Urinary tract infections in children

Towards optimal management in primary care

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Urinary tract infections in children

Towards optimal management in primary care

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op het gebied van de Medische Wetenschappen

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Mirjam Harmsen

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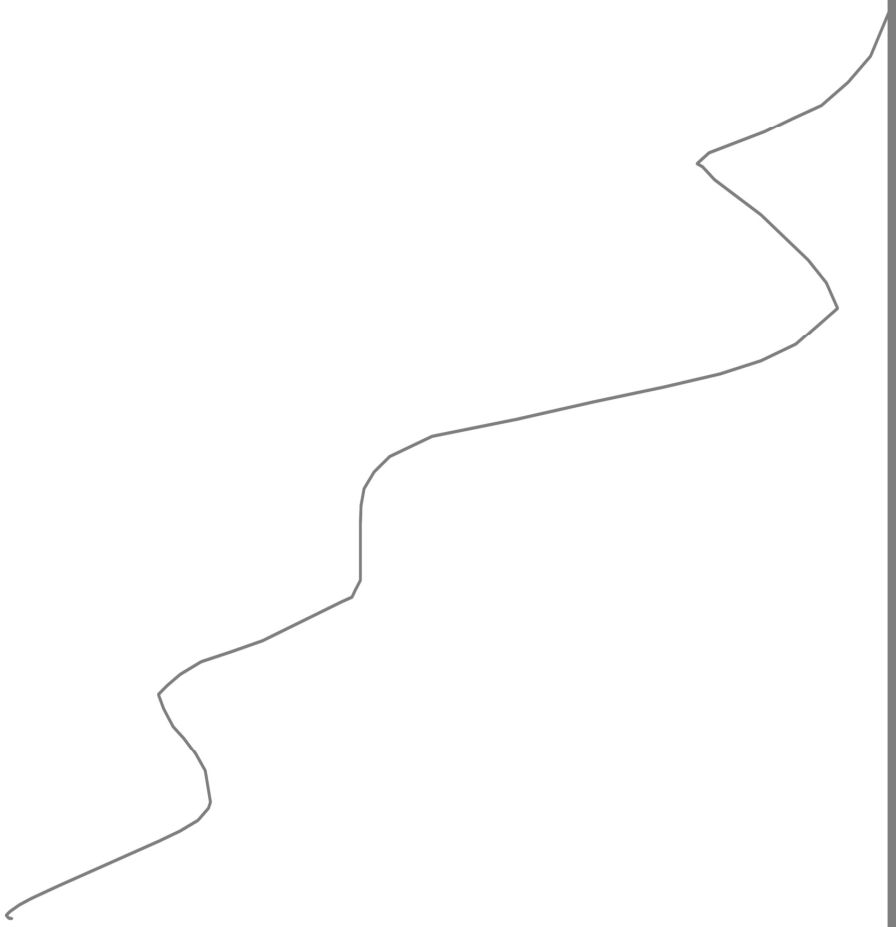
General introduction



Urinary tract infections (UTIs) in children might lead to serious health problems at an older age.[1] A timely and accurate diagnosis and treatment of childhood UTIs are considered to be important in order to prevent future renal problems.[2] The aim of the research in this thesis is to give an overview of the current diagnosis and treatment of UTIs in children in Dutch general practice, and to explore methods to improve current practice.

Clinical problem

The urinary tract infections we focus on in this thesis are cystitis and pyelonephritis. Cystitis is an inflammation of the bladder and is most times accompanied by a painful micturition (strangury) in combination with frequent micturition (pollakiuria). Sometimes there is also a painful urgency (dysury), abdominal pain, or blood in the urine (haematuria). Pyelonephritis is an infection of the upper urinary tract, causing inflammation of the kidney(s). Symptoms are (high) fever, cold shivers, vomiting, and flank pain. It is possible that there are no micturition problems. The most common causing bacterium is *Escherichia coli*, generally originating from the faecal flora. For adults, having a UTI is most times harmless. The problem is, however, that UTIs in children might lead to persistent renal scarring, which might lead to e.g. hypertension, complications during pregnancy, and even terminal renal failure.[1] Renal scarring associated with UTI varies according to the features of the UTI itself, from 1% in children with a UTI not requiring hospitalisation to 22% of hospitalised children.[3] Recurrent acute pyelonephritis is associated with a higher risk of renal damage.[4] The annual incidence of UTIs for girls and boys in the 1-6-year-old group in the Netherlands is respectively 2.6% and 0.5%.[5] About 20% of these children will have a recurrent infection.[6-8]

So, although having a UTI in adulthood is often harmless, having one at a younger age might have serious consequences. A timely and accurate diagnosis and treatment of UTIs in childhood are considered to prevent renal problems at an older age.[2] On the other hand, over-diagnosis and over-treatment need to be prevented, considering for example antibiotic resistance, medicalisation and health care costs. Besides that, diagnosing a UTI in young children is difficult. Most of their complaints are non-specific, like failure to thrive, vomiting and fever.[9] And although fever is almost always present in childhood UTIs,[10] it is also a common manifestation in all childhood illnesses. There is also the problem with obtaining a

urine sample, which can be time consuming, and special equipment may be necessary.[11]

There are several guidelines about the management of childhood UTIs,[12-16] but there are hardly any scientific studies focusing on this topic. Questions that remain are whether these guidelines are followed, and whether it is worthwhile to act according to the guidelines.

Guidelines on urinary tract infections in children

Guidelines across different countries advocate an active approach concerning diagnosis, prescription, follow-up, and referral of childhood UTIs.[12-16] Because the research in this thesis was based on the Dutch situation, in which the general practitioner is the first one to see the child with a (possible) UTI, we will from now on focus on the guideline developed by the Dutch College of General Practitioners.[15] Although this guideline does not focus exclusively on childhood UTIs, it does contain some recommendations particularly focusing on children. Following the terminology of the guideline, childhood UTIs are considered as complicated UTIs.

To diagnose a UTI, the first step is to perform a nitrite test. A negative test means the urine should also be tested using a dipslide or urine culture. A negative results means the probability of having a UTI is low. In case of a positive nitrite test and/or culture/dipslide test, a UTI is presumable. Before starting antibiotic treatment, urine for a culture should be collected, if not already done so. Medication of first choice for children under the age of 12 years is a combination of amoxicillin and clavulanic acid, or co-trimoxazole. After the treatment, the urine should be tested again by using a dipslide. A UTI in several groups of children might be caused by anatomical abnormalities of the urinary tract system, which means these children have to be referred to secondary care for further investigation. These groups are: all infants 6-12 months, all boys under the age of 12 years, girls aged 1 to 5 years with one recurrent UTI and girls aged 5 to 12 years with more than one recurrence. Infants younger than six months have to be referred for diagnostics and treatment.[15]

Health care professionals and others involved in the diagnosis and treatment of urinary tract infections in children

For a timely diagnosis and treatment, it is important that parents recognise a probable UTI in their child. As stated before, children with UTIs might have very non-specific symptoms, which makes it even harder for the parent to decide what to do. If they decide to seek medical advice, the first contact with a healthcare provider is almost always in general practice or, during out of hours, in general practice co-operatives. Practice assistants or triage nurses have to determine the need for urine testing and/or the need for the child to be seen by a general practitioner. There are protocols they have to follow, developed in accordance with the general practitioner, like the Telephone Triage Guide of the Dutch College of General Practitioners.[17] Often, the practice assistants also perform the urine tests. The general practitioner sometimes has to initiate urine testing, and has to initiate the antibiotic treatment, has to decide whether a child has to be referred to secondary care and has to initiate a follow-up contact. So, there are many people involved in a timely diagnosis and treatment of UTIs in children.

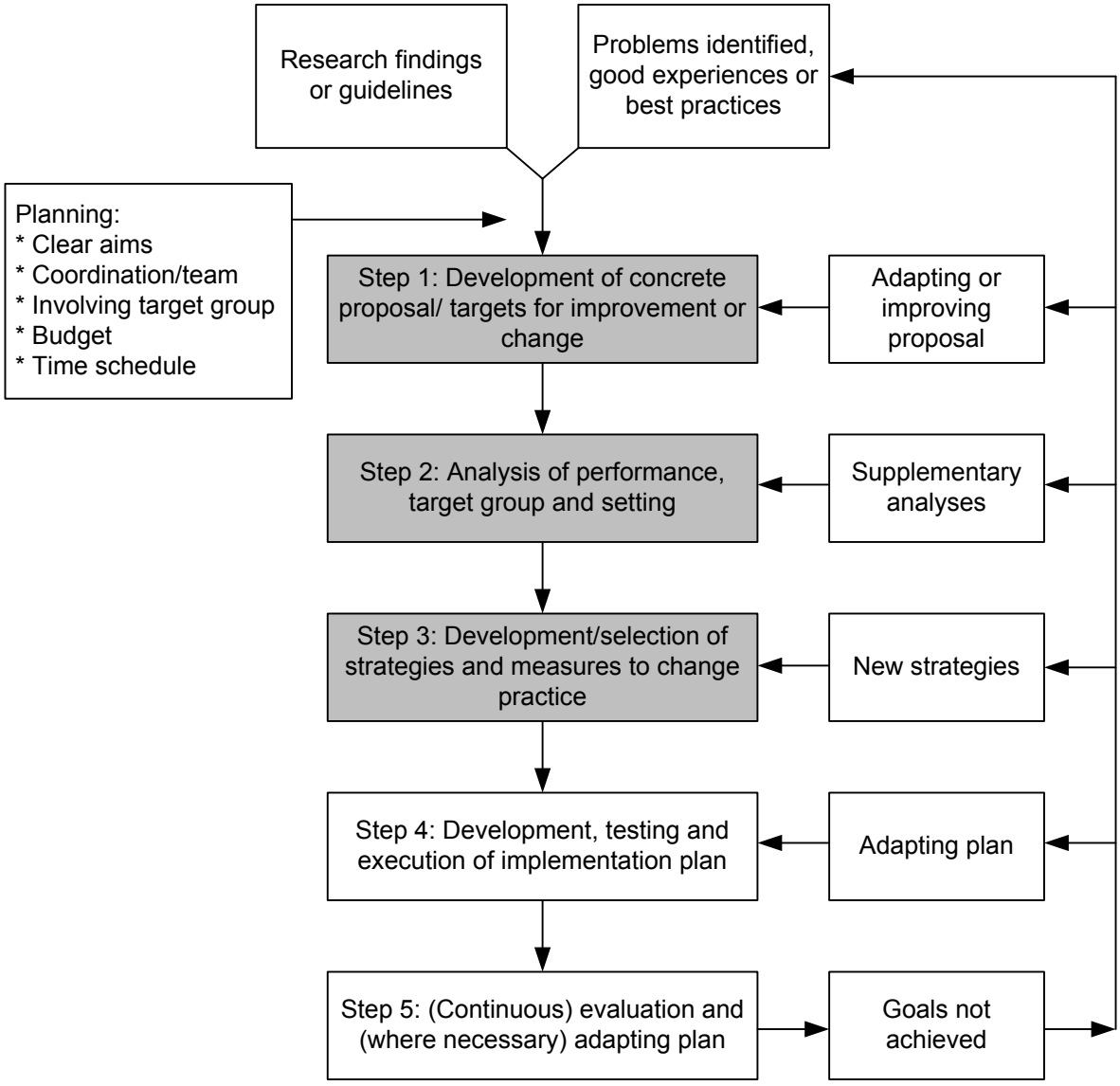
Improving quality of care

It is important to get insight into the current management of childhood UTIs in Dutch primary care, because professional performance, but also parent performance, might substantially improve clinical outcomes. To develop an effective intervention, it is important to adjust the intervention to the target group, because they are the ones who have to change their behaviour.[18] In the case of childhood UTIs, this means involving all groups mentioned above (i.e. parents, practice assistants/triage nurses, and general practitioners). Besides that, a systematic approach is recommended, including e.g. a pre-test of the intervention.[18]

Aims of this thesis

The overall aim of the research in this thesis is to give an overview of the current diagnosis and treatment of UTIs in children in Dutch general practice, and to explore methods to improve current practice. In order to end up with a solid intervention, several steps had to be taken. We followed the steps of the Model of Effective Implementation by Grol and Wensing (see figure).[18]

Figure. Model of Effective Implementation[18]



Following the steps in the model, our research questions were:

- Step 1 (chapters 1 and 7): What are the incidence rates of UTIs among children in Dutch general practice care and might there be problems in general practice management of UTIs in children? And, what aspects of the management of childhood UTIs in general practice care should be focused on?
- Step 2 (chapters 2-6): What are the strong and weak aspects of Dutch general practice performance concerning childhood UTIs?
- Step 3 (chapter 7): What methods can be used to improve general practice management?

Information from prevailing steps was used for the next steps. But also the other way around, which means for example that the information from step 2 was used to specify the information from step 1. Steps 5 and 6 will not be addressed in this thesis, however, some implications for future research and health policy are mentioned in the general discussion.

Outline of the thesis

In **chapter 1**, a study mainly focussing on incidence rates and their association with gender, season and urbanisation level is presented. It also presents a broad overview of the GPs' management in case of UTI, regarding prescription and referral to secondary care. The target group in this study were children 0-18 years old. From chapter 2 on, this thesis will focus on children aged 0-12 years. In **chapter 2**, an interview study about parents' awareness of and knowledge about young children's UTIs is presented. **Chapter 3** describes a study on guideline adherence of triage nurses at general practice co-operatives. In acute primary care, triage nurses are the first to have contact with worried parents who call because their child is ill. For a timely diagnosis and treatment of UTIs it is important triage nurses are aware of the fact that a child might have a UTI, especially since the symptoms may only be non-specific. How general practitioners in Dutch primary care diagnose childhood UTIs is described in **chapter 4**. The last source we used for getting insight into the management of UTIs in primary care was the database of the Netherlands Information Network of General Practitioners (LINH). The results of this study are presented in **chapter 5**, focussing on prescribing antibiotics, referral and follow-up. **Chapter 6** describes an economic modelling study. In this economic evaluation a maximum care strategy is compared to current care and to an improved version of current care, taking into account health care costs and QALYs (quality adjusted life years). Together with some general practitioners we set goals and developed an intervention to improve the quality of the management of UTIs in young children in primary care. **Chapter 7** describes the results of this process. This thesis concludes with a **general discussion**, giving an overview of all results and discussion of these in a greater context. The limitations of our studies as well as implications for future research and health policy are also discussed in this part of the thesis.

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Chapter 1

Incidence rates and management of urinary tract infections among children in Dutch general practice: results from a nation-wide registration study

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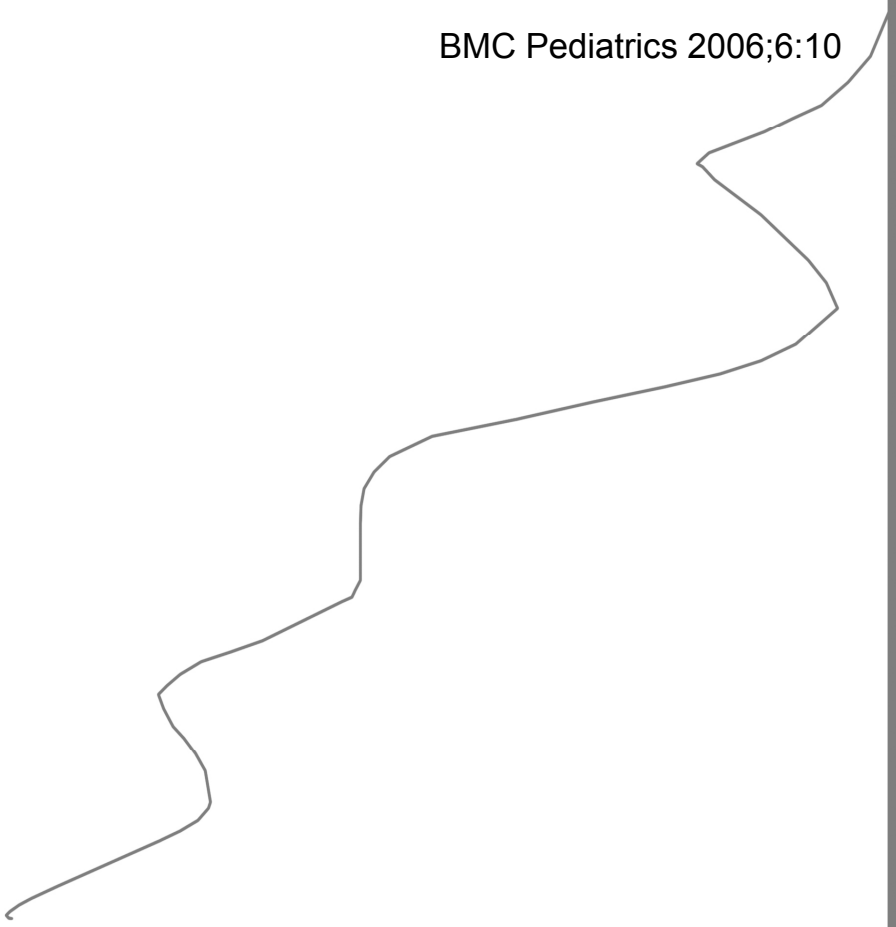

Abstract

Background: We aimed to investigate incidence rates of urinary tract infections in Dutch general practice and their association with gender, season and urbanisation level, and to analyse prescription and referral in case of urinary tract infections.

Method: During one calendar year, 195 general practitioners in 104 practices in the Netherlands registered all their patient contacts. This study was performed by the Netherlands Institute for Health Services Research (NIVEL) in 2001. Of 82,053 children aged 0 to 18 years, the following variables were collected: number of episodes per patient, number of contacts per episode, month of the year in which the diagnosis of urinary tract infection was made, age, gender, urbanization level, drug prescription and referral.

Results: The overall incidence rate was 19 episodes per 1000 person years. The incidence rate in girls was 8 times as high as in boys. The incidence rate in smaller cities and rural areas was 2 times as high as in the three largest cities. Throughout the year, incidence rates varied with a decrease in summertime for children at the age of 0 to 12 years. Of the prescriptions, 66% were in accordance with current guidelines, but only 18% of the children who had an indication were actually referred.

Conclusion: This study shows that incidence rates of urinary tract infections are not only related to gender and season, but also to urbanisation. General practitioners in the Netherlands frequently do not follow the clinical guidelines for urinary tract infections, especially with respect to referral.

Background

Urinary tract infections in childhood are common and may be difficult to diagnose in young children because of non-specific symptoms. Symptoms such as fever, vomiting, screaming, anorexia and irritability may indicate a urinary tract infection, but they are also common in other childhood diseases.[1,2]

The incidence of urinary tract infections during childhood is not only influenced by age, but also by gender. Before the age of 3 months, urinary tract infections are more common in boys; thereafter the incidence is considerably higher in girls.[3,4] In younger children, urinary tract infections are mainly caused by autoinfection with commensals from the intestinal tract,[5] whereas urinary tract infections in adolescent girls are often related to sexual activity.[6]

Reported incidence rates of childhood urinary tract infections vary. Table 1 shows incidence rates and study characteristics of eight studies that covered a substantial age range.[2,7-13] For boys the reported incidence rates range from 0.17 to 18 per 1000 person years and for girls from 0.4 to 66 per 1000 person years. This variation may be explained by differences in setting, health care system, age range, case definition, or study period. The range of occurrence rates found in the studies carried out in general practice is much smaller.

Urinary tract infections in children are an important cause of renal damage and chronic renal failure. Early diagnosis, treatment, investigation and follow-up of children with urinary tract infections are likely to reduce such long-term complications.[14,15] A guideline developed by the Dutch College of General Practitioners is available.[16] According to this guideline, nitrite testing should be performed, which, in case of a negative outcome, should be followed by a culture. Medication of first choice for children under the age of 12 years is a combination of amoxicillin and clavulanic acid or co-trimoxazole. For children older than 12 years, trimethoprim and nitrofurantoin are alternatives. The following patients should be referred for further investigation: all infants under the age of 1 year, all boys under the age of 12 years, girls aged 1 to 5 years with only one recurrence and girls aged 5 to 12 years with more than one recurrence.

The frequency of urinary tract infections in relation to age and gender, as well as diagnostic procedures and treatment, were investigated in several studies.[1,2,4,9,17-19] However, little is known about seasonal variation and urbanisation. Seasonal variations in the incidence of human disease are commonplace, but in the case of urinary tract infections this aspect has rarely been addressed.[7,9,20] Therefore, our first aim is to describe incidence rates of

Table 1. Incidence rates of urinary tract infections in children reported in previous studies

author	country, period	setting	age group	incidence (per 1000)	
				boys	girls
Stansfield 1966[7]	UK 1957-1964	child referred to hospital for UTI	0-14	0.17	0.4
Winberg 1974[8]	Göteborg 1960-1966	hospital	0-11	11	30
Uhari 1988[10]	Finland 1978-1984	hospital admission for UTI	0-14	2	7.5
Pead 1994[11]	UK 1991-1992	culture requests positive	0-12	13.9	37
Mårild 1998[9]	Sweden 1979-1981	UTI diagnosed in hospital	0-6	18	66
Brooks 1977[12]	UK 1970-1974	UTI diagnosed in general practice	0-14	3.8	7.7
Dickinson 1979[13]	UK (period unknown)	UTI diagnosed in general practice	0-14	1.7	3.1
Van de Lisdonk 2000[2]	Netherlands 1971-1990	diagnosed in general practice	0-12	2.9	24.3

UK=United Kingdom, UTI=Urinary tract infection

urinary tract infections among children in Dutch general practice in 2001 by age, gender and in relation to season and urbanisation level. It is important to know if there is a relation between these factors and urinary tract infections, because this could provide general practitioners information about patients in which they should be more alert for urinary tract infections. In addition, we are interested if general practitioners follow the clinical guideline for urinary tract infections with respect to prescription and referral.

Methods

Design

We used data from the Second Dutch National Survey of General Practice, which was performed by the Netherlands Institute for Health Services Research (NIVEL) between April 2000 and January 2002.[21,22] During the study period, 195 general practitioners in 104 practices throughout the Netherlands prospectively registered data about all their patient contacts during one calendar year. The participating general practitioners and practices were representative for all Dutch general practitioners and practices with regard to age, gender and location, including deprived areas.

In the Dutch health care system, general practitioners act as gatekeepers for secondary care. Every Dutch citizen is registered in general practice.

Measurements

For socio-demographic characteristics (among which urbanisation) a short questionnaire was used and sent by mail to all patients registered in the participating practices (n=385,461). Response on the questionnaire was 76%. Characteristics, such as date of contact, type of contact, diagnosis (coded by the general practitioner (GP) using the International Classification of Primary Care, ICPC),[23] drug prescription and referrals by the general practitioner, were registered for each contact by the general practitioner. The contact database was episode orientated, meaning that different consultations concerning the same health problem were clustered into one episode.[21] Only new episodes, starting during the registration period, were included in our analysis. We excluded eight practices, because of incomplete registration.

Patients

Data were used from all children who were aged 0 to 18 years any time during the registration period. Of these, we selected all children with the diagnosis urinary tract infection (ICPC-code U71). This code excludes pyelonephritis, but does include recurring infections.[19]

For all selected cases, the following variables were examined: number of episodes per patient, number of contacts per episode, month of the year in which the diagnosis was made, age, gender and urbanisation. Urbanisation was divided into the following four categories: <30,000 inhabitants, 30,000–50,000 inhabitants, >50,000 inhabitants and the 3 largest cities (Amsterdam, Rotterdam, The Hague).

Ethical approval

The study was carried out according to Dutch legislation on privacy. The privacy regulation of the study was approved by the Dutch Data Protection Authority. According to Dutch legislation, obtaining informed consent is not obligatory for observational studies.

Statistical analysis

Statistical analyses were performed using SPSS 11 and Stata 8 SE. We first computed the incidence rate of urinary tract infections in general practice. To determine the incidence rate, the denominator was calculated by summating the total time period children were followed during the study period (patient years). The 95% confidence intervals of incidence rates were calculated assuming a Poisson distribution.

We analysed drug prescription and referral by general practitioners anywhere during the episode, comparing these to the recommendations in the guideline on urinary tract infections developed by the Dutch College of General Practitioners.[16] We used cut-off points for age with respect to prescription and referral, similar to the guideline for urinary tract infection of the Dutch College of General Practitioners.

Results

The total patient population consisted of 385,461 persons, of which 82,053 were at the age of 0 to 18 years.

Of all episodes of children at the age of 0 to 18 years, 1.15% (1695 episodes) was diagnosed as a urinary tract infection (95% confidence interval [CI], 1.10-1.21).

Of all children with a urinary tract infection (n=1460), the mean number of episodes per year was 1.2 per child, with a maximum of 5 episodes during the registration period of one year. For each episode of urinary tract infection, the mean number of consultations was 1.7, with a maximum of 13 consultations. The proportion of episodes with only one consultation was 66%.

We found an overall incidence rate of 19.0 episodes of urinary tract infections presented in general practice per 1000 person years for children under the age of 18 years (95% CI: 18.1-19.9). In other words; if 1000 children, aged 0 to 18 years, are followed for one year, their general practitioner will have made 19 times a diagnosis of a urinary tract infection. The incidence rate in girls was almost 8 times as high as in boys (respectively 34.4 episodes per 1000 person years vs. 4.4 episodes per 1000 person years, $p<0.001$). Incidence rates of urinary tract infections for each year of age for both girls and boys are given in Figure 1. For girls the incidence gradually increased after the age of 12.

Furthermore, the incidence rates varied throughout the year. A decrease of incidence rates in summertime was mainly found in children at the age of 0 to 12 years, with a range from 27 episodes in March per 1000 person years to 13 episodes in July (Figure 2).

