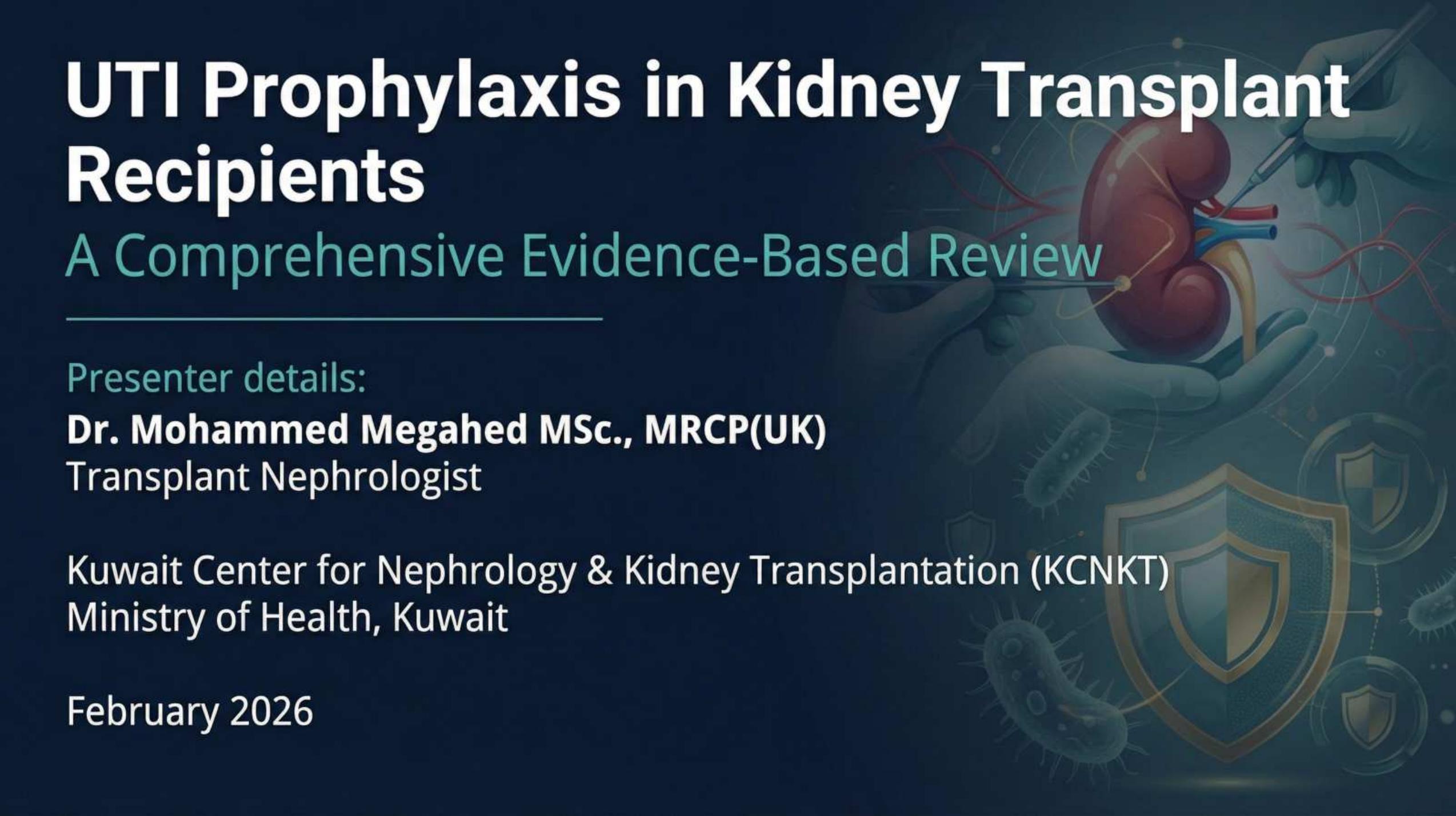


UTI Prophylaxis in Kidney Transplant Recipients



A Comprehensive Evidence-Based Review

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UTI Is the Most Common Infection After Kidney Transplantation

