

Do procedure codes within population-based administrative datasets accurately identify patients undergoing cystectomy with urinary diversion?

James Ross MD FRCSC

Thesis submitted to the University of Ottawa
in partial fulfillment of the requirements
for the Master of Science Degree in Clinical Epidemiology

Department of Epidemiology and Public Health
Faculty of Medicine
University of Ottawa

© James Ross, Ottawa, Ontario, 2024

Table of Contents

1. Abstract	viii
1.1. Introduction	viii
1.2. Methods.....	viii
1.3. Results	ix
1.4. Conclusions	x
2. Legend	x
3. Acknowledgements	xi
4. Introduction	1
4.1. Overview of Cystectomy and Urinary Diversion.....	1
4.2. Morbidity of Cystectomy and Urinary Diversion	2
4.3. Use of Large Administrative Databases to Study Cystectomy and Diversion	3
4.4. Overview of ICES	6
4.5. Existing Studies Using Large Administrative Databases to Study Cystectomy in Ontario	7
4.6. Existing Studies on the Accuracy of Cystectomy Coding.....	10
4.7. Rational for Thesis	14
5. Study Proposal	14
5.1. Significance of the Proposed Thesis.....	15
5.2. Study Questions	16
5.3. Study Hypotheses	16
6. Methods	17
6.1. Terminology.....	17
6.2. Study Objectives	19
6.3. Study Design Overview	20
6.4. Creating the Gold Standard Reference Cohort	21
6.5. Creating the Analytical Dataset	24
6.5.1. Identifying Every TOH Hospitalization During the Study Period	25
6.5.2. Determining Cystectomy Status Using Administrative Database Codes	25
6.5.3. Creating Study Co-Variates.....	27
6.5.4. Merging to Gold Standard Cohort (And Determining True Cystectomy Status)	29
6.6. Creating the Ottawa Cystectomy Identification Model (OCIM)	29
6.6.1. Modeling Method Selection.....	29
6.6.2. Determining Allowable Degrees of Freedom Based on Sample Size.....	31
6.6.3. OCIM Variable Selection.....	31
6.6.4. Fitting Continuous Co-Variables using Fractional Polynomial Terms	35

6.7. Measuring OCIM Performance	36
6.7.1. Discrimination	36
6.7.3. Calibration	38
6.7.4. Optimism Correction of Model Performance Measures	40
6.8. Creating and Calculating Accuracy Measures of Code Algorithm.....	41
6.8.1. Identifying Cystectomies Using Administrative Codes	41
6.8.2. Calculating Code Algorithm Accuracy	44
6.9. Calculating and Comparing Misclassification Bias	45
7. Results	47
7.1. Gold Standard Reference Cohort Description	47
7.2. Analytical Dataset Description	50
7.2.1. Difference in Baseline Co-Variables for Cystectomy vs. Non-Cystectomy Hospitalizations.....	50
7.3. Code Algorithm Accuracy	53
7.3.1. Cystectomy with Incontinent Diversion	53
7.3.2. Cystectomy with Continent Diversion	54
7.4. Fitting of Continuous Co-Variables	55
7.5. Creating the Ottawa Cystectomy Identification Model (OCIM)	56
7.6. The Ottawa Cystectomy Identification Model (OCIM)	58
7.7. Distribution of Predicted Probabilities	61
7.8. Model Accuracy	63
7.8.1. Model Discrimination	63
7.8.2. Model Calibration.....	63
7.9. Assessment of Misclassification Bias	66
8. Discussion	70
8.1. Summary of Results	70
8.2. Notable Results.....	70
8.2.1. Accuracy Measures of Coding Algorithms.....	70
8.2.2. OCIM Accuracy	73
8.2.3. Differences in Misclassification Bias.....	75
8.3. Study Limitations	77
8.4. Next Steps.....	79
9. References.....	81

Table Index

Table 1. 2x2 frequency table for a hypothetical database of 10,000 patients with a 1% prevalence of cystectomy using a code algorithm with a sensitivity and specificity of 90%.	5
Table 2. Description and grading of published cystectomy cohort studies using large administrative datasets.	8
Table 3. 2x2 frequency table for the code algorithm proposed by Lyon et al. for identification of radical cystectomy.	11
Table 4. 2x2 frequency table for the ICD-9 code algorithm used by Tan et al. for identification of cystectomy with any type urinary diversion.	12
Table 5. 2x2 frequency table for code algorithm used by Tan et al. for identification of cystectomy with continent urinary diversion.	13
Table 6. List of TOH-specific procedure codes within the SIMS registry used to create the gold standard cohort.	24
Table 7. CCI and OHIP coding used to identify cystectomy with incontinent or continent urinary diversion.	26
Table 8. Definitions for all co-variables contained within the final analytical dataset.	28
Table 9. A list of co-variables thought to be predictive of cystectomy and urinary diversion and their rank of perceived importance.	33
Table 10. Code algorithm for identifying patients undergoing cystectomy with incontinent or continent urinary diversion.	43
Table 11. 2x2 frequency table for code status vs true cystectomy status.	44
Table 12. The actual procedures and number performed for patients misclassified as having a cystectomy within the SIMS registry.	49
Table 13. Description of co-variables among cystectomy and non-cystectomy admissions to TOH.	52
Table 14. Accuracy of code algorithm for cystectomy with incontinent diversion.	53
Table 15. Accuracy of code algorithm for cystectomy with continent diversion.	54
Table 16. Fractional polynomial transformations for continuous co-variables using the MFP8 macro in SAS.	56
Table 17. Co-variable selection for final predictive model using the log likelihood ratio test.	57

Table 18. Multinomial model parameter estimates and odds ratios for cystectomy with incontinent urinary diversion.	59
Table 19. Multinomial model parameter estimates and odds ratios for cystectomy with continent urinary diversion.	60
Table 20. Distribution of model probabilities based on true admission status for no cystectomy, cystectomy with incontinent urinary diversion, and cystectomy with continent urinary diversion.	62

Figure Index

Figure 1. Example of a ROC plot indicating different curves with better and worse model discrimination. 38

Figure 2. Example of a calibration plot demonstrating the calibration curve of a model with 95% confidence intervals as well as a 45-degree line representing perfect calibration as a comparison. 39

Figure 3. Flowchart demonstrating the creation of the Gold Standard Reference Cohort..... 48

Figure 4. Calibration curve for cystectomy with incontinent urinary diversion..... 64

Figure 5. Calibration curve for cystectomy with continent urinary diversion. 65

Figure 6. Forest plots demonstrating misclassification for cystectomy with incontinent urinary diversion using the predictive model with bootstrap imputation vs coding algorithm..... 68

Figure 7. Forest plots demonstrating misclassification for cystectomy with continent urinary diversion using the predictive model with bootstrap imputation vs coding algorithm..... 69

Equation Index

Equation 1. Sensitivity.....	5
Equation 2. Specificity	6
Equation 3. Positive Predictive Value	6
Equation 4. Negative Predictive Value.....	6
Equation 5. Calculating Outcome Probability from Logistic Regression	30
Equation 6. Likelihood Ratio Calculation	35
Equation 7. Calculation of Model Optimism Using Bootstrap Resampling	40
Equation 8. Calculation of Optimism-Corrected C-Statistic	41
Equation 9. Calculation of Optimism-Corrected ICI.....	41
Equation 10. Calculation of Misclassification Bias.....	46

1. Abstract

1.1. Introduction

Cystectomy with urinary diversion (i.e. bladder removal surgery) is commonly studied using large health administrative databases. These databases often use diagnoses or procedure codes with unknown accuracy to identify cystectomy patients, thereby resulting in significant misclassification bias. The primary objective of this study is to develop a predictive model that will return an accurate probability that patients recorded in the discharge abstract database have undergone cystectomy with urinary diversion, stratified by type of urinary diversion (continent vs incontinent). Secondary objectives of this study include: 1) to internally validate our predictive model to determine its accuracy using a cohort of all adults admitted to The Ottawa Hospital (TOH) within the study period; and 2) compare the accuracy of this model to that of code-based algorithms used previously in published studies to identify cystectomy.

1.2. Methods

A gold standard reference cohort (GSC) of all patients who underwent cystectomy and urinary diversion at TOH between 2009 and 2019 was created by using the SIMS registry within the TOH data warehouse which captures all primary surgical procedures performed. The GSC was then confirmed by manual chart review to ensure accuracy. Through ICES, the GSC was linked to the provincial Discharge Abstract Database (DAD), physician billing records (OHIP), and Ontario Cancer Registry (OCR) and a new combined dataset containing all admissions at TOH during the study period was created. Clinical information, billing, and intervention codes within these databases were reviewed and the co-variables thought to be predictive of

cystectomy were selected a priori. A multinomial logistic regression model (i.e. The Ottawa Cystectomy Identification Model or OCIM) was created using these co-variables to determine the probability of a patient undergoing cystectomy, stratified by continent vs incontinent diversion, during an admission in the DAD. Using the OCIM and bootstrap imputation methods, co-variable values and 95% confidence intervals were calculated. The values of these same co-variables were then measured using a code algorithm (the presence of either a procedure code or billing code for cystectomy with incontinent or continent diversion). Misclassification bias was then measured by comparing the values of co-variables using the OCIM or code algorithm to the true values obtained from the gold standard reference cohort.

1.3. Results

Five hundred patients were included in the GSC [median age 68.0 (IQR 13.0); 75.6% male; 55.6% incontinent diversion]. The prevalence of cystectomy within the DAD over the study period was 0.12% (500/428697 total admissions). Sensitivity and positive predictive values for cystectomy codes were 97.1% and 58.6% for incontinent diversions and 100.0% and 48.4% for continent diversions, respectively. The OCIM accurately predicted cystectomy with incontinent diversion (c-statistic [C] 0.999, Integrated Calibration Index [ICI] 0.000) and cystectomy with continent diversion (C:1.000, ICI 0.000) probabilities. Misclassification bias was lower when identifying cystectomy patients using the OCIM with bootstrap imputation compared to the use of the code algorithm alone.

1.4. Conclusions

A model using administrative data accurately returned the probability that cystectomy by diversion type occurred during a hospitalization. Using this model to impute cystectomy status minimized misclassification bias.

2. Legend

CCI	-	Canadian Classification of Interventions
CPT	-	Current Procedural Terminology
ICD	-	International Classification of Diseases
OHIP	-	Ontario Health Insurance Plan
ICES	-	Institute for Clinical Evaluative Sciences
DAD	-	Discharge Abstract Database
OCR	-	Ontario Cancer Registry
OCIM	-	Ottawa Cystectomy Identification Model
TOH	-	The Ottawa Hospital
REB	-	Research Ethics Board
TOHDW	-	The Ottawa Hospital Data Warehouse
OR	-	Operating Room
C-Statistic	-	Concordance Statistic
ROC	-	Receiver Operating Characteristics
ICI	-	Integrated Calibration Index

3. Acknowledgements

Dr. Carl van Walraven

For all of your help and support in the development and creation of this Thesis. I thoroughly enjoyed all of our early morning meetings and appreciate your availability and assistance. It was a pleasure to have you as a research mentor.

Dr. Luke Lavallee

For inspiring me to pursue research and this Master's degree and supporting me every step along the way. Also, for all of the teaching and personal support throughout my residency and fellowship.

Dr. Duane Hickling

For inspiring me to pursue training in functional and reconstructive urology and being a great mentor and friend.

Functional and Reconstructive Urology Fellowship

For the great training in this unique and exciting field of urology and for helping to achieve my goals and aspirations.

Division of Urology, The Ottawa Hospital

For urology training and support of my research interests.

Janice

For being the best and most supportive partner that I could have asked for. I wouldn't be where I am today without you.

4. Introduction

4.1. Overview of Cystectomy and Urinary Diversion

Urine is constantly being created in the kidneys and flows through the ureters to be stored in the bladder. During urination, urine is excreted from the bladder through the urethra.

Cystectomy with urinary diversion is the standard surgical treatment for both muscle invasive and high-risk non-muscle invasive bladder cancer. Less commonly, it is also a treatment option for patients with severe voiding dysfunction from benign bladder conditions including radiation cystitis, neurogenic lower urinary tract dysfunction, and interstitial cystitis/bladder pain syndrome. **Radical** cystectomy requires removal of the urinary bladder along with the prostate and seminal vesicles (in males) or the uterus, anterior vaginal wall, and ovaries (in females). A **simple** cystectomy involves removal of just the urinary bladder.^{1,2} Radical cystectomies are usually required for malignant indications while simple cystectomies are performed for benign (i.e. non-malignant) indications.

Following bladder removal, urinary diversion must be performed in order to maintain continuous urine drainage and preserve renal function. Urinary diversion is commonly performed using a segment of intestine to which the ureters are attached. This urinary diversion can be either continent or incontinent. A **continent** diversion usually includes a “neobladder” in which a segment of intestine is reconfigured in a spherical fashion and placed in the bladder’s usual location that is attached to the urethra. Therefore, patients store urine in the neobladder and then voluntarily pass urine when able. An alternative continent form of diversion, termed a “continent cutaneous diversion”, may be created wherein a catheterizable pouch is formed by

attaching the neobladder to the abdominal wall with a continent stoma through which patients can insert a catheter to drain the stored urine. An *incontinent* diversion includes a urinary conduit created by attaching a segment of intestine to the abdominal wall which continuously drains into an adherent stoma appliance. Less commonly, the ureters can be attached directly to the abdominal wall to allow for continuous drainage (i.e. cutaneous ureterostomy).³

Several factors may favor proceeding with a continent or incontinent diversion. These include patient comorbidities (the incontinent diversion with ileal conduit is a shorter surgery and preferred for more comorbid patients), renal or liver function (continent diversions are contraindicated in patients with significantly impaired renal and liver function due to risk of metabolic abnormalities), need for concomitant urethrectomy (due to inability to obtain a negative margin for cancer control), as well as the ability to self-catheterize (patients with neobladders may need to perform intermittent catheterization if unable to empty bladder via volitional voiding).³ Patient preference, including desire to maintain normal anatomy and avoid any external appliances, must also be considered.³⁻⁵ Other factors, including surgeon training and cystectomy volume, academic vs. community setting, as well as local practice patterns may also play a role in diversion selection.⁶

4.2. Morbidity of Cystectomy and Urinary Diversion

Cystectomy with urinary diversion may be associated with significant patient morbidity. Studies using single or multi-institutional cystectomy registries have reported an overall incidence of any post-operative complication within 90-days of cystectomy with urinary diversion between 30% and 67%, of which 5% to 13% were considered ‘major complications’

(Clavien-Dindo Grade 3-5).^{7,8} The 90-day incidence of all-cause mortality is between 1% and 9%.^{9,10} Finally, the incidence of unplanned readmission to hospital within 90-days of discharge following cystectomy with diversion varies between 26% and 34%.^{11,12} The type of urinary diversion may also be associated with post-operative outcomes, with some (but not all) studies demonstrating significantly higher odds of 30-day post-operative complications and readmission in patients undergoing continent vs. incontinent diversion, with odds ratios between 1.4 and 1.7.¹³⁻¹⁵ Further patient and procedure specific research is required to accurately quantify and predict outcome risk for patients undergoing cystectomy with urinary diversion.

4.3. Use of Large Administrative Databases to Study Cystectomy and Diversion

Many studies on cystectomy with urinary diversion have been conducted using large health-care administrative databases (Table 1). Health-care administrative databases record data required for the administration of health care delivery for regulatory or financial purposes. They have several potential advantages for studying cystectomy. First, they can potentially identify every case (i.e. cystectomy) conducted in a defined population. This aspect maximizes study sample sizes and increases the precision of statistical measures. Second, this population-based view avoids biases resulting from the use of select cases, which can occur when individual surgeons or centres are studied, allowing results to be more generalizable. Third, studies using health-care administrative databases are much less expensive and quicker than those requiring primary data collection.¹⁶ This is especially true for relatively uncommon diseases or procedures like cystectomy.

Most large health-care administrative databases use codes to identify diagnoses or procedures. Codes can be procedural (i.e. Canadian Classification of Intervention (CCI) codes, Current Procedural Terminology (CPT) codes), diagnostic (i.e. International Classification of Diseases (ICD) codes), or billing-based (i.e. Ontario Health Insurance Plan (OHIP) codes). Studies may use individual codes or combination of codes (i.e. code algorithms) to identify study cohorts. The accuracy of these codes, however, is not 100% and can cause misclassification bias (deviation from true results due to incorrect assignment of case status).¹⁷ For example, one study found that 21% for patients coded as having had an acute myocardial infarction using the ICD diagnostic codes did not actually meet the diagnostic criteria for this event.¹⁸ Another study demonstrated that only 67.6% of patients undergoing oral maxillofacial surgery were correctly coded for the surgery using the Healthcare Resource Group procedure coding system.¹⁹ Despite these known inaccuracies, most health-care administrative database studies continue to generate cohorts and conclusions using coding algorithms with unknown accuracy.²⁰ Performing large database research without knowledge of code accuracy measures prevents proper quantification of, and correction for, misclassification. This may cause misleading or invalid results and conclusions which could be harmful for patients and the health care system.

Misclassification bias is particularly relevant for studies using large health care administrative databases to study uncommon diagnoses or procedures. This is because unlike sensitivity and specificity, which are relatively constant regardless of prevalence, the positive predictive value of a code algorithm is strongly influenced by disease or procedure prevalence. For a condition or procedure with a low prevalence (i.e. a relatively uncommon surgery such as cystectomy), the positive predictive value of a test or code will be lower as compared to a

condition or procedure with a high prevalence. As a result, even a code with a high sensitivity and specificity may have a low positive predictive value (i.e. a low probability of actually having undergone a surgery or having a diagnosis if coded as such) if the baseline prevalence of the condition or procedure is low.

