeks or longer for surgery jumped by 20 per cent from 1990 to 2002, said Ar-

men Aprikian, chief urologist of the McGill University Health Centre.

"A 20-per-cent increase in the death rate is huge," said Aprikian, whose Quebec-wide study on bladder cancer is published in this month's Journal of Urology.

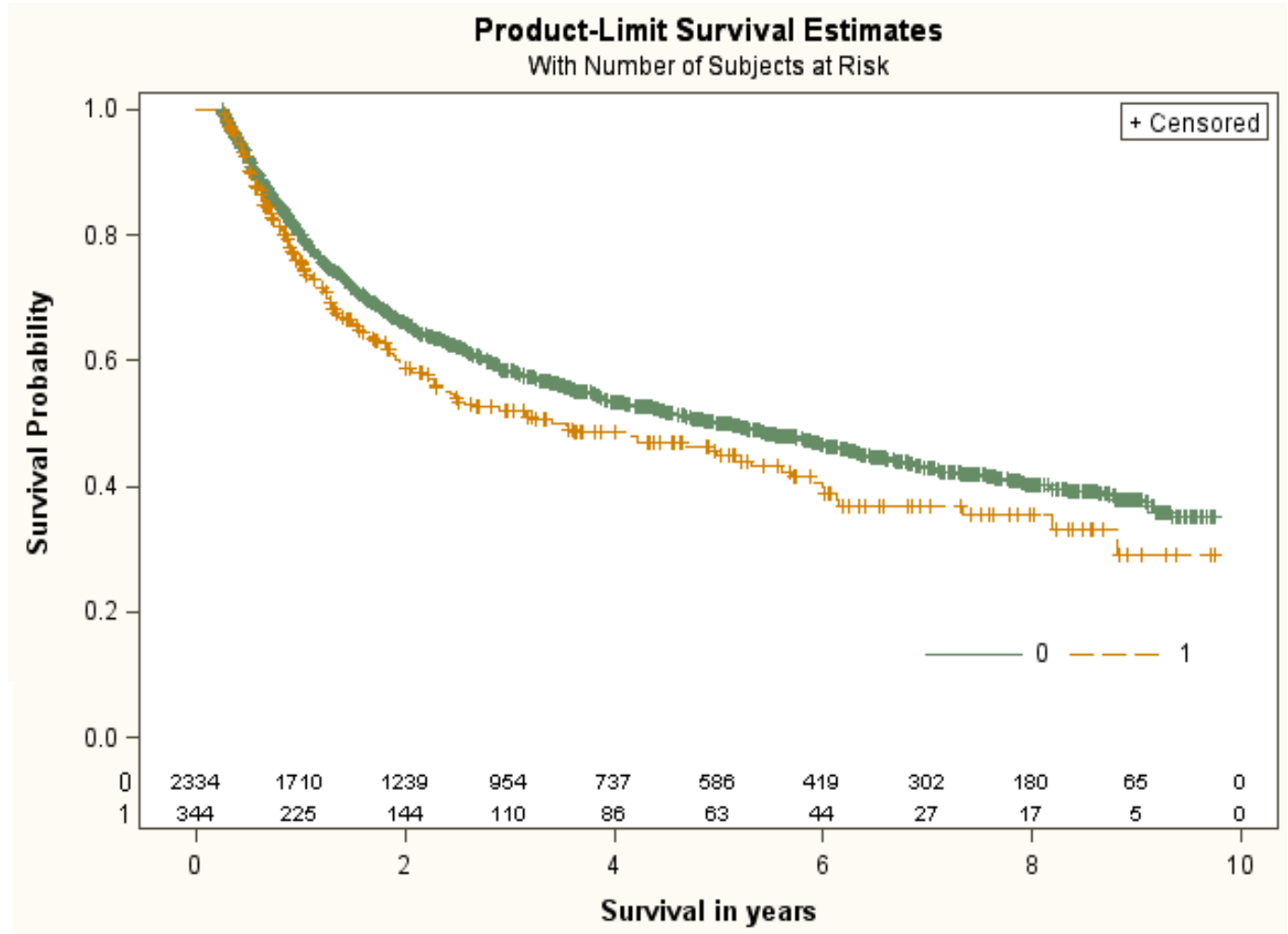
"It's clear some patients are waiting beyond the safety margin."

The study results are expected to influence provincial standards on wait times, health officials said.

Aprikian's study followed 1,592 patients.

It found the average delay time for surgery more than doubled in 12 years, to 50 days in 2002 from 23 days in 1990.

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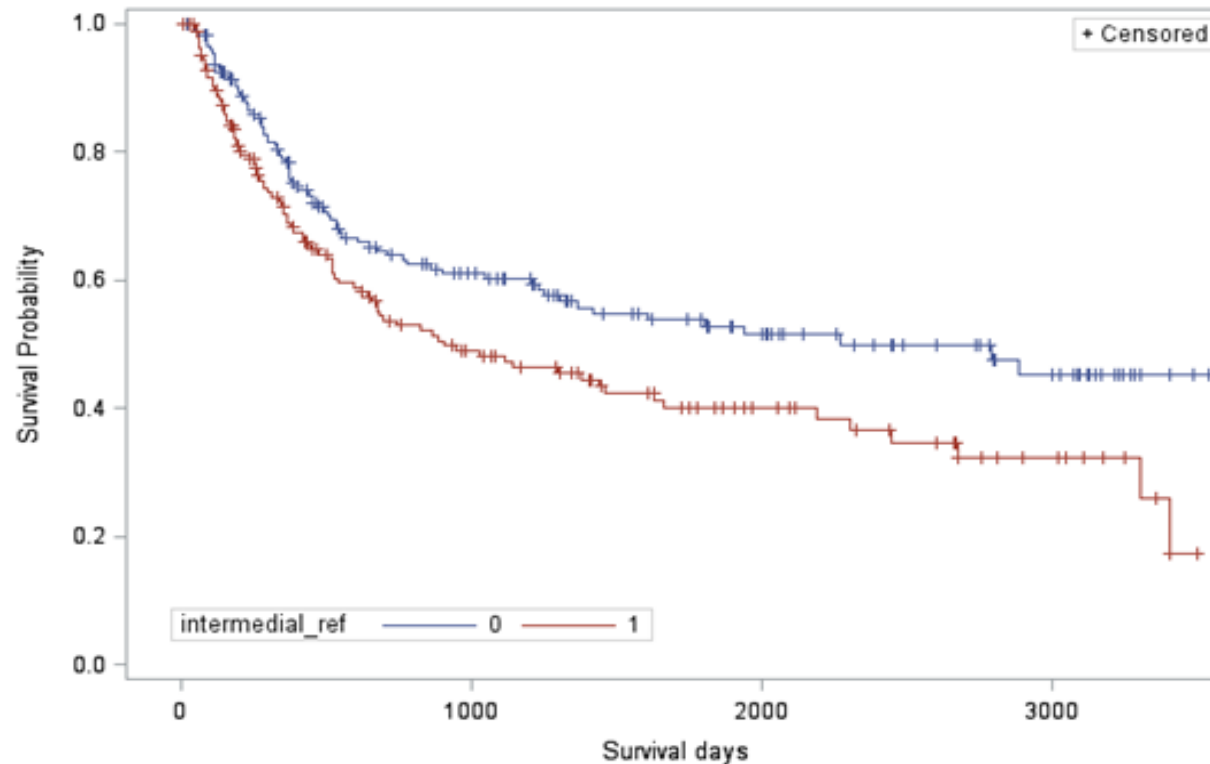
$P < 0.001$

1 - High: more than 12 weeks

Santos, Aprikian; BJU Int 2015

Delays in Referral and Overall Survival – Impact in Women much Greater

- ✓ 2– Impact of an indirect referral before the 1st urologist visit



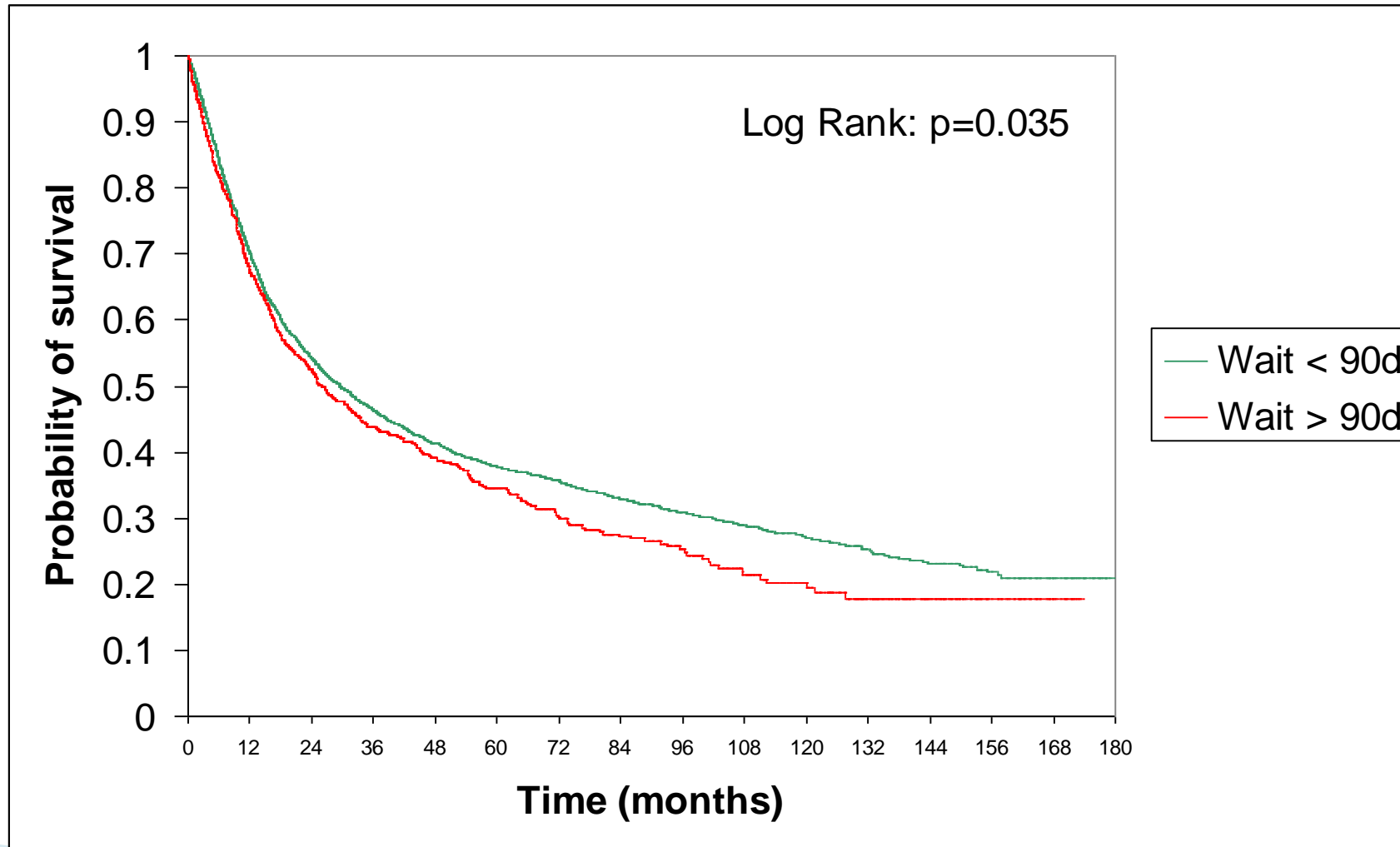
- ▶ HR= 1.55
(95% CI: 1.14–2.11)
- Women who had more than 5 FP or gynecologist visits before being referred to an urologist, had a 55% increased chance of mortality after RC.