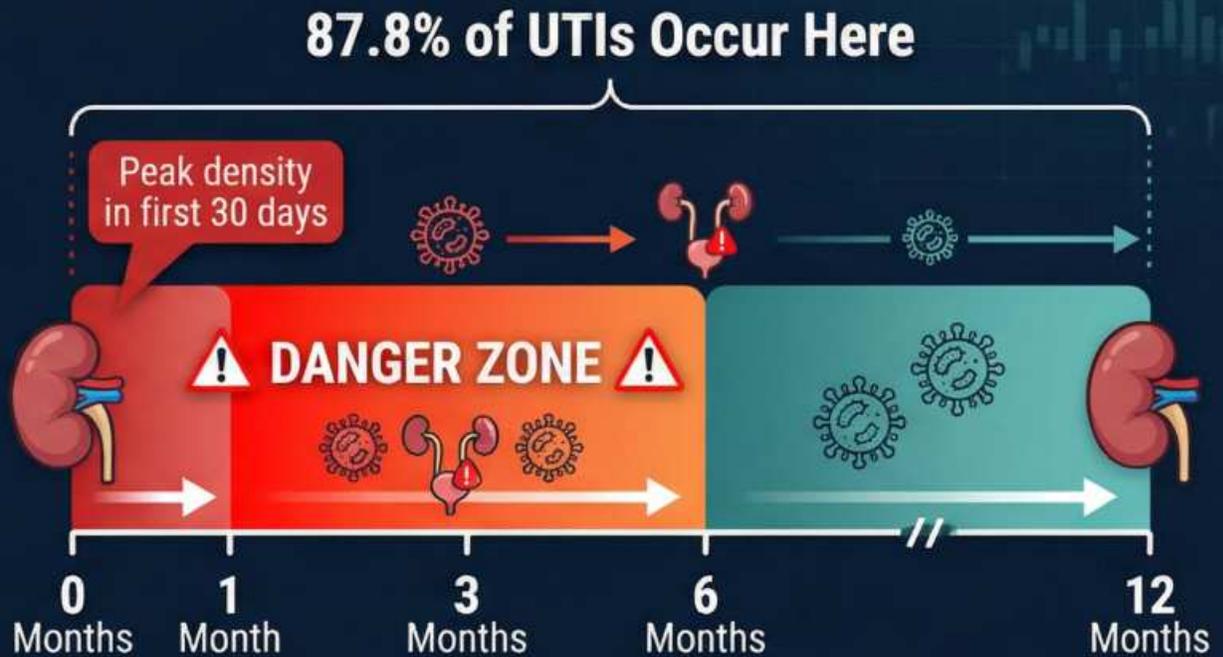
 Highest burden of **post-transplant infections** (Incidence 7–80% in 1st year)

 Risk greatest in **first 1–6 months** (Peak density in first 30 days)

 **87.8%** of UTIs occur within first **6 months**

 Associated with **increased graft loss, hospitalization, & costs**

 Early UTIs often **healthcare-associated & MDR organisms**



Who Is at High Risk?

Key Risk Factors for Post-Transplant UTI

Risk Factor	Evidence
 Female sex	Strongest predictor
 Ureteral stent	Prolonged stenting risk
 Delayed graft function	Independent risk factor
 Diabetes mellitus	Pre-transplant & NODAT
 Intense immunosuppression	ATG induction
 Anatomical abnormalities	VUR, neurogenic bladder

The Critical Timeline – When to Prophylax



Month 0–1 (Perioperative) – HIGHEST RISK

Indwelling catheter, ureteral stent, maximal immunosuppression.

Healthcare-associated MDR organisms.

Months 1–6 – HIGH RISK

Core Prophylaxis Window.
87.8% of UTIs occur here.
Stent removal at 4-6 weeks.

Beyond 6 Months – LOWER RISK

Risk decreases.
Late UTIs less severe.

Month 0

Month 1

6 Months

Primary Prophylaxis – TMP-SMX Is the Standard of Care

KDIGO Recommendation

Daily TMP-SMX (80/400 mg) for ≥ 6 months post-transplant (Grade 2B for UTI; 1B for PCP).

Dual-purpose coverage

Protects against UTI, *Pneumocystis jirovecii* pneumonia (PCP), *Nocardia*, *Toxoplasma*, *Listeria*.



