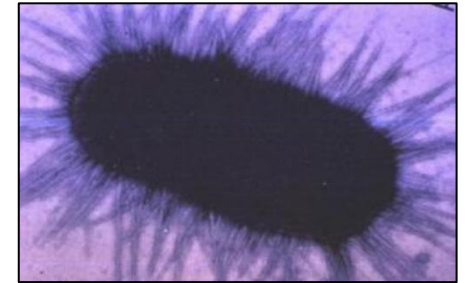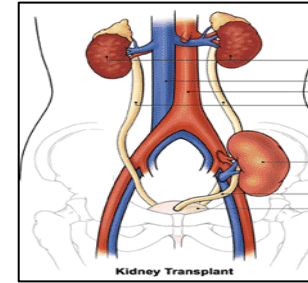# Impact of symptomatic UTI on long term transplant function

Rhana Hassan Zakri, Theo Kasimatis, Pinkie Kotecha, Rohit Srinivasan, Katie Wong,

Sandeep Sasuke, Elham Asgari, Jonathon Olsburgh

Guy's & St Thomas' NHS Trust, London

‘Urinary tract infection (UTI) is the commonest infection post renal transplant’ (RTx)

Unanswered questions

- Long term effect of symptomatic UTI on RTx function?

  - The role of ABU. Should all ABUs be treated?

- Is the effect of cystitis and pyelonephritis the same on graft function?

  - Is one post RTx UTI one too many?

1 Year

Urinary Tract Infections in Kidney Transplant Recipients Hospitalized at a Transplantation and Nephrology Ward: 1-Year Follow-up

J. Gozdowska[a,*], M. Czerwińska[a], Ł. Chabros[b], G. Młynarczyk[b], A. Kwiatkowski[c], A. Chmura[c], and M. Durlik[a]

3 Year

Late Urinary Tract Infection After Renal Transplantation in the United States

Kevin C. Abbott, MD, S. John Swanson, MD, Erich R. Richter, MD, Erin M. Bohen, MD, Lawrence Y. Agodoa, MD, Thomas G. Peters, MD, Galen Barbour, MD, Robert Lipnick, ScD, and David F. Cruess, PhD

Urinary Tract Infections in Renal Transplant Recipients

1 Year

J. Gołębiewska, A. Dębska-Ślizień, J. Komarnicka, A. Samet, and B. Rutkowski

Hypothesis

**'Long-term graft dysfunction occurs in patients
with upper tract UTI (pyelonephritis)
as a result of renal scarring'**

Material & Methods

- **Population:**
  - Renal transplant recipients 2010 -2012
- **Retrospective analysis from EPR**
- **Inclusion:**
  - Adult patients
  - Transplant follow-up at Guy's
- **Exclusion:**
  - Primary non function/graft nephrectomy <1 month post transplant

- **Follow-up:**
  - 5 year: Number of UTIs
    eGFR
- **Primary outcome:**
  - **Δ Graft function** eGFR ml/min
- **Secondary outcome:**
  - **Graft Survival**

Definitions

UTI

Asymptomatic Bacteriuria (ABU)

Urine culture proven bacteriuria. Absent clinical symptoms, RTx dysfunction or biochemical inflammatory response.

Symptomatic UTI

Lower UTI (Cystitis)

Absent systematic upset. Localised cystitis symptoms and CRP <50

Upper UTI (RTx or native kidney pyelonephritis)

CRP >50, pyrexia >38°C, RTx dysfunction, systemic symptoms, RTx/native pain
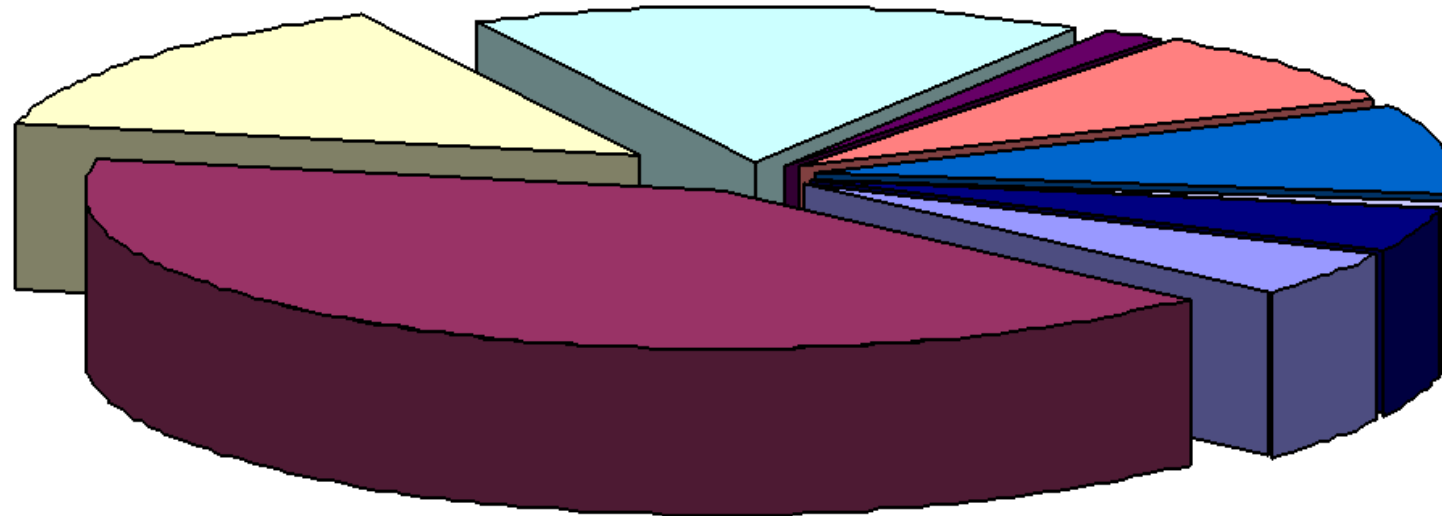
Results

