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Management of Infection Patients in Health Centres

Final Report of the MIKSTRA Programme

REPORT

36 | 2010

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Foreword

Antimicrobials are life-saving, downright miracle drugs. Penicillin is considered one of the ten most important discoveries of mankind. Since it was discovered some 70 years ago, millions of human lives have been saved. During this time, the range of antimicrobials available and their uses have diversified constantly. Today, there are hundreds of different preparations available, for a great variety of different uses.

Antimicrobials have freed up a great deal of health-care resources, particularly in hospitals, since infections that previously might have been extremely serious can now be treated in outpatient care, with patients no longer needing to be isolated. In the early twentieth century, four fifths of hospital patients sought care for an infection, compared with one sixth of patients in the 1980s. Not only has this trend been very beneficial to the well-being of the population at large, it has also impacted favourably on health-care expenditure.

However, there is also a downside to the increased use of antimicrobials. Bacterial resistance is increasing and it is one of the most serious problems faced by health care today. As the effect of antimicrobials declines, the treatment of infections takes longer, complications become more frequent and, at the same time, health care expenditure grows considerably. At this juncture, it is crucial to ask how we can use antimicrobials sparingly while obtaining the best possible effects from their use.

The majority of antimicrobials are used in outpatient care. The way antimicrobials are used varies considerably across Europe, and no rational explanation has been found for this variation. Finland is average on the European level, but tops the statistics for the Nordic countries. According to experts, there is a tendency in Finland to overuse antimicrobials, particularly when it comes to mild respiratory infections.

The MIKSTRA programme included the aim of optimal diagnostics and care for infections treated in outpatient care. The programme's steering group proposed that care recommendations for the most prevalent infections treated in outpatient care be included in the Current Care guidelines of the Finnish Medical Society Duodecim. The recommendations in question were published in 1999 and in 2000 and were among the first Current Care guidelines to be issued. Also included in the programme aims were disseminating the recommendations for use in practice, and research into the impact of the recommendations on the use of antimicrobials.

The MIKSTRA programme is one of the most extensive national research programmes on antimicrobial use in the world. During the programme period, outpatient infection treatment improved considerably in line with the programme's recommendations. The programme's main findings have been published in

highly regarded scientific forums and the programme has also received deserved international acclaim.

However, the foremost finding of the MIKSTRA programme is surely that it demonstrated that care recommendations and co-ordinated co-operation can exert an impact on the use of antimicrobials in outpatient care. Nearly 1000 physicians in outpatient care were involved in the implementation of the programme; they treated nearly 35 000 patients, thus making a considerable contribution to the programme's success.

I would like to extend my warmest thanks and congratulations to all who participated in the MIKSTRA programme for their successful work in the interests of our health and welfare.

Pekka Puska
Director General, National Institute for Health and Welfare (THL)

Acknowledgements

We wish to express our heartfelt thanks to the staff and patients at the MIKSTRA health centres and the control health centres for their active participation: the programme would not have succeeded without you. We also wish to extend our warmest thanks to the contact persons at the MIKSTRA health centres; they each worked hard in their own health centres without remuneration to help bring a programme lasting several years to a successful conclusion.

We wish to thank all the researchers listed in the report who contributed to the implementation of MIKSTRA in different ways while on fixed-term contracts. We thank Taina Mäntyranta and Mats Brommels for their many valuable comments and for their external evaluation of the programme. Thanks to Arja Helin-Salmivaara and Taina Mäntyranta in their capacities as representatives of the ROHTO programme and the ROHTO centre for the productive cooperation in the implementation of training. Thanks to Tuuli Nikkarinen, Kirsti Lonka and Annamari Ranki for participating in MIKSTRA training as external experts. Thanks to Aala Koski and Monika Fredriksson and the many students of pharmacy and health science who have helped encode MIKSTRA forms over these years.

We offer our thanks to Airi Salminen and Leila Rantanen at the Social Insurance Institution for doing the data selection from prescription files and for their help in preparing the MIKSTRA maps and some of the poster illustrations. Thanks also to Seppo Y.T. Junnila at the Salo regional health centre and Ilkka Kunnamo at the Saarijärvi-Karstula health centre for the data on patient numbers we received from their patient files. Thanks also to FiRe representatives Antti Hakanen and Miika Bergman for the information we received on the resistance of pneumococci.

This final report has been peer reviewed and accepted for publication by the scientific committee of Finohta. We thank everyone involved for their suggestions for improvements. We would also like to thank Professor Olli Ruuskanen for his insightful comments.

Implementation of the MIKSTRA programme and publication of this report were made possible by funding received from the Social Insurance Institution (Kela), the former National Agency for Medicines (now FIMEA), the former National Public Health Institute (KTL) and the former National Research and Development Centre for Welfare and Health (STAKES) (the latter two have now merged as the National Institute for Health and Welfare, THL) and the Finnish Medical Society Duodecim.

We would also like to extend our thanks to the quality committee of the Finnish Medical Association, which granted the MIKSTRA health centres an honourary mention in 2007 in recognition of their work to develop care practices.

Timo Klaukka, Research Director for Health Services Research at the Social Insurance Institution, played a key role in the birth and implementation of the

entire MIKSTRA programme, but he sadly passed away after a serious illness in June 2009, shortly before this report was finished. We look back with gratitude on his extremely valuable contribution to the programme and we will miss the active and innovative colleague we have lost.

Content

Summary

Ulla-Maija Rautakorpi, Solja Nyberg, Pekka Honkanen, Timo Klaukka, Helena Liira, Marjukka Mäkelä, Erkki Palva, Risto Roine, Hannu Sarkkinen ja Pentti Huovinen. Management of infection patients in health centres – final report of the MIKSTRA programme. National Institute for Health and Welfare, Report 36/2010. Helsinki 2010. ISBN 978-952-245-373-0. ISSN 1798-0070.

The aim of the Antimicrobial Treatment Strategies (MIKSTRA) programme has been to optimise the diagnostics and treatment of common infections in outpatient care. The programme started in autumn 1998 and ran until the end of 2003. This report describes the implementation, methods and most important results of the programme. The purpose of this report is to serve as a source of information for research and development purposes in further improving the diagnostics and treatment of infections.

Uncontrolled use of antimicrobials has led to increasing bacterial resistance all around the world, both in hospitals and in outpatient care. This development has already led to failures in treatment with common antimicrobials. To preserve the effect of existing antimicrobials, it has become necessary to re-evaluate current treatment practices and introduce new evidence-based Current Care guidelines on common infections.

Even on an international scale, MIKSTRA has been an exceptional programme in extensively and persistently collecting data on the diagnostics and treatment of infections and on the influence of guidelines and further education. MIKSTRA was a comprehensive public health programme that integrated several health centres and research institutions into a joint network.

For the first time, there is now a clear overall view of established practices in the treatment of infection patients in outpatient care in Finland. The programme has also aroused discussion about the prevailing practices in the country. Overall use of antimicrobials has somewhat decreased in the whole country during and after the programme. At the same time, several positive changes have taken place in the use of antimicrobials. Use of recommended first-line drugs has increased and the duration of treatment has been reduced. In addition, the use of diagnostic aids has become more rational. However, it is important to ensure that future health personnel have access to necessary diagnostic aids, for example by correcting the observed deficiencies. The division of tasks between physicians and nurses could also be improved.

The MIKSTRA programme faced a challenge in arranging further education in health centres. Due to some unpredictable changes in the composition of the research team, the training did not go quite as planned. The long implementation phase of the programme was further complicated by the increasing shortage of

physicians in the health centres. However, the training programme was successful in many respects, giving valuable information for future planning of continuing medical education.

As a whole, the comprehensive, multi-year programme was successful. The co-operation between health centres, research organisations, universities and the Finnish Medical Association Duodecim worked exceptionally well. There was also close co-operation with other national programmes, for example, the Rohto programme (later the Rohto-centre) and the Finnish Study Group for Antimicrobial Resistance FiRe, as well as with several international programmes.

MIKSTRA has produced a great deal of information and identified needs for improvement, and laid the foundation for the planning of future follow-up of treatment practices in health centres by means of electronic patient records. The obtained information supports a controlled and safe move towards practices that are in line with evidence-based guidelines. The experiences obtained can be useful also in considering a more rational use of resources and planning continuing medical education. Several scientific articles on the results of MIKSTRA programme have already been published and analysis of the results and planning of future activities will continue.