TMP-SMX

UTI

Pneumocystis jirovecii
pneumonia (PCP)

Nocardia

Toxoplasma

Listeria

Key Study Finding

Extending TMP-SMX from 3 to 6 months reduced overall UTI rate and eliminated multi-resistant UTIs entirely (28 MDR-UTIs vs. 0, $p=0.004$).

Extended & Alternative Primary Prophylaxis Strategies



When to Extend (>6 months)



After acute rejection treatment (≥6 weeks)



After CMV infection (6–9 months)



Heavily immunosuppressed patients



TMP-SMX Intolerance Alternatives

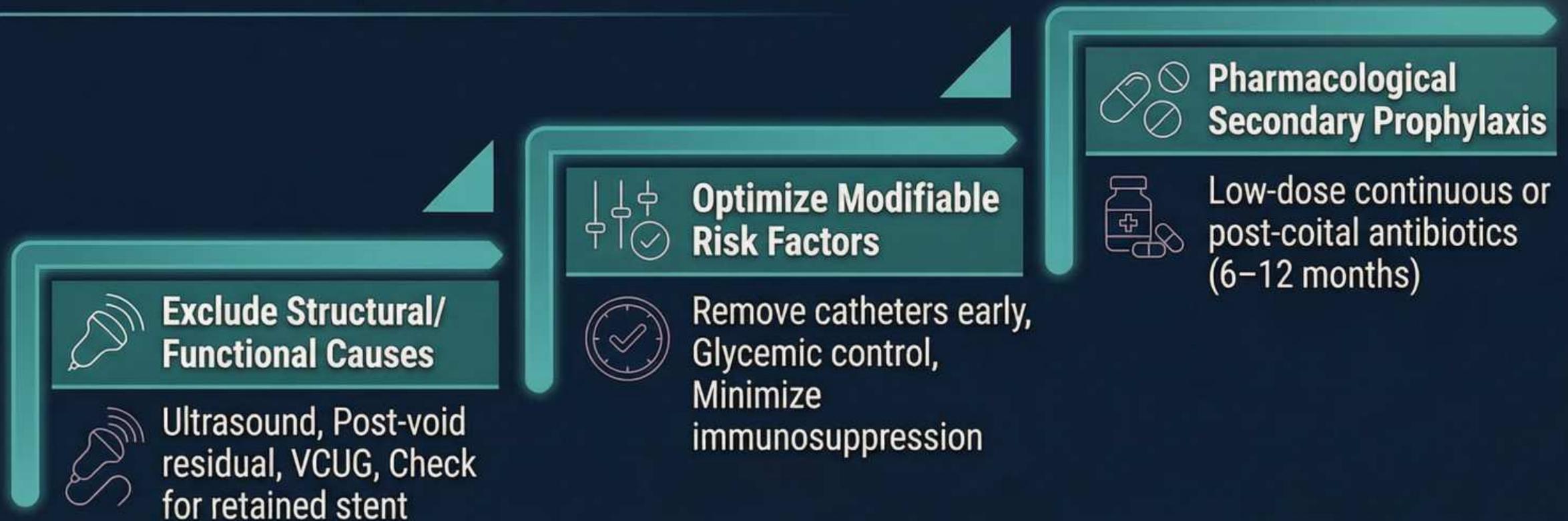
Prophylaxis Target	Alternative Agents
 PCP prophylaxis:	Dapsone or Atovaquone
 UTI prophylaxis only:	Nitrofurantoin or Fosfomycin
 Combined approach:	Dapsone (PCP) + Nitrofurantoin (UTI)



Important: Nitrofurantoin and fosfomycin **do NOT** cover PCP

Secondary Prophylaxis – A Stepwise Approach to Recurrent UTI

Recurrent UTI = ≥ 3 episodes/year or ≥ 2 in 6 months



Evidence-Based Non-Pharmacological Measures

Intervention	Evidence in KTR	Verdict
Early Foley removal (day 3–5)	Strong consensus	✓ RECOMMENDED
Early stent removal (4–6 wks)	Stent = risk factor	✓ RECOMMENDED
Topical vaginal estrogen	Grade A for rUTI	✓ RECOMMENDED
Methenamine hippurate	45–66% reduction	✓ PROMISING
D-Mannose (MANOTRAS RCT)	Did NOT reduce UTI	✗ NOT RECOMMENDED
Cranberry products	No convincing data	✗ NOT RECOMMENDED

