## RAPID Pathway

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with any prostate cancer and 456 of 836 (54%) with clinically significant prostate cancer. Of the patients with a negative TP-Bx 60 of 198 (30%) had known causes of mpMRI false-positives such as inflammation or atrophy. A flow chart of these diagnostic outcomes of the combined mpMRI and TP-Bx is shown in figure 3.

Complications after transperineal biopsy were rare, as 7 of 836 (0.8%) developed acute urinary retention, 3 of 836 (0.36%) required catheterization for bleeding and 1 of 836 (0.12%) had culture proven urinary tract sepsis.

### Discussion

Optimal prostate cancer diagnostic pathways should demonstrate maximal significant cancer detection, minimal insignificant cancer detection and a minimal repeat biopsy rate. They should also diagnose men in good time. After the introduction of RAPID the time from referral to biopsy decreased to 10 days.

mpMRI has demonstrable advantages when it comes to localizing discrete cancer lesions within the prostate.[1] Its widespread adoption has allowed image guided prostate biopsy strategies to be contemplated. We now know that an image targeted approach improves significant cancer detection rates while minimizing the diagnosis of indolent cancers.[2,3] It was with this in mind that the RAPID pathway was developed.

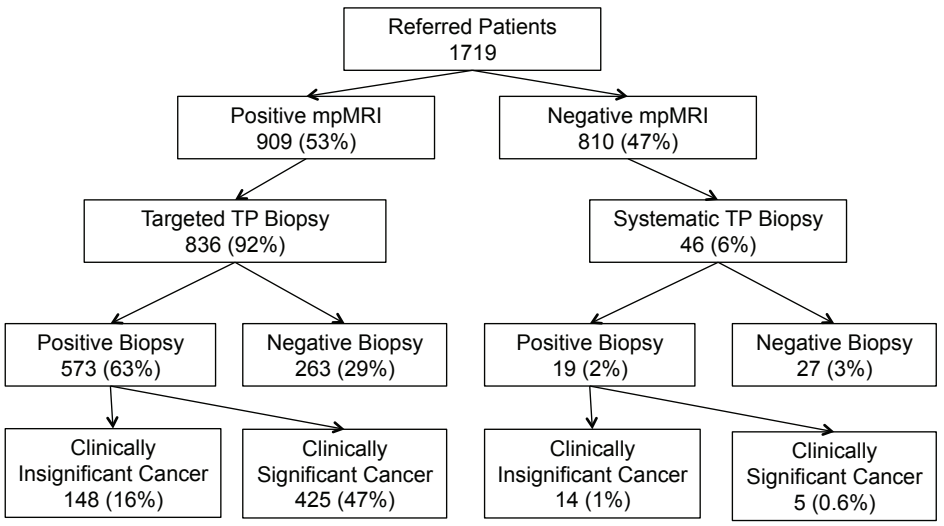


**Figure 3.** Diagnostic outcome flowchart of men entering RAPID pathway.

After the introduction of RAPID we saw a significant increase in the proportion of diagnosed significant cancers in men biopsied at 47% compared to 23% under the old pathway. The proportion of indolent cancers diagnosed also decreased to 8% from 12% under the old pathway. A mpMRI first approach also allowed 2 in 5 men to avoid a biopsy.

An area of debate is whether not sampling "normal" areas of the prostate risks missing significant cancer. This risk is unlikely to be any higher than 1 minus the negative predictive value of mpMRI for detecting such disease (in other words, around 20%).[1] The real question is what is the risk of missing significant disease in men with a lesion on mpMRI that is biopsy negative? Again, it is unlikely to be any higher than the aforementioned figure especially in the absence of independent risk factors such as a positive family history or high PSA density. Alternatively if a targeted biopsy is negative is it reasonable to be more concerned with potentially missed significant cancer outside of a mpMRI lesion when significant cancer in the lesion may have been genuinely missed? If the latter is of greater concern we know that a false-negative rate due to procedural error is mitigated by increasing biopsy density.[3]

Regardless, the risk of missing significant cancer in this group of men seems exceptionally low. In our RAPID group 46 of 810 (6%) of men referred had a nonsuspicious mpMRI but underwent TP-Bx due to risk factors or personal choice. Clinically significant disease was extremely low in this group of men at 0.6% of all with nonsuspicious mpMRIs. In those without risk factors the rate is likely to be even lower.

