OPEN

The Role of the Urobiome in Kidney Transplantation: A Systematic Review

Alberto Costa Silva, MD,[1,2] Teresa Pina-Vaz, MD,[1,2] Afonso Morgado, MD,[1,2] Carlos Martins-Silva, PhD,[1,2] Tiago Antunes-Lopes, PhD,[1,2] and João Alturas Silva, PhD[1,2]

Background. The urinary microbiome, also known as the urobiome, was traditionally considered sterile. However, emerging evidence suggests its presence in the urinary tract. Urobiome dysbiosis has been associated with various urologic conditions, making it a topic of interest also in kidney transplantation. This systematic review examines the evidence of urobiome changes in kidney transplant recipients (KTRs). **Methods.** Systematic literature searches in the PubMed and SCOPUS databases. **Results.** Of the 770 articles identified, 8 met the inclusion criteria. The urobiome showed reduced diversity in KTRs compared with healthy controls and patients on dialysis. Proteobacteria enrichment was associated with graft stability or spontaneous tolerance in KTRs without immunological events. Kidney interstitial fibrosis and tubular atrophy were associated with changes in resident urinary microbes and increased pathogenic bacteria. Additionally, KTRs with chronic allograft dysfunction had a higher prevalence of *Corynebacterium*. **Conclusions.** The review highlights the importance of studying the urobiome in KTRs and its potential impact on transplant outcomes. The field remains largely unexplored, and further research is needed to establish consistent study designs and objectives. Future studies could lead to biomarker discovery, personalized therapies, and improved outcomes and graft survival in KTRs.

(*Transplantation Direct* 2024;10: e1643; doi: 10.1097/TXD.0000000000001643.)

The term "microbiome" encompasses the entire collection of microbes within a specific anatomical niche, including commensal, symbiotic, and pathogenic microbes.[1,2] Since the Human Microbiome Project began, significant advancements have been made in understanding the microbiome. Because of technical limitations, our comprehension of the microbiome was primarily limited to bacteria.[3]

In the past, the urinary microbiome, or urobiome, received little attention because of the traditional belief that the urinary tract was a sterile environment. However, contrary to that dogma, recent research has revealed the presence of a microbiome inhabiting the urinary tract.[3,4] Recent research has identified a distinct urobiome in healthy individuals and established that its presence is not only because of fecal, urethral, or skin contaminations.[1,5–7] Urobiome imbalances, or dysbiosis, have been associated with various urologic conditions, including neurogenic bladder dysfunction, urgency urinary incontinence, and lower urinary tract symptoms.[8–16]

The first kidney transplant (KT) was performed by Joseph Murray in Boston in 1954, heralding the dawn of a new medical era.[17,18] Over time, KT has been consistently established as the most effective therapeutic method for end-stage renal disease.[19]

The relationships between other human microbiomes, particularly in the gut, have been explored in the post-KT setting.[20–22] There has been a recent interest in publications on the urobiome's significance in KT recipients (KTRs).[22–29] This systematic review aims to analyze the existing literature about urobiome in KTRs.

MATERIALS AND METHODS

Evidence Acquisition

This systematic review was performed according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement recommendations.[30] the study protocol was registered in international prospective register of systematic reviews (CRD42023458389). Its search strategy used a combination of the following terms: "(microbiome OR microbiota) AND (kidney transplant* OR renal transplant*)." Its search range was between January 2003 and July 2023 in the PubMed and SCOPUS

Received 12 February 2024. Revision received.

Accepted 29 February 2024.

[1] *Urology Department, University Hospital Center of São João, Porto, Portugal.*

[2] *Faculty of Medicine, University of Porto, Porto, Portugal.*

Correspondence: Alberto Costa Silva, MD, Urology Department, University Hospital Center of São João, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal. (albertocsilva8@gmail.com).

The authors declare no funding or conflicts of interest.

A.C.S., T.P.-V., A.M., C.M.-S., T.A.-L., and J.A.S. participated in research design, writing of the article, performance of the research, and data analysis.

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantationdirect.com).

ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001643

databases. All series written in English, retrospective or prospective, comparative or noncomparative, were included in the selection process. Articles with no full text available or not written in English were excluded. All retrieved articles were first reviewed by title and abstract, identifying 816. Two review team members (A.C.S. and T.P.-V.), assisted by collaborators, screened the retrieved articles' titles and abstracts. Reasons for exclusions were noted, and the selected articles' relevance was confirmed after the data extraction process. Disagreements were resolved by consultation with a third coauthor (J.A.-S.). The entire review team cross-checked the reliability and completeness of the extracted data. Full-text analysis was performed, and articles were selected based on their relevance to the theme and quality. Of the 770 articles analyzed, 15 were excluded because of language, and 9 because of the unavailability of their full text. The study process is summarized in Figure 1.

Risk of Bias

The risk of bias was assessed independently by 2 review team members (A.C.S. and T.P.-V.) using the Quality in Prognosis Studies (QUIPS) tool[31] (**Supplemental material, SDC**, http://links.lww.com/TXD/A656). Two authors extracted the study characteristics (A.C.S. and T.P.-V), and any disagreements were resolved by discussion with a third author (J.A.-S.).

RESULTS

The identified studies were divided into 3 categories based on their content: characterization of the urobiome in KTRs after KT, urobiome and immunological tolerance in KTRs after KT and the role of the urobiome in kidney lesions in KTRs after KT. Each article is summarized in Table 1.

Characterization of the Urobiome in KTRs After KT

Rani et al[28] compared the urobiomes of 21 KTRs with those of 8 healthy controls using shotgun metagenomics DNA from urogenital samples 12 mo after KT. They found that KTRs had lower microbial diversity and Actinobacteria but higher Proteobacteria and Firmicutes, including potentially pathogenic species (*Escherichia coli* and *Enterococcus faecalis*), than healthy controls.

