

**Antibiotic prophylaxis for the prevention  
of urinary tract infection in children with  
low grade vesicoureteral reflux :  
Results from a prospective randomized  
study**

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# Introduction

- Antibioprophylaxis significantly reduced the rate of urinary tract infection (UTI) in children without vesicoureteral reflux (VUR) (Smellie, *Lancet*, 1978)
- Until recently, no prospective study had evaluated the interest of prophylaxis for children with VUR (Williams.G, *J Pediatr* 2001, *Cochrane Database Syst Rev* 2006 )
- Antibioprophylaxis does not prevent further UTI in children after a first pyelonephritis (Garin, *Pediatrics*, 2006)

# Objectives

- Evaluate the effectiveness of prophylaxis in young children with a low grade VUR
- Compare the rate of urinary infection after the diagnosis of VUR in children receiving or not prophylaxis.

# Inclusion criteria

- Children between one-month and 3 –years
- Grade I, II or III VUR (according to the international VUR classification) diagnosed on a radiologic voiding cystourethrogram (VCUG) performed after a first episode of febrile UTI
- Absence of pyelic or ureteral dilatation, obstructive uropathy
- Approval by the University Hospital Ethical Committee and the local Committee for the Protection of Patients for Biomedical Research. Written informed consent before inclusion.

# Study design

- Randomization by sex in each participating center
- Patients were allocated to receive antibiotic prophylaxis (10 mg/kg sulfamethoxazole and 2mg/kg trimethoprim once a day) OR no treatment.
- No placebo was administered.
- Follow-up period: 18 months
- Renal US at 9 and 18 months following inclusion
- VCUG at 18 months for all patients who completed the study