- **Adult renal transplants 2010 – 2012**   **n = 610**

- **Total patients followed up at Guy's**   **n = 213**

- **Total patients in analysis after exclusions**   **n = 206**

  (1° non-function =6, Graft nephrectomy <1 month =1)

Results

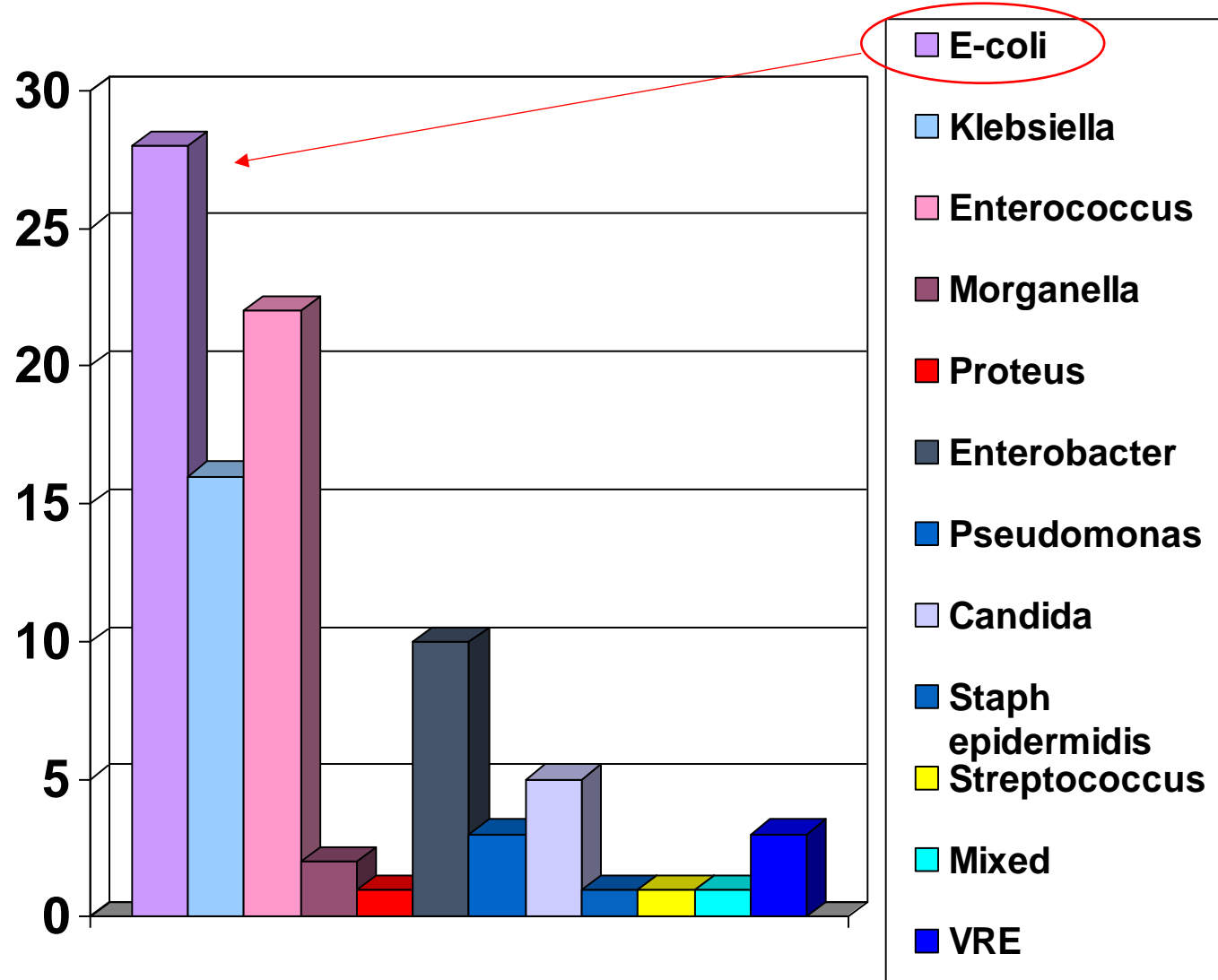**Mean recipient age:** 47.3Yrs

Male : Female 129:77 (62.6% : 37.3%)

Cause of End Stage Renal Disease

Legend:
- Unknown
- Intrinsic renal disease
- Diabetes
- HTN
- Renal vascular disease
- ADPKD
- VUR
- Stones
- Congenital Urological

Bacterial Incidence: 1st year post RTx

UTIs

- **Positive urine cultures**   206 pts over 5 years   n = 447

Unanswered questions

- Long term effect of symptomatic UTI on RTx function?