List of figures and tables

Tables

Terms and abbreviations

AD	Academic detailing
EBMeDS	Evidence-Based Medicine electronic Decision Support
CC guideline	Current Care (Käypä hoito) is a registered trademark of the Finnish Medical Society Duodecim referring to national, evidence-based clinical practice guidelines based on a systematic literature search and drawn up by volunteer health care top professionals on the field in question
CRF	Case Report Form
CRP	C-reactive Protein
Finohta	Finnish Office for Health Technology Assessment
FiRe	Finnish Study Group for Antimicrobial Resistance
ICPC	International Classification of Primary Care
ICD-10	International Classification of Diseases
Kela	Social Insurance Institution
KTL	Public Health Institute (from 2009 onwards THL)
MIKSTRA	Antimicrobial treatment strategies (MIKSTRA) -programme
PBL	Problem Based Learning
ROHTO	Centre for Pharmacotherapy Development ROHTO
RSV	Respiratory Syncytial Virus
Stakes	National Research and Development Centre for Welfare and Health (from 2009 onwards THL)
STD	Sexually Transmitted Disease
THL	National Institute for Health and Welfare
URTI	Upper Respiratory Tract Infection
UTI	Urinary Tract Infection

Introduction

The increased use of antimicrobials, the trend towards increasingly broad-spectrum drug preparations and increasing bacterial resistance all around the world prompted the Ministry of Social Affairs and Health to appoint a microbial expert group at the National Agency for Medicines in 1993 to discuss how antibiotics policy should be applied in Finland. The group eventually proposed a nationwide programme for antimicrobial treatment strategies (MIKSTRA). The means proposed included further education for physicians, public education, monitoring of consumption of antimicrobials, and bacteria sensitivity reporting (1). The last-mentioned task was assigned to the FiRe network set up by Finnish antimicrobial laboratories and the National Public Health Institute in 1992 and the rest primarily to the MIKSTRA programme. At the same time, the indication-specific use of antimicrobials was surveyed at health centres in the Pirkanmaa region with the support of the Social Insurance Institution (Kela) (2). It was found in the Pirkanmaa study that reliable data could be collected by relatively simple means and that there were shortcomings in existing practices. The study provided a good foundation for further planning of the MIKSTRA programme.

Antimicrobials are among the most frequently used of all drugs. In Finland, more than 2 million courses of antimicrobial treatment are prescribed at outpatient appointments every year. Three out of four of these are for respiratory tract infections (2). The costs of outpatient antimicrobial treatment in 1998 were FIM 360 million (EUR 61 million). In the context of international practices, it is highly likely that some of these courses of treatment are unnecessary and that some could be replaced by more specifically targeted and more affordable antimicrobials and shorter courses of treatment.

The uncontrolled use of antimicrobials has led to increasing bacterial resistance all around the world, both in hospitals and in outpatient care (3). This development has already led to failures in treatment with first-line antimicrobials (4). Increased bacterial resistance to drugs causes increases in morbidity and mortality and in the costs of health care (5). There is also an underlying fear that antimicrobials will gradually lose their efficacy in the treatment of infectious diseases. Because there are no new antimicrobials for outpatient care on the horizon that would solve the emerging resistance problems, it is important to aim for conservative use of antimicrobials.

MIKSTRA was a broad-based programme that encompassed several projects; its purpose was to optimise the diagnostics and drug treatment of the infections most commonly encountered in outpatient care. Another purpose was to establish a procedure whereby the diagnostics and treatment of infections in outpatient care could be monitored and optimised pursuant to new research data and updated treatment recommendations. Preparation of the programme began in 1997.

Information collecting for MIKSTRA began in autumn 1998 and continued until the end of 2002. Since then, the extensive material collected in the course of the programme has been thoroughly studied and analysed.

The purpose of this final report of the MIKSTRA programme is to describe how the programme was run and what its key findings were, and to communicate those findings to parties that will benefit from them. The report is in two sections. The first section describes the general implementation of the programme, its materials, its methods and its process. This comprehensive description and the experiences gained may be of use to those who contemplate and plan similar studies or training projects in the area of primary health care. The second section discusses the principal findings of the programme. The majority of this information has already been published in various scientific forums, but the report also contains previously unpublished material. We hope that the information in this second section will serve as a background databank when clinicians consider improving their work or when the people in charge of health care training and development discuss further improvement of infection diagnostics and treatment practices. This information will most likely also serve as the foundation of antimicrobial policy pending the arrival of newer research data.

In addition to the material in this printed version of the report, there is also material available in electronic form at the MIKSTRA website, www.mikstra.fi; this may be freely used for research purposes and as material for teaching and presentations as long as the source is referenced.

SECTION 1:
METHODOLOGY REPORT

1 Background

1.1 Infections in outpatient care

Infections in outpatient care are a significant cause of morbidity and an important reason for using health care services. In the Health2000 study, 7,000 Finns over the age of 30 were interviewed in 2000–2001 (6). According to the section of the survey concerning infection symptoms, 19% of the respondents had had respiratory symptoms during the previous two months, and no fewer than 10% of them had had diarrhoea symptoms during the previous two weeks. Two out of five of those with respiratory symptoms had used health care services, and 2% of them had been hospitalised.

According to the Pirkanmaa study, about 1% of the population sought medical care because of an infection during one week in November (2). Infections accounted for one third of all emergency duty consultations at health centres according to this study conducted in 1995, and respiratory tract infections accounted for 80% of all infections. The largest group of diagnoses was that of unspecified upper respiratory tract infections (URTI; 22%), followed by otitis media (16%), bronchitis (13%) and sinusitis (11%).

At the Salo regional health centre in 1998, outpatient care infections accounted for 29% of all appointments with a health centre physician, and in week 46 in the years 1999 to 2001 this figure varied between 26% and 28% (Seppo Y.T. Junnila, unpublished observation). In 1998, 47% of appointments at the Salo regional health centre were ICPC coded, as opposed to 91% to 94% in 1999–2001. By comparison, in a two-week sample at Saarijärvi-Karstula health centre in January 2006, 48% of all appointments were ICD-10 or ICPC coded, and out of these 18% had an infection diagnosis (Ilkka Kunnamo, unpublished observation).

There is great seasonal variation in the incidence of respiratory tract infections. Their most common pathogen is rhinovirus, which causes about half (or during an epidemic up to 80%) of all respiratory tract infections. Rhinovirus epidemics typically develop in early autumn and late spring. Influenza A and respiratory syncytial (RS) viruses typically propagate in mid-winter, and the RS virus also does so in spring every other year (Figure 1). Because these viruses cause a great deal of illness particularly in children, often with otitis media as a complication, the seasonal variation also manifests itself in the use of antimicrobials and the demand for health care services. For this reason, a conscious effort was made to time the collecting of information for the MIKSTRA programme so as to avoid predictable epidemic peaks. The purpose of this was to avoid having an epidemic bias the range of infection patients and to avoid burdening health care employees at a time when they are overworked anyway and thus more reluctant to respond to surveys. The

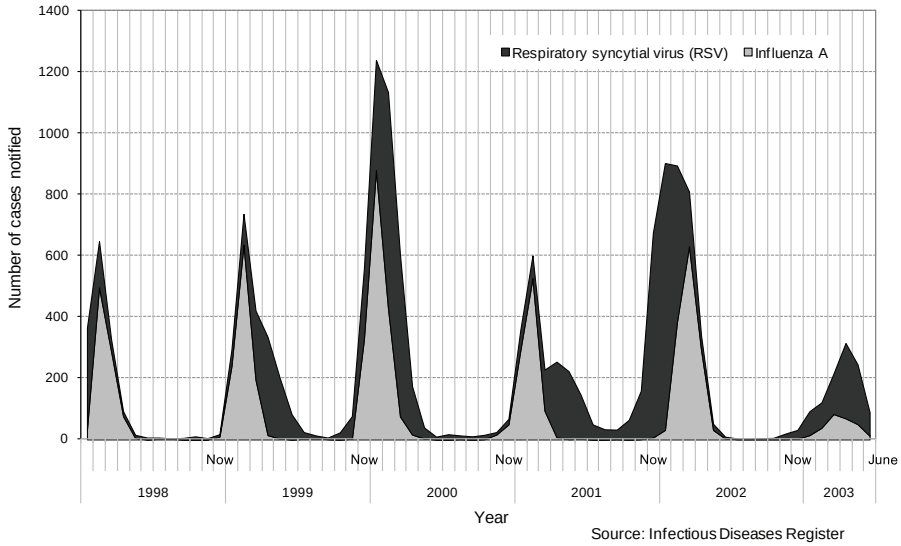


Figure 1. Influenza A and RSV cases notified to the Infectious Diseases Register by month in 1998–2003.

second week of November that was eventually selected for information collecting proved to be a fortunate choice.

1.2 Factors affecting the use of antimicrobials

Antimicrobials are the drug group with the largest number of users. The level of consumption and the range of drugs chosen vary by country, region and physician.

