The Missing Link: Evaluating Economic Outcomes of an Uncoded Novel Diagnostic From Claims Data

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BACKGROUND | OBJECTIVES

Retrospective claims-based outcomes studies have well-known strengths (e.g., standardized event indicators, access to individuals' continuum of care, clean inpatient and SNF healthcare resource utilization—HCRU—and costs) and limitations (e.g., variable non-IP/SNF diagnosis accuracy, lack of test results, limited access to potential confounding variables).

Also limited is claims' ability to assess the value of a novel diagnostic (NDx) in use but not yet assigned a CPT or HCPCS code. This is particularly problematic for novel molecular diagnostics (MolDx). The Palmetto GBA Medicare administrative contractor handles applications for unique Diagnostic Exchange (DEX) Z-Codes for use on claims along with MolDx CPTs to indicate exactly which tests were performed. Eventually, the AMA may assign such tests unique CPT codes.

Objective 1: To retrospectively evaluate the value of a particular NDx, we needed to identify in claims a NDx that has been in use since mid-2017, but was not assigned a unique DEX Z-code until 2022. We therefore aimed to develop an algorithm to identify its claims for use and outcomes studies. If successful, similar approaches may be useful for identifying and evaluating outcomes of novel diagnostics in claims data.

Objective 2: To compare the effectiveness of the uncoded NDx to the standard urine culture (SUC) for individuals with complicated urinary tract infections (cUTI), which are associated with poorer UTI-related outcomes. cUTIs arise in patients with various risk factors, may be polymicrobial, and may involve organisms missed by SUC. Also, polymicrobial infection may alter susceptibilities due to organisms' metabolic interactions. The NDx was an outpatient pathogen and sensitivities test comprised of multiplex PCR (mPCR), antimicrobial resistance genes, and a pooled antimicrobial sensitivity performed directly in urine sample. We hypothesized that the accelerated turnaround of mPCR, improved pathogen identification, and more accurate determination of susceptibilities in polymicrobial infections would result in reduced UTI frequency and lower UTI-related HCRU and cost.

TABLE 1. COMPLICATED URINARY TRACT INFECTIONS: RISK FACTORS

FACTOR	EXAMPLES
Male gender	
Recurrent UTI	2 UTIs in 6 months or 3 in 12 months
Diabetes	
Immunosuppression (disease or drugs in past 6 months)	Rheumatoid arthritis; innate or acquired immunodeficiencies; treatment for cancer or to suppress rejection
Urinary tract anatomy	Obstructive and reflux uropathy; vesicoureteral reflux with reflux nephropathy
Urinary tract functional disorders	Neuromuscular dysfunction of bladder; neuropathic bladder
Urinary tract instrumentation in prior 6 weeks	Ureterosigmoidostomy; ureterotomy for implantation of indwelling stent
Long term indwelling urinary drainage	Indwelling stents; implanted urinary sphincter; indwelling cystostomy drainage
Pelvic radiotherapy	Pelvic brachytherapy; stereotactic radiosurgery; beam radiation of pelvic lymphatics
Inherently-complicated UTI	Acute: pyelonephritis; epididymitis; perinephric abscess; infection of cystostomy catheter

DISCLOSURES

Iver Juster is an independent healthcare outcomes consultant. Dicken Ko, Emily Lukacz, and Annah Vollstedt serve as urological consultants to Pathnostics, a specialized molecular diagnostics company. Timothy Niecko is an independent statistician and health economics consultant. David Baunoch and Mohit Mathur are employed at Pathnostics.

METHODS

We aimed to compare 1-year UTI-related clinical, utilization, and cost outcomes in Original Medicare beneficiaries with cUTI diagnosed by SUC vs. by the NDx.