Wait Times- Diagnosis to Cystectomy

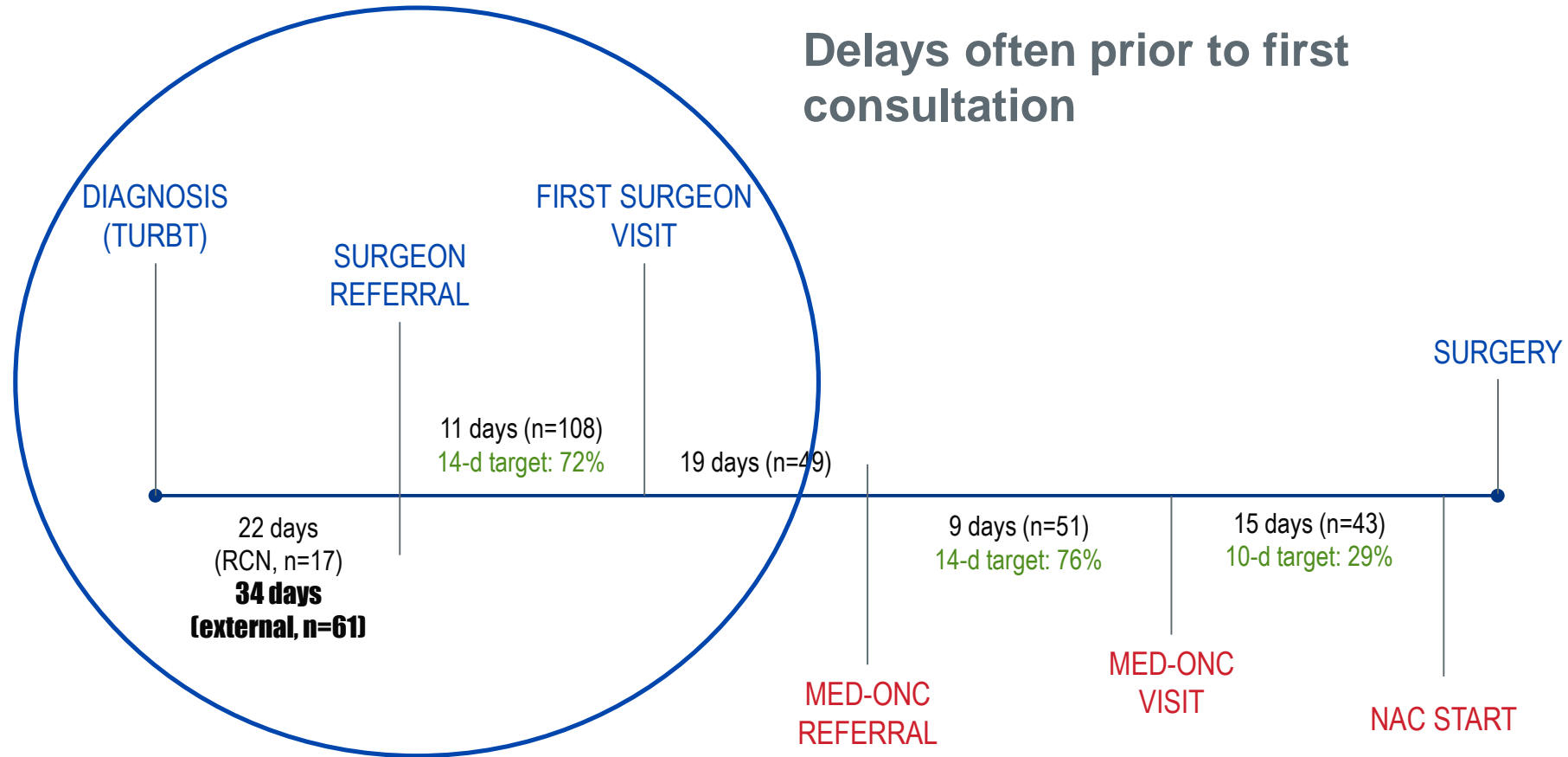


VARIABLE	VALUE	1994-1998 N=927	1999-2003 N=1,231	2004-2008 N=1,721	2009-2013 N=1,695	P- VALUE
Interval from diagnosis to date of cystectomy, months	Mean \pm SD	13.58 \pm 25.95	15.08 \pm 30.83	17.32 \pm 35.20	13.84 \pm 32.65	0.005
	Median (IQR)	3 (1-12)	3 (1-13)	3 (1-13)	4 (2-9)	<.001
	<u>01-3 mos</u>	531 (57%)	664 (54%)	884 (51%)	794 (47%)	<.001
	<u>04-6 mos</u>	103 (11%)	147 (12%)	218 (13%)	346 (20%)	
	<u>07-12 mos</u>	65 (7%)	110 (9%)	176 (10%)	198 (12%)	
	<u>13-24 mos</u>	81 (9%)	108 (9%)	134 (8%)	140 (8%)	
<u>>24 mos</u>	147 (16%)	202 (16%)	309 (18%)	217 (13%)		

Overall Survival – Delays to Surgery



TIMELINE (median days)



Postoperative Mortality, Outcomes & Hospital-Surgeon Volume

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Surgeon Volume and Operative Mortality in the United States

John D. Birkmeyer, M.D., Therese A. Stukel, Ph.D., Andrea E. Siewers, M.P.H.,
Philip P. Goodney, M.D., David E. Wennberg, M.D., M.P.H.,
and F. Lee Lucas, Ph.D.

N ENGL J MED 349;22 WWW.NEJM.ORG NOVEMBER 27, 2003

Do Cancer Centers Designated by the National Cancer Institute Have Better Surgical Outcomes?

CANCER February 1, 2005 / Volume 103 / Number 3

Linda S. Elting, Dr.P.H.¹
Curtis Pettaway, M.D.²
B. Nebiyu Bekele, Ph.D.¹
H. Barton Grossman, M.D.²
Catherine Cooksley, Dr.P.H.¹
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Correlation between Annual Volume of Cystectomy, Professional Staffing, and Outcomes

A Statewide, Population-Based Study

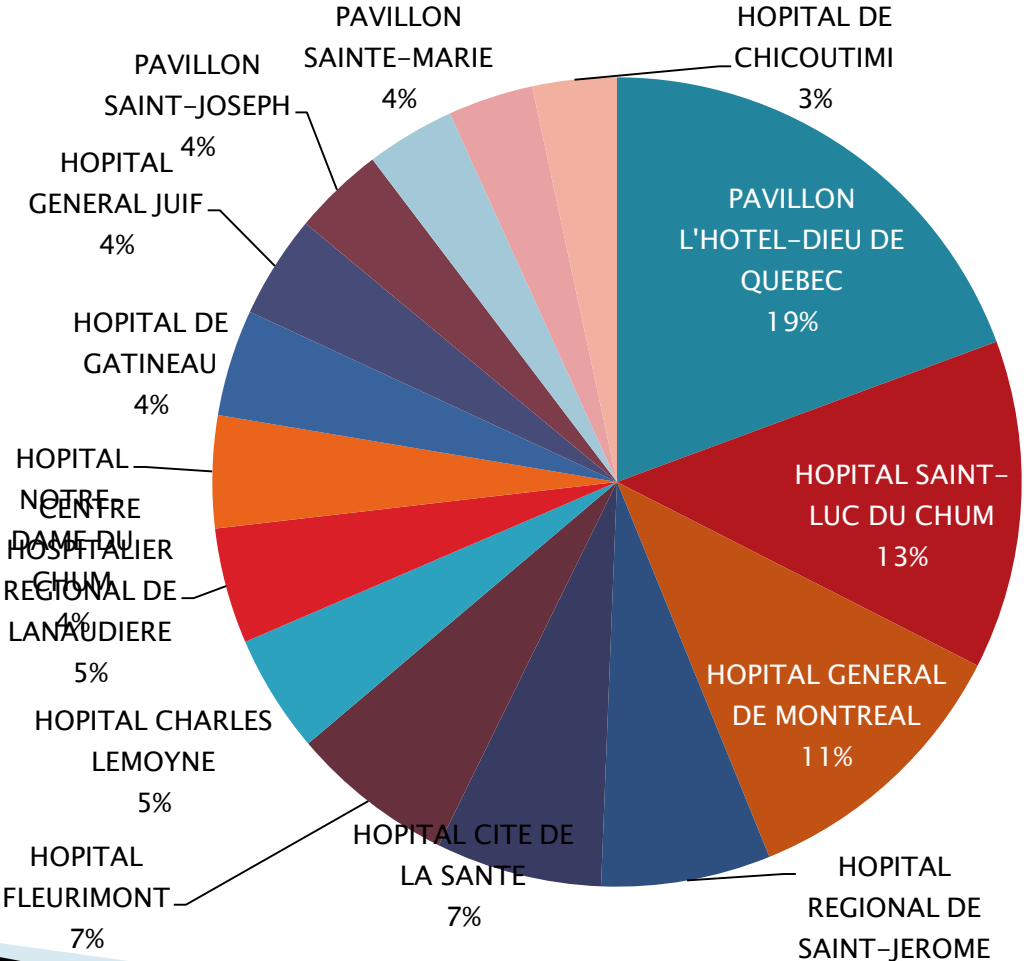
CANCER September 1, 2005 / Volume 104 / Number 5