Ref: MANOTRAS RCT (2024); EAU Guidelines (2025)

MANOTRAS RCT – D-Mannose Failed in Kidney Transplant Recipients

Study Overview

- **Study Design:** Randomized Controlled Trial (transplant-specific)
- **Population:** KTRs with recurrent UTI
- **Intervention:** D-Mannose + Proanthocyanidins vs. Placebo
- **Mechanism:** Blocking *E. coli* FimH adhesin

Clinical Implication

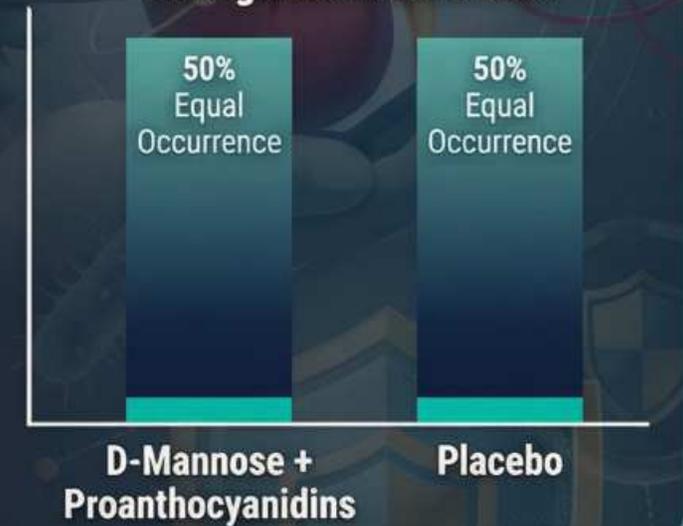
D-Mannose should **NOT** be recommended for UTI prophylaxis in KTR.

Results Section

NEGATIVE TRIAL

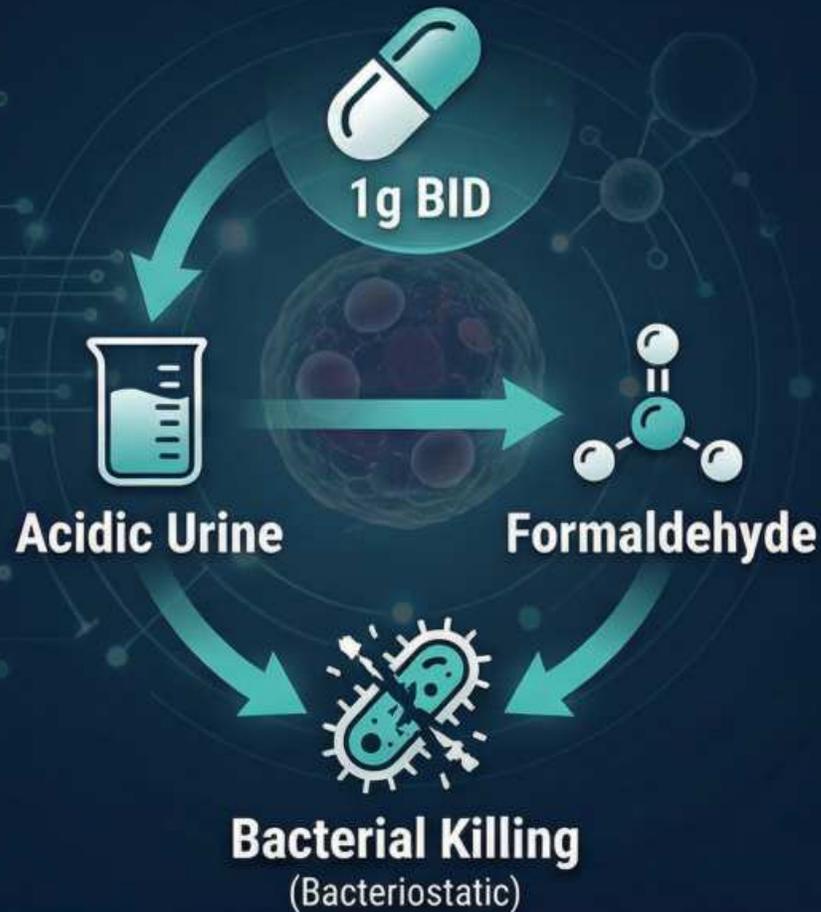
- D-Mannose **did NOT** reduce UTI episodes
- D-Mannose **did NOT** reduce asymptomatic bacteriuria
- **No significant benefit** on any endpoint

