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Complications Following Needle Prostate Biopsy: A Systematic Review and Meta-Analysis

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Abstract:

Objective:

To compare the safety profile between Trans-rectal Ultrasound guided biopsy (TR) and Trans-perineal biopsy (TP) in patients undergoing prostate biopsy. This systematic review and meta-analysis aimed to evaluate the incidence and severity of post-biopsy complications.

Methods:

A systematic search of Scopus, Pubmed, and Web of Science was performed per PRISMA guidelines. Studies including patients undergoing TR, TP biopsy, or both reporting complications (infection, bleeding, acute urinary retention [AUR], and other minor complications) were included. Risk of bias was assessed using NOS and RoB2. Data synthesis used a random-effects model with odds ratio (OR) and 95% confidence intervals (CI). Heterogeneity was assessed using I^2.

Results:

A total of 141 studies (>1.1 million patients) were included. TP was associated with significantly lower rates of infection (OR: 2.62; 95% CI: 1.69-4.09) and sepsis (0.28% vs 0.98%) compared to TR. Overall hospitalization rates were also lower with TP (OR 2.43, 95% CI: 1.14-5.15). However, TP was associated with higher rates of AUR (OR: 0.32; 95% CI: 0.19-0.54).

Conclusion:

TP demonstrates a superior safety profile for infectious complications and sepsis. However, TP carries higher AUR rates, likely related to increased core and tissue sampling. Despite this trade-

off, the transition from TR to TP as the preferred biopsy approach is supported by its lower infection and sepsis rates.

Introduction/Background:

Prostate cancer is one of the most prevalent malignancies among the male population and has a survival rate of 97% at 5 years (Ilic et al. 2018). Prostate cancer screening has resulted in earlier diagnosis and reduction in prostate cancer-related mortality. Testing using the prostate specific antigen (PSA) is used to identify cases of prostate cancer. Screening guidelines recommend testing in males aged 45-70 supported by clinical suspicion to then be followed by imaging and prostate biopsy if any abnormalities are observed (McLaughlin, 2024). The exact method of conducting a prostate biopsy has been debated. Studies have compared the effectiveness of ultrasound-guided biopsies vs computed tomography/magnetic resonance imaging (CT/MRI)-guided alternatives, which method of anesthesia is most appropriate, and the optimal anatomical point from which access to the prostate can be achieved (Bass et al. 2022). The current approach and most appropriate method to date to obtaining core biopsies is trans-rectal (TR) or a trans-perineal ultrasound guided needle biopsy where a single needle is used to obtain roughly ten to sixteen core biopsies from the gland (Davis et al. 2015). There are variations in the gauge of the needle used as well as the number and template availability for performing biopsies. Newer methods of imaging-guided biopsying include ultrasound and MRI fusion guided techniques. The use of MRI-ultrasound fusion techniques offers improved targeting of suspected lesions and can reduce the number of cores required (Kasivisvanathan et al. 2018); however, their reliance on MRI imaging pre-biopsy and the need for specialized fusion equipment limit their accessibility. Due to this, TR and TP biopsy methods remain the most widely used and

accessible approaches in clinical practice worldwide. Biopsy is associated with complications including bleeding, hematuria, rectal bleeding, hematospermia, lower urinary tract (LUT) symptoms and acute urinary retention (AUR), erectile dysfunction, pain, infection, and in rare cases mortality. These complications vary depending on the approach of the procedure. A trans rectal prostate biopsy will increase the risk of infection due to the introduction of enterococcal and other native gastrointestinal flora as well as rectal bleeding. (Anastasiadis et al., 2013).

Historically the favored approach to biopsy has been the trans-rectal ultrasound-guided biopsy, given its long-established use and accessibility. This method allows analysis of multiple tissue cores from various parts of the prostate. There are multiple pre-procedure aspects that must be taken into account when performing TR or TP guided biopsies such as antibiotic use, anesthetic type, and medication interactions.

Due to the high false negative rates associated with the six-core biopsy approach, the number of cores taken was increased to 8, 12, or 14 after 2004 according to findings by Ghani et al. (2004) and Berger et al. (2004) This, however, increases the risk of complications and thus higher core numbers are only preferred when there is high clinical suspicion of malignancy previously missed on another biopsy.

As compared to the trans-rectal approach, the trans-perineal prostate ultrasound-guided biopsy has slight differences in complication rates and prostate gland access. The patient is placed in the dorsal lithotomy position, and the biopsy needles will go through the perineum. The US probe is inserted into the rectum for view of the prostate. This allows greater access to the apex and anterior transition zone of the gland. TP guided biopsy can be done via the freehand method or via a template grid. Unlike the TR guided biopsy, TP guided biopsy requires more cores to be taken (upwards of 20-40). The trans-perineal approach provides a lower infection risk as the area can be sterilized beforehand; whereas the trans-rectal approach has an increased risk of inoculating colonic bacteria into the insertion site. However, the trans-perineal approach increases the risk of post procedure pain and urinary retention as the perineum is a highly innervated anatomical structure. The evaluation of these complications and how they vary by approach is the rationale for this study. International guidelines differ on this question. The European Association of Urology (EAU) Guidelines on Urological Infections recommend the trans-perineal route as the preferred method, a position based on a guidelines-panel meta-analysis of randomized controlled trials showing significantly fewer infectious complications with the TP biopsy (risk ratio 0.55) (Pilatz et al. 2026). In contrast, the American Urological Association (AUA) guidelines continue to permit either, citing a lack of adequately powered randomized control trials comparing infectious risk between the two methods. This divergence between major international guidelines reflects the gap in the evidence base for biopsy-related complications, which this study aims to address. This study will focus on complications arising directly from the anatomical approach taken via the widely accepted practice of TR or TP biopsy.

Review Objectives: This systematic review and meta-analysis address the following question: among patients who have undergone prostate biopsy and reported complications, how does trans-rectal biopsy compare to trans-perineal biopsy as it pertains to incidence and severity of biopsy complications including infection, sepsis, hematuria, rectal bleeding, acute urinary retention, hospitalization, emergency department presentations, and mortality?

Methods:

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines and the protocol registered with PROSPERO (registration ID: CRD420251019935).

Databases searched

Papers to be screened for this systematic review were first collected via a key word search of 'prostate' 'biopsy' 'complications' in Pubmed, Scopus, and Web of Science. The search was run on February 18,2025 and a reran on November 25, 2025. The identified articles were imported into an Endnote library where duplicates were removed before exporting the remaining studies into Covidence for title and abstract screening, full text screening and data extraction (Figure 1). All stages of the review were conducted by two independent reviewers with any discrepancies resolved through discussion or by a third reviewer.

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria: 1) participants had undergone a trans-rectal (TR) or trans-perineal (TP) prostate needle biopsy, 2) the study reported greater than or

equal to one complication arising from the procedure, 3) reported complications were attributable to the needle biopsy itself and not anesthesia, radical prostatectomy, or other interventions, 4) the biopsy was performed in a hospital or clinical setting, and 5) the study is a primary research article published in a peer-reviewed journal.

Studies were excluded if: 1) no biopsy was performed (i.e. PSA or imaging only), 2) a biopsy approach other than TR or TP was used, 3) the study compared antibiotic prophylaxis protocols, anesthesia used, or other confounding interventions, 4) a radical prostatectomy was performed immediately following biopsy so that complications could not be attributed to the biopsy itself, and 5) the study was a case report, editorial, commentary, or letter. There were no restrictions placed on study design, country of origin, year of study, or sample size analyzed.

Risk of Bias Assessment

Risk of bias was assessed using tools appropriate to the design of this study. The Newcastle-Ottawa Scale (NOS) was applied to observational studies for evaluation of selection and comparability (Wells et al. 2000). NOS was chosen over ROBINS-I given the broad range of complication outcomes and high volume of observational studies included. The Cochrane Risk of Bias 2 (RoB 2) was applied to randomized controlled trials to assess for bias arising from the randomization process, deviations of intended interventions, and missing outcome data (Sterne et al. 2019).

Data Extraction

Two individual reviewers extracted the data into a generic data extraction form. The following data was extracted: study year, country, study sample characteristics, biopsy details such as the

approach, and number of cores, and complications following biopsy including any ER visits, hospitalization, and mortality. To assess any confounding principles for the narrative synthesis, needle gauge, antibiotic prophylaxis regime, anesthesia type, and outpatient vs inpatient were also collected. Complications were extracted separately for TR and TP arms where available. Studies reporting both approaches were treated as comparative; single-approach studies contributed to approach-specific rates. Data that could not be separated by arm were marked as not reported or excluded.

Narrative synthesis

A narrative synthesis was performed to provide a descriptive overview of the available evidence. Studies were grouped into whether they were TP biopsy or TR biopsy approach and complication type. The overall direction and magnitude of the complication rates were compared, while giving consideration to differences in study design, patient populations, technique, quantity of cores obtained, definitions of outcomes, and length of follow-up. For each complication, where there was availability of sufficient and comparable arm-specific data, outcomes were included in the quantitative meta-analysis. Outcomes that were insufficiently reported or not comparable were not pooled and only narratively discussed. There was particular consideration given to clinically important complications such as infectious complications, sepsis/sepsis-related hospitalization, acute urinary retention, hematuria, overall hospitalization, emergency department presentations, and mortality. Variation in the definitions of varying complications and their reporting across studies was considered in the interpretation of the consistency and applicability of the evidence.

Meta-analysis

Data synthesis was performed using a random-effects model using the DerSimonian-Laird method, with individual study proportions logit-transformed prior to pooling in order to stabilize variance. Pooled proportions and odds ratios (OR) for the comparison between TR and TP were calculated using a custom Python tool (PROBE-Meta v1.0) made with assistance of a generative AI tool for code writing, with 95% confidence intervals (CI). This was created for this study and verified via pandas (McKinney, 2010). Heterogeneity across the studies were assessed using the I^2 statistic; values greater than 75% were considered indicative of substantial heterogeneity. Publication bias was assessed using Egger's regression test, which was performed separately for each outcome and biopsy arm (Supplementary figure S10). Given the high study heterogeneity observed across all outcomes, funnel plot asymmetry should be interpreted cautiously given Egger's test high false-positive result under high heterogeneity. Statistically significant findings were considered with a p-value <0.05.

Results:

Narrative synthesis:

Complications following prostate biopsy were consistently reported in both trans-rectal (TR) and trans-perineal (TP) approaches, although there was substantial variation in the definition and severity of various reported complications. The 141 studies that were included gave a broad representation of clinical settings, geographic areas, study designs, and biopsy techniques. TR biopsy had a wider breadth of representation at 61% of studies, which reflects its history as the predominant approach, whereas the TP biopsy was represented in 15.6% but in newer studies (2006-2024).

Of all the complications reported, infectious complications represented the clearest difference in the approaches. The TR biopsy was more frequently associated with infectious complications post-biopsy across the literature with varying reported rates. The variation seems to reflect the extensive variation in the definitions of infection, as the reported complications ranged from post-biopsy fever to culture-confirmed infection or bacteremia. Despite this heterogeneity, the direction of effect was generally consistent with TP biopsy tending to report fewer infectious complications. This finding was also reflected in the reported rates of sepsis and sepsis-related hospitalization, where the TP approach had lower complication burden. Sepsis and sepsis-related hospitalization were analyzed as a combined outcome as a majority of studies reported them jointly rather than independently.

Figure 1. PRISMA 2020 flow diagram of study identification, screening, and inclusion.

Despite this, acute urinary retention has been shown to be an important complication associated with TP biopsy. The magnitude represented by this association appears to be based on surgical technique and number of core sampling. The studies that had the highest rates of reported AUR were those that used saturation biopsy techniques involving more than 30 cores. TP biopsy studies that used standard core or freehand techniques generally reported lower rates of AUR and were more comparable with those of the TR approach.

The other complications showed less consistent differences between the two approaches. Hematuria occurred at similar rates following TP or TR biopsy, this is consistent with the required use of needle penetration into the highly vascularized prostate in both approaches.