Radical Cystectomy for Bladder Cancer in Quebec

3- Hospital facility and year of RC

N = 51 hospitals

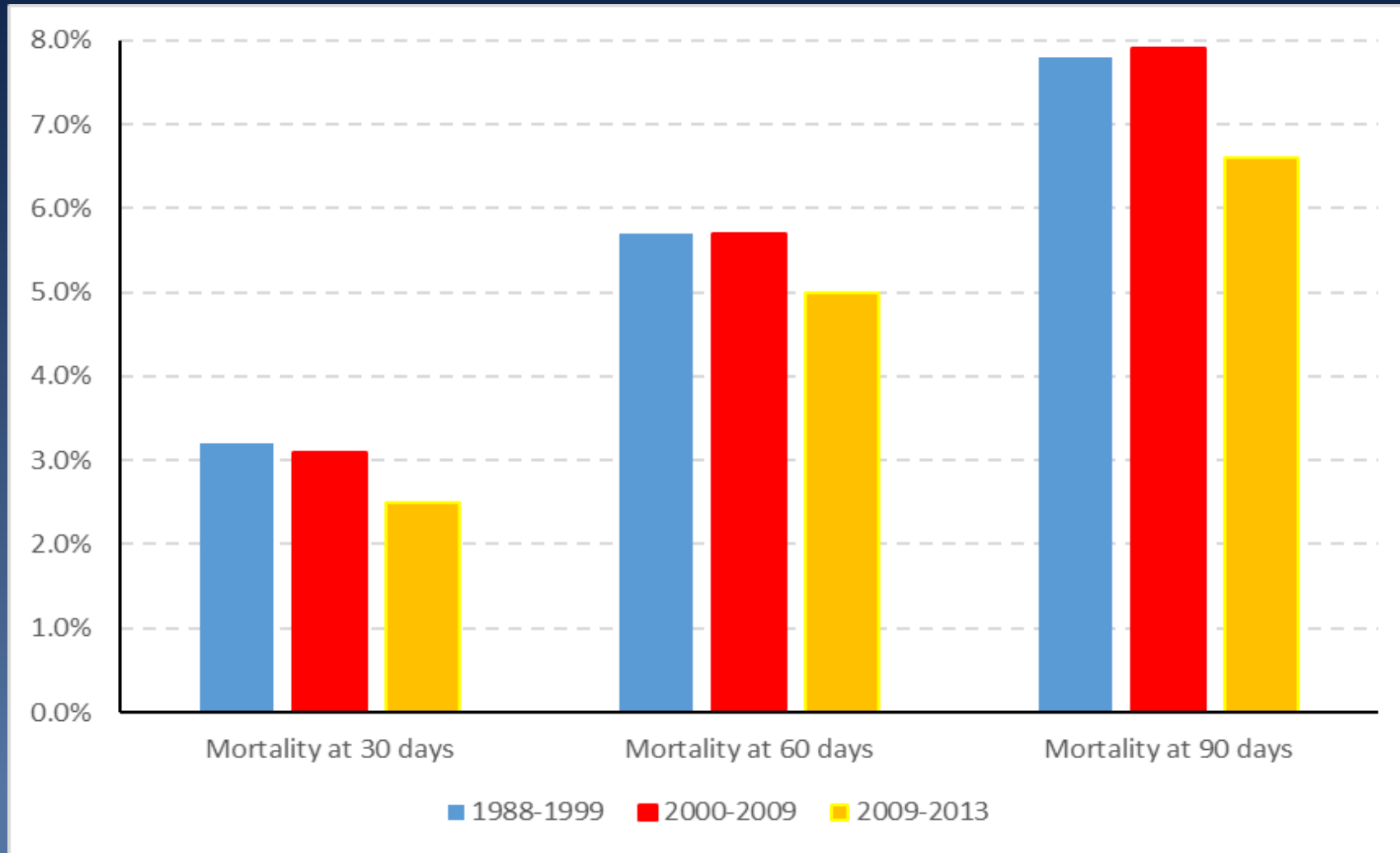
N = 122 surgeons



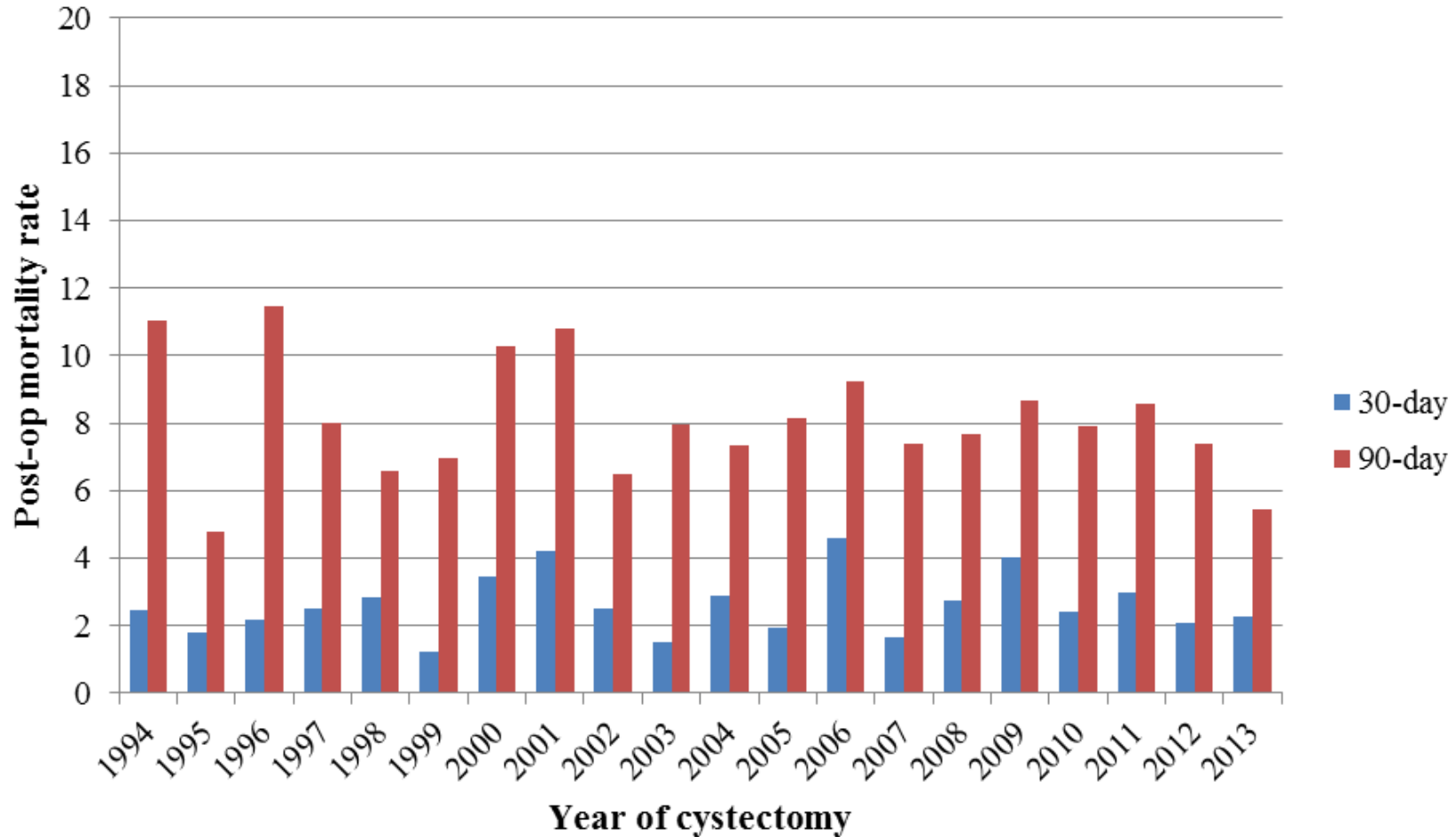
N = 2988

year	Frequency	Percent
2005	323	10.81
2006	311	10.41
2004	309	10.34
2008	309	10.34
2001	304	10.17
2007	302	10.11
2000	288	9.64
2002	287	9.61
2003	279	9.34
2009	276	9.24

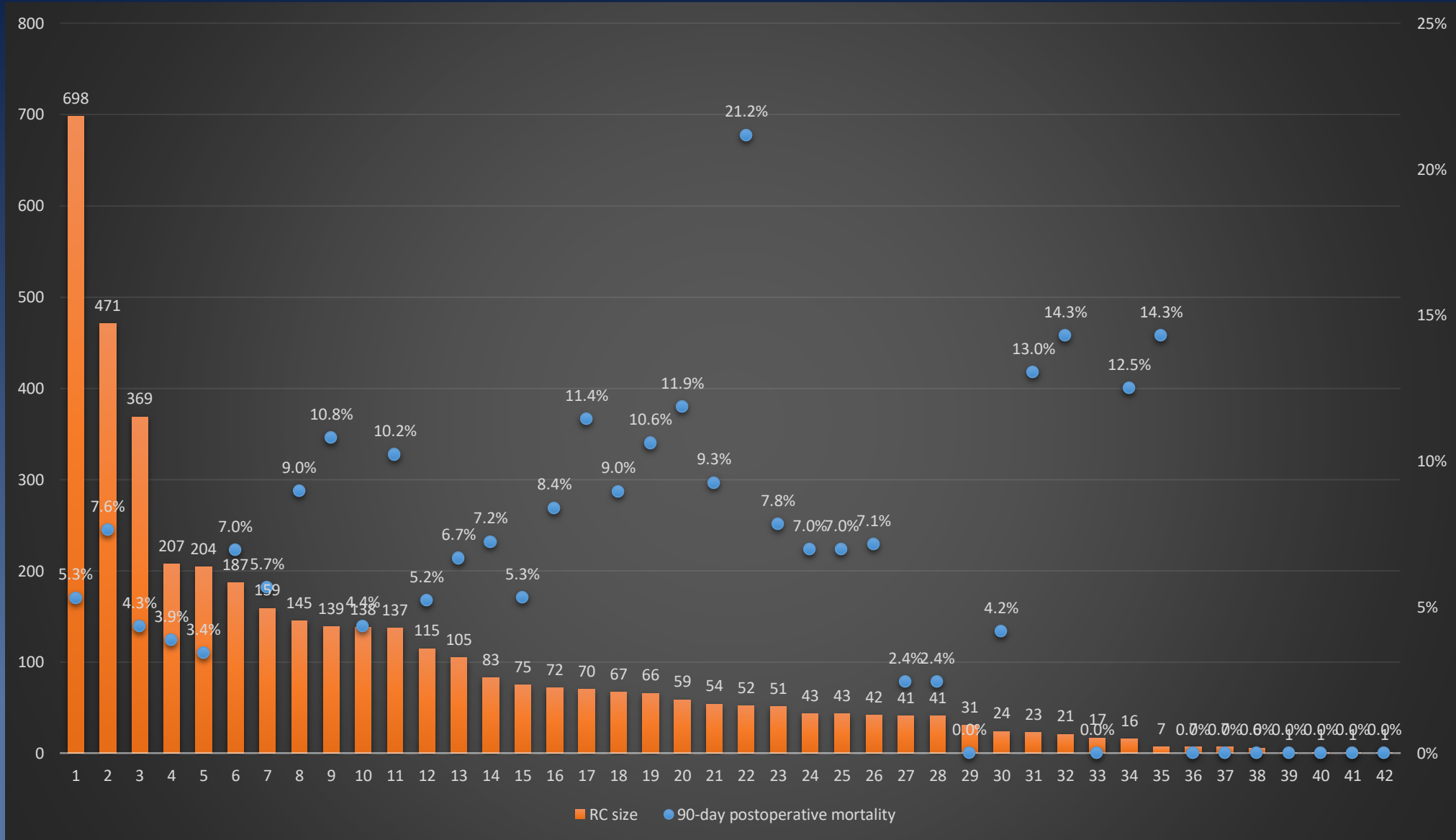
Post-Operative Mortality in Quebec



90-day Mortality ~5-9%



90-Day post-operative mortality after radical cystectomy for bladder cancer in Quebec - 2015