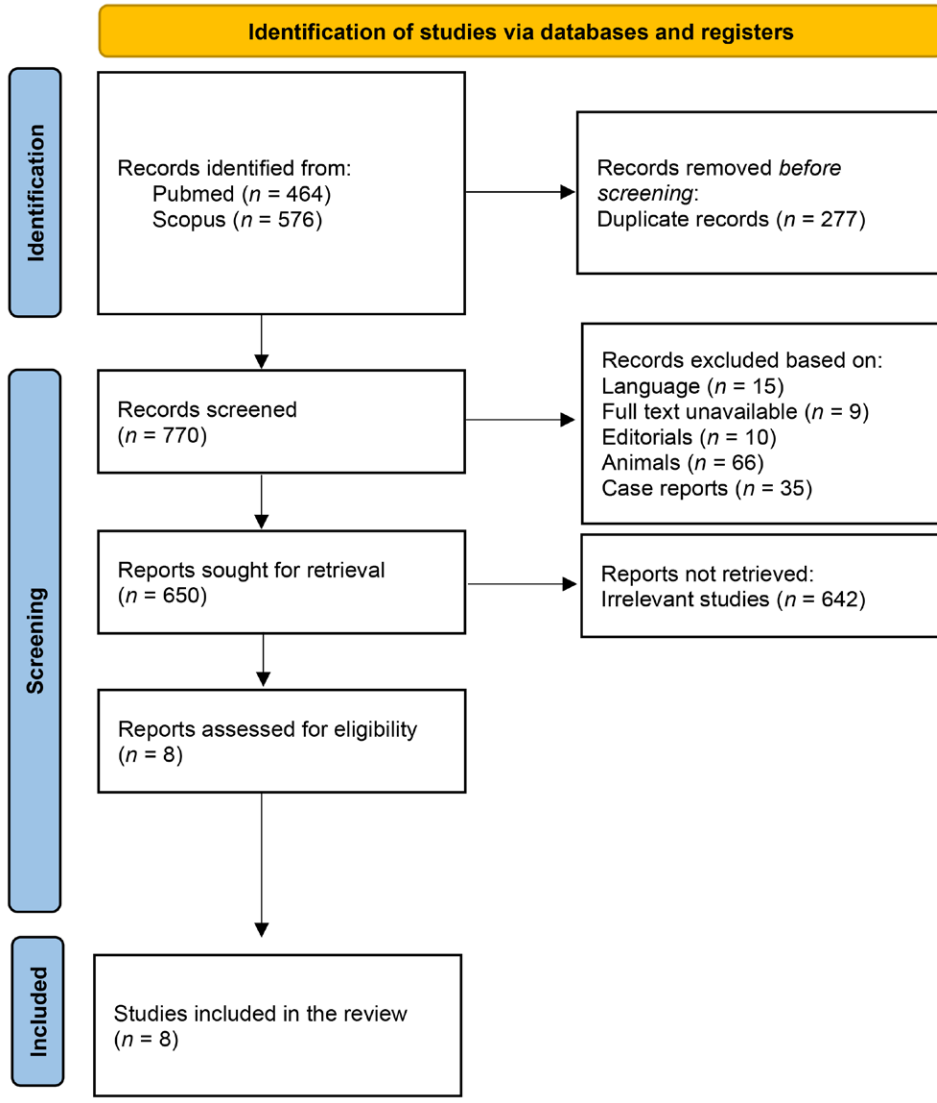

FIGURE 1. PRISMA flowchart.

TABLE 1.

Characteristics of the included studies

Study	Country	Study type	Sample and method	Sample size	IMS and ABT	Aim	Relevant microbiota
Jaworska et al[23]	Poland	Prospective	UG 16S rRNA gene sequencing (V3–V4)	50 KTR vs 50 patients on dialysis vs 50 healthy controls Time after KT: unspecified	IMS: unspecified ABT: no use 3 mo prior	Compare urobiomes between KTRs, patients on dialysis, and healthy controls	KTRs had higher prevalence of genera *Sphingomonas*, *Ochrobactrum*, and *Actinocorallia* than the healthy controls Patients on dialysis had higher prevalence of genera *Moryella*, *Shuttleworthia*, *Finegoldia*, *Gallicola*, and *Propionigenium* than KTRs KTRs had higher prevalence of genera *Ochrobactrum* and *Sphingomonas* than patients on dialysis
Gerges-Knafl et al[24]	Austria	Prospective	UG 16S rRNA gene sequencing (V3–V4)	21 KTRs with AKI vs 9 nKTRs with AKI Time after KT: 5 mo	IMS: TAC + MMF + corticosteroids ABT: 14 in KT vs 2 in nKT	Compare urobiomes between KTRs with AKI and nKTRs with AKI	KTRs with AKI had higher prevalence of *Gemella*, *Pseudomonas*, *Arthrobacter* and *Rothia* (genera) *and* Flavobacteriaceae and Phyllobacteriaceae (family) nKTRs with AKI had higher prevalence of *Facklamia*, *Faecalibacterium*, *Alistipes*, *Collinsella*, *Ruminococcus*, *Fusobacterium*, *Actinotignum*, *Mobiluncus*, *Peptoniphilus*, *Barnesiella*, *Clostridium*, *Coprococcus*, *Parabacteroides*, *Propionimicrobium* (genera), Veillonellaceae, Ruminococcaceae (family), Bacteroidetes (class), Firmicutes (phylum)
Colas et al[25]	France	Prospective	UG 16S rRNA gene sequencing	51 KTRs with stable IMS status vs 19 KTRs with MIS vs16 KTRs spontaneously tolerant Time after KT: 90 mo	Stable: CNI + AM ± corticosteroids MIS: AM or corticosteroids Tolerant: no IMS ATB: unspecified; 7 of the Stable used it at the time of the sample	Urobiome's effects on IMS status after KT	KTRs with spontaneous tolerance had greater urobiome diversity and elevated Proteobacteria phylum that remained stable for a long time. KTRs on CNI or mTOR inhibitors had decreased *Lactobacillales* order KTRs on corticosteroids had increased order *Clostridiales* order
Burnham et al[26]	USA	Prospective	UG and urinary bladder Shotgun DNA sequencing- cell-free DNA	85 KTRs Time after KT: first 4 d	IMS and ABT: unspecified	Role of cell-free DNA in KTRs	KTRs had lower urobiome diversity Urobiome diversity was lower in KTR bladder catheter than UG within the first four days after KT
Wu et al[27]	USA	Prospective	UG 16S rRNA gene sequencing (V4, ITS1, and ITS2)	32 KTRs with CAD vs 35 KTRs without CAD Time after KT: 3 mo	IMS: TAC or CsA ATB: not used	Evaluate urobiome and CAD development in KTRs	KTRs with CAD had a higher prevalence of *Corynebacterium* genus
Rani et al[28]	USA	Prospective	UG DNA shotgun metagenomics	21 KTRs vs 8 healthy controls Time after KT: 12 mo	IMS: CNI + AM + PRED ATB: KTR on TMP-SMX	KT effects on the urobiome	KTRs had lower urobiome diversity and Actinobacteria and higher Proteobacteria (*Escherichia coli*) and Firmicutes (*Enterococcus faecalis*)
Modena et al[29]	USA	Prospective	UG 16S rRNA gene sequencing (V2–V4 and V6–V9)	25 KTRs with IFTA vs 23 KTRs without IFTA vs 20 healthy controls Time after KT: 1 and 6–8 mo	IMS: TAC + MMF + PRED ATB: unspecified	Evaluate urobiome and IFTA development in KTRs	KTRs with IFTA had lower prevalence of *Lactobacillus* and *Streptococcus* genera and higher prevalence of *Propionibacterium acnes*, *Prevotella disiens*, *Gardnerella vaginalis*, and *Finegoldia magna* genera
Fricke et al[22]	USA	Prospective	UG 16S rRNA gene sequencing (V1, V2, and V3)	60 KTRs evaluated before and at 1 and 6 mo after KT	IMS: unspecified ATB: TMP-SMX	Compare urobiomes before and after KT	Urobiomes had lower diversity and prevalence of Proteobacteria, Synergistetes, and Fusobacteria phyla but a higher prevalence of Firmicutes 1 mo after KT. The higher prevalence of Firmicutes was maintained 6 mo after KT