The incidence rate in smaller cities and rural areas was 2.1 times as high as in the three largest cities, respectively 18.9 episodes per 1000 person years vs. 8.9 episodes per 1000 person years, $p<0.001$ (Figure 3).

Figure 1. **Incidence rates of urinary tract infections by age for boys and girls, 95% error bars**

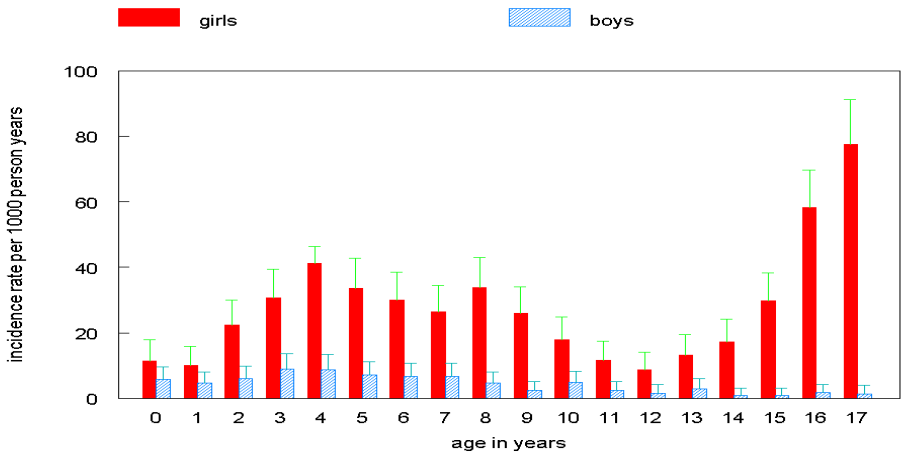

Figure 2. **Incidence rates throughout the year by age group, 95% error bars**

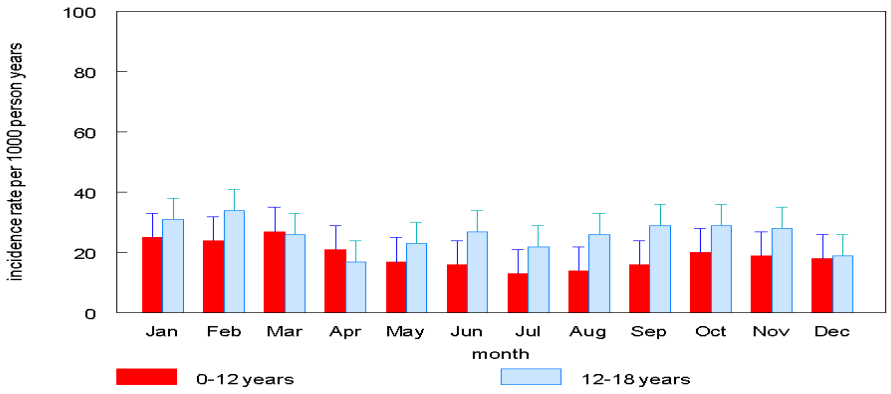

Figure 3. **Incidence rates according to urbanisation, 95% error bars**

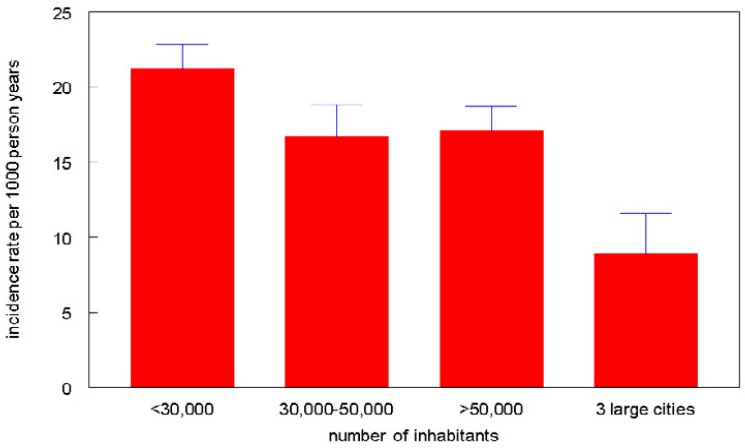

Table 2. Number and proportion of prescriptions in accordance with the Dutch guideline for urinary tract infections, by age and sex group

age group (in years)	total number of prescriptions			prescriptions for medication of first choice number (%)		
	girls	boys	total	girls	boys	total
0-2	59	26	85	45 (76%)	12 (46%)	57 (67%)
2-7	485	83	568	261 (54%)	33 (40%)	294 (52%)
7-12	387	39	426	166 (43%)	26 (67%)	192 (45%)
12-18	669	28	697	605 (90%)	23 (82%)	628 (90%)
total	1600	176	1776	1077 (67%)	94 (53%)	1171 (66%)

Table 3. Number of children to be referred in accordance with the guideline for urinary tract infections, and actual referrals, by age and sex group (n=225)

category	number of children to be referred according to guideline	actual referrals number (%)
girls and boys, 0-year of age	42	13 (31%)
boys, aged 1-12 years	147	18 (12%)
girls, 1 recurrence, aged 1-5 years	27	6 (22%)
girls, >1 recurrence, aged 5-12 years	9	3 (33%)
total	225	40 (18%)

General practitioners prescribed medication for urinary tract infections 1776 times, to 1131 children (77% of all children in whom a urinary tract infection was diagnosed). When they chose to prescribe medication, 66% (1173 times) of the prescriptions were in accordance with the guideline of the Dutch College of General Practitioners. This percentage varied with age. The general practitioners deviated more frequently from the guideline for children under the age of 12 years than for children older than 12 years (Table 2). Children approaching the age of 12 years more often received medication for urinary tract infection advised in older children, such as trimethoprim and nitrofurantoin. Differences between boys and girls in the proportion of first choice medication were statistically significant for the first three age groups ($p<0.05$), favouring girls for age groups 0-2 and 2-7, but favouring boys for age group 7-12.

In total 120 children were referred 134 times, of which 67% (90 times) to secondary care and 33% (44 times) to primary care. Of the children who should be referred according to the guideline (n= 225), only 18% (40 children) were actually referred. This percentage varied with age and gender (Table 3). Especially boys under the age of 12 were seldom referred (12%). The remaining 80 children had no indication for referral according to the guideline.

Discussion

In this study, we found an overall incidence rate of 19 episodes of urinary tract infections presented by children in general practice per 1000 person years. This is strikingly similar to the incidence rate of 18.6 episodes per 1000 person years in 1987, found in the first National Survey, the design of which was very similar.[22] It appears that the incidence rate hardly changed over the past 15 years. Our results may be considered representative for all children treated in primary care in the Netherlands.

We found a significantly higher incidence rate for girls (34.4 episodes per 1000 person years) than for boys (4.4 episodes per 1000 person years). Earlier studies also showed that urinary tract infections are more common in girls, but the male/female ratio of incidence rates varied. Comparing our results to those of earlier studies in other countries (Table 1), shows that our findings for boys are comparable to the other studies in general practice (range 1.7-3.8), but for girls our results are much higher (range of other studies in general practice (3.1-24.3). Especially the UK studies performed in the seventies[12,13] show very low figures. A possible explanation of the higher incidence we found in girls than the Dutch study by Van de Lisdonk[2] is the greater age range in our study.

Our results showed a variation of the incidence rate throughout the year, with a decrease in summertime. This decrease was mainly found in children below the age of 12 years. Elo et al.[3] and Stansfeld[7] also found a decrease of incidence rates during the summer. A possible explanation, suggested by Stansfeld,[7] is that upper respiratory tract infections may precede urinary tract infections. Since cough and colds are more common in the winter months, the same would apply to urinary tract infections.[7]

On the other hand, Jakobsson[20] found a higher diagnostic rate during the summer months, and a Korean study found pyelonephritis incidence peaking in summer.[24] Mårild[9] found no seasonal variation at all. Differences in age groups and composition of study populations may contribute to these conflicting results.

For example, the study of Jakobsson[20] only collected information from children under the age of two years, whereas the children in the study of Mårild[9] were younger than six years. The age groups of children in the studies of Elo et al.[3] and Stansfeld[7] were more similar to our age group, and the Korean study[24] included patients of all ages. Moreover, none of these studies were carried out in general practice, but obtained their information from pediatric centers or from health insurance claims data.

The incidence rate in smaller cities and rural areas is significantly higher than in the three largest cities. Although less clear, a similar trend was found in the first National Survey. An explanation could be that children with urinary tract infections in the three largest cities are more inclined to visit the hospital (emergency department) instead of the general practitioner. General practitioners in the three largest cities will miss these episodes during their registration period, resulting in a lower incidence rate. It is not likely that the discrepancy could be fully attributed to this explanation, therefore the clinical and epidemiological significance of urbanisation remains to be determined. A study carried out in Northern Norway (all ages) did not show a difference.[25]

When general practitioners chose to prescribe medication for urinary tract infections, 66% of the prescriptions were in accordance with the guideline of the Dutch College of General Practitioners. This percentage varied with age. It is possible that general practitioners are less familiar with prescription of medication for urinary tract infections in younger children.

Our analyses showed that only 18% of the referrals corresponded with this guideline. This could be an underestimation, because some of the patients may have had episodes of urinary tract infections before the registration period started. It appears that general practitioners are reluctant to refer children with urinary tract infections. It is also possible that they do not know the guideline or that they do not agree with it. Further investigations into this referral behaviour are necessary. Dependent on the findings, consequences for education of general practitioners may be considered.

Conclusion

In conclusion, this study shows that incidence rates of urinary tract infections are not only related with gender and season, but also with urbanisation. Furthermore, general practitioners in the Netherlands do not always follow the guideline for urinary tract infections developed by the Dutch College of General Practitioners

concerning prescription and referral. Especially the referral behavior of general practitioners differs considerably from the guideline.

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Chapter 2

Parents' awareness of and knowledge about young children's urinary tract infections

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Abstract

Objective: To provide insight into parents' awareness of and knowledge about urinary tract infections (UTIs) in young children.

Methods: Twenty interviews with parents who had a child recently diagnosed with a UTI were audiotaped, transcribed verbatim, and qualitatively analysed.

Results: Most parents knew the typical symptoms related to UTI. But, according to the parents, neither they nor all general practitioners (GPs) thought of a UTI in case of atypical symptoms. The awareness that UTI can be a serious illness usually came to parents later, partly because health care workers often did not explicitly mention this. According to the parents, health care workers should be more aware of UTIs in children. Parents felt that health education or mass screening might not be desirable because it would increase anxiety or would be perceived as not relevant.

Conclusion: Parents could not consistently recognise UTI in their children and were most times unaware of the possible consequences of a UTI. Nevertheless, parents were sceptical about health education and mass screening.

Practice implications: There seems little scope for health education addressed at parents or screening for UTI in young children. Instead, physicians and nurses should be alert for the possibility of UTIs in young children, and more information should be given once a UTI is diagnosed.

Introduction

The annual incidence of urinary tract infections (UTIs) is 2.6% for girls and 0.5% for boys in the 1-6-year-old group in the Netherlands.[1] Besides pneumonia, UTIs were the most prevalent serious infections in Belgian children.[2] A timely diagnosis and treatment of children's UTIs is presumably required to avoid adverse outcomes such as renal scarring, which is likely to affect 5-15% of young children with UTI.[3-6] Renal scarring is associated with serious health problems in later life, such as hypertension, complications during pregnancy, and renal failure.[7] About 20% of children will have a recurrent infection,[5,8,9] which will increase the chance on adverse outcomes. Awareness of the importance of timely diagnosis and treatment of children's UTIs is growing. For example, clinical practice guidelines on UTI recommend an active diagnostic approach in young children.[10-13] The Dutch guideline on UTIs states that children with a UTI can be treated in primary care, unless they are male or have recurrent infections; then they should be referred to hospital for further diagnostics. Antibiotics should always be given, and after the treatment urine should be tested to find out whether the UTI is cured.[11]

The problem with detecting UTIs in children is that most children do not have the typical symptoms adult patients have, like pain when voiding and frequent voiding. Children have more atypical symptoms, like fever (Box 1 gives an overview of the typical and atypical symptoms related to UTIs).[14] So it is hard for parents, and general practitioners (GPs), to detect a UTI in children. There is, however, little research into parents' perspectives on the detection and treatment of children's UTIs, despite the fact that parents are the ones who decide to seek medical advice and who have to comply with medical treatment advice. The only study found focused mainly on parents' opinions of the diagnosis of UTI and how helpful parents had found the information they had been given.[15]

As far as we know, no other study focused on awareness of parents themselves and their knowledge about UTIs in children. Better insight into these topics could point out ways to improve the detection of UTIs in general practice. The aim of this study is to provide insight into parents' awareness of and knowledge about UTIs in young children, in order to identify areas for quality improvement in the general public and in general practice. In the light of this, we also explored parents' ideas about mass media to improve public awareness, and their ideas about mass screening.

Box 1. Overview of atypical and typical symptoms related to urinary tract infections (UTIs) in children[21]

Atypical UTI-related symptoms	Typical UTI-related symptoms
• General malaise • Fever • Abdominal pain, flank pain • Diarrhea • Vomiting • Weight reduction, delayed height growth	• Dysury, strangury (painful micturation) • Pollakiuria (frequent micturation) • Haematuria (blood in urine) • Incontinence

Methods

Design

We performed a qualitative interview study with parents of children diagnosed with UTI. The Regional Committee on Medical Research Ethics, Nijmegen, the Netherlands, approved the study, and all parents provided written consent.

Participants

The participants in this study were parents who had a child (aged ≤ 12 years old) recently diagnosed with a UTI (<1 year ago) or still in the middle of a UTI episode; this last criterion to prevent recall bias as much as possible. In the Netherlands, all UTIs in children are considered to need medical attention,[11] so no distinction was made between cystitis or pyelonephritis. The diagnosis was made by the GP by means of urine tests, with bag samples or midstream samples. The parents were recruited through their GPs, who were participating in our GP-interview study. These GPs were a random selection from a database with GP addresses, working within a 2h drive by public transport from Nijmegen, The Netherlands. The interviews were conducted at the parents' homes. In order to collect a variety of viewpoints, a total of 20 interviews were planned in a predefined period of time.

Interview protocol

Two researchers conducted semi-structured interviews, which lasted 30-60 min. First, the parents were asked to tell the story about their child's UTI. Questions in the interview guide were used as a helping hand, to ensure that all participants touched on a list of predefined topics: awareness of UTI, knowledge of UTI, and health education and screening (see Box 2 for more details). These topics were

Box 2. Interview topics and related questions

Topic	Interview question
Awareness of UTI	• Reason going to the GP • Thought of a UTI (parents, GP) • Questions asked by GP • Possibility of 'missing' a UTI
Knowledge about UTI	• Explained why it is important to detect UTIs in time • Current knowledge and ideas about UTI • Knowledge other parents
Health education and screening	• Written information • Advice (from GP, assistant, others) • Mass media • Mass screening

GP=General practitioner, UTI=Urinary tract infection

derived from literature, like guidelines[11-13] and another study that addressed this topic.[15]

Analysis

The interviewers audiotaped and transcribed the interviews verbatim with the computer programme Atlas.ti 4.2.[16] Broad categories of interest that corresponded to the main topics of the interview guide were chosen before the analysis was done. One investigator read and condensed the transcripts. Extracts of statements were made from the transcripts for each identified view within the categories of interest. Because of the predefined questions that had to be addressed during the interviews and the predefined categories for analysis, another researcher only checked these extracts. In the results section, 'some' is used for less than 10 parents, 'many' for 10-15 parents, and 'most' for 16-20 parents.

Results

A total of 20 interviews were conducted: 18 times with the mother alone, 1 time with the father alone and 1 time with both. In five families, two children had had a UTI; in two interviews both children were discussed, while in the other three interviews only the most problematic case was discussed. In all these cases, the inclusion criterion of 'recently diagnosed' was applied. The interviews were about 4 boys and 18 girls, and all but 1 was younger than 6 years when their first UTI occurred. Nine children had one UTI, four had two UTIs, and eight had more than

Table 1. Parent and child characteristics

Id	Parents (n=20)		Children (n=22)			
	Sex interviewed parent	First child with UTI in family?	Sex	Age first UTI	Age last UTI	Total number of UTIs
1	F	Y	F	4	4	1
2	F	n.a.	F	5	5	1
3	F	N	F	<1	1	>>1
4	F	Y	M	<1	<1	1
5	F	Y	F	5	8	3
6	F	Y	M	<1	<1	1
7	M, F	Y	F	7	7	1
8	F	Y	F	3	3	2
9	F	Y	F	3	12	>>1
10	F	Y	F	<1	1	?
11	F	Y	F	<1	7	>>1
12	F	N	F	<1	6	6
13	F	Y	F	4	6	10
14	F	n.a.	F	6	8	2
15	F	N	M	1	1	1
			F	3	4	2
16	F	n.a.	F	11	12	2
17	F	N	F	1	1	1
18	M	Y	M	<1	<1	1
19	F	N	F	5	5	1
			F	2	4	3
20	F	Y	F	6	10	>>1

F=Female, M=male, Y=yes, N=no, n.a=not applicable, >>1=a lot more than 1 (exact number unknown), ?=unknown

three UTIs. Of one child it is unknown how many UTIs it had. See Table 1 for an overview of the parents and their children. The quotes in Box 3 are presented to illustrate the various viewpoints. No new topics derived from the interviews.

Awareness of UTI

When parents visited the general practice because their child had typical UTI symptoms such as pain when voiding, then they often thought of a UTI themselves. Parents visiting the practice with their child for more atypical symptoms, like abdominal pain (sometimes extreme), abdominal pain for a long time, vomiting, high fever (possibly fluctuating), and general malaise, most times

Box 3. Illustrating viewpoints

Awareness of UTI

''... The persisting pain was really strange for her. And on the second day we were really worried. Because if you see your child so listless... it is so unlike her even if she has a cold or fever ...'' (parent 2)

''... What I found most unpleasant was that the GP did not think of it. A lot of problems could have been prevented ...'' (parent 3)

''... If they are somewhat older, then you will probably notice if it hurts. When they are very small, then ... I knew she was in pain, but we did not know where ...'' (parent 3:31/41)

''... I think that a parent knows what a UTI is like. When your child goes to the toilet a lot and voids little bits, then you can't help thinking, 'this is not normal'. That is what I think. ..'' (parent 20:21)

Knowledge of UTI

''... But yes, I did not think of the consequences, that it can damage the kidneys. If you know about the process, then it is easy to understand. But if the GP says, 'Well, she has a UTI', I would not think that it might be dangerous to the kidneys ...'' (parent 7)

''... What was lacking in the information given was information about the future, what you can expect with such a child. When I asked questions, they kind of ignored them: 'We can't tell you anything about that.' I found that hard ...'' (parent 6)

Health education and screening

''... I think you only get really interested when your child actually has something. Or, with those symptoms, that people start to think 'Yeah, I read something about that ...'' (parent 1)

''... I think it is of no use because it is possible the child does not have a UTI just at that moment. It will only cause you and the GPs a lot of work''' (parent 13)

GP=General practitioner, UTI=Urinary tract infection

did not think of a UTI. The reasons for many parents to contact the GP even though their child had only atypical symptoms were that the child's behaviour was different and the atypical symptoms looked more severe than when the child had a common illness. But also the GP did not always think of a UTI, even when the child had typical symptoms. With hindsight, some parents felt disappointed that their GP had not thought of a UTI or, in some cases, that the GP had said that there was nothing to be worried about. In about a fourth of the cases a delay in diagnosis was on the GP's side. In a smaller number of cases the delay was on the parent's side.

There was discrepancy between parents about the idea that UTIs in children can easily be missed. Some parents thought so if children have atypical symptoms. Some other parents thought it to be very unlikely that they would miss

a UTI, especially if they have good contact with the child. They would expect to observe a change in voiding, for example.

There was also discrepancy between parents in recognizing a recurrent infection or a UTI in one of the other children in the family. Some parents were very alert regarding a future episode of UTI, and brought a urine sample to the general practice very quickly. In another case, a UTI in a second child was missed because this one had different symptoms.

Knowledge about UTI

As long as it was uncertain what was wrong with the child, parents were worried. After the UTI was diagnosed, the parents were more reassured. Most parents did not think of UTIs as being a serious condition in children; they usually realised this later. Some parents were a bit afraid of what the future might bring. Fear of an inflammation of the brain and renal failure were among the concerns that were mentioned. Especially the lack of communication of healthcare workers about the prognosis dissatisfied the parents.

In general practice, almost no information was given about the consequences a UTI can have if it is not detected and treated in time. One reason for not giving the desired information was because the medical personnel did not think it was important at the time. Parents found their own information on the Internet, in leaflets from general practice, and in lay books.

Health education and screening

The parents mentioned several ways to be sure of identifying children's UTIs, such as distributing information via leaflets, posters, and presentations at general practices, day-care centres, child health centres, schools, and libraries. The Internet has also become more important. However, some parents thought that people only look for information if the topic concerns them. Others were afraid such information could scare people. Therefore most parents did not think health education through mass media campaigns would be of help in raising awareness of UTIs in children.

According to the parents, screening is not a good method for identifying the UTIs of asymptomatic children, even though some think it might be a relatively easy and cheap method.

Discussion and conclusion

Discussion

This study gave some insight in parents' awareness of and knowledge about childhood UTIs and possible ways to improve this. At the time of diagnosis, most parents knew about the typical symptoms of a UTI. However, they did not know about many atypical symptoms related to UTI. Since most of the UTI symptoms in children are atypical,[14] parents might not think of a UTI and this might be a barrier for diagnosing it in time. The insight that UTI is a serious illness usually came later, and was not always communicated by the healthcare workers. Despite raising awareness in general, as seen by the development of guidelines on UTIs specific addressed to children, the parents in our study felt that GPs should be more aware on UTIs and should be more alert about follow-up and referral. It is striking that, although some of the parents did not know about the UTI symptoms, they knew something was wrong with the child, and therefore made an appointment with the GP. Of course we do not know in how many cases in general this feeling is wrong because we only interviewed parents whose children did have a UTI. But the fact that the parents did come to the general practice because of the different behaviour of their child is a facilitating factor in the early diagnosis of UTIs in children.

Parents had mixed feelings about receiving more information about the possible consequences of a UTI. Some were afraid such information would scare people off, while others thought it would not work because people only look for information if the topic concerns them. Lagerløv et al.[17] also reported this and identified three attitudes towards the importance of obtaining information about childhood diseases: some parents were curious to know about common childhood illnesses and had already acquired information beforehand; some parents actively sought information only when the child was ill; and some parents did not like information at all, saying it only added to the burden of the situation or made them anxious.[17] This tells us that increasing alertness, e.g. via mass media campaigns, would probably only be effective for parents who are curious to know about common childhood illnesses. It is probably better to give information at the child's first diagnosis of UTI. Some parents wanted to know more about the possible consequences of their child's UTI. Kai[18] also found that most parents thought that being more informed would reduce, rather than increase, their anxiety.

General practitioners could probably test urine in more cases, especially when a child has typical UTI symptoms or persisting fever without focus. However,

several studies found negative results for screening in absence of symptoms; even the most favourable strategies require testing of thousands of children and unnecessarily treating hundreds for each case of end-stage renal disease that screening would prevent.[19,20] Also, in our study parents were not keen on mass screening.

A qualitative approach was used to provide insight into parents' concerns and thinking, which we preferred to producing statistically representative results. Perhaps we could have uncovered other opinions by interviewing more fathers. Nonetheless, this study reflects the contemporary reality of childcare, which remains largely the responsibility of mothers. The group interviewed was heterogeneous, e.g. parents of children with their first UTI and parents of children with several, severe, UTIs, and this could have had an effect on parent's awareness and knowledge. But because the parents were asked to tell each story from the beginning on, we do not think this has influenced the results. There are two reasons for the fact that the results may look more negative than they actually are. Because barriers are more likely to be remembered than facilitating factors, there might be some recall bias in cases in which the last UTI was diagnosed about 1 year before the interview. Another reason is the fact that the GPs selected the children about whom an interview could be conducted; they may have chosen the more memorable cases, e.g. the more severe cases. But this does not mean that these barriers and more severe cases do not exist and that solutions have to be found for them. The total number of 20 interviews was a convenience sample over a predefined period of time. Even though the stories were different from each other, the overall conclusions were more or less the same and more interviews would not have revealed any more or completely different conclusions.

Because our results are to some extent comparable to the results of Owen's study,[15] we think our (and their) results are generalisable to most parents of children with a UTI. What our study added to the Owen study are the topics awareness in parents, and parents' ideas about how to prevent adverse effects of UTIs, e.g. through health education and/or screening. Conversely, Owen's study paid more attention to diagnostic problems.

Conclusion

Lack of knowledge about the atypical symptoms and the possible serious consequences of childhood UTIs were the most important ideas derived from this study. This knowledge is important for effecting timely diagnoses and treatment adherence. The parents in our study did not think screening or raising awareness

through mass media, in order to detect UTIs in time, is recommended. They preferred information given at the time a diagnosis of UTI was made.

Practice implications

Because raising awareness in parents prior to an actual UTI is difficult and not always wanted as well, GPs and nurses should be more aware of atypical symptoms and improve the detection and management of UTIs in young children. To prevent possible future UTIs, more information should be given to the parents about the complications a childhood UTI may have.