Sales of antimicrobials, as of all drugs, have been monitored systematically in Finland since the 1970s. Since 1987, the National Agency for Medicines and Social Insurance Institute (Kela) have been jointly publishing Finnish drug statistics based on registers maintained by the two institutions. The register of the National Agency for Medicines is derived from statutory reporting by wholesalers, while the Kela register is derived from pharmacy sales reports on prescription drugs qualifying for national health insurance reimbusement.

The problem with both registers as far as the evaluation and governing of the use of antimicrobials is concerned is that they contain no information on why the drugs were prescribed or on the infection patients who were not prescribed an antimicrobial.

The use of most antimicrobials tends to be weighted towards winter, particularly the first quarter of the year, because the consumption of antimicrobials always spikes during viral respiratory tract infection epidemics. Annual variation can largely be explained by variation in the extent of these epidemics.

Seasonal variation in the use of antimicrobials can be seen for instance in the Kela prescription statistics (Figure 2). In this seasonal cycle, November is in a high

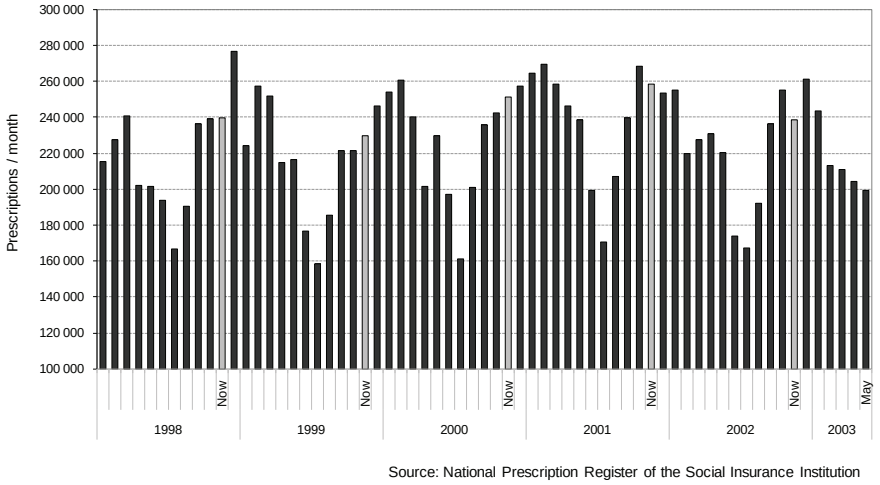


Figure 2. Reimbursed prescriptions of antimicrobials (J01) per month in Finland in 1998–2002

season but not in the peak season. This was the other reason, apart from avoiding epidemic spikes, for settling on the second week of November for collecting data for the MIKSTRA programme.

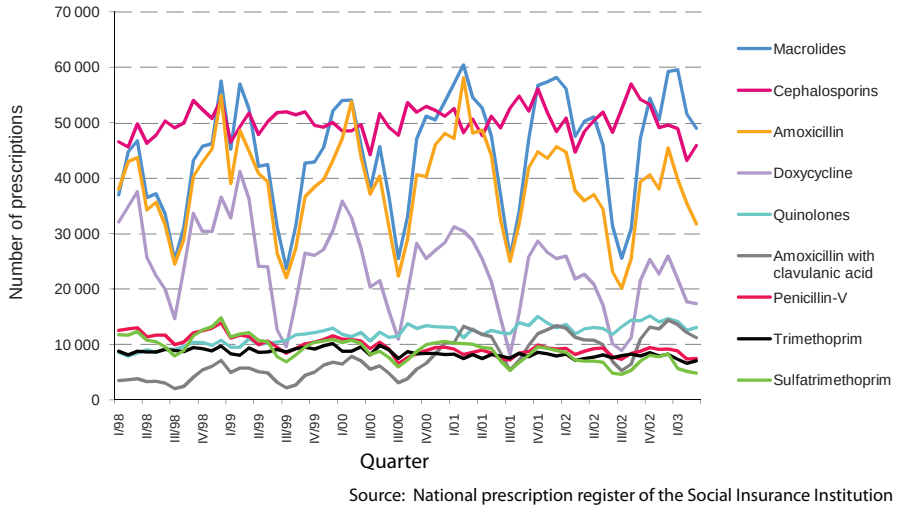


Figure 3. Number of reimbursed prescriptions of antimicrobials per quarter, January 1998 to March 2003.

Seasonal variation in the sales of antimicrobials is particularly clear for those antimicrobials that are used to treat respiratory tract infections (e.g. penicillins, doxicycline and macrolides (Figure 3)).

In the international context, the consumption of antimicrobials in Finland is average by European standards but high by Nordic standards (8). Finland differs

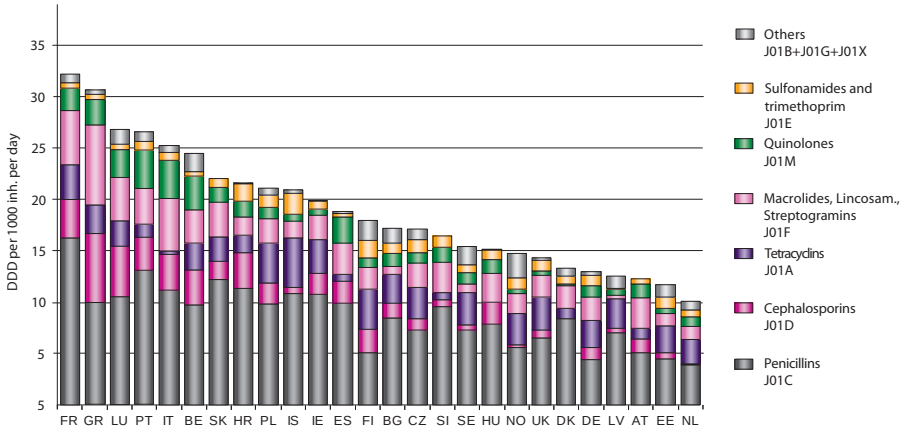


Figure 4. Total outpatient antibiotic use in 26 European countries in 2002 (Source: ESAC 1, European Surveillance of Antimicrobial Consumption 2001-2004; www.esac.ua.ac.be).

from other countries in having for a long time had higher consumption levels of tetracyclins and sulpha-trimethoprim, for instance (Figure 4).

1.3 Antimicrobial resistance

Bacterial resistance to drugs has been monitored nationwide in Finland by the National Public Health Institute since the beginning of 1991. Initially, this monitoring consisted of collecting samples of the most common types of bacteria from clinical microbiology laboratories. Since 1997, monitoring has been handled by the Finnish Study Group for Antimicrobial Resistance (FiRe), a network of these laboratories that currently includes 25 clinical microbiology laboratories around the country. All the central hospital and university laboratories and major private laboratories are members.

The FiRe network publishes annual nationwide statistics which are available on the network's website (www.finres.fi). The clinical microbiology laboratories of central hospital districts also publish their own regional reports including results specific for individual health centres.

Because a bacterial resistance survey system was already in place, the MIKSTRA programme did not collect bacterial resistance statistics at the health

centres studied. It also became apparent at an early stage in the programme that the annual bacterial samples collected at MIKSTRA health centres were small and that the material would not thus have been sufficiently large or comprehensive for a study of the relationship between the use of antimicrobials on the one hand and bacterial resistance on the other. However, this research is being carried out on the basis of materials produced by the FiRe network, the National Agency for Medicines and Kela.

Resistance status

Notwithstanding the above, the MIKSTRA programme monitored changes in bacterial resistance to drugs very closely. The most important change in the resistance situation to affect antimicrobial treatment was the increased resistence of pneumococci to macrolides, which was written up in the Finnish Medical Journal as early as in 2000 (9). Following this, the MIKSTRA working group stressed the importance of reducing the use of macrolides particularly in treating upper respiratory tract infections in accordance with the Current Care guidelines.