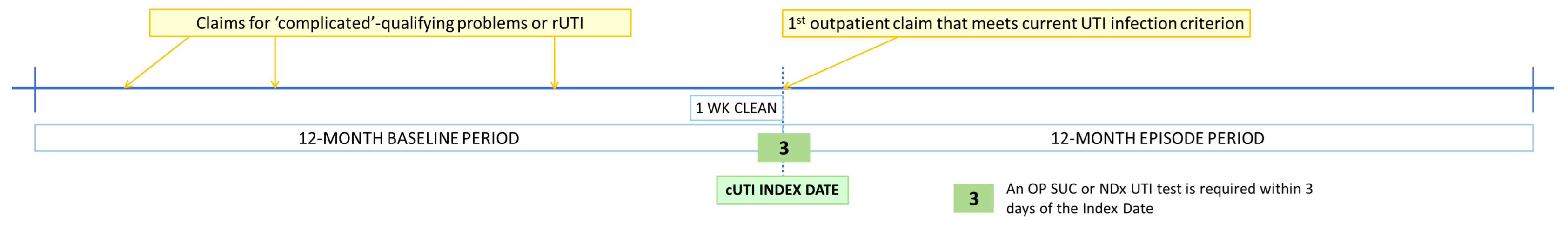
Data: A 5% Limited Data Set deidentified sample of Medicare beneficiaries with any Medicare coverage in 2017-19. Data include limited demographics, monthly eligibility, and healthcare claims, but not Part D drug claims. ResDAC, CMS' research assistance contractor, approved the use of the data for the study, subject to its Data Use Agreements.

Identifying the NDx: To be able to compare cUTI managed with SUC versus the NDx, we first developed an algorithm to identify the NDx, which lacked a specific CPT code. We identified 9 labs (from their NPI numbers) that performed the NDx at various times in 2017-19; they confirmed that the NDx was the sole molecular diagnostic for UTI performed during specific date ranges. Due to the wide range of organisms tested, NDx claims had multiple CPT codes, but always contained 87798, 87640, 87653, or 87801. Thus, instances of NDx were identified from a combination of lab NPI, test date, and presence of qualifying CPT codes.

Validating identification of NDx: Because the proportion of Original Medicare Parts A+B (OM/A+B) beneficiaries to the entire Medicare population varies with time, we used CMS' data on US Medicare enrollment to derive an 'expected' annual OM/A+B denominator, proportion, and NDx rate on our data.

Identifying individuals with cUTI: Following published criteria, UTIs were considered to be 'complicated' if the individual was male or had at least 1 other qualifying criterion in **Table 1**, based on diagnoses (ICD10-CM) in the first or second position, Part B drugs (HCPCS), or urologic procedures (CPT). Individuals with no enrollment in OM/A+B or who were in hospice at any point were excluded.

One-year cUTI episode schema



Matched 1-year cUTI episodes: The first *outpatient* UTI after at least 12 months' continuous OM/A+B enrollment during which at least 1 cUTI criterion was met—and with a 7-day period free of UTI claims—was designated as a *potential* episode Index Date. Further required was 12-months' continuous enrollment following the Index Date. To be placed in the SUC or the NDx cohort, (1) there must be a SUC or NDx claim ± 3 days of the Index Date, and (2) all outpatient UTI tests must be SUC or NDx for the duration of the episode.

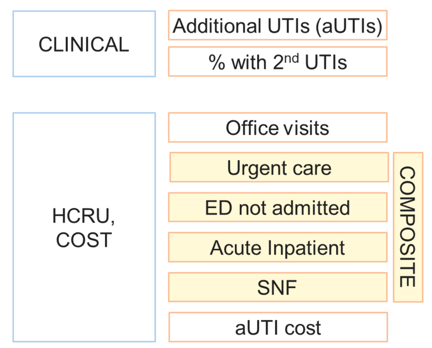
SUC and NDx individuals were matched 10:1 along criteria (**Table 2**) deemed to be relevant to UTI outcomes by a panel of Board-certified practicing and academic urologists. Initially, 30-day episodes were matched, but because of too few UTI outcomes for an adequately-powered study, we matched the subset of individuals with 1-year episodes, again aiming for 10:1.