- Is the effect of cystitis and pyelonephritis the same on graft function?

Type of UTI

Worst clinical episode	No UTI	UTI		
		ABU	Symptomatic UTI	
			Cystitis	Pyelonephritis
n = 206	118	29	25	34
Overall	57%	14%	12%	17%
			Recurrent n = 14 (6.8%)	Recurrent n = 11 (5.3%)
Mean age/yrs	47.5	47.0	49.9	44.9
Ratio Male:Female	2:1	1:1.8	1:2.5	1:2.7

ΔGraft function over 5 years

	No UTI n=118	UTI n= 88
Mean baseline eGFR mL/min	59	58
Mean eGFR 5 yr post RTx mL/min	50.9	39.3
Mean ΔeGFR mL/min	8.1	18.7

Mann Whitney U Test P <0.001

ΔGraft function over 5 years

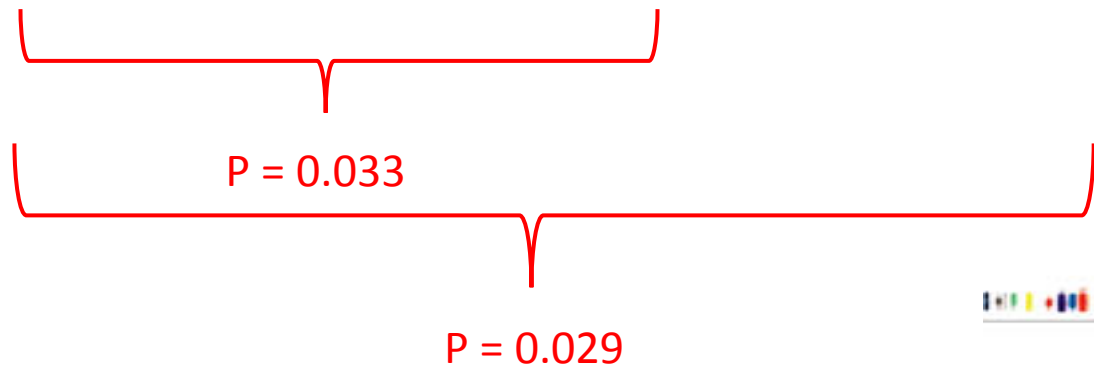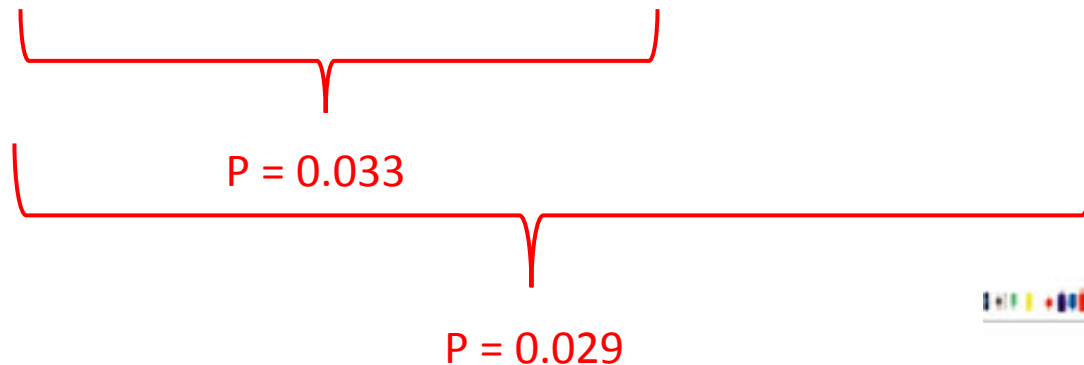|	No UTI n=118	ABU n=29	SYMPTOMATIC UTI n= 59	
Mean baseline eGFR mL/min	59	58	59.2	57
Mean eGFR 5 yr post RTx mL/min	50.9	43.6	37.4	37.1
Mean ΔeGFR mL/min	8.1	14.4	20.9	

Kruskal-Wallis Test

Pair wise analysis

ΔGraft function over 5 years

	No UTI n=118	ABU n=29	Cystitis n=25	Pyelonephritis n=34
Mean baseline eGFR mL/min	59	58	59.2	57
Mean eGFR 5 yr post RTx mL/min	50.9	43.6	37.4	37.1
Mean ΔeGFR mL/min	8.1	14.4	21.8	19.9

Kruskal-Wallis Test

Pair wise analysis

P = 0.033

P = 0.029

ΔGraft function over 5 years

	No UTI n=118	ABU n=29	Cystitis n=25	Pyelonephritis n=34
Mean baseline eGFR mL/min	59	58	59.2	57
Mean eGFR 5 yr post RTx mL/min	50.9	43.6	37.4	37.1
Mean ΔeGFR mL/min	8.1	14.4	21.8	19.9