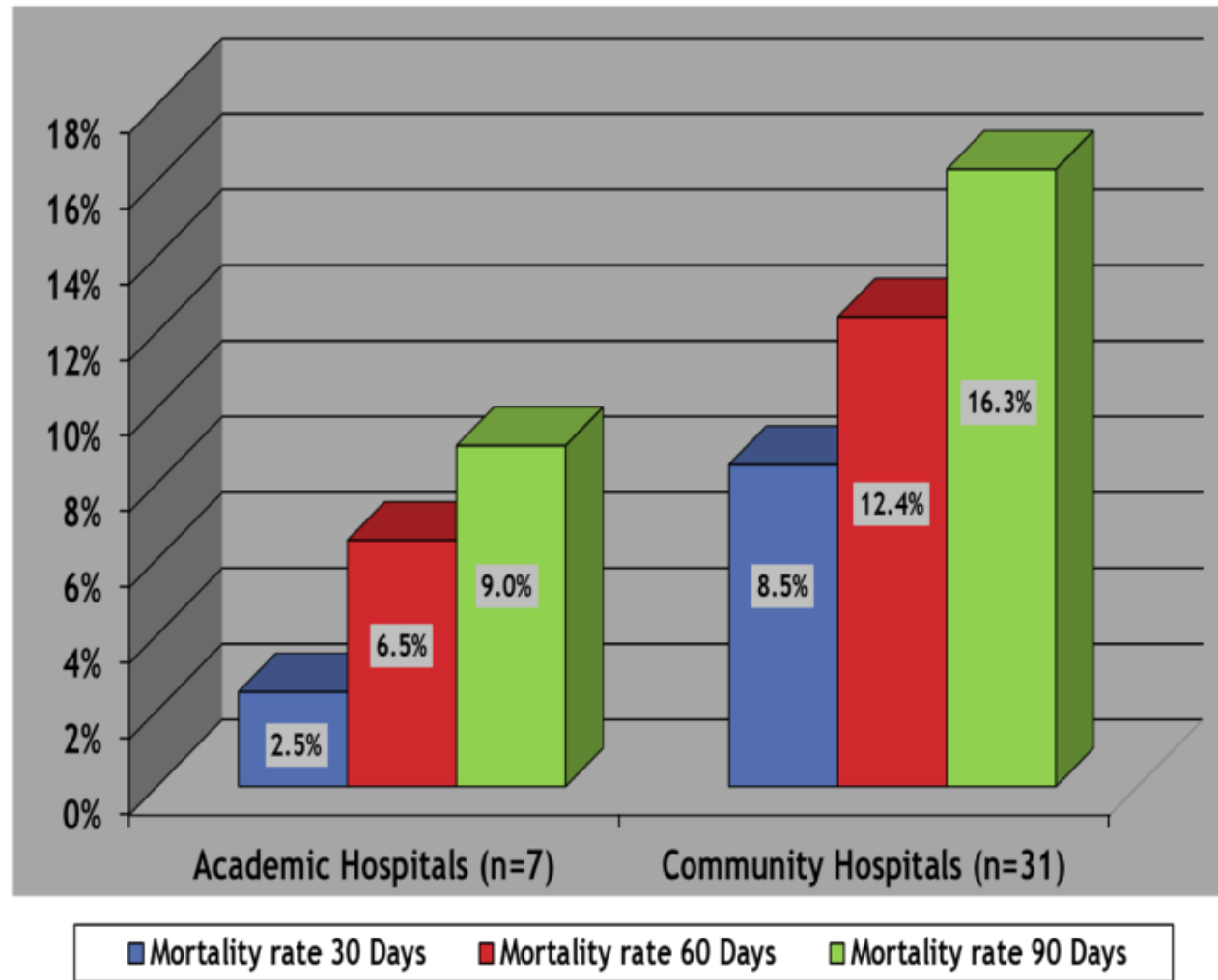
Post-Operative Mortality

	Rapport de hasards (Hazard ratio)	
	Univarié	Multivarié ¹
Année du CR (2010–2014)	0.74 (0.57–0.95)	0.76 (0.58–0.99)
Âge (par incrément de 5 ans)	1.33 (1.24–1.43)	1.33 (1.24–1.43)
Sexe (femme)	1.21 (0.93–1.58)	1.15 (0.87–1.51)
Région de résidence au moment du CR (référence: régions avec des villes de >40000 habitants)		
– Régions avec des villes de 100000–250000 habitants	0.92 (0.72–1.17)	0.78 (0.54–1.13)
– Régions rurales (plus grande ville de la région <100000 habitants)	0.80 (0.47–1.37)	0.68 (0.27–1.71)
Région de l'hôpital où CR a été conduit (référence: régions avec des villes de >40000 habitants)		
– Régions avec des villes de 100000–250000 habitants	1.21 (0.95–1.54)	1.25 (0.82–1.90)
– Régions rurales (plus grande ville de la région <100000 habitants)	1.03 (0.33–3.23)	1.59 (0.32–7.91)
Distance entre la résidence et l'hôpital (par incrément de 50km)	0.99 (0.95–1.04)	1.05 (0.97–1.13)
Le type d'hôpital (hôpitaux universitaires)	0.74 (0.58–0.94)	0.99 (0.66–1.48)
La taille de l'hôpital (référence: <250 lits)		
– 250–499 lits	0.78 (0.51–1.20)	0.78 (0.49–1.25)
– ≥500 lits	0.80 (0.52–1.23)	0.75 (0.46–1.22)
CR volume de l'hôpital, par année active (par incrément de 5 / an)	0.96 (0.92–1.00)	1.06 (0.97–1.16)
CR volume du chirurgien, par année active (par incrément de 5 / an)	0.84 (0.75–0.94)	0.74 (0.59–0.91)
Temps entre la dernière cystoscopie / TUR-B et CR (par incrément de 30 jours)	0.96 (0.89–1.03)	0.95 (0.87–1.04)

Radical Cystectomy in 80+ Years Old

Base line characteristics of the study population	
Cohort:	
- Number of patients:	275
Sex:	
- Males:	188 (68%)
- Females:	87 (32%)
Type of hospital where RC performed :	
- Academic hospitals (n=7) :	122 (44%)
- Community hospitals (n=31)	153 (56%)
Post Operative Complications (first 90 days) :	
- At least one complication:	91 (33%)
- More than one complication:	44 (16%)
- Urinary tract complications:	38 (13.8%)
- GI tract complications:	12 (4.3%)
- Wound complications:	8 (2.9%)
- CT scan in the 1 st six weeks	84 (30.5%)
Post Operative Mortality Rates :	
- Mortality at 30 days:	16 (5.8%)
- Mortality at 60 days:	27 (9.8%)
- Mortality at 90 days:	36 (13%)

Post operative mortality by hospital type ($p < 0.001$)



Post-Operative Hospital Duration



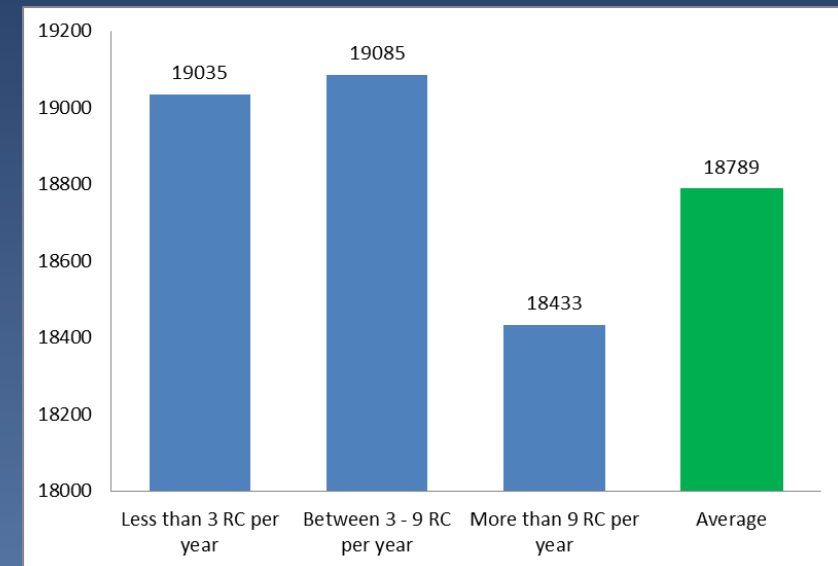
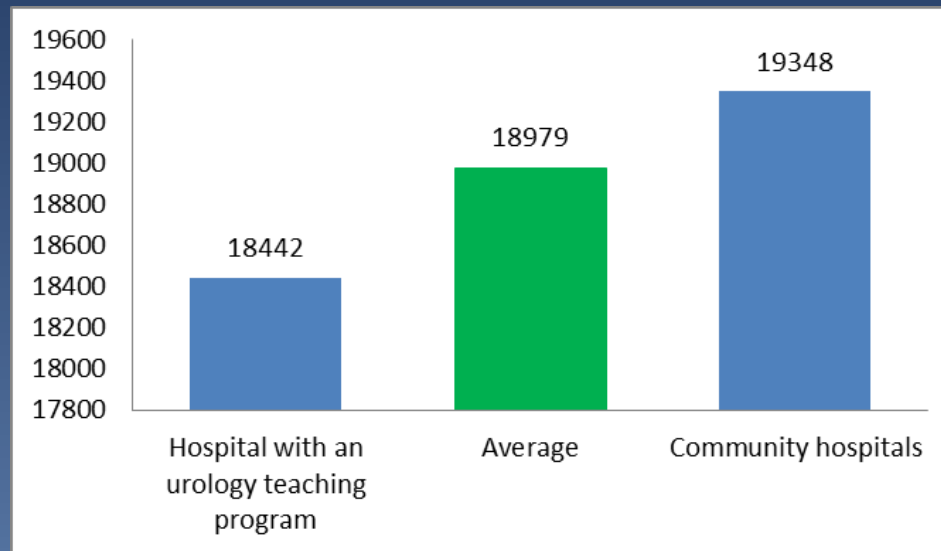
Baseline characteristics

- ▶ The number of hospitalized days in the year after radical cystectomy for bladder cancer is lower in:
 - younger patients
 - men
 - patients treated in centers with high annual radical cystectomy volumes

Patients (n)	3975
Median age group (inter-quartile range (IQR))	65-69 (60-79)
Sex (male)	2995 (75.3%)
Hospital size	
- 0-99 beds (small)	17 (0.4%)
- 100-249 beds (medium)	651 (16.4%)
- 250+ beds (large)	3307 (83.2%)
Median distance in km to hospital (IQR)	18.2 (7.2-62.1)
- # patients >100 km to hospital	814 (20.5%)
Median time (days) to discharge after surgery	13 (9-22)
Median number of hospitalized days	
- within 1 month after RC	15 (11-23)
- within 3 months after RC	16 (11-29)
- within 1 year after RC	21 (13-38)
Median number of cystectomies/year (IQR)	280 (267-303)
- 2000-2009	274 (263-287)
- 2009-2013	309 (303-315)
Median hospitals' annual RC load (range)	5.5 (2-47)
Median surgeons' annual RC load (range)	3.4 (1-23)

Medical Costs Associated with Radical Cystectomy in Quebec

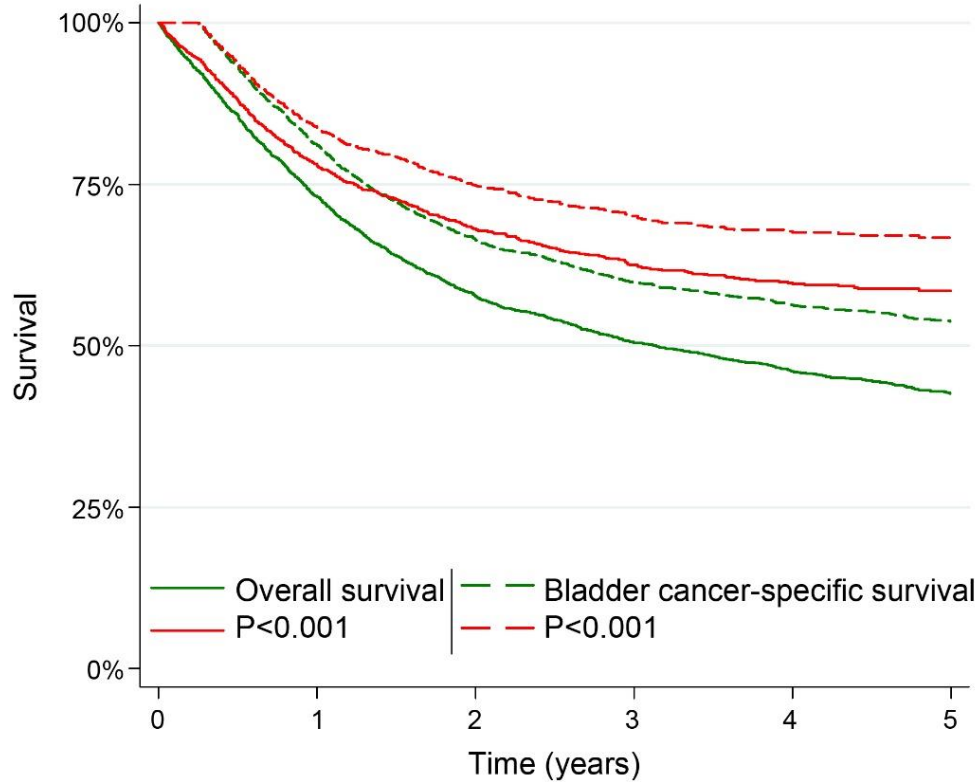
- Cost estimates
- N = 2759
- Average cost = \$18989 (range: \$16005 – \$25684)



Health-care services utilization and costs associated with radical cystectomy for bladder cancer: a descriptive population-based study in the province of Quebec, Canada.