For example, assume a pre-test probability of 1% for having undergone a cystectomy and urinary diversion during any admission within a database containing information on 10,000 patients (i.e. only 100/10000 or 1% of patients within this hypothetical database truly underwent cystectomy and urinary diversion). If a coding algorithm used to identify cystectomy and urinary diversion patients had a sensitivity of 90%, a specificity of 90%, the calculated positive predictive value of the code algorithm (i.e. the probability of having actually undergone cystectomy with urinary diversion if coded as such) would only be 8.3%.

Table 1. 2x2 frequency table for a hypothetical database of 10,000 patients with a 1% prevalence of cystectomy using a code algorithm with a sensitivity and specificity of 90%.

		True Cystectomy Status		Total
		Cystectomy +	Cystectomy -	
Code Status	Code +	90	990	1080
	Code -	10	8910	8920
Total		100	9900	10000

Equation 1. Sensitivity

$$\begin{aligned}
 \text{Sensitivity} &= [\text{True Positives}] / [\text{True Positives} + \text{False Negatives}] * 100\% \\
 &= 90 / [90+10] * 100\% \\
 &= 90.0\%
 \end{aligned}$$

Equation 2. Specificity

$$\begin{aligned}\text{Specificity} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Positives}] * 100\% \\ &= 8910 / [8910+990] * 100\% \\ &= 90.0\%\end{aligned}$$

Equation 3. Positive Predictive Value

$$\begin{aligned}\text{Positive Predictive Value} &= [\text{True Positives}] / [\text{True Positives} + \text{False Positives}] * 100\% \\ &= 90 / [90+990] * 100\% \\ &= 8.3\%\end{aligned}$$

Equation 4. Negative Predictive Value

$$\begin{aligned}\text{Negative Predictive Value} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Negatives}] * 100\% \\ &= 8910 / [8910 + 10] * 100\% \\ &= 99.9\%\end{aligned}$$

4.4. Overview of ICES

ICES (formerly the Institute for Clinical Evaluative Sciences) is an independent non-profit organization that houses population-based collections of health administrative datasets for the province of Ontario. Data in ICES is captured through the routine administration of Ontario's publicly funded health care system and includes data on physician service claims, health care encounters, cancer diagnoses, and surgical procedures.²¹ ICES contains a number of health administrative datasets which can be used to study specific patient cohorts. Commonly used datasets contained within ICES includes the Discharge Abstract Database (DAD), The Ontario Health Insurance Plan (OHIP) database, and The Ontario Cancer Registry (OCR). The DAD records demographic, diagnostic, and procedural data for all hospitalizations in Ontario. The OHIP database records all remunerated health-care services provided in Ontario and includes patient and physician identifiers as well as service date. Finally, the OCR includes all incident cases of malignant cancers. The OCR's data comes from regional cancer centers, hospital

discharge/day surgery records, and laboratory pathology reports.^{22,23} It records the cancer type along with date of diagnosis.

4.5. Existing Studies Using Large Administrative Databases to Study Cystectomy in Ontario

Table 1 provides a sample of published population-level studies that used codes within large health databases contained within ICES to identify their cystectomy cohort. The name of the databases and the coding system used to identify patients with cystectomy are cited. We developed a letter-grading system to identify how researchers measured and dealt with potential misclassification which was applied to each study listed. Grade ‘**E**’ indicates that the study did not measure code accuracy or even acknowledge the potential for misclassification in the methods or discussion. Grade ‘**D**’ indicates that the study acknowledged that misclassification bias might exist but did not measure it or the code’s accuracy. Grade ‘**C**’ indicates that the study did not measure code accuracy but cited a previous study that measured the code accuracy; however, the final results did not account for coding inaccuracies. Grade ‘**B**’ indicates that a study had been done by the researcher (or someone at their center) which actually measured code accuracy but did not correct for misclassification in the study analysis. Finally, Grade ‘**A**’ indicates a study that both measured and accounted for misclassification bias due to coding.

Table 2. Description and grading of published cystectomy cohort studies using large administrative datasets.

Author	Region (Time Period)	Database(s)	Case Identification	Grade
Lusty et al ²⁴	Ontario (2009-2013)	DAD	CCI	D
Siemens et al ²⁵	Ontario (1994-2003)	DAD	CCP/CCI	D
Raphael et al ²⁶	Ontario (2004-2013)	DAD	CCP/CCI	D
Kulkarni et al ²⁷	Ontario (1992-2004)	DAD, OHIP	CCP/CCI, OHIP	D
Leveridge et al ²⁸	Ontario (1994-2008)	DAD, OCR, OHIP	CCI	D
Jaeger ²⁹	Ontario (1994-2008)	DAD, OCR, OHIP	CCI	D
Siemens ³⁰	Ontario (2000-2008)	OCR, DAD	CCI	D
Brennan ³¹	Ontario (1994-2013)	OCR, DAD	CCI	D
Doiron et al ³²	Ontario (1994-2008)	OCR, DAD	CCI	D
Booth et al ³³	Ontario (1994-2008)	OCR, DAD	CCI	D
Raphael et al ²⁶	Ontario (2004-2013)	OCR, DAD	CCI	D
Izard et al ³⁴	Ontario (1994-2008)	OCR, DAD	CCI	D
Booth et al ³⁵	Ontario (1994-2008)	OCR, DAD, OHIP	CCI	D
Siemens et al ³⁶	Ontario (1994-2008)	OCR, DAD		D
Siemens et al ³⁷	Ontario (1994-2008)	OCR, DAD	CCI	D
Kulkarni ³⁸	Ontario (1992-2004)	OCR, DAD	CCI	D
Kulkarni ³⁹	Ontario (1992-2004)	OCR, DAD	CCI	D
Richard ⁴⁰	Ontario (1994-2014)	OCR, DAD, OHIP	CCI, OHIP	D

- DAD = Canadian Institute for Health Information Discharge Abstract Database
- OHIP = Ontario Health Insurance Plan
- CCI = Canadian Classification of Health Interventions
- CCP = Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures

All of these studies used diagnostic codes within the Ontario Cancer Registry (OCR), CCI procedure codes within the Discharge Abstract Database (DAD), and/or billing codes within the OHIP database to identify patients with bladder cancer and those undergoing cystectomy with urinary diversion respectively. *None of these studies* used a code or code algorithm whose accuracy had actually been measured (Grade B) or that subsequently corrected for misclassification (Grade A). None of the studies cited validation of cystectomy procedure coding specifically within the database being used nor did they cite the accuracy of bladder cancer diagnosis using the OCR. No studies validating the use of OHIP billing codes in the identification of cystectomy (or any other surgery) were cited.

Most studies cited a single source commenting on the validity of ICD-9 coding to identify surgeries performed in Calgary, Alberta as a means of validating use of any code algorithm to identify a diagnosis or procedure.⁴¹ The authors of this study performed a manual chart review on randomly selected patients who were discharged from three acute care hospitals in Calgary to determine what surgeries they actually received. This gold standard cohort was then compared to the codes recorded in one of two administrative databases used for recording patient discharge information. Of note, this study did not study CCI coding (the study pre-dated the introduction of CCI in Canada) and was not specific to cystectomy. Furthermore, the study was not performed in Ontario or using Ontario health administrative databases such as those contained within ICES.⁴¹

4.6. Existing Studies on the Accuracy of Cystectomy Coding

Although no formal validation of cystectomy coding using databases within ICES has been performed, there have been two published studies looking at coding accuracy for cystectomy with urinary diversion using other health administrative databases. Lyon et al. used an ICD-10-based coding algorithm in the United States to identify patients who underwent cystectomy with urinary diversion for bladder cancer from their institutional billing database.⁴² This billing database contained all claims the hospital and its clinicians submitted to insurance companies and the government for remuneration. To be identified with cystectomy, patients during a particular encounter required an ICD-9/10 diagnosis code for bladder cancer *and* an ICD-10-PCS procedure code for cystectomy with urinary diversion. The reference standard recording all hospital cystectomies (n=234) was the urologists' prospectively maintained registry of cystectomies. There were no quality control methods identified in the study to ensure that this cystectomy registry was in fact complete and contained all cystectomies performed at their institution. The prevalence of cystectomy within the institutional database of all billed procedures was not provided; therefore, the specificity and negative predictive values of this algorithm was not measured. Finally, this algorithm has not been externally validated. A description of accuracy measures for the coding algorithm used in this study can be seen in Table 2.

Table 3. 2x2 frequency table for the code algorithm proposed by Lyon et al. for identification of radical cystectomy.

		True Cystectomy Status		Total
		Cystectomy +	Cystectomy -	
Code Status	Code +	227	12	230
	Code -	7	Not Provided	Unknown
Total		234	Unknown	Unknown

Equation 1: Sensitivity

$$\begin{aligned} \text{Sensitivity} &= [\text{True Positives}] / [\text{True Positives} + \text{False Negatives}] * 100\% \\ &= 227 / [227+7] * 100\% \\ &= 97.0\% \end{aligned}$$

Equation 2: Specificity

$$\begin{aligned} \text{Specificity} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Positives}] * 100\% \\ &\bullet \text{ Cannot Calculate (True Negatives Unknown)} \end{aligned}$$

Equation 3: Positive Predictive Value

$$\begin{aligned} \text{Positive Predictive Value} &= [\text{True Positives}] / [\text{True Positives} + \text{False Positives}] * 100\% \\ &= 227 / [227 + 12] * 100\% \\ &= 95.0\% \end{aligned}$$

Equation 4: Negative Predictive Value

$$\begin{aligned} \text{Negative Predictive Value} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Negatives}] * 100\% \\ &\bullet \text{ Cannot Calculate (True Negatives Unknown)} \end{aligned}$$

Tan et al. developed an enhanced natural language processing tool to identify patients having undergone radical cystectomy for bladder cancer from textualized data in electronic medical records.⁴³ As a comparison, a code-based algorithm, specifically the presence of an ICD-9 diagnosis code for bladder cancer in combination with an ICD-9/CPT procedure code for cystectomy and urinary diversion was also developed. The authors also attempted to identify cystectomy patients who underwent continent urinary diversion using the code-based algorithm

by adding an ICD-9 billing code for continent urinary diversion. To identify a gold-standard cohort, a manual chart review was done on patients having at least one billing claim submitted by a urologist during the hospitalization *plus* one or more of the following: diagnostic code for bladder cancer; procedure code for cystectomy; an operative log entry that included the terms ‘cystectomy’ or ‘cystoprostatectomy’. A total of 497 patients were screened by manual chart review of which 84 had confirmed cystectomies (84/497 x 100% = 16.9% overall prevalence of cystectomy). Of those with confirmed cystectomies, 32 had continent diversions (32/497 x 100% = 6.4% overall prevalence of cystectomy with continent diversion). A description for the accuracy measures for the code algorithm used in this study can be seen in Tables 3 and 4.

Table 4. 2x2 frequency table for the ICD-9 code algorithm used by Tan et al. for identification of cystectomy with any type urinary diversion.

		True Cystectomy Status		Total
		Cystectomy +	Cystectomy -	
Code Status	Code +	83	6	89
	Code -	1	407	408
Total		84	413	497

Equation 1: Sensitivity

$$\begin{aligned} \text{Sensitivity} &= [\text{True Positives}] / [\text{True Positives} + \text{False Negatives}] * 100\% \\ &= 83 / [83+1] * 100\% \\ &= 98.8\% \end{aligned}$$

Equation 2: Specificity

$$\begin{aligned} \text{Specificity} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Positives}] * 100\% \\ &= 407 / [407+6] * 100\% \\ &= 98.5\% \end{aligned}$$

Equation 3: Positive Predictive Value

$$\text{Positive Predictive Value} = [\text{True Positives}] / [\text{True Positives} + \text{False Positives}] * 100\%$$

$$= 83 / [83+6] * 100\%$$

$$= 93.3\%$$

Equation 4: Negative Predictive Value

$$\text{Negative Predictive Value} = [\text{True Negatives}] / [\text{True Negatives} + \text{False Negatives}] * 100\%$$

$$= 407 / [407 + 1] * 100\%$$

$$= 99.8\%$$

Table 5. 2x2 frequency table for code algorithm used by Tan et al. for identification of cystectomy with continent urinary diversion.

		True Cystectomy + Continent Diversion Status	
		Cystectomy +	Cystectomy -
Code Status	Code +	27	80
	Code -	5	385

Equation 1: Sensitivity

$$\text{Sensitivity} = [\text{True Positives}] / [\text{True Positives} + \text{False Negatives}] * 100\%$$

$$= 27 / [27 + 5] * 100\%$$

$$= 84.4\%$$

Equation 2: Specificity

$$\text{Specificity} = [\text{True Negatives}] / [\text{True Negatives} + \text{False Positives}] * 100\%$$

$$= 407 / [407+6] * 100\%$$

$$= 82.8\%$$

Equation 3: Positive Predictive Value

$$\text{Positive Predictive Value} = [\text{True Positives}] / [\text{True Positives} + \text{False Positives}] * 100\%$$

$$= 27 / [27+80] * 100\%$$

$$= 25.2\%$$

Equation 4: Negative Predictive Value

$$\text{Negative Predictive Value} = [\text{True Negatives}] / [\text{True Negatives} + \text{False Negatives}] * 100\%$$

$$= 385 / [385 + 5] * 100\%$$

$$= 98.7\%$$

4.7. Rational for Thesis

In summary, many studies have identified cohorts of patients receiving cystectomy with urinary diversion using data from health administrative databases, including those contained within ICES. Cystectomy cases in these studies are identified using code algorithms with unknown accuracy. Without knowing the accuracy of codes being used to identify cases, it is impossible to measure or correct for misclassification bias, therefore these studies could have erroneous results and conclusions, potentially impacting patient care and health care policy. The studies that have attempted to determine the accuracy of cystectomy codes in administrative data are few in number (there are only two published studies to our knowledge), have methodology limitations, and have never been externally validated. No studies on the accuracy of CCI codes within the DAD and billing codes within the OHIP database have ever been performed; despite this, several studies using these codes to identify cystectomy patients have been published. Given these observations, further measurement of cystectomy code accuracy in large health administrative databases, including the DAD and OHIP database within ICES, is required.

5. Study Proposal

I believe that using procedural and physician billing codes to identify cystectomy with urinary diversion will result in important misclassification due to the low prevalence of cystectomy among all hospitalizations. I also believe that creating a predictive model using patient demographics and clinical data, hospitalization data, physician billing information, and cancer registry data can be developed to accurately quantify the probability that patients had undergone cystectomy and urinary diversion. Finally, I believe that using this expected

cystectomy probability to impute cystectomy status in analyses will decrease misclassification bias.

This study will aim to create a multinomial logistic regression model that I will call the “Ottawa Cystectomy Identification Model” (or “OCIM”) using patient, hospital, procedural, and coding co-variables contained within linked ICES databases. The goal of the OCIM will be to accurately predict the probability that a patient has actually undergone a 1) cystectomy with incontinent urinary diversion OR 2) a cystectomy with continent urinary diversion, during any hospitalization to The Ottawa Hospital (TOH) recorded within the DAD. This study will also perform an internal validation of the OCIM using the TOH cohort. Finally, it will quantify misclassification bias when cystectomy-diversion is identified using procedural and billing coding alone vs. an analysis in which cystectomy status is imputed using expected cystectomy probability from the OCIM.

5.1. Significance of the Proposed Thesis

The development of the OCIM to accurately identify the probability that patients having undergone cystectomy with urinary diversion at TOH can be extrapolated to assess whether health administrative data can accurately study population-based cystectomy in Ontario. If the OCIM decreases misclassification bias compared to coding alone, future health administrative data research on cystectomy using similar case identification methods will be less biased. This will improve population-level data for patients undergoing cystectomy which we hope will translate into improved patient outcomes within this population.

The methods used to derive and internally validate the OCIM can also be used to build and validate similar models for other diagnoses and procedures or using other health administrative databases. By demonstrating the potential for misclassification bias within large administrative datasets when inaccurate codes are used for case identification, particularly for diseases or procedures having a very low prevalence, we hope to bring further attention to the importance of using accurate coding algorithms to minimize misclassification bias in large health database research as well as the statistical methods that correct for misclassification bias.

5.2. Study Questions

1. What is the accuracy of Ontario procedural and billing codes used in previously published studies to identify cystectomy and urinary diversion within the DAD?
2. Can a multinomial logistic regression model using patient, hospital, procedural, and coding data accurately quantify the likelihood that a cystectomy with urinary diversion, stratified by diversion type, has been performed during a hospitalization to TOH recorded in the DAD?
3. Does misclassification bias decrease when cystectomy with urinary diversion surgery status is imputed using the multinomial model compared to procedure or billing codes alone?

5.3. Study Hypotheses

1. Procedural and billing codes for cystectomy with urinary diversion will have a high sensitivity and specificity. However, when these codes are applied to all records within the DAD at TOH, in which <1% of all hospitalizations are anticipated to truly include a

cystectomy, there will be a significant number of patients with these procedural or billing codes applied who did not actually undergo cystectomy with urinary diversion.

2. A multinomial logistic regression model using patient demographics and comorbidities, hospitalization data, physician billing data, and information from a cancer registry can be developed and used to accurately return the probability that a cystectomy with incontinent urinary diversion OR cystectomy with continent urinary diversion had occurred during any TOH hospitalization recorded within the DAD.
3. Analysis using the predictive model with probabilistic imputation methods will decrease misclassification bias for cystectomy with urinary diversion patients compared to the use of procedural or billing codes alone.