Changes in the sensitivity of Streptococcus pneumoniae between 1995 and 2008 are shown in Figure 5. The percentage of macrolide-resistant pneumococci has increased from 0.6% in the early 1990s to 24.6% in 2008. The percentage of strains with decreased penicillin sensitivity has also increased to 15.2% in 2008, while 3.1% of strains were fully penicillin-resistent. Resistance to sulpha-trimethoprim was between 14.1% and 19.4% for six years but rose to 22.3% in 2008. The percentage of tetracyclin-resistant strains is also slowly increasing. In

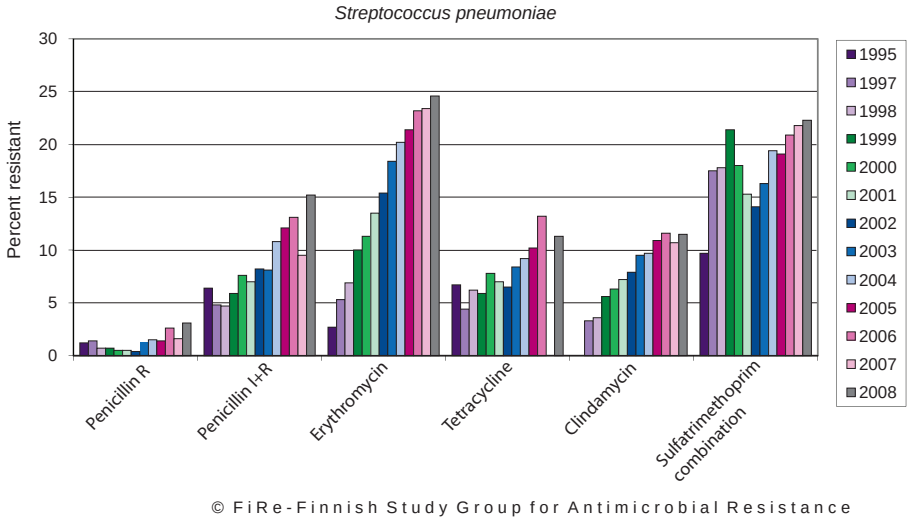


Figure 5. Antibacterial resistance of Streptococcus pneumoniae in Finland 1995–2008 (Source: FiRe, Finnish Study Group for Antimicrobial Resistance, www.finres.fi) (R = resistant, I = reduced susceptibility).

many cases pneumococci are multi-resistent, which restricts the range of treatment options available.

Other common pathogens in outpatient care do not show as dramatic a change in their sensitivity as pneumococci do (www.finres.fi). However, the resistance of gonococci to fluoroquinolones is increasing, and so is that of imported salmonella. Most campylobacteria have been resistent to fluoroquinolones for a long time.

Changes in bacterial resistance have already caused changes in the treatment recommendations for outpatient care infections, and these are taken into account when treatment recommendations are updated.

1.4 Guidance for the use of antimicrobials

Before the MIKSTRA programme, the use of antimicrobials was mainly governed by textbooks and recommendations issued by individual experts. There was also a series of publications by the National Agency for Medicines named Kapseli in which issue no. 10, published in 1981, was titled Antimikrobinen lääkehoito (Antimicrobial treatment) (10). This was, apart from textbooks, the only official guidance available for the use of antimicrobials until 1995 and the publication of a new, updated version in Kapseli 24, Avohoidon mikrobilääkkeet (Antimicrobials in outpatient care) (11).

The use of antimicrobials and bacterial resistance affects many areas of medicine, which may be one reason why no systematic treatment recommendations have been issued earlier. Changes in bacterial resistance have led to recommendations being issued for the use of individual antimicrobial products, though. The broadest of these was the recommendation to avoid the use of macrolides in the treatment of throat and skin infections because of the increased macrolide resistance of streptococcus A (12). The recommendation was issued primarily because of patient safety, since macrolide-resistant streptococcus A had been found to cause life-threatening complications when patients were treated with macrolides (13). The recommendation led to a significant decrease in the use of macrolides and, in the longer term, to a decrease in the percentage of macrolide-resistant streptococcus A (14).

The overall image of the use of antimicrobials in Finland is quite good by international standards, thanks to the annual drug statistics published by the National Agency for Medicines and Kela. The greatest shortcoming in these statistics regarding the governing of the use of antimicrobials was that there was no information on the indication-specific use of the drugs. Indeed, one of the aims of the MIKSTRA programme was to obtain diagnosis-specific information on the diagnostics and treatment of the most common types of infection in outpatient care.

The issuing of Current Care guidelines for outpatient care infections was begun at the initiative of the MIKSTRA programme. Recommendations were requested for acute otitis media, acute bronchitis, sinusitis, throat infection, skin infection and urinary tract infections (www.duodecim.fi/kh/). These were among the first Current Care guidelines to be issued. Each Current Care working group issuing recommendations included one or more members of the MIKSTRA working group.

The MIKSTRA programme took it upon itself to convey these recommendations into the field in outpatient care through a specially designed training programme. The purpose was to compare treatment practices for the outpatient care infections in question before and after the recommendations were issued. The MIKSTRA programme thus helped the research on how the Current Care guidelines become established practice. Current Care guidelines and training material created in the MIKSTRA programme have later been used as additional and background material in the ROHTO programme and in the Evidence-Based Medicine Electronic Decision Support (EBMeDS) project.

2 Objectives of the MIKSTRA programme

The purpose of the MIKSTRA programme was to gain an overall picture of how infection diagnostics and treatment are handled at health centres and what antimicrobials are used for in outpatient care.

Another purpose was to guide the use of antimicrobials in a direction optimal for infection diagnostics and treatment, hence reducing their costs, through further education based on the Current Care guidelines. The long-term objective was that all outpatient care infections would be treated in the similar way nationwide, according to local applications based on evidence-based national recommendations.

It was also explored whether further education at the workplace would be suitable for introducing treatment recommendations into practice. Two proven training methods were tested in the day-to-day work of health centres in the practical implementation of the training.

The programme further aimed to establish a procedure whereby the diagnostics and treatment of infections in outpatient care could be monitored and further optimised pursuant to new research data and updated treatment recommendations.

3 Materials and methods

3.1 Research domain and actors

3.1.1 Component projects

The objectives of the programme were fulfilled through the following independent but interlinked component projects:

1. producing evidence-based treatment recommendations for the commonest types of outpatient care infections jointly with the Current Care programme of the Finnish Medical Society Duodecim,
2. gathering information on the diagnostics and treatment of outpatient care infections at the health centres studied, annually in the second week of November,
3. gathering information annually on patient expectations, attitudes and treatment behaviour with regard to outpatient care infections and antimicrobial treatment,
4. training instructor physicians to take charge of the implementation of a training programme based on the Current Care recommendations at their respective health centres,
5. distributing information on diagnostic and treatment procedures, bacterial resistance and consumption of antimicrobials to health centre personnel through their contact persons and through the media,
6. analysing the impact of treatment recommendations on diagnostics and treatment practices and related costs, and
7. analysing the impact of two different training methods on treatment practices.

3.1.2 Health centres

The backbone of the MIKSTRA programme was a network of 30 MIKSTRA health centres located around the country (Figure 6; Appendix 1). These health centres were recruited in 1998. All health centres in Finland (n=256) were sent a letter inviting them to participate in the project, and a notice was published in the Finnish Medical Journal (15). Out of the 83 health centres expressing interest (32% of the total), a sample representative of the entire country was chosen. The parameters taken into account in the selection were the size of the municipality (small: population under 10,000; medium: population 10,000 to 50,000; large:

population over 50,000), the type of municipality (rural – urban), the provision of health care services (own health centre vs. inter-municipal federation for health care), and sales of antimicrobials per 1,000 residents. The aim was also to have all regions and all hospital districts represented.

The 30 health centres selected for the MIKSTRA programme serve a combined population of about 820,000 (about 16% of the national population) and employed some 450 physicians.

In the final year of data collection, 2002, 20 control health centres also participated in the programme (Figure 6; Appendix 2). The control health centres were chosen from among those which had expressed willingness to join the project in 1998 but which had been excluded from the sample. The same criteria were applied in this selection as in the selection of health centres for the actual research. Originally, 30 health centres agreed to serve as controls, but 10 of these later withdrew. These withdrawals made the control health centre sample somewhat less representative. The 20 control health centres serve a combined population of

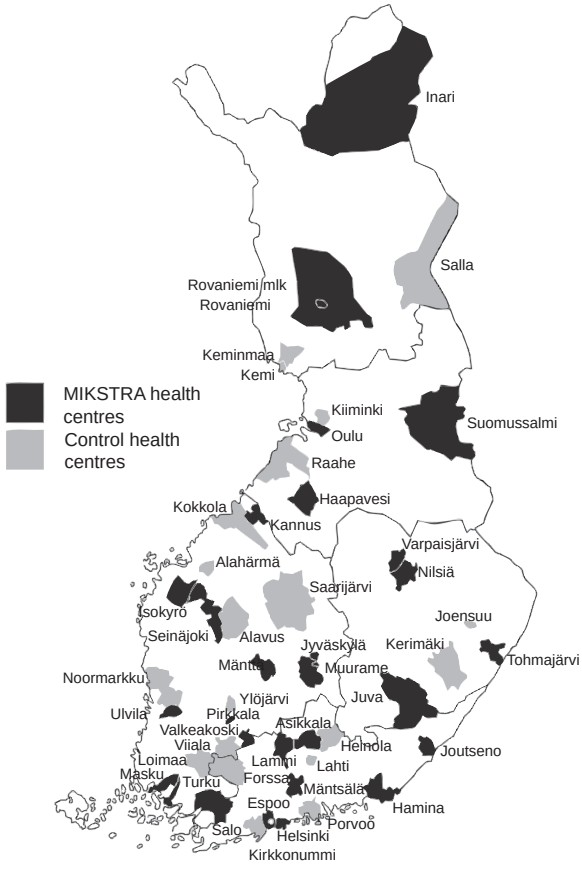


Figure 6. MIKSTRA study and control health centres.

about 545,000 (about 10% of the national population) and employed some 350 physicians.