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Chapter 3

Urinary tract infections in young children: high guideline adherence of triage nurses at general practice co-operatives

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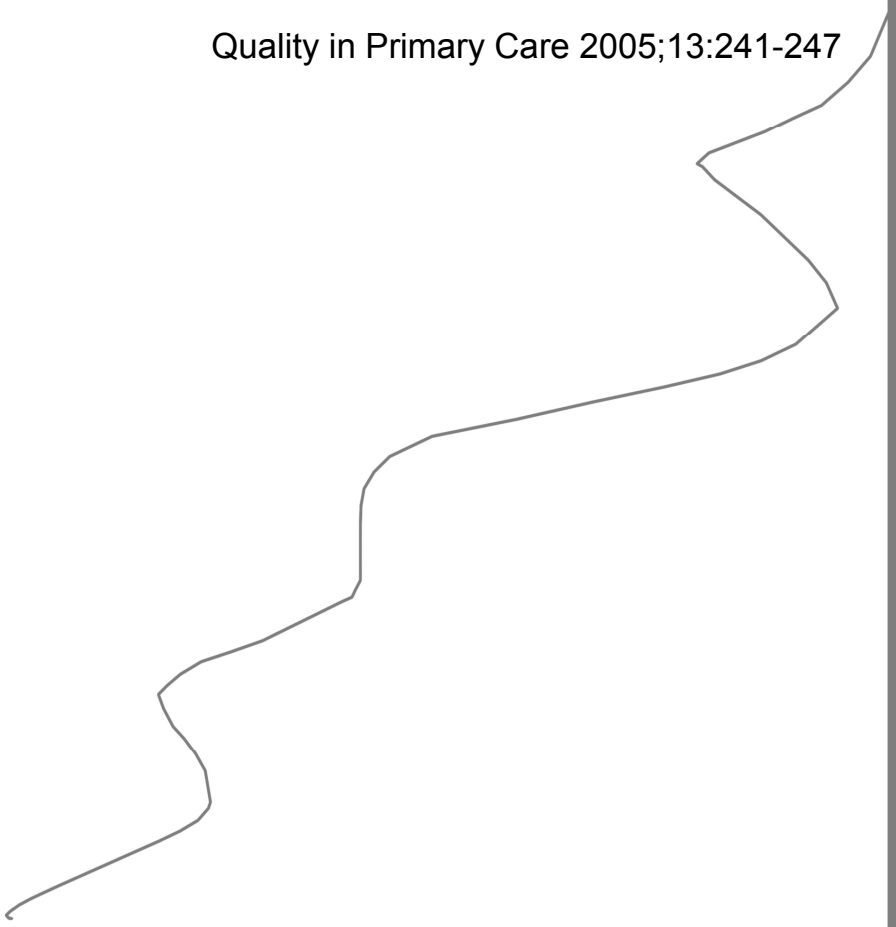

Abstract

Background: Urinary tract infection (UTI) is one of the most common bacterial infections among children, and it can have serious consequences including renal failure. Triage nurses at general practice (GP) co-operatives play an important role in identifying UTI in young children, but diagnosis is difficult because the symptoms tend to be non-specific.

Aim: The aim of this study was to determine what triage nurses at GP co-operatives do when UTI in a child is suspected, or when a feverish child is presented.

Methods: A survey study of triage nurses at Dutch GP co-operatives based on four vignettes was carried out. The information in the vignettes consisted of data about one 5-year-old child with suspected UTI and three children with fever without focus (a 14-month-old boy with a 3-day fever, a 2-month-old girl with a 2-day fever, and a 4-year-old child with a 5-day fever).

Results: A total of 145 questionnaires (59% response rate) were returned. If UTI was suspected, all triage nurses requested the parents to provide a sample of the child's urine, but only 70% gave instructions on how to collect the urine. More than 90% of the triage nurses requested the feverish children aged 2 months and 4 years to appear at the GP co-operative. Eighty percent also requested the 14-month-old boy with fever without focus to appear, even though there was no direct need for this request. In most cases, the triage nurses did not think UTI was likely, mainly because they thought another focus was more likely.

Discussion: More than 90% of triage nurses at GP co-operatives acted according to the guidelines if UTI was suspected. Even though UTI was not the first focus a triage nurse thought of when a child with fever without focus was presented, she requested the child to be brought to the GP co-operative almost every time. Possible interventions to improve the detection of children's UTIs could focus on the importance of the timeliness of detection, while over-diagnosis should be prevented.

Introduction

The incidence of urinary tract infections (UTIs), one of the most common kinds of bacterial infections among children, is 2.6% for girls and 0.5% for boys in the 1 to 4-year-old group in general practice.[1] Diagnosing UTI in young children is difficult because most of their complaints are nonspecific, like failure to thrive, vomiting and fever.[2] Four to five percent of feverish children have UTI.[3,4] Without timely treatment, renal scarring can occur, which can lead to hypertension, complications during pregnancy, and renal failure.[5] UTIs are likely to cause renal scarring in 5-15% of young children, particularly those less than 1 year old. Children older than 5 years hardly ever suffer renal scarring caused by UTIs.[6-8] Thus, the challenge is to detect and treat UTIs in young children appropriately, while avoiding over-diagnosis and over-treatment.

In The Netherlands, the first contact with a healthcare provider is almost always in general practice (GP).[9] Out of hours GP care is provided by GP co-operatives, established mainly about the millennium.[10] A patient's first contact with the GP co-operative is usually with a triage nurse by telephone. Triage nurses determine the level and urgency of care needed to address the health issue and give advice in non-urgent cases. They use the Telephone Triage Guide,[11] developed by the Dutch College of General Practitioners, which gives information on what questions to ask, what advice to give, and which situations are cases of emergency, urgency, or routine. Triage nurses on the alert for UTIs in children can initiate timely treatment so that fewer renal scars will occur.

The aim of this study was to determine what triage nurses at GP co-operatives do when a child with a suspected UTI or a feverish child is presented.

Material and methods

Participants

The study participants were triage nurses working at GP co-operatives. All 117 Dutch GP co-operatives were telephoned or e-mailed. Altogether, 247 questionnaires were sent to 54 GP co-operatives (approximately 3-5 per GP co-operative). The remaining GP co-operatives declined to participate or did not respond. Reminders were sent to GP co-operatives that had returned fewer than 65% of their questionnaires 1-2 months after the mailing.

Box 1. Vignettes

- Vignette 1. A parent of a 5-year old child calls the GP co-operative. The child has some non-specific complaints, but is not seriously ill. The child has no previous medical history. You think it might be a urinary tract infection.
- Vignette 2. On Saturday at 9.30 a.m., a worried mother calls the GP co-operative: her 14-month-old son has a fever (40 ^{0}C) for the 3rd day. According to the mother, the child does not look very ill and does not have any serious symptoms.
- Vignette 3. On a Wednesday at 11 p.m. a father calls about his 2-month-old daughter. She has a fever of 40 ^{0}C for the 2nd day.
- Vignette 4. A mother calls about her 4-year-old child on Sunday afternoon. Her child has had a fever for 5 days now.

GP=General practice

Questionnaire

We constructed four vignettes (Box 1) on the basis of the Telephone Triage Guide[11] and two national guidelines on UTIs[12] and feverish children.[13]

The guidelines are clear about whether a child must be seen at the GP co-operative. For example, feverish children younger than 3 months (vignette 3) must be seen by a general practitioner anyway, but this is not recommended for a child older than 3 months with fewer than 4 days of fever and no other symptoms (vignette 2). The vignette information consisted of only a few patient characteristics, in which age, gender, and duration of fever varied according to the various guideline decision points.

Structured questions with prespecified answers asked background information such as gender, background profession, knowing and using the Telephone Triage Guide, and questions to assess routines. The questions about vignette 1 focused on the complaints perceived as being associated with UTIs, the questions to be asked, the decision whether to see the child, the advice and instructions to be given (e.g. when to call again), to provide a urine sample if the child was to be seen and advice about how to collect the urine. The questions about vignettes 2, 3, and 4 focused primarily on the estimation of whether a UTI was likely and why. Another question concerned the decision whether to see the child at the GP co-operative, and if not, whether advice was given on when to call again.

The questionnaire was tested on three GP nurses and eight general practitioners.

Analyses

We calculated the differences between participating and non-participating GP co-operatives and responding and non-responding GP co-operatives with independent samples *t*-tests ($p<0.05$) on the number of years since the GP co-operative was founded, number of GP co-operatives within the organisation, total number of inhabitants in the catchment areas, degree of triage (e.g. who does the triage, which method is used) and degree of working according to protocols. These data were obtained from a study of the Dutch Health Care Inspectorate on GP co-operatives.[10] No data were available on individual non-responding triage nurses.

Questionnaire data were entered into the computer programme Access 2000 and analysed with the statistical computer programmes SAS 8.2 for Windows and SPSS 12.1. Frequencies were calculated for the background variables gender, background profession, knowing and using the Telephone Triage Guide, and the questions about the four vignettes. Means and standard deviations were calculated for the variables years of working experience in the background profession and at the GP co-operative, and number of days a week working at the GP co-operative.

Results

Response

Of 247 questionnaires, 145 were returned (59%). No differences were found between the participating and non-participating GP co-operatives and the responding and non-responding GP co-operatives.

Respondents

Table 1 presents the characteristics of the triage nurses. All respondents but one were women. Most triage nurses had a background as a GP nurse or hospital nurse. Almost all triage nurses said they knew the Telephone Triage Guide and most said they used it.

Table 1. Respondent characteristics (*n* = 145)

Gender (% women)	99
Background profession (%):	
• GP nurse	79
• Nurse	21
Mean (sd) number of years of working experience in background profession	14.1 (7.8)
Mean (sd) number of years of working experience at the GP co-operative	2.5 (0.9)
Mean (sd) number of days a week working at the GP co-operative	2.0 (1.0)
Telephone Triage Guide (%):	
• Knows the guide	99
• Uses the guide	89

GP=General practice, Sd=Standard deviation

Table 2. Triage nurses (n=145) who think the symptom is related to urinary tract infection

	Percentage of triage nurses
Nonspecific complaints:	
• Abdominal pain	100
• Fever	95
• Flank pain	93
• General malaise	90
• Incontinence	81
• Vomiting	24
• Diarrhoea	7
• Weight loss	6
• Delayed height growth	5
Typical UTI-related complaints:	
• Haematuria	99
• Dysury	98
• Pollakiuria	98
• Strangury	87

The child with suspected UTI

Table 2 shows that most nurses thought that abdominal pain, fever, flank pain, general malaise, and incontinence are related to UTI, as well as the more typical symptoms like haematuria, dysury, pollakiuria, and strangury. Complaints like diarrhoea, vomiting, and delayed height growth were not frequently associated with UTI (<25% thought so). The non-specific symptoms most relevant to UTIs in

Table 3. Alertness of the 145 triage nurses to child urinary tract infection or fever without focus (%)

	Vignette 1	Vignette 2	Vignette 3	Vignette 4	
	♂/♀	♂	♀	♂	♀
UTI likely	n.a.	19	18	17	46
Reason why UTI is likely:					
• Gender	n.a.	13	38	10	50
• Age	n.a.	17	33	19	25
• No focus	n.a.	88	50	76	48
• Duration of fever*	n.a.	4	0	3	6
Reason why UTI is not likely:					
• Other focus	n.a.	89	81	92	94
• No specific UTI complaints*	n.a.	0	5	1	4
• Incidence UTI low*	n.a.	0	10	2	0
• Persistent fever without focus*	n.a.	4	0	0	1
Child to appear at GP co-operative	92	80	90	96	98
Urine sample	99	n.a.	n.a.	n.a.	n.a.
Instructions about collecting urine	70	n.a.	n.a.	n.a.	n.a.
If not presented at GP co-operative, advice given	100	100	93	100	100

♂=Male, ♀=Female, n.a.=not asked; * open answers

children were perceived to be abdominal pain, fever, flank pain, and general malaise. If parents called about their child (vignette 1), the triage nurses wanted to know the duration (94%) and seriousness (74%) of the symptoms and what parents themselves thought about the complaints (85%). Some triage nurses also asked about the gender, age, and medical history of the child.

Most nurses would ask that the child be brought to the GP co-operative (Table 3). They would ask for a urine sample in such a case, and usually gave instructions about how to collect the urine: washing the genitals, using a urine collection bag for very young children or a clean jar, sampling morning and midstream urine, and keeping the urine refrigerated or delivering it within 2 hours. If the child was not asked to appear at the GP co-operative, all triage nurses gave advice or information about drinking liquids, alarming symptoms, when to contact the GP co-operative again (each item ≥60%); micturition, temperature, and hygiene (each item <20%).

The feverish child

Table 3 shows that fewer than 20% of the triage nurses thought UTI to be likely in vignettes 2 and 3 and for the case of a boy in vignette 4. For the case of a girl in vignette 4, less than half thought UTI was likely. The main reasons for suspecting UTI for boys was fever without focus; and for girls, fever without focus and gender. The main reason for not suspecting UTI was that another illness might be causing the fever. Other, open answers given were that the incidence of UTI in the vignettes is low and that there were no specific UTI complaints. The great majority of the triage nurses would ask the parents to bring the child to the GP co-operative if vignettes 3 and 4 applied. If a child was not asked to appear, advice would be given about when to contact the GP co-operative again.

Discussion

This study shows that more than 90% of triage nurses at GP co-operatives acted in accordance with the guidelines concerning asking the parents to bring the children in vignettes 1, 3, and 4 to the GP co-operative and providing a urine sample if UTI is suspected. However, the proportion of triage nurses who would advise how to collect the urine was smaller. Also, many triage nurses wanted to see the patient in vignette 2, although this is not recommended: advice by telephone is considered sufficient if the child is older than 3 months, has had fever for 3 days or less, does not have severe symptoms, and is not seriously ill.[13] Besides this all, most triage nurses did not think UTI was likely when a child with fever without focus was presented.

As far as we know, no other studies have reported on this topic. Most studies about the management of children with UTI or fever dealt with GP management. Vernon et al.[14] found a wide variation in clinical practice by and between GPs. Although the guideline adherence of triage nurses was generally high, it is likely that their practice varies as well.

There are some explanations for our results. Triage nurses at GP co-operatives usually know nothing about the child's medical history, and therefore want the child to appear (e.g. vignette 2). The setting can also explain why relatively few triage nurses advised how to collect urine, more specifically, morning urine (47% of the triage nurses who gave advice). Because of the opening hours of the GP co-operatives, collecting morning urine is usually impossible, so this instruction was not relevant. Many triage nurses did not give instructions about using a urine collection bag (42% of triage nurses who gave advice) because

toilet-trained children do not need a bag. As in vignette 1, it was logical not to give this advice. Furthermore, urine collection bags are sometimes unavailable at GP co-operatives and must then be obtained from pharmacies, which have limited openings hours or are closed at night and on weekends. Although UTIs were not the first thing on a triage nurse's mind when a child with fever without focus was presented, it is encouraging that they wanted the child to appear anyway. Then it is up to the general practitioner to decide whether a UTI is likely. However, caution is advocated because even if a focus like otitis media exists, there might still be UTI as well.[15] These results may be considered representative for all Dutch triage nurses, seeing that there were no significant differences in background variables among the GP co-operatives.

This study has some limitations. Because of the limited information in the vignettes, more triage nurses might have decided to request the child in vignette 2 to appear than they otherwise would. The reason for not giving more information was, as already stated, that UTI might exist even if another focus is found. A second limitation is the use of self-reporting behaviour, which may lead to overly optimistic adherence. However, Peabody et al.[16] showed that vignettes appear to be a valid and comprehensive method that directly focuses on the process of care provided in actual clinical practice. Furthermore, Bonetti et al.[17] showed that using case descriptions predicts actual behaviour better than the more usual format (i.e. using self-reports of beliefs) when measuring intention. The high proportion of triage nurses not suspecting a UTI might be explained by the way the question was asked ('Do you think a UTI is likely?): 'likely' may mean '10% chance' to one person and '50% chance' to another.

This study only gives a first impression about UTI and fever in children at GP co-operatives. Future research could focus on motives for the way triage nurses act, or use administration systems as a data source to measure actual behaviour. Possible interventions to improve the detection of child UTI could focus on the importance of timely detection. Information could be given about the non-specific complaints children with UTIs have, even if another focus exists. Triage nurses should ask parents to provide a sample of the child's urine more often; however, over-diagnosis should be prevented.

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Chapter 4

How do Dutch general practitioners diagnose children's urinary tract infections?

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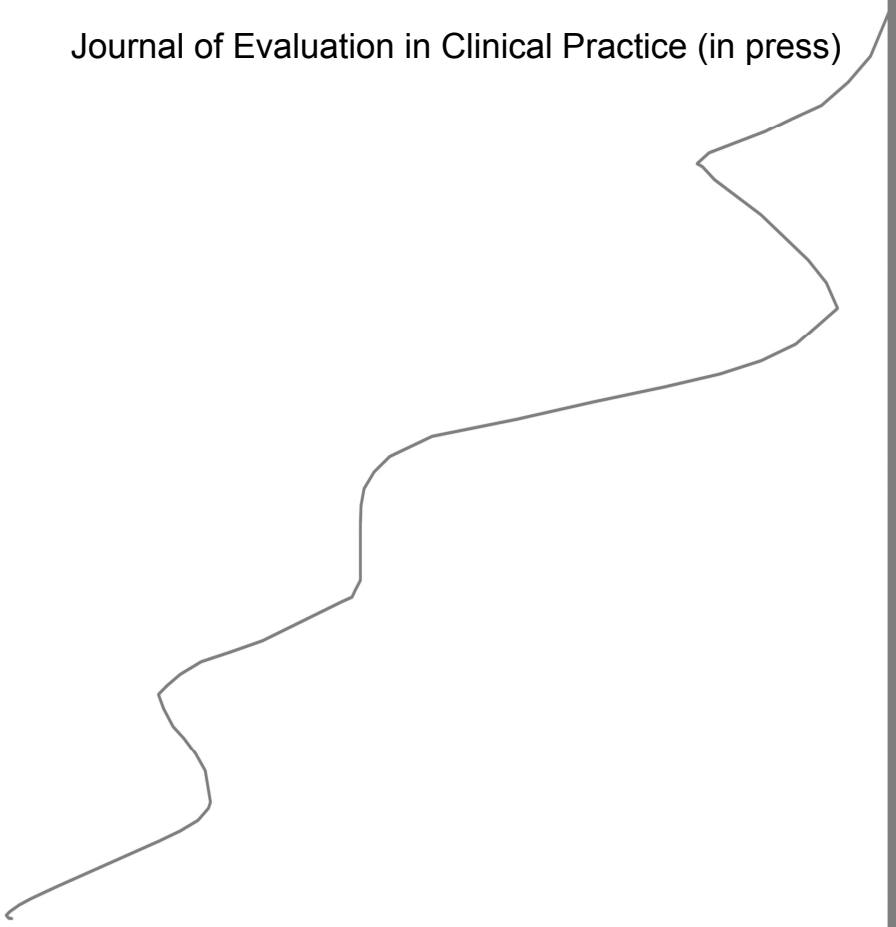


Abstract

Objective: To study which tests general practitioners used to diagnose a urinary tract infection (UTI) in children and which patient characteristics were associated with test choice.

Design: Retrospective chart review on the diagnosis of UTIs in children in Dutch general practices who were diagnosed as having a UTI. A total of 49 general practices participated in the study, and provided information on 148 children aged 0-12 years old.

Results: The nitrite test, which is recommended as first step, was performed in 87% of the children during the first contact. Less than 30% of the children had a dipslide and 37% a cultured urine. About half of all children with a UTI diagnosis had a follow-up contact in general practice, and an average of 83% of these children had their urine tested. The recommended test, a dipslide, was performed in 26% of the children with a follow-up contact. Patient age and UTI history were associated with choice of test.

Conclusions: The diagnostic procedures for UTIs in children in general practices could be improved, with focus on the importance of an accurate UTI diagnosis in all children, and explaining which tests should be performed and what the test results mean.

Introduction

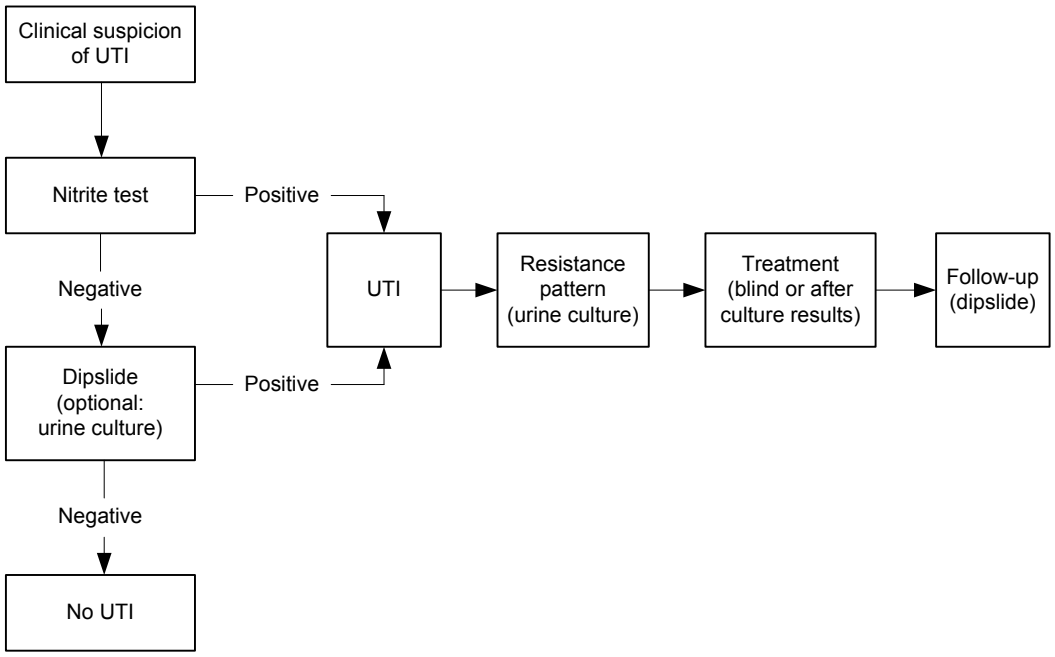
Clinical guidelines on urinary tract infections (UTIs) give clear recommendations on the diagnostic workup of a child with a suspicion of UTI.[1-4] A timely diagnosis, and subsequent treatment, of UTIs in children is important to prevent possible negative consequences.[5] UTIs in childhood may have renal scarring as a consequence, which may lead to hypertension, complications during pregnancy and even renal failure in later life.[5] In Dutch general practices, the incidence of UTIs in 0-6 year old children is 2.6% for girls and 0.5% for boys.[6] But many more children are suspected to have a UTI, and should be tested accurately. A false-negative diagnosis will leave patients with UTI at risk for serious complications. A false-positive diagnosis may lead to unnecessary, invasive, and expensive follow-up procedures.[7]

According to prevailing clinical guidelines,[1-4] a combination of tests is recommended (Figure 1). The nitrite test is the first test to use. A meta-analysis by Devillé et al.[8] showed that a positive nitrite test gives good arguments to confirm a UTI. A dipslide test has to be performed in case of a negative nitrite test. The dipslide is a good, quick test to rule out, as well as to rule in, UTIs.[3] An alternative for the dipslide is a urine culture, which has high predictive values as well.[4] The urine of every child with a UTI should be cultured anyway, before the start of the antibiotic treatment, to give information about precise microbiological species, number of colony forming units and resistance pattern. This allows a quick and adequate change in therapy in case of treatment failure. After 3 to 5 days following the end of the antibiotic treatment, the child's urine should be tested again by using a dipslide.[3]

Tests not recommended in prevailing guidelines are the leukocyte test and the determination of a urine sediment, as well as tests on haemoglobin and erythrocytes, because they have lower predictive value than those mentioned above and very little additional value.[3,7-9]

Given these complex decisions in children at risk, a good understanding of actual care in general practices would be important to identify gaps in performance. Such performance data are currently lacking. The aim of this paper was to study which diagnostic tests general practitioners (GPs) used to diagnose a UTI in children. We were also interested whether patient characteristics were of influence, although there should be no difference in choice of tests.

Figure 1. Recommended workup for the diagnosis of urinary tract infections (UTIs), according to Dutch general practice guidelines[3]



Methods

The study design was a retrospective chart review on the diagnosis of UTIs in children who were diagnosed as having a UTI.

Population and data collection

A random selection of 124 general practices from a nationwide Dutch database was asked to participate in the study. The general practices were asked to select all children aged 0-12 years old having had a UTI in the first 10 months in the year 2006 in their electronic medical record systems, using the codes U70 (pyelonephritis) and U71 (cystitis) of the International Classification of Primary Care (ICPC),[10] or free text words related to UTIs. Information from these patient records was summarised by the general practices on a standardized form for use by the researchers. These forms were anonymous to the researchers; only the practices were able to relate the forms to the medical records.

Analyses

Data from the forms were entered into an SPSS 14.0 data file. To give insight into the actual performance of general practices concerning urine testing in children, frequencies were calculated for all possible tests. Secondly, chi-square tests were performed to give insight into associations between the different tests (Pearson Chi-square $p<0.05$).

To measure the influence of patient characteristics (sex and age of the child, UTI history, other relevant medical history) as independent variables on the tests (urine test in general, nitrite, leucocytes, erythrocytes, urine culture, dipslide and sediment), logistic regression analyses were performed. Excluded were independent variables with little variance in the answers (≥90% in one category), more than 20% of the expected frequencies lower than 5 (in the dependent-independent variables cross-tabulation), less than 10 cases in one cell, and with weak relations with the dependent variables ($p\geq0.10$). Because statistical interaction between sex and age of the patient was suspected, an interaction term was included in the analyses. First the backward likelihood method was used. The final model was analysed using the method 'Enter'.