6. Methods

6.1. Terminology

The following is a list of key terms used in this study and their respective definitions:

- **ICES:** Formally known as the Institute for Clinical Evaluative Science. ICES is an organization that houses health administrative datasets for the province of Ontario. Data in ICES is captured through the administration of Ontario's publicly funded health care system. The databases used in this study (DAD, OHIP, and OCR) were all contained and access within ICES. Although databases in ICES contain data for the entire province of Ontario, in this study the cohort was restricted to patients hospitalized at TOH, which corresponds to our ability to generate a gold standard reference cohort of true cystectomy and urinary diversion cases limited to this centre.

- **Hospitalization:** Includes any inpatient admission to TOH during the study period. Excludes ambulatory visits to clinic or emergency rooms as well as any day surgery procedures. Admissions to other hospitals in Ontario were also excluded as the gold standard reference cohort was limited to just cystectomies with urinary diversions performed at TOH.
- **Gold Standard Reference Cohort:** All patients who actually underwent cystectomy with urinary diversion at TOH during the study period. Patients undergoing cystectomy and urinary diversion were identified using an operative database within TOH (i.e. the SIMS registry) and confirmed by manual chart review. This cohort was imported to ICES and merged with the analytical dataset containing all hospitalizations at TOH during the same period to determine true cystectomy status (stratified by incontinent vs continent diversion) for each hospitalization.
- **OCIM (Ottawa Cystectomy Identification Model):** Multivariable multinomial logistic regression model that provides the probability of 1) cystectomy with incontinent diversion, 2) cystectomy with continent diversion, or 3) no cystectomy for each hospitalization at TOH within the DAD during the study period.
- **Cystectomy with Incontinent Diversion:** Surgery in which the bladder is removed and a piece of intestine is used to create an ileal conduit or the ureters are attached directly to the abdominal wall (cutaneous ureterostomy) which then allows for continuous drainage into a stoma bag attached to the abdomen. In this study, cystectomy with incontinent diversion also refers to patients who had their bladder removed but did not receive any urinary diversion procedure (either because the remainder of the urinary tract was also removed or the patient was already anuric due to end stage renal failure).

- **Cystectomy with Continent Diversion:** Surgery in which the bladder is removed and bowel is used to create an orthotopic neobladder in the pelvis or a catheterizable pouch to store the urine until the patient is ready to void/empty.
- **Misclassification Bias:** Deviation from true results due to incorrect assignment of case status. In this study, misclassification bias refers to the difference between the true values of co-variables as measured from the gold standard cohort (identified by manual chart review) and the values of co-variables calculated using the OCIM or the code-algorithm.
- **Bootstrap Resampling:** A statistical method of estimating measures and distribution of a measure by resampling with replacement from the original sample to create a new sample of the same size as the original.
- **Bootstrap Imputation:** The application of bootstrap resampling techniques to calculate co-variable values using the OCIM for cystectomy identification.

6.2. Study Objectives

1. Create a gold standard reference cohort of all patients at TOH who underwent a cystectomy with urinary diversion (stratified by diversion type – incontinent vs continent) during the study period.
2. Develop a multivariable multinomial regression model (i.e. the OCIM) that returns the probability that patients recorded in population-based hospitalization databases actually underwent cystectomy with urinary diversion (stratified by diversion type – incontinent vs continent).
3. Internally validate the OCIM with bootstrap sampling methods to measure its discrimination and calibration.

4. Compare the accuracy of the OCIM to that of cystectomy billing and procedure codes alone (which have previously been used to identify cystectomy patients in health administrative databases) when measuring cystectomy incidence and its association with patient factors (age, sex, comorbidities), hospitalization factors (intensive care unit utilization, cardiac arrest), and outcomes (death in hospital, length of stay, return to emergency within 30-days of discharge, unplanned readmission to hospital within 30-days of discharge).

6.3. Study Design Overview

This study was a retrospective observational study using health administrative data from hospitalizations at TOH between January 1st, 2009 and June 1st, 2019. TOH is a tertiary-care facility in Ottawa, Ontario, Canada that has two acute care inpatient campuses containing approximately 1100 beds. Research Ethics Board (REB) approval was obtained (REB # 20220112-01H).

The study had five parts:

- 1) ***Creating the Gold Standard Reference Cohort (Section 6.4)***: A gold-standard reference cohort of *all* patients who truly underwent cystectomy with urinary diversion as a primary procedure at TOH during the study period was first identified using The Ottawa Hospital Data Warehouse (TOHDW). This dataset was transferred to ICES.
- 2) ***Creating the Analytical Dataset (Section 6.5)***: At ICES, we used population-based hospitalization data to identify every adult admission to TOH during the study period. By linking to the gold standard reference cohort, we determined who had cystectomy. We then

created all *a priori* identified covariates that could be used to identify cystectomy using administrative data.

- 3) ***Creating the Ottawa Cystectomy Identification Model (OCIM) and Measuring its Performance (Section 6.6 and Section 6.7):*** This section created the OCIM which used covariates created with administrative data to return the probability that a cystectomy with urinary diversion (stratified by incontinent vs continent diversion type) truly occurred during each hospitalization.
- 4) ***Identifying a Code Algorithm to Detect Cystectomy Patients and Calculating Its Accuracy Measures (Section 6.8):*** CCI procedure codes and OHIP billing codes were used to create a code algorithm that could identify patients undergoing cystectomy with incontinent diversion or cystectomy with continent diversion. The accuracy measures of this code algorithm were determined using the analytical dataset.
- 5) ***Calculating and Comparing Misclassification Bias (Section 6.9):*** This section measured cystectomy incidence or its association with covariables using true cystectomy status. These measures were compared to outputs when cystectomy status was determined using codes or with the OCIM and bootstrap imputation. Differences in these measures from true values were termed misclassification bias.

6.4. Creating the Gold Standard Reference Cohort

The gold-standard reference cohort included all patients undergoing cystectomy with urinary diversion at The Ottawa Hospital between January 1st, 2009 and June 1st, 2019. These patients were identified in the SIMS registry (which is a component of TOHDW). The SIMS registry contains information on all primary operative procedures performed at TOH. Prior to any

operation, surgeons complete forms capturing patient and procedural information (including the type of procedure that is planned to be done). If these forms are not completed, operations cannot be booked or conducted and hospitals cannot receive remuneration. Completion rates for these forms are essentially 100% since hospital remuneration is a function of these data and the importance of their completion to hospital function has been highlighted to operation room managers (who ensure form completion from surgeons). Data from these forms are inputted by hospital records staff into SIMS. In particular, the primary procedure actually done during the operation is registered as a TOH-specific alpha-numeric code.

The SIMS registry was queried for all potential primary cystectomy with urinary diversion procedures using TOH-specific procedure codes listed in Table 6A. To ensure that no true cystectomies were missed, codes for other surgeries that are similar to cystectomy and may be misclassified were also included in the query (Table 6B). These procedures included partial cystectomy without urinary diversion and nephroureterectomy (which includes removal of a small piece of the bladder).

True cystectomy with urinary diversion status of all potential cases identified in the SIMS registry was then determined by manual chart review by a single reviewer (JR). Cystectomy and urinary diversion status was confirmed by reviewing the operative note on the date recorded for the surgery in the SIMS registry. If the operative note was incomplete or unclear, supplemental review of associated progress notes and discharge summaries were performed. Those identified as having undergone cystectomy were stratified by urinary diversion type (incontinent vs continent). Patients undergoing just cystectomy without urinary diversion (i.e. if both kidneys

were simultaneously removed or the patient was already on dialysis for renal failure) were classified as incontinent diversions. Any case that was unclear regarding its cystectomy-urinary diversion status was reviewed with a second expert reviewer to provide a final opinion.

Patients less than 18 years of age or those patients who underwent cystectomy with urinary diversion as a secondary surgery as part of a larger operation (e.g. total pelvic exenteration for locally invasive rectal cancer) were excluded. These patients were excluded as they represent a different patient cohort with distinct diagnoses, risk factors and outcomes that could contaminate our cohort of primary cystectomy with urinary diversion cases because their outcomes may be influenced by the other (non-cystectomy) procedures they are receiving. This could bias future population-based studies using our model. Furthermore, these cases would not be identifiable within the SIMS registry, which only records the primary operation performed. Patients without valid Ontario health cards were also excluded since they could not be linked to the Ontario health databases required for analysis.

A dataset containing the final gold-standard reference cohort was then created which included all patients from TOH who underwent a cystectomy during the study period. Therefore, any person who was *not* included in this dataset *did not* have a cystectomy. The gold-standard dataset contained three variables: 1) Ontario Health Card Number, 2) Cystectomy Date, and 3) Diversion Type (Incontinent vs Continent). Members of the TOHDW analytical team linked patient health card number to the gold-standard dataset. This was transferred to ICES via an encrypted data portal.

Table 6. List of TOH-specific procedure codes within the SIMS registry used to create the gold standard cohort.

Procedure Code	Description
A - Cystectomy and Diversion Codes	
BLCYSTECT	Complete removal of bladder (cystectomy)
BLCYSTILCD	Complete removal of bladder (cystectomy) with creation of non-continent urinary diversion (i.e. ileal conduit)
BLCYSTILNB	Complete removal of bladder (cystectomy) with creation of continent urinary diversion (i.e. neobladder)
B - Non-Cystectomy and Diversion Codes (included in search to account for misclassification)	
BLCYSTECTP	Partial removal of bladder without urinary diversion
NEPHURETEC	Removal of kidney, ureter, and bladder cuff without urinary diversion

6.5. Creating the Analytical Dataset

Creation of the analytical dataset had four steps. First, we identified every inpatient hospitalization at TOH during the study period. Second, we determined cystectomy status for each hospitalization using database codes in the administrative data. Third, we determined values of all co-variables that we considered potentially important *a priori* for determining true cystectomy status based on coded cystectomy. Finally, we linked back to the gold standard cohort to determine true cystectomy status.

6.5.1. Identifying Every TOH Hospitalization During the Study Period

A dataset containing *all* inpatient hospitalizations at TOH during the study period (between January 1st, 2009 and June 1st, 2019) was created using the DAD, which is a database contained within ICES that contains information on all hospitalizations in the province of Ontario.

6.5.2. Determining Cystectomy Status Using Administrative Database Codes

Procedure and billing codes were identified by both reviewers as likely being predictive of cystectomy with urinary diversion. For procedure coding, the DAD uses CCI codes. CCI codes with descriptions in the CCI manual for cystectomy with incontinent or continent diversion were identified with the assistance of a coding expert at the Health Records Department at TOH to ensure the correct codes were being used. The OHIP billing codes for cystectomy with incontinent or continent diversion were identified with the assistance of a urologist who regularly performs and bills for cystectomy with urinary diversion (LL). The CCI and OHIP billing codes used to identify cystectomy with urinary diversion are presented in Table 7.

Table 7. CCI and OHIP coding used to identify cystectomy with incontinent or continent urinary diversion.

Cystectomy Type	CCI Coding (Procedure Codes)	OHIP Coding (Billing Codes)
Cystectomy and Incontinent Diversion	1PM89RR	S453
	1PM89EN	S484+S452
	1PM89DA	S484+S454
	1PM91LA	
	1PM91DA	
	1PM91RR	
	1PM91EN	
	1PM90LAXXG	
Cystectomy and Continent Diversion	1PM89LA	S440
	1PM89DAXXG	S484+S441
	1PM89LAXXG	S485+S441
	1PM89RRXXG	
	1PM89ENXXG	
	1PM90RDXXG	
	1PM91DAXXG	
	1PM91LAXXG	
	1PM91RRXXG	
	1PM91ENXXG	
	1PM92LAXXG	
	1PM92DAXXG	
	1PM92RDXXG	

6.5.3. Creating Study Co-Variates

Variables listed in databases contained within ICES (specifically the DAD, OHIP database, and OCR) were reviewed independently by two reviewers with experience in performing cystectomy with urinary diversion (JR and LL). Patient-, hospital-, and procedure-level co-variables from these databases that were thought to possibly be predictive of a patient actually undergoing cystectomy with urinary diversion were selected by consensus between reviewers. Any disagreements in co-variable selection were discussed between reviewers until an agreement was reached. If no agreement could be reached then a third expert reviewer was asked to provide a final decision. All co-variables selected by the two reviewers were then created within the ICES dataset containing all TOH hospitalizations during the study period. The co-variables selected and their definitions are presented in Table 8.

Table 8. Definitions for all co-variables contained within the final analytical dataset.

Co-Variable	Definition
Cystectomy with incontinent urinary diversion	The patient truly had a cystectomy with an incontinent urinary diversion (from gold standard cohort)
Cystectomy with continent urinary diversion	The patient truly had a cystectomy with a continent urinary diversion (from gold standard cohort)
Cystectomy Index Date	The date of true cystectomy and urinary diversion (from gold standard cohort)
Male Sex	Patient is of male sex
Age	Patient age at time of admission
OHIP billing code for cystectomy with incontinent diversion	OHIP billing codes S453, S484+S452, or S484+S454 are present for patient
OHIP billing code for cystectomy with continent diversion	OHIP billing codes S440, S484+S441, or S485+S441 are present for patient
OCR diagnosis of bladder cancer	Patient is recorded in OCR as having bladder cancer prior to admission
CCI code for cystectomy and incontinent diversion	CCI codes 1PM89RR, 1PM89EN, 1PM89DA, 1PM91LA, 1PM91DA, 1PM91RR, 1PM91EN, or 1PM90LAXXG are present for patient
CCI code for cystectomy and continent diversion	CCI codes 1PM89LA, 1PM89DAXXG, 1PM89LAXXG, 1PM89RRXXG, 1PM89ENXXG, 1PM90RDXXG, 1PM91DAXXG, 1PM91LAXXG, 1PM91RRXXG, 1PM91ENXXG, 1PM92LAXXG, 1PM92DAXXG, or 1PM92RDXXG are present for patient
CIHI-DAD diagnosis code for bladder cancer	Diagnosis of bladder cancer in CIHI-DAD record
Main provider service	Urology is the primary service during admission
Operative time	Coded cystectomy or primary procedure operative time in minutes
Intervention in primary operating room	Coded cystectomy or primary procedure occurred in main operating room
Intervention in other setting	Coded cystectomy or primary procedure occurred in a location other than the main OR
Acute length of stay	Acute length of hospital admission
Elective admission	Elective admission to hospital
General anesthesia	General or combined general/neuraxial anesthesia for cystectomy or primary procedure
Readmission/death within 28 days	Patient died or was readmitted within 28 days of index admission
Discharge home	Patient discharged home without supports following admission
Blood Transfusion	Blood transfusion administered during admission
Unplanned Return to the OR	Unplanned patient return to the main OR within 28 days of coded cystectomy or primary procedure

6.5.4. Merging to Gold Standard Cohort (And Determining True Cystectomy Status)

The final gold standard reference cohort was imported via encrypted data portals to ICES. The gold standard reference cohort was then merged with the ICES dataset containing all admissions. The final dataset contained A) all adult (≥ 18 years old) hospitalizations to TOH between January 1st, 2009 and June 1st, 2019, B) all of the selected potential co-variables for the model from the two reviewers for each hospitalization, C) whether a cystectomy was truly performed during the hospitalization, D) if ‘Yes’ to ‘C’, then the date of the true cystectomy, and E) if ‘Yes’ to ‘C’, then what type of urinary diversion was performed (incontinent vs continent).

6.6. Creating the Ottawa Cystectomy Identification Model (OCIM)

6.6.1. Modeling Method Selection

To create the OCIM, a multivariable multinomial logistic regression model was used to return the probabilities of patients in any admission identified in the DAD being in any of the following 3 classes: i) cystectomy with incontinent diversion, ii) cystectomy with continent diversion, or iii) no cystectomy.

For basic logistic regression, the result is the log odds of a binary outcome (Equation 5). In this sense, each parameter estimate ‘ β_1 ’ to ‘ β_p ’ represents the change in log odds for a single unit increase in the corresponding variable (‘ X_1 ’ to ‘ X_p ’). By exponentiating any parameter estimate, one can calculate the odds ratio for the outcome given a unit change of that variable providing all other variables in the model remain constant. By inputting the values for each

variable, the linear predictor (i.e. the ‘x-beta’) can be calculated which can be used to calculate the outcome probability (Equation 5).

Equation 5. Calculating Outcome Probability from Logistic Regression

$$P(x_1, x_2, \dots, x_p) = \frac{\exp(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p)}{1 + \exp(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_p x_p)}$$

- P = Probability
- β_0 = Intercept (log odds if X_1 to $X_p = 0$)
- β_1 to β_p = Co-efficients for variables X_1 to X_p

Unlike binomial logistic regression, the multinomial model allows for assessment of outcomes with multiple categories. A multinomial model can be used when the outcome levels do not have a defined order, as is the case with cystectomy and type of urinary diversion, where the diversion type is a category with no particular rank or order (i.e. nominal categorical outcome).

The multinomial logistic regression model implies that, for a single predictor ‘ X_1 ’ to ‘ X_p ’, each outcome category follows a logistic regression model with a specific category assigned as the reference (Equation 7). Therefore, parameter estimates for a particular predictor variable are different for each outcome category. For the OCIM, this means that there would be a different parameter estimate for each predictor variable when ‘cystectomy with incontinent diversion’ is the outcome and when ‘cystectomy with continent diversion’ is the outcome. These parameter estimates reflect changes in outcome log-odds compared to ‘no cystectomy’.

6.6.2. Determining Allowable Degrees of Freedom Based on Sample Size

Creating a predictive model with a dataset that is too small or with an insufficient number of outcome events may result in model overfitting. With overfitting, model generalizability is limited and poor model performance in external data is seen. In order to prevent model overfitting in the OCIM, we used the methods proposed by Riley et al to determine the allowable degrees of freedom for co-variable selection.⁴⁴

This calculation assumed that there would be 429,000 admissions to TOH during the study period with an estimated 250 cystectomies with each type of diversion (out of a total of 500 cystectomy with diversion admissions) giving a prevalence of cystectomy with incontinent or continent diversion among all admissions of 0.0583%. We then calculated the number of degrees of freedom permitted in the regression model to return a precise estimate of the model intercept (error +/- 1%), to achieve a small mean error across individual predictions (error +/- 1%), to minimize the risk of overfitting (shrinkage of 90%), and finally to minimize optimism in model fit (optimism of 0.05). The final allowable degrees of freedom in the model was calculating by determining the mean average of the sample sizes for each calculation.