ABT, antibiotic therapy; ALM, antimetabolite; AKI, acute kidney injury; CAD, chronic allograft dysfunction; CsA, cyclosporin A; CNI, calcineurin inhibitor; IFTA, interstitial fibrosis and tubular atrophy; IMS, immunosuppression therapy; MIS, minimal immunosuppression; KTRs, kidney transplant recipients; MMF, mycophenolate mofetil; nKTR, nonkidney transplant recipient; PRED, prednisolone; TAC, tacrolimus; TMP-SMX, trimethoprim-sulfamethoxazole; UG, urogenital sample.

Burnham et al[26] examined the urobiomes of 82 KTRs using shotgun DNA sequencing obtaining cell-free DNA from urogenital and urinary bladder samples. They found that urobiome abundance and diversity were influenced by the sex of the KTR but not the donor. Moreover, they found that urobiome diversity was lower in the Foley catheter than urogenital samples from KTRs within the first 4 d after KT.

Fricke et al[22] examined 60 KTRs' urogenital samples using 16S rRNA gene sequencing before and at 1 and 6 mo after KT. They found that urobiome diversity decreased from before to 1 mo after KT. Specifically, Proteobacteria, Synergistetes, and Fusobacteria decreased, whereas Firmicutes increased. The increase in Firmicutes was maintained 6 mo after KT. They found no relationship between urobiome changes and rejection episodes.

Jaworska et al[23] performed 16S rRNA gene sequencing on urogenital samples from 50 KTRs, 50 patients on dialysis, and 50 healthy controls. They found higher prevalence of genera *Mogibacterium*, *Sphingomonas*, and *Ochrobactrum* in KTRs than in controls. Furthermore, they found higher prevalence of genera *Ochrobactrum* and *Sphingomonas* but lower prevalence of *Moryella*, *Shuttleworthia*, *Finegoldia*, *Gallicola*, and *Propionigenium* in KTRs than in patients on dialysis.

Urobiome and Immunological Tolerance in KTRs After KT

Colas et al[25] compared 51 KTRs with stable status (on calcineurin inhibitors, antimetabolites, ± corticosteroids), 19 KTRs with minimal immunosuppression (on antimetabolites or corticosteroids), and 16 KTRs who were spontaneously tolerant (on no immunosuppression) with a median follow-up time of 90 mo using total DNA isolation with 16S rRNA gene sequencing from urogenital samples. The objective was to examine whether urobiome changes after KT were associated with posttransplantation immunosuppressive status. They found reduced urobiome diversity within the first month after KT in all groups. KTRs with spontaneous tolerance had higher microbiome diversity and Proteobacteria that remained stable for a long time. They concluded that Proteobacteria enrichment was associated with graft stability or spontaneous tolerance without immunological events such as acute or chronic rejections. Additionally, they revealed that calcineurin inhibitors were negatively associated with Lactobacillales, whereas corticosteroids were positively correlated with Clostridia, suggesting a 2-way interaction between immunosuppressive drugs and the urobiome.