Rectal bleeding was numerically less in TP vs TR biopsy, but the difference did not reach statistical significance. In a similar manner, UTI/prostatitis rates tended to be lower in TP biopsy but did not demonstrate statistical significance. Mortality and the need for emergency room presentations were uncommon among both approaches and thus limited the ability to identify meaningful differences between the two. Erectile dysfunction and post-procedural pain were described qualitatively in the literature but couldn't be pooled quantitatively due to varying measurement tools and insufficient reporting across studies.

The PERFECT trial, included in this review, illustrated that lesion location may also influence the diagnostic performance of TR vs TP biopsy. The posteriorly located lesions favored the trans-rectal route, whereas anteriorly located lesions favored the trans-perineal route. Complications such as hemospermia, and lower urinary tract symptoms were subsequently dropped from the discussion due to insufficiency of data on these from the completed data extraction.

Meta-Analysis:

The complications that were assessed in this study were infection, sepsis, hematuria, rectal bleeding, acute urinary retention, UTI/prostatitis, hemospermia, hospitalization, mortality, and ER visits (figure 2). There were 141 total studies analyzed with 86 relating to trans-rectal only, 22 being trans-perineal only, and 33 reporting both approaches by study design (of the 141 studies, 31 studies did not contribute usable arm-specific data to the pooled analyses) (Supplementary table 1). Of the complications reported in these studies the complications with the most significance was infection, sepsis/sepsis-related hospitalization, urinary retention, and

overall hospitalization rate. Infection was reported in 77 and 27 of the TR and TP studies with a median of 2.97% (2.46-3.60 CI; I^2=99%) and 1.15% (0.78-1.71 CI; I^2=85%) respectively (p=<0.0001). The range of reported infection rates were wide; ranging from 0% (Cronin et al. 2017; Thurtle et al. 2018) to 34.97% (Bissada et al. 1977). The studies included in this review showed that the median TR infection rate had a decade trend: in the 1990s: 3.22%, 2000s:4.49%, 2010s: 3.03% and 2020s: 2.24%. Sepsis with subsequent hospitalization was reported in 72 and 32 of the TR and TP studies with a median of 0.98% (0.76-1.26 CI; I2=99%) and 0.28% (0.15-0.52 CI; I2=76%) respectively (p=0.0002). Three of the studies provided population-level pictures. Anastasiadis et al. (2015; England, n=198,361) demonstrated a 1.1% sepsis/sepsis-related hospitalization rate, while Nam et al. (2010, 2013; Canada, 2013, n=75,190) and Loeb et al. (2010, 2011, 2012; SEER-Medicare, USA, 2011, n=17,472) had an increase from 1.0% in 1996 to 4.1% in 2005, and an overall 6.9% vs 2.7% in controls in 30-day hospitalizations respectively. Hematuria was reported in 57 and 25 of the TR and TP studies with a median of 8.66% (5.02-14.54 CI; I2=99.8%) and 8.64% (4.33-16.51 CI; I2=99.1%) respectively (p=0.995). Rectal bleeding was reported in 42 and 16 of the TR and TP studies with a median of 1.63% (1.00-2.63 CI; I2=99%) and 0.67% (0.28-1.62 CI; I2=88%) respectively (p=0.086). Acute urinary retention was reported in 51 and 33 of the TR and TP studies with a median of 1.31% (1.01-1.70 CI; I2=96%) and 3.94% (2.56-6.01 CI; I2=97%) respectively (p=<0.0001). The highest rates of urinary retention came from Merrick et al. (USA, 2008) with 39.4% and the Brun et al. (France, 2023) study comparing switching from TR to TP with 43.0%. The studies that reported on the use of freehand or standard TP biopsy with 10-14 cores had retention rates closer to 1-7% which is more comparable to the TR rates. UTI/Prostatitis was reported in 53 and 22 of the TR and TP studies with a median of 2.77% (1.97-3.87 CI; I2=99%) and 1.15% (0.43-3.05 CI;

I2=99%) respectively (p=0.096). Overall hospitalization rates were reported in 58 and 24 of the studies with the median being 2.82% (2.30-3.45 CI; I2=99%) and 1.18% (0.58-2.41 CI; I2=97%) respectively (p=0.021). Overall mortality was reported in 36 and 11 studies in the TR and TP cohorts with median of 0.07% (0.05-0.10 CI; I2=26%) and 0.12% (0.05-0.29 CI; I2=38%) respectively (p=0.217). The reporting of mortality of TR biopsy did range from 0.003% in Roth et al. 2015 (Australia) to 0.224% in the Carmignani et al. 2012. The need for ER presentations was reported in 14 and 8 of the TR and TP studies with the median being 4.45% (1.21-15.02 CI; I2=100%) and 3.09% (1.60-5.89 CI; I2=91%) respectively (p=0.620).

Egger's test indicated significant funnel plot asymmetry ($p<0.05$) in 7 of 18 outcome-arm combinations: UTI/Prostatitis (TR and TP), rectal bleeding (TP), sepsis/sepsis-related hospitalization (TP), mortality (TR), ER visits (TP), hospitalization (TP). The remaining 11 combinations showed no significant asymmetry.

To explore the trends in infection rates, a meta-regression of infection rate on publication year was performed for both TR and TP arms. Meta-regression of infection rate against publication year showed a significant downward trend in the TR arm (slope=-0.250%, P,0.001) but no significant change in the TP arm (slope=-0.042%/year, p=0.514) illustrated in Figure 4. This suggests a gradual improvement in TR infection control over time but has not shown a corresponding change in the TP infection rate.

Figure 2. Pooled outcomes summary table — TR vs TP prostate biopsy complications (n=141 studies).

Figure 3. TR vs TP Pooled Arm Comparisons — Odds Ratios by Complication (n=141 studies).

Full outcome-specific forest plots for each complication, stratified by TR and TP arms, are provided in the Appendix (Supplementary Figures S1–S9).

Discussion:

Higher infectious complication rate following TR biopsy (OR 2.624, 95% CI 1.685-4.087, p=<0.0001) is a key finding of this review. The range of reported infection rates was wide. This stems from the inconsistent definitions of "infection" across the studies rather than true differences biologically. Some studies counted any post-biopsy fever as evidence of infection while other studies required culture-confirmed bacteremia. The variance in the definition of what constitutes an infection explains the considerably high heterogeneity as demonstrated by the I2 of 99% in the TR studies and 85% for the TP studies. A comparison of infection definitions across studies to determine whether this is definitional heterogeneity, rather than a true difference was not feasible; this is a proposed target for future analysis. This is acknowledged to be a core limitation in this systematic review. The range of studies across decades also gives

insight into the challenges with the TR approach. Despite antibiotic prophylaxis refinement over the decades the infection complications rate has not significantly improved until the recent decades. In fact, some studies such as Loeb et al. (2010, 2011, 2012) saw increased rates of infectious complications highlighting the global rise of antibiotic resistance. As antibiotic resistance increases, recent studies in this review emphasize the limitations of relying on the use of antimicrobial prophylaxis to mitigate the risks associated with trans-rectal access. The ability of the clinician to sterilize the perineal skin pre-procedure provides a plausible explanation for the lower risk of infectious complications with the TP approach.

Figure 4. Meta-regression of infection rate by publication year, TR and TP arms (marker size proportional to study N).

Sepsis and sepsis related hospitalizations complement the points illustrated by the data reflected in the infectious complication. There was 3.1 times increase in the risk of sepsis/sepsis-related hospitalizations post TR biopsy than in the TP arm (OR 3.48, 95% CI 1.79-6.79, p=0.0002). The all-cause hospitalization within 30 days of biopsy was 2.5 times higher (OR 2.43, 95% CI 1.14-5.15, p=0.0213). These three studies represent a combined population of nearly 300,000 patients and consistently show that TR biopsy carries a hospitalization burden nearly four times higher than the background rate. This is in contrast to the TP hospitalization rates which had a median of approximately zero percent across those reporting TP biopsy complications. Hospital or system level biopsy volumes were not extracted beyond these three studies; such data could enable clinically useful triage estimates in future work.

One of the trade offs with the TP approach arose from the data on acute urinary retention (OR 0.324, 95% CI 0.193-0.542, p=<0.0001). This represents a clinically significant difference between TP and TR. In the TP the way the biopsy needle traverses the perineum is more likely to cause swelling and block the urethra thus causing urinary retention. These high rates of urinary retention likely reflect the use of saturation biopsy approaches where >30 cores are taken rather than the standard TP approach where number of cores is comparable to those of TR biopsies. This suggests that the increased risk of AUR may not be attributable solely to the trans-perineal route but may be influenced by the extent of tissue sampled causing prostatic edema. Core number was not consistently reported across studies, limiting formal stratification of retention rates by technique which is a target for future subgroup analysis.

The other complications mentioned were not statistically significant between the two approaches. Hemospermia was omitted from the meta-analysis due to insufficiently reported cases throughout TR, TP, and studies comparing both. Hematuria (OR 1.003; CI 0.391-2.568, p=0.995) was present in both approaches. Both approaches involve needle punctures in highly vascularized tissues, and near identical rates (8.66% TR vs 8.64% TP) confirm no true difference in bleeding risk. However, variation can be explained by the varying definitions of Hematuria across studies from discoloration to frank hematuria. Rectal bleeding was not significant in this systematic review with an OR of 2.44 (CI 0.88-6.72) and a p value of 0.086. While it is possible that there is an increased risk with the TR approach given the anatomical approach taken, there was limited TP data (k=16) that could have impacted the analysis. Mortality was near zero across both arms (OR 0.558; CI 0.221-1.409, p=0.217). Mortality risk is rare in both groups and did not

differ between approaches. Although relative mortality rates were low, this risk remains clinically relevant when counseling patients.

Mehtodological heterogeneity limited interpretation of complication rates. Differences in complication rates, follow-up, number of cores, biopsy technique, antibiotic prophylaxis, clinical setting, and patient selection likely contributed to the high heterogeneity observed across pooled outcomes. The 1977-2025 study period also spans major changes in biopsy practice and antimicrobial resistance.

There was definitional variation across several of the complications reported. As previously mentioned, infection had a varied range in definition from self-reported fever to bacteremia requiring ICU admission. There was no standardized complication reporting tool such as the Clavien-Dindo tool used consistently across the studies. The other major source of the high variation within the study is operator and setting variation. Some studies such as Young et al. (Australia, 2019) were done by a single surgeon and displayed careful patient selection and needle disinfection protocols achieving a sepsis rate of 0.36%. Whereas other studies represented population-level demographics capturing the full distribution of operating skills and institutional practice. Of the nine complications reported, mortality was the exception. With an I^2 of 26% for TR and 38% for TP we see moderate variation due to the near zero mortality reported regardless of approach, era, or location.

It is also important to consider the range in geographic location and populations. TR studies represented in this systematic review had great geographical diversity with the USA, Italy,

Netherlands, Canada, Taiwan, UK, Sweden, Australia, Thailand, France, Finland, and others being included. The studies that represented the TP biopsy approach were more confined to the UK, USA, and Italy with emerging representation from France and Australia. This reporting imbalance reflects TR's long-standing status as the historical gold standard, with TP more recently gaining traction. In places where many enteric flora species have gained antibiotic resistance and where the health systems can better respond to infection rates, we see the TP approach being preferred. Such as in the UK, where the British Association of Urological Surgeons recommends the TP approach (BAUS, n.d.). Figures 5-8 represent the geographic data discussed.

Figure 5. Geographic distribution of included studies by country (n=141 studies, 43 countries; some studies span multiple countries).

Figure 6. Geographic distribution of included studies by country, shown as a choropleth map (n=141 studies, 43 countries; some studies span multiple countries).

Figure 7. Geographic distribution of TR (trans-rectal) studies by country (k=86 TR-only + 33 combined-arm studies; 40 countries).

Figure 8. Geographic distribution of TP (trans-perineal) studies by country (k=22 TP-only + 33 combined-arm studies; 27 countries).

The PERFECT trial (Ploussard et al., 2024), a randomized head-to-head RCT of TR vs TP MRI-targeted biopsy, found no superiority of TP over TR in significant cancer detection. The trial illustrated that MRI lesion location played a role in performance. For lesions found in the posterior aspect of the prostate, the TR approach was superior, whereas if the lesion were in the anterior aspect, then the TP approach was superior. This suggests that perhaps the optimal approach may be decided by lesion location rather than a universal policy approach.