6.6.3. OCIM Variable Selection

6.6.3.1. Ranking Candidate Variables

After variable selection by the two reviewers was complete (Table 8), each reviewer ranked the co-variables by perceived importance in identifying cystectomy with urinary diversion status (i.e. rank '1' would indicate the most important co-variable). This ranking was

performed to determine a logical order by which co-variables are added to the model during model creation. The final ranking of co-variables was determined by calculating the mean of both reviewer's rank scores. The co-variables were then sorted based on mean rank, with the lower mean rank scores corresponding to higher importance ranking for identifying patients undergoing cystectomy with urinary diversion during hospital admission (Table 9).

Table 9. A list of co-variables thought to be predictive of cystectomy and urinary diversion and their rank of perceived importance.

Variable	JR Rank	LL Rank	Mean Rank Score	Final Rank
OHIP Billing Code for Cystectomy	2	1	1.5	1
OCR Diagnosis of Bladder Cancer	3	2	2.5	2
CCI Code for Cystectomy	1	5	3	3
DAD Diagnosis Code for Bladder Cancer	4	3	3.5	4
Main Provider Service	5	4	4.5	5
Operative Time	6	7	6.5	6
Intervention Location	11	6	8.5	7
Acute Length of Stay	7	11	9	8
Patient Age	8	10	9	9
Elective Admission	10	9	9.5	10
Anesthetic Type	12	8	10	11
Readmission/Death within 28 days	9	13	11	12
Discharge Disposition	9	14	11.5	13
Blood Transfusion	14	12	13	14
Unplanned Return to the OR	13	15	14	15

6.6.3.2. Selecting Variables for OCIM

Section 6.6.3.1 discusses how variables for the model were identified and prioritized (ranked) based on their perceived importance. Variables were individually added to the multinomial model based these reviewer rankings (Table 9). Each individual variable was kept in the model if the variable's addition resulted in a significant improvement in model fit. In regression analysis, model fit refers to the difference between the observed and predicted values. As such, an improvement in model fit implies a smaller difference between observed and predicted values in the updated model.⁴⁵

Model fit after the addition of each new co-variable was measured using the *likelihood ratio test*. The likelihood for a given model measures the joint probability of the observed outcomes expressed as a function of the regression model. Lower likelihoods reflect better model fit. The likelihood ratio test is used to compare two nested models: the model before and the model after adding a new variable. The likelihood ratio statistic is computed as twice the difference between the log-likelihoods of the two models (Equation 6). The statistical significance of this difference can be measured by comparing it to the chi-squared (X^2) distribution for significance testing with the degrees of freedom equal to the difference in the number of parameters between the two models.⁴⁵ If the log likelihood statistic is greater than the X^2 for given degrees of freedom, then the difference is considered 'significant'.

Equation 6. Likelihood Ratio Calculation

$$\begin{aligned} \text{LR} &= -2\log[L(M1)/L(M2)] \\ &= -2\log[L(M1) - L(M2)] \end{aligned}$$

- LR = Likelihood Ratio
- L = Likelihood
- M1 = Nested Model 1
- M2 = Nested Model 2

In this study, the likelihood ratio test was performed for each additional co-variable added to the model. If the addition of a co-variable significantly improved model fit (as determined by a significant likelihood ratio test), it was kept in the updated base model. Whenever a new co-variable was added to the model, the statistical significance of all co-variables in the model was reviewed; those no longer statistically significant for both cystectomy with incontinent and continent diversion were removed. Following co-variable removal, the likelihood ratio test was once again applied to ensure there was no significant difference in model fit after variable removal. The updated model was then compared to the next model which added the next ranked co-variable. This process was repeated until all ranked co-variables were either included or excluded from the final model.

6.6.4. Fitting Continuous Co-Variables using Fractional Polynomial Terms

An assumption of logistic regression modelling is that co-variables within the model maintain a linear relationship with the log odds of the outcome. If this assumption of linearity is not met for continuous co-variables, one option is to categorize the continuous variable using pre-defined cut-points. Conversion from continuous to categorical co-variable has several disadvantages and may result in biased results or loss of data and significance of association between an outcome and variable.⁴⁶

To preserve the continuous nature of a co-variable in the case of a non-linear relationship, fractional polynomial transformation was used. The process of fractional polynomial transformation involves two main steps, 1) backwards elimination of model co-variables that are not associated with the outcome (in this study an alpha of 0.2 was used for step #1) and 2) assessment of whether transformation should be performed for continuous co-variables in order to improve model fit (in this study an alpha of 0.05 was used for step #2).⁴⁷ In SAS, we used the MFP8 macro to assess for the need for fractional polynomial transformation of all continuous co-variables (age, acute length of stay, and operative time).⁴⁸

6.7. Measuring OCIM Performance

6.7.1. Discrimination

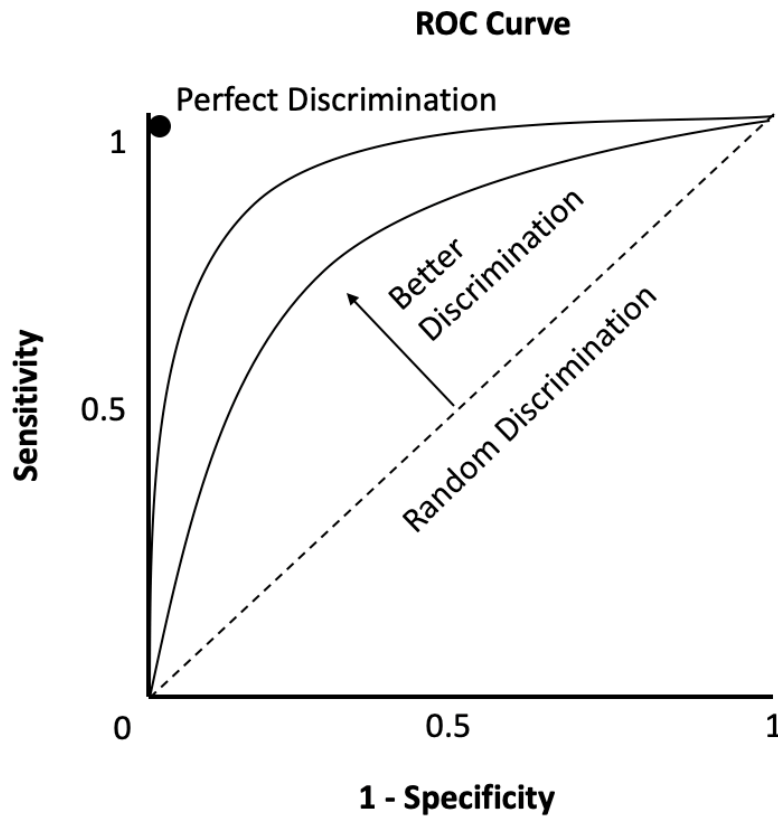
Model discrimination quantifies its ability to distinguish between those with and without an outcome. In this study, model discrimination refers to the model's ability to correctly differentiate between each of the three potential outcomes: cystectomy with incontinent diversion, cystectomy with continent diversion, or no cystectomy.

In this study, the concordance-statistic (c-statistic) was used to measure model discrimination. The c-statistic ranges from 0 to 1 and corresponds to the area under the receiver operating characteristics (ROC) curve (Figure 1). The ROC curve plots the model's false-positive rate (or 1-specificity, see x-axis in Figure 1) against the true positive rate (or sensitivity, see y-axis in Figure 1). Curves are generated by calculating these statistics for varying

probability thresholds of the model that are used to distinguish expected cases. For example, when the probability thresholds is very low (i.e. very close to 0), 1-specificity (x-axis) will be close to 1 (since the specificity will be very low) and the sensitivity will also be close to 1; as a result, this threshold will therefore produce a point that is close to the top-right portion of the ROC curve in Figure 1.

Repeating these calculations for all potential probability thresholds creates the ROC curve. This plot graphically represents the model's ability to distinguish between patients with and without an outcome. A model that randomly assigns outcome status will have a ROC curve that lies on the diagonal and a c-statistic of 0.5. As a model's ability to discriminate between those with and without an outcome increases, its ROC curve stretches towards the upper-left corner of the plot. The c-statistic is the area under this ROC curve and has a value range from 0.5 to 1.0. C-statistics closer to 1 indicate a model with greater discrimination.

Figure 1. Example of a ROC plot indicating different curves with better and worse model discrimination.

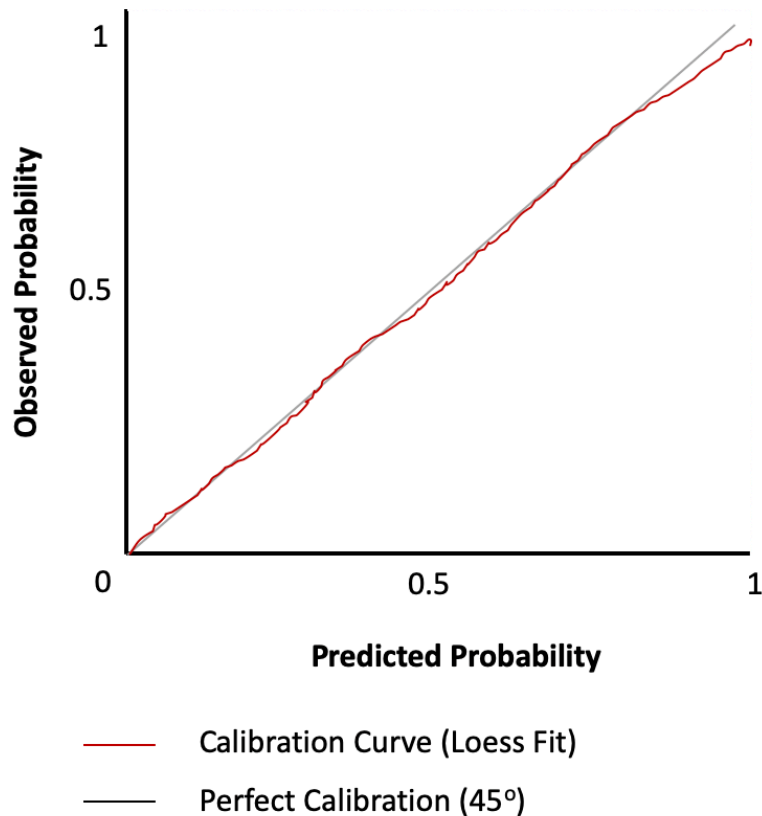


6.7.3. Calibration

Model calibration quantifies the agreement between observed and predicted outcomes of a model. In this study, calibration plots were created for both cystectomy with incontinent and cystectomy with continent urinary diversion. A calibration plot displays the predicted probabilities (x-axis) and observed probabilities (y-axis) of an outcome. Given the binary outcome in this study (i.e. cystectomy yes or no), smoothing of the observed outcome probabilities was conducted using the loess algorithm. The loess algorithm returns outcome values between 0 and 1 by combining the outcome values of patients with similar predicted outcome probabilities.⁴⁹ In the calibration plot, a 45-degree line indicates perfect model

calibration and acts as a point of comparison for the model calibration (Figure 2). Deviations from the 45-degree line indicate worsening calibration.

Figure 2. Example of a calibration plot demonstrating the calibration curve of a model with 95% confidence intervals as well as a 45-degree line representing perfect calibration as a comparison.



In this study, model calibration was measured using the integrated calibration index (ICI).⁵⁰ The ICI represents the weighted average absolute difference between the observed and predicted probabilities. Similar to the c-statistic, the ICI can range from 0 to 1; however, for the ICI, a lower number (i.e. closer to 0) indicates a better model calibration.⁵⁰

6.7.4. Optimism Correction of Model Performance Measures

Model overfitting, as described in Section 3.6.2., results from a model having too many predictors given the size of the study cohort or from excessive data analysis to identify best fitting models. Model overfitting may exaggerate model performance that would be expected when the model is applied to a new patient cohort. “Optimism” is the difference between model performance within the population in which it was created and a different population.⁴⁹

In this study, bootstrap resampling methods were used calculate model optimism. Bootstrap resampling is a statistical method of estimating measures and distribution of a measure by resampling with replacement from the original sample to create a new sample of the same size as the original. In each bootstrap sample, a new model (with the same co-variables as our original model) was created and its performance – namely the c-statistic and ICI – was measured. This “bootstrap model” was then applied to the original study cohort and its performance – the C-statistic and ICI – was re-measured. The optimism was calculated as the difference in performance between the bootstrap model and the original model (Equation 7).

Equation 7. Calculation of Model Optimism Using Bootstrap Resampling

Optimism = Bootstrap Sample Performance – Original Sample Performance

This process was repeated in all 250 bootstrap samples and the mean optimism for both the C-statistic and the ICI was calculated. Optimism corrected c-statistic was calculated by subtracting this optimism from the model’s original c-statistic (Equation 8). Optimism corrected ICI was calculated by *adding* this optimism to the model’s original ICI (Equation 9).

Equation 8. Calculation of Optimism-Corrected C-Statistic

Optimism-Corrected C-Statistic = C-statistic from original sample – mean average of c-statistic optimism from bootstrap resampling

Equation 9. Calculation of Optimism-Corrected ICI

Optimism-Corrected ICI = ICI from original sample + mean average of ICI optimism from bootstrap resampling

6.8. Creating and Calculating Accuracy Measures of Code Algorithm

6.8.1. Identifying Cystectomies Using Administrative Codes

There have been no previously published studies that have attempted to differentiate between incontinent vs continent diversion for patients undergoing cystectomy with urinary diversion using databases within ICES. As such, no previously utilized code algorithm could be evaluated in this study. As demonstrated in Table 1, a number of studies using databases within ICES have been performed. These studies, however, looked at all patients undergoing cystectomy and did not differentiate between diversion type (incontinent vs continent). All studies using the ICES database used CCI codes to identify cystectomy and some used a combination of CCI and OHIP billing codes. Studies looking specifically at radical cystectomy (for bladder cancer) only included patients meeting the code criteria that had a diagnosis of bladder cancer within the OCR.

Based on previously used code algorithms to identify cystectomy patients, we decided to use a combination of the presence of *either* a CCI code **OR** an OHIP billing code as a means of identifying 1) cystectomy with incontinent diversion or 2) cystectomy with continent diversion

(Table 10). This combination of both codes was used because we thought it had the highest face validity and would provide the highest likelihood of identifying a patient that actually underwent cystectomy with diversion compared to the use of CCI and OHIP codes independently. This code algorithm was also similar to the codes used in previously published studies on cystectomy with any urinary diversion. Any patient meeting one of these code algorithms were deemed to be coded for that procedure.

Table 10. Code algorithm for identifying patients undergoing cystectomy with incontinent or continent urinary diversion.

Procedure	Code Algorithm
Cystectomy with Incontinent Urinary Diversion	<p>Any CCI Procedure Code for Cystectomy with Incontinent Urinary Diversion (Includes Any One of the Following):</p> <p>1PM89RR: Excision total, bladder open approach with non-continent urinary diversion 1PM89EN: Excision total, bladder endoscopic approach with non-continent urinary diversion 1PM89DA: Excision total, bladder using endoscopic approach 1PM91LA: Excision radical, bladder open approach with simple apposition technique 1PM91DA: Excision radical, bladder endoscopic approach with simple apposition 1PM91RR: Excision radical, bladder open approach with non-continent urinary diversion 1PM91EN: Excision radical, bladder endoscopic approach with non-continent urinary diversion 1PM90LAXXG: Excision total with reconstruction, bladder using open approach with stoma formation and pedicled distant flap</p> <p>OR</p> <p>Any OHIP Billing Code for Cystectomy with Incontinent Urinary Diversion (Includes Any One of the Following):</p> <p>S453: Complete cystectomy with ureteroileal conduit S484+S452: Complete cystectomy + Ureteroileal conduit S484+S454: Complete cystectomy + Ureteroileal conduit with ureterectomy and ileal replacement</p>
Cystectomy with Continent Urinary Diversion	<p>Any CCI Procedure Code for Cystectomy with Continent Urinary Diversion (Includes Any One of the Following):</p> <p>1PM89LA: Excision total, bladder with simple apposition which does not involve creation of a cutaneous stoma 1PM89DAXXG: Excision total, bladder endoscopic (laparoscopic) approach with creation of neobladder (pouch, reservoir) using pedicled flap 1PM89LAXXG: Excision total, bladder with creation of neobladder using pedicled flap 1PM89RRXXG: Excision total, bladder open approach with creation of continent urinary stoma with or without formation of neobladder using pedicled flap 1PM89ENXXG: Excision total, bladder endoscopic approach with creation of continent urinary stoma with or without formation of neobladder using pedicled flap 1PM90RDXXG: Excision total with reconstruction, bladder with creation of a continent rectal bladder to function without a stoma with pedicled flap 1PM91DAXXG: Excision radical, bladder endoscopic approach with creation of neobladder using pedicled flap 1PM91LAXXG: Excision radical, bladder open approach with creation of neobladder using pedicled flap 1PM91RRXXG: Excision radical, bladder open approach with creation of continent urinary stoma with or without formation of neobladder using pedicled flap 1PM91ENXXG: Excision radical, bladder endoscopic approach with creation of continent urinary stoma with or without formation of neobladder using pedicled flap 1PM92LAXXG: Excision radical with reconstruction, bladder with creation of continent urinary reservoir and permanent cutaneous stoma 1PM92DAXXG: Excision radical with reconstruction, bladder endoscopic approach with creation of continent urinary reservoir and permanent cutaneous stoma 1PM92RDXXG: Excision radical with reconstruction, bladder with creation of a continent neobladder to function without a stoma</p> <p>OR</p> <p>Any OHIP Billing Code for Cystectomy with Continent Urinary Diversion (Includes Any One of the Following):</p> <p>S440: Complete cystectomy with continent urinary diversion S484+S441: Complete cystectomy + Creation of continent urinary diversion S485+S441: Complete cystectomy with ureteroileal transplant + Creation of continent urinary diversion</p>

6.8.2. Calculating Code Algorithm Accuracy

The accuracy measures of the code algorithm were calculated using 2x2 contingency tables as presented in Table 10. The sensitivity of a code refers to the codes ability to correctly identify patients who actually have a disease or underwent a procedure (Equation 1). The specificity refers to the codes ability to correctly identify patients who actually do not have a disease or did not undergo a procedure (Equation 2). The positive predictive value refers to the proportion of patients who are assigned a code for a diagnosis or procedure who actually have the diagnosis or received the procedure (Equation 3). Finally, the negative predictive value refers to the proportion of patients who are not assigned a code for a diagnosis or procedure who actually do not have the diagnosis or did not receive a procedure (Equation 4).⁵¹

Table 11. 2x2 frequency table for code status vs true cystectomy status.