Results

A total of 49 general practices participated in the study, and provided information on 148 children. This average of three children per practice in 10 months is approximately equal to the five children per practice in one year found in a previous study.[11]

Characteristics of the children are presented in Table 1. Most of the 148 children were girls (80%); most of them between 5 and 11 years old. About 25% of the children had at least one UTI previously mentioned in the medical history, of which half had more than one. Other relevant aspects of the medical history, like constipation and vesicoureteric reflux, was present in 11 children. Table 1 shows that the sex and age distribution of children in our study is equal to the distribution in a large national study on illnesses and disorders in general practice, based on more than 50 000 children aged 0-12 years old.[6]

Table 1. Characteristics of children with urinary tract infections (UTIs)

Patient characteristics	N (%) this study (n=148)	N (%) national reference data (n=767)[6]
Gender (female)	118 (80)	647 (84)
Age:		
• <1 year old	4 (3)	32 (4)
• 1-4 years old	54 (37)	262 (34)
• 5-12 years old	90 (60)	473 (62)
Age and gender:		
• Girls <1 year old	1 (1)	28 (4)
• Girls 1-4 years old	38 (26)	215 (27)
• Girls 5-12 years old	79 (53)	404 (53)
• Boys 0-12 years old	30 (20)	120 (16)
UTI in medical in medical history	38 (26)	
• One previous UTI	16 (11)	
• 2-5 previous UTIs	12 (8)	
• More than 6 previous UTIs	4 (3)	
Other relevant medical history	11 (7)	

Table 2. Urine tests (%) in children diagnosed as having a UTI, compared to the recommendations in the guidelines

	First visit		Follow-up visit	
	% this study (n=142)	Guidelines	% this study (n=76)	Guidelines
Any urine test:	97		83	
• Nitrite	87	+	79	-
• Leucocytes	74	+/-	68	-
• Erythrocytes	62	-	54	-
• Urine culture	37	+	11	-
• Dipslide	31	+	26	+
• Sediment	14	+/-	17	-

UTI=Urinary tract infection, + =Recommended, +/- =Optional, - =Not recommended

Table 2 presents the use of urine tests in children who were diagnosed with a UTI. At the first visit, almost all children had a urine test (97%). The test recommended to perform first, the nitrite test, was performed in 87% of the children. Less than 30% had a dipslide. The percentage of children with a cultured urine was low (37%), despite the recommendation to culture all urines. High percentages of children had leucocyte and erythrocyte tests performed (respectively 74% and 62%), although these tests are not recommended by the guidelines.

There was a strong association between the erythrocyte test and the leukocyte test ($p<0.001$), and the erythrocyte test and the nitrite test ($p<0.001$). The leucocyte test had also an association with urine culture ($p=0.020$).

About half of all children diagnosed as having a UTI had a follow-up contact in general practice. In this contact, on average, 83% of the children had their urine tested. The recommended test, a dipslide, was performed in 26% of the children with a follow-up contact. At follow-up, the dipslide test had a strong association with the erythrocyte and leukocyte tests. These two tests were also strongly correlated to each other and to the nitrite test (all p-values<0.001).

Patient's age was associated with performing sediment at the first contact (odds ratio 0.77 [95% confidence interval 0.63;0.94]) and on performing a urine culture (0.48 [0.28;0.85]) or a dipslide and/or urine culture (0.74 [0.61;0.89]) at follow-up. For these tests, a younger age was related to a higher proportion of tests. Having a history of UTIs meant less testing on erythrocytes (0.35 [0.16;0.76]) and leucocytes (0.34 [0.13;0.88]), and more testing using the dipslide and/or urine culture (2.84 [1.20;6.70]) at the first contact.

Discussion

Our findings suggest that the use of the nitrite test was largely appropriate, but that other tests may be either overused (e.g. erythrocytes) or underused (e.g. urine culture) at first visits of children with suspected UTI in Dutch general practice. Striking was that only half of the children had a follow-up contact, and only a quarter of these children's urine was tested by the recommended dipslide. Patient age and UTI history were associated with choice of tests.

This study was based on a large sample of children who presented with a new episode of UTI and which seemed to be representative. A limitation of the study was that the sample did not include children suspected of having a UTI, but who in the end were diagnosed as not having one.

Although our samples of patients and practices were reasonably large, we cannot completely rule out the possibility of selection bias. A strong aspect might be that our sample comprised of normal practices, not a special research network. Also, the characteristics of the children in this study are comparable with the children in a national study on 767 children with UTI.[6]

There are several possible explanations for the findings. Using a dipslide in general practices may have disadvantages, for instance, because of the short shelf life.[2] This means a lot of practices may not have a dipslide available. The high percentages of erythrocyte and leukocyte tests can be explained by the fact that most general practices use combination strips (dipsticks), which means that nitrite, erythrocytes, leucocytes, etc. are tested at the same time. Dipstick tests have the advantage of being quick and easy to perform and can be carried out in general practice giving an immediate result.[12] A study in UK general practices by Robinson[13] showed nitrite testing by 64% of the GPs, leukocyte testing by 53%, and 94% reported sending all samples to the laboratory for microscopy and culture. No respondents used dipslides.

Better performance according to the guidelines seemed to be related to a younger age of the child and a UTI in the medical history. Although the guidelines do not discriminate on age, sex or UTI history in diagnosing children, it is easy to understand why GPs act like this. Young children and children with a recurrent UTI seem to be more vulnerable for complications.

To get good test results, an uncontaminated urine sample should be collected. This is not easy, especially in young children.[14] The gold standard for urine collection is suprapubic aspiration (SPA), but this method is not child friendly and not very feasible in general practice. Therefore other collection methods are used, most times clean voided urine, which showed reasonably good agreement with SPA. Use of bag or nappy/pad specimens may be used as substitutes for SPA, especially in non-toilet trained children, but till now, there is insufficient data available.[4]

Future studies should focus on the gaps in the knowledge of the diagnosis of UTIs in children, like the tests that are performed when a child is suspected to have a UTI or the ways urine is collected. Interventions aimed at general practice staff to improve the diagnosis of childhood UTIs should focus on the importance of accurate UTI diagnosis in all children, and explain which tests should be performed and what the test results mean.

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Chapter 5

Management of children's urinary tract infections in Dutch family practice: a cohort study

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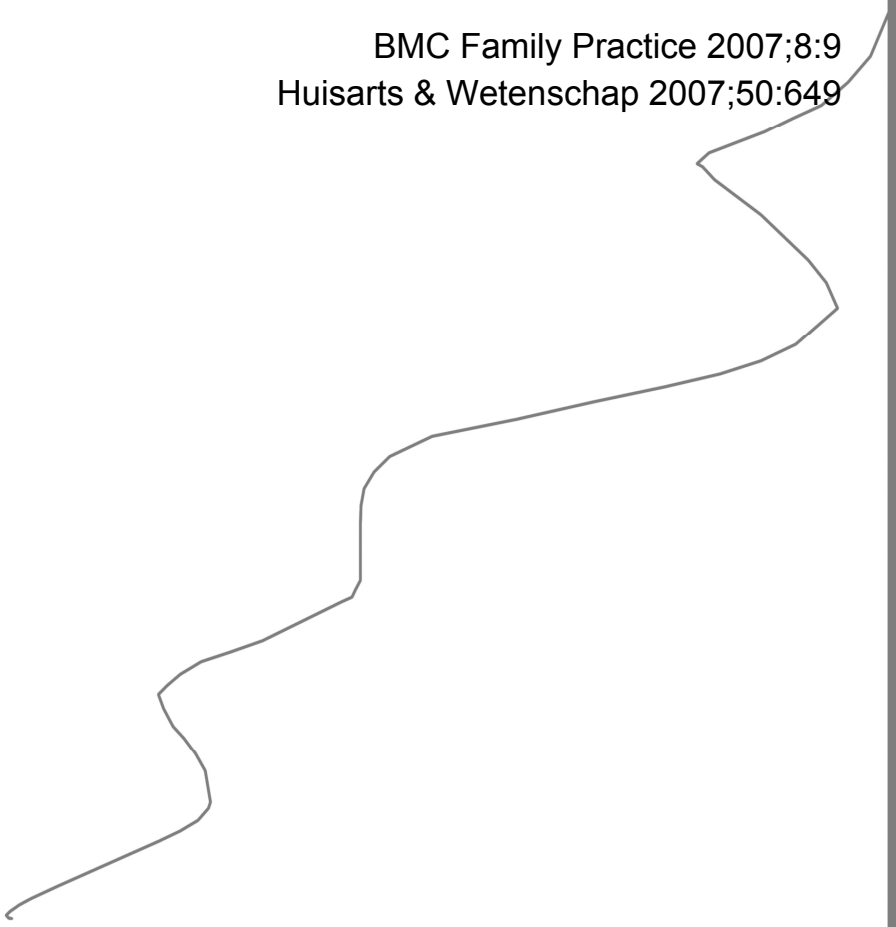
Huisarts & Wetenschap 2007;50:649



Abstract

Background: Optimal clinical management of childhood urinary tract infections (UTI) potentiates long-term positive health effects. Insight into the quality of care in Dutch family practices for UTIs was limited, particularly regarding observation periods of more than a year. Our aim was to describe the clinical management of young children's UTIs in Dutch primary care and to compare this to the national guideline recommendations.

Methods: In this cohort study, all 0 to 6-year-old children with a diagnosed UTI in 2001 were identified within the Netherlands Information Network of General Practitioners (LINH), which comprises 120 practices. From the Dutch guideline on urinary tract infections, seven indicators were derived, on prescription, follow-up, and referral.

Results: Of the 284 children with UTI who could be followed for three years, 183 (64%) were registered to have had one cystitis episode, 52 (18%) had two episodes, and 43 (15%) had three or more episodes. Another six children were registered to have had one or two episodes of acute pyelonephritis. Overall, antibiotics were prescribed for 66% of the children having had $\leq$3 cystitis episodes, two-thirds of whom received the antibiotics of first choice. About 30% of all episodes were followed up in general practice. Thirty-eight children were referred (14%), mostly to a paediatrician (76%). Less than one-third of the children who should have been referred was actually referred.

Conclusion: Treatment of childhood UTIs in Dutch family practice should be improved with respect to prescription, follow-up, and referral. Quality improvement should address the low incidence of urinary tract infections in children in family practice.

Background

Awareness of the importance of timely diagnosis and treatment of childhood urinary tract infections (UTIs) is growing. Without timely treatment, renal scarring can occur,[1] which is likely to affect approximately 5-15% of young children with a UTI.[2-5] Renal scarring is associated with serious health problems in later life, such as hypertension, complications during pregnancy, and renal failure.[1] Optimal clinical management of childhood UTI potentiates long-term positive health effects. Therefore, guidelines across different countries advocate an active approach concerning prescription, follow-up, and referral.[6-9]

The guideline on UTIs of the Dutch College of General Practitioners (DCGP) states that every childhood UTI should be treated with antibiotics because of the risk of renal scarring. Amoxicillin/clavulanic acid or co-trimoxazole are the medications of choice in an attempt to reach effective tissue levels and to maximize the chance of the most effective medicine until test results are available. The follow-up recommendation takes into account that young children may not express their complaints clearly, while they have a high risk of renal scarring. The referral recommendations are based on the patients' age and sex, which predict the probability of anatomical abnormalities of the urinary tract system.[9]

The one-year incidence of UTIs in 0 to 6-year-old children in Dutch family practices averages for girls 25.7 and for boys 4.5 per 1000 life-years.[10] Insight into the quality of care for UTI was limited, particularly regarding observation periods of more than a year. We have acquired the necessary prospective data to provide insight into the primary-care-based management of childhood UTIs in the Netherlands. We aimed to describe the clinical management of young children's UTIs in Dutch primary care and compare this to the national guideline recommendations.

Methods

Design and setting

A prospective cohort study in Dutch family practice was performed.

Study population

We identified all children 0-6 years old (born between 1994 and 2001) with UTI diagnosed in 2001 within the Netherlands Information Network of General Practice (LINH). The LINH network contains 120 practices and is representative of the Dutch population of patients, family practitioners, and types of practices.[11]

Informed consent was arranged within the network (general board of the National Institute for Health Services Research (NIVEL), general board of the Centre for Quality of Care Research (WOK), general board of the Dutch College of General Practitioners (NHG), and the general board of the National Association of General Practitioners (LHV)). According to the Dutch Central Committee on Research Involving Human Subjects (CCMO) regulations only research in which the study participant has to be physically present during the study is subject to the Medical Research Involving Human Subjects Act (WMO) and therefore ethical approval is not required for studies that use patient databases.

The International Classification of Primary Care (ICPC)[12] defines UTI as acute pyelonephritis (ICPC code U70) or cystitis (ICPC code U71). These definitions imply that UTI was diagnosed by urine testing, not just suspected or assumed.

Measurements

Although there is no specific DCGP guideline on UTIs in children, the Dutch UTI guideline does include specific recommendations for children.[13] We derived seven clinical indicators of appropriate performance. Two indicators focused on medication, one on follow-up, and four on referring (Table 1).

Data collection

In the LINH network, the family practice staff routinely records the encoded patient information in electronic medical records (EMR). For the period 2001–2003 data were extracted from the EMR, concerning contacts with the family practice, prescriptions, referrals, and patient characteristics (age, sex).

Practices were excluded from the analyses if they had registered fewer than 46 weeks in 2002 or 2003. Patients who were not on the practice list and patients who had left the practice before 1 January 2004 were also excluded.

Table 1. Indicators urinary tract infections (UTIs) in children in general practice

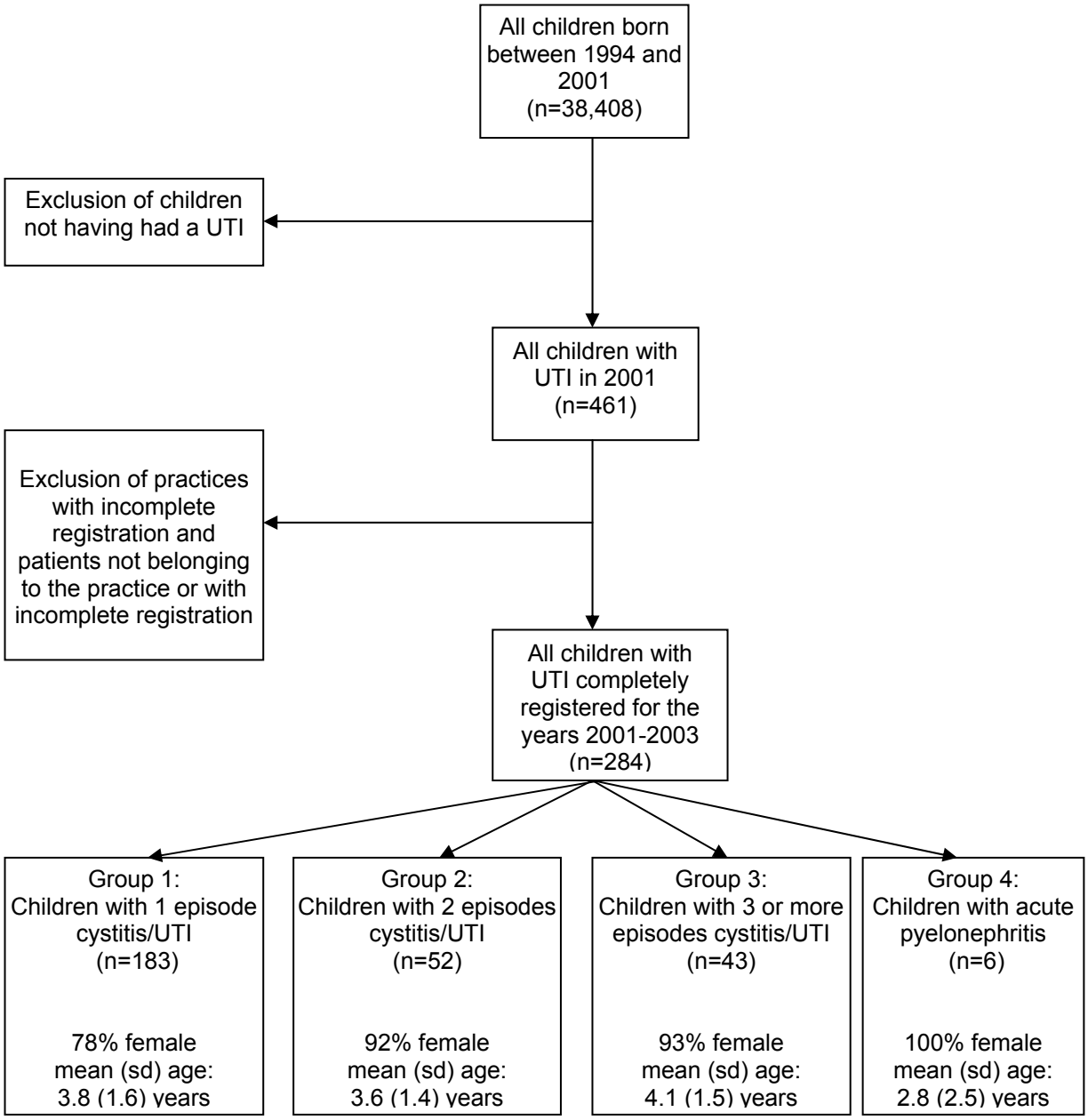
Indicator	Measurement	
	Numerator	**Denominator**
First-choice antibiotics		
1. Antibiotics given	All children receiving antibiotics	All children
2. Amoxicillin/clavulanic acid OR co-trimoxazole	Children receiving first-choice antibiotics	All children receiving antibiotics
Follow-up		
3. Episodes with at least one follow-up contact	Number of UTI episodes with >1 contact	All UTI episodes
Referral	For all groups:	For all groups:
4. Children <1 year old	Total referred within the group	Total within the group
5. Boys <12 years old		
6. Girls 1-4 years old with second UTI		
7. Girls 5-12 years old with >1 recurrent UTI		

Analyses

The contacts were expressed in units of episodes. Episodes were considered new episodes if the preceding contact for UTI occurred more than 28 days previously. Prescriptions and referrals within 28 days after the last contact for an episode were linked to that episode. The first UTI in 2001 was assumed to be the child's first episode ever. To be able to compare groups, four groups of children were created, based on ICPC code and number of UTI episodes: group 1 (1 episode cystitis), group 2 (2 episodes cystitis), group 3 (≥ 3 episodes cystitis) and group 4 (1 or 2 episodes acute pyelonephritis).

Descriptive statistics were applied to patient characteristics, and the numbers of children receiving medication, follow-up, or referrals. For each indicator, the number of children (or episodes in the case of follow-up) to whom family practitioners (FPs) offered the appropriate care was divided by the total number of children (or episodes in the case of follow-up) needing the provision of such care (Table 1). We calculated the percentage of children with more than one contact during a UTI episode as an indicator of follow-up. Age groups were based on age when having the first UTI.

Figure 1. Selection of children with urinary tract infections for the analyses



Mean (sd) age=Age during first episode, sd=standard deviation, UTI=Urinary tract infection

Student's *t*-test or chi-square tests, as appropriate, were used to investigate whether more boys or girls were treated as recommended by the guideline, and whether younger children were treated more consistently with the guideline than older children. We also investigated whether recurrent childhood UTIs were more often treated according to the guideline than single episodes. We considered a probability level of $P<0.05$ statistically significant.

Results

Study population

Figure 1 shows the selection of children included in this study. Of 38,408 children in the 120 practices in the year 2001, 461 from 92 practices had a diagnosed UTI (1.2%). Of these 461 children, 284 (62%) in 59 practices could be followed for three years. There were no age or sex differences between included children and children excluded in step 2 of the flow chart.

Of the 284 children included, 278 (98%) were diagnosed with cystitis. Of these children, 66% had one episode (group 1), 19% had two (group 2), and 15% had 3 to 10 (group 3). Six children were diagnosed with acute pyelonephritis (2%; group 4).

During the first UTI episode, the mean age varied from 2.8 (SD 2.5) to 4.1 years (SD 1.5). About 80% of the children in group 1, 90% in groups 2 and 3, and 100% in group 4 were girls (Figure 1). Because of the small numbers, no further data are presented for group 4 and for episodes 4-10 in group 3.

Prescriptions

Table 2 shows that, overall, 66% of the children received antibiotics, varying from 61% to 70%. First choice medication, amoxicillin/clavulanic acid or co-trimoxazole, was prescribed for 55% to 83% of the children with antibiotics (overall 66%). Another 4% to 25% (overall 13%) of the children with antibiotics received ceftibuten, ofloxacin, or nitrofurantoin. Since childhood UTIs should be treated as complicated UTIs according to the DCGP-guideline, these last three antibiotics should not be prescribed according to the guidelines. Furthermore, 10% to 25% (overall 19%) of the children with antibiotics received amoxicillin without clavulanic acid, which is also not according to the DCGP-guideline. In eight cases, a child

Table 2. Prescription of antibiotics in children with urinary tract infections

	Group 1 (n=183)	Group 2 (n=52)	Group 3 (n=43)	Total (n=278)
Percentage (number) of children/antibiotic prescription				
Overall children with antibiotics (indicator 1)	66 (121/183)	70 (73/104)	61 (79/129)	66 (273/416)
• First episode	66 (121/183)	73 (38/52)	67 (29/43)	68 (188/278)
• Second episode		67 (35/52)	63 (27/43)	65 (62/95)
• Third episode			53 (23/43)	53 (23/43)
Percentage (number) of children with antibiotics/choice of antibiotic				
Amoxicillin/clavulanic acid or co-trimoxazole				
Overall first-choice antibiotics (indicator 2)	65 (79/121)	56 (41/73)	76 (60/79)	66 (180/273)
• First episode	65 (79/121)	55 (21/38)	69 (20/29)	64 (120/188)
• Second episode		57 (20/35)	78 (21/27)	66 (41/62)
• Third episode			83 (19/23)	83 (19/23)
Ceftibuten, ofloxacin, or nitrofurantoin				
Overall	7 (9/121)	21 (15/73)	14 (11/79)	13 (35/273)
• First episode	7 (9/121)	18 (7/38)	14 (4/29)	11 (20/188)
• Second episode		23 (8/35)	15 (4/27)	19 (12/62)
• Third episode			13 (3/23)	13 (3/23)
Amoxicillin				
Overall	25 (30/121)	18 (13/73)	10 (8/79)	19 (51/273)
• First episode	25 (30/121)	18 (7/38)	17 (5/29)	22 (42/188)
• Second episode		17 (6/35)	7 (2/27)	13 (8/62)
• Third episode			4 (1/23)	4 (1/23)

who did not receive medication was referred to a medical specialist directly after seeing the GP. No differences in prescription for age or sex were found in any group.

Follow-up

Twenty-eight percent to 37% of all episodes was followed up (Table 3). The overall follow-up rate was 32%. About 60% of all episodes with follow-up contacts consisted of two contacts. The second contact took place within 14 days of the first for 90% of the episodes. There were no differences for age or sex groups.

Table 3. Follow-up and referrals in children with urinary tract infections

	Group 1 (n=183)	Group 2 (n=52)	Group 3 (n=43)	Total (n=278)
Pecentage (number) of episodes with more than one contact during the episode				
Overall episodes with more than one contact (indicator 3)	28 (52/183)	34 (35/104)	36 (46/129)	32 (133/416)
• First episode	28 (52/183)	35 (18/52)	33 (14/43)	30 (84/278)
• Second episode		33 (17/52)	37 (16/43)	35 (33/95)
• Third episode			37 (16/43)	37 (16/43)
Percentage (number) of children with a referral				
Overall	8 (14/183)	19 (10/52)	33 (14/43)	14 (38/278)
• First episode	8 (14/183)	12 (6/52)	9 (4/43)	9 (24/278)
• Second episode		8 (4/52)	16 (7/43)	12 (11/95)
• Third episode			7 (3/43)	7 (3/43)
Percentage (number) of children with a referral, special groups of children				
Children <1 year of age (indicator 4)	67 (2/3)	100 (1/1)	0 (0/0)	75 (3/4)
Boys overall (indicator 5)	18 (7/40)	25 (1/4)	0 (0/3)	17 (8/47)
Girls overall	5 (7/143)	19 (9/48)	38 (15/40)	13 (31/231)
Girls 1-4 years, second episode (indicator 6)		9 (2/22)	33 (7/21)	21 (9/43)
Girls 5-9 years, third episode (indicator 7)			7 (2/27)	7 (2/27)

Referrals

Table 3 shows that overall 38 of 278 (14%) children were referred for specialist treatment (range: 8-16%). Seventysix percent was referred to a paediatrician; 8% to a urologist; 3% to radiography; and from 13% it is not clear to what specialist they were referred.

Less than one-third of the children who should have been referred concerning the guideline on referring specific age and/or sex categories, was actually referred. Three of four children younger than one year were referred, and fewer than 25% of the boys were referred during at least one episode.

In group 2, 9% of the girls aged 1-4 years were referred during the second episode, and in group 3 33%. Two girls in the 5-9 year olds group (7%) were referred during the third episode. No differences regarding age and sex subgroups were found.

Discussion

This study showed that the management of childhood UTIs in the Netherlands varied substantially across patients. Only 66% of the children received antibiotics

and of these 66% was prescribed first choice antibiotics. There was no follow-up in the majority of the episodes. Referral of children younger than one year was generally consistent with the guidelines, but the referral rates for boys, girls 1-4 years old with a second UTI, and girls 5-12 years old with more than one recurrent UTI should have been much higher, if we consider the guidelines.

We found that the proportion of children receiving amoxicillin decreased proportionally to the number of episodes. Perhaps FPs prescribe amoxicillin routinely because this medication is much older than the combined form with clavulanic acid, and has less side effects than amoxicillin/clavulanic acid. If amoxicillin alone does not work, they prescribe the combination. Prescribing ceftibuten, ofloxacin, or nitrofurantoin suggests that not all FPs are aware that, according to the guidelines, childhood UTI should be treated as complicated UTI. This is confirmed by the fact that, for 98% of all children, the FP had registered the ICPC for cystitis instead of the code for complicated UTI (pyelonephritis). No significant differences of age or gender might imply that GPs are unaware of the increased risk of complications or underlying pathology in boys and younger children. Such unawareness may lead to health complications when the child is older.