The evidence that has been compiled across the complications reported in this meta-analysis support the interpretation of several clinical practice points. This significance was carried across the population-level databases, single-center series, and the RCT.

Egger's test identified funnel plot asymmetry in several outcome-arm combinations. However, due to the substantial heterogeneity across nearly all pooled outcomes (I^2>85%), the asymmetry cannot be reliably attributed to publication bias over genuine clinical and methodological heterogeneity between studies. This is a recognized limitation of Egger's test under high heterogeneity and should be considered a limitation of the current synthesis rather than definitive evidence of publication bias.

Finally, this review suggests that the optimal approach to biopsy may not be determined solely based on overall complication rates. With all of this taken together, the narrative evidence supports the TP biopsy as having an important infectious safety advantage, while indicating that biopsy technique, intensity of tissue sampling, lesion location, and patient-specific factors should be considered when selecting which approach to utilize. The overall mortality risk was extremely

low for both approaches; however, was not zero as particular populations such as those that are elderly and comorbid tend to have an increased 30 day all cause mortality rate (Brewster et al. 2017). One of the largest drawbacks was the lack of standardized reporting (i.e. mandatory Clavien-Dindo grading) (Soliman et al. 2026).

Conclusion:

This systematic review and meta-analysis illustrate that trans-perineal prostate biopsy is associated with a more favorable infectious safety profile over the trans-rectal approach. Across the 141 studies and more than 1.1 million patients, TP biopsy had a significantly lower rate of post-biopsy infection, sepsis, and overall hospitalization. The consistency of these results persisted across different study designs and clinical settings and are relevant in the context of antimicrobial resistance and antibiotic prophylaxis. The main trade-off with the TP biopsy is an increased risk of acute urinary retention. However, the range that is seen with this complication could be associated with biopsy technique and extent of the tissue sampled. The saturation biopsy protocols were observed to have the highest rates. Complications such as hematuria, rectal bleeding, UTI/prostatitis, emergency department presentations, and mortality did not demonstrate any significant differences between approaches. Overall, the findings support the continuation of transition toward the TP approach as the preferred method to minimize infectious complications and sepsis. However, evidence does not support any single approach for universal use in every patient. There are multiple considerations when choosing which method including biopsy technique, number of cores, patient-related factors, and lesion location. Future comparative studies should have standardized definitions and severity grading for complications, clearly distinguish standard-core vs saturation TP techniques, and evaluate outcomes according

474 to lesion location. The use of this standardization could improve the comparability of future
475 evidence and help delineate which approach would be of most benefit to each individual patient.
476

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List of Supplementary Materials:

The following supplementary materials accompany this manuscript and are provided as a separate file: Supplemental_Figures.docx

Supplementary Table 1. Full reference list of included studies provided as: Supplemental_References.docx

Figure 1. PRISMA 2020 flow diagram.

Flow diagram showing the identification, screening, eligibility assessment, and inclusion of studies in the systematic review and meta-analysis.

Figure 2. Pooled outcomes summary: TR versus TP prostate biopsy complications.
Summary of pooled complication rates for transrectal (TR) and transperineal (TP) prostate biopsy across the nine assessed outcomes (n=141 studies).

Figure 3. TR versus TP pooled arm comparisons.
Odds ratios comparing complication rates between transrectal (TR) and transperineal (TP) prostate biopsy across the assessed outcomes (n=141 studies).

Figure 4 file. Meta-regression of infection rate by publication year, TR and TP arms.

Figure 5. Geographic distribution of included studies by country.
Geographic distribution of the included studies by country (n=141 studies, 43 countries). Some studies included data from multiple countries.

Figure 6. Geographic distribution of included studies by country: choropleth map.
Choropleth map showing the geographic distribution of included studies by country (n=141 studies, 43 countries). Some studies included data from multiple countries.

Figure 7. Geographic distribution of TR studies by country.
Geographic distribution of transrectal (TR) studies by country (k=86 TR-only studies + 33 combined-arm studies; 40 countries).

Figure 8. Geographic distribution of TP studies by country.
Geographic distribution of transperineal (TP) studies by country (k=22 TP-only studies + 33 combined-arm studies; 27 countries).

Supplementary Figures S1–S9. Forest plots (TR vs TP, DerSimonian-Laird random-effects) for each of the nine complications assessed.

Supplementary Figure S10. Funnel plots (logit-proportion vs. standard error) for all nine outcomes, with Egger's regression test results.

Supplementary Materials

Figure 1. PRISMA 2020 flow diagram of study identification, screening, and inclusion.

Figure 2. Pooled outcomes summary table — TR vs TP prostate biopsy complications (n=141 studies).

Figure 3. TR vs TP Pooled Arm Comparisons — Odds Ratios by Complication (n=141 studies).

Figure 4. Meta-regression of infection rate by publication year, TR and TP arms.

Figure 5. Geographic distribution of included studies by country (n=141 studies, 43 countries; some studies span multiple countries).

Figure 6. Geographic distribution of included studies by country, shown as a choropleth map (n=141 studies, 43 countries; some studies span multiple countries).

Figure 7. Geographic distribution of TR (trans-rectal) studies by country (k=86 TR-only + 33 combined-arm studies; 40 countries).

Figure 8. Geographic distribution of TP (trans-perineal) studies by country (k=22 TP-only + 33 combined

arm studies; 27 countries).

Supplementary Figure S1. Infection: TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S2. Sepsis/Hospitalization: TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S3. UTI/Prostatitis: TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S4. Hematuria: TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S5. Rectal bleeding: TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S6. Urinary retention: TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S7. Hospitalization (all-cause): TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S8. Mortality: TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S9. Emergency department visit: TR vs TP forest plot (DerSimonian-Laird random-effects).

Supplementary Figure S10. Funnel plots (logit-proportion vs standard error) for all nine outcomes, TR and TP arms, with Egger's regression test for funnel asymmetry. Egger's regression test intercepts and p-values for each outcome-arm combination are summarized in the Results section. Given the high heterogeneity observed across outcomes, funnel asymmetry should be interpreted cautiously as a limitation of the evidence base rather than definitive evidence of publication bias.

Figure 1. PRISMA 2020 flow diagram of study identification, screening, and inclusion.

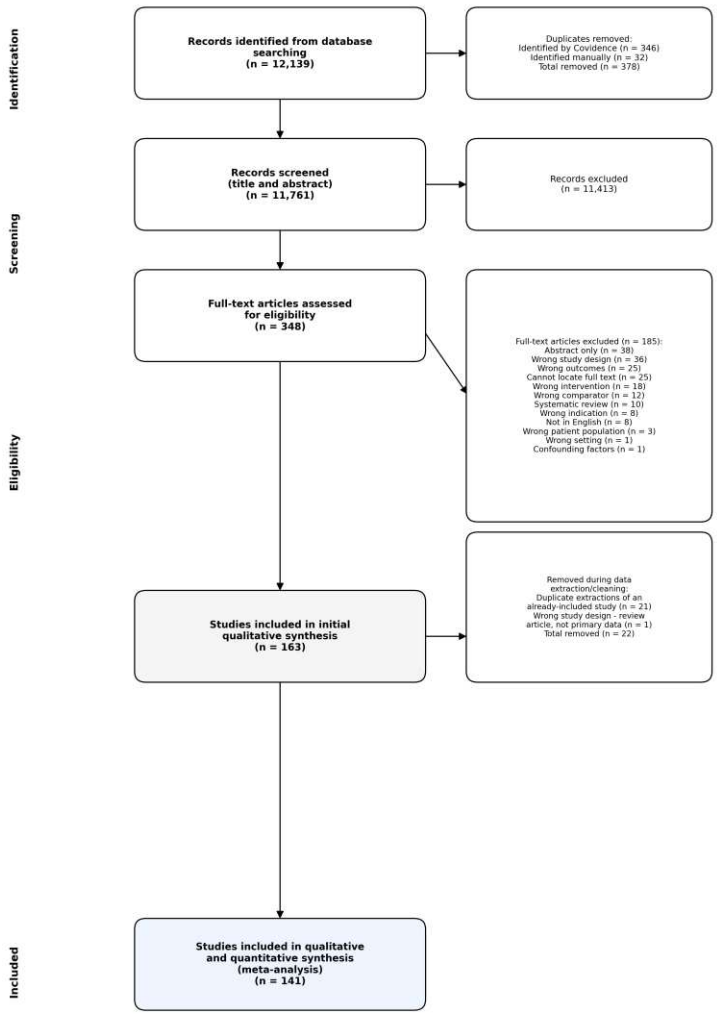


Figure 2. Pooled outcomes summary table — TR vs TP prostate biopsy complications (n=141 studies).

Pooled Outcomes Summary — TR vs TP Prostate Biopsy Complications (n=141 studies)

Outcome	TR k	TR %	TR 95% CI	TR I²	TP k	TP %	TP 95% CI	TP I²	OR (TR vs TP)	95% CI	Sig.
Infection	77	2.97%	2.46-3.60	99%	27	1.15%	0.78-1.71	85%	2.624	1.685-4.087	Yes
Sepsis/Hospitalization	72	0.98%	0.76-1.26	99%	32	0.28%	0.15-0.52	76%	3.483	1.788-6.786	Yes
UTI/Prostatitis	53	2.77%	1.97-3.87	99%	22	1.15%	0.43-3.05	99%	2.446	0.854-7.005	No
Hematuria	57	8.66%	5.02-14.54	99.8%	25	8.64%	4.33-16.51	99.1%	1.003	0.391-2.568	No
Rectal Bleeding	42	1.63%	1.00-2.63	99%	16	0.67%	0.28-1.62	88%	2.435	0.882-6.724	No
Urinary Retention	51	1.31%	1.01-1.70	96%	33	3.94%	2.56-6.01	97%	0.324	0.193-0.542	Yes
Hospitalization all cause	58	2.82%	2.30-3.45	99%	24	1.18%	0.58-2.41	97%	2.425	1.141-5.154	Yes
Mortality	36	0.07%	0.05-0.10	26%	11	0.12%	0.05-0.29	38%	0.558	0.221-1.409	No
ER Visit	14	4.45%	1.21-15.02	100%	8	3.09%	1.60-5.89	91%	1.46	0.327-6.516	No

OR > 1 favors higher event rate in TR relative to TP (i.e., TP safer) for that outcome, and vice versa.
'Sig.' = statistically significant (95% CI for OR excludes 1). I² = heterogeneity (I² statistic), reported separately for TR and TP arms.
Pooling: DerSimonian-Laird random-effects model on logit-transformed proportions, TR and TP arms pooled independently (see PROBE-Meta v1.0 methodology).

Figure 3. TR vs TP Pooled Arm Comparisons — Odds Ratios by Complication (n=141 studies).

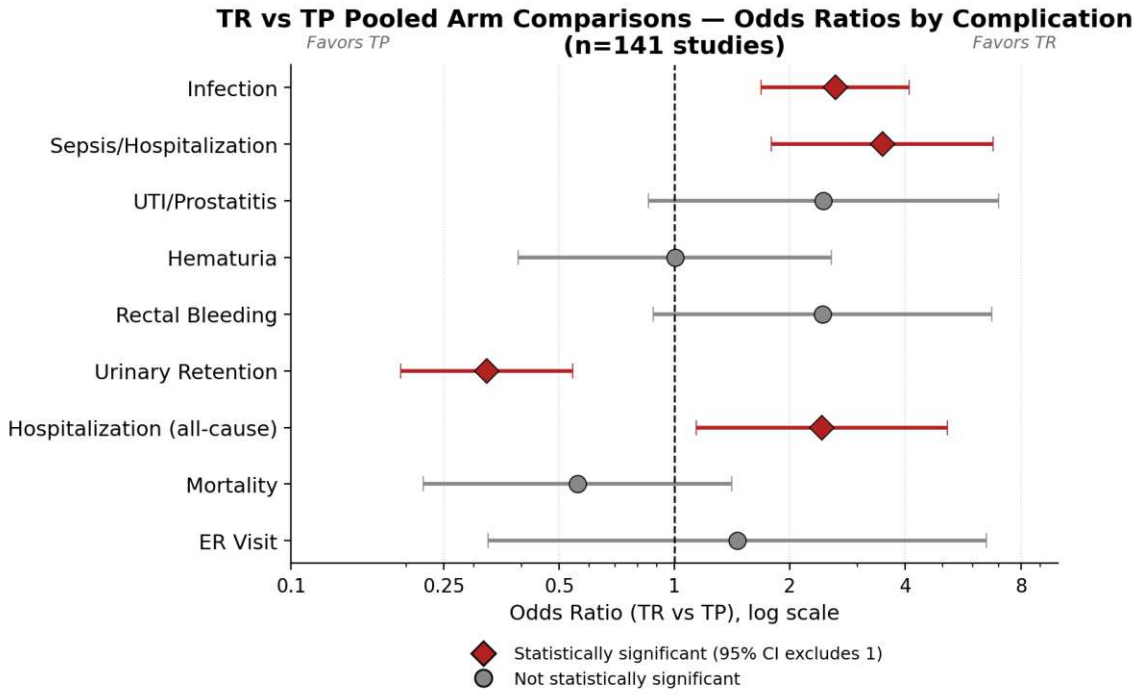


Figure 4. Meta-regression of infection rate by publication year, TR and TP arms.