		True Cystectomy Status	
		+	-
Code Status	+	A – True Positive	B – False Positive
	-	C- False Negative	D – True Negative

Equation 1: Sensitivity

$$\text{Sensitivity} = [\text{True Positives}] / [\text{True Positives} + \text{False Negatives}] * 100\%$$

Equation 2: Specificity

$$\text{Specificity} = [\text{True Negatives}] / [\text{True Negatives} + \text{False Positives}] * 100\%$$

Equation 3: Positive Predictive Value

$$\text{Positive Predictive Value} = [\text{True Positives}] / [\text{True Positives} + \text{False Positives}] * 100\%$$

Equation 4: Negative Predictive Value

$$\text{Negative Predictive Value} = [\text{True Negatives}] / [\text{True Negatives} + \text{False Negatives}] * 100\%$$

Both sensitivity and specificity are constant measures of the code accuracy and are not influenced by the prevalence of a disease or procedure (i.e. the pre-test probability). The positive and negative predictive values, however, are influenced by the disease or procedure prevalence. To this end, a higher prevalence of a disease or procedure will result in a higher positive predictive value (and lower negative predictive value) for the identifying code whereas a lower prevalence will result in a lower positive predictive value (and higher negative predictive value) for the identifying code. Therefore, in the case of uncommon surgeries such as cystectomy, which would have a low prevalence within the DAD, even codes with a high specificity may have a low positive predictive value and are thus subject to significant misclassification bias.

6.9. Calculating and Comparing Misclassification Bias

Once the final OCIM was created and its accuracy assessed (Section 3.7), misclassification bias from the model was measured and compared to that resulting from identifying cystectomy with incontinent or continent diversion using the procedure and billing code algorithm (Section 6.8). Misclassification bias is the difference between a statistic's true value (i.e. that measured when true cystectomy status was used from the reference gold standard cohort) and that measured when cystectomy status was determined by a surrogate method (administrative codes or predictive models). Therefore, true values for a statistic were measured when true cystectomy status was used in its calculation. "Surrogate values" for a statistic were measured when cystectomy status was determined with one of two surrogates: i) code algorithm (Table 10); or ii) expected cystectomy probability from the OCIM.

With code algorithms, cystectomy was deemed present if code criteria were met. For expected cystectomy probability from the OCIM, we used “Bootstrap Imputation” to assign cystectomy status.⁵²⁻⁵⁴ Bootstrap imputation starts by using bootstrap resampling techniques to creating 10 000 bootstrap samples having original sample size with replacement. Then, the statistic is calculated in each bootstrap sample. This calculation is done by first imputing cystectomy status for each patient based on his / her *expected cystectomy probability* from OCIM. Cystectomy status was imputed by randomly selecting a number from a uniform distribution between 0 and 1. If this number was *less than* the expected cystectomy probability from OCIM, cystectomy was deemed present; if this number *exceeded* the expected cystectomy probability from OCIM, cystectomy was deemed absent. This process was done for all observations in the bootstrap sample and the statistic was calculated.

These steps were repeated in all 10 000 bootstrap samples, returning 10 000 statistics. The final statistic point estimate was the mean of these 10 000 estimates with 95% confidence intervals calculated as the 2.5 and 97.5 percentiles of these values.⁴⁹ Misclassification bias for a statistic was calculated as the absolute difference between its true value and the surrogate value, with the latter calculated when cystectomy status was determined by the code algorithm or by OCIM with bootstrap imputation (Equation 10). This process was performed for both cystectomy with incontinent and cystectomy with continent urinary diversion.

Equation 10. Calculation of Misclassification Bias

Misclassification Bias = True Value of Co-Variable (Using Gold Standard Cohort) – Surrogate Value of Co-Variable (Using Code Algorithm or OCIM + Bootstrap Imputation)

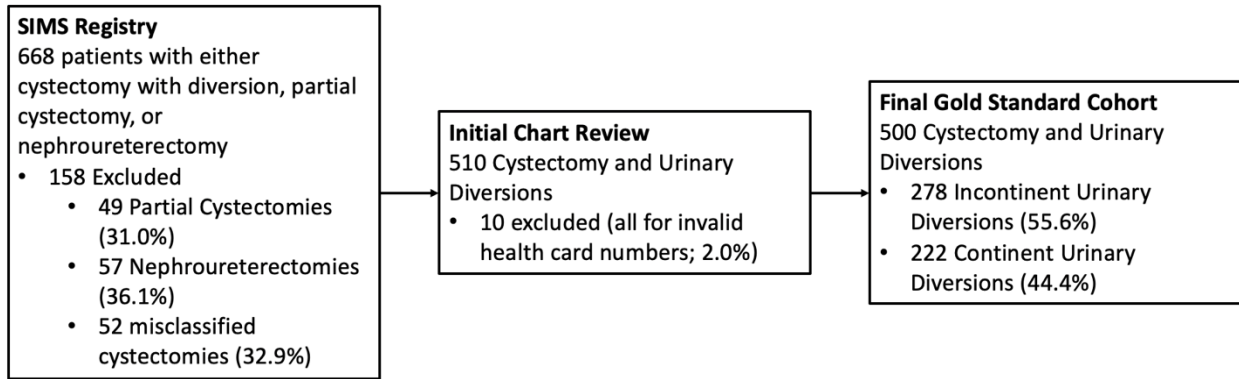
7. Results

7.1. Gold Standard Reference Cohort Description

During the study period, 668 patients were identified as having undergone cystectomy with urinary diversion, partial cystectomy, or nephroureterectomy within the SIMS registry. Of these, 158 patients were excluded after manual chart review ($158/668 \times 100\% = 23.6\%$). Of the 158 excluded, 49 had undergone partial cystectomy ($49/158 = 31.0\%$), 57 underwent nephroureterectomy ($57/158 = 36.0\%$), and 52 were misclassified as cystectomy with urinary diversion ($52/158 = 32.9\%$).

After exclusions, we identified 510 patients who truly underwent cystectomy with urinary diversion during the study period at TOH (Figure 3). Ten of these patients were subsequently excluded because they did not have valid Ontario Health Card numbers ($10/510 \times 100\% = 2.0\%$). The final gold standard reference cohort thus contained 500 cystectomies with urinary diversions. Of these, 278 were cystectomy with incontinent urinary diversion ($278/500 \times 100\% = 55.6\%$) and 222 were cystectomy with continent urinary diversion ($222/500 \times 100\% = 44.4\%$; Figure 3).

Figure 3. Flowchart demonstrating the creation of the Gold Standard Reference Cohort.



Fifty-two patients were miscoded in the SIMS registry as having had a cystectomy with urinary diversion. Of these patients, 26 patients ($26/52 = 50.0\%$) actually had an ileal conduit urinary diversion alone without a cystectomy and seven ($7/52 = 13.5\%$) had an aborted cystectomy in which the abdomen was opened but the bladder was deemed to be unresectable and thus the surgery was not completed. Reasons for the remaining misclassified patients are presented in Table 12.

Table 12. The actual procedures and number performed for patients misclassified as having a cystectomy within the SIMS registry.

Actual Procedure Performed	n (%)
Just ileal conduit performed without cystectomy	26 (50.0)
Cystectomy aborted without bladder being removed	7 (13.5)
Revision of previously performed neobladder diversion	3 (5.8)
Conversion of previously performed neobladder to an ileal conduit	3 (5.8)
Repair of fistulous communication with the bladder	3 (5.8)
Augmentation of bladder with piece of intestine without bladder removal	2 (3.8)
Creation of catheterizable channel without bladder removal	1 (1.9)
Partial cystectomy without urinary diversion	1 (1.9)
Transurethral resection of bladder tumor	1 (1.9)
Resection of peri-vesicular pheochromocytoma	1 (1.9)
Pelvic lymph node resection without bladder removal	1 (1.9)

7.2. Analytical Dataset Description

The final analytical dataset included 428 697 hospitalizations to TOH during the study period. The overall incidence of hospitalizations for cystectomy with any urinary diversion (incontinent or continent) was 1.2 per 10 000 admissions per year. The incidence of cystectomy and incontinent urinary diversion was 0.6 per 10 000 hospitalizations per year and the incidence of cystectomy with continent urinary diversion was 0.5 per 10 000 hospitalizations per year.

Based on our sample size and prevalence of cystectomy, as per the methods described by Riley et al., the OCIM would be allowed a maximum of 27 degrees of freedom for co-variable selection.⁴⁴ After co-variable selection was complete by the two reviewers, our total number of degrees of freedom from all selected co-variables was 15, indicating that our model was not overfit for the sample size and number of cystectomies within the sample.

7.2.1. Difference in Baseline Co-Variables for Cystectomy vs. Non-Cystectomy Hospitalizations

There were notable differences between hospitalizations for cystectomy with urinary diversion compared to non-cystectomy hospitalizations (Table 13). Hospitalizations during which a cystectomy with urinary diversion was performed were more likely to have a higher prevalence of male sex, elective admission, blood transfusion administration, diagnosis of bladder cancer within the DAD or OCR, use of general anesthetic for coded cystectomy or primary procedure, have the coded cystectomy or primary procedure being performed in the main OR, unplanned return to the OR within 28 days, and urology as the primary service. The prevalence of patients being discharged home without supports and primary procedure or coded

cystectomy not being performed in the main OR was lower in cystectomy patients. Mean age was higher, and operative time was longer in cystectomy patients as well (Table 12).

Within cystectomy patients, those with incontinent diversions were more likely to have a lower prevalence of male sex, diagnosis of bladder cancer within the DAD or OCR, and discharge home without support; the prevalence of blood transfusion was higher; operative time was shorter, and mean age was higher. The code algorithm for cystectomy with incontinent or continent diversion was much more prevalent in patients who truly underwent each respective surgery. This being said, 150 patients (54.0%) who actually underwent cystectomy with incontinent urinary diversion also met the code definition for cystectomy with continent urinary diversion. Likewise, 23 patients (28.4%) who actually underwent cystectomy with continent urinary diversion also met the coding definition for cystectomy with incontinent urinary diversion (Table 13).

Table 13. Description of co-variables among cystectomy and non-cystectomy admissions to TOH.

Co-Variable	Cystectomy and Incontinent Urinary Diversion (n = 278)	Cystectomy and Continent Urinary Diversion (n = 222)	No Cystectomy (n = 428 197)	Overall (n = 428 697)
Male Sex n (%)	201 (72.3)	177 (79.7)	173 465 (40.5)	173 843 (40.6)
Age mean (SD)	71.2 (10.4)	63.6 (8.5)	57.5 (20.6)	57.5 (20.6)
CCI or OHIP Code for Cystectomy and Continent Diversion n (%)	150 (54.0)	222 (100.0)	87 (0.0)	459 (0.1)
CCI or OHIP Code for Cystectomy and Incontinent Diversion n (%)	270 (97.1)	23 (28.4)	128 (0.0)	461 (0.1)
Elective Admission n (%)	265 (95.3)	218 (98.2)	143 112 (33.4)	143 595 (33.5)
Blood Transfusion During Admission n (%)	165 (59.4)	122 (55.0)	53 547 (12.5)	53 834 (12.6)
Diagnosis of Bladder Cancer in DAD n (%)	234 (84.2)	218 (98.2)	2 732 (0.6)	3 184 (0.7)
Diagnosis of Bladder Cancer in OCR n (%)	218 (78.8)	204 (91.9)	6 112 (1.4)	6 535 (1.5)
General Anesthetic n (%)	265 (95.3)	215 (96.8)	114 629 (26.8)	115 109 (26.9)
Coded Cystectomy or Primary Procedure in Main OR n (%)	275 (98.9)	222 (100.0)	145 473 (34.0)	145 970 (34.0)
Coded Cystectomy or Primary Procedure Not in Main OR n (%)	<= 5 (0.7)	0 (0.0)	177 602 (41.5)	177 604 (41.4)
Operative Time of Coded Cystectomy or Primary Procedure median (1 st quartile, 3 rd quartile)	526.5 (468.0, 590.0)	641.0 (576.0, 695.0)	0.0 (0.0, 113.0)	0.0 (0.0, 113.0)
Unplanned Return to OR Within 28 days of Coded Cystectomy or Primary Procedure n (%)	21 (7.6)	19 (8.6)	12 (0.0)	52 (0.0)
Death or Readmission within 28 days of Coded Cystectomy or Primary Procedure n (%)	25 (9.0)	19 (8.6)	37 587 (8.8)	37 631 (8.8)
Discharged Home Without Supports Following Admission n (%)	36 (12.9)	48 (21.6)	266 924 (62.3)	267 008 (62.3)
Urology was the Primary Service During Admission n (%)	276 (99.3)	222 (100.0)	20 846 (4.9)	21 344 (5.0)
Acute Length of Hospital Admission median (1 st quartile, 3 rd quartile) n (%)	11.0 (8.0, 19.0)	10.0 (8.0-19.0)	3.0 (2.0, 7.0)	3.0 (2.0, 7.0)

7.3. Code Algorithm Accuracy

7.3.1. Cystectomy with Incontinent Diversion

There were 278 hospitalizations where a cystectomy with incontinent urinary diversion actually occurred within the gold standard reference cohort. When applying the coding algorithm for cystectomy with incontinent urinary diversion, a total of 461 hospitalizations were identified ($461/428\ 697 \times 100\% = 0.11\%$). The code algorithm identified 97.1% of cystectomy with incontinent diversion. However, only 58.6% of people with the code algorithm actually underwent cystectomy with incontinent diversion (Table 14).

Table 14. Accuracy of code algorithm for cystectomy with incontinent diversion.

		True Cystectomy with Incontinent Diversion		Total
		+	-	
Code Status	+	270	191	461
	-	8	428 228	428 236
Total		278	428 419	428 697

Equation 1. Sensitivity

$$\begin{aligned} \text{Sensitivity} &= [\text{True Positives}] / [\text{True Positives} + \text{False Negatives}] * 100\% \\ &= 270 / [270 + 8] * 100\% \\ &= 97.12\% \end{aligned}$$

Equation 2. Specificity

$$\begin{aligned} \text{Specificity} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Positives}] * 100\% \\ &= 428\ 228 / [428\ 238 + 191] * 100\% \\ &= 99.95\% \end{aligned}$$

Equation 3. Positive Predictive Value

$$\begin{aligned} \text{Positive Predictive Value} &= [\text{True Positives}] / [\text{True Positives} + \text{False Positives}] * 100\% \\ &= 270 / [270 + 191] * 100\% \\ &= 58.57\% \end{aligned}$$

Equation 4. Negative Predictive Value

$$\begin{aligned} \text{Negative Predictive Value} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Negatives}] * 100\% \\ &= 428\,228 / [428\,228 + 8] * 100\% \\ &= 100\% \end{aligned}$$

7.3.2. Cystectomy with Continent Diversion

There were 222 hospitalizations where a cystectomy with continent urinary diversion actually occurred within the gold standard reference cohort. When applying the coding algorithm for cystectomy with continent urinary diversion, a total of 459 hospitalizations were identified ($459/428\,697 \times 100\% = 0.11\%$). The code algorithm identified 100% of cystectomy with continent diversion. However, only 48.37% of people with the code algorithm actually underwent cystectomy with continent diversion (Table 15).

Table 15. Accuracy of code algorithm for cystectomy with continent diversion.

		True Cystectomy and Continent Diversion Status		Total
		+	-	
Code Status	+	222	237	459
	-	0	428 238	428 238
Total		222	428 475	428 697

Equation 1: Sensitivity

$$\begin{aligned}\text{Sensitivity} &= [\text{True Positives}] / [\text{True Positives} + \text{False Negatives}] * 100\% \\ &= 222 / [222 + 0] * 100\% \\ &= 100\%\end{aligned}$$

Equation 2: Specificity

$$\begin{aligned}\text{Specificity} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Positives}] * 100\% \\ &= 428\ 238 / [428\ 238 + 237] * 100\% \\ &= 99.94\%\end{aligned}$$

Equation 3: Positive Predictive Value

$$\begin{aligned}\text{Positive Predictive Value} &= [\text{True Positives}] / [\text{True Positives} + \text{False Positives}] * 100\% \\ &= 222 / [222 + 237] * 100\% \\ &= 48.37\%\end{aligned}$$

Equation 4: Negative Predictive Value

$$\begin{aligned}\text{Negative Predictive Value} &= [\text{True Negatives}] / [\text{True Negatives} + \text{False Negatives}] * 100\% \\ &= 428\ 238 / [428\ 238 + 0] \\ &= 100\%\end{aligned}$$

7.4. Fitting of Continuous Co-Variables

The continuous variables were assessed using the MFP8 macro within SAS to determine best transformations to maintain a linear relationship with the log odds of the outcome. Age, acute length of stay, and operative time all required fractional polynomial transformation. These transformations are presented in Table 16.