Santos F1, Dragomir A2, Zakaria AS3, Kassouf W4, Aprikian A. BMC Health Services Research, 2015

Overall Survival



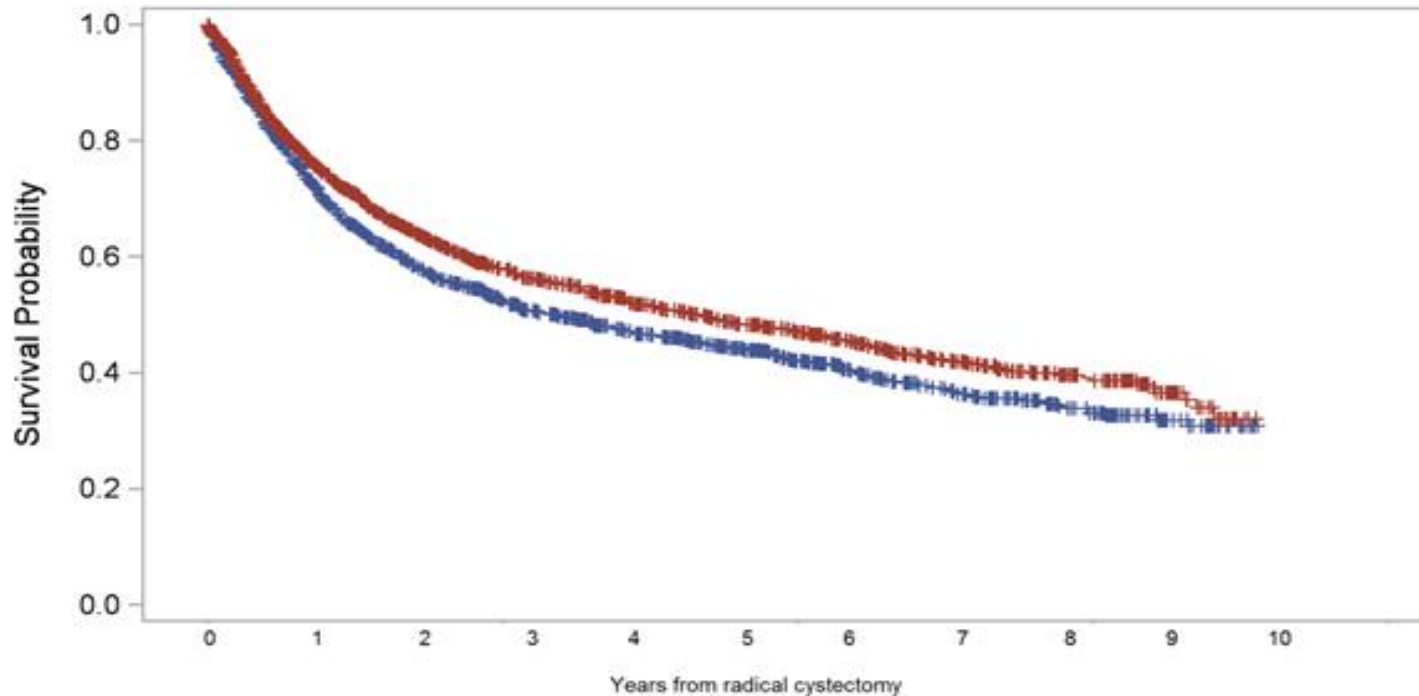
Number at risk:

Time (years)	0	1	2	3	4	5
2000-2009	2579	1876	1477	1286	1171	1081
2010-2014	1518	1143	857	590	371	201

Taux de survie à cinq ans	2000-2009	2010-2014
La survie spécifique du cancer de la vessie	55.5% (53.4%–57.4%)	61.3% (58.3%–64.2%)
La survie globale	42.7% (40.7%–44.6%)	50.9% (48.0%–53.8%)

Effect of High-Volume Hospital on Overall Survival ($p < 0.05$)

Santos, Aprikian, World J Urol 2016

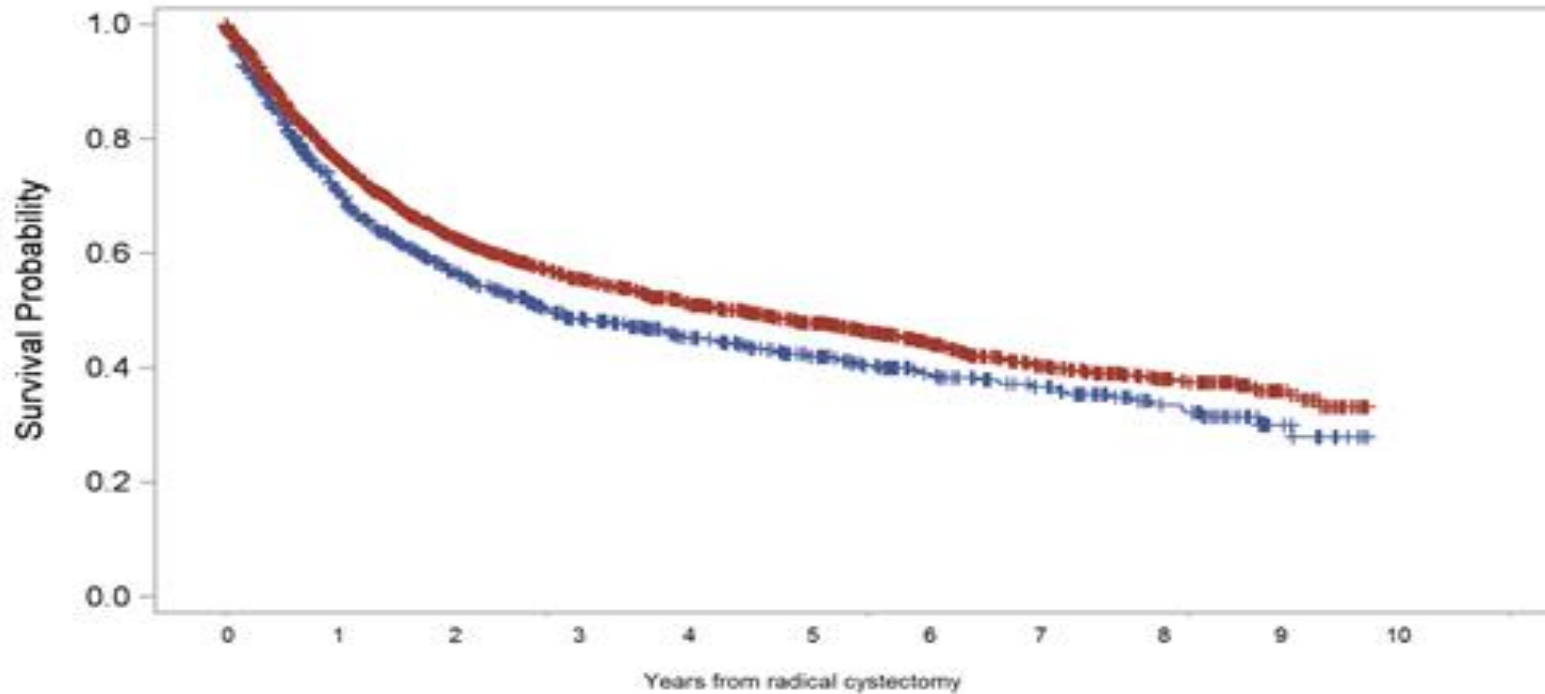


HR= 0.87
(0.78-0.97)

- Red curve: 3rd and 4th quartile of hospital volume distribution (> 15)
- Blue curve: 1st and 2nd quartile of hospital volume distribution (< 10)

Effect of High-Volume Hospital and Surgeon on Overall Survival

Santos, Aprikian, World J Urol 2016



HR= 0.80
(0.70-0.91)
P < 0.05

- Red curve: 3rd and 4th quartile of H-S volume distribution (> 7)
- Blue curve: 1st and 2nd quartile of H-S volume distribution (< 2)

Cancer. 2013 Oct 1;119(19):3546-54. doi: 10.1002/cncr.28235. Epub 2013 Jul 9.

Higher surgeon and hospital volume improves long-term survival after radical cystectomy.

Kulkarni GS¹, Urbach DR, Austin PC, Fleshner NE, Laupacis A.

	ONTARIO	QUEBEC
HOSPITAL LOAD ACROSS QUARTILES	2.1, 4.5, 10.4 and 26.1	5, 9.6, 17.5 and 36
SURGEON LOAD ACROSS QUARTILES	0.96, 2, 4.4 and 11.5	1, 2, 3.4 and 9
5-YEARS OVERALL SURVIVAL	35%	46%

Table 2. Early and late outcomes of 2802 patients with muscle-invasive bladder cancer by hospital and surgeon cystectomy volume quartiles*

	Hospital Volume			
	Q1, <4.1 Cases/y (N = 763)	Q2, 4.1-8.2 Cases/y (N = 730)	Q3, 8.3-20.0 Cases/y (N = 648)	Q4, >20.0 Cases/y (N = 661)
Median/mean LOS, d	16/13	16/12	16/11	13/9
Postoperative mortality, n (%)				
30-D mortality rate	26 (3)	20 (3)	15 (2)	10 (2)
90-D mortality date	76 (10)	77 (11)	47 (7)	44 (7)
Postoperative morbidity, n (%) [†]				
30-D readmissions	104 (14)	85 (12)	111 (17)	124 (19)
90-D readmissions	236 (31)	200 (27)	206 (32)	254 (38)
5-Y OS (95% CI), % [‡]	27 (24-31)	28 (25-32)	29 (26-32)	35 (31-38)
5-Y CSS (95% CI) [‡]	31 (28-36)	32 (28-36)	35 (30-38)	38 (33-42)