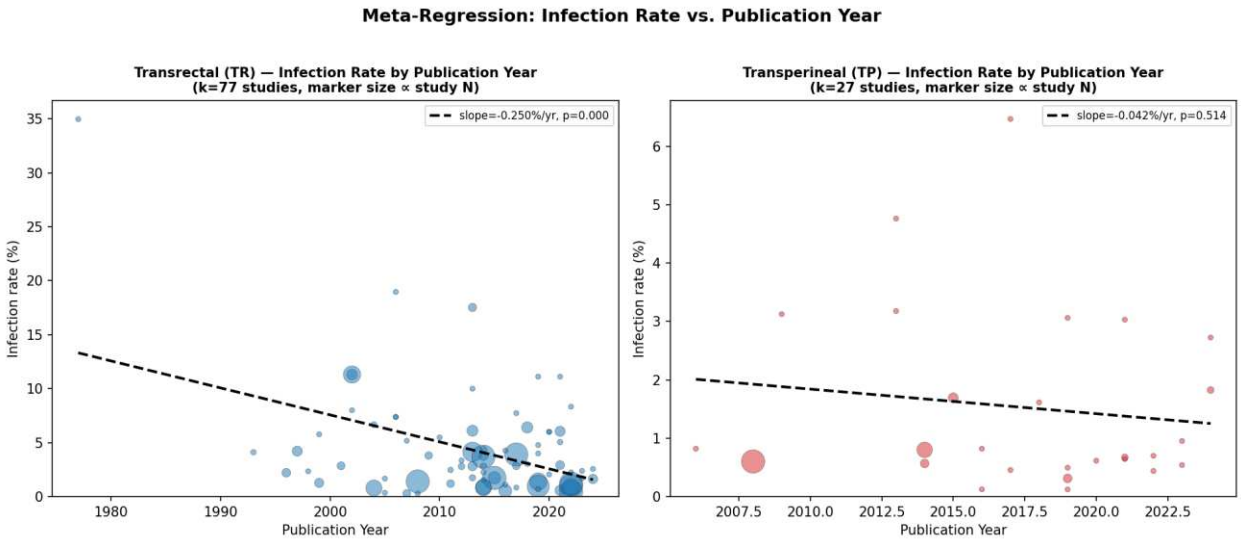


Figure 5. Geographic distribution of included studies by country (n=141 studies, 43 countries; some studies span multiple countries).

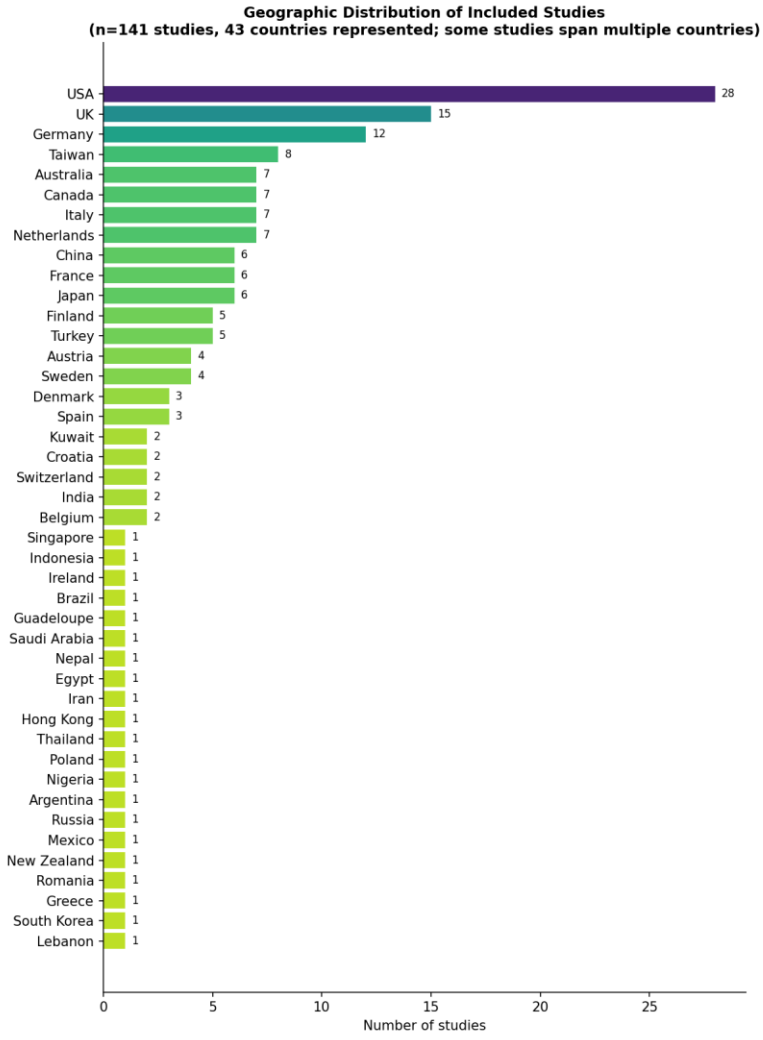


Figure 6. Geographic distribution of included studies by country, shown as a choropleth map (n=141 studies, 43 countries; some studies span multiple countries).

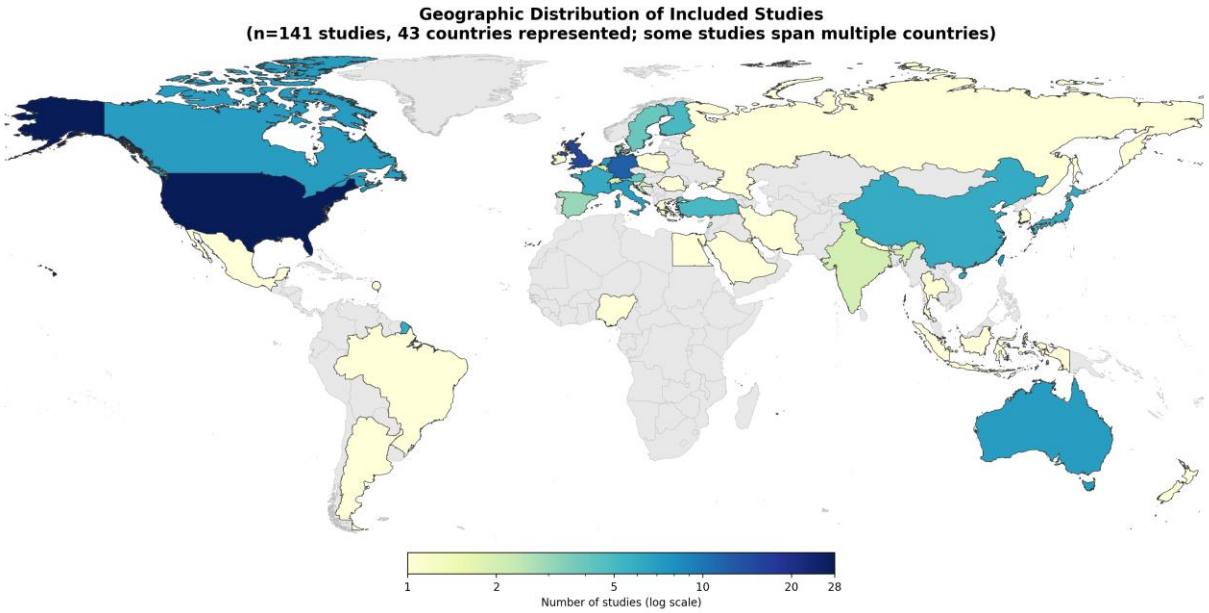


Figure 7. Geographic distribution of TR (trans-rectal) studies by country (k=86 TR-only + 33 combined-arm studies; 40 countries).