Table 2. Propensity scoring covariates

Age Gender Race Baseline year rUTI Urinary tract anatomy Urinary tract dysfunction Diabetes

Elixhauser variables: Heart failure, Cardiac arrhythmia, Valvular disease, Peripheral vascular disease, Complicated hypertension, Paralysis, Other neurological disorders, Chronic obstructive pulmonary disease, Renal failure, Liver disease, Lymphoma, Metastatic cancer, Solid tumor without mets, Obesity, Drug abuse, Psychoses, Depression

Figure 2. Outcomes assessed



Unique UTI: 1st claim with UTI in 1st or 2nd diagnosis after a 7-day 'clean period' free of UTI claims.

aUTI: Any unique UTI following the Index UTI

Office visits: Clinician encounters in a non-facility or facility setting with Place of Service code = Office visit with UTI in 1st or 2nd diagnosis

ED not admitted: Patient was discharged; ED billed for the encounter. UTI in 1st or 2nd diagnosis.

Acute inpatient: ED services are included in claim. UTI in 1st diagnosis, or if in 2nd, the claim must include sepsis or UTI admitting diagnosis

SNF: Counted only if immediately follows an acute inpatient UTI discharge, and the SNF claim has UTI in 1st or 2nd diagnosis

Costs are measured as Medicare-allowed

ABBREVIATIONS:

NDx: Novel Diagnostic
SUC: Standard urine culture
LDS: Medicare 5% Limited Data Sample
CPT: Common Procedural Terminology
mPCR: Multiplex polymerase chain reaction
cUTI: Complicated urinary tract infection
ResDAC: The Research Data Assistance Center which contracts with CMS to provide data
HCRU: Healthcare resource utilization
P-AST: Pooled antimicrobial sensitivity testing
NPI: National Provider Identifier

RESULTS

Population and cohorts

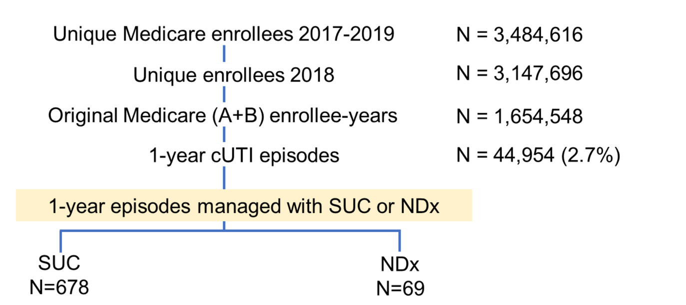
The waterfall from all Medicare enrollees in the 5% sample to the 69 NDx and 678 SUC propensity-matched episodes is shown below. The rate of 1-year cUTI episodes in the entire population was 2.7 per 100 enrollees.

Episode descriptives

NDx N	NDx %	SUC N	SUC %	Signif	
69		678			
74.28		74.79		0.69	Average age
42	60.9%	408	60.2%	0.91	Male
58	84.1%	594	87.6%	0.41	Race: White
11	15.9%	84	12.4%		Race: Non-white
14	20.3%	192	28.3%	0.16	rUTI
*	*	*	*	0.74	Immunosuppression
22	31.9%	239	35.3%	0.56	Anatomic and functional
16	23.2%	138	20.4%	0.58	Diabetes
15	21.7%	139	20.5%	0.81	Heart failure
26	37.7%	238	35.1%	0.67	Cardiac arrhythmia, valvular
17	24.6%	126	18.6%	0.22	Peripheral vascular disease
13	18.8%	155	22.9%	0.45	HTN complicated
*	*	*	*	0.60	Paralysis and other neuro
21	30.4%	211	31.1%	0.90	Renal failure, liver dz, COPD
13	18.8%	160	23.6%	0.37	Cancers
*	*	*	*	0.42	Obesity
12	17.4%	86	12.7%	0.27	Drug abuse, psychoses, depression

* indicates cell sizes <10 in the NDx cohort.

