

Validation of Breast Cancer and Bladder Cancer Among Patients With Type 2 Diabetes Mellitus in US Medicare: A Pilot Study

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Disclosures

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METHODS

Eligible patients:

- The study population included enrolled beneficiaries of fee-for-service US Medicare, aged ≥ 65 years, and initiating an antidiabetic drug from January 1, 2014 to December 31, 2015.
- Patients were prescribed the study drug, dapagliflozin (a sodium-glucose co-transporter-2 [SGLT2] inhibitor), or another oral antidiabetic drug (i.e., dipeptidyl peptidase-4 [DPP-4] inhibitors, glucagon-like peptide-1 [GLP-1] receptor agonists, thiazolidinediones, or alpha glucosidase inhibitors).
- Patients were excluded if there was evidence of the following within 180 days before study entry:
 - Female breast cancer cohort: breast biopsy
 - Bladder cancer cohort: cystoscopy, bladder biopsy, urine cytology, or hematuria diagnosis

We used prespecified algorithms (Figure 1) to identify cases of female invasive breast cancer and in situ or invasive bladder cancer. The validation process is outlined in Figure 2, and the clinical case definitions used for confirming cases of female breast cancer and bladder cancer are outlined in Table 1.

PPVs and 95% confidence intervals (CI) were estimated in two ways depending on assumptions about postreview provisional cases (i.e., patients with insufficient information to confirm as a case or a non-case):

- (1) PPV 1: The proportion of confirmed cases among all cases included in the adjudication review, assuming all postreview provisional cases are noncases (more conservative approach)

$$PPV\ 1 = \frac{\text{Confirmed cases}}{\text{All reviewed cases}}$$

- (2) PPV 2: The proportion of confirmed cases among only cases where a definitive case status was assigned (i.e., confirmed cases and confirmed noncases)

$$PPV\ 2 = \frac{\text{Confirmed cases}}{\text{(Confirmed cases + Confirmed noncases)}}$$

RESULTS

Table 2. Disposition of Requested Medical Records and Adjudicated Cases

	Female Breast Cancer	Bladder Cancer
Validation sample		
Medical records requested, n	109	87
Medical records retrieved, n (%) ^a	42 (39)	52 (60)
Adjudication review		
Medical records included in adjudication review, n ^b	42	48
Medical records with sufficient information to assign case status, n (%) ^c	36 (86)	45 (94)
Confirmed cases, n (%) ^d	28 (78)	43 (96)
Confirmed noncases, n (%) ^d	8 (22)	2 (4)
Medical records with insufficient information to assign case status (postreview provisional cases), n (%) ^c	6 (14)	3 (6)

^a Percentage among cases with medical cases requested.

^b For this pilot assessment, up to 50 cases were included in the adjudication review for each outcome based on the number of algorithm-identified cases and the number of cases for whom medical records were retrieved. Only medical records that were retrieved prior to initiating adjudication review were included in the adjudication review (for the bladder cancer outcome, 4 additional records were retrieved after the adjudication period initiated).

^c Percentage among cases included in adjudication review.

^d Percentage among cases included with definitive case status.

DISCUSSION

- Limited medical records were available for most postreview provisional cases, leading to an incomplete assessment of the clinical case definition criteria for either a cancer-specific therapy or related clinical event.
- PPV values from other published breast cancer algorithms in US Medicare claims are higher than those observed in our study; however, previous studies validated cases using the Surveillance, Epidemiology, and End Results (SEER) database or state cancer registry linkage data.^{1,2}
- A validation study using claims data from the HealthCore Integrated Research Database (HIRD) used the same algorithms and clinical case definitions as this study, and observed similar PPVs for female breast cancer (PPV 2 = 84% [95% CI, 70%-93%]) and bladder cancer (PPV 2 = 90% [95% CI, 56%-100%]).³

Limitations

- We are limited in interpreting the lower PPV for the female breast cancer algorithm given the scarcity of data, as only 2 years of data were included in this pilot assessment. More years of data will be included in the final validation of these outcomes during a future interim analysis planned for the year 2022.