The LINH network provided a unique opportunity for collecting prospective data regarding clinical management in routine healthcare settings, but one can question FP registration behaviour and whether all childhood UTIs were identified with the ICPC codes 'acute pyelonephritis' and 'cystitis'. However, the incidence we found for 0 to 6-yearolds, which is 12.0 (461*1000/38408), is comparable to those in other Dutch studies: 15.1[10] and 13.2.[14] Since direct observation and hand-searching medical records are infeasible, using databases of consultation registrations seems to be the optimal method for collecting information about FP clinical behaviour.

It is difficult to compare our results on FP management with other studies because our data are prospectively collected, had a follow-up period of three years, and focused on primary care and individual young children; this in contrast to other studies. A study by Kwok et al.[15] already gave some insight in the management of children's UTIs in Dutch family practice. But compared to our study, this study concentrated on a much wider age range, although the children most vulnerable to renal scarring are the younger ones. The study also had a follow-up period of only one year and did not pay attention to follow-up after the antiobiotic treatment. One British study found that 37% of children with proven UTI were sent for renal tract imaging,[16] and another Dutch study reported 4% of the

children being referred.[14] Two other British studies found much higher rates of referral.[17,18] However, these last two studies used postal questionnaires to measure FP behaviour, whereas our study and the first two studies used medical records. Reporting behaviour retrospectively may lead to overestimation of guideline adherence because of social desirability bias.[19]

Improvement of professional performance might substantially improve clinical outcomes. This is demonstrated in Sweden, where a more aggressive approach led to no new cases of uraemia caused by non-obstructive pyelonephritis during the years 1986-1995.[20] But, development and distribution of guidelines do not necessarily lead to better patient care.[21] Future research could focus on developing interventions to improve prescription, follow-up, and referrals, but should also consider motives for not following the guidelines. Because not many childhood UTIs appear in family practice in the Netherlands –our study saw an average of five children per practice in one year– interventions should not be too time consuming for the FPs.

Conclusion

In order to prevent negative health outcomes, treatment of childhood urinary tract infections in Dutch family practice should be improved with respect to prescription, follow-up, and referral. Quality improvement should address the low incidence of urinary tract infections in children in family practice.

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Chapter 6

Management of childhood urinary tract infections: an economic modelling study

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Abstract

Introduction: Childhood urinary tract infections (UTIs) can lead to renal scarring and ultimately to terminal renal failure, which has a high impact on quality of life, survival and health care costs. Variation in the treatment of UTIs between practices is high.

Objective: To assess the cost-effectiveness of a maximum care model for UTIs in children, implying more testing and antibiotic treatment, compared to current practice in primary care in The Netherlands.

Methods: We performed a probabilistic modelling study using Markov models. Figures used in the model were derived from a systematic review of the research literature. Multi-dimensional Monte Carlo simulation was used for the probabilistic analyses.

Results: Maximum care gained 0.00102 (males) and 0.00219 (girls) QALYs (quality adjusted life years) and saved €42.70 (boys) and €77.81 (girls) in 30 years compared to current care, and was thus dominant. Net monetary benefit of maximum care ranged from €20 to €200 for a willingness to pay for a QALY ranging from €0 to €80,000 respectively. Maximum care was also dominant over improved current care, although less dominant than to current care.

Conclusions: This study suggested that maximum care for childhood UTI was dominant in the long run to current care, meaning that it delivered more quality of life at lower costs. However, making firm conclusions is not possible, given the limitations of the input data.

Introduction

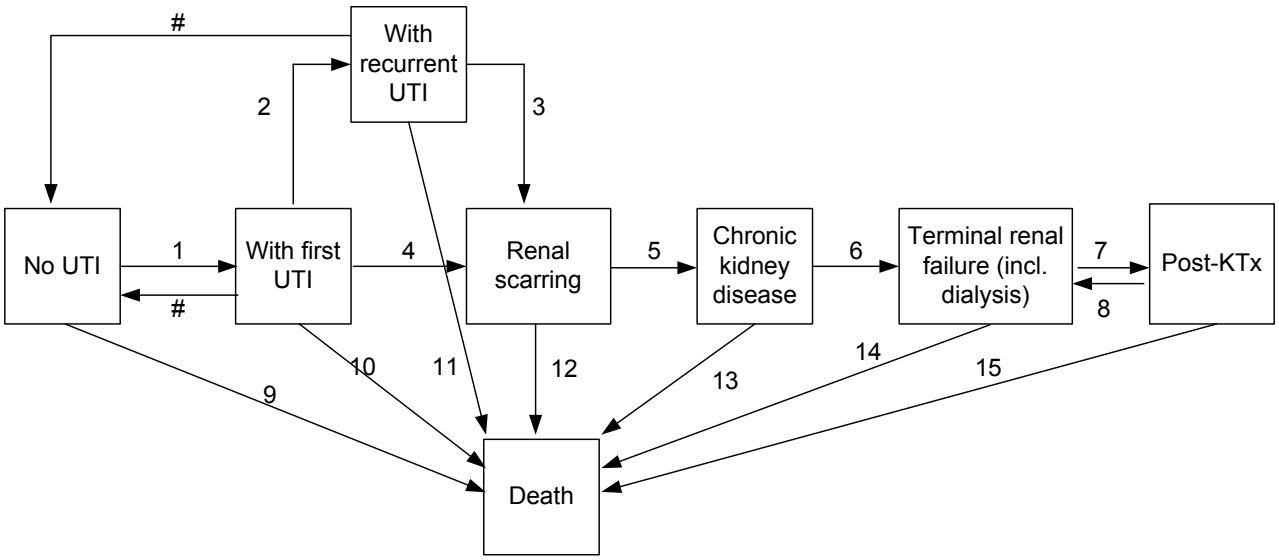
Urinary tract infections (UTIs) in children can lead to Renal scarring (RS), which can subsequently lead to hypertension, complications during pregnancy, and even chronic kidney disease stages 3-5 (TRF, terminal renal failure).[1] In 1997, 1.1% of the total health care budget of The Netherlands was spent on renal replacement therapy (RRT; i.e. dialysis or kidney transplantation), serving only 0.0006% of the total population.[2] This figure is similar in other developed countries. It is important to know whether strategies to reduce the number of children with a UTI and developing TRF are effective and cost-effective.

A number of clinical guidelines on UTIs have been developed to enhance timely diagnosis and adequate treatment.[3-7] Some guidelines recommend ultrasonography and voiding cystourethrogram (VCU) in all children with a UTI to detect respectively dilatation secondary to obstruction and vesicoureteric reflux (VUR). Subsequently, children with abnormalities of the urinary tract (e.g. VUR) are recommended antibiotic prophylaxis to prevent recurring UTIs. Some guidelines even recommend a ^{99m}Technetium-dimercaptosuccinic acid (DMSA) renal cortical scintigraphy in all children to detect RS.[3-5]

All these actions imply substantial health care costs. On the other hand, each case of TRF prevented will increase the quality of life, improve survival rates, and save health care resources in the longer run. A study in primary care in The Netherlands showed that adherence to the guidelines on UTI was not optimal; for instance, only 70% of the children with UTI received antibiotics treatment.[8] Dutch guidelines,[6,9,10] and also the more recent NICE-guideline,[7] recommend tests like VCU and DMSA only in specific groups of children. Current health care costs may thus be lower, but its cost-effectiveness in the long run remains unclear.

Two other economic modelling studies on UTIs in children have been performed. Whiting et al.[11] performed a study on the clinical and cost-effectiveness of tests for diagnosis and investigation of UTIs in children. Alternative strategies for diagnosis and management of UTIs in infants were analysed by Downs.[12] The aim of our study was to assess the cost-effectiveness of a maximum care model for UTIs in children, implying comprehensive diagnostic testing and antibiotics treatment, compared to current practice in primary care in The Netherlands.

Figure 1. Markov model



UTI=Urinary tract infection, KTx=Kidney transplantation

Methods

We compared two strategies for the management of UTI in children: 1) maximum care, assuming comprehensive diagnostic testing and antibiotics treatment, and 2) current care, with less diagnostic testing and antibiotics treatment in primary care, although assuming maximal guideline adherence in patients referred to hospital. If maximum care turned out to be cost-effective, we planned to compare maximum care with an improved version of current care. Table 1 describes the differences in the three strategies for UTI treatment.

Our research question, whether a maximum care approach will be more cost-effective than current care, was answered by applying probabilistic modelling. We developed a decision model to evaluate the potential cost-effectiveness of several approaches to UTI treatment from a health care perspective (Figure 1). Data from a systematic review of the research literature was used, because performing an empirical study to answer our questions was not feasible for practical and ethical reasons.

Literature review

In order to obtain transition probabilities –the probability for a patient with a certain condition to move to another condition– a systematic literature review was carried out.

Search strategy

Medline (last major up-date: January, 2007) was searched using the search strategies: ((“Urinary-Tract-Infections”/all SUBHEADINGS in MIME,MJME) OR urinary tract infection* OR UTI”), and (“Kidney-Failure-Chronic”/ economics ,epidemiology ,history ,mortality ,prevention-and-control ,radiography ,urine in MIME,MJME,PT). The reference lists of papers thus found were also checked for other potentially relevant studies.

Inclusion of studies

Included studies had to be written in English or Dutch, and be original studies or reviews of original studies. Other inclusion criteria were: absolute numbers of children had to be provided or could be calculated, it had to be clear that the study design was prospective, and the studies had to report on numbers of children rather than kidneys.

Studies on children of all ages were included as long as they included at least some children aged less than 13 years. Studies conducted in adults and children were only included if data for children were reported separately. No distinction was made between cystitis or pyelonephritis, because in children it is hard to make this distinction.[13] Concerning the probability to develop RS after UTI, we restricted ourselves to studies based on DMSA scintigraphy performed $\geq$6 months after the initial UTI, because by then the scars can be presumed to be persistent.

Data extraction

A single reviewer extracted data from each publication that satisfied the inclusion criteria, and compiled these in structured tables. Information to be collected in the tables were the percentage and number of children with the specific condition, total number of children included in the study, primary or secondary care, country, age, and remarks like whether the study also included children with VUR. Where possible, distinctions were made between boys and girls. If a single publication reported on two or more separate studies, then each study was extracted separately. If the findings of a single study were spread across two or more publications, then these publications were extracted as one. A second researcher checked the data extraction.

Table 1. Differences between maximum care, current care and improved current care

Stage	Maximum care	Current care	Improved current care
Perfect health	--- None ---		
Perfect health with UTI	• 100% 1st visit to GP + 1st urine test + quantitative urine culture + serum creatinine + blood pressure • 100% 2nd visit to GP + 2nd urine test + quantitative urine culture • 100% visit to paediatrician + ultrasonography + VCU + DMSA + abdominal radiograph • 100% antibiotics + antibiotic prophylaxis till diagnostic tests (6 months) + 35% antibiotic prophylaxis for 12 months	• 100% 1st visit to GP + 1st urine test + 40% quantitative urine culture + 0% serum creatinine + blood pressure • 32% 2nd visit to GP + 2nd urine test + 12% quantitative urine culture • 17% (♂) or 7% (♀) visit to paediatrician + ultrasonography + VCU + DMSA + abdominal radiograph • 66% antibiotics + 17% (♂) or 7% (♀) antibiotic prophylaxis till diagnostic tests (6 months) + 11% (♂) or 5% (♀) antibiotic prophylaxis for 12 months	• 100% 1st visit to GP + 1st urine test + quantitative urine culture + serum creatinine + blood pressure • 100% 2nd visit to GP + 2nd urine test + quantitative urine culture • 35% visit to paediatrician + ultrasonography + VCU + DMSA + abdominal radiograph • 100% antibiotics + 35% antibiotic prophylaxis till diagnostic tests (6 months) + 35% antibiotic prophylaxis for 12 months
Perfect health with recurrent UTI	--- Identical to perfect health with UTI, but without VCU ---		
Renal scarring	--- 100% yearly visit to paediatrician --- --- 100% yearly monitoring[1] + 93% DMSA scintigraphy ---		
Chronic kidney disease	--- 100% yearly visit to paediatrician or paediatric nephrologist --- --- 100% yearly monitoring[2] + ultrasonography --- --- 100% antihypertensive drug therapy (ACE Inhibitors) ---		
Terminal renal failure	--- Dialysis[3] ---		
Post-KTx	--- Kidney transplant and post-transplantation treatment ---		
Death	--- None ---		

UTI=Urinary tract infection, KTx=Kidney transplantation, [1] of serum creatinine, albumin, urine test (dipstick) for red blood cells (hemoglobin) and white blood cells (leukocyte esterase); [2] of serum creatinine, albumin, bicarbonate, sodium, haemoglobin, potassium, calcium, phosphate, cholesterol, blood glucose, blood pressure, urine test (dipstick) for red blood cells (hemoglobin) and white blood cells (leukocyte esterase); [3] Combination of all dialysis method

Analyses

If more than one study provided data for a transition probability, these data were pooled. An exception to the rule to weigh studies by the total number of children was the probability to get from CKD to TRF. For this probability both studies were weighted equally because the age groups were supplementary. A second researcher checked the data for input in the evaluation.

Economic evaluation

In the model each strategy was incorporated as a separate branch, representing the sequence of events related to UTI that an initially healthy child might experience within a time frame of 30 years. Effectiveness was expressed in terms of quality adjusted life years (QALYs) and costs in euros (indexed to 2006). Both costs and effects were discounted at a 4% discount rate, following the prevailing guidelines.[14]

Markov model

Figure 1 describes the sequential model used in the study. The results of the literature review were used as input to calculate the probabilities to get from one stage to the other (for results see Table 2). Boys and girls were evaluated separately because of the differences in some probabilities.

Components of maximum care were derived from North American, Swedish and English guidelines on UTI.[3-5] Input for current care was based on a study in Dutch primary health care[8] and Dutch primary care guidelines on UTIs.[6,9,10] These guidelines were also used to define improved current care.

A small number of children develops a UTI and visits a GP or paediatrician. Each UTI episode can result in a cured UTI, a recurrent UTI or RS. The probability of getting RS (kidney damage with normal or high glomerular filtration rate (GFR) [$\geq$90 mL/min/1.73m^2]) is higher for infants and young children with recurrent infections. A person with RS can get CKD (GFR 15-89) and some children eventually get TRF (defined as a person's life depending on RRT or GFR <15).[15] In our model TRF patients are treated by dialysis. People might get a kidney transplant, and therefore move to the post-kidney transplant state (post-KTx). In some persons the graft will not survive and they will return to the TRF state. Individuals in all states have a risk of dying, depending on the seriousness of the state. Each state generates costs (Table 3) and QALYs over time.

Model assumptions

The Quality of Life (QoL) weights were based on patient preferences. For chronic kidney disease (CKD)[16] the QoL weight was measured with the Standard Gamble method, and for TRF and post-kidney transplant (post-KTx)[17] the Time Trade Off method was used. For one year in the CKD state we counted 0.63 QALY[16] and for TRF and post-KTx respectively 0.57 and 0.75 QALY.[17] For all other states, except death (0.00 QALY), we counted 1.00 QALY.

The costs were based on current guideline prices for The Netherlands; costs per unit are reported in Table 3.[2,14,18-20] Following a health care perspective, only direct medical costs were used for analysis. Costs of over-the-counter treatments were not included. Medical care for RS, CRF, TRF and post-KTx was assumed to be of high clinical quality, and the values associated with these states were identical for all strategies.

Patients were assumed to fully comply with the course of antibiotic treatment. The percentage of boys and girls getting prophylactic antibiotics for six months (till diagnostic testing was performed) was assumed to be similar to the proportion of boys and girls referred to a paediatrician. The total percentage of children getting prophylactic antibiotic treatment for 12 months in maximum care was estimated to be 35%. This is based on the percentage of children with a first UTI in which VUR is detected (30%),[21-24] and the low probability for a child to have urinary tract abnormalities[25,26] or to have more than three UTIs in one year.[8] As not all high risk children were referred to a paediatrician in current care, the percentage of children getting antibiotic prophylaxis for one year was assumed to be 67% of the children referred to a paediatrician. Improved current care is identical to maximum care, except that only problematic children were referred to hospital (35% of all children).

In case of maximum care, we estimated a 10-11% probability of getting a recurrent infection.[27,28] We estimated the probability of getting a recurrent infection in current care and improved current care based on the figure for maximum care and results of two literature reviews.[29,30] The number of recurrent infections was assumed to be one per child.

A time horizon of 30 years was chosen because causal relationships between care and outcomes can be expected to prevail over that period. Considering the increasing prevalence of most chronic diseases in later life, a lifetime perspective would make causal relationships weak and consequently more speculative.

Table 2. Transition probabilities

	Transition	Yearly probability (95%CI) and sources
1	No UTI → With first UTI	Boys: 0.876% (0.874;0.878)[21,26,36] Girls: 1.482% (1.474;1.489) [21,26,36]
2	With first UTI → With recurrent UTI	• Maximum care: Boys: 10.2%[27] Girls: 11.375 (11.275;11.475)[27,28] • Current care*: Boys: 12.898% Girls: 14.711% • Improved current care*: Boys: 11.91% Girls: 13.28%
3	With recurrent UTI → Renal scarring	42.0%[27]
4	With first UTI → Renal scarring	20.282% (10.281;30.284)[23,27,32,41,42]
5	Renal scarring → Chronic kidney disease	2.280%[1,43-45]
6	Chronic kidney disease → Terminal renal failure	11.400% (-1.628;13.028)[33,35]
7	Terminal renal failure → Post-KTx	7.812% (7.754;7.847)[33,34,37,39,40]
8	Post-KTx → Terminal renal failure	5%[39,40]
9	No UTI → Death	Natural course[31]
10	With first UTI → Death	Natural course[31]
11	With recurrent UTI → Death	Natural course[31]
12	Renal scarring → Death	Natural course[31]
13	Chronic kidney disease → Death	Natural course[31] + 2%[33]
14	Terminal renal failure → Death	5.189% (5.161;5.216)[35,37]
15	Post-KTx → Death	1.093% (1.091;1.094)[37,38]

UTI=Urinary tract infection, KTx=Kidney transplantation, # Complementary probability, * These transition probabilities are based on figures for maximum care

Analyses

Probabilistic Markov-based modelling using first and second order Monte Carlo simulation simultaneously was used for the analyses. To examine the robustness of the model, one-way sensitivity analyses were performed with regard to the discount rate (0%, 8%). Parametric uncertainties in the input parameters were taken into consideration by performing probabilistic sensitivity analyses (second order Monte Carlo simulation). Distributions were available for the yearly transition probabilities and the QoL weight for CKD. All costs and the QoL weights for TRF and post-KTx were considered to be fixed. Also some yearly probabilities were assumed fixed, because no information on the distribution was available.

Table 3. Cost prices per unit of care or state

Unit of care or state	Costs per unit (€)
Visit to the GP	21.00[14]
Visit to a paediatrician or nephrologist	58.29[14]
Urine test	1.97[18]
Quantitative urine culture (dipslide)	2.28[20]
Ultrasonography	70.17[18]
VCU	220.07[18]
DMSA	131.60[18]
Abdominal radiograph	45.13[18]
Serum creatinine, albumin, potassium, phosphate, blood glucose, sodium, cholesterol	1.47[18]
Haemaglobin	11.53[18]
Calcium	5.78[18]
Bicarbonate	4.04[18]
Blood pressure measurement	none
Antibiotics	6.50[19]
Antibiotic prophylaxis	0.29 per week[19]
ACE-inhibitors	8.79[18]
RF/dialysis	70,213 (1st year)[2]
	66,120 (later years)[2]
KTx	51,002[2]
Post-KTx	10,206[2]
Death	none

ACE-inhibitor = Angiotensin-converting enzyme, DMSA = ^{99m}Technetium-dimercaptosuccinic acid (renal cortical scintigraphy), GP = general practitioner, KTx = kidney transplantation, RF = renal failure, VCU = voiding cystourethrogram

Results

Table 2 shows the results of the literature review. A total of 16 studies completely matched our inclusion criteria.[21,23,26,28,31-42] Unfortunately, no prospective studies were available for calculating the risk of getting CKD after RS. Therefore, we had to use retrospective studies.[1,43-45] The criterion of at least 30 children per study was not met for the only study focussing on the probability of getting RS when having recurrent UTIs; this study involved 26 children.[27] Numbers of children used for calculating the other transition probabilities ranged from 150 (RS to CKD) to >100,000 (no UTI to UTI).

Table 4 reports on findings regarding cost-effectiveness. We found that maximum care dominated current care for both boys and girls, meaning that it delivered more quality of life and saved money. In boys, maximum care gained more QALYs than current care (0.00102 QALYs over 30 years). It also saved

Table 4. Results base-case analyses maximum care vs. current care

Strategy	Costs (€)	Incremental costs (€)	Effect (QoL)	Incremental Effect	Costs/ Effect
Males:					
• Maximum care	998.10		17.32014		57.62
• Current care	1040.70	42.70	17.31913	-0.00102	60.09
Females:					
• Maximum care	1625.20		17.30207		93.93
• Current care	1703.00	77.80	17.29988	-0.00219	98.44

QoL=Quality of life

€42.70 per boy over 30 years. In girls the gain in QALYs was 0.00219 and the cost saving was €77.81 over 30 years.

In the comparison of improved current care with maximum care, we found again that maximum care dominated, but less than compared to current care. In boys, maximum care gained 0.0012 QALY and saved €27.81 over 30 years. In girls, these figures were respectively 0.00125 QALY and €42.99.

Both 'costs' and 'QALYs' were calculated to present values (discounted at 4%). Sensitivity analyses on the discount rate (0%, 8%) did not alter the results in a meaningful way.

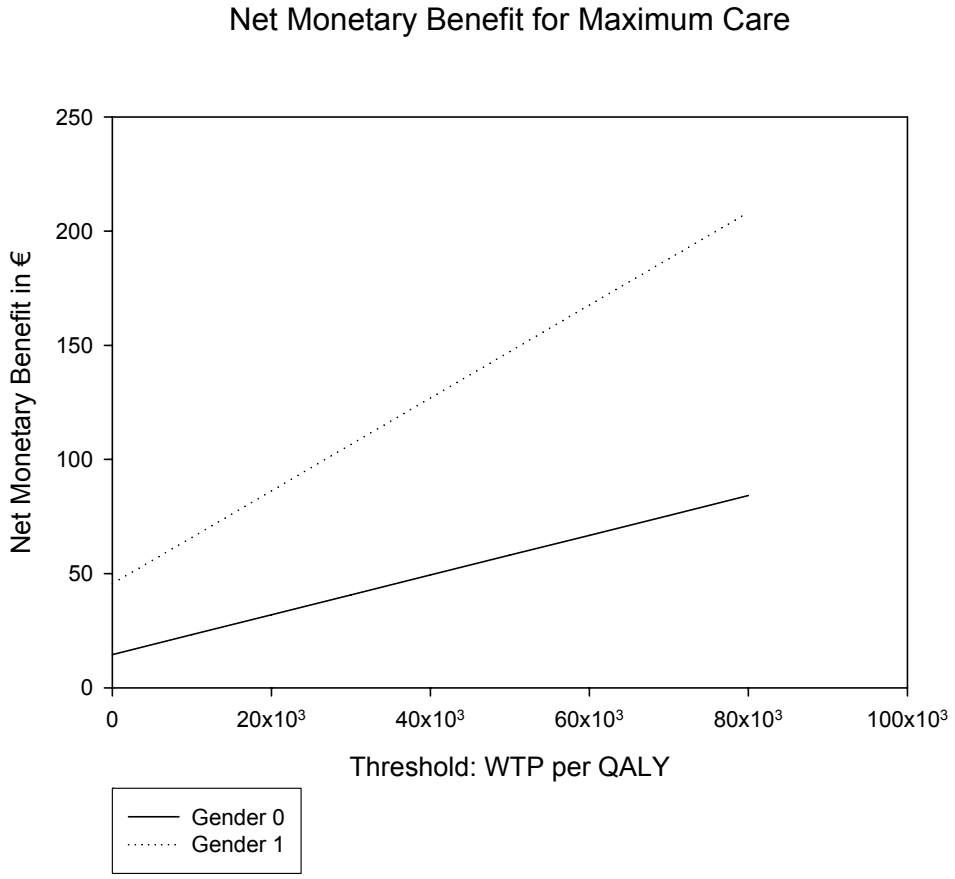
Figure 2 shows that, in boys, the net monetary benefit (NMB) of maximum care (compared to current care) ranged from €20 to €80 for a willingness to pay (WTP) for a QALY ranging from €0 to €80,000 respectively. In girls, the NMB ranged from €50 to €200. For maximum care compared to improved current care, the NMBs were lower, for both boys and girls (respectively €30 to €120 and €40 to €140 for a WTP of €0 to €80,000). A positive NMB implies that the costs of a new therapy is less than the value of the additional benefit achieved.[46]

Discussion

This study found that maximum care for UTI in children was dominant in the long run to current care and improved current care for boys and girls. This implies that it delivered more quality of life at lower cost.