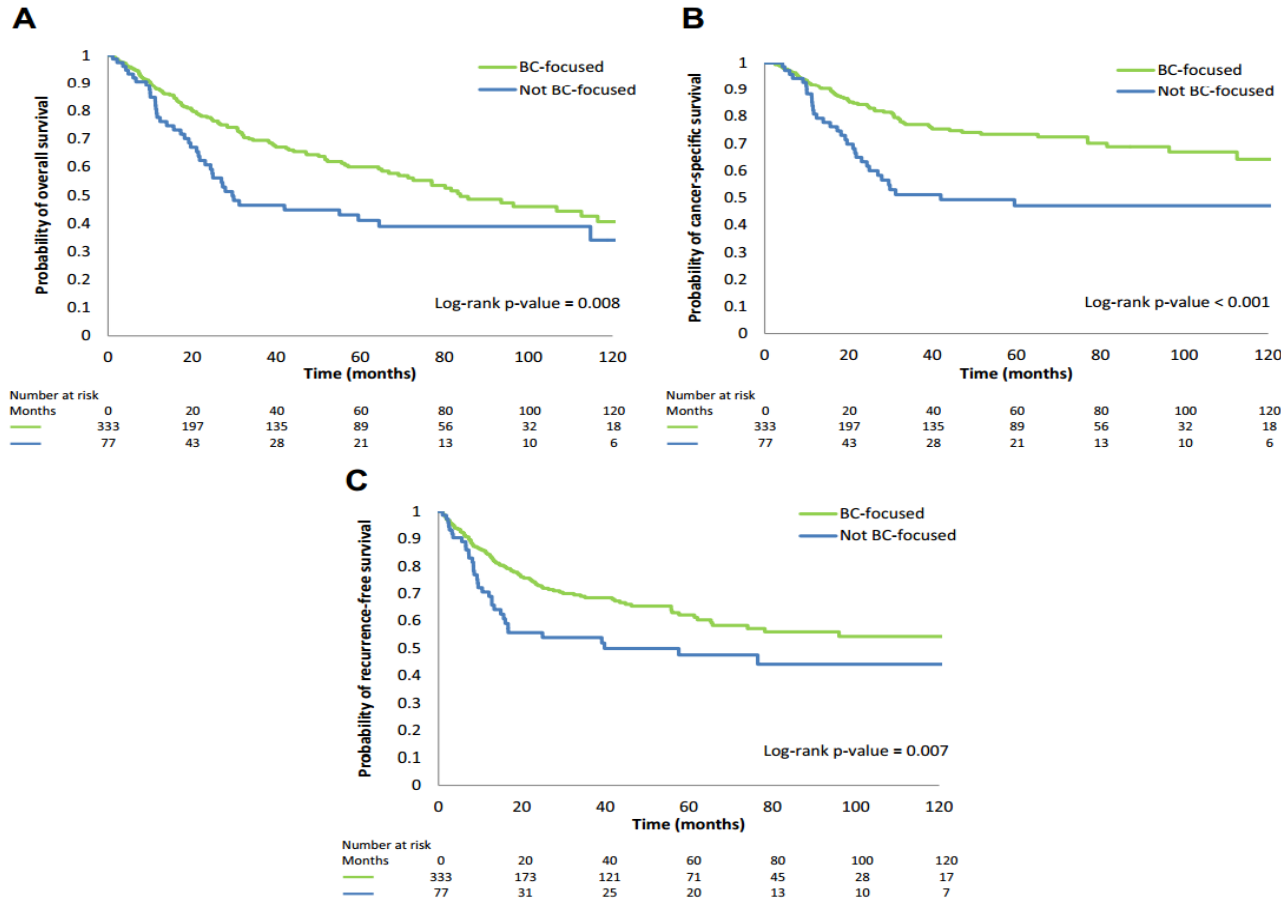
	Surgeon Volume			
	Q1, <1.3 Cases/y (N = 705)	Q2, 1.3-2.4 Cases/y (N = 797)	Q3, 2.5-6.2 Cases/y (N = 676)	Q4, >6.2 Cases/y (N = 624)
Mean/median LOS, d	17/12	16/12	15/11	13/10
Postoperative mortality, n (%)				
30-D mortality rate	22 (3)	23 (3)	16 (2)	10 (2)
90-D mortality date	79 (11)	69 (9)	56 (8)	40 (6)
Postoperative morbidity, n (%) [†]				
30-D readmissions	223 (32)	216 (27)	201 (30)	256 (41)
90-D readmissions	93 (13)	91 (11)	97 (14)	143 (23)
5-Y OS (95% CI), % [‡]	28 (25-32)	28 (24-31)	27 (24-31)	36 (32-40)
5-Y CSS (95% CI), % [‡]	31 (27-35)	33 (29-37)	33 (29-38)	39 (34-44)

The Importance of Surgeon Characteristics on Impacting Oncologic Outcomes for Patients Undergoing Radical Cystectomy

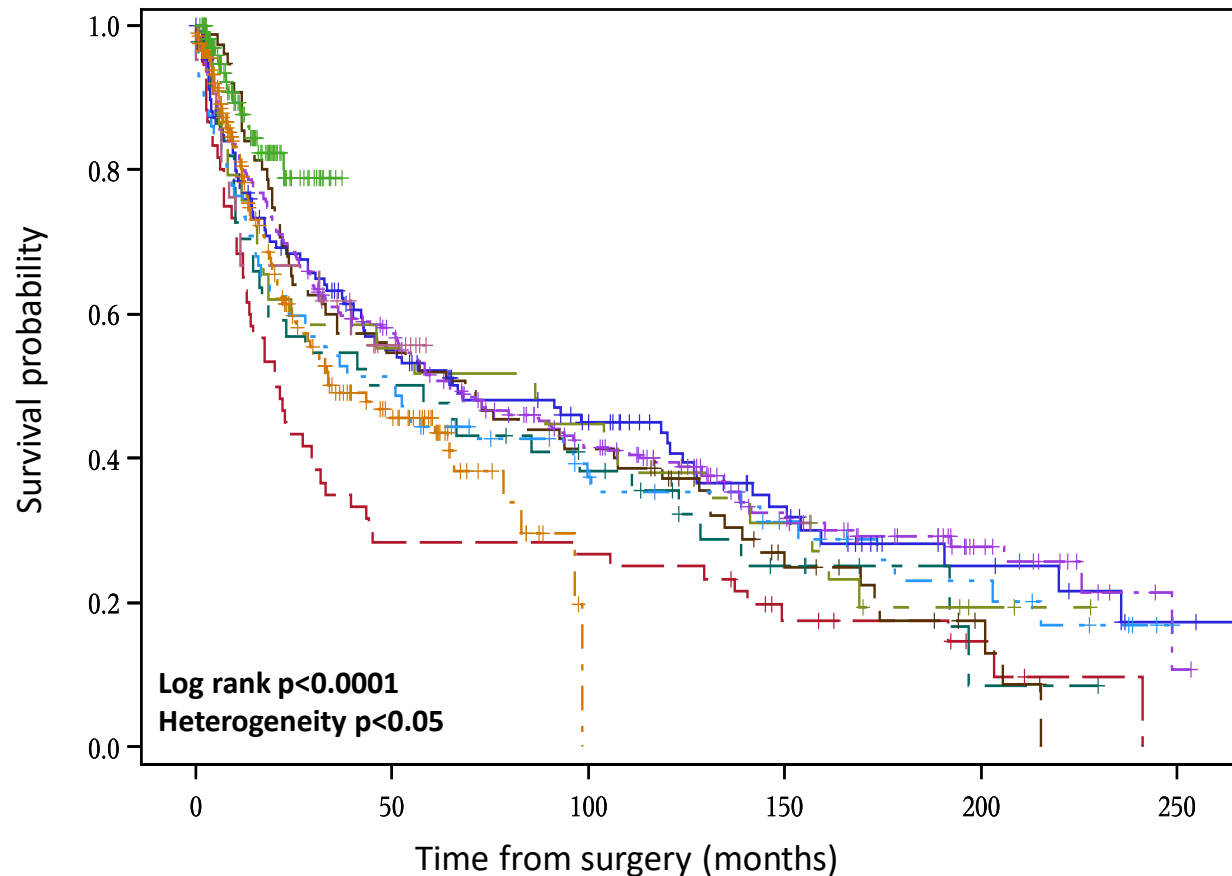


Bimal Bhindi,^{*,†} Julie Yu,[†] Cynthia Kuk,[†] Srikala S. Sridhar,[†] Robert J. Hamilton,[†] Antonio Finelli,[†] Michael A. S. Jewett,[‡] Andrew Evans,[†] Neil E. Fleshner,[§] Alexandre R. Zlotta^{||} and Girish S. Kulkarni[†]

From the Division of Urology, Department of Surgery (BB, RJH, AF, MASJ, NEF, ARZ, GSK), Department of Medical Oncology (SSS) and Department of Pathology (AE), University Health Network, Faculty of Medicine (JY), Institute for Clinical and Evaluative Sciences (GSK), University of Toronto, and Division of Urology, Department of Surgery, Mount Sinai Hospital (CK, ARZ), University of Toronto, Toronto, Ontario, Canada



Overall survival stratified by surgeon



Surgeon	2-year OS (%)
1	67
2	42
3	55
4	65
5	69
6	59
7	60
8	62
9	60
10	78

Figure 1. Kaplan-Meier estimate of OS stratified by surgeon. There was statistically significant between surgeon variation in OS. 3 surgeons had 2-year OS rates $>65\%$, whereas 6 surgeons had 2-year OS rates of 55-65%.

A. Fairey et al



90-day mortality rate

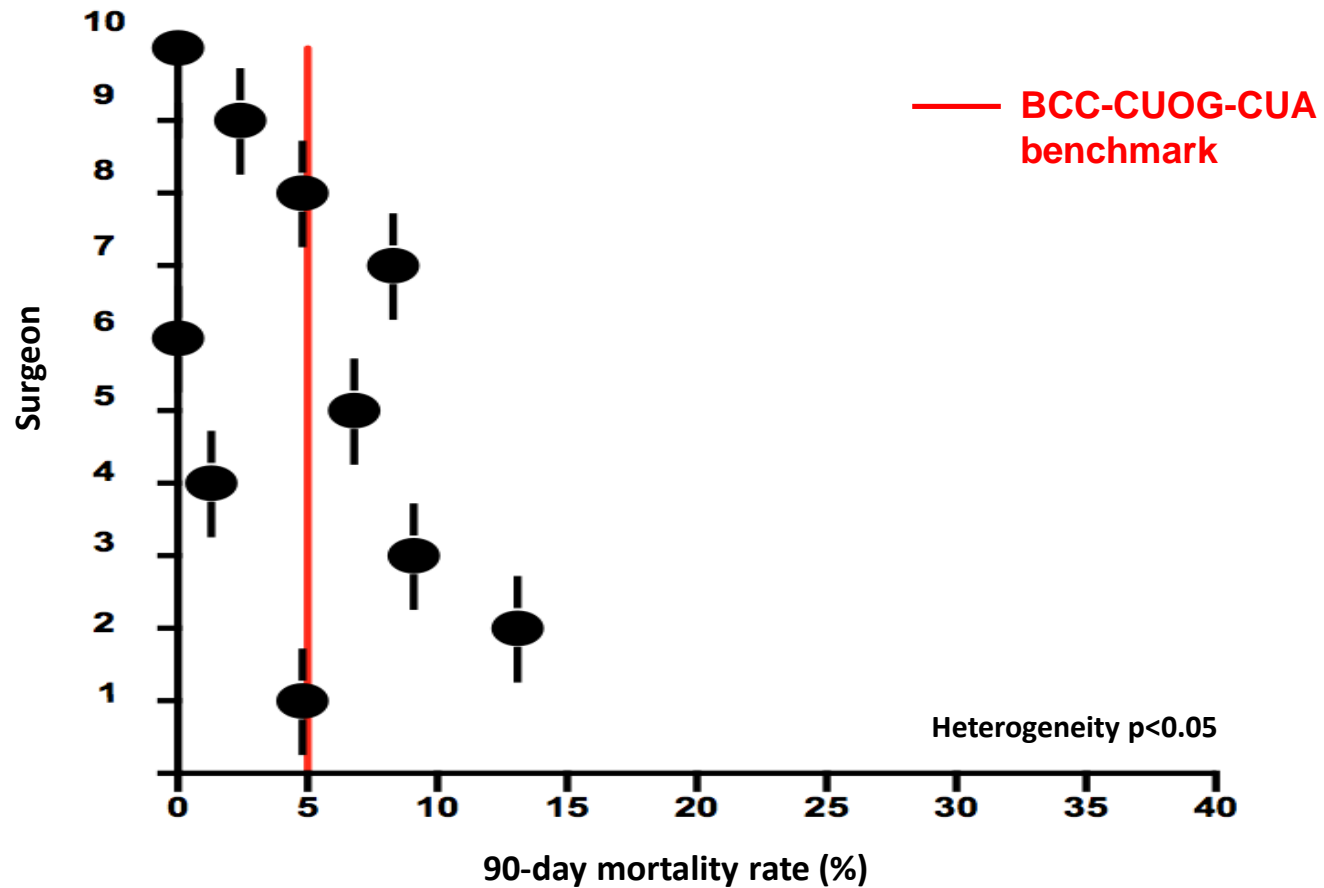


Figure 3. Between surgeon variation in 90-day mortality. There was statistically significant between surgeon variation in 90-day mortality rate. In addition, 4 out of 10 surgeons met the BCC-CUOG-CUA surgical quality performance indicator benchmark for 90-day mortality rate. 4 surgeons had 90-day mortality rate of <3% whereas 5 surgeons had 90-day mortality rate of $\geq 5\%$.