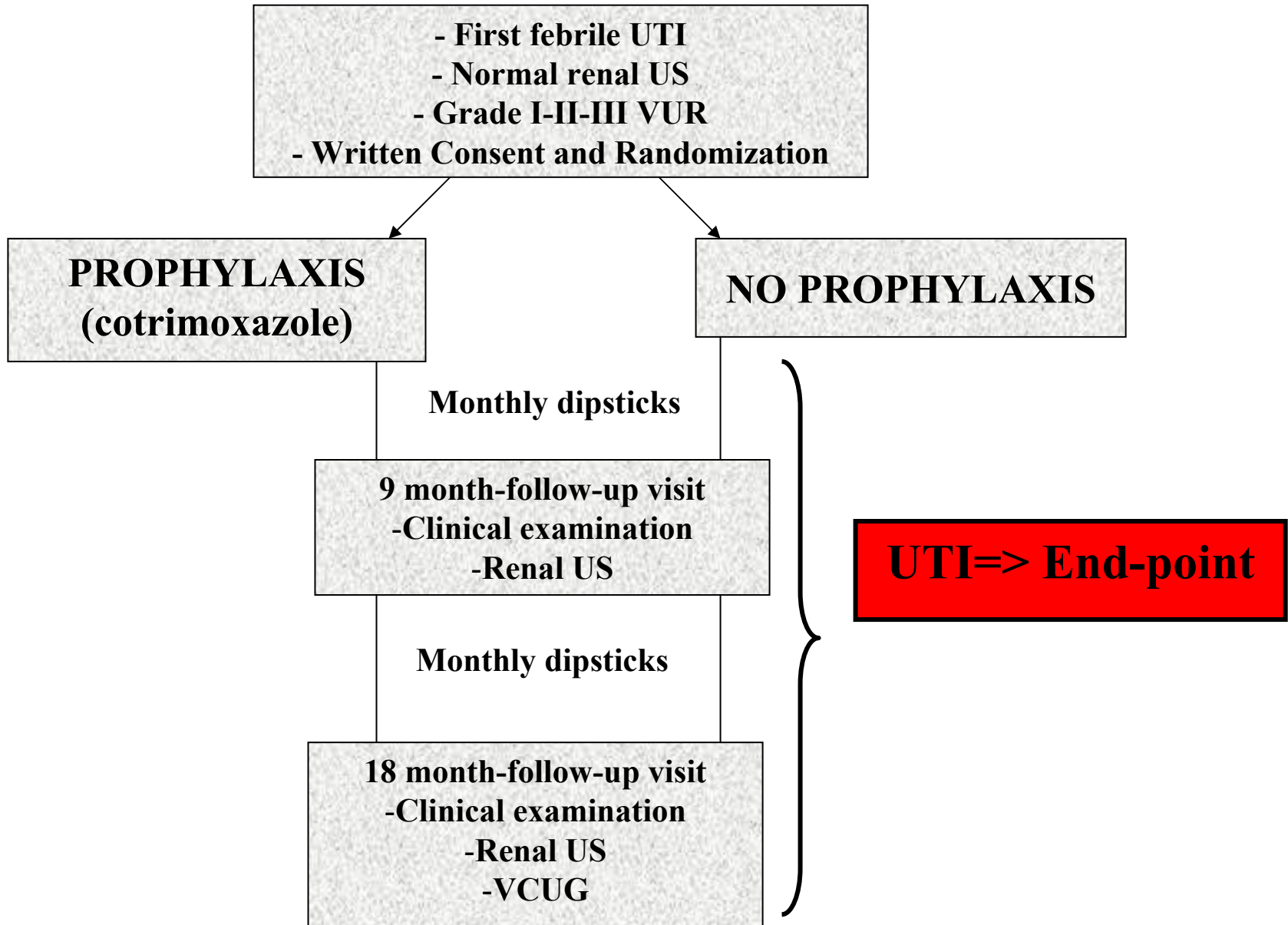
# Study design

- Urinary dipsticks every month and if symptoms of UTI in both groups.
- Urine culture performed if positive leukocyte and/or nitrite test.
- Urinary infection defined as a significant bacteriuria (more than  $10^5$  bacteria/ml)
- Urine collection with sterile bags
- **The occurrence of a urinary infection was an endpoint and the patient accordingly removed from the study**

# Statistical analyses

- Comparison of characteristics of each group: Chi-2 test or Student test according to the variables.
- UTI-free survival rates performed using the Kaplan-Meier method and compared by the log-rank test.
- Logistic regression analysis with a Cox model
- Intention to treat analyses.
- $p < 0.05$  was considered as significant.

# Study design



# Demographic Data

	<b>Prophylaxis Nb (%)</b>	<b>No Prophylaxis Nb (%)</b>	<b>p</b>
<b>Number</b>	102 (100%)	121 (100%)	
<b>Female</b>	72 (71%)	82 (68%)	0.65
<b>Male</b>	30 (29%)	39 (32%)	
<b>Age at inclusion</b>	12+/-8.1 months	10,6+/-8,4 months	0.18
<b>Grade I VUR</b>	8 (8%)	14 (12%)	0.58
<b>Grade II VUR</b>	70 (68%)	76 (63%)	
<b>Grade III VUR</b>	24 (24%)	30* (25%)	
<b>Unilateral VUR</b>	61 (60%)	61 (51%)	0.28
<b>Bilateral VUR</b>	41 (40%)	59* (49%)	