3.1.3 Working group

The working group responsible for planning and controlling the programme had representatives from the National Public Health Institute, Kela, the National Agency for Medicines, the National Research and Development Centre for Welfare and Health (Stakes), the Health Care Method Assessment Unit (Finohta), and the Finnish Medical Society Duodecim (Table 1). Researchers from the Universities of Helsinki, Tampere and Turku and from the Centre for Pharmacotherapy Development (ROHTO) also participated.

Table 1. Members of the MIKSTRA Steering Group.

		Organisation Current position
Pentti Huovinen	Research professor (Chair)	**National Public Health Institute** National Institute for Health and Welfare THL
Pekka Honkanen	Professor (Researcher)	**Stakes, Finohta** University of Oulu
Timo Klaukka†	Research professor Head of Health Research	**Social Insurance Institute**
Kalevi Lauslahti	Research Professor emeritus (Chair until 5/1998)	**Stakes, Finohta**
Marjukka Mäkelä	Research professor Director	**Stakes, Finohta** National Institute for Health and Welfare THL, Finohta
Solja Nyberg	MSc, Researcher (1/2002 onwards)	**MIKSTRA Programme** National Institute for Health and Welfare THL
Erkki Palva	Professor, Director	**National Agency for Medicines** Fimea
Ulla-Maija Rautakorpi	MD PhD, Chief Medical Officer (Project manager)	**MIKSTRA Programme** National Institute for Health and Welfare THL, Finohta
Risto P. Roine	Docent Chief Medical Officer	**Stakes, Finohta** Hospital District of Helsinki and Uusimaa
Hannu Sarkkinen	Docent, Director	**Finnish Medical Society Duodecim** Päijät-Hämeen keskussairaala

Virpi Semberg	Director (until 5/2000)	**Stakes, Finohta** Hospital District of Helsinki and Uusimaa
Helena Liira	Docent Medical Director	**Finnish Medical Society Duodecim** Kirkkonummi Municipality
Temporary researchers		
Heidi Anttila	PhD, Researcher	**Stakes, Finohta**
Arja Helin-Salmivaara	MD PhD, Training officer	**ROHTO Programme**
Hanna Koskinen	MSc, Health economist	**Stakes, Finohta**
Pekka Laippala†	Professor	**Stakes, Finohta, University of Tampere**
Jorma Leistevuo	PhD, Researcher	**Centre for Pharmacotherapy Development ROHTO**
Tiina Leistevuo	MD PhD, Physiatrist	**National Public Health Institute**
Eeva Mäkinen	MD, Researcher	**National Institute for Health and Welfare THL, Finohta**
Tuuli Nikkarinen	MD PhD, Senior physician	**Finnish Medical Society Duodecim**
Johanna Pulkki	Pharmacist, Researcher	**National Public Health Institute**
Martti Teikari	MD, Managing editor	**Stakes, Finohta**
Petter Tuderman	Chemist, Researcher	**University of Helsinki**
Hanna Virkkunen	MSc, Researcher	**Centre for Pharmacotherapy Development ROHTO**

†Timo Klaukka passed away in June 2009 and Pekka Laippala in 2003.

3.1.4 Funding

Funding for the programme was contributed by Kela, the National Public Health Institute, the National Agency for Medicines, Stakes and the Finnish Medical Society Duodecim. The programme employed a full-time project manager from 1998 to 2003 and a part-time one from 2004 to 2008, one or more part-time researchers from 2000 to 2008, and a full-time biostatistician from 2002 to 2003 and a part-time one from 2004 to 2008. Finohta, the Finnish Office for Health Technology Assessment based at Stakes, provided office space for the project manager and the statistician and obtained the necessary tools for them and the fixed-term researchers, while also providing secretarial assistance, IT support and publicity support. Financial administration of the programme was undertaken by the Turku office of the National Public Health Institute: from 2003 in the microbiology and infectious diseases department and from 2005 in the bacterial and infectious diseases department.

The background organisations funded the coordination of actions out of their own budgets to a total of EUR 76,000 to 170,000 annually. This sum covered the salaries of the project manager, the statistician and the fixed-term researchers including ancillary personnel costs, the costs of the annual meetings with contact persons at the health centres involved, and other running programme costs. Moreover, the organisations involved also provided funding for the MIKSTRA component projects that were their responsibility. The costs do not include the participating organisations' own work input or the substantial input of the participating health centres.

3.2 Materials and methods

Information on the diagnostics and treatment of infection patients in outpatient care and on patient expectations and recovery was collected in three different surveys between 1998 and 2002. An indication survey was circulated among health care professionals in the second week of November (week 46) each year. A patient survey was circulated simultaneously, and phone interviews with patients were conducted 10 to 14 days later.

3.2.1 Information collection by physicians and nurses (indication survey)

The aim of information collection was for each physician and nurse involved in treating outpatient care infections at the MIKSTRA health centres to keep a record of his/her practices in the diagnostics and treatment of infection patients for the duration of the survey week. A case-report form (CRF) was prepared for this survey; it was slightly augmented and altered in the course of the study (Table 2; Appendices 3 and 4). In the final year, the corresponding information was also collected at the control health centres.

Table 2. Topics included in the case-report forms of MIKSTRA study.

1.	Sex and year of birth of the patient
2.	Smoking status of the patient or child's parents at home (no/yes, how much)*
3.	Type of consultation (scheduled or home visit, out-of-hour visit, telephone consultation, scheduled control visit**)
4.	Main diagnosis (only the one(s) ruling the treatment decisions)
5.	Duration of symptoms, in days (classified into four categories)
6.	Diagnostic procedures (14 options including 'non' and 'other', with a definition which)
7.	Referrals and (internal or external) consultations (six options including 'neither')
8.	Sick leave or parental-leave (no/yes, for how many days)
9.	Patient's expectations on antibiotic prescription (demanded–resisted, scale 1-5)
10.	Treatment with antibiotic per os, im. or iv. (yes/no, had already, delayed prescription)
11.	Prescribed antibiotic (name, strength, dose and package, duration of treatment in days if other than that calculated from dose and package)
12.	Factors influencing the choice of antibiotic treatment***
13.	Prescribed or recommended symptomatic or topical medication (name, strength, dose, package and duration in days)
14.	First or re-consultation for the infection episode (how many consultations in all)
15.	New appointment (no/yes/if needed/by telephone)**
16.	Doctor's/nurse's signature, doctor's stamp or nurse's initials and stamp of the health centre)
17.	Participation in MIKSTRA-training (no/yes, how many occasions)****

*	from year 2000 onwards only
**	from year 1999 onwards only
***	four options in 1998; six including ‘other’, with a definition which, from 1999 onwards only
****	years 2001 and 2002 only

3.2.2 Patient survey

All patients who sought treatment because of an infection during the information collection week were offered a questionnaire form while they were waiting for their appointment. The questionnaire gauged the patient's symptoms and expectations with regard to the appointment and his/her general views on the treatment of infections (Table 3; Appendix 5). A code number was used to link the patient's questionnaire form with the CRF regarding him/her.

Table 3. Topics included in the patient questionnaire forms of MIKSTRA study.