Waterfall: Data sample to episode cohorts



Algorithmic NDx identification

NDx identification validation

Because of the deidentified data, accuracy was estimated by comparing expected to identified tests per 1,000 enrollee-years (EY), where

$$\text{Expected tests} = \text{Lab-reported tests} \times \frac{EY_{\text{data sample}}}{EY_{\text{CMS-reported Parts A+B}}}$$

	2017	2018	2019
Lab-reported tests	10,928	26,717	20,139
EY (data sample)	1,665,856	1,654,548	1,639,885
EY(CMS-reported)	33,242,085	33,052,639	32,758,741
EY ratio (data/CMS)	0.0501	0.0501	0.0501
Expected tests	548	1,337	1,008
Identified tests	549	1,658	1,099
Delta %	0.2%	24.0%	9.0%

Additional UTIs (aUTIs) beyond the Index

Additional UTIs and their costs

	NDx	SUC
Total N in cohort	69	678
Number of additional UTIs (aUTIs)	126	1513
Patients with aUTIs	45	488
Average aUTIs per cohort member	1.83	2.23
Excess average aUTIs per SUC episode	0.41	
...% of total episode cost	79.5%	82.9%
…Average for patients with aUTIs	$767.48	$1,303.20
Average cost per aUTI	$274.10	$420.33

65.2% of NDx vs. 72.0% of SUC episodes contained at least 1 aUTI (p=0.24). Average cost per aUTI was $146.23 less in NDx episodes (p=0.0013). HCRU component analysis found that SUC aUTIs were likelier to advance to emergent or inpatient care.

UTI-related costs

HCRU components were consistent with the costs reported here. Total and HCRU Composite costs were 44% and 77% lower in the NDx cohort; NDx patients received a greater proportion of their care as outpatients. The mean $437.47 difference in cost of aUTIs per episode could, if causal, be conceptualized as the potentially-preventable cost of aUTIs.

UTI-related costs

	NDx	SUC	Delta	Delta %	Significance
Total	$629.55	$1,131.39	$501.84	-44%	0.004
Composite	$141.60	$605.06	$463.46	-77%	0.04
Additional UTIs	$500.52	$938.00	$437.47	-47%	0.02
Outpatient	$487.95	$526.33	$38.38	-7%	0.67
% of cost from outpatient services	77.5%	46.5%			
% of cost from Composite	22.5%	53.5%			

CONCLUSIONS

- Novel diagnostics (NDx) without specific claims codes can be identified for monitoring usage and tracking outcomes with cooperation from the manufacturer or performing labs, though caution should be exercised with validating with deidentified data. We developed an algorithm to identify an NDx from standard CPTs, the performing labs' NPIs, and the labs' NDx implementation dates, and evaluated the algorithm's identification vs. expected rates.
- Applying the algorithm to create matched cohorts of individuals with complicated urinary tract infections (cUTI) managed for 1 year with the NDx or with standard urine culture (SUC), we found that NDx was associated with a nonsignificant 9.4% reduction in second UTIs and mean reduction of 0.4 UTIs per cohort member.
- However, the NDx was associated with significant 44% reductions in total UTI-related cost, and 77% related to a composite of UTI-related urgent care, ED, inpatient, and SNF costs,
- These observations are compatible with the previously-reported biologic rationale for the NDx and an earlier time-series study.

DISCUSSION

In-vitro studies can suggest the biologic plausibility of a novel diagnostic (NDx), but a translational approach is needed to demonstrate real-world applicability. When its limitations are understood and to a feasible extent ameliorated, claims data can help gain insight into an NDx' clinical and economic value—but only if the NDx can be identified in the data.

We showed that in cooperation from the manufacturer or labs, an uncoded NDx can be reliably identified for retrospective outcomes research. Our possible mild over-identification may imply that NDx-favoring outcomes were understated. That the study's outcomes were compatible with the NDx' biologic rationale and a prior time-series study suggests the value of this approach.[7]

In assessing the validity of the outcomes in this study, the usual caveats on claims-based retrospective studies apply. Through its contracted administrator Palmetto GBA, CMS has provided a Local Coverage Determination and DEX Z-Code that can be used in concert with established CPTs on claims. This will facilitate future cUTI studies with sufficient N to reveal the scenarios in which the NDx has greatest value and may be a springboard to stratified randomized formal or pragmatic clinical trials.

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