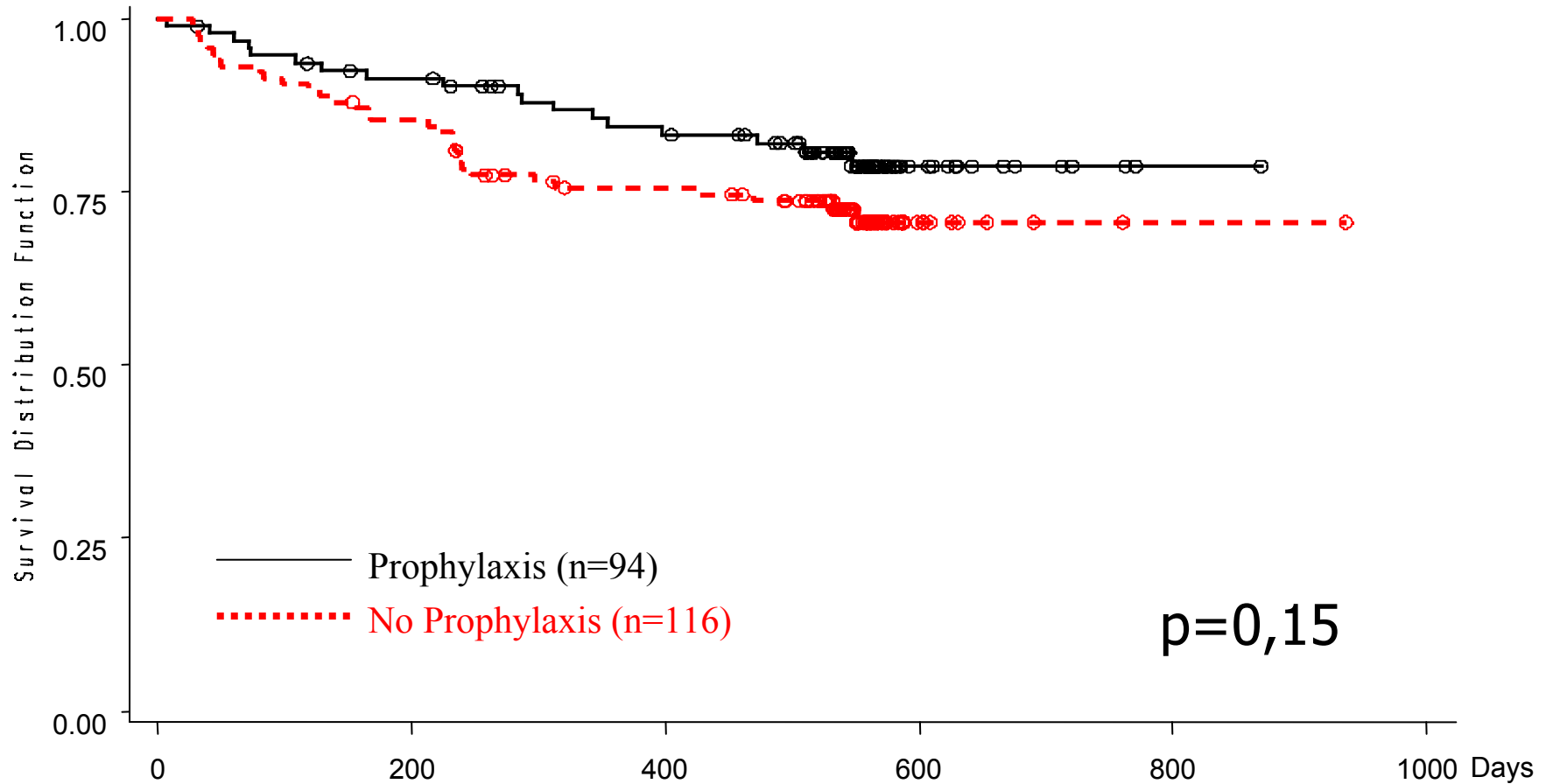
# Demographic Data according to sex

	<b>Female Nb (%)</b>	<b>Male Nb (%)</b>	<b>p</b>
<b>Number</b>	154 (100%)	69 (100%)	
<b>Prophylaxis</b>	71 (46%)	39 (56%)	0.19
<b>No prophylaxis</b>	83 (54%)	30 (44%)	
<b>Age at inclusion</b>	<b>13+/-8.1 months</b>	<b>7+/-7 months</b>	<b>&lt;0.01</b>
<b>Grade I VUR</b>	18 (12%)	5 (7%)	0.09
<b>Grade II VUR</b>	104 (67%)	41 (60%)	
<b>Grade III VUR</b>	31* (20%)	23 (33%)	
<b>Unilateral VUR</b>	<b>91 (59%)</b>	<b>30 (44%)</b>	<b>0.038</b>