1. Date of appointment
2. Sex and year of birth of the patient
3. Which of the following symptoms of infection are you (or your child as a patient) suffering from at the moment (16 options including 'other, what'; one or more options allowed)?
4. Which of the symptoms you chose above was/were the main reason for you to seek for medical help today (max to two options). Please indicate your choice(s) by using the numbers from the above list or write down your symptoms.
5. For how long have you, or your child, had these symptoms during this particular illness? (classified into same four categories as in the case-report form)
6. Have you had previous appointments during this episode of illness and if so, how many appointments have you had before this one? (no/yes a doctor/yes a nurse and how many times each)
7. How ill do you feel yourself, or how ill do you think your child is at the moment? (very ill to almost or totally symptomless; scale 1–4)
8. What are your expectations regarding antibiotics for treatment of your, or your child's, current infection? (Ring the number that best corresponds to your expectation). (I want to – I don't want to have an antimicrobial, scale 1–5)
9. What kind of help are you hoping to receive from the doctor or nurse at this appointment? (10 options including 'other, please specify', one or more responses allowed))
10. What is your opinion on the following statements? (fully agree to fully disagree; scale 1–5):
    - One recovers from a cold more quickly with antibiotics.
    - Penicillin is just as efficient as other antibiotics.
    - Antimicrobials become less effective if you take them frequently.
    - Antimicrobials are not effective against infections caused by viruses.
    - Doctors prescribe antimicrobials too readily.
    - Bronchitis needs always to be treated with antibiotics.
    - Unnecessary course of antimicrobials will not cause any harm
    - One can prevent catching a cold by washing hands well.

3.2.3 Patient phone interviews

Patients taking the survey were requested, on a separate form, to agree to a follow-up interview by phone about two weeks after their health centre appointment.

The phone interviews were targeted at those infection patients for whose diagnostics and care a Current Care guideline existed that was being put into practice through training at the participating health centres. The relevant infections were otitis media, throat infection, sinusitis, acute bronchitis, skin infection and urinary tract infection. A sample of patients with an unspecified upper respiratory tract infection (i.e. common cold) was also interviewed. The aim was to interview a sample of 200 patients for each type of infection each year. The interviewees were initially selected at random by choosing every fifth patient out of the infection patients giving consent for the interview until the sample of 200 patients was complete. However, because this method causes too much of a bias towards the patients of large health centres, from year 2000 onwards the selection was made so that all applicable patients from small health centres were included, while a percentage relative to the population was included from medium-size and large health centres.

The purpose of the phone interview was to find out about how the patients had recovered and how satisfied they were, what other treatments than the ones prescribed at the health centre they had used (if any), and what the costs caused to them by the illness had been. The outline of the phone interview remained the same throughout, but some more specific questions for instance gauging customer satisfaction were added.

3.2.4 Training intervention for medical personnel

Previous research indicated that simply publishing and distributing treatment recommendations does not have an appreciable impact on treatment practices (16). It has also been found that traditional teaching in a lecture setting does not have very large an impact on treatment practices. The aim in the MIKSTRA programme was to find out whether further education at the workplace would be suitable for introducing treatment recommendations into practice. A further aim was to compare two proven interactive training methods.

The purpose was to train a physician instructor for each MIKSTRA health centre to manage and organise training and other actions locally and to act as the local change agent. At most of the health centres, the instructors were also the programme contacts or local coordinators. The coordinators and instructors were not paid bonus for their work; they did this work on the side of their normal work. The control health centres got no training, but the treatment recommendations were normally published on completion in the national Duodecim journal and in the general practice medical database.

Randomisation

The participating health centres were randomly chosen first to implement training in two stages (groups A and B) and then to use either the problem-based learning (PBL) or the academic detailing (AD) method. At phase I, group A health centres were to cover the treatment recommendations for otitis media, throat infection and urinary tract infections (A recommendations), while group B health centres were to cover the treatment recommendations for bronchitis, sinusitis and skin infection (B recommendations) (Figure 7). Phase I lasted from September 1999 to November 2000, i.e. until the data collecting week that year. Phase II began after data collecting in 2000 and lasted until the data collecting week in 2001. During the latter phase, the A health centres were intended to cover the B recommendations and vice versa. The purpose of this was that in the 2000 data collection the health centre groups would act as controls for each other. The randomisation was performed by picking the names of the health centres out of a hat.

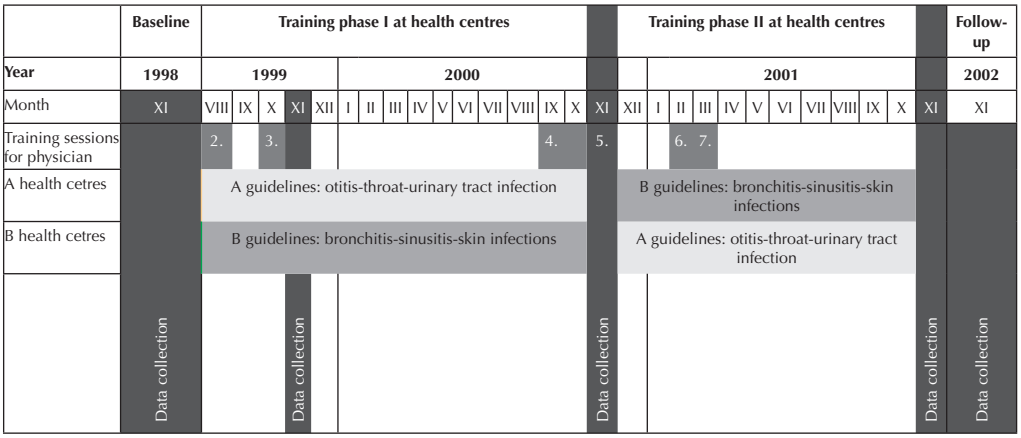


Figure 7. Randomisation of health centres and training schedule (numbers refer to the list of training sessions for physician instructors presented in Table 4).

Instructor training

A total of seven training sessions were held for instructors (Table 4), two of them being method-oriented two-day sessions jointly held with the ROHTO programme (November 2000 and March 2001).

Table 4. Training of MIKSTRA instructors and contact persons (time, target group and main topics).

When, where	To whom	Topic(s)e
Year 1999:		
1. Orientation, IV/-99 Helsinki	Instructor physicians and contact persons in two groups	Orientation to the theme and training methods
2. Regional training, IIX/-99 Helsinki, Tampere, Turku, Kuopio, Oulu, Jyväskylä	Instructor physicians and contact persons	Practical exercise on training methods, guidelines for otitis media and bronchitis as examples
3. General meeting, X/-99 Helsinki	Instructor physicians and contact persons	Training methods; feedback on the results of the first data-collection
Year 2000:		
4. Regional training, IX/-00 Turku, Helsinki, X/-00 Oulu, Tampere, Kuopio	Instructor physicians, contact persons and health centre staff	Urinary tract- and skin-infections; feedback on the previous results
5. Method training, XI/-00 Majvik	MIKSTRA- and ROHTO-instructors	Group-dynamics, role of a physician instructor; public performance: experience swapping
Year 2001:		
6. Regional training, II/-01 Tampere, Kuopio, Salo, Helsinki, III/-01 Oulu	Instructor physicians and contact persons and health centre staff	Impact of the MIKSTRA programme; future training; questions and answers
7. Method training, III/-01 Unitas-opisto	MIKSTRA- and ROHTO-instruktors	Interaction skills; group process; management of change

Training methods

The two training methods chosen differ in their theoretical background, and both had been proven through research to be effective in changing established treatment practices (17, 18).

In problem-based learning (PBL), a change in procedure derives from the individual learning of the participants and the development of their competence. Discussing a case or a practical problem in a group initiates the learning process and a critical evaluation of one's own actions. Evaluation of existing information and learning of new information is assumed to change practices; in other words, the focus is on the learning process.

The other method chosen, academic detailing (AD), involves guidance or feedback and guidance given by an expert and involves creating a local operating model. This is based on practical action, scientific evidence and specific, concrete

instruction given by experts and aiming at a tangible change in operating procedures, augmented by discussion and feedback on employees' actions. The focus is thus on actions and how to change them. Each health centre was also instructed to document the created local operating models.

Training material

The key training material consisted of the newly completed Current Care guidelines jointly produced by the Finnish Medical Society Duodecim, specialist medical associations (www.duodecim.fi/kh), and members of the MIKSTRA working group. The Current Care guidelines were published in October 1999 (otitis media, throat infection, sinusitis, bronchitis and skin infection) and March 2000 (urinary tract infection). Some of these recommendations have already been updated. At the request of the health centres, overhead slides of the treatment recommendations were made in 2000 to assist in training; these are also available on the MIKSTRA website (www.mikstra.fi). Because the optimum use of antimicrobials requires the general population too to be aware of the information in the recommendations, concise patient instructions were drawn up for each of the recommendations. A short print run of patient instructions was produced and sent out to the health centres; further copies could be printed online (www.mikstra.fi/potilasohjeet or www.duodecim.fi/kh).

Feedback on the health centres' own practices

The annual numbers of patients per diagnosis at individual health centres were in most cases so low that it was not feasible to give feedback on them. In practice, feedback on an individual health centre's results was given by reporting the group-level results of earlier surveys at training sessions.