Table 16. Fractional polynomial transformations for continuous co-variables using the MFP8 macro in SAS.

Variable	Transformations
Age	Term 1: $1/\text{Age}^2$ Term 2: $\log(\text{Age})/\text{Age}^2$
Acute Length of Stay (LOS)	Term 1: LOS Term 2: $1/\text{LOS}^{0.5}$
Operative Time (OPT)	Term 1: $\text{OPT}^{0.5}$ Term 2: OPT^3

7.5. Creating the Ottawa Cystectomy Identification Model (OCIM)

Based on the likelihood ratio test, the following co-variables significantly improved model fit and were therefore kept in the final predictive model: 1) OHIP code for cystectomy with incontinent urinary diversion, 2) OHIP code for cystectomy with continent urinary diversion, 3) CCI code for cystectomy with incontinent urinary diversion, 4) CCI code for cystectomy with continent urinary diversion, 5) diagnosis of bladder cancer within the DAD, 6) urology as the primary service, 7) acute length of stay, 8) elective admission, and 9) unplanned return to the OR within 28 days. A diagnosis of bladder cancer within the OCR was initially significantly associated with an admission for cystectomy with urinary diversion, however, the significant association was lost and the co-variable was removed after ‘Urology as the Primary Service’ was added to the model. None of the other variables offered to the model significantly improved model fit. A summary of the steps used to create the OCIM are presented in Table 17.

Table 17. Co-variable selection for final predictive model using the log likelihood ratio test.

Model	Co-Variables Added/Removed	Log Ratio Test	Decision
#1	Intercepts	8440.176	NA
#2	1) OHIP codes for cystectomy and incontinent diversion 2) OHIP codes for cystectomy and incontinent diversion	8440.176 <u>- 1021.313</u> 7418.863	OHIP codes for cystectomy and urinary diversion Included
#3	Diagnosis of bladder cancer in OCR	1021.313 <u>- 821.024</u> 200.289	Diagnosis of bladder cancer in OCR included
#4	1) CCI code for cystectomy and incontinent diversion 2) CCI code for cystectomy and continent diversion	821.024 <u>- 616.097</u> 204.927	CCI codes for cystectomy and urinary diversion included
#5	Diagnosis of bladder cancer in DAD	616.097 <u>- 585.280</u> 30.817	Diagnosis of bladder cancer in DAD included
#6	Urology as primary service	585.280 <u>- 454.221</u> 131.059	1) Urology as primary service included 2) Diagnosis of bladder cancer in OCR no longer significant and removed
#7	Diagnosis of bladder cancer in OCR REMOVED	455.923 <u>- 454.221</u> 1.702	No significant difference in model with 'Diagnosis of bladder cancer in OCR' removed
#8	OR Time (two terms)	No Convergence	OR time not included
#9	1) Cystectomy/primary procedure in main operating room 2) Cystectomy/primary procedure in other operating room	455.923 <u>- 455.528</u> 0.395	Cystectomy/primary procedure in the main OR or not in the main OR not included
#10	Acute length of stay (two terms)	455.923 <u>- 441.660</u> 14.263	Acute length of stay included
#11	Age (two terms)	441.660 <u>- 431.478</u> 10.182	Age not included
#12	Elective admission	441.660 <u>- 429.174</u> 12.486	Elective admission included
#13	General anesthetic	429.174 <u>- 424.902</u> 4.272	General anesthetic not included
#14	Death or readmission within 28 days	429.174 <u>- 425.862</u> 3.312	Death or readmission within 28 days not included
#15	Discharge home without supports	429.174 <u>- 428.387</u> 0.787	Discharge home without supports not included
#16	Blood transfusion	429.174 <u>- 424.942</u> 4.232	Blood transfusion not included
#17	Unplanned return to the OR within 28 days	429.174 <u>- 420.966</u> 8.208	Unplanned return to the OR within 28 days included

7.6. The Ottawa Cystectomy Identification Model (OCIM)

The final Ottawa Cystectomy Identification Model (OCIM) was a multinomial model provided the log odds of 1) cystectomy with incontinent urinary diversion, 2) cystectomy with continent urinary diversion, or 3) no cystectomy (which represents the reference level by which the log odds of cystectomy with urinary diversion is compared). As such, each co-variable had two parameter estimates (one for cystectomy with incontinent diversion vs no cystectomy and one for cystectomy with continent diversion vs no cystectomy). The parameter estimates and odds ratios for co-variables predictive of cystectomy with incontinent urinary diversion and cystectomy with continent urinary diversion can be seen in Table 18 and Table 19, respectively.

Table 18. Multinomial model parameter estimates and odds ratios for cystectomy with incontinent urinary diversion.

Co-Variable	Parameter Estimate (95% CI)	Odds Ratio (95% CI)
Intercept	-10.97	NA
OHIP for Cystectomy and Continent Diversion	0.67 (-0.47, 1.81)	1.95 (0.62, 6.12)
OHIP for Cystectomy and Incontinent Diversion	3.66 (2.52, 4.79)	38.82 (12.50, 120.55)
CCI for cystectomy and Continent Diversion	4.85 (3.67, 6.04)	129.21 (39.17, 419.69)
CCI for Cystectomy and Incontinent Diversion	5.87 (4.68, 7.06)	352.76 (107.32, >999.99)
Diagnosis of Bladder Cancer in DAD	-0.03 (-1.08, 1.02)	0.97 (0.34, 2.77)
Urology as the Primary Service	6.58 (4.86, 8.31)	722.60 (128.94, >999.99)
Acute Length of Stay	-0.05 (-0.08, -0.02)	0.95 (0.92, 0.98)
1/(Acute Length of Stay) ^{0.5}	-9.37 (-14.41, -4.32)	<0.001 (<0.001, 0.01)
Elective Admission	1.66 (0.63, 2.70)	5.28 (1.88, 14.83)
Unplanned Return to OR within 28 Days	1.99 (-0.17, 4.14)	7.29 (0.84, 63.12)

Table 19. Multinomial model parameter estimates and odds ratios for cystectomy with continent urinary diversion.

Co-Variable	Parameter Estimate (95% CI)	Odds Ratio (95% CI)
Intercept	-26.64 (-881.30, 820.00)	NA
OHIP for Cystectomy and Continent Diversion	7.16 (4.82, 9.50)	>999.99 (123.72, >999.99)
OHIP for Cystectomy and Incontinent Diversion	0.22 (-1.13, 1.57)	1.25 (0.32, 4.81)
CCI for cystectomy and Continent Diversion	6.21 (3.74, 8.68)	498.53 (42.05, >999.99)
CCI for Cystectomy and Incontinent Diversion	3.65 (0.83, 6.46)	38.39 (2.30, 640.69)
Diagnosis of Bladder Cancer in DAD	2.40 (0.62, 4.17)	10.98 (1.86, 64.82)
Urology as the Primary Service	14.27 (-840.40, 868.90)	>999.99 (<0.001, >999.99)
Acute Length of Stay	-0.03 (-0.07, 0.01)	0.97 (0.93, 1.01)
1/(Acute Length of Stay) ^{0.5}	-4.59 (-14.66, 5.49)	0.01 (<0.001, 241.16)
Elective Admission	2.52 (0.52, 4.54)	12.50 (1.67, 93.28)
Unplanned Return to OR within 28 Days	3.99 (1.18, 6.80)	54.22 (3.26, 901.47)

OHIP billing codes for cystectomy with incontinent or continent diversion was highly associated with true cystectomy status for both diversion types. The presence of a CCI code for cystectomy with any diversion type (incontinent or continent) was positively associated with the presence of cystectomy with both incontinent or continent diversion, regardless of diversion type, however, in both cases the OR was higher corresponding with the true cystectomy and diversion status. Urology as the primary service was highly associated for cystectomy with both diversion types. Unplanned return to the OR within 28 days was significantly associated with cystectomy with continent diversion but not for cystectomy with incontinent diversion (Table 18 and Table 19).

7.7. Distribution of Predicted Probabilities

Expected probabilities at the 1st, 25th, 50th, 75th, and 99th percentile for each outcome (no cystectomy, cystectomy with incontinent urinary diversion, and cystectomy with continent urinary diversion) are presented in Table 20 and stratified by true cystectomy with urinary diversion status. The median probability (i.e. 50th percentile) for each outcome was significantly higher for the corresponding true cystectomy status. For admissions where no cystectomy was performed, the model probability for no cystectomy was 100% compared to a probability of 0% for cystectomy with incontinent or continent diversion for all percentiles (Table 20).

Table 20. Distribution of model probabilities based on true admission status for no cystectomy, cystectomy with incontinent urinary diversion, and cystectomy with continent urinary diversion.

True Cystectomy Status	Outcome	OCIM Expected Probability of Outcome at Specific Percentiles				
		1 st Pctl	25 th Pctl	50 th Pctl	75 th Pctl	99 th Pctl
No Cystectomy	1) No Cystectomy	1.00	1.00	1.00	1.00	1.00
	2) Cystectomy and Incontinent Diversion	0.00	0.00	0.00	0.00	0.00
	3) Cystectomy and Continent Diversion	0.00	0.00	0.00	0.00	0.00
Cystectomy-Incontinent Diversion	No Cystectomy	0.01	0.03	0.053	0.08	1.00
	Cystectomy and Incontinent Diversion	0.00	0.89	0.93	0.96	0.98
	Cystectomy and Continent Diversion	0.00	0.00	0.00	0.01	0.98
Cystectomy-Continent Diversion	No Cystectomy	0.00	0.01	0.01	0.02	0.07
	Cystectomy and Incontinent Diversion	0.00	0.01	0.01	0.08	0.24
	Cystectomy and Continent Diversion	0.25	0.83	0.98	0.98	0.98

7.8. Model Accuracy

7.8.1. Model Discrimination

The OCIM demonstrated excellent discrimination for both cystectomy with incontinent diversion and cystectomy with continent diversion. The optimism corrected c-statistic was 0.9986 (95% CI 0.9964, 0.9994) for cystectomy with incontinent urinary diversion and was 1.0000 (1.0000, 1.0000) for cystectomy with continent diversion.

7.8.2. Model Calibration

The OCIM also demonstrated excellent calibration between the observed and expected probabilities for both cystectomy with incontinent diversion and cystectomy with continent diversion. In this case, the optimism corrected ICI was 0.000 (95% CI 0.00, 0.00) for both predicted outcomes (Figure 4 and Figure 5).

Figure 4. Calibration curve for cystectomy with incontinent urinary diversion.

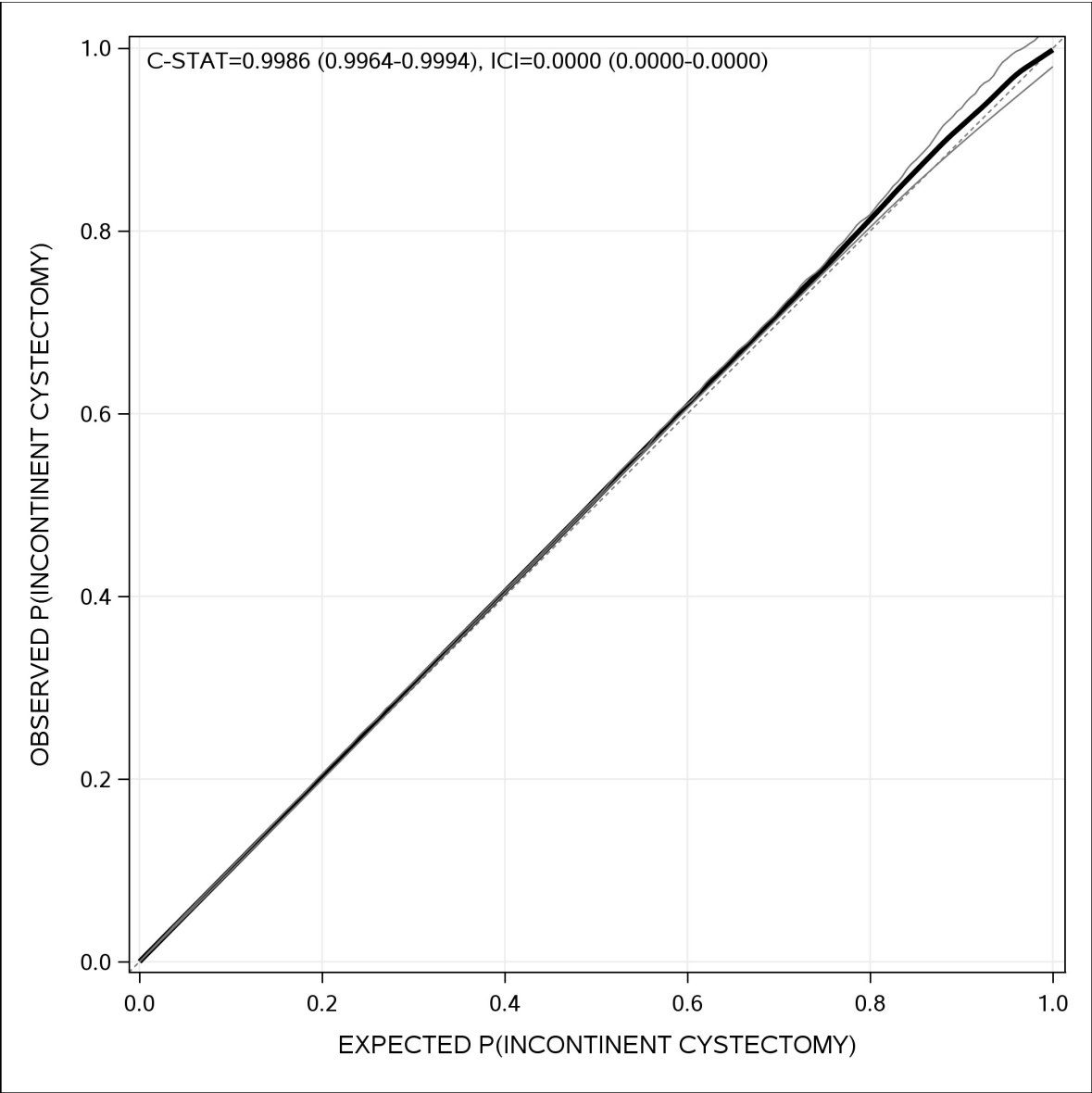
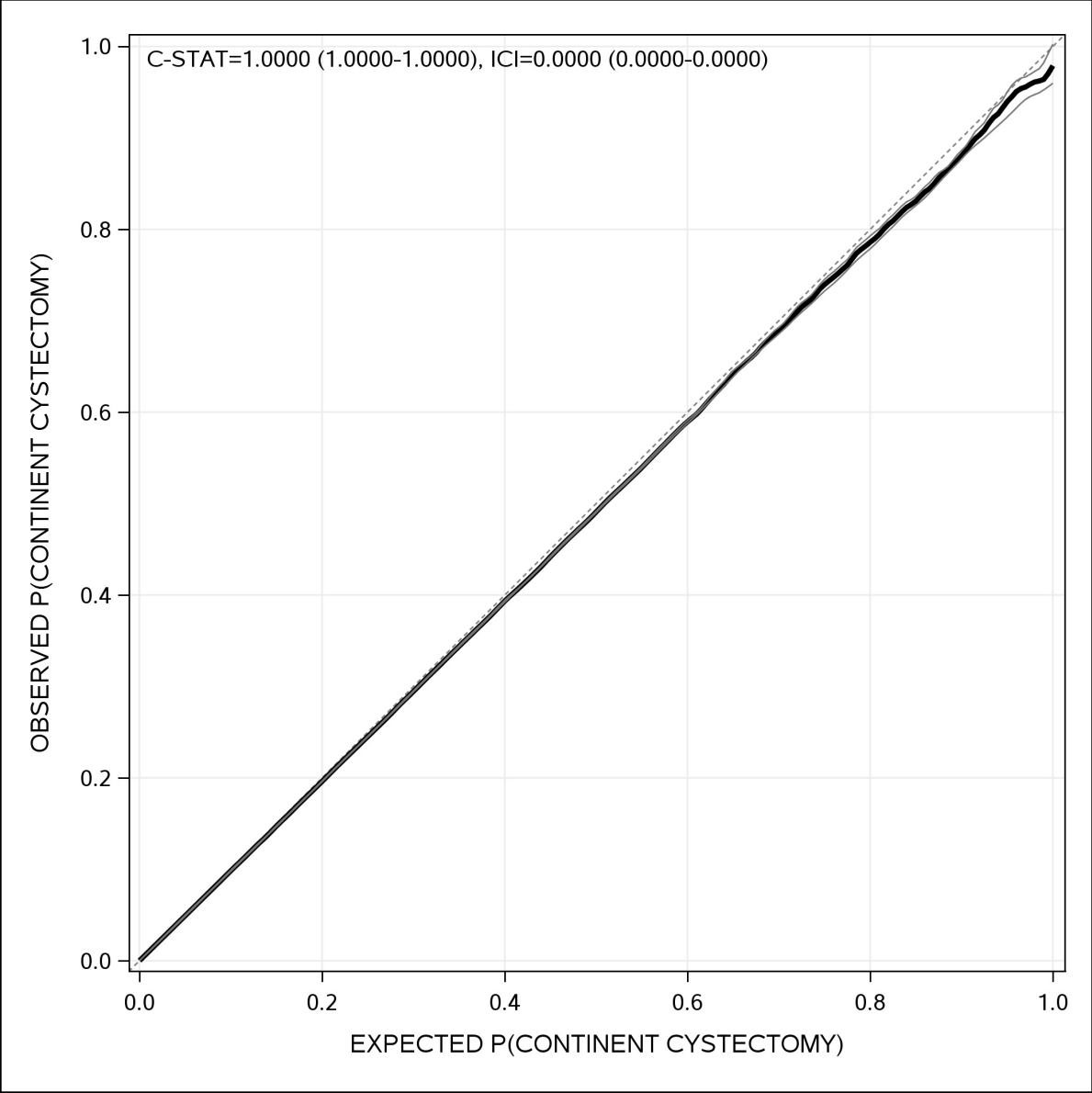


Figure 5. Calibration curve for cystectomy with continent urinary diversion.