A. Fairey et al



Perioperative outcomes

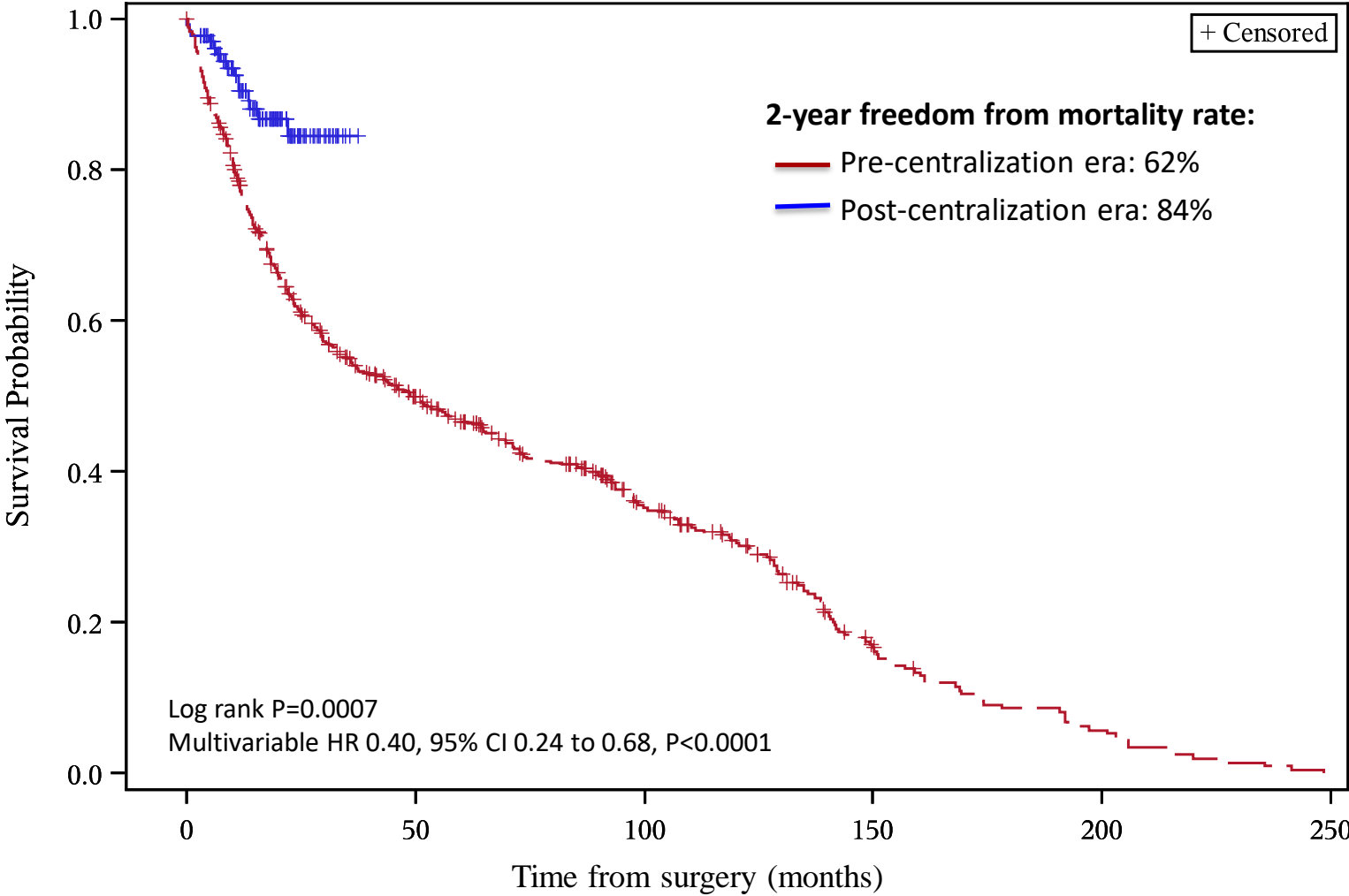
Variable	Pre-centralization	Post-centralization	P value
90-day mortality – no.(%)	33 (6.4)	2 (1.5)	0.02
90-day transfusion – no. (%)	237 (59)	7 (5)	<0.01

Legend: Multivariable analysis showed an independent association between treatment in post-centralization era and decreased 90-day mortality (OR 0.23, 95% CI 0.06 to 0.99, P=0.049).

A. Fairey et al



Freedom from mortality stratified by era



GUIDELINES

- Few recommendations in Guidelines
- EAU
 - Higher surgeon and hospital volume decrease morbidity and mortality (LOE 3)
 - Surgical outcomes associated with provider volume (LOE 2)
 - No delay of wait time to cystectomy > 3 months (Grade B)



CPAC Report on Surgical Oncology – Health Canada

- Pan-Canadian analysis (except Quebec), 2002-2012
- Esophageal, pancreatic, liver, lung, ovarian cancer surgery
- Higher volumes correlated with less post-op mortality and length of stay
- For every 10-case increase in volume leads to a 10-20% decrease in post-op mortality
- Recommend > 10-50 procedures per year per surgeon
- Prevent deaths



Surgical Oncology Re-Organization

- Cancer Care Ontario – designated centres for thoracic surgery, hepatobiliary surgery
volume based (150 major lung/20 esophagus per year)
- Quebec – Thoracic Surgery (Deslauriers, Mulder et al)
centres of thoracic surgery – Sept 2015
volume based (MUHC, CHUM, CHUQ, CHUS, Sacre Coeur)

Experience with Centralization in Bladder Cancer

Centralisation of radical cystectomies for bladder cancer in England, a decade on from the 'Improving Outcomes Guidance': the case for super centralisation.

Afshar M et al. BJU Int 2017

RESULTS:

In all, 15 292 RCs were identified.

Improvement in 30-day mortality from 2.7% to 1.5% ($P = 0.024$).

Better 1-year mortality (21.5% vs 25.6%; $P < 0.001$), LoS (14 vs 16 days; $P < 0.001$), and re-intervention rates (30.0% vs 33.6%; $P < 0.001$).

Each single extra surgery per centre reduced the odds of death at 30 days by 1.5% (odds ratio [OR] 0.985, 95% confidence interval [CI] 0.977-0.992) and 1% at 1 year (OR 0.990, 95% CI 0.988-0.993), and significantly reduced rates of re-intervention.

BJUI
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“Volume” not an adequate indicator

- Access (delays)
- Volume
- Post-operative mortality
- Morbidity
- Pathology
- Disease-specific mortality
- Overall survival
- Cost

Surgical Scorecard



Bladder Cancer Quality-of-Care Consensus Meeting

Wes Kassouf, MD.

Chair

CONSENSUS STATEMENT

Improving patient journey and quality of care: Summary from the second Bladder Cancer Canada-Canadian Urological Association-Canadian Urologic Oncology Group (BCC-CUA-CUOG) bladder cancer quality of care consensus meeting

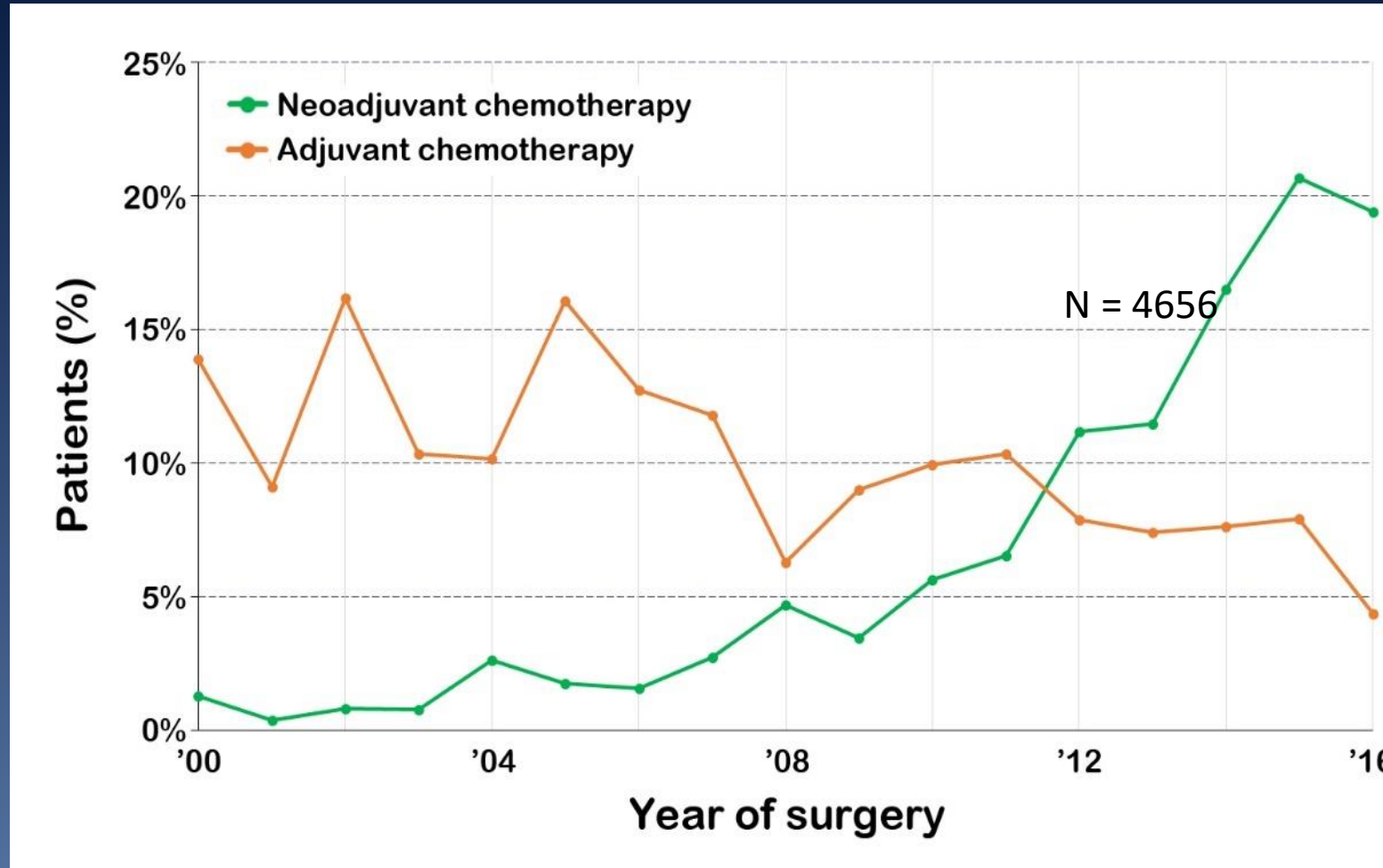
Wassim Kassouf, MD¹; Armen Aprikian, MD¹; Fred Saad, MD²; Rodney H. Breau, MD³; Girish Kulkarni, MD⁴; David M. Guttman⁵; Ken Bagshaw⁵; Jonathan Izawa, MD⁶; Libni Eapen, MD⁷; Adrian Fairey, MD⁸; Alan So, MD⁹; Scott North, MD¹⁰; Ricardo Rendon, MD¹¹; Srikala S. Sridhar, MD¹²; Fadi Brimo, MD¹³; Peter Chung, MD¹⁴; Darrel Drachenberg, MD¹⁵; Yves Fradet, MD¹⁶; Niels Jacobsen, MD⁸; Chris Morash, MD³; Bobby Shayegan, MD¹⁷; Geoffrey Gotto, MD¹⁸; Alex Zlotta, MD⁴; Neil Fleshner, MD⁴; D. Robert Siemens, MD¹⁹; Peter C. Black, MD⁹