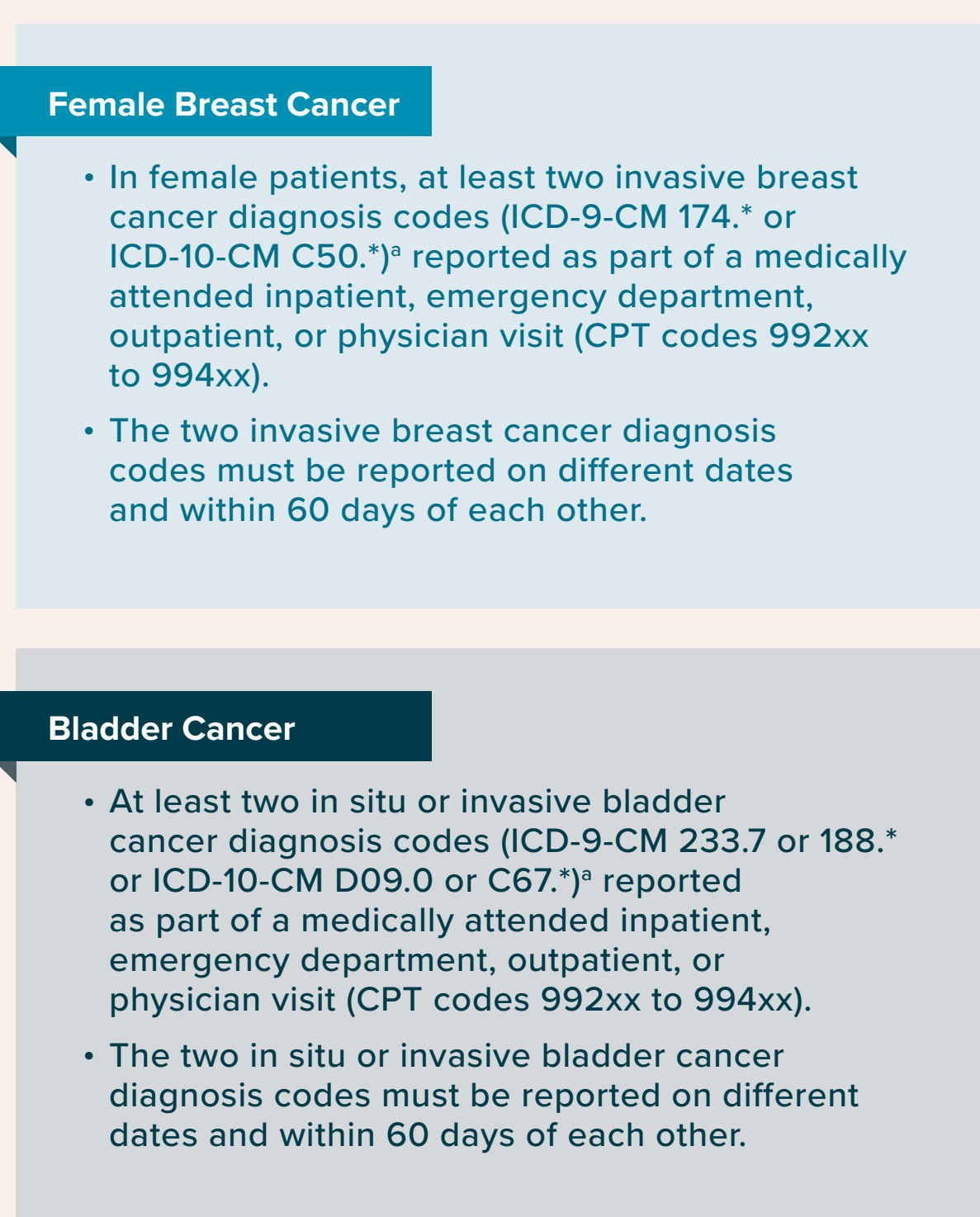
BACKGROUND

- Outcome validation is often required in postauthorization drug safety studies conducted in medical record or insurance claims databases to evaluate and quantify possible outcome misclassification.
- In an ongoing postauthorization drug safety study, we conducted a pilot assessment in the United States (US) Medicare claims database to evaluate the positive predictive performance of algorithms to identify breast cancer and bladder cancer outcomes among individuals with type 2 diabetes mellitus who initiated an antidiabetic drug.