Kruskal-Wallis Test

Pair wise analysis

P = 0.033

P = 0.029

Graft survival – UTI

Survival Functions

Overall worst clinical 0 = No UTI, 1 = ABU, cystitis = 2, Pyelonephritis = 3

- 0
- 1
- 2
- 3
- 0-censored
- 1-censored
- 2-censored
- 3-censored

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	1.029	3	.794

Test of equality of survival distributions for the different levels of Overall worst clinical 0 = No UTI, 1 = ABU, cystitis = 2, Pyelonephritis = 3.
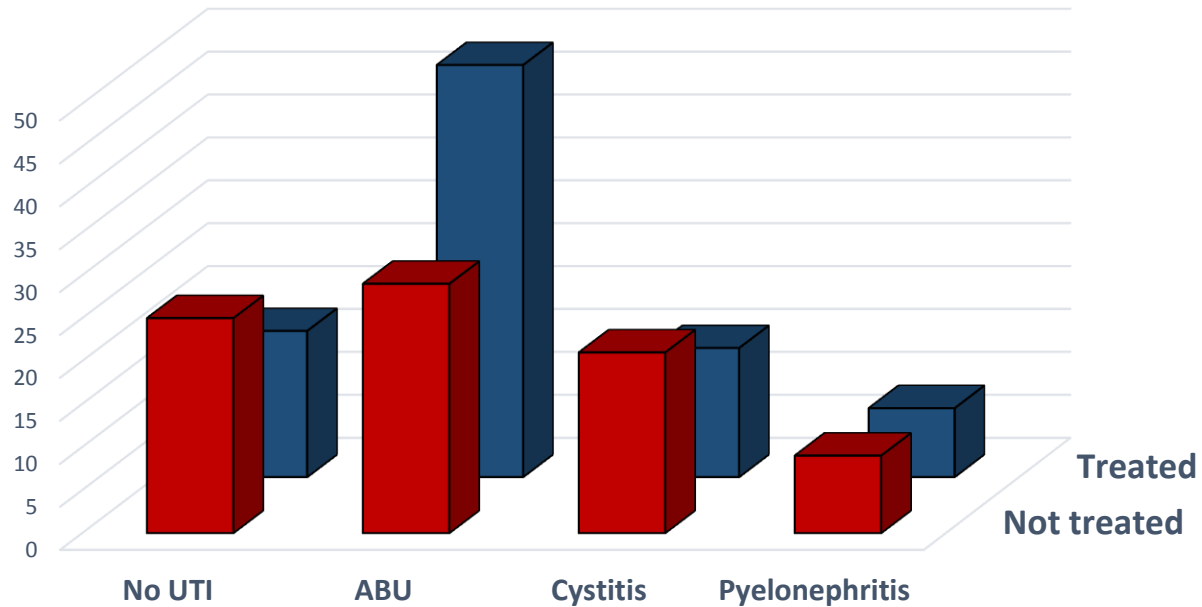
Asymptom

- The role of ABU
  be treated?

ABUs

Treated Vs non-treated ABU:
Further episodes in next 5Yrs

Unanswered questions

- Is one post RTx UTI one too many?
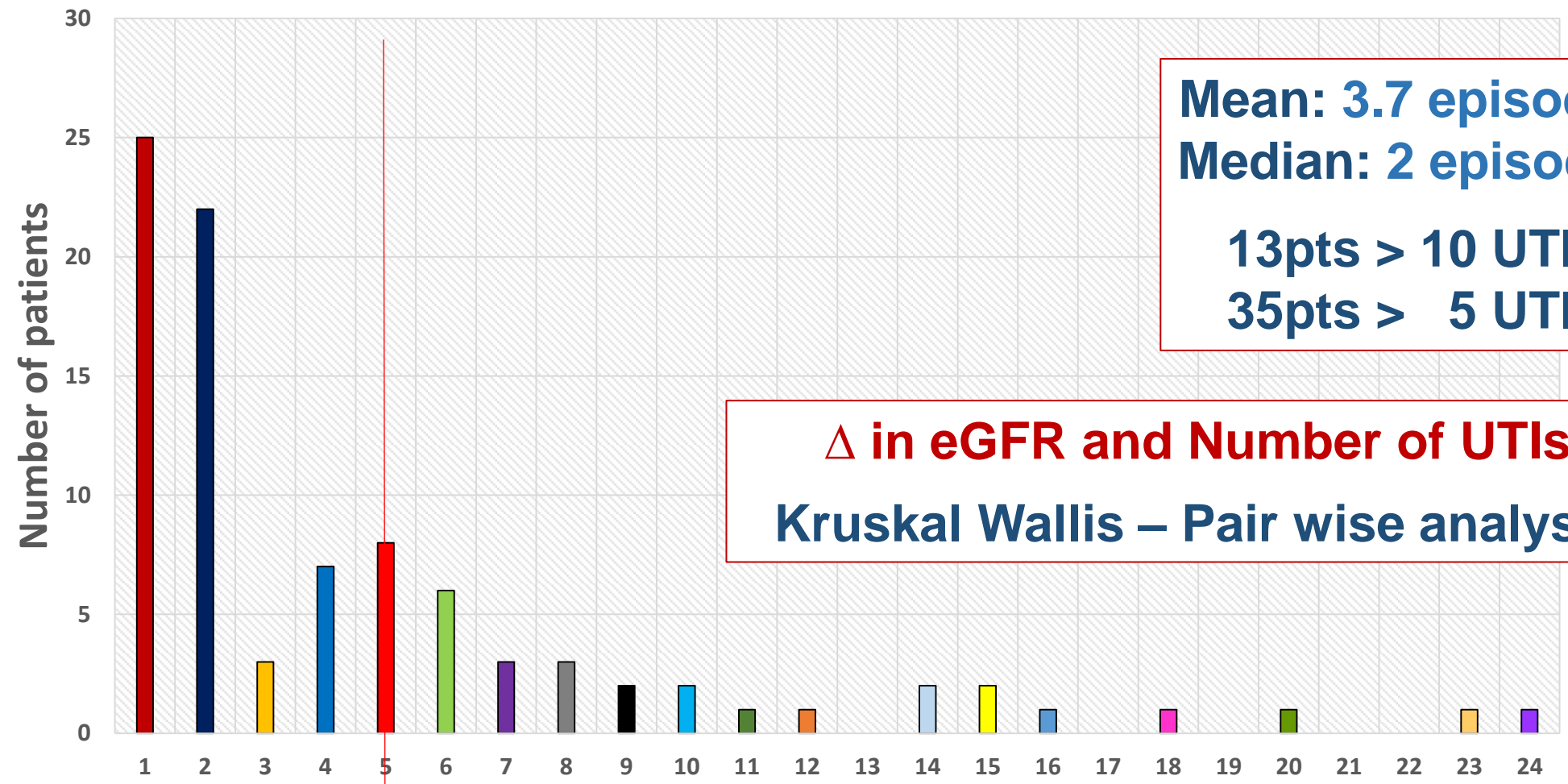
Summary