<b>Bilateral VUR</b>	62* (41%)	39 (56%)	

# Performed analysis

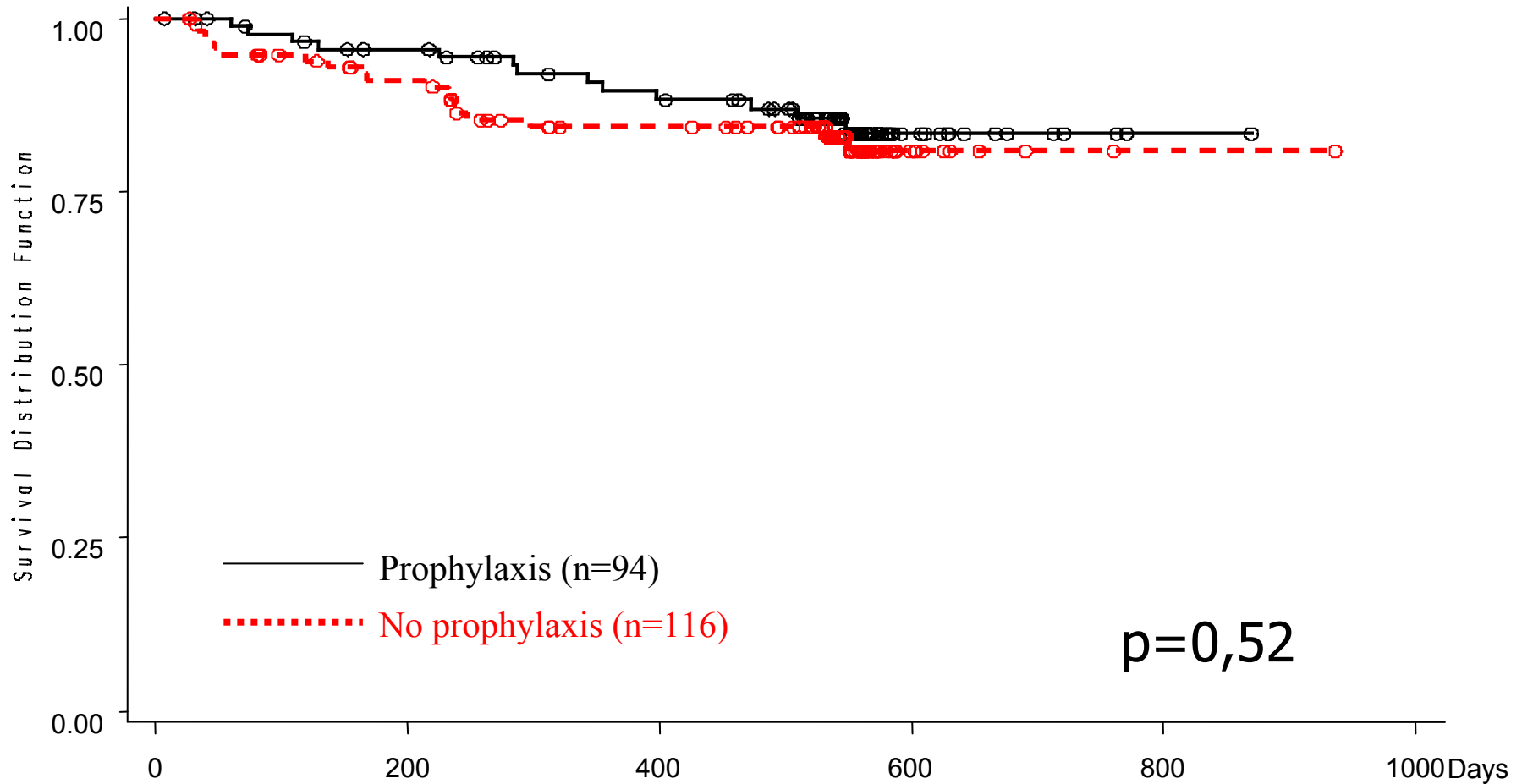
- 24 children (11%) did not complete the study.
- No follow-up data for 13 of them (8 in the prophylaxis group)
- 11 remaining children attended the 9-month check-up but not the end-study check-up, and were considered for the analysis.
- The analyses were therefore performed on 210 children, 94 treated with cotrimoxazole and 116 who received no prophylaxis.