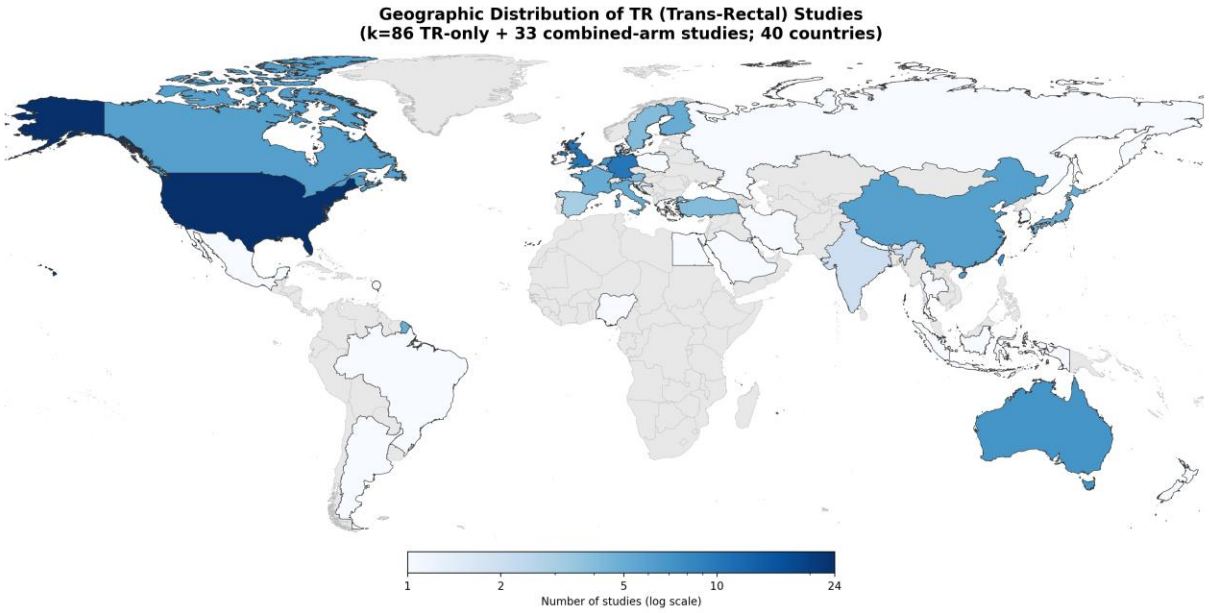
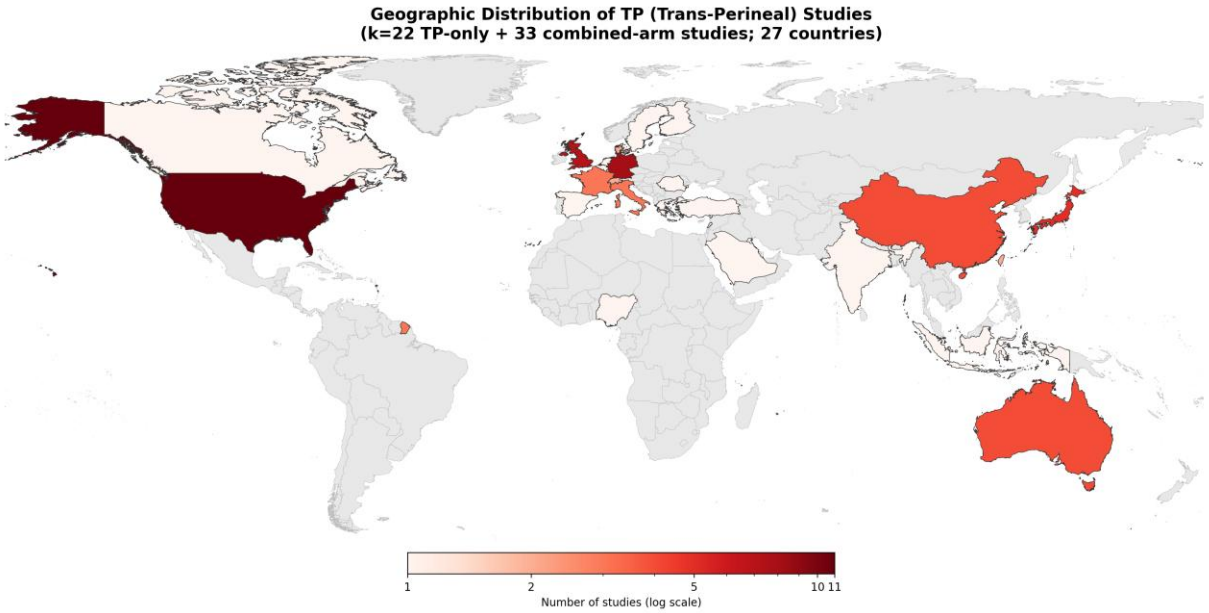
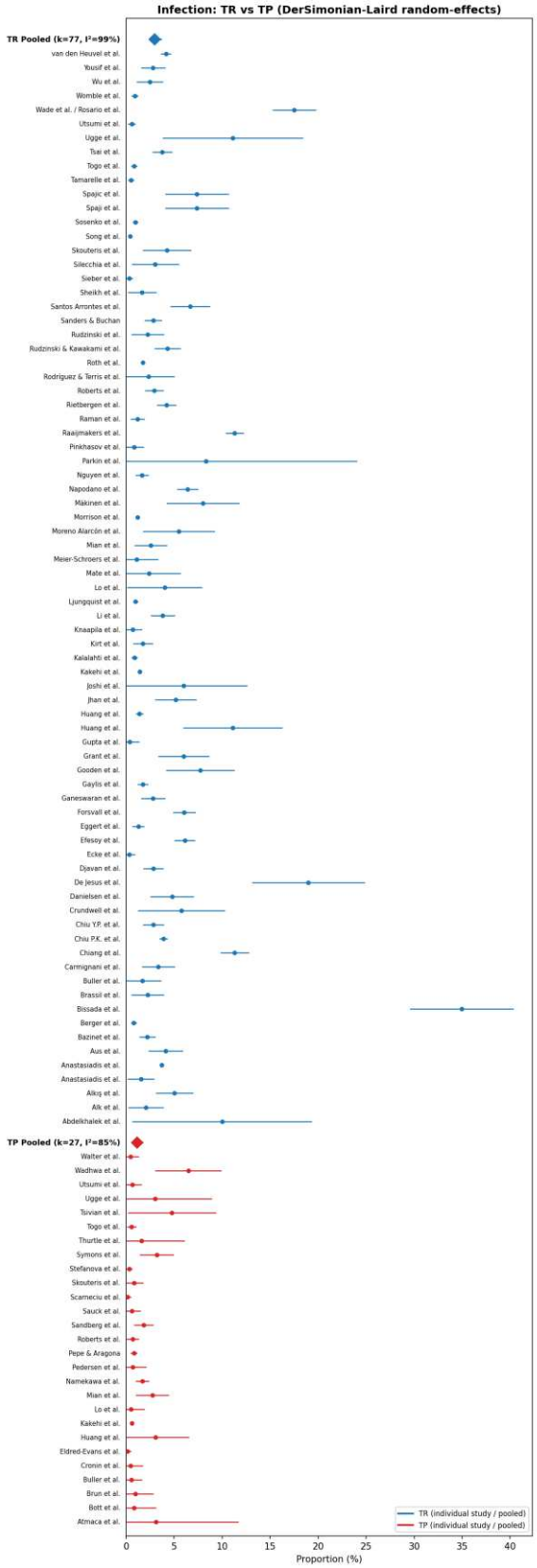


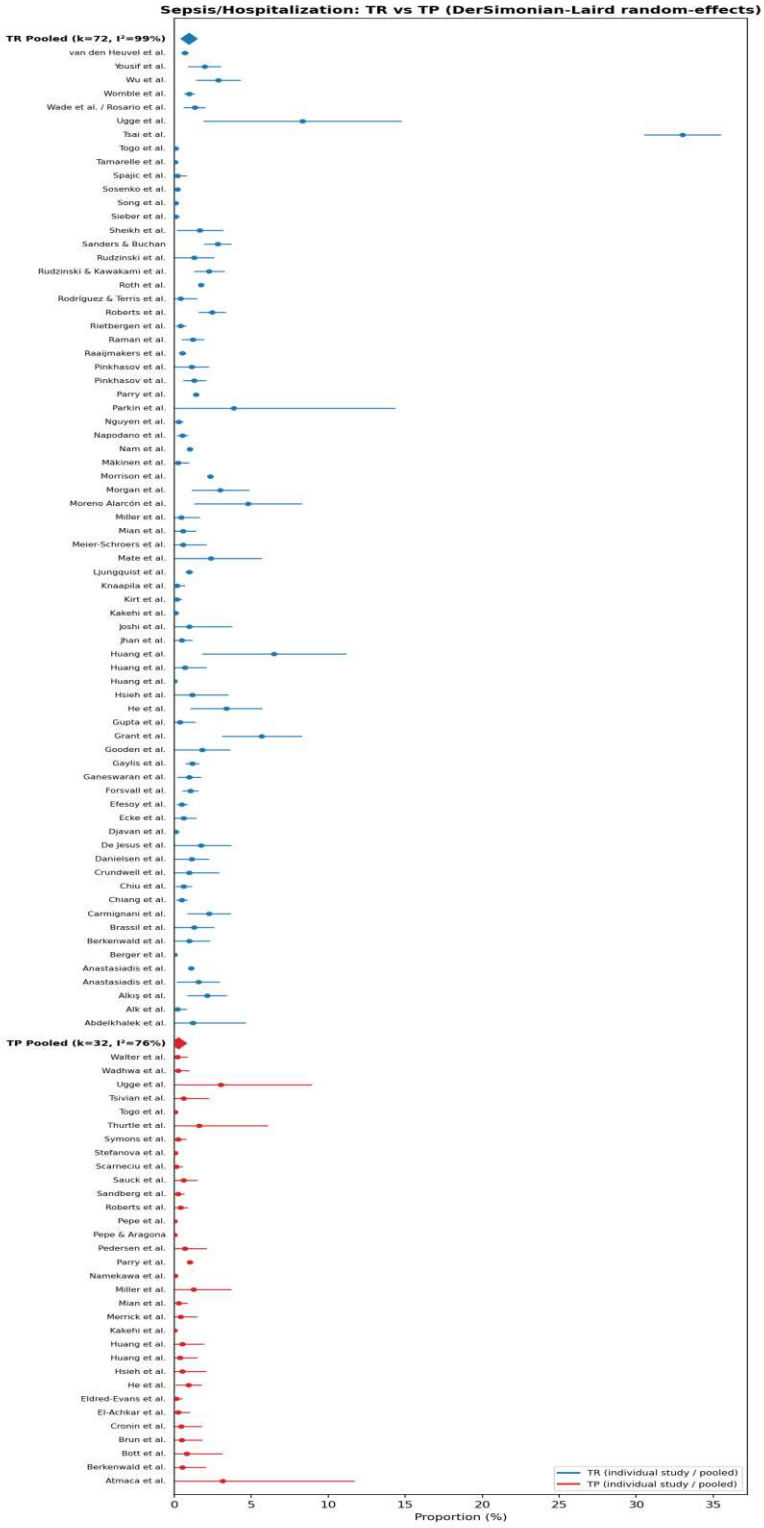
Figure 8. Geographic distribution of TP (trans-perineal) studies by country (k=22 TP-only + 33 combined-arm studies; 27 countries).



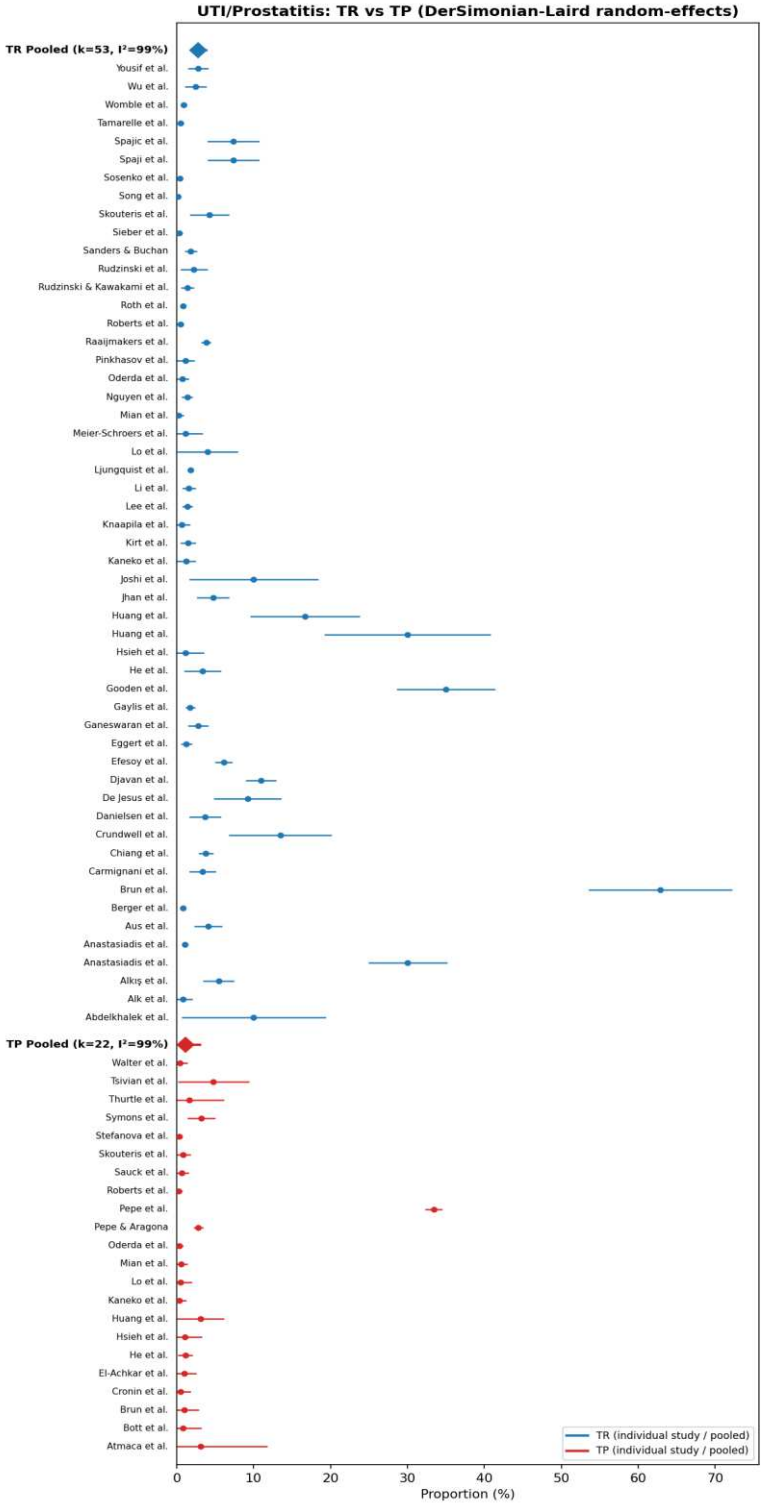
Supplementary Figure S1. Infection: TR vs TP forest plot (DerSimonian-Laird random-effects).