The Role of the Urobiome in Kidney Lesions in KTRs After KT

Gerges-Knafl et al[24] examined the association between the urobiome and acute kidney injury (AKI) in 21 KTRs (5 mo after KT) and 9 non-KTRs (nKTRs) using 16S rRNA gene sequencing from urogenital samples. They found genera *Flavobacteriaceae*, *Gemella*, *Pseudomonas*, *Arthrobacter*, *Phyllobacteriaceae*, and *Rothia* more prevalent in KTRs with AKI. In contrast, Facklamia, Faecalibacterium, Alistipes, Collinsella, Ruminococcus, Fusobacterium, Actinotignum, Mobiluncus, Peptoniphilus, Barnesiella, Clostridium, Coprococcus, Parabacteroides, Propionimicrobium, Veillonellaceae, Ruminococcaceae, Bacteroidetes, and Firmicutes were more prevalent in nKTRs with AKI. This evidence suggests some bacteria preferentially inhabit the urinary tract of KTRs with AKI but not nKTRs with AKI, and vice versa.[24]

Modena et al[29] compared 25 KTRs who developed interstitial fibrosis and tubular atrophy (IFTA) to 23 KTRs with normal allograft biopsy findings and 20 nKTRs as controls. The KTRs were evaluated using 16S rRNA gene sequencing from urogenital samples 1 and 6–8 mo after KT. Among KTRs with IFTA, they found decreased *Lactobacillus* in women but *Streptococcus* in men, and increased pathogenic bacteria, such as *Propionibacterium acne*, *Prevotella disiens*, *Gardnerella vaginalis*, and *Finegoldia magna*. They concluded that IFTA was associated with a loss in dominant resident urinary microbes and a parallel increase in nonresident pathogenic bacteria.

Wu et al[27] compared the urobiomes of 32 KTRs with chronic allograft dysfunction (CAD) and 35 without CAD using 16S rRNA gene sequencing from urogenital samples. CAD was defined as creatinine levels consistently ≥25% above the 3-mo post-KT baseline. They found that, although urobiome diversity was similar across groups, KTRs with CAD had a higher prevalence of *Corynebacterium* genus.

DISCUSSION

The interplay between bacteria and the urinary environment can contribute to normal physiological processes and predisposition to certain diseases. It seems reasonable that the urobiome and its dysbiosis may be associated with allograft-host dynamics, immunosuppression, and antibiotic therapy after KT. The urobiome shows lower microbial biomass than the in other body regions, such as the gut or mouth, making it challenging to study.[32] This study has focused on describing the urobiome in KTRs and its association with disease mechanisms.

KTRs represent a heterogeneous population who suffer from diverse comorbidities and with frequent healthcare contacts before and after transplantation. A dysregulated urobiome can be present in these individuals even before transplantation, and this condition can potentially worsen posttransplant. The use of antibiotics can lead to microbial imbalance.[33] For example, trimethoprim/sulfamethoxazole is part of standard care following transplantation as prophylaxis for *Pneumocystis* pneumonia[34] and by inhibition of enzymes in the folate metabolic pathway, can also have impact on urinary tract, and it is also used as a prophylaxis against urinary tract infections. Rani et al[28] showed that urobiome in KTRs has the potential to avoid the inhibition by trimethoprim/sulfamethoxazole. Thus, they suggest that prophylactic antibiotics could alter the urinary microbiome following transplantation and select bacterial species. Also, immunosuppressants can selectively stimulate or inhibit growth of bacteria.[35]

Rani et al[28] showed that there may be no effect of different primary diagnoses of chronic kidney disease on microbial composition. In terms of anatomical differences, KTRs are subjected to surgical manipulation, have a shorter distance between kidney pelvis and bladder, and some still have diuresis from native kidneys. All these factors can also have a role in microbiome changes.