OBJECTIVE

- To estimate the positive predictive values (PPV) of claims algorithms for female invasive breast cancer and in situ or invasive bladder cancer

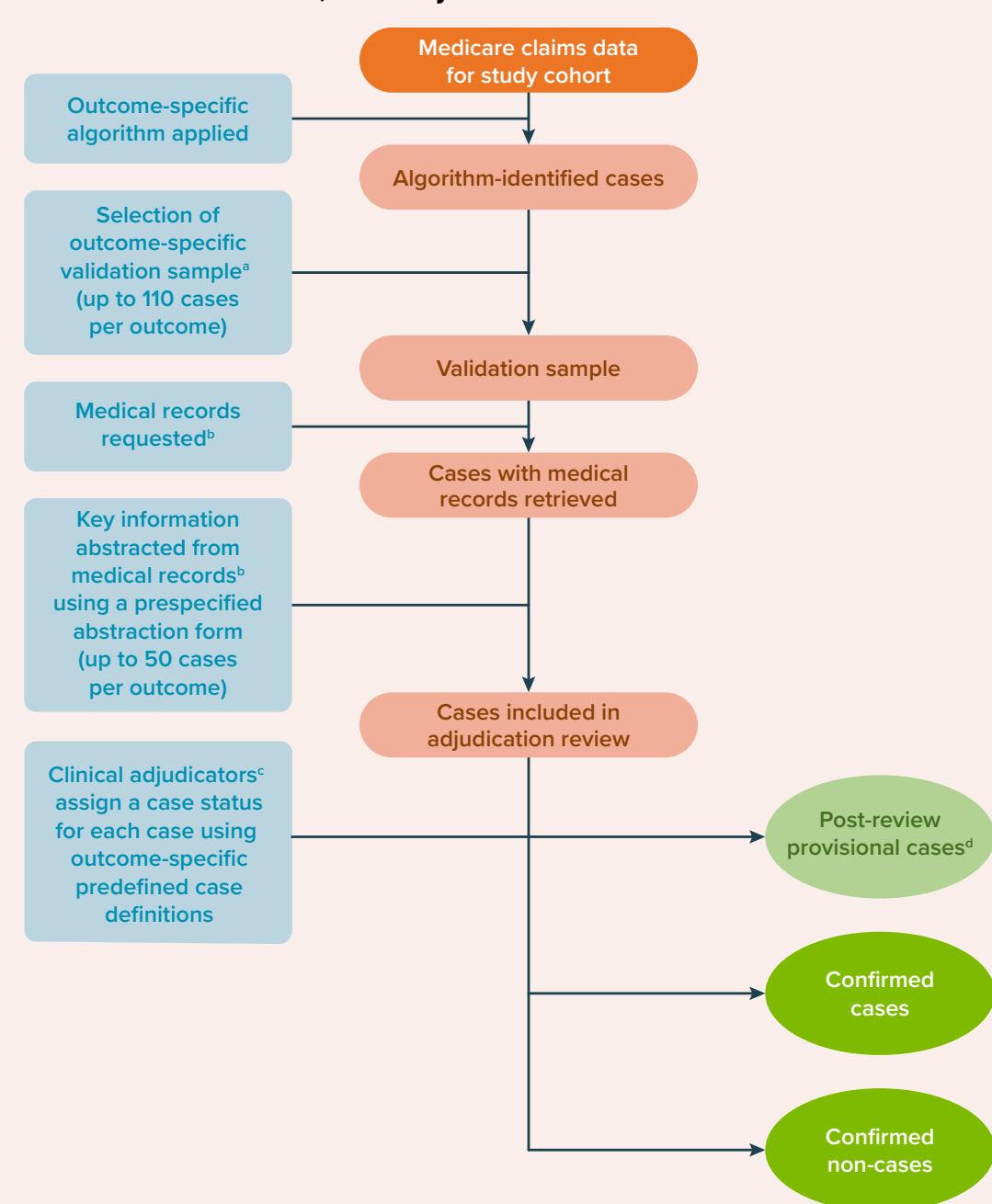
Figure 1. Claims Algorithms for Female Invasive Breast Cancer and In Situ or Invasive Bladder Cancer