	No UTI n=118	ABU n=29	Cystitis n=25	Pyelonephritis n=34
Mean baseline eGFR mL/min	59	58	59.2	57
Mean eGFR 5 yr post RTx mL/min	50.9	43.6	37.4	37.1
Mean ΔeGFR mL/min	8.1	14.4	21.8	19.9

Kruskal-Wallis Test

Pair wise analysis

P = 0.033

P = 0.029

Hypothesis

'Long-term graft dysfunction occurs in patients
with upper tract UTI (pyelonephritis)
as a result of renal scarring'

....but have we underestimated the effect of
'cystitis' and 'number of hits' on graft
dysfunction?

The Future

- **Tx UTI clinic:** MDT / 'One stop model'
  - **Transplant UTI 'Care bundle'**
  - **Streamline, early management**
  - **Prospective 10-15yrs follow-up data**

- **Consider Post RTx RCT:** Aim to prevent Tx UTI
  - **Standard practice Vs prophylactic abx Vs Probiotic**
  - **Necker technique v Lich-Gregoir (Campos Freire)**

Thank-you!

Antibiotic stewardship   *E-Coli* resistance patterns
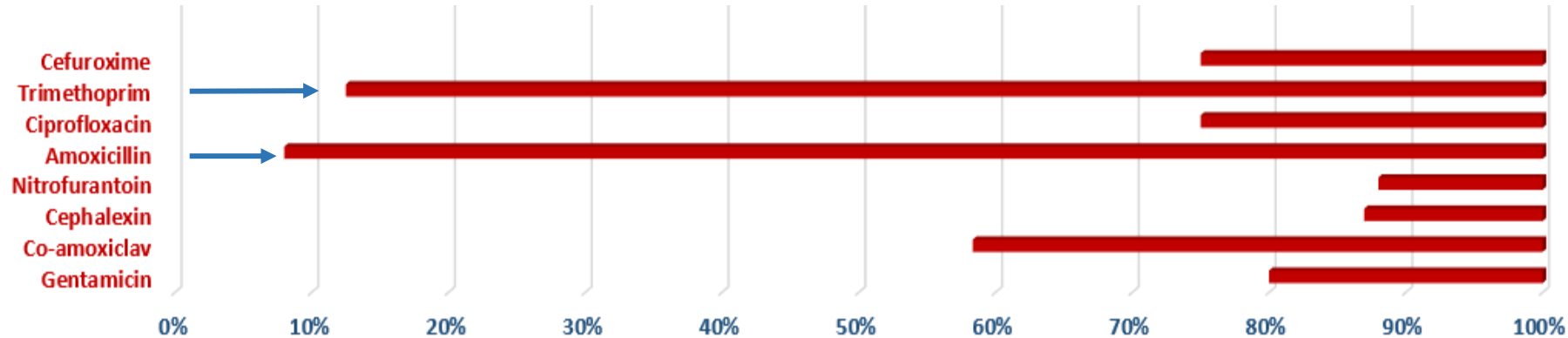
2010 -2012