### Conclusions

The RAPID pathway is safe and effective for diagnosing suspected prostate cancer. Our MRI triage approach allows 2 in 5 men to avoid an immediate biopsy. Half of men who undergo biopsy have clinically significant disease.

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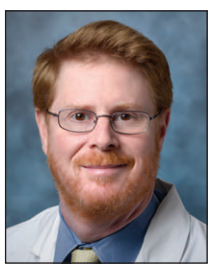
# Misdiagnosis of Interstitial Cystitis: Rates and Reasons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Interstitial cystitis/bladder pain syndrome (IC/BPS) is defined by the Society of Urodynamics, Female Pelvic Medicine, and Urogenital Reconstruction (SUFU) as "an unpleasant sensation (pain, pressure, and discomfort) perceived to be related to the urinary bladder associated with lower urinary tract symptoms of more than 6 weeks duration, in the absence of infection or other identifiable causes."[1] There is significant diagnostic uncertainty of IC/BPS. This is due to the lack of a definitive diagnostic test for IC/BPS as well as a lack of definite diagnostic criteria for IC/BPS.

Diagnosis is a key challenge in managing the disease as it is essentially a diagnosis of exclusion. Misdiagnosis may result from the failure to recognize a separate underlying condition that would explain symptoms (incorrectly assigning a diagnosis of IC/BPS) or vice versa (incorrectly assigning a separate diagnosis when the true clinical picture is IC/BPS). Making the distinction between IC/BPS and other benign conditions is not always straightforward as there is significant overlap (eg urinary frequency may be present in overactive bladder and IC/BPS).

These challenges in diagnosis make the true prevalence of IC/BPS notoriously difficult to estimate. For example, the prevalence of IC/BPS for women in the literature has ranged from as low as 0.045% in administrative claims data to 6.5% in a population based telephone study.[2]

This translates to an approximately twentyfold range in prevalence estimates of IC/BPS in women and an approximately eightfold range in men (based on administrative studies alone). When combining survey and administrative studies there is an astounding 150-fold range in prevalence estimates for women and a greater than 500-fold range for men. These wide ranges in prevalence estimates suggest that IC/BPS is likely frequently misdiagnosed (either under or over diagnosed). In this study we used a national data set to assess the reasons for misdiagnosis of IC/BPS by primarily assessing whether an ICD code for IC/BPS truly represents IC/BPS. Furthermore, we sought to identify patients who truly met IC/BPS diagnostic criteria but were never assigned an ICD code

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## Misdiagnosis of Interstitial Cystitis

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for IC/BPS.

The Veterans Affairs Informatics and Computing Infrastructure (VINCI) was used to identify all living patients in the Veterans Affairs (VA) system between 1999 and 2016 who had an ICD-9/10 code for IC/BPS (9,503, 595.1/ N30.10). Further identified were patients with ICD codes for "IC/BPS-like" conditions, which were defined as conditions that are frequently misdiagnosed for IC/BPS (prostatitis, vagismus, vulvar vestibulitis, vulvodynia and dyspareunia). All other patients were considered controls (5,346,866). A key advantage of the VINCI database is that it combines the scope of a large population based administrative database with in-depth chart abstraction.

To assess the accuracy of an ICD code for IC/BPS representing true IC/BPS as well as cases of true IC/BPS that were potentially missed, random and balanced samples of patients were selected from those with an ICD code for IC/BPS, those with an "IC/BPS-like" code and controls. In-depth chart review was performed on these samples to determine who actually met diagnostic criteria for IC/BPS (see Appendix). If a patient's medical record was not sufficient to make a determination the diagnosis was considered equivocal. Patients were excluded if they had concomitant conditions that would make it difficult or impossible to assess the true presence of IC/BPS. These conditions included a history of cancer (aside from nonmelanoma skin cancers), dementia, HIV, cystectomy or if the patient was deceased at the time of query. If chart abstraction revealed that a patient did not meet criteria for IC/BPS, the actual diagnosis or reason for not meeting IC/BPS diagnostic criteria was determined.

In-depth chart abstraction revealed that of the 1,334 patients with an ICD code for IC/BPS only 48.8% met diagnostic criteria for IC/BPS. The most common single reason for not meeting criteria was the lack of pain or discomfort as a symptom followed by the existence of another condition that explained the symptoms. A total of 11 (4.0%) and 4 (0.6%) patients from the IC/BPS-like and control groups, respectively, met criteria for true IC/BPS (see figure).