Infection: TR vs TP (DerSimonian-Laird random-effects)
TR Pooled (k=77, I²=99%)
van den Heuvel et al.
Yousif et al.
Wu et al.
Womble et al.
Wade et al. / Rosario et al.
Utsumi et al.
Ugge et al.
Tsai et al.
Togo et al.
Tamarelle et al.
Spajic et al.
Spaji et al.
Sosenko et al.
Song et al.
Skouteris et al.
Silecchia et al.
Sieber et al.
Sheikh et al.
Santos Arrontes et al.
Sanders & Buchan
Rudzinski et al.
Rudzinski & Kawakami et al.
Roth et al.
Rodríguez & Terris et al.
Roberts et al.
Rietbergen et al.
Raman et al.
Raaijmakers et al.
Pinkhasov et al.
Parkin et al.
Nguyen et al.
Napodano et al.
Mäkinen et al.
Morrison et al.
Moreno Alarcón et al.
Mian et al.
Meier-Schroers et al.
Mate et al.
Lo et al.
Ljungquist et al.
Li et al.
Knaapila et al.
Kirt et al.
Kalalahti et al.
Kakehi et al.
Joshi et al.
Jhan et al.
Huang et al.
Huang et al.
Gupta et al.
Grant et al.
Gooden et al.
Gaylis et al.
Ganeswaran et al.
Forsvall et al.
Eggert et al.
Efesoy et al.
Ecke et al.
Djavan et al.
De Jesus et al.
Danielsen et al.
Crundwell et al.
Chiu Y.P. et al.
Chiu P.K. et al.
Chiang et al.
Carnignani et al.
Buller et al.
Brassil et al.
Bissada et al.
Berger et al.
Bazinet et al.
Aus et al.
Anastasiadis et al.
Anastasiadis et al.
Alkış et al.
Alk et al.
Abdelkhalek et al.
TP Pooled (k=27, I²=85%)
Walter et al.
Wadhwa et al.
Utsumi et al.
Ugge et al.
Toivian et al.
Togo et al.
Thurtle et al.
Symons et al.
Stefanova et al.
Skouteris et al.
Scarneciu et al.
Sauck et al.
Sandberg et al.
Roberts et al.
Pepe & Aragona
Pedersen et al.
Namekawa et al.
Mian et al.
Lo et al.
Kakehi et al.
Huang et al.
Eldred-Evans et al.
Cronin et al.
Buller et al.
Brun et al.
Bott et al.
Atmaca et al.
TR (individual study / pooled)
TP (individual study / pooled)
0
5
10
15
20
25
30
35
40
Proportion (%)

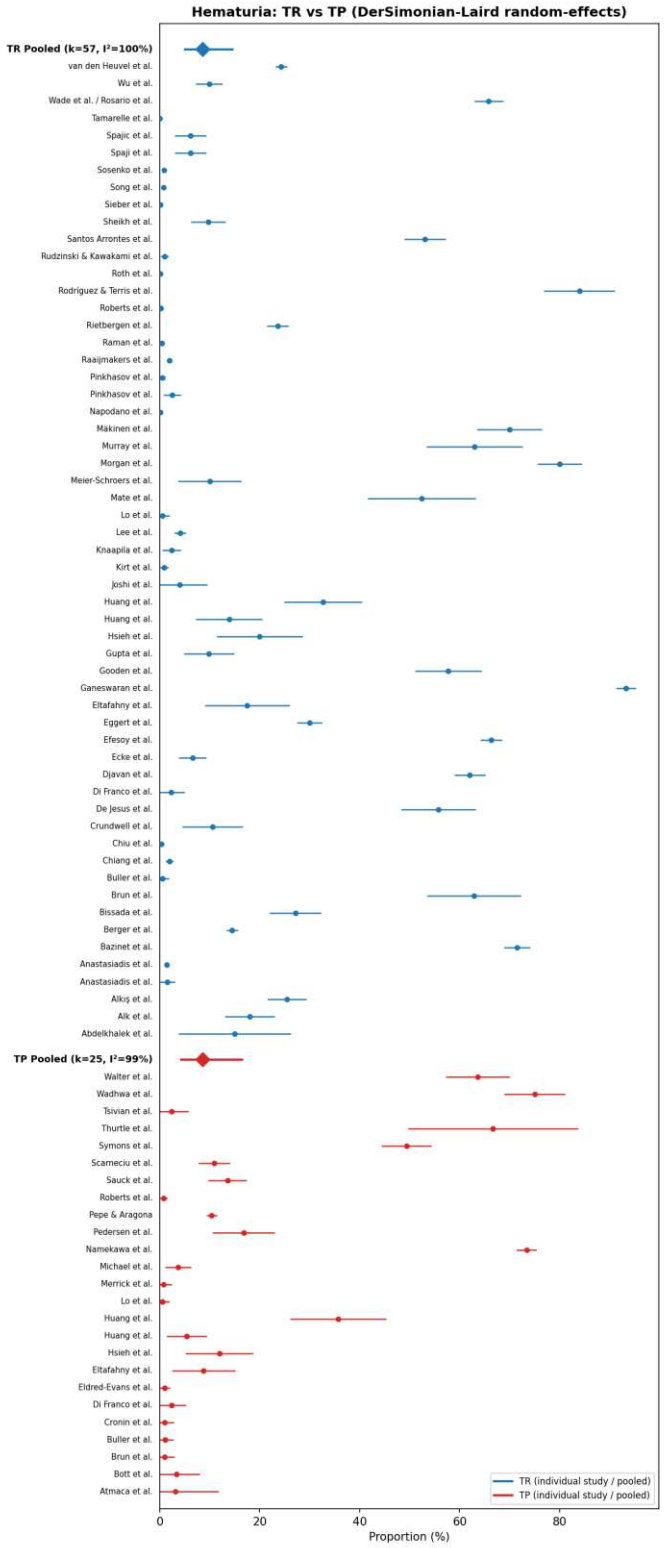
Supplementary Figure S2. Sepsis/Hospitalization: TR vs TP forest plot (DerSimonian-Laird random-effects).


Sepsis/Hospitalization: TR vs TP (DerSimonian-Laird random-effects)
TR Pooled (k=72, I²=99%)
van den Heuvel et al.
Yousif et al.
Wu et al.
Womble et al.
Wade et al. / Rosario et al.
Ugge et al.
Tsai et al.
Togo et al.
Tamarelle et al.
Spajic et al.
Sosenko et al.
Song et al.
Sieber et al.
Sheikh et al.
Sanders & Buchan
Rudzinski et al.
Rudzinski & Kawakami et al.
Roth et al.
Rodríguez & Terris et al.
Roberts et al.
Rietbergen et al.
Raman et al.
Raaijmakers et al.
Pinkhasov et al.
Pinkhasov et al.
Parry et al.
Parkin et al.
Nguyen et al.
Napodano et al.
Nam et al.
Mäkinen et al.
Morrison et al.
Morgan et al.
Moreno Alarcón et al.
Miller et al.
Mian et al.
Meier-Schroers et al.
Mate et al.
Ljungquist et al.
Knaapila et al.
Kirt et al.
Kakehi et al.
Joshi et al.
Jhan et al.
Huang et al.
Huang et al.
Huang et al.
Hsieh et al.
He et al.
Gupta et al.
Grant et al.
Gooden et al.
Gaylis et al.
Ganeswaran et al.
Forsvall et al.
Efesoy et al.
Ecke et al.
Djavan et al.
De Jesus et al.
Danielsen et al.
Crundwell et al.
Chiu et al.
Chiang et al.
Carmignani et al.
Brassil et al.
Berkenwald et al.
Berger et al.
Anastasiadis et al.
Anastasiadis et al.
Alkış et al.
Alk et al.
Abdelkhalek et al.
TP Pooled (k=32, I²=76%)
Walter et al.
Wadhwa et al.
Ugge et al.
Tsivian et al.
Togo et al.
Thurtle et al.
Symons et al.
Stefanova et al.
Scarneciu et al.
Sauck et al.
Sandberg et al.
Roberts et al.
Pepe et al.
Pepe & Aragona
Pedersen et al.
Parry et al.
Namekawa et al.
Miller et al.
Mian et al.
Merrick et al.
Kakehi et al.
Huang et al.
Huang et al.
Hsieh et al.
He et al.
Eldred-Evans et al.
El-Achkar et al.
Cronin et al.
Brun et al.
Bott et al.
Berkenwald et al.
Atmaca et al.
TR (individual study / pooled)
TP (individual study / pooled)
0
5
10
15
20
25
30
35
Proportion (%)

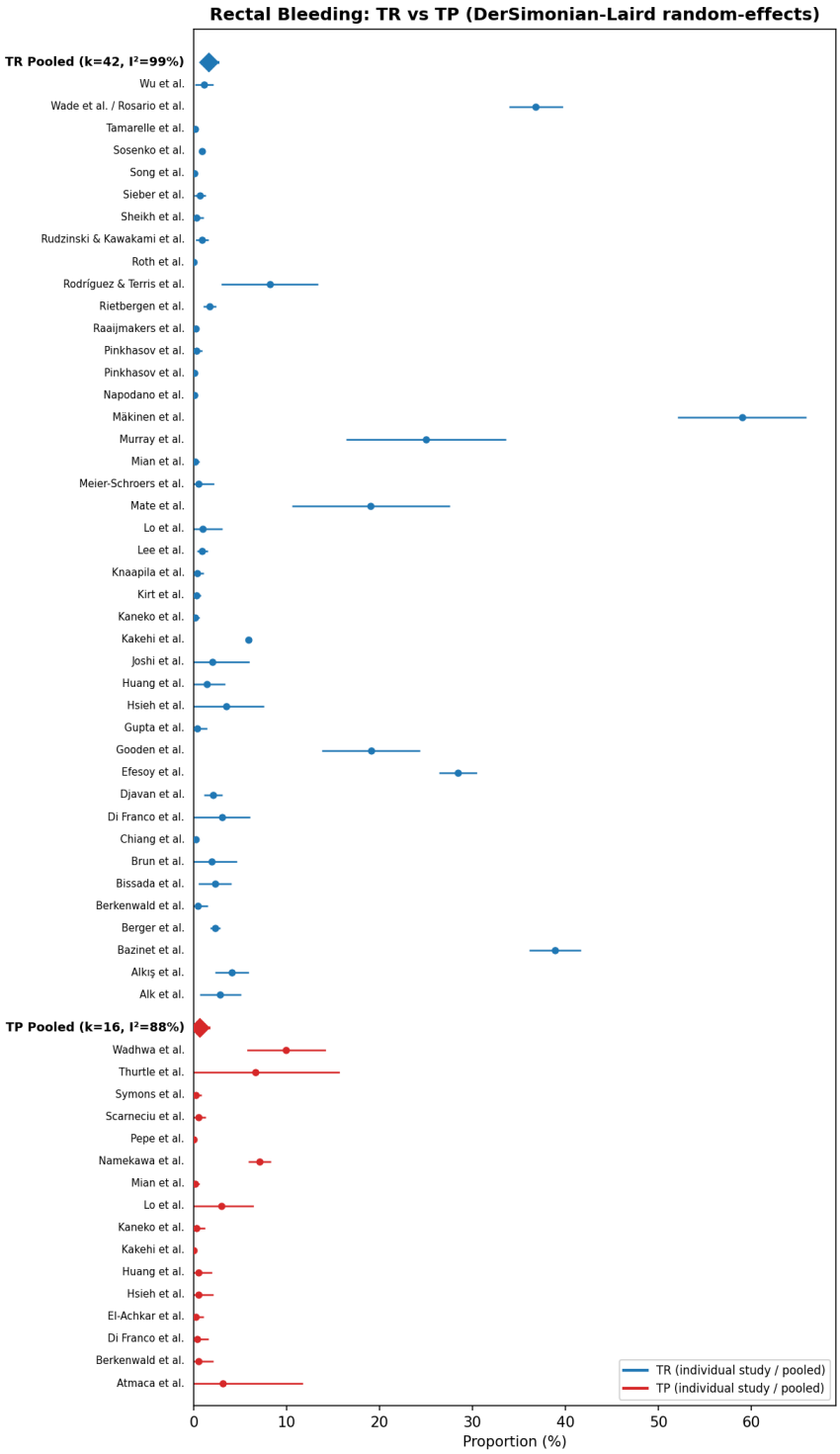
Supplementary Figure S3. UTI/Prostatitis: TR vs TP forest plot (DerSimonian-Laird random-effects).