The key findings of MIKSTRA were published in Finnish and international scientific publications. The articles were circulated to the health centre contacts before publication, and these contacts were also highlighted at press briefings and in press releases. Information was conveyed to other health care personnel and to the general population through the media. Local media in particular were approached to support the successful conducting of the programme at the MIKSTRA health centres.

Once the information was collected and the material verified, each MIKSTRA health centre received a customised final report, comparing their individual results to the results of all MIKSTRA health centres and those of all control health centres.

3.2.5 Internal evaluation

Implementation of the MIKSTRA programme was monitored on several occasions using different methods. Basic data on the health centres (including availability of diagnostic aids) was collated at the baseline in 1998 and again in 2002

(www.mikstra.fi, in Finnish). The latter of the two surveys also included questions on how positions were filled at the health centres and what their personnel turnover was.

The start-up and implementation of training and the role of local media were evaluated in discussions at annual meetings but also through dedicated 'Local publicity/training monitoring' and 'Feedback/evaluation' forms in 1999 and 2000 (www.mikstra.fi, in Finnish). The Department of Public Health at the University of Helsinki surveyed instructor experiences using a mailed questionnaire in autumn 1999. In summer 2000, the MIKSTRA training officer interviewed all contacts by phone. Experiences of MIKSTRA and ROHTO instructors were also collated at the joint methodology training session in spring 2001. In summer 2001, a survey on how visible and functional MIKSTRA and the treatment recommendations are was conducted among physicians at the MIKSTRA health centres and a random sample of other physicians selected from the database of the Finnish Medical Association.

3.2.6 External evaluation

An external evaluation of the MIKSTRA training intervention was conducted by Taina Mäntyranta, MD, from the Department of Public Health at the University of Helsinki. The evaluation explored how the Current Care guidelines had been implemented at the health centres and which factors enabled or hindered the training. The evaluation was based on the monitoring data collected in the internal evaluation and interviews with members of the project working group, the health centre contacts and the instructors.

As part of the Stakes project feedback, an e-mail questionnaire was circulated among representatives of the organisations participating in the MIKSTRA programme in autumn 2005. The principal purpose of this questionnaire was to find out how the people involved in Stakes development projects saw the actions of Stakes.

3.2.7 Data processing and statistical methods

Data encoding and storage

The paper questionnaire forms were duplicated at the Kela in-house printing shop in Pitäjänmäki in Helsinki and mailed directly to the health centres. They were returned by mail from the health centres to the Stakes office, where each form was reviewed and encoded. All text information on the indication and patient survey forms was standardised and tagged with uniform number codes (e.g. drug choices, diagnostic aids). Year of birth, gender and symptoms were also checked to see that they matched on forms with the same ID number.

Some interpretative policy decisions had to be made at the encoding stage for instance because of missing information. For instance, regarding the prescribing of

antimicrobials the decision was made that an antimicrobial drug had been prescribed if details of a specific antimicrobial treatment was documented on the form although it was not ticked as having been prescribed. Also, a decision had to be made on how to treat the cases where two diagnoses had been entered for one patient, and neither had been clearly labelled the primary diagnosis. The policy decisions made at the encoding stage are listed in an online appendix at www.mikstra.fi (in Finnish).

Once the encoding was completed, the indication and patient survey forms were entered into the computer system, in each year by Helsingin Päätepalvelu Oy. They returned the material initially in Excel format and in later years in SPSS format. The data from each survey are saved as a separate file and can be combined on the basis of ID numbers.

The phone interviews were conducted in the first year by pharmacist students, and the results were entered onto computer by Helsingin Päätepalvelu Oy. In the following years, both the interviews and the entering of data were outsourced from ASM-tutkimus Oy.

Checking and correcting the files

After the data were entered onto computer, the files were reviewed to spot any entry errors. The frequency distributions of all variables were verified, and most were checked individually for each health centre. All values that on the basis of the frequency distributions were too small, too large or deviant in view of the question were checked. Also, pairs of interrelated variables were cross-checked, and in some situations three or more variables were co-checked.

Data on the indication and patient survey forms, e.g. year of birth and gender, were checked to make sure they matched. For unmatched forms, matches were sought among forms from the same health centre on the basis of background information, date and information entered on the forms that had not been entered onto computer. Similarly, some ID numbers had to be altered and some pairs of forms separated because the information they contained clearly showed that the two forms could not be a match. The number of forms from each health centre was counted, because it was found that in one year some forms had been left completely out of the computerisation. Some spot checks were also made. Some systematical entry errors were found during the checking process, and the fields in question were checked for all other forms too.

The sections on the indication survey forms regarding the prescribing of antimicrobials were checked with particular care. If there was no answer on the form to the question regarding the prescribing of antimicrobials, and no antimicrobial was named on the form, the missing information was replaced with a ‘no antimicrobials’ response if the form was otherwise appropriately filled in. However, the original information was also retained in the data. Also, if the patient had been prescribed an antimicrobial but the form had not been filled in by a physician, the original form was checked.

Phone interview responses on paper were not available at the Stakes office except for 1998, so checking could not be similarly conducted. From 1999 onwards, ASM-tutkimus Oy performed the interviews and entered them onto computer and checked them itself before delivery. Suspicious answers to key questions and any errors discovered through frequency distributions were returned to ASM-tutkimus Oy for rechecking.

All of the contradictory, suspicious and erroneous entries discovered in the aforementioned checks were re-checked on the original forms and corrected as necessary. Changes made to the materials following the checks are documented in the correction files and, where necessary, marked with a red pen on the study forms themselves. The checking took up a lot of time because there was so much material, but the investment was worthwhile to minimise entry errors in the materials and in the results.

The paper forms are archived and accessible if necessary. The forms from each health centre are in a separate bundle in numerical order.

Statistical methods

The statistical methods were chosen according to the context. Basically, the statistical unit is a single patient, for instance in reporting percentages. In practice, however, patients are clustered by health centre and by physician or nurse. In analyses where clustering is used, this is done at the health centre level. The method used is a mixed model with the health centre as a random factor. The identity of the health care professional who took the appointment (physician or nurse) could not be used for clustering, because the physician's unique identifier or 'SV code' is missing from some of the physicians' forms (1%) and is missing from all of the forms filled in by interns (B.Med.) (about 4% of all forms) and by nurses and public health nurses. Also, for each diagnosis there were usually only a handful of forms filled in by the same doctor.

The materials and results were mainly processed using SPSS software (versions 11 to 16). The mixed models were created using GLIMMIX in the SAS software – a macro in version 8 and a procedure in version 9. Graphs were mainly processed in Excel.

Missing information in the study forms occasionally causes slight variation in the figures, meaning that the total numbers of patients in various sub-totals or percentage calculations do not always add up.

3.2.8 Ethical issues

The ethical approvement was obtained from the City of Helsinki research ethics committee in 1998. Patients were asked in writing for their consent to a phone interview. Apart from age and gender, no identifying information was stored for any of the patients.

4 Process description

4.1 Participation

MIKSTRA was a long-term data collection project with broad geographical coverage, and during its course many changes occurred in the field of health care. Health centres largely remained stable, though, and only one health centre was unable to collect information in one year (2001) because of personnel turnover and lack of manpower. The occupancy rates of health centre physicians' positions and the permanence of physicians in those positions had been good since the recession of the early 1990s. This is why the increasing turnover and shortage of physicians towards the end of the programme came as a surprise. About half of the 953 physicians who participated in data collecting in the MIKSTRA programme were involved only in one year, and only about one in five were involved in four years or more (Table 5). Such a high turnover among physicians inevitably influenced the results of the project.

Table 5. How many times (years) did the physicians participate in MIKSTRA data collection during the five years of the study?

Number of data collections (years)	Number of physicians	Percent of all participated physicians over five years	Cumulative percentage
5	86	9,0	9,0
4	101	10,6	19,6
3	135	14,2	33,8
2	156	16,4	50,2
1	475	49,8	100
Total number of participating physicians during the five years of the study	953	100	

However, the physicians' participation was commendably active each year. Relative to the number of health centre physicians' posts in 1998, the participation percentage was 99% in the first year and 88%, 85%, 81% and 88% in the following years.

4.2 Changes in the operating environment

In 1998, the MIKSTRA health centres served a combined population of 819,777. In the course of the programme, the population decreased in some municipalities and increased in others (Table 6, p. 42). Overall, the combined population served by MIKSTRA health centres increased by just over 20,500 (3%), and the number of health centre physicians' positions increased by 41 (9%) over the same period of time according to the health centres. However, the number of actual doctors employed during the last information collecting week in 2002 was roughly the same as in 1998, because on average 8% of all posts were unfilled. According to our survey, some MIKSTRA health centres had up to one in four physicians' positions unfilled in week 46 in 2002 (Table 6). The control health centres also had a shortage of doctors in the week studied (8% on average).