CPT = Current Procedural Terminology; ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification.

^a ICD-10-CM codes were used for diagnoses on or after 01 October 2015.

Figure 2. Validation Process: Sample Selection, Medical Record Request and Abstraction, and Adjudication Review



^a It was planned to sample an equal number of algorithm-identified cases (≥ 55) from the dapagliflozin group and the comparator group for each outcome. However, because fewer than 55 cases for each outcome were identified by the algorithm in the dapagliflozin group, all such cases were selected into the validation sample.

^b Medical record requests and abstractions were conducted by a third-party vendor.

^c Two clinical adjudicators independently reviewed information on each algorithm-identified case to assign case status. Disagreements between the two clinical adjudicators were resolved through discussion among an adjudication committee consisting of three clinical adjudicators.

^d Insufficient information to assign a case status.

Table 1. Clinical Case Definitions for Female Breast Cancer and Bladder Cancer

Outcome	Criteria for Confirmed Cases
Female Breast Cancer	A confirmed case met Criterion 1 and either Criterion 2 or 3: 1) Diagnosis of breast cancer 2) Evidence of breast cancer-specific therapy ^a within the period of 1 month before the first recorded breast cancer diagnosis and 3 months after the second recorded breast cancer diagnosis 3) Evidence of a related clinical event (i.e., visit to an oncologist, a hospitalization associated with a breast cancer diagnosis, or death with cancer as the cause of death) after the first recorded breast cancer diagnosis
Bladder Cancer	A confirmed case met Criterion 1 and either Criterion 2 or 3: 1) Diagnosis of bladder cancer 2) Evidence of bladder cancer-specific therapy ^b within the period of 1 month before the first recorded bladder cancer diagnosis and 3 months after the second recorded bladder cancer diagnosis 3) Evidence of a related clinical event (i.e., visit to an oncologist, a hospitalization associated with a bladder cancer diagnosis, or death with cancer as the cause of death) after the first recorded bladder cancer diagnosis

^a Includes mastectomy, radiation therapy, chemotherapy, hormonal therapy, or other targeted or biological therapy.

^b Includes cystectomy, radiation therapy, chemotherapy, immunotherapy, or other targeted or biological therapy.

Table 3. Positive Predictive Values of Algorithms for Adjudicated Cases

PPV Estimation Approach	Female Breast Cancer	Bladder Cancer
PPV 1, ^a % (95% CI)	66.7 (50.5-80.4)	89.6 (77.3-96.5)
PPV 2, ^b % (95% CI)	77.8 (60.8-89.9)	95.6 (84.9-99.5)

CI = confidence interval; PPV = positive predictive value

^a PPV 1: Numerator is confirmed cases; denominator is the sum of all algorithm-identified cases included in the adjudication review.

^b PPV 2: Numerator is confirmed cases; denominator is the sum of confirmed cases and confirmed noncases. Postreview provisional cases (insufficient information to assign case status) are excluded from the numerator and denominator.

CONCLUSIONS

- In this pilot validation study, the claims algorithms resulted in moderate PPVs for identifying female invasive breast cancer and high PPVs for identifying bladder cancer among older patients in the US Medicare claims database with type 2 diabetes mellitus who initiated an antidiabetic drug.

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