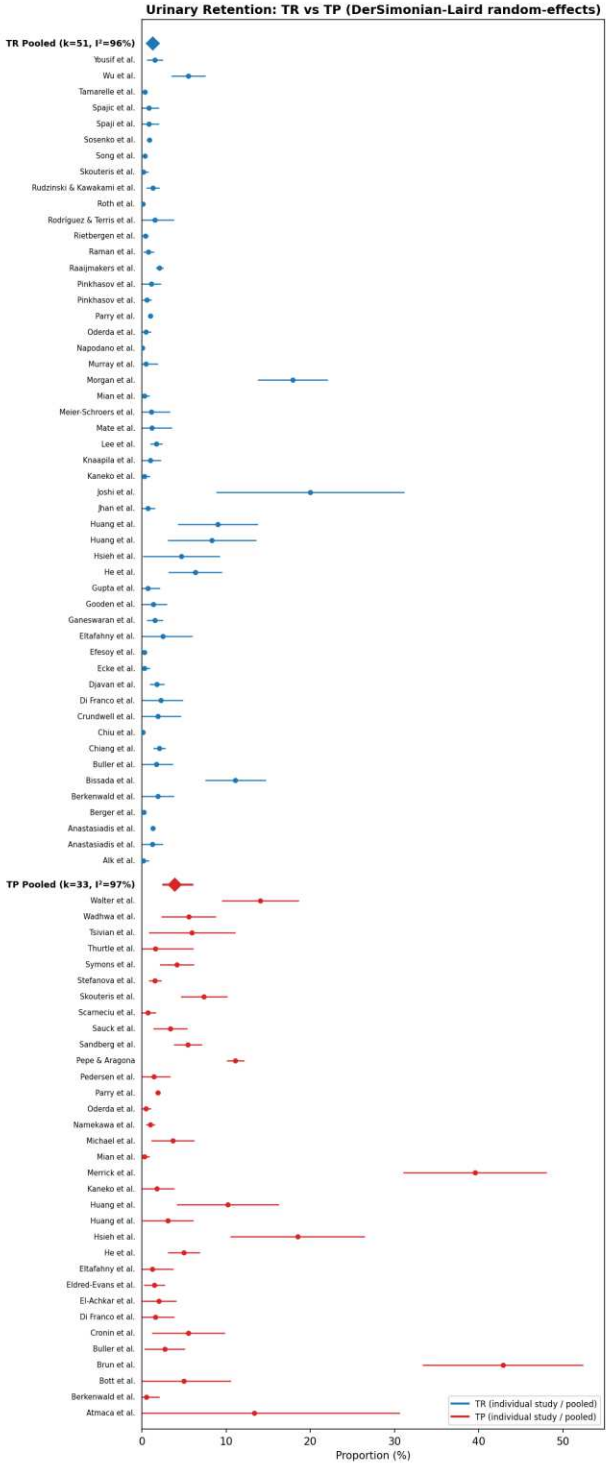
Supplementary Figure S4. Hematuria: TR vs TP forest plot (DerSimonian-Laird random-effects).


Hematuria: TR vs TP (DerSimonian-Laird random-effects)
TR Pooled (k=57, I²=100%)
van den Heuvel et al.
Wu et al.
Wade et al. / Rosario et al.
Tamarelle et al.
Spajic et al.
Spaji et al.
Sosenko et al.
Song et al.
Sieber et al.
Sheikh et al.
Santos Arrontes et al.
Rudzinski & Kawakami et al.
Roth et al.
Rodríguez & Terris et al.
Roberts et al.
Rietbergen et al.
Raman et al.
Raaijmakers et al.
Pinkhasov et al.
Pinkhasov et al.
Napodano et al.
Mäkinen et al.
Murray et al.
Morgan et al.
Meier-Schroers et al.
Mate et al.
Lo et al.
Lee et al.
Knaapila et al.
Kirt et al.
Joshi et al.
Huang et al.
Huang et al.
Hsieh et al.
Gupta et al.
Gooden et al.
Ganeswaran et al.
Eltafahny et al.
Eggert et al.
Efesoy et al.
Ecke et al.
Djavan et al.
Di Franco et al.
De Jesus et al.
Crundwell et al.
Chiu et al.
Chiang et al.
Buller et al.
Brun et al.
Bissada et al.
Berger et al.
Bazinet et al.
Anastasiadis et al.
Anastasiadis et al.
Alkış et al.
Alk et al.
Abdelkhalek et al.
TP Pooled (k=25, I²=99%)
Walter et al.
Wadhwa et al.
Tsivian et al.
Thurtle et al.
Symons et al.
Scarneciu et al.
Sauck et al.
Roberts et al.
Pepe & Aragona
Pedersen et al.
Namekawa et al.
Michael et al.
Merrick et al.
Lo et al.
Huang et al.
Huang et al.
Hsieh et al.
Eltafahny et al.
Eldred-Evans et al.
Di Franco et al.
Cronin et al.
Buller et al.
Brun et al.
Bott et al.
Atmaca et al.
TR (individual study / pooled)
TP (individual study / pooled)
0
20
40
60
80
Proportion (%)

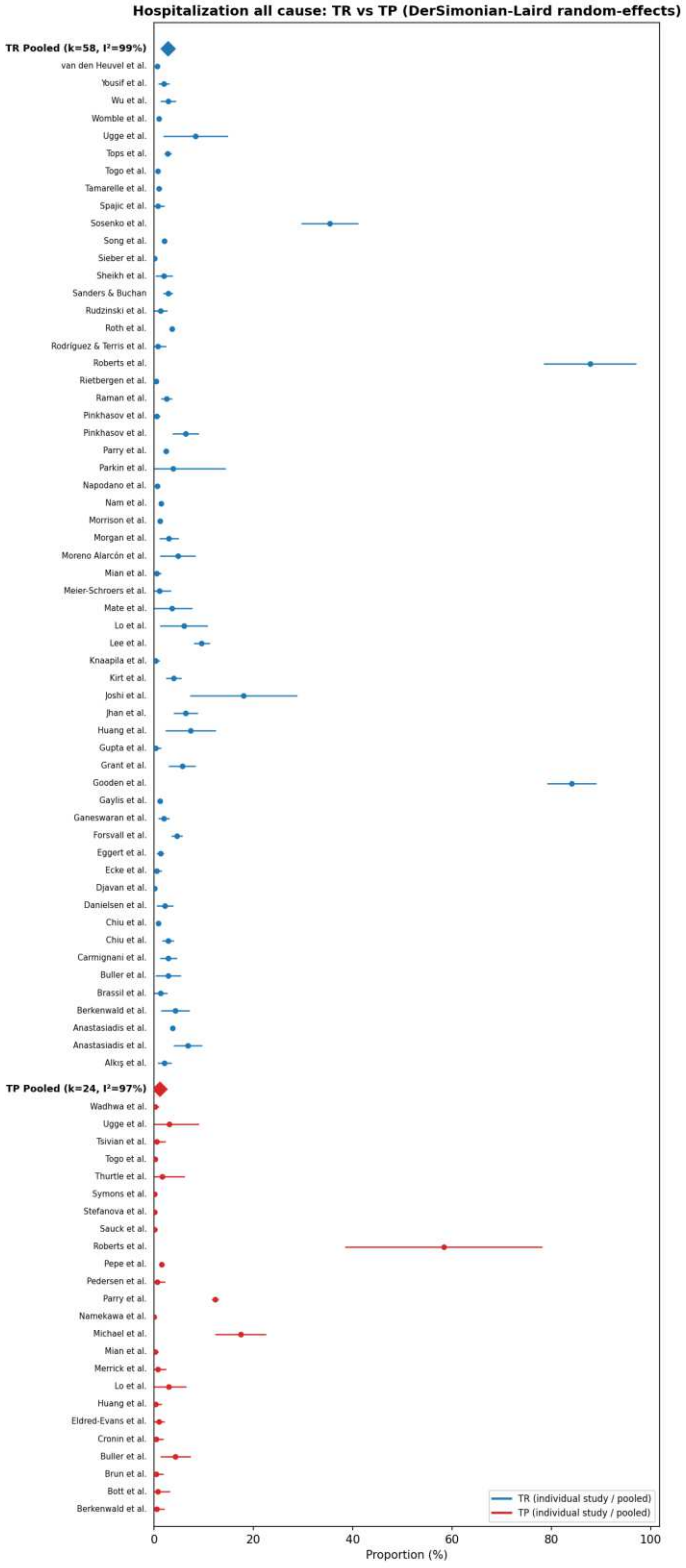
Supplementary Figure S5. Rectal Bleeding: TR vs TP forest plot (DerSimonian-Laird random-effects).


Rectal Bleeding: TR vs TP (DerSimonian-Laird random-effects)
TR Pooled (k=42, I²=99%)
Wu et al.
Wade et al. / Rosario et al.
Tamarelle et al.
Sosenko et al.
Song et al.
Sieber et al.
Sheikh et al.
Rudzinski & Kawakami et al.
Roth et al.
Rodríguez & Terris et al.
Rietbergen et al.
Raaijmakers et al.
Pinkhasov et al.
Pinkhasov et al.
Napodano et al.
Mäkinen et al.
Murray et al.
Mian et al.
Meier-Schroers et al.
Mate et al.
Lo et al.
Lee et al.
Knaapila et al.
Kirt et al.
Kaneko et al.
Kakehi et al.
Joshi et al.
Huang et al.
Hsieh et al.
Gupta et al.
Gooden et al.
Efesoy et al.
Djavan et al.
Di Franco et al.
Chiang et al.
Brun et al.
Bissada et al.
Berkenwald et al.
Berger et al.
Bazinet et al.
Alkış et al.
Alk et al.
TP Pooled (k=16, I²=88%)
Wadhwa et al.
Thurtle et al.
Symons et al.
Scarneciu et al.
Pepe et al.
Namekawa et al.
Mian et al.
Lo et al.
Kaneko et al.
Kakehi et al.
Huang et al.
Hsieh et al.
El-Achkar et al.
Di Franco et al.
Berkenwald et al.
Atmaca et al.
TR (individual study / pooled)
TP (individual study / pooled)
0
10
20
30
40
50
60
Proportion (%)

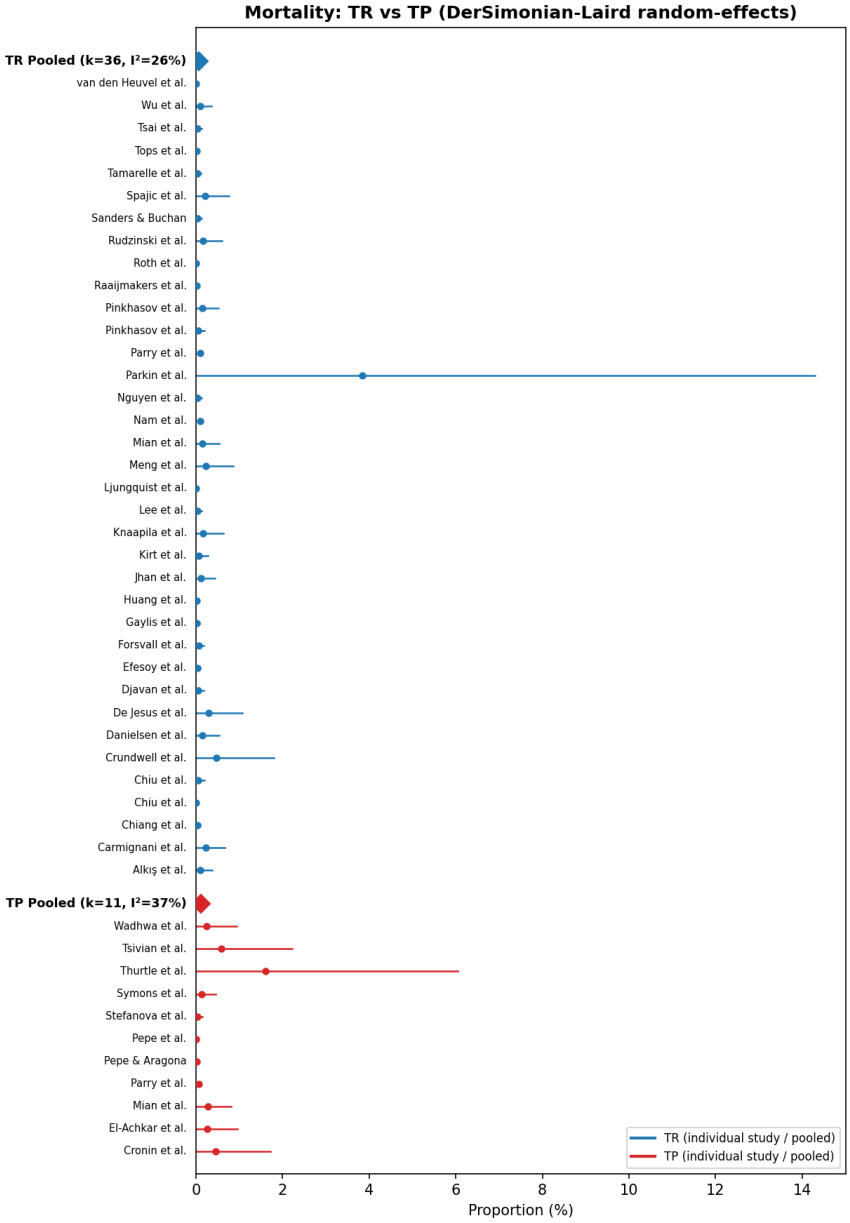
Supplementary Figure S6. Urinary Retention: TR vs TP forest plot (DerSimonian-Laird random-effects).