Improved genome sequencing analyses have led to the reclassification of numerous bacteria, causing notable changes in their nomenclature. For instance, *Propionibacterium acnes* has been rebranded as *Cutibacterium acnes*. This shift can introduce complexity in data interpretation. Considering the 2021 Consensus To Advance Urobiome Research,[36] expressions such as "midstream urine" and "catheterized urine samples," which appears in the articles, were renamed as "urogenital" and "urinary bladder samples," respectively, in writing this article. The adoption of this terminology is based on the observation that voided samples can contain microbiota from urinary tract and, potentially, genitalia as posturethral contamination.

Culture-based studies are known to have a limited role in understanding the urobiome and metaculturomics, or enhanced culture techniques, surpass conventional methods by allowing the detection of microbes comparable to sequencing techniques.[37] The enhanced culture method called Expanded Quantitative Urine Culture allows the growth of most urinary species, allows for the growth of slow-growing microbes, for the morphological differences between species to develop, and can grow about 70% of all taxa identified by 16S rRNA gene sequencing or shotgun metagenomic sequencing. It also functions as a control for sequencing.[36,38] The studies included in this systematic review used either 16S rRNA gene sequencing or DNA shotgun sequencing of urogenital samples. Although human microbiome profiling often relies on sequencing the hypervariable regions of the 16S rRNA, this approach limits evaluating bacteria at the species level.[39] Adopting the cell-free DNA shotgun sequencing assay developed by Burnham et al[26] is an alternative approach for monitoring KTRs, detecting bacteria and viruses, profiling resistance, and assessing graft injury. The process of gene sequencing, though highly useful, presents its own set of difficulties, such as the uneven lysis of bacterial taxa and universal primer bias.[40] Third-generation sequencing and whole-metagenome shotgun sequencing can be useful tools in this setting. It is possible that not all microbiota share the same level of importance, and the concept of "functionally" or "metabolically" active microbiota could also be relevant in the context of the urobiome.[41]

Fricke et al[22] have presented taxa at the phylum level in their research, which include both pathogens and commensals microorganisms. For example, Firmicutes contain *Lactobacillus species*, which are typically beneficial. However, this same phylum also houses *Staphylococcus aureus*, known for its opportunistic pathogenicity. The report of differences at such a high taxonomic level is indicative of the early publication date and specific findings from early short read next-generation sequencing approaches should be judged with caution.

The reviewed studies suggest a reduced urobiome diversity among KTRs compared with healthy controls or patients on dialysis. KTRs with spontaneous tolerance, considered the holy grail of transplantation, showed an increase in Proteobacteria.[25] However, Proteobacteria in ileal or oral microbiota is associated with pathological states such as acute rejection in small-bowel transplant recipients and infections in kidney or heart recipients.[42,43] Future studies should explore this divergent role of Proteobacteria in transplantation. IFTA or AKI development poses a significant challenge for KTRs, potentially affecting their transplant outcomes.[32,44] Urobiome changes have been described in KTRs with AKI, and urinary dysbiosis has been associated with IFTA.[24,29] KTRs with CAD had a higher prevalence of *Corynebacterium*, a bacterial genus also known for its potential uropathogenic activity in encrusted urinary tract infections.[27,45]

The scarcity of studies and the low sample sizes in each study impose constraints on the conclusions. The studies designs and objectives lacked clear uniformity. Furthermore, high heterogeneity among studies precluded a meta-analysis. Most articles lacked sufficient information to determine whether the donor involved was living, brain-dead, or died from a cardiac event. Although immunosuppression and prophylactic antibiotic regimens are commonly referenced in studies, their effects on the urobiome remain unclear. Research findings were presented at various taxonomic levels, including the phylum and genus levels, thereby complicating the drawing of conclusions.

The emerging but early state of research in urobiome in KT field requires careful consideration when forming conclusions. Despite recent advancements, the field remains largely unexplored, offering great potential for future research. Prospective studies with standardized nomenclature and methodology are needed. The prospects for discovering biomarkers, predicting transplant outcomes, developing therapeutic interventions (eg, tailored immunosuppressive therapies), and implementing personalized approaches based on the urobiome to enhance patient outcomes and long-term graft survival are promising.