Our findings here highlight the high rates of misdiagnosis of IC/BPS. Misdiagnosis frequently occurred when an ICD code for IC/BPS was assigned to patients who did not actually meet true IC/BPS criteria. Furthermore, although the rates of true IC/BPS for patients with an IC/BPS-like code or controls appear low (4.0% and 0.6%, respectively), given the large cohorts sampled these low percentages actually translate to a large number of patients potentially suffering from IC/BPS who are not properly identified. For example, if extrapolated our results would suggest that there are more than 35,000 patients in the VA system who meet IC/BPS criteria but are not identified.

Our study suggests that the inaccuracy of the diagnosis of IC/BPS stems from misclassifying patients as having IC/BPS when it is not actually present and failing to identify cases where IC/BPS is truly present. Crudely, our results suggest that an ICD code for IC/BPS is associated with a low positive predictive value (only 48.8% of those with an ICD code actually met diagnostic criteria) and low sensitivity (12.5%).

Future directions will involve the development and implementation of strategies to improve the accuracy of the identification of patients suffering from IC/BPS and further improving treatment modalities and outcomes.

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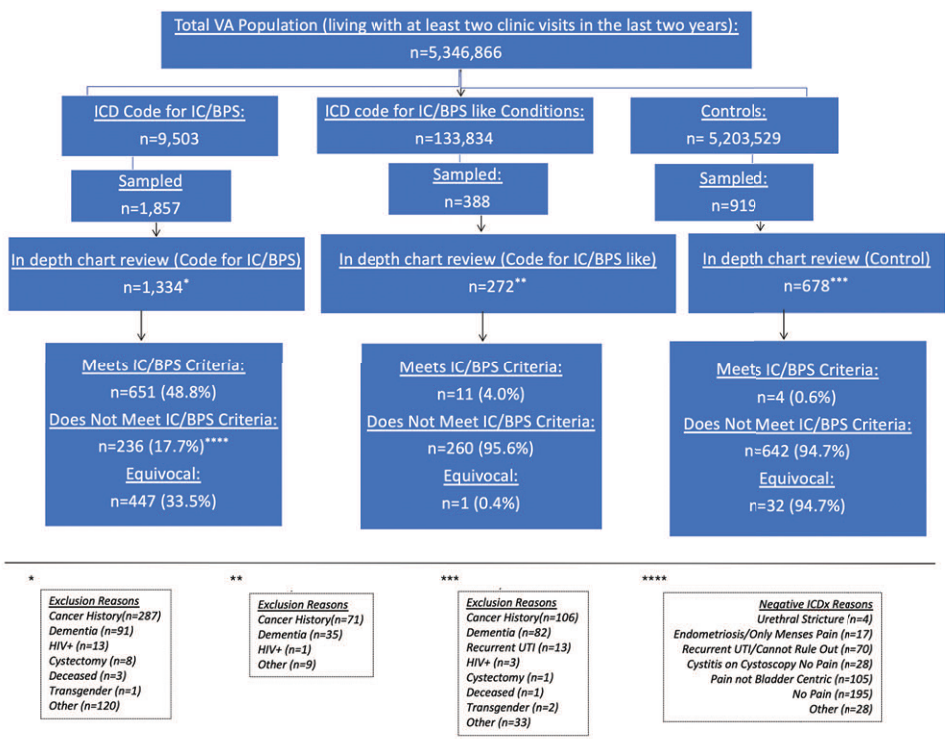


**Figure.** Consort diagram of rates of and reasons for misdiagnosis of IC/BPS in large national cohort.

**Appendix.** Diagnostic criteria for IC/BPS.

Patients who were a correct IC/BPS diagnosis met at least one of the following criteria:

1. Two visits (in the VA system) complaining of unpleasant *bladder centric* sensation in the absence of positive urine culture at least 6 weeks apart.
2. One visit complaining of bladder centric pain/unpleasant bladder centric sensation and a second visit complaining of "likely" IC/BPS-related pain in the absence of positive urine culture at least 6 weeks apart (both at the VA). We defined "likely" IC/BPS-related pain as pain that could be due to IC/BPS but without a specific complaint of bladder-centric pain or bladder tenderness on exam. Symptoms of "likely" IC/BPS include dysuria, pelvic pain, chronic lower abdominal pain, dyspareunia.
3. A history of bladder pain and/or a history of IC/BPS (in the VA or other system) with one additional visit complaining of bladder centric pain in the absence of a positive urine culture.

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