Urinary Retention: TR vs TP (DerSimonian-Laird random-effects)
TR Pooled (k=51, I²=96%)
Yousif et al.
Wu et al.
Tamarelle et al.
Spajic et al.
Spaji et al.
Sosenko et al.
Song et al.
Skouteris et al.
Rudzinski & Kawakami et al.
Roth et al.
Rodríguez & Terris et al.
Rietbergen et al.
Raman et al.
Raaijmakers et al.
Pinkhasov et al.
Pinkhasov et al.
Parry et al.
Oderda et al.
Napodano et al.
Murray et al.
Morgan et al.
Mian et al.
Meier-Schroers et al.
Mate et al.
Lee et al.
Knaapila et al.
Kaneko et al.
Joshi et al.
Jhan et al.
Huang et al.
Huang et al.
Hsieh et al.
He et al.
Gupta et al.
Gooden et al.
Ganeswaran et al.
Eltafahny et al.
Efesoy et al.
Ecke et al.
Djavan et al.
Di Franco et al.
Crundwell et al.
Chiu et al.
Chiang et al.
Buller et al.
Bissada et al.
Berkenwald et al.
Berger et al.
Anastasiadis et al.
Anastasiadis et al.
Alk et al.
TP Pooled (k=33, I²=97%)
Walter et al.
Wadhwa et al.
Tsivian et al.
Thurtle et al.
Symons et al.
Stefanova et al.
Skouteris et al.
Scarneciu et al.
Sauck et al.
Sandberg et al.
Pepe & Aragona
Pedersen et al.
Parry et al.
Oderda et al.
Namekawa et al.
Michael et al.
Mian et al.
Merrick et al.
Kaneko et al.
Huang et al.
Huang et al.
Hsieh et al.
He et al.
Eltafahny et al.
Eldred-Evans et al.
El-Achkar et al.
Di Franco et al.
Cronin et al.
Buller et al.
Brun et al.
Bott et al.
Berkenwald et al.
Atmaca et al.
TR (individual study / pooled)
TP (individual study / pooled)
0
10
20
30
40
50
Proportion (%)

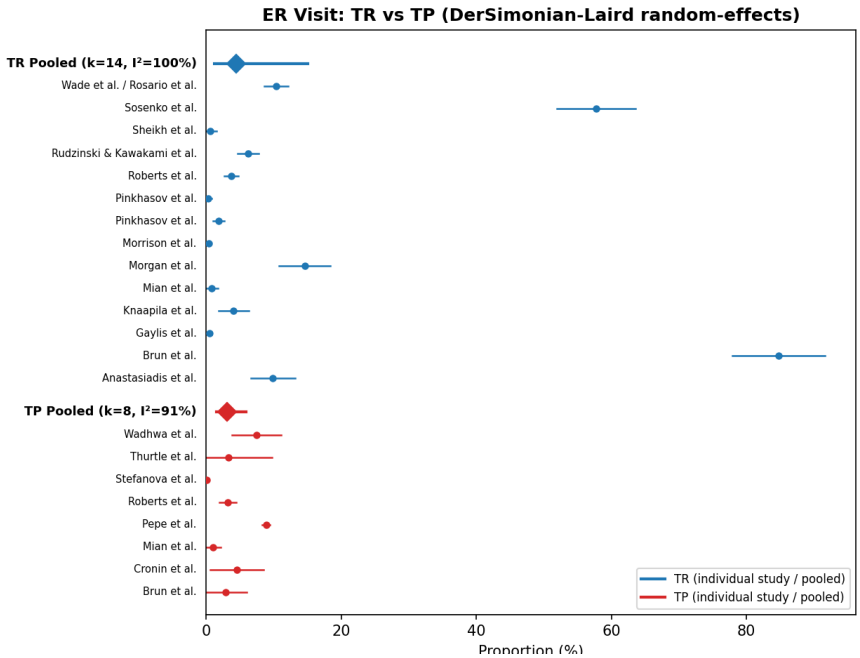
Supplementary Figure S7. Hospitalization (all-cause): TR vs TP forest plot (DerSimonian-Laird random-effects).


Hospitalization all cause: TR vs TP (DerSimonian-Laird random-effects)
TR Pooled (k=58, I²=99%)
van den Heuvel et al.
Yousif et al.
Wu et al.
Womble et al.
Ugge et al.
Tops et al.
Togo et al.
Tamarelle et al.
Spajic et al.
Sosenko et al.
Song et al.
Sieber et al.
Sheikh et al.
Sanders & Buchan
Rudzinski et al.
Roth et al.
Rodriguez & Terris et al.
Roberts et al.
Rietbergen et al.
Raman et al.
Pinkhasov et al.
Pinkhasov et al.
Parry et al.
Parkin et al.
Napodano et al.
Nam et al.
Morrison et al.
Morgan et al.
Moreno Alarcón et al.
Mian et al.
Meier-Schroers et al.
Mate et al.
Lo et al.
Lee et al.
Knaapila et al.
Kirt et al.
Joshi et al.
Jhan et al.
Huang et al.
Gupta et al.
Grant et al.
Gooden et al.
Gaylis et al.
Ganeswaran et al.
Forsvall et al.
Eggert et al.
Ecke et al.
Djavan et al.
Danielsen et al.
Chiu et al.
Chiu et al.
Carmignani et al.
Buller et al.
Brassil et al.
Berkenwald et al.
Anastasiadis et al.
Anastasiadis et al.
Alkış et al.
TP Pooled (k=24, I²=97%)
Wadhwa et al.
Ugge et al.
Tsivian et al.
Togo et al.
Thurtle et al.
Symons et al.
Stefanova et al.
Sauck et al.
Roberts et al.
Pepe et al.
Pedersen et al.
Parry et al.
Namekawa et al.
Michael et al.
Mian et al.
Merrick et al.
Lo et al.
Huang et al.
Eldred-Evans et al.
Cronin et al.
Buller et al.
Brun et al.
Bott et al.
Berkenwald et al.
TR (individual study / pooled)
TP (individual study / pooled)
0
20
40
60
80
100
Proportion (%)

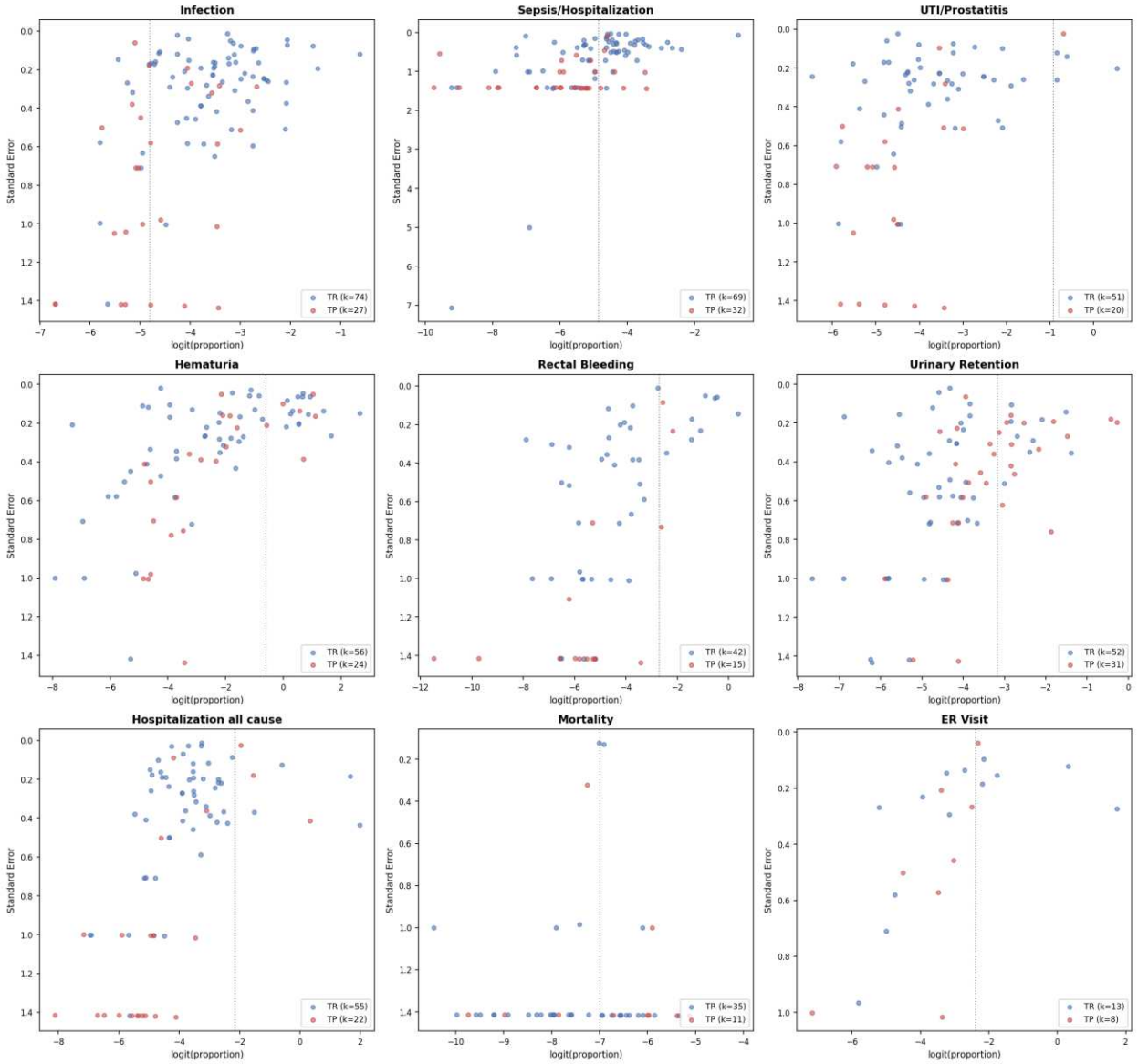
Supplementary Figure S8. Mortality: TR vs TP forest plot (DerSimonian-Laird random-effects).



Supplementary Figure S9. ER Visit: TR vs TP forest plot (DerSimonian-Laird random-effects).



Supplementary Figure S10. Funnel plots (logit-proportion vs. standard error) for all nine outcomes, TR and TP arms, with Egger's regression test for funnel asymmetry.



Egger's regression test intercepts and p-values for each outcome-arm combination are summarized in the Results section above. Given the high heterogeneity (I^2 generally >85%) observed across outcomes, funnel asymmetry should be interpreted as a limitation of the evidence base rather than definitive evidence of publication bias.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFunnelPlotsTRvsTP.png
- SupplementalReferences.docx