As far as we know, our study is the first study to focus on the benefits of maximum care to prevent the development of future kidney failure as a result of UTIs in childhood. A review by Hoomans et al.[47] showed there are not many good costing studies on guideline implementations. However, costing studies on these topics

Figure 2. Net Monetary Benefit for maximum care vs. current care



€ = euro's; WTP = Willingness to pay; QALY = Quality adjusted life year; Gender 0 = boys; Gender 1 = girls

are indeed hard to do. Our study was obviously limited by the availability and quality of the data. For instance, only one prospective study focused on the probability of getting RS when having recurrent UTIs using DMSA scintigraphy, and this study included only 26 children.[27] On the other hand, we compared this study to results from other studies, which were retrospective and/or used other methods than DMSA scintigraphy to detect RS. Altogether these studies [48-50] showed similar percentages. Likewise, in the only prospective study found on RS and CKD [51] the follow up time was not specified. We therefore were unable to use this study, and decided to include retrospective studies to estimate the probability to get from RS to CKD.[1,43-45] Despite a systematic literature search and checking reference lists, it might be possible we have missed relevant papers. For some items we did not have the true cost per unit. Uncertainty was dealt with by using a probabilistic method, using 95% confidence intervals for most probabilities.

The Markov model also had some limitations. It ignored the costs of productivity loss as well as health consequences in other areas than renal failure, such as hypertension resulting from untreated RS. This means the model cannot be applied to the individual child. The model probably underestimated the impact of initial antibiotic treatment, because the figures used were based on a comparison between single dose and 7-10 days of antibiotic treatment. The reviews used for calculating the effects of antibiotic prophylaxis[29,30] did not show significant results, but all showed a trend towards a clinically relevant effect. We also could not take into account the effects of early diagnosis of RS, just because no figures were available from the literature. Inclusion of these important effects would probably not change conclusions.

Despite the limitations of our study, it is intriguing that maximum care turned out to be both more effective and less costly. Does this imply that all children with UTI should be send to hospital for comprehensive diagnostic testing and antibiotic treatment? Other factors come into play here, such as hospital capacity for managing this large patient population and the burden posed on children and parents by invasive testing. The debate about the cause of renal damage in children is still going on. Despite the well defined evidence base for reflux nephropathy, many paediatricians now appear to consider congenital dysplasia to be the cause of most parenchymal defects. This belief is reflected throughout the NICE guidelines, and in their advice to dramatically reduce management activity from previous standards.[7] However, some authors have strongly argumented against this view. For instance, Coulthard[52] pointed out that both congenital dysplastic defects and reflux nephropathy occur. Consequently, he argues that scarring rates are likely to be reduced if more attention is focussed on minimising treatment delay and attempting to prevent UTIs in children with VUR.[52] An obvious alternative to current care would be that more children with UTI in primary care receive antibiotic treatment. In addition, perhaps more children with UTI at risk for RS should be referred to hospital. This would be consistent with prevailing guidelines in The Netherlands[6] and e.g. the recommended approach by Marks et al.[53] that all high risk children require imaging investigations to identify those with congenital malformations, obstruction, abnormal renal tract and/or bladder. Children with their first, uncomplicated, febrile or non-febrile UTI caused by *Escherichia coli* and responding well to treatment will, therefore, not undergo imaging, unless they have recurrent infections.[53] In addition to this approach, extra attention should have to be paid to young children.[6] However, as also said by

Marks et al.,[53] these recommendations are based on opinion rather than on firm evidence, which is lacking in the literature.[53]

Implementation of maximum care may be hard to accomplish, as it has major impact on the capacity to diagnose and treat UTIs, especially in hospital care. Therefore, improving current primary care remains an important objective. Because the differences in QALYs and costs between current care and improved current care were relatively small, interventions to change physician behaviour should not imply high investments. Future research should focus on the impact of various strategies of diagnostic testing in UTI on both quality of life and costs.

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Chapter 7

Towards optimal management of urinary tract infections in children: development of a quality improvement intervention

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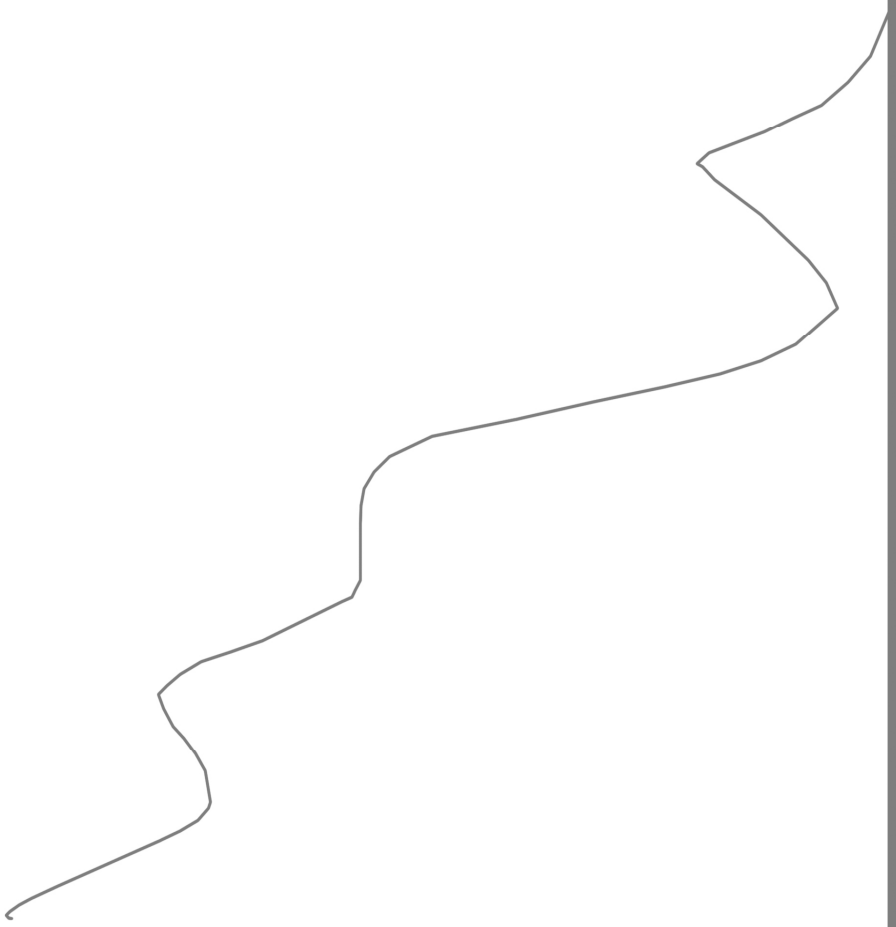


Abstract

Objective: To systematically develop and pre-test an intervention to improve the quality of the diagnosis and treatment of (suspected) urinary tract infections in children in general practice.

Methods: A multi-centre pilot study in Dutch general practices, in which, together with general practitioners (GPs), practice assistants and parents, targets for improvement of the treatment were defined, strategies and measures for improvement were selected, and interventions were pre-tested.

Results: In two Delphi rounds seven treatment targets were selected, concerning diagnostics, treatment, referral and follow-up. GPs recommended to make some small changes to the suggested intervention materials. This resulted in summary charts and written individual training packages for practice assistants and GPs, which were pre-tested on appreciation and use in daily practice. Use of the intervention materials could be better, but those who used the materials for the first time, appreciated these as pleasant and said to use it rather often in daily practice. Half of the GPs said to have really made changes to their daily practice.

Conclusions: The results of the study were promising. A pre-tested intervention is ready for evaluation in a rigorous study.

Introduction

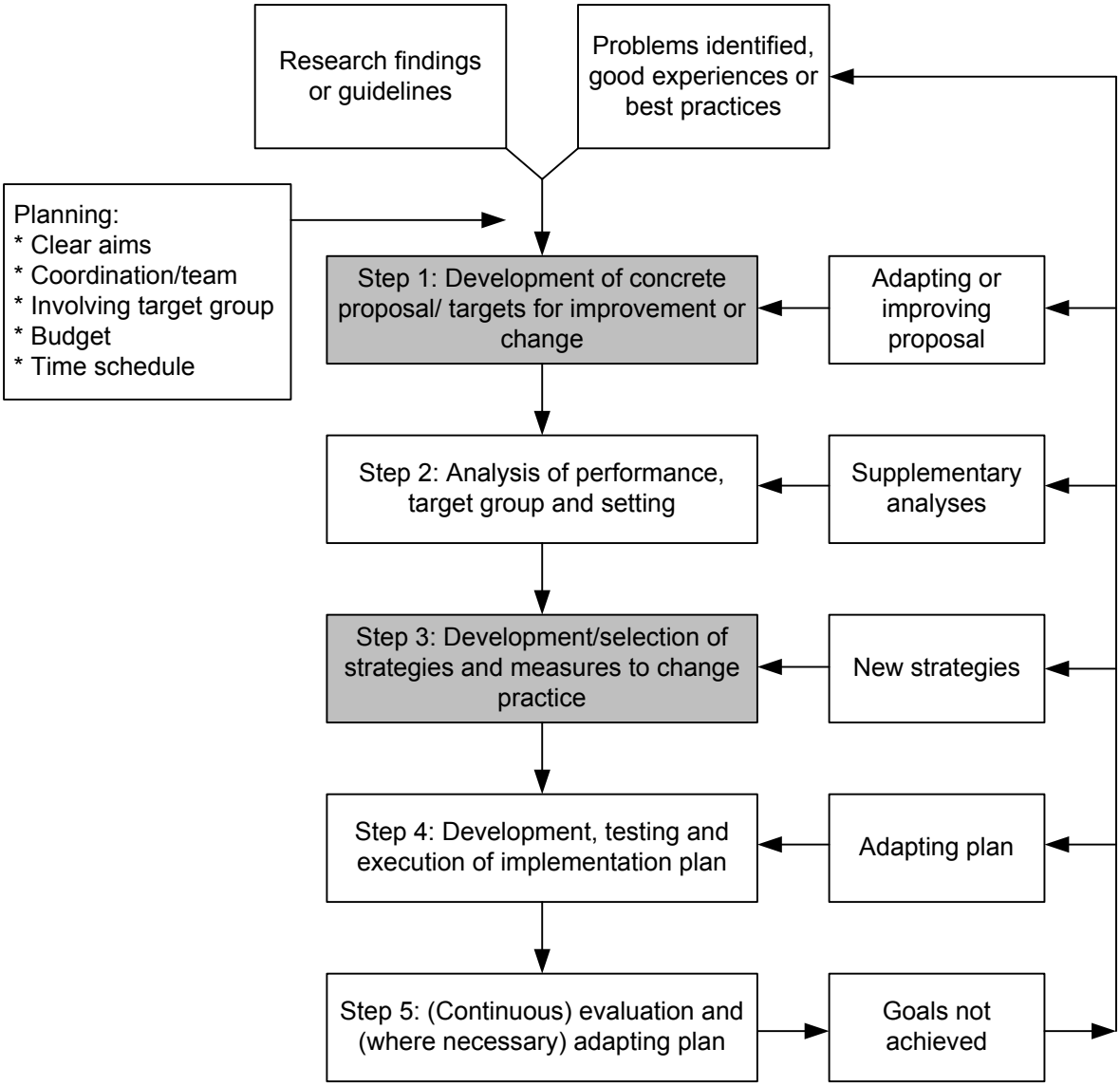
The consequences of childhood urinary tract infections (UTIs) not diagnosed and treated in time can be serious, and include problems such as hypertension, complications during pregnancy and even renal failure later in life.[1] Previous research showed that there is room for improvement concerning the whole process of being on the alert for a UTI, diagnostics, treatment, follow-up and referral in general practice care.[2-6] Besides that, an economic evaluation study showed that improvement of current care delivers more quality of life at lower costs.[7]

Which interventions to improve healthcare practice work best in particular situations is not yet clear. The scientific literature concerning implementation interventions offers little specific assistance to the introduction of changes, so it is necessary to develop strategies and measures for each clinical problem and target group.[8] Successful implementation of innovations or changes in health care performance requires good preparation and rigorous planning of the steps in the change process (Figure 1).[9] Small-scale testing of the plan and its components can be seen as a crucial element in preparing the implementation.[8]

Several groups are involved in the management of UTIs in childhood. The parents have to be on the alert for UTIs in their child and have to decide to go to the general practice, the practice assistant has to recognise signs that are related to a UTI in children and perform the appropriate urine tests, and the general practitioner (GP) also sometimes has to initiate urine testing and has to take care of adequate antibiotic treatment, follow-up of the child and referral to secondary care. Representatives of general practices and parents can play a crucial role in designing and testing a plan for better performance. They often know best what is feasible and potentially effective. Furthermore, commitment from those involved to the entire process ultimately contributes to successful large scale improvement.[9]

This chapter describes the systematic development and pilot testing of an intervention to improve the quality of the diagnosis and treatment of (suspected) UTIs in children in general practice care.

Figure 1. Model of Effective Implementation[9]



Methods

The study presented in this chapter was a multi-centre pilot study in Dutch general practices. Together with the GPs and the practice assistants of these practices we: 1) defined concrete key targets for improvement of the treatment of childhood UTIs (step 1 in the model), 2) developed and selected strategies and measures to change practice (step 3 in the model), and 3) pre-tested a quality improvement intervention (step 3 in the model). Parents were involved in step 3 of the process.

Step 1: Defining targets for improvement

Previous research showed on which aspects the diagnosis and treatment of childhood UTIs could be improved.[2-7] This resulted in a list of possible targets for optimal general practice care, which was tested in two written Delphi rounds.[10,11] In the first Delphi round nine GPs were asked to what extent they found the listed targets relevant and feasible. In the second Delphi round the GPs once again judged the relevancy and feasibility of the selected targets, and also made adjustments with respect to the contents. The GPs were recruited from a group of GPs who had participated in previous research of our group on childhood UTIs.[3]

Step 2: Developing and selecting strategies and measures to change practice

In the second Delphi round the GPs were also asked to judge on relevancy and feasibility a couple of ideas about possible interventions for improving UTI care in general practice, and whether these materials should focus on UTIs in general or on childhood UTIs in particular. Given the small number of children with UTI in a single practice (i.e. approximately five in one year),[4] we preferred a relatively simple, individual intervention; a method that proved to be effective for improving medical behaviour in primary care concerning men with lower urinary tract symptoms.[12]

Step 3: Pre-testing the quality improvement intervention

After defining the objectives and developing and selecting methods for change, we pre-tested the quality improvement intervention stepwise in two pilot studies.

Pilot study on lay-out and contents of the quality improvement intervention

The first pilot study focused on lay-out and contents of the training packages. Participants were seven GPs from steps 1 and 2 and their practice assistants. Four parents also participated in this step. These parents came to the general practice for testing their child's urine and were handed over an envelope containing two letters about childhood UTIs (one by the Dutch College of General Practitioners (DCGP) and one by the Dutch Kidney Foundation) and an invitation to participate in the project. Two months after sending the intervention materials to

Box 1. Final set of targets

1. Practice assistants order children with more than three days of fever (>38 ^{0}C) without focus to come to the general practice, in order to be seen by a GP.
2. Practice assistants order children with a suspected UTI to come to the general practice, in order to be seen by a GP.
3. Boys till 12 years of age and girls trough 4 years of age with a proven UTI have to be treated with a 10-day antibiotic course amoxicillin/clavulanic acid, unless there is a contra indication.
4. Girls aged 5-12 years old with a proven UTI without signs of renal involvement have to be treated with a 7-day antibiotic course nitrofurantoin, unless there is a contra indication.
5. Children aged less than 6 months old with a (suspected) UTI have to be referred to secondary care for treatment. The GP does not start any treatment.
6. Girls aged through 4 years, girls aged 5-12 years old with pyelonephritis or more than one UTI and boys till 12 years of age have to be referred to secondary care for further diagnostics.
7. All children with a UTI have to have a follow-up contact within three to five days after finishing the antibiotic treatment, in which the urine is tested by using a dipslide or urine culture.

GP=General practitioner, UTI=Urinary tract infection

the general practices, the GPs, practice assistants and parents were interviewed by telephone, using a semi-structured interview format.

Pilot study on use and appreciation of the quality improvement intervention

The second pilot study focused on the use and appreciation of the quality improvement intervention. Participants were 19 GPs recruited from a random selection from a database with GP addresses, and 33 of their practice assistants. For practical reasons it was not feasible to evaluate the intervention materials for parents in this second step.

Three months after sending the adjusted intervention materials to the general practices, they were sent a questionnaire. Questions focussed on whether they used the intervention materials during the second pilot study (yes/partly/no), how they experienced it (pleasant/neutral/not pleasant) and whether they used it in daily practice (always/most times/sometimes/most times not/never). Besides these more general questions, GPs and practice assistants were asked to rate five statements on the training packages on a 5-point Likert scale. We also asked GPs whether they had made changes in their routines concerning the management of childhood UTIs.

Box 2. Intervention materials as suggested (left column) and after Delphi round 2 (right column)

Intervention materials as suggested	R	F	Intervention materials pre-tested
Parents			
• Information leaflet	5	6	• *DCGP patient letter* 'Urinary tract infections: Cystitis in a child'. • Part of the *Dutch Kidney Foundation leaflet* 'Wanted! Recognising urinary tract infections in children – a tool for parents', namely the cases and the texts on UTIs and being on the alert.
Practice assistants			
• Information leaflet with a summary of the most important information derived from the DCGP guideline for general practitioners and the DCGP guideline for telephone triage	7	7	*Summary chart* about the management of UTIs in children, and also with a flow chart on diagnosing UTIs and a checklist about use of the dipslide method.
• Flow chart	5	5	
• Training course	7	5	• *Reader* 'Urinary tract infections in children – Training for practice assistants'. • Chapter on urinary tract infections from the *DCGP guidelines for practice assistants*.
General practitioners			
• Information leaflet with a summary of the most important information derived from the DCGP guideline for general practitioners	4	5	*Summary chart* about the management of UTIs in children, and also with a flow chart.
• Flow chart	5	5	
• Training by use of the PIN (program for individual training)	4	6	• *PIN* urinary tract infections: a booklet with an introduction on the topic, work sheets with questions on the topic and background information on the answers, and a test.

R=Relevancy, F=Feasibility (number of GPs who agreed [total N = 9]), DCGP=Dutch College of General Practitioners, UTIs=Urinary tract infections

Results

Step 1: Defining targets for improvement

Nine GPs helped us to define the improvement targets. After judging a list of 22 possible targets on relevancy and feasibility, a set of seven targets was selected, concerning diagnostics, treatment, referral and follow-up. Box 1 presents the final set of seven targets.

Step 2: Developing and selecting strategies and measures to change practice

The left three columns of Box 2 show the intervention materials as suggested and the ratings on relevancy and feasibility of the nine GPs in the second Delphi round. Based on these results, for both the GPs and the practice assistants the leaflet and the flow chart were added together in a summary chart. Material focussing on childhood UTI was preferred over material on UTIs in general. However, this last adjustment was not possible for the PIN (Programma Individuele Nascholing = program for individual training), because this is an existing method developed by the DCGP. The PIN is a booklet with an introduction to the topic, work sheets with questions about the topic and background information on the answers, and a test which can be handed in to the DCGP in order to get accreditation points.[13]

Step 3: Pre-testing the quality improvement intervention

Pilot study on lay-out and contents of the quality improvement intervention

The GPs and practice assistants were in general satisfied with the intervention materials they received, except for some remarks about the lay-out. The chapter on urinary tract infections from the DCGP guidelines for practice assistants[14] was perceived as a bit boring to read and they felt that it should focus more on UTIs.

The parents were very satisfied with the DCGP patient letter, but the contents of the Dutch Kidney Foundation letter were perceived as somewhat aggressive. On the other hand, parents thought it would be good if all parents would be aware of the serious side consequences childhood UTIs may have. All these comments led to adjustments to the intervention materials. The set tested on

Table 1. Use and appreciation of intervention materials (number of general practitioners and practice assistants)

	Use		Appreciation		Use in daily practice	
Practice assistants (n=33)						
Summary chart	Yes:	8/33	Pleasant:	11/14	Always/most times:	5/15
	Partly:	7/33			Sometimes:	9/15
Guidelines	Yes:	11/33	Pleasant:	14/18	Always/most times:	13/17
	Partly:	7/33			Sometimes:	3/17
Reader	Yes:	9/33	Pleasant:	12/14	Always/most times:	1/14
	Partly:	5/33			Sometimes:	10/14
General practitioners (n=19)						
Summary chart	Yes:	7/19	Pleasant:	10/16	Always/most times:	7/16
	Partly:	9/19			Sometimes:	7/16
PIN	Yes:	10/19	Pleasant:	8/12		
	Partly:	2/19				

use and appreciation in the second pilot study is shown in the right column of Box 2.

Pilot study on use and appreciation of the quality improvement intervention

Table 1 shows that altogether 14-18 of 33 practice assistants had used the different intervention materials during the pilot study. Most of them rated the materials as pleasant, and said to use it rather frequently during daily practice. The reader was used slightly less often in daily practice than the summary chart and the guidelines.

The practice assistants who used the reader during the pilot study (n=14) were also asked to react on five statements about the reader. All practice assistants found the time spent on the reader worthwhile, and 11 said it helped to perform better according to the guidelines. Using the reader gave almost all practice assistants new information on UTIs in children, and ten practice assistants said it really changed their way of acting. Twelve practice assistants would certainly recommend this training to colleagues.

Table 1 also shows the GP results on use and appreciation of the intervention materials. The summary chart was used by 16 of 19 GPs, and ten of them rated it as pleasant. Ten GPs used the PIN and most of them rated it as pleasant to use. Use in daily practice was not applicable for the PIN, because this is more like a knowledge test than a reader.

A total of 12 GPs, those who had used the PIN, answered to the statements. Ten of them agreed with the statement that the time spent on the PIN was worthwhile, and also ten would recommend the PIN to colleagues. Ten GPs said the PIN would help them to better adhere to the guidelines. Part of the information was new to seven GPs. The statement 'The PIN changed my daily practice concerning UTIs in children' was agreed with by seven GPs.

To a somewhat different question on changing behaviour, ten GPs said to really have made changes in their daily practice. All had made agreements with the practice assistants about the policy on childhood UTI, and two had bought dipslides for a better diagnosis of UTIs. Other changes were: making changes to prescribing and referring, using a dipslide at follow-up, or using the dipslide more often (n=1 for all).

Discussion

Through a step-by-step process, we developed a new intervention to help practices to follow UTI guidelines. The results of the studies were promising. Although not all practice assistants and GPs used the change materials during the pilot study period, almost all who did use it were positive. Besides that, ten of 16 GPs reported to have made changes in their daily practice, varying from making more agreements with the practice assistants to buying a dipslide.

This pilot study resulted in intervention materials adjusted to the users. Cooperating with enthusiastic GPs was a very positive point in this project. Experience in many projects has shown that it is best to start with a small group of enthusiastic care providers, practices or institutions.[15] Also the participation of practice assistants and parents was important, because part of the intervention focused on them. In future, participation of the practice assistants might get improved when approaching them directly (bottom-up) in stead of through the GPs (top-down). After all, the practice assistant is the one who is the first to deal with a (suspected) UTI. Unfortunately, the number of participating parents was small. This is probably due to the small number of children having a UTI in a single practice and the relatively short study period.

Box 3. Contents of future intervention to test in a randomised controlled trial

Training packages to be send by mail to general practices and/or general practice co-operatives (self-study):

- Reader and guidelines for practice assistants and triage nurses by the Dutch College of General Practitioners
- Program for Individual Training (PIN) for general practitioners

Workshops for practice assistants, triage nurses of general practice co-operatives, and general practitioners (for instance 4-6 months after sending the intervention materials to the practices or co-operatives):

- Discussing the guidelines
- Discussing 'homework' (i.e. the answers to the questions in the reader for practice assistants and triage nurses, and the PIN for general practitioners)
- Defining targets to change behaviour for individual practice assistants and general practitioners
- Handing over the summary charts

To develop an effective intervention, a systematic approach is recommended.[9] Furthermore it is important to adjust the intervention to the target group, because they are the ones who have to change their behaviour. The systematic approach we used, the Model of Effective Implementation,[9] and the Delphi procedure[10,11] helped us to a large extent. We performed the first steps from identifying the problem to identifying barriers and facilitators in an earlier stage of the project,[2-7] and these steps gave a lot of information that could be used in the steps described in this chapter. Subsequently, the results from the steps described in this chapter will give good starting-points for the next step, i.e. adjusting the current intervention and testing the interventions on effectively changing behaviour in a randomised controlled trial. To measure sustainable behaviour change in a trial, the period between receiving the intervention materials and the evaluation has to be longer than in the study presented in this chapter. A disadvantage might be that, given the low yearly prevalence of childhood UTI in a single general practice,[4] a lot of general practices should participate to be able to measure effects.

The results of the pilot study were certainly promising. To make the intervention more complete, it might be wise to use more active interventions, for instance workshops. These could focus on more than just childhood UTIs, to equalise the time spend on workshops and the number of childhood UTIs in a single general practice. These workshops could also focus more on organisational issues to change routines. Box 3 describes the elements of the intervention which we would like to implement and evaluate in future. Our pilot study only focussed on

general practices, but of course general practice co-operatives can be involved as well. To evaluate the intervention materials for parents, i.e. the DCGP letter and the Dutch Kidney Foundation letter, a separate study has to be conducted.