REFERENCES

1. Wolfe AJ, Brubaker L. Sterile urine and the presence of bacteria. *Eur Urol*. 2015;68:173–174.
2. Turnbaugh PJ, Ley RE, Hamady M, et al. The human microbiome project: exploring the microbial part of ourselves in a changing world. *Nature*. 2007;449:804–810.
3. Whiteside SA, Razvi H, Dave S, et al. The microbiome of the urinary tract—a role beyond infection. *Nat Rev Urol*. 2015;12:81–90.
4. Wolfe AJ, Toh E, Shibata N, et al. Evidence of uncultivated bacteria in the adult female bladder. *J Clin Microbiol*. 2012;50:1376–1383.
5. Lewis DA, Brown R, Williams J, et al. The human urinary microbiome; bacterial DNA in voided urine of asymptomatic adults. *Front Cell Infect Microbiol*. 2013;4:1–14.
6. Pearce MM, Hilt EE, Rosenfeld AB, et al. The female urinary microbiome: a comparison of women with and without urgency urinary incontinence. *MBio*. 2014;5:1–12.
7. Nelson DE, Dong Q, van der Pol B, et al. Bacterial communities of the coronal sulcus and distal urethra of adolescent males. *PLoS One*. 2012;7:e36298–e36299.
8. Bae S, Chung H. The urobiome and its role in overactive bladder. *Int Neurourol J*. 2022;26:190–200.
9. Bilski K, Dobruch J, Kozikowski M, et al. Urobiome in gender-related diversities of bladder cancer. *Int J Mol Sci* . 2020;21:4488–4413.
10. Shoemaker R, Kim J. Urobiome: an outlook on the metagenome of urological diseases. *Investig Clin Urol*. 2021;62:611–622.
11. Jacobs KM, Price TK, Thomas-White K, et al. Cultivable bacteria in urine of women with interstitial cystitis: (not) what we expected kristin. *Female Pelvic Med Reconstr Surg*. 2021;27:322–327.
12. Joyce C, Halverson T, Gonzalez C, et al. The urobiomes of adult women with various lower urinary tract symptoms status differ: a re-analysis. *Front Cell Infect Microbiol*. 2022;12:1–9.
13. Price TK, Huaiying LIN, Gao X, et al. Bladder bacterial diversity differs in continent and incontinent women: a cross-sectional study. *Am J Obs Gynecol*. 2020;223:729–747.
14. Brubaker L, Putonti C, Dong Q, et al. The human urobiome. *Mamm Genome*. 2021;32:232–238.
15. Bajic P, Van Kuiken ME, Burge BK, et al. Male bladder microbiome relates to lower urinary tract symptoms. *Eur Urol Focus*. 2020;6:376–382.