UTI Episodes & Bacteriuria Rates: No Significant Difference



Methenamine Hippurate – A Promising Non-Antibiotic Alternative

Mechanism Flow



Key Evidence

45–66% Reduction in UTI Episodes

- Retrospective KTR Studies
- Reduced antibiotic days & hospitalizations

Advantages

- No antimicrobial resistance
- Antibiotic-sparing strategy
- Safe for long-term use
- No drug interactions

Limitation: Retrospective data only; RCTs needed

Chronic Suppressive Antibiotic Therapy

Indications & Agents

Indications for Suppression

- ≥ 3 symptomatic UTIs/year
- Recurrent graft pyelonephritis
- Structural abnormalities (e.g., VUR)
- Recurrent MDR UTIs

Agents Table

Agent 	Dose 	Key Notes 
Nitrofurantoin	50–100 mg nightly	Preferred if eGFR >30
TMP-SMX	SS tab nightly or 3x/week	Monitor K+ & CBC
Fosfomycin	3 g every 10 days	For ESBL organisms
Cephalexin	250 mg nightly	Less preferred (resistance)

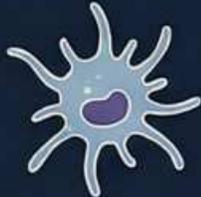
Duration: 6–12 months, then reassess. Monitor for breakthrough UTI.

UTI Vaccines – Uromune (MV140): Mechanism & Evidence

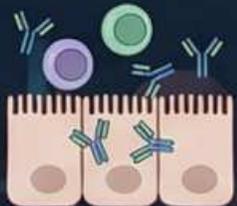
Mechanism of Action



Sublingual Spray



Dendritic Cell Activation
(Syk/MyD88)



Mucosal Immunity
(Th1/Th17, IgA/IgG)

Key Evidence – Pivotal RCT (n=240)

Median UTI reduced 3.0 → 0.0



UTI-free rate: 56–58% vs 25% (Placebo)



Time to first UTI: 275 days vs 48 days



Long-term (9-year): 54% remained UTI-free

In KTR: Pilot study showed trend toward reduction; controlled trials needed.

UTI Vaccines – Head-to-Head Comparison

Uromune (MV140) vs. Uro-Vaxom (OM-89)

 Uromune (MV140)	 Uro-Vaxom (OM-89)
<ul style="list-style-type: none">✓ Sublingual Spray✓ 4 Species Coverage✓ Effect up to 9 years✓ Pilot KTR data	<ul style="list-style-type: none">✓ Oral Capsule✓ <i>E. coli</i> only✓ Effect wanes (needs booster)✓ No KTR data

Clinical Implication: Uromune has broader coverage & mucosal immunity, theoretically better for KTR, but robust transplant-specific RCTs are lacking for both. 

Next-Generation Sequencing (mNGS) — Revolutionizing UTI Diagnostics

Feature	mNGS	Standard Culture
Turnaround Time	 ~24 hours	 48–72 hours
Positive Rate (KTR)	 100%	31.6%
Polymicrobial Detection	 89.5%	10.5%
Viral/Fungal Detection	  Yes (BKV, CMV)	 No
Resistance Genes	 Direct Detection	 Requires Isolate



Clinical Impact: Guided therapy changes in **76.9%** of cases vs **33.3%** by culture

mNGS — Clinical Applications & Limitations in KTR



When to Consider mNGS

- ✓ Recurrent UTI with culture-negative results
- ✓ Suspected polymicrobial infections
- ✓ Rapid resistance profiling
- ✓ Detection of rare/atypical pathogens (Nocardia, BKV)
- ✓ Antimicrobial stewardship



Current Limitations



- ⚠ High cost limits routine use
- ⚠ Difficulty distinguishing colonizer vs. pathogen
- ⚠ Host DNA contamination reduces sensitivity
- ⚠ No standardized laboratory protocols

Recommendation: Consider mNGS for recurrent/refractory UTIs or culture-negative cases. Complements but does not replace standard culture.