# UTI-free survival



**Prophylaxis did not significantly reduce the UTI occurrence**

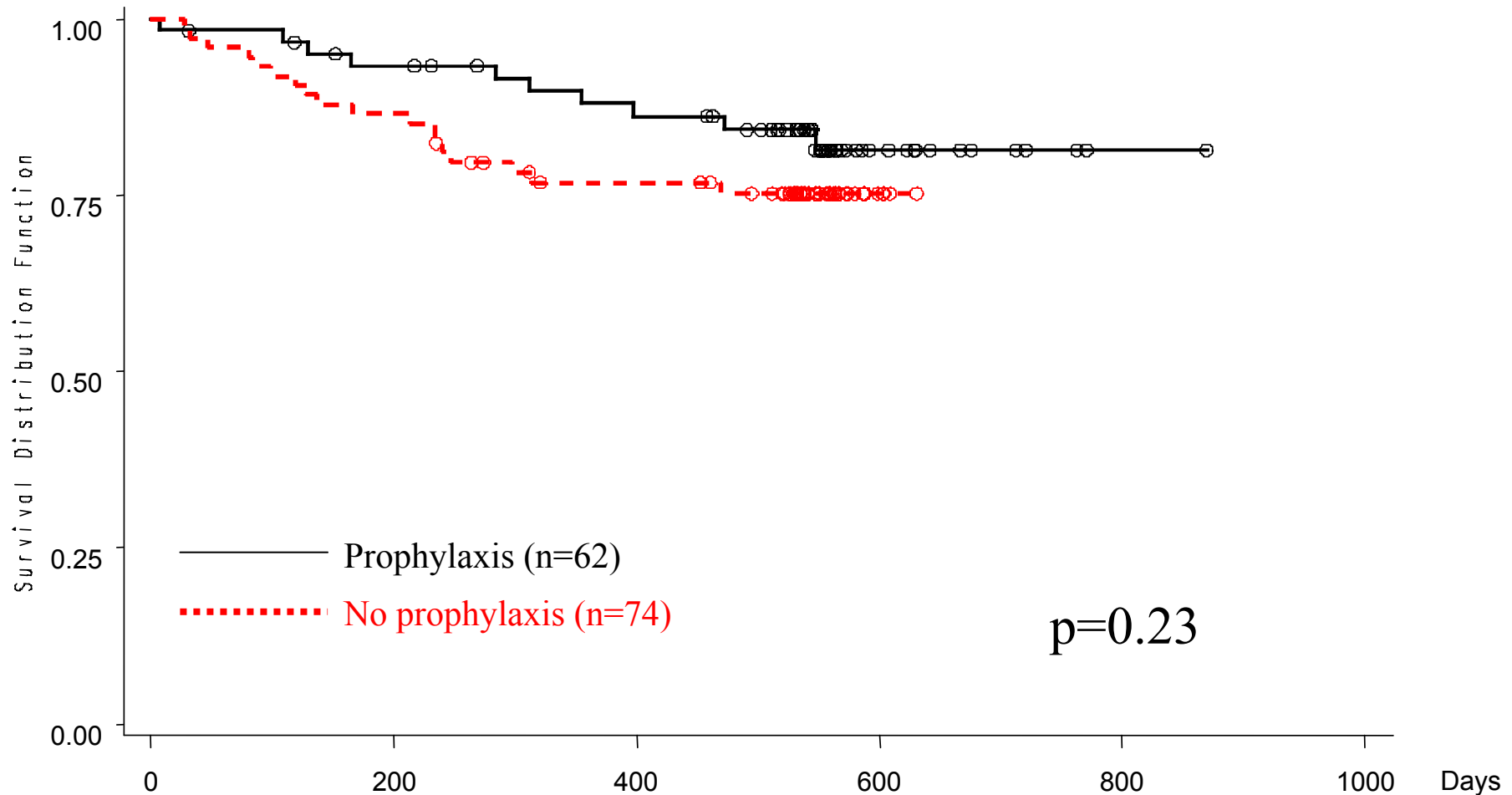
# Febrile UTI-free survival



**Prophylaxis did not significantly reduce the febrile UTI rate**

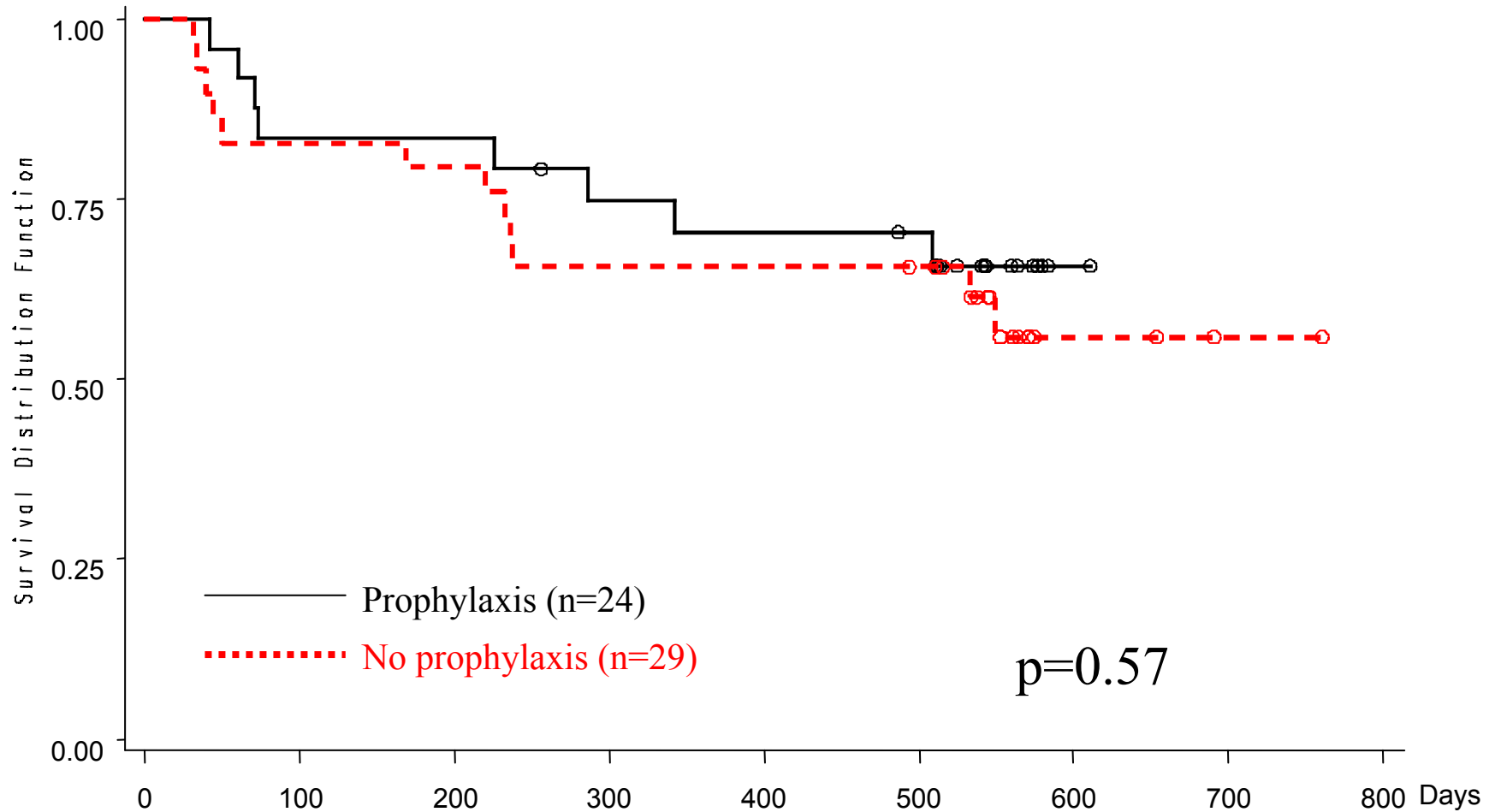