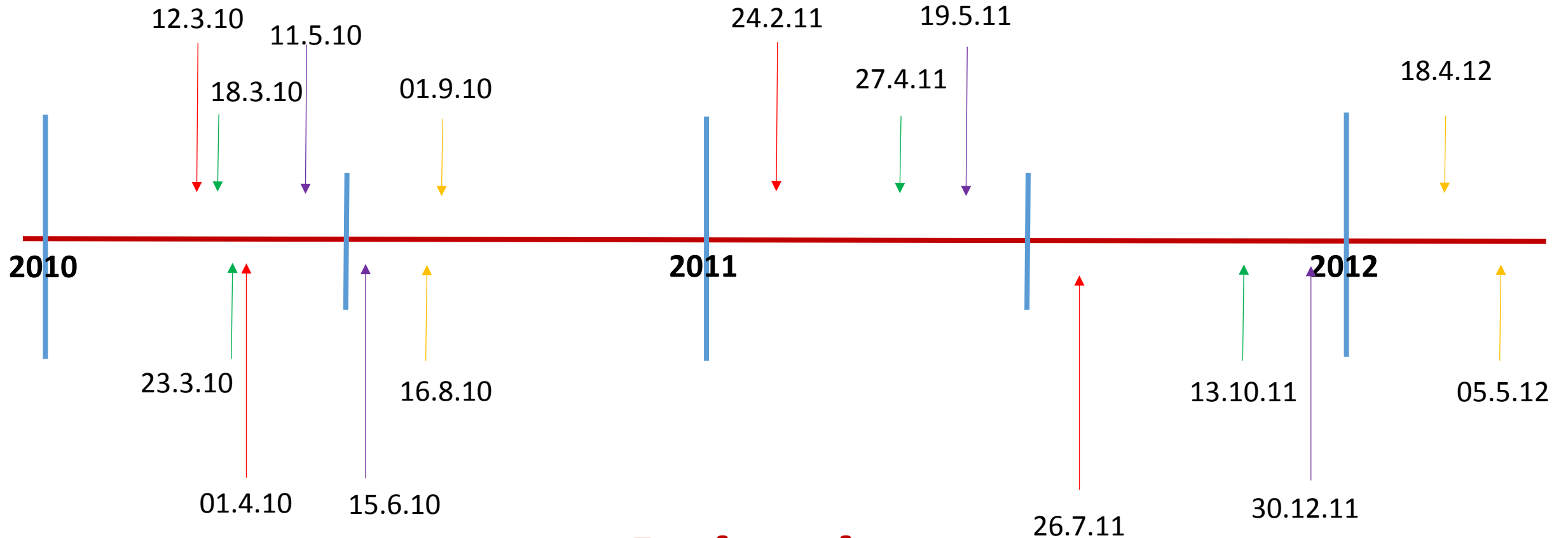# UTIs and Rejection

- **Total patients with rejection**   n = 50
- **Patients with rejection on first Bx**   n = 44

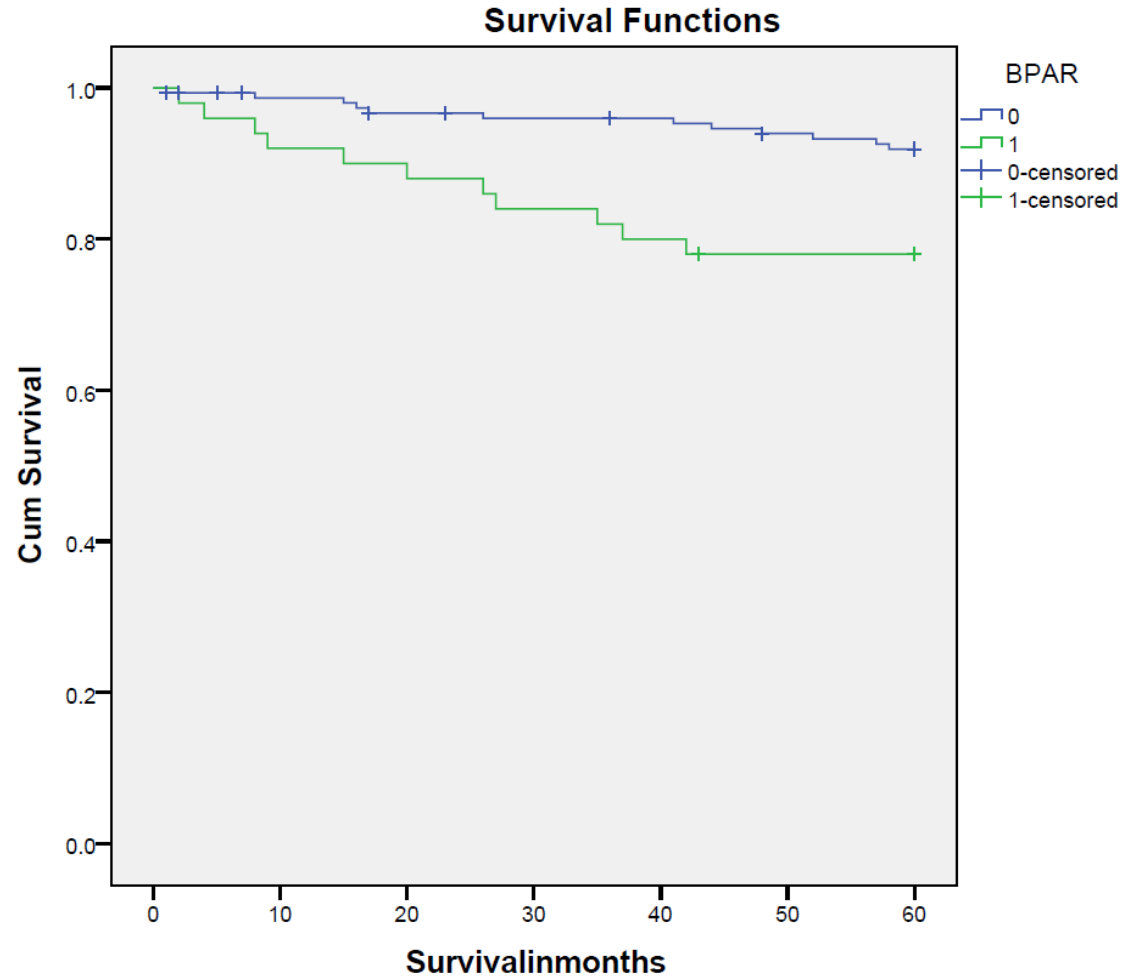- **Patients with rejection but no UTI excluded**   n = 32