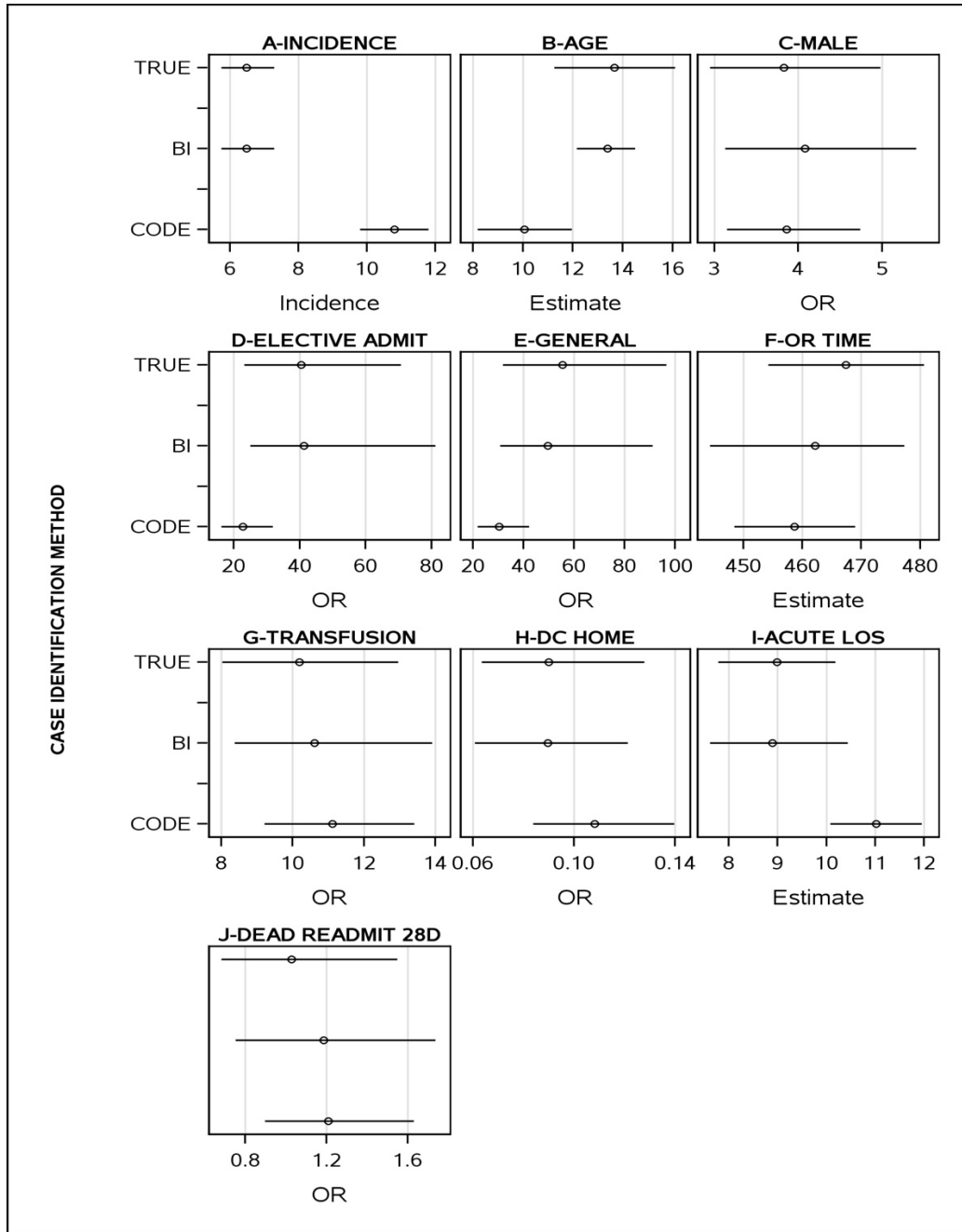
7.9. Assessment of Misclassification Bias

The predictive mode (i.e. the OCIM) resulted in significantly less misclassification with true cystectomy status as compared to the code algorithm (i.e. the presence of a CCI procedure code OR OHIP billing code for cystectomy with incontinent/continent urinary diversion). When identifying cystectomy cases using the OCIM compared to the code algorithm, cystectomy incidence as well as most other co-variables more closely resembled the actual estimates from the gold standard reference cohort. The one exception is for the odds ratio for male sex for cystectomy with incontinent diversion where the code algorithm was slightly closer to the true value, however, this was not significant.

For both cystectomy with incontinent and continent urinary diversion, the code algorithm significantly overestimated the incidence of cystectomy admissions when used to identify potential cystectomy cases. Similarly, identifying cases of cystectomy with incontinent urinary diversion using the code algorithm resulted in a significant underestimation of patient age compared to the true value (Figure 6). For cystectomy with continent urinary diversion, the coding algorithm also significantly underestimated operative time (Figure 7). The difference in misclassification did not always bias towards the null hypothesis. The incidence and acute length of stay as well as the odds ratio for transfusion, discharge home without supports, and death or readmission within 28 days was higher when using the code algorithm to identify patients undergoing cystectomy with incontinent diversion. The incidence and acute length of stay as well as the odds ratios for transfusion and death or readmission within 28 days was also higher when using the code algorithm to identify patients undergoing cystectomy with continent

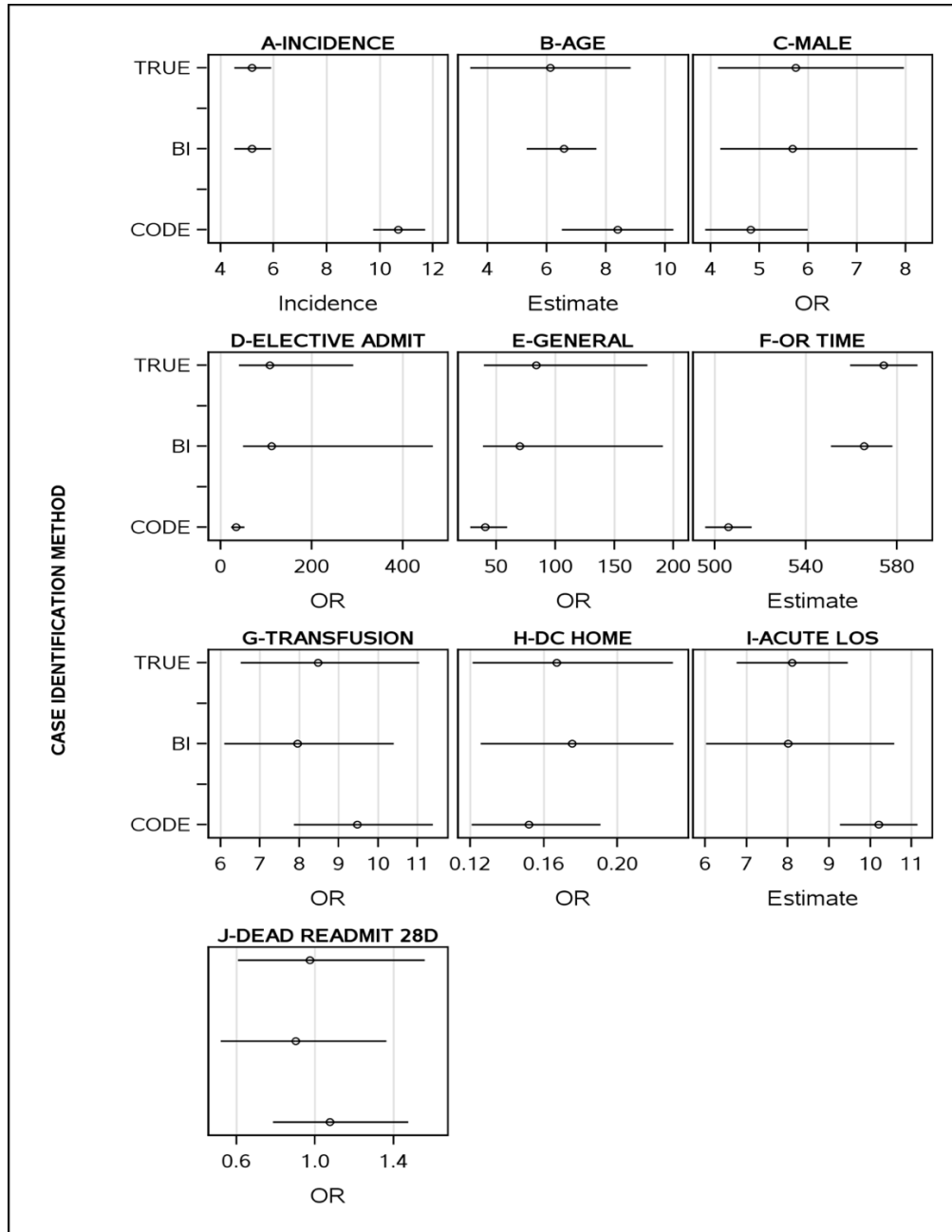
urinary diversion. Variables from Tables 18 and 19 whose association with true cystectomy status returned invalid results (i.e. parameter estimates <0.001 or >999.9) were excluded.

Figure 6. Forest plots demonstrating misclassification for cystectomy with incontinent urinary diversion using the predictive model with bootstrap imputation vs coding algorithm.



- True = The actual value based on the gold standard cohort
- BI = Value estimate calculated using OCIM with bootstrap imputation
- Code = Value based on coding algorithm
- OR = Odds Ratio
- Estimate = Parameter Estimate

Figure 7. Forest plots demonstrating misclassification for cystectomy with continent urinary diversion using the predictive model with bootstrap imputation vs coding algorithm.



- True = The actual value based on the gold standard cohort
- BI = Value estimate calculated using OCIM with bootstrap imputation
- Code = Value based on coding algorithm
- OR = Odds Ratio
- Estimate = Parameter Estimate

8. Discussion

8.1. Summary of Results

This study found that hospitalizations in which cystectomy with urinary diversion (incontinent or continent) were performed are uncommon in comparison to all hospitalizations to TOH during the same study period. When a code algorithm using either intervention (CCI) or billing (OHIP) codes were used to identify cystectomy with urinary diversion patients, the coding algorithms had high sensitivities and specificities but resulted in significant misclassification (positive predictive values of 58.6% for cystectomy with incontinent diversion and 48.4% for cystectomy with continent diversion). Using procedure and billing codes as well as other clinical data within health administrative databases in ICES, a multinomial logistic regression model (the OCIM) was successfully created that accurately returned the probability that cystectomy with incontinent or continent urinary diversions occurred during hospitalization recorded in the discharge abstract database (Figure 4 and Figure 5). When compared to the use of the code algorithm alone, the cystectomy status determined using OCIM and bootstrap imputation resulted in less misclassification bias for cystectomy incidence and all co-variables except one (Figure 6 and Figure 7).

8.2. Notable Results

8.2.1. Accuracy Measures of Coding Algorithms

The coding algorithms used in this study included either a CCI procedure code or an OHIP billing code to identify patients undergoing cystectomy with incontinent urinary diversion or

cystectomy with continent urinary diversion (Table 10). These code algorithms had very high sensitivities (97.1% and 100.0% for cystectomy with incontinent diversion and continent diversion, respectively) and specificity (100.0% and 99.9% for cystectomy with incontinent diversion and continent diversion, respectively). Despite the high sensitivity and specificity of the code algorithms, the positive predictive values were much lower, with just over half (58.6%) of patients coded for cystectomy with incontinent urinary diversion actually receiving the surgery and just under half (48.4%) of patients coded for cystectomy with continent urinary diversion actually receiving the surgery.

Unlike sensitivity and specificity, which are relatively constant regardless of prevalence, the positive predictive value of a code algorithm is strongly influenced by disease or procedure prevalence. For a condition or procedure with a low prevalence, the positive predictive value of a test or code will be lower as compared to a condition or procedure with a high prevalence. As a result, even a code with a high sensitivity and specificity may have a low positive predictive value if the baseline prevalence of the condition or procedure is low.⁵¹

For example, for cystectomy with incontinent diversion, a total of 461 hospitalizations were identified using the coding algorithm. Of these 461 hospitalizations, 270 were true positives and 191 were false positives. Because the code algorithm identified 270 out of 278 actual cystectomies with incontinent diversions, the code algorithm was very sensitive (97.1%). Although there were 191 false positives, because there were 428 288 true negatives, the code algorithm was also very specific (100.0%). Given that 191/461 hospitalizations identified using the code algorithm identified were false positives, however, the positive predictive value of the

code algorithm was only 58.6%. Similarly, for cystectomy with continent urinary diversion, 459 hospitalizations were identified of which 222 were true positives. Although the code was very sensitive and specific, because 237/459 hospitalizations were false positives, the positive predictive value of the code algorithm was only 48.4%.

Although sensitivity and specificity are often cited when referencing code accuracy, this study highlights the importance of reporting the positive predictive value of the code being used along with the prevalence of the condition. Positive predictive value reports the proportion of ‘code positive’ cases that actually have the diagnosis or underwent the procedure and is therefore most reflective of potential code misclassification. Furthermore, as highlighted in this study, for uncommon diagnoses or procedures, even codes with high sensitivity and specificity (prevalence independent) may have a low positive predictive value (prevalence dependent) and therefore still result in significant misclassification.

Despite the importance of reporting these accuracy measures, a previous study by van Walraven et al (2011) found that validated coding algorithms to identify diagnoses or procedures are rarely applied in studies using health administrative datasets. This study performed a random review of 150 Medline cited studies using administrative databases. Of these studies, 115 ($115/150 \times 100\% = 76.7\%$) used codes to identify diagnoses or procedures of which only 14 ($14/115 \times 100\% = 12.1\%$) reported any measure of code accuracy for the diagnosis or procedure that it was supposed to represent. Furthermore, of the studies reporting on code accuracy, only 8 ($8/115 \times 100\% = 7.0\%$) reported positive predictive values for the codes used.²⁰

In our review on cystectomy studies using large health administrative databases, no study directly cited or referenced the accuracy measures of the code algorithm used to identify cystectomy patients (Table 1). There was also a paucity of validation studies on coding algorithms for cystectomy in the published literature. Of the two cystectomy validation studies identified, neither provided full assessment of all measures of code accuracy and both used a gold standard reference cohort of unknown accuracy or completeness.^{42,43} For cystectomy studies using databases within ICES, many used a diagnosis of bladder cancer within the OCR in addition to CCI coding to identify cystectomy patients. Interestingly, in this study, a diagnosis of bladder cancer within the OCR, despite being the presumed gold standard, did not result in significant improvement in model fit of the OCIM and was not included in the final model. A diagnosis of bladder cancer within the DAD did result in a significant improvement in model fit and therefore was included in the final OCIM.

By providing a full and precise assessment of cystectomy coding accuracy, this study will help to facilitate future validated research on cystectomy and urinary diversion using large health administrative databases and will also allow for proper review and analysis of previously published administrative database studies on cystectomy.

8.2.2. OCIM Accuracy

The OCIM demonstrated excellent discrimination (high optimism adjusted c-statistic) and calibration (low optimism-adjusted ICI) for the identification of hospitalizations during which cystectomy with diversion occurred. Although both procedure and billing codes were highly associated with cystectomy and diversion status, other clinical variable within ICES databases

proved to be independently predictive and resulted in further significant improvement in overall model fit (Table 17).

Other studies have also created logistic regression models which combine diagnostic or procedure codes and clinical co-variables to allow for accurate identification of cases using large health administrative databases. A study by Adamczyk et al. (2021) created a gold standard reference cohort by applying a text search algorithm developed for acetabular fracture patients in the TOH trauma registry which was then applied to all CT Pelvis studies at TOH between 2008 to 2013. The diagnosis of acetabular fracture identified via the text search was then confirmed by manual chart review. This gold standard reference cohort was then linked to all non-psychiatric hospitalizations within the TOH-DAD during the same period. A binomial logistic regression model using diagnostic codes for acetabular fracture as well as other clinical co-variables within the DAD was created. Similarly, this model demonstrated excellent discrimination (optimism adjusted c-statistic 0.99) and calibration (calibration slope 1.06) for the identification of hospitalizations during which an actual acetabular fracture was diagnosed.⁵⁵

To our knowledge, this is the first study to use a multinomial predictive model to identify and distinguish between procedures within large health administrative databases. Through the use of a multinomial logistic regression model, we were able to accurately identify and distinguish between incontinent and continent diversion for patients who underwent cystectomy using a single model. As highlighted in the introduction, distinguishing between type of urinary diversion is important due to differences in patient population and expected post-operative course. By creating an accurate model for identification of patient's undergoing cystectomy with

urinary diversion, we hope to facilitate future validated population-based research for cystectomy patients with both incontinent and continent urinary diversions.