# UTI and grade II VUR



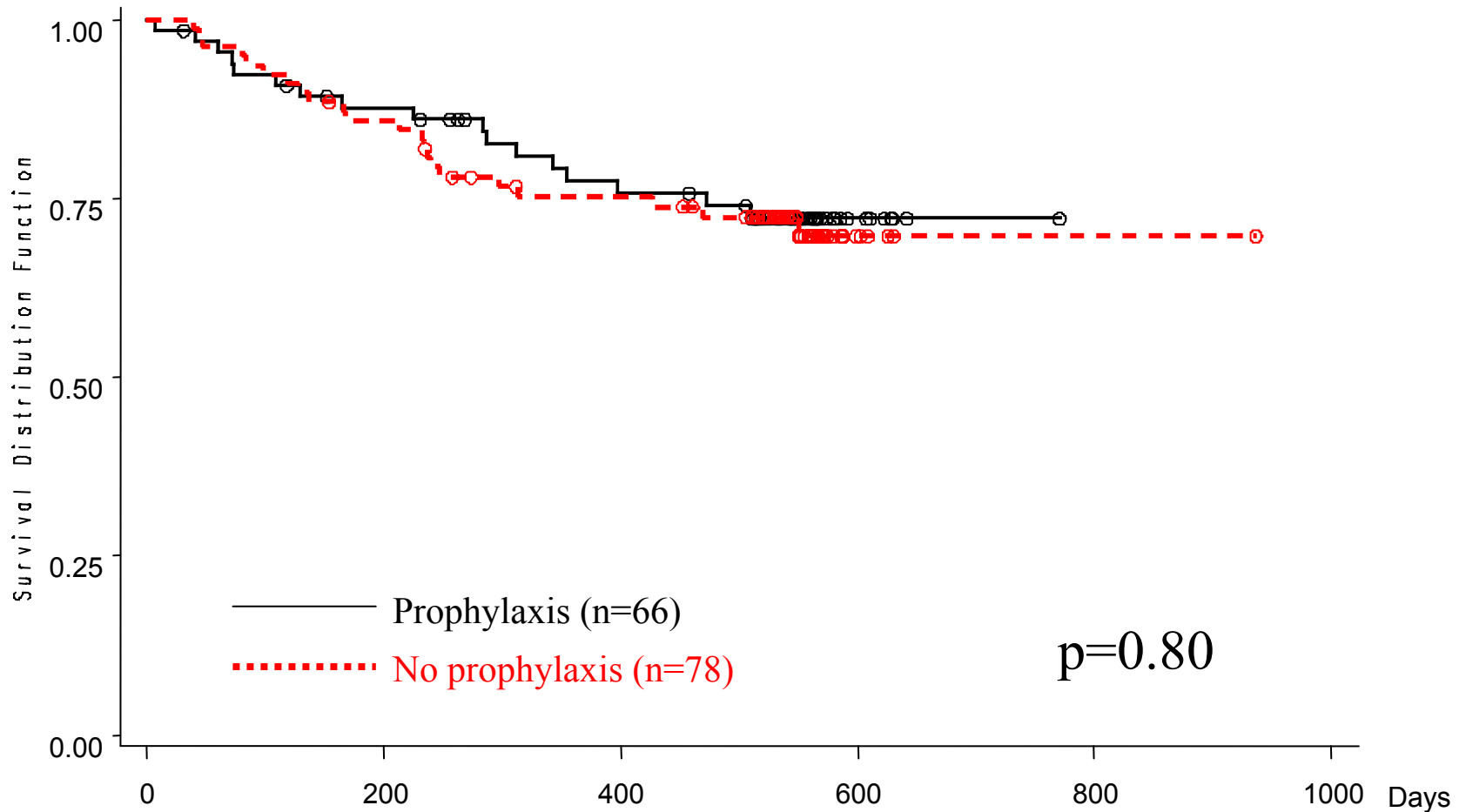
**Prophylaxis did not significantly reduce the UTI occurrence for children with grade II VUR**

# UTI and grade III VUR



Prophylaxis **did not significantly reduce** the UTI occurrence for children with **grade III VUR**