- **Total patients in analysis after exclusions**   n = 18

BTS
British Transplantation Society

The Voice of Transplantation in the UK

KING'S HEALTH PARTNERS
Pioneering better health for all

UTIs

12.3.10

11.5.10

18.3.10

01.9.10

24.2.11

19.5.11

27.4.11

18.4.12

2010

2011

2012

23.3.10

16.8.10

13.10.11

05.5.12

01.4.10

15.6.10

30.12.11

26.7.11

Rejection

Graft survival – Rejection

Survival Functions

BPAR
- 0
- 1
- 0-censored
- 1-censored

Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	7.862	1	.005

Test of equality of survival distributions for the different levels of BPAR.
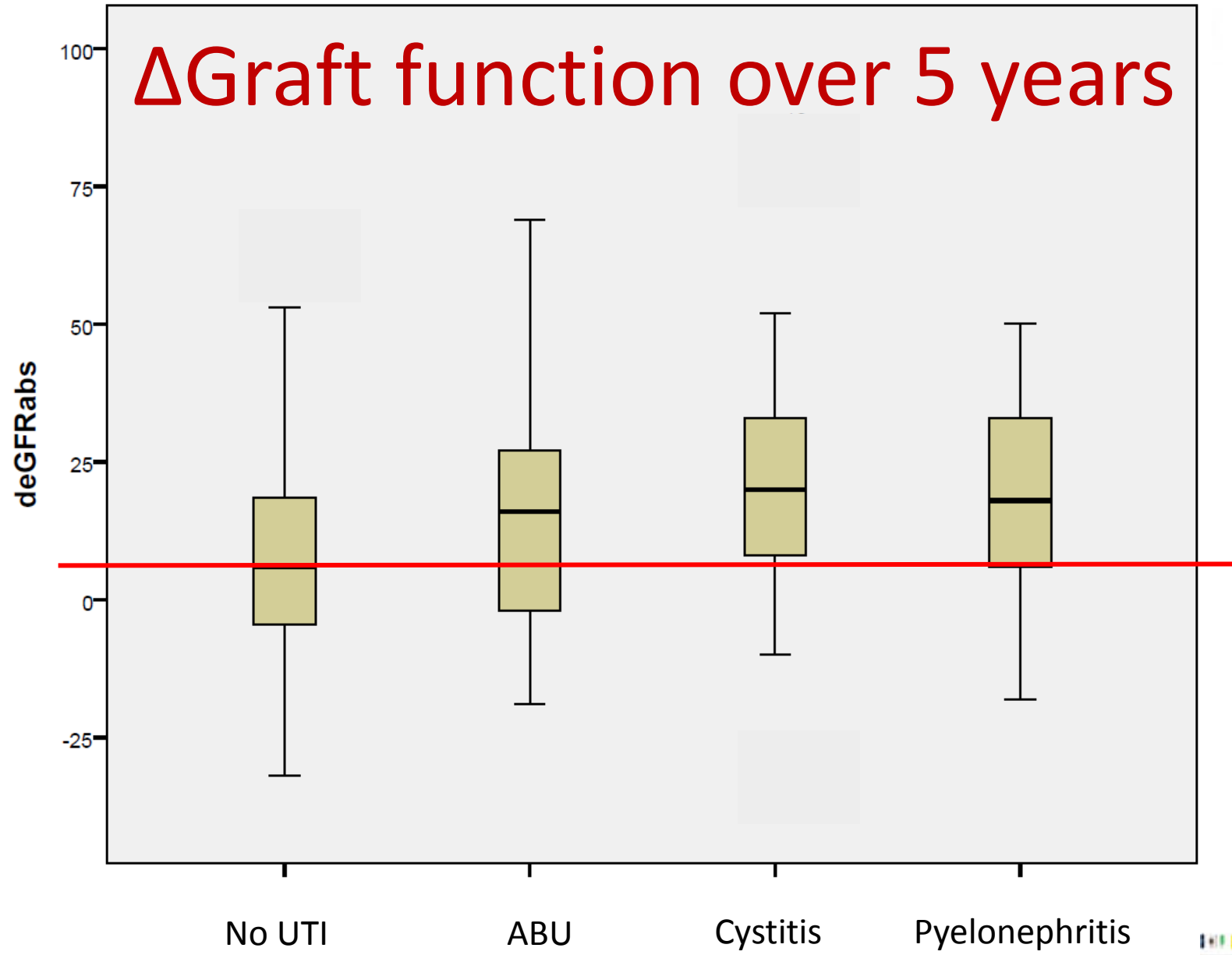
Graft survival – DGF
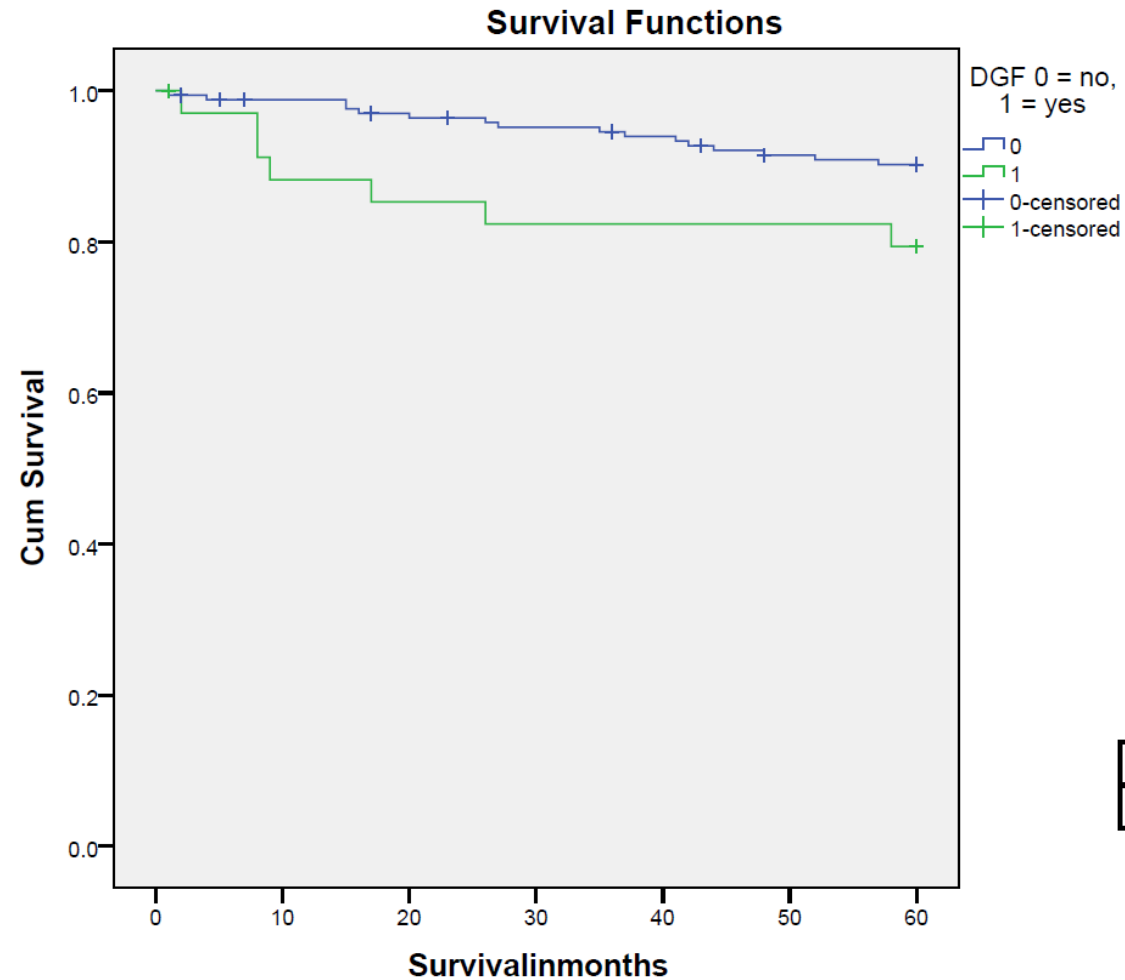
Limitations