8.2.3. Differences in Misclassification Bias

Use of just the coding algorithms significantly *overestimated* the incidence of both cystectomy with incontinent and continent urinary diversions. Furthermore, use of the OCIM with bootstrap imputation resulted in closer estimates for most co-variables to the true values from the reference cohort as compared to the use of the code algorithm alone. The one exception was the association of male sex with cystectomy with incontinent urinary diversion for which the OCIM slightly overestimated the odds ratio as compared to the code algorithm; however, this difference was not significant. Adamczyk et al. (2021) also demonstrated reduced misclassification using their model with bootstrap imputation methods as compared to coding alone for acetabular fractures.⁵⁵

When assessing misclassification, one can employ two different methods. One method involves the use of probability cut offs based on the predictive model to classify patients as having the disease/procedure or not (i.e. if patient probability is above a certain cut off then disease positive and if below then disease negative). By comparing classification based on these probability cut offs to the true values, misclassification can be calculated and corrected. This method, although less laborious, has been shown to increase misclassification as compared to other methods which allow for uncertainty of case ascertainment. Bootstrap imputation, as applied in this study, avoids the need for probability cut offs and has been shown to result in reduced misclassification.^{52,53,55}

There are two main types of misclassification bias, differential and non-differential. Differential misclassification bias occurs when the probability of misclassification differs between groups. Non-differential misclassification bias occurs when members of all groups have the same probability of misclassification. Although the impact of differential misclassification can be difficult to predict, it is generally assumed that non-differential misclassification bias will bias towards the null hypothesis.⁵⁶

The predictable effect of non-differential misclassification bias is often used to justify ignoring the impact of misclassification in large administrative database studies. In this study, however, it is clear that non-differential misclassification did not always bias towards the null. For example, when identifying cystectomy with incontinent urinary diversion cases using the code algorithm as compared to the OCIM, the incidence of cystectomy, acute length of stay, as well as the odds ratio for transfusion, discharge home without supports, and death or readmission within 28 days was higher than the true value (Figure 6). The incidence and acute length of stay as well as the odds ratios for transfusion and death or readmission within 28 days was also higher than the true values when using the coding algorithm to identify patients undergoing cystectomy with continent urinary diversion compared to the OCIM (Figure 7). These results demonstrate the importance of proper measurement and correction for misclassification regardless of type of misclassification bias.

In this study, cystectomy with urinary diversion, although a definitive operative (i.e. a patient has either had their bladder removed or has not) and thus seemingly easier to identify,

had significant misclassification bias when using procedure and billing coding alone. The exact reasons for misclassification are not fully clear but are likely reflective of the low overall prevalence of cystectomy as compared to all hospitalizations within the study period. There may also be some misclassification attributed to the diversion status (incontinence vs continent) which may be more difficult to identify with coding. Further review of false negative and false positive cystectomy-coded patients would be useful in determining potential causes for misclassification and could also help in improving upon future coding accuracy, however, this was outside of the scope of this thesis.

8.3. Study Limitations

There are some limitations of this study to consider. Firstly, this study has not been externally validated. As such, in order to apply the OCIM to populations at other centers, the model must first be validated within that center's population in order to ensure accuracy of case identification. Such external validation is important to allow the model to be applied to broader population-based data and without this it would be impossible to measure and correct for misclassification that may arise within populations external to TOH.

Second, even once externally validated, this model only applies to population data within the ICES database, which uses CCI intervention codes and OHIP billing codes and is limited to the population of Ontario. If the model is to be applied to populations external to Ontario or other databases, then further validation using equivalent procedure or billing codes must be performed. This being said, the ICES databases captures a majority of medical encounters within the Canadian province of Ontario. With a population of almost 15 million people, Ontario is the

largest province within Canada and has a diverse population. As such, it remains a useful collection of databases by which high quality population-based study can be performed. The OCIM may also be extended to other health jurisdictions within Canada, as long as the intervention and billing code system distinguishes between cystectomy and diversion type, as it does in Ontario.

The final limitation is in regards to how the gold standard reference cohort was created. In this study, the SIMS database was queried to identify all cystectomy patients at TOH during the study period. One limitation of the SIMS registry is that it will only capture surgeries performed as a primary operation. For example, if a cystectomy is performed as a secondary surgery for an invasive rectal cancer where the resection of the rectum is considered the primary surgery, only the rectal resection will be recorded in SIMS.

Although the SIMS registry may miss some patients who have undergone cystectomy as a secondary surgery, this was not deemed to be a significant weakness of the study methodology for two main reasons. First is that such surgeries are fairly uncommon and therefore we would not expect as many cases to have occurred during the study period in comparison to cystectomy performed as a primary surgery. Secondly, patient's undergoing cystectomy as a secondary operation as part of a larger surgery represents a completely different cohort with unique diagnoses, outcomes and expected post-operative recovery and, therefore, we would want to exclude these patients regardless when identifying cystectomy and urinary diversion using our predictive model.

The process of validation using gold standard reference cohorts can require significant resources and may not be practical in all cases. Although ideally all code algorithms used to identify diagnosis or procedures within health care administrative datasets would have measured accuracy within the database being used, based on the results of this study, particular attention should be drawn to those diagnosis or procedures with low prevalence as they are at particular risk of misclassification. Other diagnosis or procedures without specific diagnosis or billing codes or that lack clear diagnostic criteria (i.e. urinary tract infection) would also be at risk for misclassification and would therefore likely benefit from validation. Finally, restricting the size of the dataset in which the cases are being identified, for example instead of using all hospitalizations (as was used in this study) only using hospitalizations to urology, may increase the prevalence of cystectomy hospitalizations and thus presumably reduce misclassification bias, however, further study would be required to confirm this.

8.4. Next Steps

This study provides an internally validated and highly predictive model for the identification of patients undergoing cystectomy with incontinent and continent urinary diversion. The next steps of this study will be to proceed with external validation of the OCIM at other centers within Ontario. Once externally validated, application of this model along with the use of bootstrap imputation methods will allow for accurate and validated population-based study of cystectomy patients within the province of Ontario using ICES. Such study will help to improve knowledge of patients undergoing cystectomy with both incontinent and continent urinary diversion and will hopefully facilitate further intervention to improve patient care. The methods for validation described in this study can also be applied to other urology diagnoses or procedures to help

facilitate further validated administrative database study not specific to just cystectomy with urinary diversion.

9. References

1. Stein JP and Skinner DG: Radical Cystectomy. *BJU International* 2004; **94**: 197–221.
2. Aisen CM, Lipsky MJ, Tran H, et al: Understanding Simple Cystectomy for Benign Disease: A Unique Patient Cohort With Significant Risks. *Urology* 2017; **110**: 239–243.
3. Bachir BG and Kassouf W: Urinary Diversions: Advantages and Disadvantages of the Major Types of Diversions. *Current Opinion in Supportive and Palliative Care* 2013; **7**: 249.
4. Lee RK, Abol-Enein H, Artibani W, et al: Urinary Diversion After Radical Cystectomy for Bladder Cancer: Options, Patient Selection, and Outcomes. *BJU International* 2014; **113**: 11–23.
5. Stein R, Hohenfellner M, Pahernik S, et al: Urinary Diversion—Approaches and Consequences. *Dtsch Arztebl Int* 2012; **109**: 617–622.
6. Hebert KJ, Matta R and Myers JB: Patient Selection and Outcomes of Urinary Diversion. *Urol Clin North Am* 2022; **49**: 533–551.
7. Shabsigh A, Korets R, Vora KC, et al: Defining Early Morbidity of Radical Cystectomy for Patients with Bladder Cancer Using a Standardized Reporting Methodology. *European Urology* 2009; **55**: 164–176.
8. Chang SS, Cookson MS, Baumgartner RG, et al: Analysis of Early Complications After Radical Cystectomy: Results of a Collaborative Care Pathway. *J Urol* 2002; **167**: 2012–2016.
9. Knorr JM, Ericson KJ, Zhang JH, et al: Comparison of Major Complications at 30 and 90 Days Following Radical Cystectomy. *Urology* 2021; **148**: 192–197.
10. Aziz A, May M, Burger M, et al: Prediction of 90-day Mortality After Radical Cystectomy for Bladder Cancer in a Prospective European Multicenter Cohort. *European Urology* 2014; **66**: 156–163.
11. Al-Daghmin A, Aboumohamed A, Din R, et al: Readmission After Robot-assisted Radical Cystectomy: Outcomes and Predictors at 90-Day Follow-up. *Urology* 2014; **83**: 350–356.
12. McIntosh AG, Li T, Ito T, et al: WBC Associates with Readmission Following Cystectomy. *Bladder Cancer* 2017; **3**: 95–103.
13. Rezaee ME, Atwater BL, Bihrlle W, et al: Ileal Conduit Versus Continent Urinary Diversion in Radical Cystectomy: A Retrospective Cohort Study of 30-day Complications, Readmissions, and Mortality. *Urology* 2022; **170**: 139–145.
14. Monn MF, Kaimakliotis HZ, Cary KC, et al: Short-term morbidity and mortality of Indiana pouch, ileal conduit, and neobladder urinary diversion following radical cystectomy. *Urologic Oncology: Seminars and Original Investigations* 2014; **32**: 1151–1157.

15. Angeles MA, Mallet E, Rouanet P, et al: Comparison of postoperative complications and quality of life between patients undergoing continent versus non-continent urinary diversion after pelvic exenteration for gynecologic malignancies. *International Journal of Gynecological Cancer* 2020; **30**: 233–240.
16. Cook JA and Collins GS: The Rise of Big Clinical Databases. *British Journal of Surgery* 2015; **102**: e93–e101.
17. Vetter TR and Mascha EJ: Bias, Confounding, and Interaction: Lions and Tigers, and Bears, Oh My! *Anesthesia & Analgesia* 2017; **125**: 1042.
18. van Walraven C, Wang B, Ugnat AM, et al: False-Positive Coding for Acute Myocardial Infarction on Hospital Discharge Records: Chart Audit Results from a Tertiary Centre. *Can J Cardiol* 1990; **6**: 383–386.
19. Khurram SA, Warner C, Henry AM, et al: Accuracy of Clinical Coding for Procedures in Oral and Maxillofacial Surgery. *British Journal of Oral and Maxillofacial Surgery* 2016; **54**: 894–897.
20. van Walraven C, Bennett C and Forster AJ: Administrative Database Research Infrequently Used Validated Diagnostic or Procedural Codes. *Journal of Clinical Epidemiology* 2011; **64**: 1054–1059.
21. Anon: About ICES. Available at: <https://www.ices.on.ca/About-ICES>, accessed November 29, 2021.
22. Lavallee L, Manuel DC and van Walraven C: Survival of Men with Prostate Cancer Undergoing Radical Prostatectomy in Ontario. *Journal of Urology* 2014; **192**: 1385–1389.
23. Anon: Ontario Cancer Registry. *Cancer Care Ontario* 2017. Available at: <https://www.cancercareontario.ca/en/cancer-care-ontario/programs/data-research/ontario-cancer-registry>, accessed April 15, 2023.
24. Lusty A, Doiron RC, Booth CM, et al: No Outcome Differences after Cystectomy between Patients with De Novo Muscle-Invasive Bladder Cancer Compared to Progressors: A Retrospective Population-Based Study. *J Urol* 2021; **206**: 260–269.
25. Siemens DR, Visram K, Wei X, et al: Effect of Centralization on Complex Surgical Care: A Population-Based Case Study of Radical Cystectomy. *Can Urol Assoc J* 2020; **14**: 91–96.
26. Raphael MJ, Griffiths R, Peng Y, et al: Mental Health Resource Use Among Patients Undergoing Curative Intent Treatment for Bladder Cancer. *J Natl Cancer Inst* 2021; **113**: 1238–1245.
27. Kulkarni GS, Urbach DR, Austin PC, et al: Higher surgeon and hospital volume improves long-term survival after radical cystectomy. *Cancer* 2013; **119**: 3546–3554.

28. Leveridge MJ, Siemens DR, Mackillop WJ, et al: Radical Cystectomy and Adjuvant Chemotherapy for Bladder Cancer in the Elderly: A Population-based Study. *Urology* 2015; **85**: 791–798.
29. Jaeger MT, Siemens DR, Wei X, et al: Association Between Anesthesiology Volumes and Early and Late Outcomes After Cystectomy for Bladder Cancer: A Population-Based Study. *Anesth Analg* 2017; **125**: 147–155.
30. Siemens DR, Jaeger MT, Wei X, et al: Peri-Operative Allogeneic Blood Transfusion and Outcomes After Radical Cystectomy: A Population-Based Study. *World J Urol* 2017; **35**: 1435–1442.
31. Brennan K, Karim S, Doiron RC, et al: Venous Thromboembolism and Peri-Operative Chemotherapy for Muscle-Invasive Bladder Cancer: A Population-based Study. *Bladder Cancer* **4**: 419–428.
32. Doiron RC, Booth CM, Wei X, et al: Risk Factors and Timing of Venous Thromboembolism After Radical Cystectomy in Routine Clinical Practice: A Population-Based Study. *BJU Int* 2016; **118**: 714–722.
33. Booth CM, Siemens DR, Li G, et al: Curative Therapy for Bladder Cancer in Routine Clinical Practice: A Population-based Outcomes Study. *Clinical Oncology* 2014; **26**: 506–514.
34. Izard JP, Siemens DR, Mackillop WJ, et al: Outcomes of Squamous Histology in Bladder Cancer: A Population-Based Study. *Urol Oncol* 2015; **33**: 425.e7–13.
35. Booth CM, Siemens DR, Peng Y, et al: Delivery of Perioperative Chemotherapy for Bladder Cancer in Routine Clinical Practice. *Annals of Oncology* 2014; **25**: 1783–1788.
36. Siemens DR, Mackillop WJ, Peng Y, et al: Processes of Care and the Impact of Surgical Volumes on Cancer-specific Survival: A Population-based Study in Bladder Cancer. *Urology* 2014; **84**: 1049–1057.
37. Siemens DR, Mackillop WJ, Peng Y, et al: Lymph Node Counts Are Valid Indicators of the Quality of Surgical Care in Bladder Cancer: A Population-Based Study. *Urologic Oncology: Seminars and Original Investigations* 2015; **33**: 425.e15-425.e23.
38. Kulkarni GS, Urbach DR, Austin PC, et al: Impact of provider volume on operative mortality after radical cystectomy in a publicly funded healthcare system. *Can Urol Assoc J* 2013; **7**: 425–429.
39. Kulkarni GS, Urbach DR, Austin PC, et al: Longer Wait Times Increase Overall Mortality in Patients With Bladder Cancer. *J Urol* 2009; **182**: 1318–1324.
40. Richard PO, Bashir S, Riverin BD, et al: Risk of Bone Fractures Following Urinary Intestinal Diversion: A Population Based Study. *Journal of Urology* 2019; **202**: 319–325.

41. Quan H, Parsons GA and Ghali WA: Validity of Procedure Codes in International Classification of Diseases, 9th Revision, Clinical Modification Administrative Data. *Med Care* 2004; **42**: 801–809.
42. Lyon TD, Faraj KS, Brennan E, et al: Defining Radical Cystectomy Using the ICD-10 Procedure Coding System. *Urol Oncol* 2021; **40**: e17–e22.
43. Tan H-J, Clarke R, Chamie K, et al: Development and Validation of an Automated Method to Identify Patients Undergoing Radical Cystectomy for Bladder Cancer Using Natural Language Processing. *Urology Practice* 2017; **4**: 365–372.
44. Riley RD, Ensor J, Snell KIE, et al: Calculating the Sample Size Required for Developing a Clinical Prediction Model. *BMJ* 2020; **368**: m441.
45. Vittinghoff E, Glidden DV, Shiboski SC, et al: *Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models*. Second Edition. New York, NY: Springer; 2012.
46. Altman DG and Royston P: The Cost of Dichotomising Continuous Variables. *BMJ* 2006; **332**: 1080.
47. Omer D and Musa AB: Modelling Logistic Regression using Multivariable Fractional Polynomials. *IJIR* 2017; **3**: 8–16.
48. Meier-Hirmer C, Ortseifen C and Sauerbrei W: Multivariable Fractional Polynomials in SAS: An Algorithm for Determining the Transformation of Continuous Covariates and the Selection of Covariates. 2003. Available at: http://people.musc.edu/~hille/2009BMTRY755_Website/LectureNotes/Diagnostics2/beschreibung.pdf, accessed April 30, 2023.
49. Steyerberg EW: *Clinical Prediction Models: A Practical Approach to Development, Validation, and Updating*. Second Edition. New York, NY: Springer; 2019.
50. Austin PC and Steyerberg EW: The Integrated Calibration Index (ICI) and Related Metrics for Quantifying the Calibration of Logistic Regression Models. *Statistics in Medicine* 2019; **38**: 4051–4065.
51. Monaghan TF, Rahman SN, Agudelo CW, et al: Foundational Statistical Principles in Medical Research: Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value. *Medicina (Kaunas)* 2021; **57**: 503.
52. van Walraven C: Improved Correction of Misclassification Bias with Bootstrap Imputation. *Med Care* 2018; **56**: e39–e45.
53. van Walraven C: Bootstrap Imputation with a Disease Probability Model Minimized Bias From Misclassification Due to Administrative Database Codes. *J Clin Epidemiol* 2017; **84**: 114–120.

54. van Walraven C: A Comparison of Methods to Correct for Misclassification Bias from Administrative Database Diagnostic Codes. *International Journal of Epidemiology* 2018; **47**: 605–616.
55. Adamczyk A, Grammatopoulos G and van Walraven C: Minimizing Misclassification Bias with a Model to Identify Acetabular Fractures Using Health Administrative Data. *Medicine (Baltimore)* 2021; **100**: e28223.
56. Chyou P-H: Patterns of Bias Due to Differential Misclassification by Case–Control Status in a Case–Control Study. *Eur J Epidemiol* 2007; **22**: 7–17.