# UTI-free survival in girls

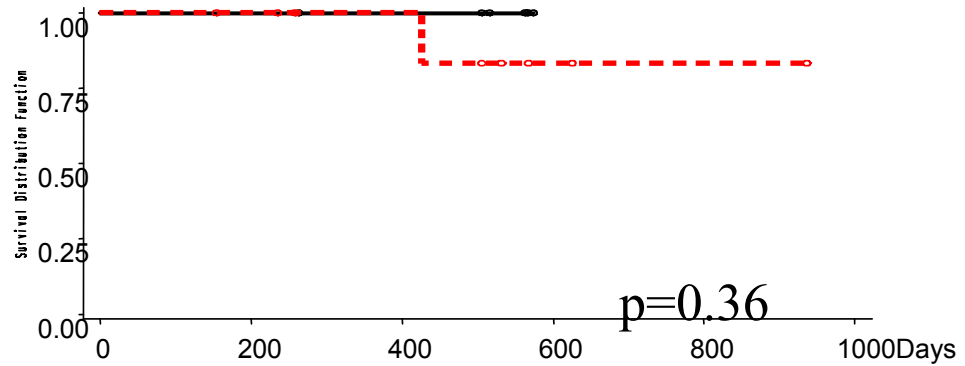


**Prophylaxis did not significantly reduce the UTI occurrence in girls....**

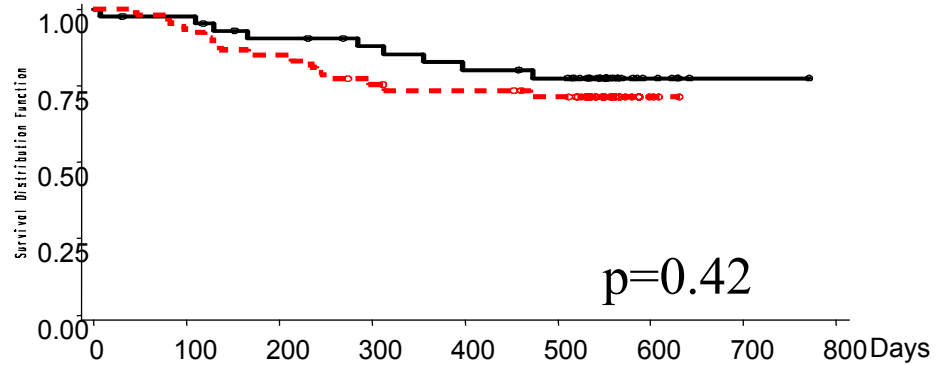
# ...for any grade of VUR

UTI-free survival in girls

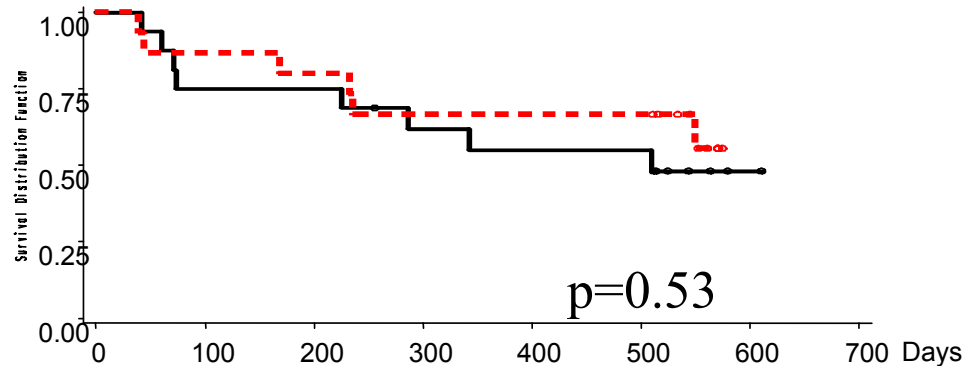
## Grade I VUR



## Grade II VUR



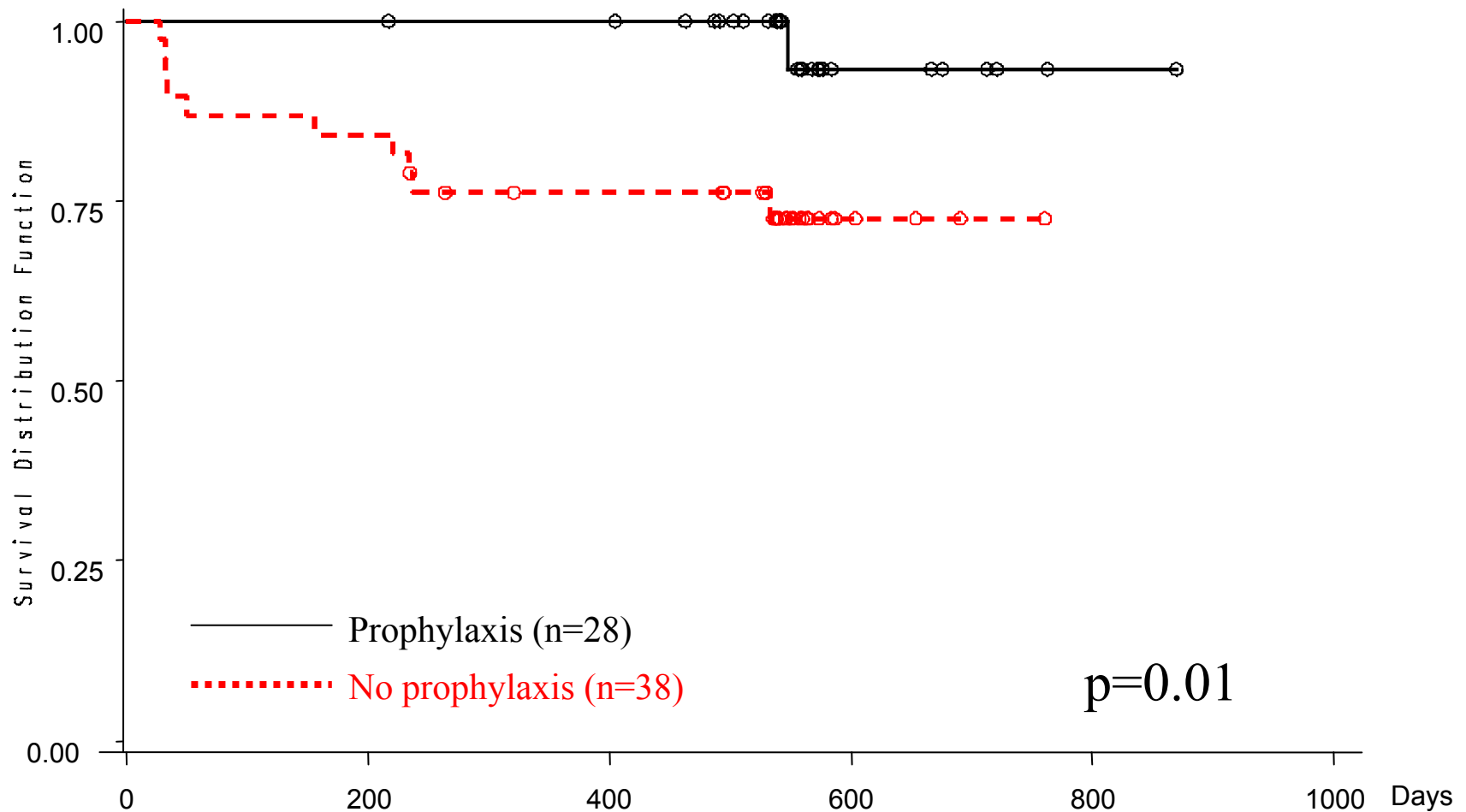
## Grade III VUR



— Prophylaxis

..... No prophylaxis

# UTI-free survival in boys

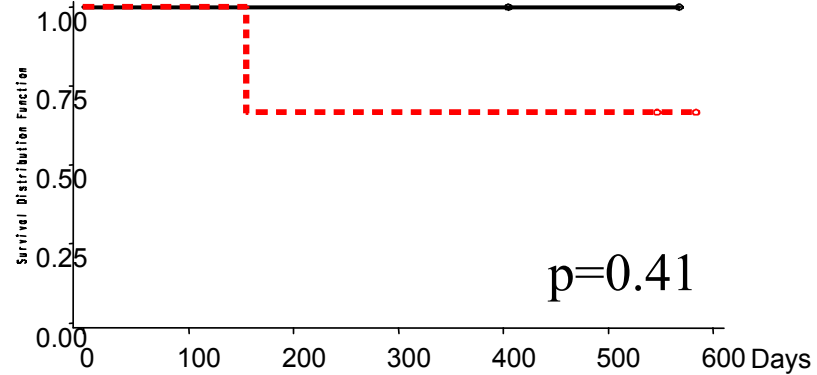


However, prophylaxis **significantly reduced** UTI in boys with low grade VUR...

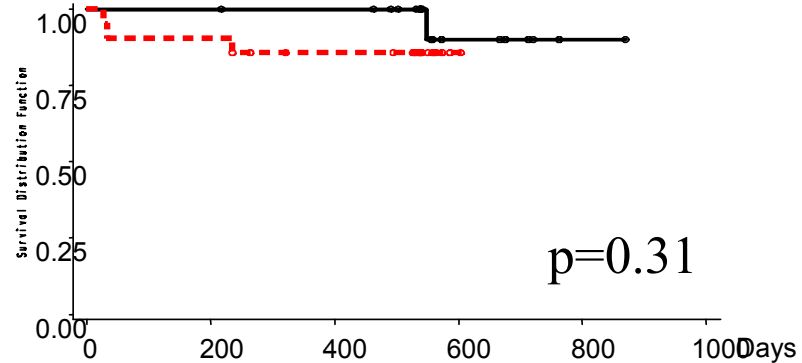
...in particular in **boys with grade III VUR**

UTI-free survival in boys

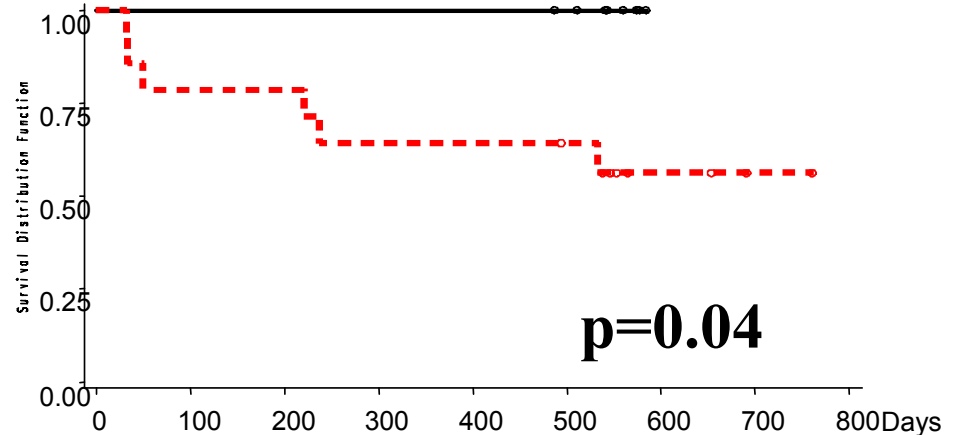
**Grade I VUR**



**Grade II VUR**



**Grade III VUR**



— Prophylaxis

..... No prophylaxis

# Methodological biases

- Absence of a placebo and lack of a double-blinded approach.
  - But similar monitoring in both groups
- Collection of urine
  - sterile bags
  - risks of contamination
  - But similar method of collection in both groups
  - Similar overestimation of UTI in the two groups?
- Absence of DMSA renal scan to define febrile UTI as acute pyelonephritis

# CONCLUSION

- No significant difference in the recurrence of UTI or febrile UTI between the treated and the control groups
- This suggested that antibiotic prophylaxis was ineffective in reducing the risk of UTI
- However, prophylaxis significantly reduced UTI in boys, specially with grade III VUR.

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