- **Retrospective observational study**
- **Confounders**
  - **E.g. changes in immune-suppression over 5yrs**
- **Assumptions**

  Cystitis – (CRP 0-10 v 10-50)

  "Statistically significant" is "clinically significant"
- **Need for further multivariate analysis / mixed repeated measure model**

ΔGraft function over 5 years

Unresolved issues

- **Literature:**
  - Inconsistent, small series, short follow-up

- **Guidelines:**
  - No national guidelines
  - Need for streamlined services

- **Is statistically significant the same as clinically significant?**

Definitions

- **ABU**

Urine culture proven bacteriuria. Absent clinical symptoms, RTx dysfunction or biochemical inflammatory response.

- **Lower UTI (Cystitis)**

Absent systematic upset. Localised cystitis symptoms and CRP <50

- **Upper UTI (RTx or native kidney pyelonephritis)**

CRP >50, pyrexia >38°C, RTx dysfunction, systemic symptoms, RTx/native pain

- **Positive urine culture**

    $>10^5$ but consider $>10^2$ with pyuria

- **Patient with UTI**

    Includes ABU (either Rx or unRx), cystitis and pyelonephritis

- **Symptomatic UTI**

    Includes cystitis + pyelonephritis

- **Worst episode recorded**
    eg ABU v cystitis v Pyelonephritis

Rejection (n=45)

	No UTI n=118	ABU n=29	Cystitis n=25	Pyelonephritis n=34
Rejection on 1st renal bx n	22	8	5	10
Type of rejection n				
Tubulo-interstitial 1A	5	1	1	2
Tubulo-interstitial 1B	6	1	1	4
Vascular 2A	0	2	2	2
Vascular2B	2	0	0	0
TMR/AMR	8	4	1	2
Type 3	1	0	0	0