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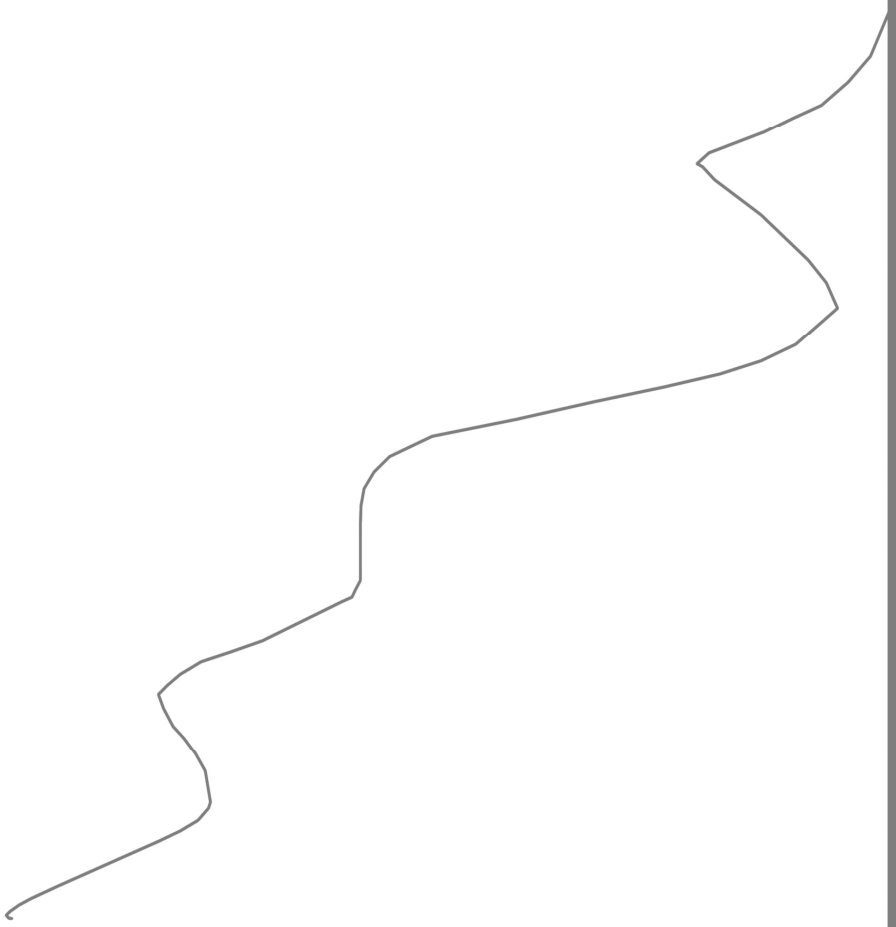
General discussion



Introduction

This thesis focussed on the current diagnostic and therapeutic approach to urinary tract infections (UTIs) in children in Dutch primary care, with a perspective on preventing renal failure in the long run.

Although having a UTI in adulthood is often harmless, having one at a younger age might have serious consequences.[1] Timely and accurate diagnosis and treatment of UTIs in childhood are considered to prevent renal problems, as well as a number of other health problems, at a later age.[2] On the other hand over-diagnosis and over-treatment need to be prevented, considering for example antibiotic resistance, medicalisation and health care costs. Given such complex decisions in children at risk, a good understanding of actual care in primary care is important to identify gaps in performance. This thesis contributes to the understanding of how childhood UTIs in general practice care are managed, and how this might be improved.

After a general introduction to the topic, the first chapter in this thesis gave an overview of incidence rates and management of UTIs in children 0-18 years old. Chapter 2 addressed parents' awareness of and knowledge about childhood UTIs. To study how UTIs in children aged <12 years old in Dutch general practice care are managed, we performed three studies (chapters 3-5). To get insight into which strategy, maximum care or current care, provides the best balance between quality adjusted life years gained and costs, an economic evaluation was performed (chapter 6). Because the management of childhood UTIs could be improved, we developed a quality improvement intervention, which is described in chapter 7.

In this general discussion, first the main findings of these studies are presented, and at the end summarised in six key messages. Thereafter, these main findings will be discussed and also methodological aspects will be considered. This part of the thesis ends with implications for future research and for health policy.

Main findings

The study in 82,053 children aged 0 to 18 years old (chapter 1) showed an overall incidence rate of UTIs of 19 episodes per 1000 person years. The incidence rates were related to gender (more in girls than in boys), season (decrease in summertime for children at the age of 0 to 12 years old) and urbanisation (more in smaller cities and rural areas than in the three largest cities). The study described

in chapter 1 also reported that the adherence of general practitioners to clinical guidelines concerning prescription and referral could be better.

Information derived from 20 interviews held with parents who had a child recently diagnosed with a UTI (chapter 2) showed that parents had knowledge of the typical symptoms related to a UTI, but not of the atypical symptoms. However, parents were sceptical about health education to broad groups of parents and mass screening, because this would be perceived as not relevant or it would unnecessarily increase anxiety. They thought it would be better if physicians and nurses would be more on the alert for possible UTIs in children, and more information should be given once a UTI is diagnosed.

Chapter 3 showed that although more than 90% of triage nurses at general practice co-operatives, providing out-of-hours primary care, acted according to the guidelines if a UTI was suspected (meaning asking the parents to bring the child to the general practice co-operative), in most cases the nurses did not think a UTI was likely. If a UTI was suspected, all triage nurses requested the parents to provide a sample of the child's urine, but only 70% gave instructions on how to collect the urine.

The diagnosis of UTIs in children can be improved (chapter 4). The use of the nitrite test was found to be largely appropriate (performance in 87% of 148 children diagnosed with a UTI), but other tests are either overused or underused. Especially the urine culture is underused. Also, in only 25% of the children having a follow-up contact the urine was tested using the recommended dipslide.

Based on data of the Netherlands Information Network of General Practitioners (LINH), 284 children aged 0 to 6 year old with a diagnosed UTI in 2001 were followed for three years (chapter 5). The results of this study showed that not all children were prescribed antibiotics, and if they were, not all received the antibiotics of first choice. Also, the follow-up rate should be better. Of the children who should have been referred, because of their age, sex and/or UTI history, less than 33% was actually referred.

A literature study (chapter 6) showed that there are still gaps in our knowledge the percentage of children with a UTI actually getting renal problems. A probabilistic modelling study using Markov models showed that maximum care, implying more testing and antibiotic treatment, gained more quality adjusted life years (QALY's) and saved more money in the end in 30 years compared to current care and to improved current care. However, drawing firm conclusions is not possible, given the limitations of the input data derived from the literature review.

Chapter 7 describes the development of a quality improvement intervention for primary care. The results of a pilot study on use and appreciation of the quality improvement intervention were promising. Although not all practice assistants and general practitioners used the intervention materials, almost all who did so rated them as pleasant to use. There were also 10 of 16 general practitioners who reported to have made changes in their daily routines.

Key messages

The results of the various studies lead to the following key messages:

- There are mixed feelings about raising parents' awareness on UTI. Giving adequate information to parents only after a UTI has been diagnosed in a child seems appropriate and sufficient.
- Quality improvement should focus on triage, diagnosis, treatment, follow-up and referral of childhood UTIs, for example, currently, not the appropriate diagnostic tests are performed and not all high risk children are referred to secondary care. Besides the general practice, the general practice co-operative is an important setting for detection and treatment of childhood UTIs.
- It seemed that maximum care, implying more testing and antibiotic treatment is better than current care and improved current care, but figures are too uncertain to draw firm conclusions.
- A promising intervention to improve management of childhood UTIs in general practice, based on written, individual change materials for general practitioners and practice assistants, is available for further testing.

Discussion of the main findings

The incidence rates found in this thesis indicate that an average Dutch general practice will see about five children with a diagnosed UTI each year. Many more children might have a UTI, which means a general practitioner has to be on the alert and has to perform the appropriate tests.

Raising awareness

The first step towards improvement is increasing the awareness of parents and GPs. Children with UTIs present themselves mostly with atypical symptoms like fever, vomiting and weight reduction, and not with the more typical symptoms like

strangury and pollakiuria.[3] But the problem of parents not knowing, identifying or correctly interpreting the symptoms of childhood UTIs might be limited. Although the parents did not know the symptoms, they felt that something was wrong with their child and therefore made an appointment at the general practice. Besides, there are mixed feelings about raising awareness, e.g. through mass media campaigns.[4,5] What is not feasible at all is screening for UTIs in children. For each case of end-stage renal disease that screening would prevent, thousands of children need to be tested and hundreds would receive unnecessary treatments.[6,7] Also, a child might not have a UTI one week, but will have it a week later. So, the focus should be on correctly identifying incident cases with an important role for practice assistants and general practitioners in the diagnosis of childhood UTIs.[8]

Of course, also the primary care workers face the problem of the atypical symptoms. Shaikh et al.[9] concluded that, although no sign or symptom by itself confirms the diagnosis of UTI in children, the presence of fever (>40^{o}C), history of a previous UTI, lack of circumcision, abdominal pain, back pain, dysuria, frequency, new-onset incontinence, and suprapubic tenderness increase the baseline likelihood of UTI by 2 to 6 fold. The absence of several key signs and symptoms can be used to identify infants at low risk for UTI.[9]

Diagnostic testing

To confirm a UTI, diagnostic tests should be performed. The nitrite test is the recommended diagnostic test to start with, and was performed by most general practitioners in our study (chapter 4). The nitrite test is based on the fact that, when present in the bladder, some bacterial species are able to convert nitrate derived from the diet into nitrite in the urine. A meta-analysis by Devillé et al.[10] showed that a positive nitrite test gives good arguments to confirm a UTI. However, the nitrite test is less good for rejecting the diagnosis, since infecting organisms may not be able to produce nitrite.[11] Therefore, a dipslide has to be performed in case of a negative nitrite test. It is also possible to perform a urine culture instead of a dipslide to confirm a UTI. A disadvantage of urine cultures is that they are performed in a microbiological laboratory, and therefore take some time before the diagnosis is determined. In any case urine should be cultured to give information about precise microbiological species, number of colony forming units and resistance pattern. In this way, there are possibilities for a quick and adequate change in therapy in case of treatment failure. A study by Prelog et al.[12] showed that many young children with UTI were infected with organisms resistant

to trimethoprim or ampicillin. There were also differences in children with first or recurrent UTIs.[12] Resistance patterns for trimethoprim are high (40%) and other antibiotics, like nitrofurantoin and cefalexin, have other disadvantages. These problems emphasise the need to avoid unnecessary use of antibiotics, and to ensure a correct diagnosis in the first instance by obtaining at least one properly collected clean catch urine sample before starting treatment.[13] The number of children with a cultured urine was strikingly low (chapter 4). Because all children in our study were diagnosed as having a UTI, the percentage should have been 100%.

The urine for culture should be collected before starting antibiotic treatment. In our study on general practice cooperatives it was shown that the performance of triage nurses on giving instructions on how to collect urine could be improved (chapter 3). Of course the reliability of the diagnostic test results relies on the reliability of the urine sample, but there are several problems collecting a good urine sample, like practical problems (e.g. getting parents' co-operation, availability of equipment) and financial implications (e.g. high costs of dipsticks and urine bags).[14] Collecting a clean catch is also a problem. Although suprapubic aspiration (SPA) is the gold standard, this method is not child friendly and not feasible in general practice. Clean voided urine shows reasonably good agreement with SPA, but is hard to catch in young children. There is insufficient data available about use of bag or nappy/pad specimens.[15] For now, the method for toilet-trained children is clean voided urine and for non-toilet trained children bag collection.

Antibiotic treatment and referral

Besides a timely diagnosis, prompt treatment is important to prevent possible negative consequences of childhood UTIs.[1,16] First of all, a proven UTI should be treated with the right antibiotics.[17] In our modelling study (chapter 6) differences in percentages of children receiving prophylactic antibiotics were the only variables relevant to change the probability of renal scarring. However, these findings were not very strong. Watson[18] state that we urgently need a controlled trial in this area, especially as compliance with long term prophylaxis is probably worse and some parents and carers express concerns about long term usage.

Concerning the Dutch guidelines,[17] two groups of children should be referred to secondary care: those aged less than 6 months (for treatment) and those in specific groups (for further diagnostics). This is in line with current opinions.[19,20] Many paediatricians are beginning to question the need to refer

every child with UTI for imaging. Imaging should be targeted at the child at risk of permanent renal damage. Its aim should be to demonstrate anatomical or functional abnormalities that predispose the urinary tract to new or progressive renal damage.[20] The number of imaging tests might also be reduced. Both Tseng et al.[21] and Preda et al.[22] found that a normal ^{99m}Technetium-dimercaptosuccinic acid (DMSA) scan makes a voiding cystourethrogram (VCU) unnecessary in the primary examination of infants with UTI. So, it is important to select those children at risk. Unfortunately, as our study showed, Dutch general practitioners have low percentages of children referred who are at high risk (chapter 5). Not referring them, might imply that general practitioners are unaware of the increased risk of complications or underlying pathology in boys, younger children and girls with recurrent infections. The influence of whether or not performing all these imaging tests remains unclear. We therefore were not able to use these figures for differences in the transition probabilities in our modelling study (chapter 6).

Improving care

The models for maximum, current and improved care, used in the modelling study, are partly hypothetical, and are therefore not applicable in daily practice (chapter 6). Besides that, maximum care may be hard to accomplish because of the required capacity, and the relevance is questionable (see discussion above about e.g. imaging), even though it delivered more quality of life at lower costs. Furthermore, a problem is the short-run inflexibility of production functions, which reduces the potential efficiency gains.[23] Improving current primary care may be the most feasible option in the short run. As shown in previous chapters, current practice needs improvement concerning diagnostic testing, prescribing antibiotics, follow-up contacts and referring. In general practice, various disorders are thought of being ‘small’, which is the case in childhood UTIs (approximately 5 cases per year per practice). For these disorders, self-education and distant learning could play a role as the method is known to be effective.[24] We therefore developed individual distance learning packages for both practice assistants and general practitioners. Our pilot study resulted in intervention materials adjusted to these users (chapter 7). Further testing is needed, before wide-scale implementation can be recommended.

Methodological considerations

Many different research designs and techniques were used in this thesis: questionnaires, interviews, computer databases, the Delphi method, and literature review in combination with a modelling study. Each of these techniques has its own strengths and limitations. But by using different techniques to collect information ('triangulation'), the results can be considered to be more than just the sum of the different studies.

To get insight into their concerns and thinking we interviewed 20 parents. A qualitative approach is a good method for revealing these views.[25] Interviewing more parents would probably not have changed the overall conclusions, because even though the stories differed from each other, the conclusions were more or less similar.

Using vignettes, with limited information, might have caused that triage nurses decided to request more children to visit the general practice co-operative than they would otherwise have been done. Self-reporting behaviour may lead to overly optimistic adherence, but other studies showed that this is not a major problem.[26,27]

Since direct observation and hand-searching of medical records are infeasible, using databases of routine consultation registrations seems to be a good method for collecting information about general practitioners' clinical behaviour, and also provide the opportunity for collecting prospective data. Nevertheless, there was debate going on about the reliability of the low numbers of antibiotic description presented in chapter 5.[28] There is always a possibility that errors of coding or searching have biased our findings, although we did all possible to reduce this problem. It can also be questioned whether all children with a UTI were identified using the International Classification of Primary Care (ICPC) codes 'acute pyelonephritis' and 'cystitis' or free text words. However, our results are based on records of 142 children (chapter 4) and of 148 children followed-up for three years (chapter 5), which allows us to draw rather firm conclusions.

Any modelling study is a reduction of the complexity of the clinical reality. In particular, the modelling study was not aimed at the individual patient but at populations. Our model relied for a great deal on probabilities found in the international literature, which was for some figures rather limited. By using a probabilistic method we dealt with these uncertainties as good as possible.

It is important to use a systematic approach when developing an intervention, and also to adjust the intervention to the target group.[29] This thesis

was based on the Model of Effective Implementation,[29] which has shown its value although it does not provide guarantees for improvement.

Implications for future research

Many important questions about the consequences and management of childhood UTI remain. Questions concern the role of vesicoureteric reflux (VUR) in causing renal damage, the risk of renal scarring and chronic renal failure in children with UTI, the effectiveness of antibiotic prophylaxis and/or surgical intervention in preventing recurrent UTI and renal damage.[20] Recent information suggests that the long-term outcome for children with UTI is much better than previously thought.[30] This means well-designed cohort studies with sufficient number of patients and controls are needed to draw firm conclusions on the link with renal failure.

Nevertheless, improvement of the diagnosis and treatment of childhood UTI seems possible and needed. Future research could focus on developing interventions to improve diagnosis, prescription, follow-up, and referrals, but should also consider motives for not following the guidelines. Another interesting research area are the children suspected of having a UTI: how to assure that they attend the GP timely?

The studies described in this theses focused on primary care. What is important as well, are the clinical pathways in out-of-hours primary care and hospital care. More research has to been done in these healthcare fields as well, to see whether quality of care has to be improved.

Implications for health policy

Interventions to improve the diagnosis and management of childhood UTIs should primarily focus on the practice assistants and general practitioners, or on the parents once a UTI is diagnosed. Spending a lot of money on raising parent awareness is probably not efficient. Because of the low number of childhood UTIs in a general practice, it is important to raise the subject from time to time, so general practitioners and their assistants will not forget about it. In Sweden, such an approach seemed to be successful.[31]

To conclude

Although there are many more aspects of childhood UTIs to explore, optimal primary care is important. This thesis showed that there are several options to improve current care.

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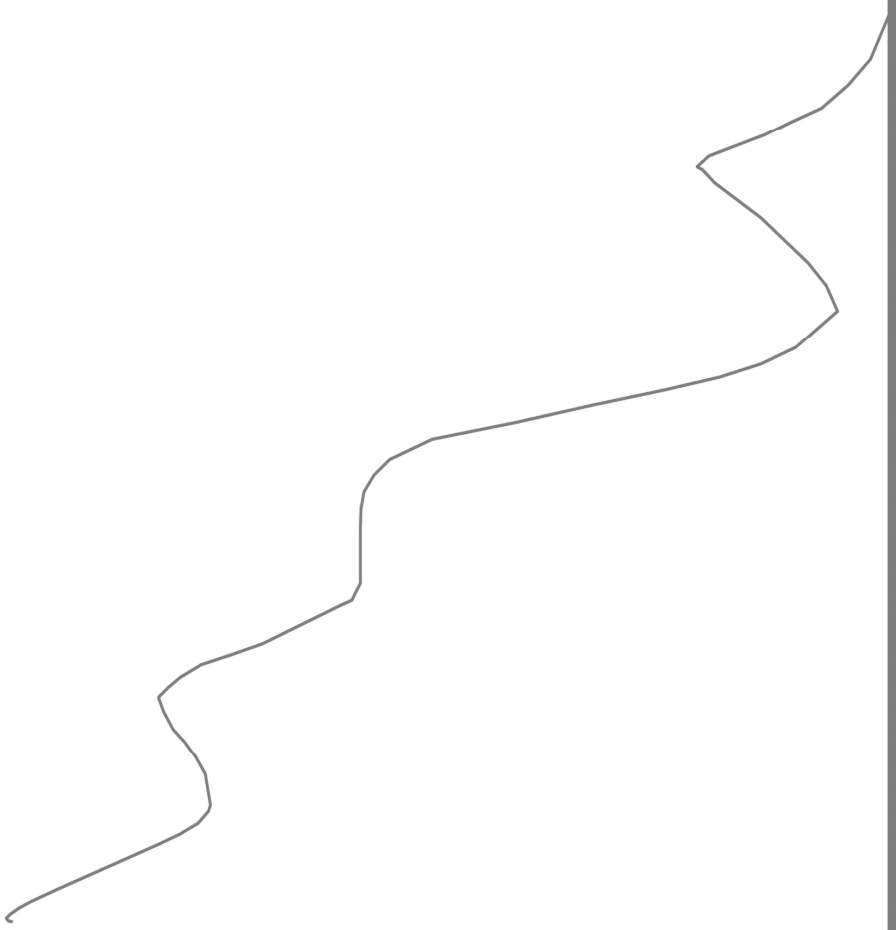
Summary



The aim of this thesis is to get insight into the current diagnostic and therapeutic approach to urinary tract infections (UTIs) in children in Dutch primary care, with a perspective on preventing renal failure in the long run. The **introduction** describes the background and research questions of the present thesis. The research questions were:

- What are the incidence rates of UTIs among children in Dutch general practice care and might there be problems in general practice management of UTIs in children? And, what aspects of the management of childhood UTIs in general practice care should be focused on? (chapters 1 and 7)
- What are strong and weak aspects of Dutch general practice performance concerning childhood UTIs? (chapters 2-6)
- What methods can be used to improve general practice management? (chapter 7)

The study described in **chapter 1** aimed to investigate incidence rates of childhood UTIs in Dutch general practice and their association with gender, season and urbanisation level, and to analyse prescription and referral in case of UTIs. Data were used from the Second Dutch National Survey of General Practice, which was performed between April 2000 and January 2002, and in which 195 general practitioners (GPs) in 104 practices throughout The Netherlands prospectively registered data about all their patient contacts during one calendar year. The study in 82,053 children aged 0 to 18 years old, described in chapter 1, showed an overall incidence rate of UTIs of 19 episodes per 1000 person years. The mean number of UTI episodes per child was 1.2 per year, with a maximum of 5. The mean number of consultations per episode was 1.7. The proportion of episodes with only one contact was 66%. The incidence rates showed association with gender, season and urbanisation. In girls the incidence rate was almost 8 times higher than in boys ($p<0.001$). Furthermore, the incidence rates varied throughout the year, with a decrease in summertime, mainly in children aged 0-12 years old. In smaller cities and rural areas the incidence rate was 2.1 times as high than in the three largest cities ($p<0.001$). In the 0-18 year old group, adhering to clinical guidelines could be better for GPs. Of all children in whom a UTI was diagnosed, 75% was prescribed medication. Two-thirds of the prescriptions were in line with the guidelines. In total 120 children were referred 134 times. Of the children who had to be referred according to the guidelines, 18% was actually referred.

Information derived from 20 interviews held with parents who had a child recently diagnosed with a UTI (**chapter 2**) showed that parents had knowledge of the typical symptoms related to a UTI, but not of the atypical symptoms (i.e. fever, diarrhoea, vomiting). The reasons for parents to contact the GP even though their child had only atypical symptoms were that the child's behaviour was different and that the atypical symptoms looked more severe than when the child had a common illness. The parents also thought that the GPs did not know the atypical symptoms, and should be more aware of UTIs in children. In about a fourth of the cases a delay in diagnosis was on the GP's side. In a smaller number of cases the delay was on the parent's side. The awareness that a UTI can be a serious illness usually came to parents later, partly because health care workers often not explicitly mentioned this. One reason for not giving the desired information was because medical personnel did not think it was important at the time. Parents were sceptical about health education to broad groups of parents and mass screening, because this would be perceived as not relevant at that time or it would unnecessarily increase anxiety. They thought it would be better if physicians and nurses would be more on the alert for possible UTIs in children, and more information should be given once a UTI is diagnosed.

Triage nurses at general practice cooperatives (out-of-hours general practice care) play an important role in identifying UTIs in young children, as many children with fever are presented out-of-hours. **Chapter 3** describes a questionnaire study in 145 triage nurses, working at Dutch general practice cooperatives. Questions were asked about four vignettes, constructed on the basis of the Telephone Triage Guide and two national guidelines on UTI and feverish children. The information in the vignettes consisted of data about a 5-year-old child with suspected UTI and three children with fever without focus (a 14-month-old boy with a 3-day fever, a 2-month-old girl with a 2-day fever, and a 4-year-old child with a 5-day fever [in this case questions were asked for both boys and girls]). Triage nurses were aware of the typical UTI symptoms, but the atypical symptoms were not frequently associated with UTI (<25% thought so). The results showed that more than 90% of these nurses acted according to the guidelines if a UTI was suspected, asking the parents to bring the child to the general practice co-operative. However, in most cases the nurses did not think a UTI was likely. If a UTI was suspected, all triage nurses requested the parents to provide a sample of the child's urine, but only 70% said to give instructions on how to collect the urine.

Clinical guidelines on UTIs give clear recommendations on the diagnostic workup of a child with a suspicion of UTI. **Chapter 4** describes a retrospective chart review study in Dutch general practices on the diagnosis of UTIs in children who were diagnosed as having a UTI. A total of 49 general practices participated in the study, and provided information on 148 children. At the first visit, 97% of the children had their urine tested. The use of the nitrite test was found to be largely appropriate (performance in 87%), but other tests were either overused or underused. Especially the urine culture was underused. Less than 40% of the children had their urine cultured, although this should ideally be 100%. Half of the children had a follow-up contact to test whether the UTI was cured. In only 25% of these children the urine was tested using the recommended dipslide. Although the guidelines do not report about distinctions in diagnosing a UTI in children of different age or sex, patient age and UTI history were identified as predictors of different tests. A younger age was related to a higher proportion of sediment testing, urine culture, and dipslide and/or urine culture at the first contact. Having a history of UTIs meant less testing on erythrocytes and leucocytes, and more testing using the dipslide and/or urine culture.

Based on data of 59 practices within the Netherlands Information Network of General Practitioners (LINH), 284 children aged 0 to 6 years old with a registered UTI in 2001 were followed for three years (**chapter 5**). Most of them had one episode cystitis/UTI during these three years, and only six children were diagnosed as having a acute pyelonephritis. During the first episode, the mean age varied from 2.8 to 4.1 years. The majority of the children was female (>80%). In the group of children with three or less cystitis episodes, 66% was prescribed antibiotics. The first choice medication, amoxicillin/clavulanic acid or co-trimoxazole, was prescribed for 66% of children with antibiotics. In eight cases, a child who did not receive medication was referred to a medical specialist directly after seeing the GP. About 30% of all episodes were followed up in general practice. In 90% of these episodes this was within 14 days from the first contact. A total of 38 children (14%) were referred, most times to a paediatrician. However, of the children who should have been referred, because of their age, sex and/or UTI history, only one in three was actually referred.