¹Department of Urology, McGill University Health Centre, Montreal, QC; ²Division of Urology, University of Montreal, Montreal, QC; ³Division of Urology, University of Ottawa, Ottawa, ON; ⁴Departments of Surgery (Urology), Princess Margaret Cancer Centre and the University Health Network, University of Toronto, Toronto, ON; ⁵Patient representatives, Bladder Cancer Canada; ⁶Division of Urology, Western University, London, ON; ⁷Division of Radiation Oncology, University of Ottawa, Ottawa, ON; ⁸Division of Urology, University of Alberta, Edmonton, AB; ⁹Department of Urologic Sciences, University of British Columbia, Vancouver, BC; ¹⁰Division of Medical Oncology, University of Alberta, Edmonton, AB; ¹¹Division of Urology, Dalhousie University, Halifax, NS; ¹²Departments of Medical Oncology, Princess Margaret Cancer Centre and the University Health Network, University of Toronto, Toronto, ON; ¹³Department of Pathology, McGill University Health Centre, Montreal, QC; ¹⁴Departments of Radiation Oncology, Princess Margaret Cancer Centre and the University Health Network, University of Toronto, Toronto, ON; ¹⁵Division of Urology, University of Manitoba, Winnipeg, MB; ¹⁶Division of Urology, Laval University, Quebec City, QC; ¹⁷Division of Urology, McMaster University, Hamilton, ON; ¹⁸Division of Urology, University of Calgary, Calgary, AB; ¹⁹Department of Urology, Queen's University, Kingston, ON; Canada

List of Quality Indicators

- Annual surgical volume of radical cystectomy by each surgeon performing this procedure (structure);
- Time from cystoscopy to TURBT (process);
- Time from TURBT to pathology report (process);
- Percent of patients without neoadjuvant chemotherapy who had radical cystectomy within six weeks of last TURBT (process);
- For patients with high-risk NMIBC, percent who had intravesical bacillus Calmette-Guerin (BCG) induction course with at least one year of maintenance (process);
- For patients with MIBC, percent who received any curative-intent definitive therapy (radical cystectomy or radiation-based therapy) (process);
- Percent of patients with adequate lymph node dissection defined as >14 nodes (process);
- Percent of patients with MIBC being referred to medical oncology preoperatively for consideration of neoadjuvant chemotherapy (process);
- For patients with MIBC and receiving neoadjuvant chemotherapy, percent who completed a minimum of three cycles of cisplatin-based combination therapy (process);
- Percent of metastatic patients offered second-line systemic therapy after receiving first-line chemotherapy (process);
- Percent of patients with MIBC on TURBT being referred to radiation oncology preoperatively for consideration of radiotherapy (process);
- Percent with positive soft tissue margin at radical cystectomy (outcome); and
- Percent of patients deceased within 90 days post-cystectomy (outcome).

Neoadjuvant Chemotherapy in Quebec

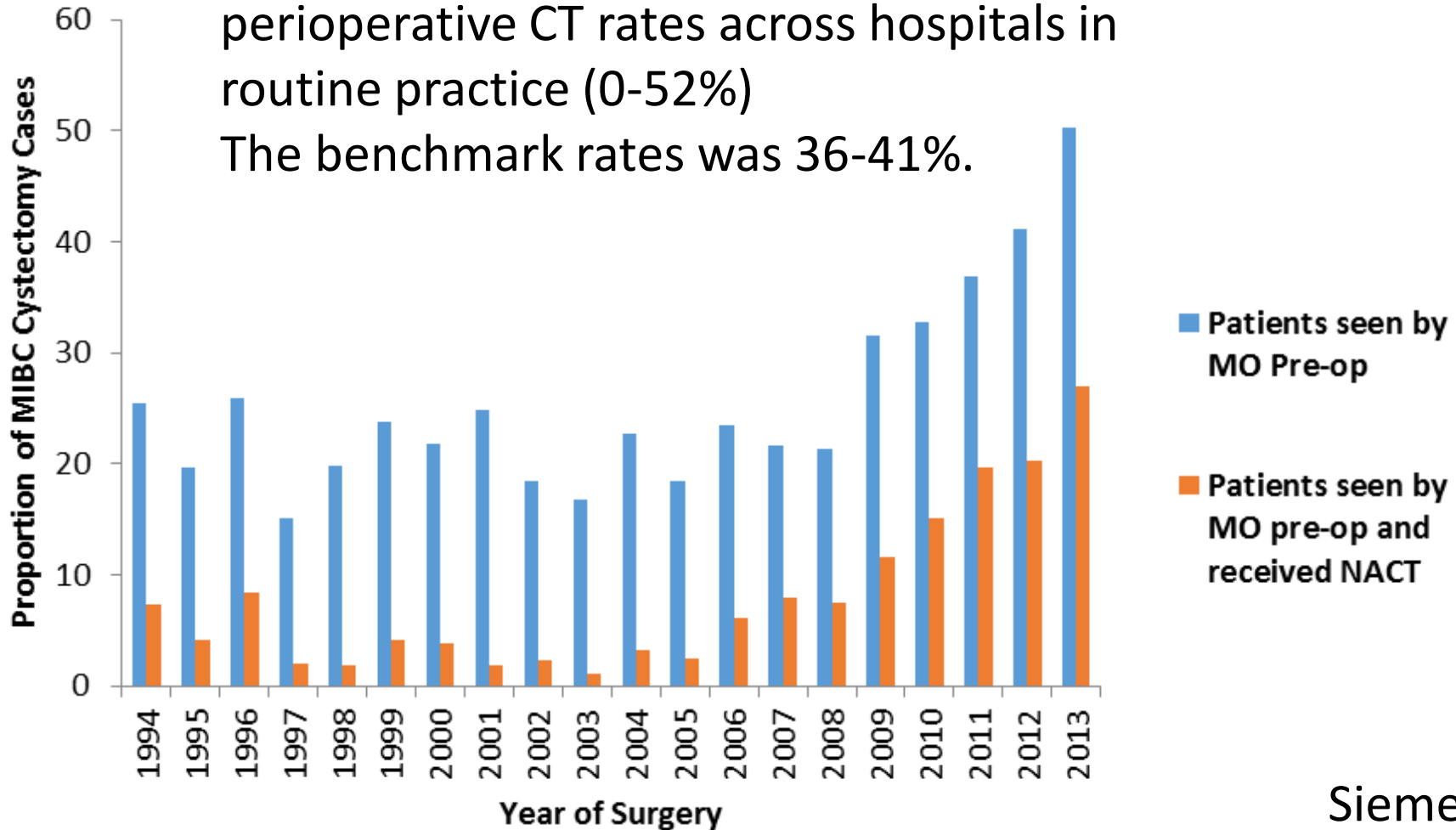


Academic hospital, younger age, and surgeon volume independently associated with NAC use

NACT Utilization



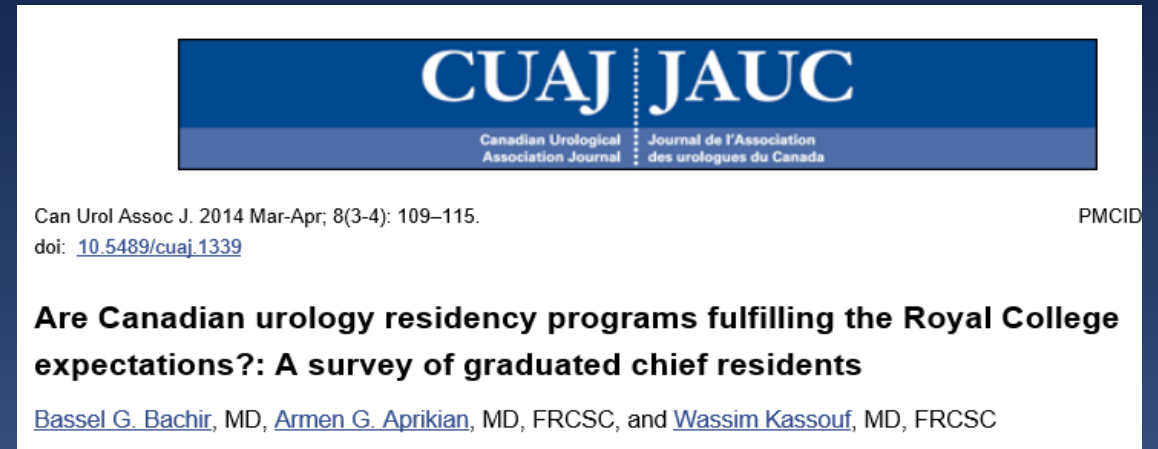
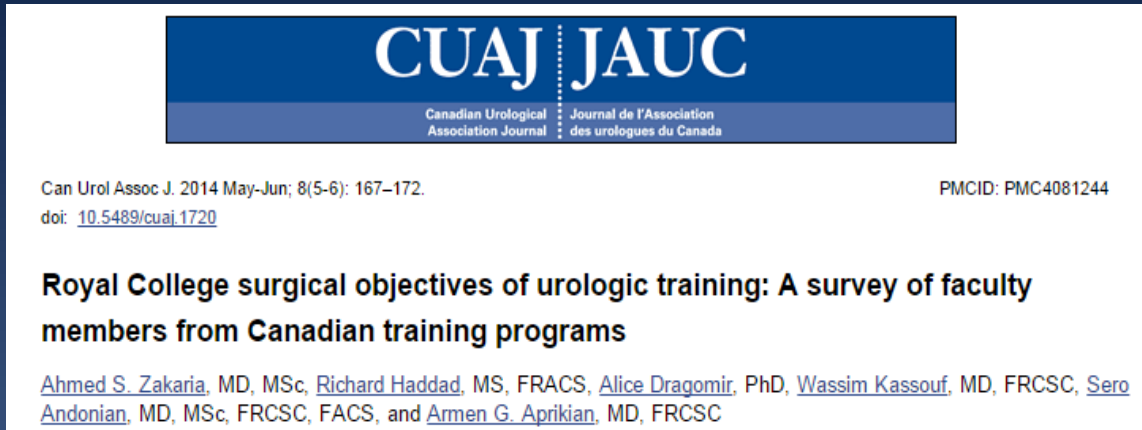
There is significant systematic variation in perioperative CT rates across hospitals in routine practice (0-52%)
The benchmark rates was 36-41%.



14 CBCIS Participating centres



Resident and Faculty Perception on the training of radical cystectomy in Canada



- Almost 50% of teaching faculty felt radical cystectomy should not be a level A procedure for training
- Almost 35% of graduating residents felt they did not achieve level A proficiency to perform radical cystoprostatectomy
- Almost 60% of graduating residents felt they did not achieve level A proficiency to perform anterior pelvic exenteration

Fellowship training improves patient outcomes

Systematic review with meta-analysis of the impact of surgical fellowship training on patient outcomes.

BJS

Johnston MJ1, Singh P2, Pucher PH2, Fitzgerald JE3, Aggarwal R4, Arora S1, Darzi A2.

Imperial College
London

- 23 large studies
- Meta-analysis
- Mortality rate and complications lower in hospitals training fellows and by fellowship trained surgeons

Subspecialization

- The urologist plays the key role
- Disease has become more complex to manage
 - Variant pathology
 - Molecular subtyping
 - Neoadjuvant chemotherapy
 - Organ preservation
- Surgery is only one part of a complex management scheme
- Systemic therapy, targeted therapy, immunotherapy: Opportunity to expand our specialty

The logo for European Urology, featuring the words "EUROPEAN" and "UROLOGY" stacked vertically in a sans-serif font. "EUROPEAN" is in a light blue color and "UROLOGY" is in a darker blue color.

Molecular Subtypes of Urothelial Bladder Cancer: Results from a Meta-cohort Analysis of 2411 Tumors, Eur Urol, 2019

Integration of Care



- All urologists (or a designate) should be integrated into a multiD team at a regional centre
- Regional centre should provide “case-manager, nurse navigator-link”
- Rapid access
- Combined clinics
- Self-assessment



- **At minimum: every case of MIBC should be discussed at a Tumour Board/Multidisciplinary Team**