Asymptomatic Bacteriuria – The BiRT Trial Changed Practice

Landmark RCT (n=199): Antibiotics vs. No Therapy for ASB >2 months post-Tx

	Antibiotics (Tx)	No Therapy (No Tx)	
Symptomatic UTI	27%	31%	NO SIGNIFICANT DIFFERENCE (p=0.49)
Pyelonephritis	17%	16%	NO DIFFERENCE
Antibiotic Burden	30 days	6 days	5-FOLD HIGHER IN TREATMENT GROUP
New Resistance Emergence	18%	4%	SIGNIFICANTLY HIGHER (p=0.003)

Treating ASB provided NO benefit but caused 5x more antibiotic exposure and significantly more resistance.

ASB Management — International Consensus & Guidelines



Updated Meta-Analysis (n=486)



No significant benefit of treating ASB (RR 0.94)



IDSA (2019)

Recommend **AGAINST** screening/treating >1 month (Strong)



AST-IDCOP (2019)

No benefit >2 months



EAU (2025)

Do **NOT** screen or treat (Strong)



The Gray Zone: 0–2 Months

No RCT evidence for this period. Practice varies.

- Consider treating if:  Stent present,  Pyuria + Symptoms, or  ESBL.

Proposed Follow-Up Protocol Framework

Evidence-Based Surveillance & Prophylaxis Timeline



Recurrent UTI Protocol: Structural Workup → Susceptibility-Guided Therapy → Methenamine/Nitrofurantoin Suppression → mNGS

Key Takeaways — Evidence-Based Summary

10 Essential Points for Clinical Practice

- 1 UTI is #1 infection post-KT (87.8% in first 6 mos)
- 2 TMP-SMX \geq 6 months is Standard of Care
- 3 Extending TMP-SMX to 6 mos eliminates MDR-UTIs
- 4 Do NOT treat ASB >2 months post-Tx (BiRT Trial)
- 5 Treating ASB causes 5x antibiotic burden & resistance
- 6 Early catheter/stent removal are key
- 7 Methenamine hippurate is a promising alternative
- 8 D-Mannose & Cranberry are NOT effective in KTR
- 9 Uromune (MV140) shows promise; needs KTR data
- 10 mNGS detects 100% pathogens; use for refractory cases

Quiz Section – Test Your Knowledge (Part 1)

Question 1: A 45-year-old female KTR is 4 months post-transplant on TMP-SMX prophylaxis. Routine urine culture shows *E. coli* $\geq 10^5$ CFU/mL. She is completely asymptomatic with stable creatinine. What is the best management?

- A) Treat with 7 days of ciprofloxacin
- B) Treat with 14 days of culture-directed antibiotics
- C) **Do NOT treat** – this is asymptomatic bacteriuria
- D) Switch TMP-SMX to nitrofurantoin

Answer: C – Do NOT treat.

Based on the BiRT Trial (n=199) and IDSA/EAU guidelines, ASB >2 months post-transplant should NOT be treated. Treatment increases antibiotic burden 5-fold and resistance emergence (18% vs. 4%, p=0.003).

Quiz Section – Test Your Knowledge (Part 2)

Question 2

Which non-pharmacological intervention has been shown to be **INEFFECTIVE** in a transplant-specific RCT for UTI prophylaxis in KTR?

- A) Early Foley catheter removal
- B) Topical vaginal estrogen
- C) D-Mannose + Proanthocyanidins
- D) Methenamine hippurate

Correct Answer: C

Explanation: The MANOTRAS RCT (2024) showed D-Mannose did NOT reduce UTI or ASB in KTR.

Question 3

What percentage of UTI cases did mNGS detect compared to standard urine culture in a KTR study?

- A) mNGS 50% vs. Culture 31.6%
- B) mNGS 75% vs. Culture 50%
- C) mNGS 100% vs. Culture 31.6%
- D) mNGS 89.5% vs. Culture 10.5%

Correct Answer: C

Explanation: mNGS achieved 100% detection vs 31.6% for standard culture.

Thank You & References

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Ministry of Health, Kuwait

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- 9. mNGS in post-KT infections — Frontiers in Cellular and Infection Microbiology (2025)