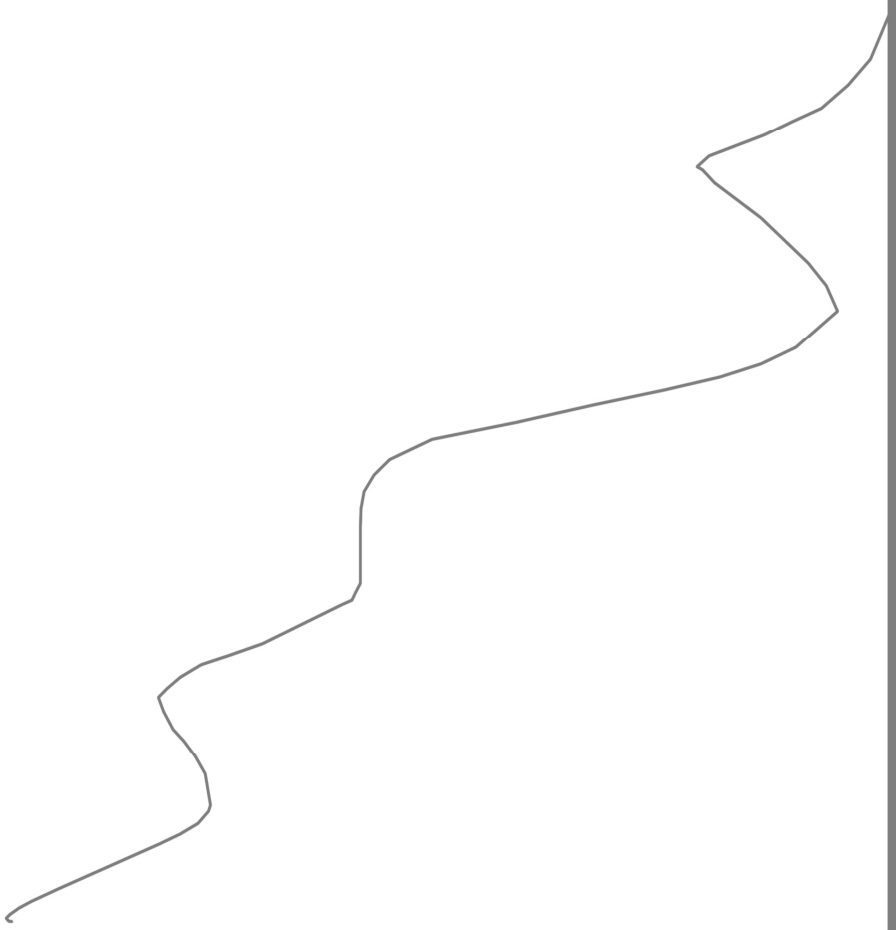
The aim of the study described in **chapter 6** was to assess the cost-effectiveness of a maximum care model for UTIs in children, implying more diagnostic testing and antibiotic treatment, compared to current practice in primary care in The

Netherlands, with less diagnostic testing and antibiotics treatment in primary care. We also compared maximum care with an improved version of current care. Because performing an empirical study was not feasible, we applied probabilistic Markov-based modelling, using data from a systematic review of the research literature. The literature study showed that there are still gaps in our knowledge about the percentage of children with a UTI getting renal problems. The modelling study showed that maximum care gained more quality adjusted life years (0.00102 QALYs in 30 years) and saved more money (€42.70 for boys and €77.81 for girls in 30 years) compared to current care, and was thus dominant. Maximum care was also dominant over improved current care, meaning care according to prevailing guidelines, although less dominant than to current care. In boys, the net monetary benefit (NMB) of maximum care, compared to current care, ranged from €20 to €80 for a willingness to pay for a QALY ranging from €0 to €80,000 respectively. In girls, the NMB ranged from €50 to €200. A positive NMB implies that the costs of a new therapy is less than the value of the additional benefit achieved. However, drawing firm conclusions is not possible, given the limitations of the input data derived from the literature review.

Chapter 7 describes the process to develop a quality improvement intervention for primary care. Together with GPs and their practice assistants a quality improvement intervention was developed by 1) defining improvement objectives, 2) developing and selecting methods for change, and 3) pre-testing the quality improvement intervention. A total of seven objectives was created on diagnostics, treatment, referral and follow-up. Based on these objectives, and after a pilot study on lay-out and contents of the quality improvement intervention, individual education materials for parents, practice assistants, and general practitioners were developed. There were two information leaflets for parents. For practice assistants a summary chart and reader were developed, and they were also handed out information on UTIs from the Dutch College of General Practitioners guidelines for practice assistants. General practitioners received a summary chart and the PIN (programme for individual education; a booklet with an introduction on the topic, work sheets with questions and answers, and a test) of the Dutch College of General Practitioners. The results of the pilot study, on use and appreciation of the quality improvement intervention, were promising. Although not all practice assistants and general practitioners used the intervention materials, almost all who did so rated them as pleasant to use. Ten out of 16 general practitioners reported to have made changes in their daily practices.

The main findings of this thesis are summarised and discussed in the **general discussion**, and refer to the topics ‘raising awareness’, ‘diagnostic testing’, ‘antibiotic treatment and referral’, and ‘improving care’. A total of four key messages is formulated. Subsequently, the most relevant methodological issues are reviewed and the general discussion ends with some implications for future research and for health policy. It can be concluded that, although there are many more aspects of childhood UTIs to explore, optimal care is important. This thesis showed that there are several options to improve current care in Dutch general practice.

Samenvatting



Het doel van het onderzoek beschreven in dit proefschrift was het verschaffen van inzicht in de huidige diagnostische en therapeutische benadering van urineweginfecties (UWIs) bij kinderen in de Nederlandse eerstelijns gezondheidszorg, met als achterliggende gedachte het voorkomen van nierfalen op latere leeftijd. De **introductie** geeft een algemene inleiding op het onderwerp en beschrijft de onderzoeksvragen van dit proefschrift, te weten:

- Wat zijn de incidentiecijfers van UWIs bij kinderen in de Nederlandse huisartspraktijk en zijn er mogelijk problemen bij de behandeling van UWIs bij kinderen? (hoofdstukken 1 en 7)
- Wat zijn in de Nederlandse huisartspraktijken de sterke en zwakke punten van het handelen bij kinderen met UWIs? (hoofdstukken 2-6)
- Welke methoden kunnen gebruikt worden om het handelen in de huisartspraktijken te verbeteren? (hoofdstuk 7)

De studie beschreven in **hoofdstuk 1** trachtte de incidentiecijfers van UWIs bij kinderen in Nederlandse huisartspraktijken te onderzoeken, en hun associatie met geslacht, seizoen en urbanisatiegraad. Daarnaast werden voorschrijf- en verwijscijfers geanalyseerd. De gebruikte data waren afkomstig uit de Tweede Nationale Studie naar Ziekten en Aandoeningen in de Huisartsenpraktijk, welke plaatsvond tussen april 2000 en januari 2002. In totaal registreerden 195 huisartsen uit 104 praktijken door heel Nederland prospectief gegevens over al hun patiëntcontacten gedurende één kalenderjaar. De studie naar 82.053 kinderen 0 tot 18 jaar oud, zoals beschreven in hoofdstuk 1, liet een incidentie zien van 19 UWI-episodes per 1000 persoonsjaren. Het gemiddelde aantal UWI-episodes per kind was 1,2 per jaar, met een maximum van vijf. Het gemiddelde aantal consulten per episode was 1,7. Het aandeel episodes met slechts één contact was 66%. De incidentiecijfers lieten een samenhang zien met geslacht, seizoen en urbanisatiegraad. Het incidentiecijfer was bij meisjes bijna 8 keer hoger dan bij jongens ($p<0,001$). Daarnaast varieerde het incidentiecijfer gedurende de seizoenen, met een verlaging in de zomerperiode voor met name de kinderen van 0 tot 12 jaar oud. In de kleinere steden en de dorpen was het incidentiecijfer 2,1 keer zo hoog dan in de drie grote steden ($p<0,001$). Het door de huisartsen volgen van de richtlijnen voor de behandeling van UWIs bij de 0 tot 18-jarigen kan beter. Van alle kinderen met een gediagnosticeerde UWI kreeg 75% medicijnen voorgeschreven. Tweederde van deze voorschriften waren in overeenstemming met de richtlijnen. In totaal werden 120 kinderen 134 keer verwezen. Van de

kinderen die volgens de richtlijnen hadden moeten worden verwezen, werd 18% daadwerkelijk verwezen.

Informatie afkomstig uit 20 interviews met ouders van kinderen recent gediagnosticeerd met een UWI (**hoofdstuk 2**) liet zien dat ouders wel de typische symptomen van een UWI kenden, maar niet de atypische symptomen zoals koorts, diarree en overgeven. Redenen voor ouders om toch contact op te nemen met de huisartspraktijk, ook al had hun kind alleen maar atypische symptomen, waren dat het kind zich anders gedroeg en dat de atypische symptomen ernstiger leken dan bij bijvoorbeeld een gewone verkoudheid. De ouders waren van mening dat de huisartsen ook niet voldoende op de hoogte waren van de atypische symptomen en dat zij meer alert moeten zijn op UWIs bij kinderen. In ongeveer één op de vier gevallen was de arts de oorzaak van een vertraging in de diagnose. Vertraging aan de kant van de ouders kwam in minder gevallen voor. Ouders beseften meestal niet meteen welke (ernstige) consequenties een UWI bij kinderen kan hebben, deels doordat gezondheidszorgmedewerkers dit vaak niet meldden. Eén van de redenen van de gezondheidszorgmedewerkers om deze informatie niet te geven was dat ze het op dat moment niet belangrijk achtten. Ouders waren sceptisch over voorlichting aan grote groepen ouders tegelijk en over massascreening, omdat de informatie op het moment van geven wellicht als niet relevant zou worden beschouwd en de ouders wellicht onnodig angst zou aanjagen. De ouders dachten dat het beter zou zijn als artsen en doktersassistenten/verpleegkundigen meer alert zouden zijn op mogelijke UWIs bij kinderen, en dat het beter zou zijn als er meer informatie werd gegeven zodra de diagnose eenmaal was vastgesteld.

De triagisten op huisartsenposten spelen een belangrijke rol bij het identificeren van UWIs bij jonge kinderen, aangezien op de huisartsenposten veel kinderen met koorts komen. **Hoofdstuk 3** beschrijft de resultaten van een vragenlijstonderzoek onder 145 triagisten werkzaam bij Nederlandse huisartsenposten. Er werden vragen gesteld over vier vignetten, samengesteld op basis van de Telefoonwijzer en twee nationale richtlijnen over UWIs en koorts. De informatie in de vignetten betrof gegevens over een vijfjarig kind met een vermoeden op een UWI en over drie kinderen met koorts zonder oorzaak (een 14-maanden oude jongen met drie dagen koorts, een 2-maanden oud meisje met twee dagen koorts, en een vierjarig kind (zowel jongen als meisje) met vijf dagen koorts). Triagisten waren zich bewust van de typische UWI symptomen, maar in slechts 25% van de gevallen werden

atypische symptomen gerelateerd aan UWIs. De resultaten van het onderzoek lieten zien dat meer dan 90% van de triagisten handelden in overeenstemming met de richtlijnen in het geval dat er een vermoeden op een UWI was, wat betekent dat ze de ouders zouden vragen met het kind naar de huisartsenpost te komen. Daarentegen dachten de triagisten in de meeste gevallen niet dat er sprake zou zijn van een UWI. Indien wel werd gedacht aan een UWI, werden de ouders gevraagd wat urine van het kind mee te brengen. Slechts 70% van de triagisten zei instructies te geven over hoe deze urine het beste kan worden opgevangen.

De klinische richtlijnen over UWIs geven duidelijke aanbevelingen over de diagnostiek die uitgevoerd moet worden indien een kind er van wordt verdacht een UWI te hebben. **Hoofdstuk 4** beschrijft een retrospectief dossieronderzoek in Nederlandse huisartspraktijken naar de diagnose van UWIs bij kinderen die waren gediagnosticeerd met een UWI. Totaal 49 huisartsen namen deel aan het onderzoek en leverden informatie aan over 148 kinderen. Tijdens het eerste bezoek aan de huisartspraktijk werd van 97% van de kinderen de urine getest. Het gebruik van de nitriettest was grotendeels volgens de richtlijnen (uitgevoerd bij 87%), maar de andere testen werden ofwel te vaak of te weinig gebruikt. Met name vonden er te weinig urinekweken plaats. Bij minder dan 40% van de kinderen werd de urine gekweekt, terwijl dit ideaal gezien bij 100% zou moeten zijn. De helft van de kinderen had een follow-up contact om na te gaan of de UWI was genezen. Bij slechts 25% van deze kinderen werd getest met de aanbevolen dipslide. Ook al maken de richtlijnen geen onderscheid in leeftijd en het al dan niet hebben van een voorgeschiedenis met betrekking tot UWIs, deze factoren werden toch gevonden als voorspellende factor voor de verschillende testen. Een jongere leeftijd was gerelateerd aan meer sedimenttesten en het uitvoeren van dipslides en/of kweken tijdens het eerste contact. Kinderen met een voorgeschiedenis van UWIs werden minder getest op erytrocyten en leukocyten, maar er werd meer gebruik gemaakt van de dipslide en/of de kweek.

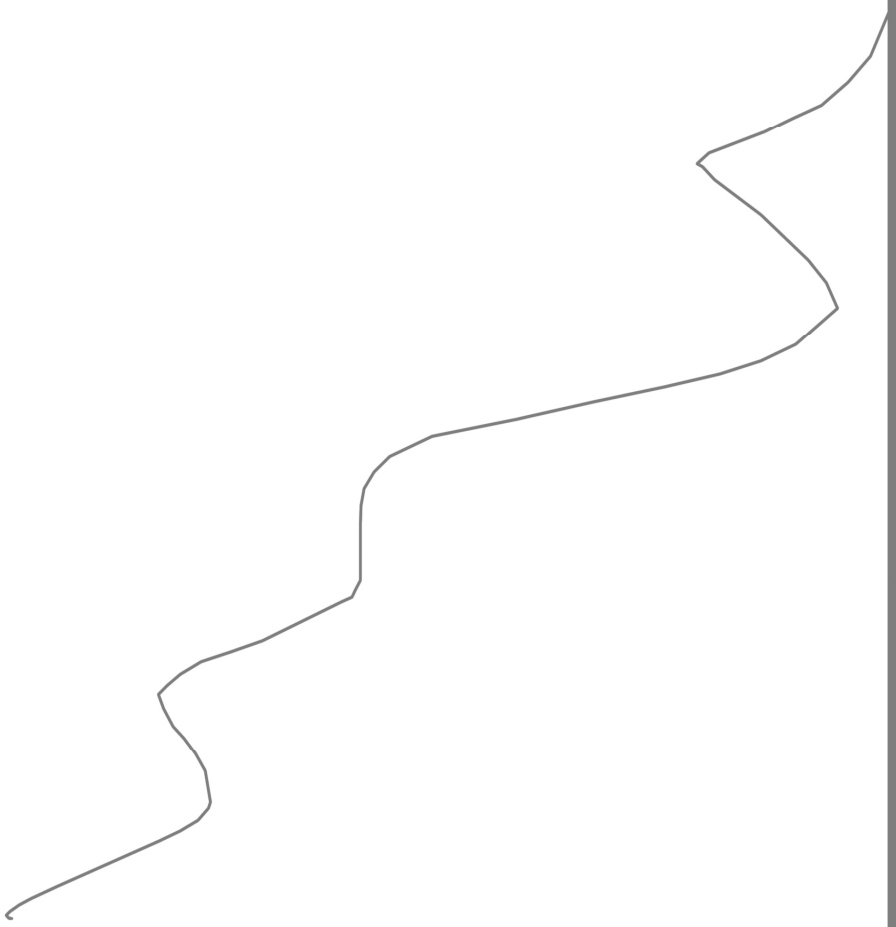
Gebruik makend van gegevens van 59 huisartspraktijken aangesloten bij het Nederlands Informatie Netwerk Huisartsenzorg (LINH) konden 284 kinderen van 0 tot 6 jaar oud met een geregistreerde UWI in 2001 gedurende drie jaar worden gevolgd (**hoofdstuk 5**). De meeste kinderen hadden één episode cystitis/UWI gedurende deze drie jaren, en maar zes kinderen waren gediagnosticeerd met een acute nierbekkenontsteking. Gedurende de eerste episode varieerde de leeftijd

van de kinderen tussen 2,8 en 4,1 jaar oud. Het merendeel van de kinderen was vrouwelijk (>80%). Antibiotica werd voorgeschreven bij 66% van de kinderen met drie of minder cystitis episodes. Het eerstekeus antibioticum, amoxicilline-clavulaanzuur, werd voorgeschreven aan 66% van de kinderen met medicatie. In acht gevallen werden kinderen zonder een medicatievoorschrift meteen doorgestuurd naar een specialist in het ziekenhuis. Follow-up vond plaats in ongeveer 30% van de episodes. Indien er een follow-up contact plaatsvond, was dit in 90% van de gevallen binnen 14 dagen na het eerste contact. Totaal 38 kinderen (14%) werden verwezen naar het ziekenhuis, meestal naar de kinderarts. Daarentegen werd maar één op de drie kinderen die volgens de richtlijnen zouden moeten worden verwezen, op basis van hun leeftijd, geslacht en/of UWI voorgeschiedenis, ook daadwerkelijk verwezen.

Het doel van de studie beschreven in **hoofdstuk 6** was om na te gaan of het maximale-zorg-model voor UWIs bij kinderen, uitgaande van meer diagnostische tests en antibioticavoorschriften, vergeleken met de huidige zorg in Nederlandse huisartspraktijken doelmatiger is. Tevens werd het maximale-zorg-model vergeleken met een verbeterde versie van de huidige zorg. Om pragmatische redenen werd gekozen voor een modelmatige benadering, gebruik makend van gegevens afkomstig uit een systematisch overzicht van de literatuur. Deze ‘systematic review’ liet zien dat er nog steeds hiaten zijn in de kennis over het percentage kinderen met een UWI dat daadwerkelijk nierproblemen krijgt. De modellering studie, geanalyseerd middels een probabilistische gevoeligheidsanalyse, liet zien dat het maximale-zorg-model meer voor kwaliteit gecorrigeerde levensjaren (QALYs) opleverde (0,00102 QALYs in 30 jaar) en meer geld bespaarde (€42,40 voor jongens en €77,81 voor meisjes in 30 jaar), vergeleken met de huidige zorg. Hetzelfde, zij het in iets mindere mate, werd waargenomen bij vergelijking met de verbeterde versie van de huidige zorg. Voor jongens varieerde de netto contante waarde van het maximale-zorg-model, vergeleken met de huidige zorg, van €20 tot €80 gegeven een bereidheid tot betalen voor een QALY variërend van respectievelijk €0 tot €80.000. Voor meisjes varieerde de netto contante waarde van €50 tot €200. Een positieve netto contante waarde impliceert dat er per saldo geld verdiend wordt. Gezien de beperkingen van de gebruikte gegevens afkomstig uit de literatuur is het echter niet mogelijk stellige conclusies te trekken.

Hoofdstuk 7 beschrijft het ontwikkelingsproces van een verbeterinterventie in de eerste lijn. In drie stappen werd samen met huisartsen en hun praktijkassistenten een verbeterinterventie ontwikkeld: 1) vaststellen van verbeterdoelen, 2) ontwikkelen en selecteren van verbetermethoden, en 3) pretesten van de verbeterinterventie. Totaal zeven verbeterdoelen werd opgesteld, gericht op diagnostiek, behandeling, verwijzing en follow-up. Aan de hand van de verbeterdoelen en een pilotonderzoek naar de lay-out en inhoud van het materiaal werd uiteindelijk gekomen tot individueel voorlichtings- en scholingsmateriaal voor ouders, praktijkassistenten en huisartsen. Voor de ouders betrof het twee informatiefolders. Voor de praktijkassistenten werden een samenvattingskaart en een scholingsreader ontwikkeld. Daarnaast ontvingen zij de informatie over UWIs uit de richtlijnen voor praktijkassistenten en -ondersteuners van het Nederlands Huisartsen Genootschap (NHG). De huisartsen ontvingen een samenvattingskaart en de PIN (Programma Individuele Nascholing, een boekje met een introductie op het onderwerp, werkbladen met vragen en antwoorden, en een schriftelijke test) van het NHG. De resultaten van het pilotonderzoek naar het gebruik van en de waardering voor de verbeterinterventie waren veelbelovend. Niet alle huisartsen en praktijkassistenten hadden het materiaal gebruikt, maar de meesten die dat wel hadden gedaan waardeerden deze als plezierig in gebruik. Tien van de 16 huisartsen gaven aan veranderingen te hebben doorgevoerd in hun dagelijkse praktijk.

De belangrijkste bevindingen van dit proefschrift zijn samengevat en bediscussieerd in de **algemene discussie** en refereren aan de onderwerpen ‘verhogen alertheid’, ‘diagnostische tests’, ‘voorschrijven van antibiotica en verwijzen’ en ‘verbeteren van de zorg’. Totaal vier sleutelboodschappen werden geformuleerd. Daarnaast werd ingegaan op de belangrijkste methodologische beperkingen. Het hoofdstuk eindigt met aanbevelingen voor verder onderzoek en beleid in de gezondheidszorg. Geconcludeerd kan worden dat optimale zorg belangrijk is, ook al zijn er nog veel meer aspecten van UWIs bij kinderen te onderzoeken. Dit proefschrift liet zien dat er verschillende mogelijkheden zijn om de zorg in Nederlandse huisartspraktijken te verbeteren.



Dankwoord

Zoals iedere promovendus die eindelijk zijn/haar dankwoord mag schrijven: ook ik deed het niet helemaal alleen. Ik ben dank verschuldigd aan een heleboel mensen, waarvan ik hopelijk niemand zal vergeten (indien wel: mijn oprechte excuses).

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En wat zouden we zijn zonder praktische ondersteuning? Het gebruik kunnen maken van de expertise en handigheden van onderzoeksassistenten zou iedere onderzoeker moeten kunnen ervaren. In mijn geval wil ik graag Geert Schattenberg, Nieke van Lin, Janine Liefers en Marjan Knippenberg bedanken

voor hun hulp bij het opzetten van Access-bestanden, Excel-bestanden, het versturen van vragenlijsten, opzoeken van literatuur, etc. etc. etc. Ook Anita Oude Bos had hier haar aandeel in, als zijnde de projectsecretaresse. De geneeskundestudenten Surayda Mahmoeb en Frank Nielander hebben voor hun wetenschappelijke stage een groot deel van de interviewstudie gedaan. En in de laatste fase, het transformeren van losse artikelen etc. in een volwaardig proefschrift en de praktische voorbereiding op de promotie zelf, is Jolanda van Haren voor iedere promovendus van onschatbare waarde, dus ook voor mij.

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Voor ouders, broertjes, overige familie en vrienden was het niet altijd makkelijk te volgen wat ik nu deed. Toch bleef de interesse. En niet altijd over het werk praten is ook best prettig. Speciale dank natuurlijk voor paps en mams, waar ik weer mocht wonen toen ik uit Australië terugkwam en die me goed hebben verzorgd in de eerste jaren van mijn promovendus zijn. Dat doet een mens goed!

Last, but not least: Stefan, mijn grote relativist. ‘Kun je er nu iets aan doen? Nee? Laat het dan los!’ Heel erg bedankt voor je liefde, begrip, reflectie en steun. Tjuskus!!!

Curriculum Vitae

Mirjam Harmsen werd op 3 februari 1976 geboren in Warnsveld. Ze woonde tot en met haar vijftiende in Hengelo (Gelderland) en verhuisde toen naar Varsseveld. Na de havo (Ulenhof College te Doetinchem en Christelijk College Schaersvoorde te Aalten) begon de reis naar het zuiden. In 1998 werd de opleiding Voeding & Diëtetiek aan de Hogeschool Arnhem Nijmegen afgerond en vervolgens in 2000 de verkorte opleiding Gezondheidswetenschappen, studierichting Gezondheidsvoorlichting, aan de Universiteit Maastricht. Daar was ook de eerste kennismaking met het fenomeen wetenschappelijk onderzoek. Omdat er al een hele tijd plannen waren om naar Australië te gaan, werd een tijdelijke baan gezocht. Deze werd gevonden in Nijmegen, bij (toen nog) de Werkgroep Onderzoek Kwaliteit (WOK). Na twee jaar gewerkt te hebben als onderzoeksassistent werden de koffers gepakt en begon het Australië-avontuur. Drie maanden heeft Mirjam gewerkt bij de Cochrane Consumers and Communication Review Group, welke gezeteld was binnen de La Trobe University in Melbourne. Daarna was het tijd om rond te reizen door Australië en Nieuw Zeeland. Terug in Nederland, eind zomer 2003, kon ze weer aan de slag in Nijmegen, bij wat tegenwoordig heet het Scientific Institute for Quality in Healthcare (IQ Healthcare), en in april 2004 startte het promotieonderzoek waarvan in dit proefschrift de resultaten worden gepresenteerd. Naast haar promotieonderzoek voerde Mirjam nog verschillende andere onderzoeken uit en had ze verschillende andere taken, te weten (vice)voorzitter van het SCHIL-overleg (overleg van onderzoeksassistenten en junior-onderzoekers), secretariaat van de PhD council (promovendivertegenwoordiging) van het Nijmegen Centre for Evidence Based Practice (NCEBP) en later ook van NCEBP zelf. In haar werk zoekt Mirjam een combinatie van wetenschappelijk en praktisch werk. Momenteel werkt ze als onderzoeker bij het Kwaliteitsbureau van Alysis Zorggroep (ziekenhuis Rijnstate, kliniek Velp, ziekenhuis Zevenaar) en als post doc bij IQ Healthcare. Mirjam woont in Varsseveld samen met Stefan Wisselink.

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