16. Antunes-Lopes T, Vale L, Coelho AM, et al; EAU Young Academic Urologists (YAU) Functional Urology Working Group. The role of urinary microbiota in lower urinary tract dysfunction: a systematic review. *Eur Urol Focus*. 2020;6:361–369.
17. Joseph EM. *Surgery of the Soul: Reflections on a Curious Career*. Science History Publications; 2001:1.
18. Barker CF, Markmann JF. Historical overview of transplantation. *Cold Spring Harb Perspect Med*. 2013;3:a014977–a014977.
19. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant*. 2011;11:2093–2109.
20. Winichakoon P, Chaiwarith R, Chattipakorn N, et al. Impact of gut microbiota on kidney transplantation. *Transplant Rev (Orlando)*. 2022;36:100668.
21. Campbell PM, Humphreys GJ, Summers AM, et al. Does the microbiome affect the outcome of renal transplantation? *Front Cell Infect Microbiol*. 2020;10:558644.
22. Fricke WF, Maddox C, Song Y, et al. Human microbiota characterization in the course of renal transplantation. *Am J Transplant*. 2014;14:416–427.
23. Jaworska MM, Pecyna P, Jaskiewicz K, et al. Differences in the composition of the bacterial element of the urinary tract microbiome in patients undergoing dialysis and patients after kidney transplantation. *Front Microbiol*. 2023;14:1187625.
24. Gerges-Knafl D, Pichler P, Zimprich A, et al. The urinary microbiome shows different bacterial genera in renal transplant recipients and non-transplant patients at time of acute kidney injury - a pilot study. *BMC Nephrol*. 2020;21:117.
25. Colas L, Mongodin EF, Montassier E, et al; DIVAT Consortium. Unique and specific proteobacteria diversity in urinary microbiota of tolerant kidney transplanted recipients. *Am J Transplant*. 2020;20:145–158.
26. Burnham P, Dadhania D, Heyang M, et al. Urinary cell-free DNA is a versatile analyte for monitoring infections of the urinary tract. *Nat Commun*. 2018;9:1–10.
27. Wu JF, Muthusamy A, Al-Ghalith GA, et al. Urinary microbiome associated with chronic allograft dysfunction in kidney transplant recipients. *Clin Transplant*. 2018;32:e13436.
28. Rani A, Ranjan R, McGee HS, et al. Urinary microbiome of kidney transplant patients reveals dysbiosis with potential for antibiotic resistance. *Transl Res*. 2017;181:59–70.
29. Modena BD, Milam R, Harrison F, et al. Changes in urinary microbiome populations correlate in kidney transplants with interstitial fibrosis and tubular atrophy documented in early surveillance biopsies. *Am J Transplant*. 2017;17:712–723.
30. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.
31. Hayden JA, Windt Van Der DA, Cartwright JL, Co P. Assessing bias in studies of prognostic factors. *Ann Intern Med*. 2006;158:280–286.
32. Perez-Carrasco V, Soriano-Lerma A, Soriano M, et al. Urinary microbiome: yin and yang of the urinary tract. *Front Cell Infect Microbiol*. 2021;11:1–17.
33. Patangia DV, Anthony Ryan C, Dempsey E, et al. Impact of antibiotics on the human microbiome and consequences for host health. *Microbiologyopen*. 2022;11:1–23.
34. Fishman JA, Gans H; AST Infectious Diseases Community of Practice. *Pneumocystis jiroveci* in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;33:e13587.
35. Emal D, Rampanelli E, Claessen N, et al. Calcineurin inhibitor tacrolimus impairs host immune response against urinary tract infection. *Sci Rep*. 2019;9:1–11.
36. Brubaker L, Gourdine J-PF, Siddiqui NY, et al. Forming consensus to advance urobiome research. *mSystems*. 2021;6:e0137120.
37. Price TK, Dune T, Hilt EE, et al. The clinical urine culture: enhanced techniques improve detection of clinically relevant microorganisms. *J Clin Microbiol*. 2016;54:1216–1222.
38. Jung CE, Chopyk J, Shin JH, et al. Benchmarking urine storage and collection conditions for evaluating the female urinary microbiome. *Sci Rep*. 2019;9:1–9.
39. Peker N, Garcia-Croes S, Dijkhuizen B, et al. A comparison of three different bioinformatics analyses of the 16S-23S rRNA encoding region for bacterial identification. *Front Microbiol*. 2019;10:1–13.
40. Pollock J, Glendinning L, Wisedchanwet T, et al. The madness of microbiome: attempting to find consensus. *Appl Environ Microbiol*. 2018;84:1–12.
41. Peris-Bondia F, Latorre A, Artacho A, et al. The active human gut microbiota differs from the total microbiota. *PLoS One*. 2011;6:e22448.
42. Oh PL, Martínez I, Sun Y, et al. Characterization of the ileal microbiota in rejecting and nonrejecting recipients of small bowel transplants. *Am J Transplant*. 2012;12:753–762.
43. Diaz PI, Hong BY, Frias-Lopez J, et al. Transplantation-associated long-term immunosuppression promotes oral colonization by potentially opportunistic pathogens without impacting other members of the salivary bacteriome. *Clin Vaccine Immunol*. 2013;20:920–930.
44. Palmisano A, Gandolfini I, Delsante M, et al. Acute kidney injury (AKI) before and after kidney transplantation: causes, medical approach, and implications for the long-term outcomes. *J Clin Med*. 2021;10:1484.
45. Sakhi H, Join-Lambert O, Goujon A, et al. Encrusted urinary tract infections due to *Corynebacteria* species. *Kidney Inter Reports*. 2021;6:179–186.