In the course of the programme, the emergency clinic functions in the Turku and Oulu regions were reorganised, and as a result these large centralised emergency clinics fell outside the data collecting – Turku from 1999 and Oulu from 2000 onwards.

4.3 Implementing the training intervention

Implementation of the intervention was evaluated using follow-up questionnaires and by interviewing contacts. The following points were taken into account in the evaluation: 1) whether the randomisation into A and B groups had held up; 2) how actively the health centre's instructor had taken part in instructor training; 3) whether a written local operating model (a 'house code') had been prepared; and 4) whether the applicable training method (AD or PBL) had been used as agreed or in a modified form. The results of the evaluation are summarised in Table 7, p 43.

At 5 health centres the intervention proceeded as planned, at 8 it proceeded almost as planned, and at 14 the training was conducted according to the health centre's own application. Three health centres never started the training at all, citing a lack of manpower.

In practice, the randomisation did not wholly hold up. At 9 health centres, one or more of the phase II treatment recommendations were discussed during phase I, although for the most part this happened in 2000, after the data collection in 1999. Some health centres felt the PBL method to be too alien and either abandoned it or used an applied version of it. Half of the health centres wrote local 'house codes' for at least part of the treatment recommendations. In just over half of the health centres randomly selected to use the PBL method, actual or fictitious case histories were used in training. Health centres sent participants to the training sessions organised by the programme variably, from two (3 health centres) to seven (4 health centres) times. On average, the health centre instructors and/or contacts participated in 5.4 training sessions out of 7.

Table 6. Change of population from 1998 to 2002, number of GP posts in 1998 and 2002 and number (%) of GP posts occupied at MIKSTRA study health centres during the study week 46 in 2002.

Health Centre	Population	Population change	Number of GP posts		Number (%) of GP posts occupied on week 46
Year	1998	1998-2002	1998	2002	2002
Asikkala	8 800	-141	6	6	6 (100)
Espoo, Tapiola	38 726	-203	15	17	17 (100)
Haapavesi	8 283	975	6	7	7 (100)
Hamina+	26 697	-1 171	15	13	10 (77)
Hki, Alppiharju	12 111	0*	7	7*	7*
Hki, Pihlajamäki-Viikki	17 200	0*	6	6	5 (83)
Inari	7 716	-490	6	7	7 (100)
Joutseno	11 423	-549	6	6	5 (83)
Juva+	14 990	-1 244	9	9	7 (78)
Jyväskylä	76 500	4 816	46	56	53 (95)
Kannus	6 300	-250	4	4	3 (75)
Korpilahti+	12 751	681	8	9	9 (100)
Kyrönmaa+	17 916	-607	12	12	11 (92)
Lammi+	7 265	-113	5	5*	5*
Masku+	13 281	927	7	7*	7*
Mäntsälä	15 700	1 515	8	10	10 (100)
Mänttä+	16 384	-3 995	11	18	15 (83)
Nilsiä	7 800	-1 121	6	7	5 (71)
Oulu	113 584	11 252	60	60*	60*
Pirkkala	11 848	1 847	8	11	11 (100)
Rovaniemi kaupunki	34 600	567	23	25	22 (88)
Rovaniemi mlk	22 000	-225	12	11	10 (91)
Salo+	44 402	1 715	29	34	30 (88)
Seinäjoki+	48 976	2 771	30	36	36 (100)
Suomussalmi	11 690	-1 121	6	7	5 (71)
Tohmajärvi+	6 131	-1 055	4	4	4 (100)
Turku	168 000	6 925	79	79*	65** (82)
Ulvila+	14 513	-527	8	8	7 (88)
Valkeakoski	20 700	-264	14	16	16 (100)
Varpaisjärvi	3 490	-333	3	3*	3*
Total (% posts occupied)	819 777	20 582	459	500	458 (92)
Number of GPs in data			454	405	405
Participation rate			99 %	81 %	88 %

+joint municipal health centre

*data from 2002 not provided; figures from 1998 used

**number of potentially participating doctors in 2002 given by the health centre

Table 7. Summary of the implementation of MIKSTRA-training in health centres.

Health centres by group	Randomization to groups A or B-held up[a]		Participation of the instructor physician in instructor training[b]	Case histories were used in training (PBL)[c]	Written local house codes were made[d]	Training method (AD or PBL) was followed[e]
	1999	2000		-		
AD - A						
2	3	4	2+5	-	?	2
3	6	6	2+4	-	6	3
13	4	5	1+5	-	3	2
19	3	3	0+4	-	0	1
20	4	3	1+4	-	1	1
21	3	3	0+4	-	1	1
22	?	3	1+3	-	0	1
25	3	3	0+3	-	0	0
AD - B						
4	5	4	1+3	-	6(?)	1
5	6	3	0+3	-	6	2
6	6	3	1+4	-	0	1
7	4	5	2+2	-	1	2
9	6	6	2+4	-	0	1
15	4	3	0+5	-	0	1
18	6	6	0+5	-	6	3
PBL - A						
12	4	5	0+2	N	0	1
14	5	6	0+5	N	0	1
16	3	3	0+2	N	0	0
40	3	3	1+5	Y	0	1
24	?	?	1+4	?	0	1
30	3	2	0+5	?	?	1
28	5	5	1+4	N	0	1
PBL - B						
1	6	3	1+3	Y	6	2
8	6	6	2+5	Y	6	3
10	5	5	0+5	Y	2	2
11	6	6	2+5	Y	0	2
17	3	3	0+2	Y	0	0
23	6	6	0+5	Y	6	3
26	(3?)6	(3?)6	2+5	Y	1	3
27	3	6	0+5	Y	0	2

[a] Number of guidelines implemented during the period of time scheduled to the groups A and B (max 6)

[b] Method training sessions 0–2 + guideline-based training sessions 0–5 (max 7)

[c] Y = Yes, N = No, ? = information not provided or unclear

[d] Number of documented local operating models (max 6)

[e] 0 = no training; 1 = training was carried out with a modified method and/or schedule; 2 = training was carried out with minor deviations from protocol; 3 = training was carried out according to the protocol: in PBL by group discussions with case histories (formal seven steps were not demanded), in AD introduction and discussion. Written local operating models were required in all groups (if written only in some cases = 2)

Implementation of the training was complicated, particularly early in the programme, by a balancing act between the requirements of research and development on the one hand and the premises of further education and treatment recommendations on the other, plus that the participant organisations had differing operating practices. Lack of resources and time, a shortage of pedagogical support at the critical early stage of the programme and the illness of the key employee in the training who had no substitute were also cited as obstacles to the starting of training. Although attitudes at the health centres were largely positive and even enthusiastic, the initial complications with the training had the effect of dampening motivation at some health centres.

A shortage of personnel, constantly changing substitutes and the resulting shortage of time were cited as principal obstacles to organising training by the health centres. Reorganisations, the population responsibility collective labour agreement, different treatment practices between hospitals and private physicians, competing training and projects on offer, and the impractical nature of some of the treatment recommendations also hampered the implementation of the programme.

However, it was a strength of the MIKSTRA programme that its subject was considered relevant and important and that there was a demand for treatment recommendations and clear ground rules. Training, networking, multi-diciplinarity and patient instructions were appreciated. The nationwide reach and visibility of the programme supported its local implementation. The participation of major actors, good cooperation within the organisation and a smoothly functioning dialogue between researchers and people in the field were also cited as positive features.

The Stakes project feedback survey conducted in autumn 2005 reached 77 representatives of organisations that had participated in the MIKSTRA programme. Out of these, 29 (38%) responded to the survey; the average response rate for all projects covered in that year's feedback survey (10 projects) was 40%. The respondents considered that the programme experts were competent in their field (4.1/5 points), that the project had been professionally prepared (4.1 points) and that its publicity had been well managed (4.0 points). The average point score for all statements concerning Stakes or the actions of Stakes personnel was 3.5 or more. The respondents' experiences of the benefits of the project were as follows: the project improves practices/tools/potential in the social and/or health care sector (4.0/5 points), the results of the project can be implemented in practice (3.97 points), the project improves the quality or functionality of social and/or health care services (3.93 points), and the project has improved the respondent's professional expertise (3.93 points).

Each health centre received a final report on their results as a final feed-back. It also included a brief description of how the implementation was organised at that health centre. The following is a sample compilation of the feedback from one AD health centre and one PBL health centre.

AD: MIKSTRA implementation at the health centre of MM

The health centre of MM was randomly assigned to group A and thus to use the academic detailing (AD) training method. The training was mainly carried out in connection with normal meetings, one treatment recommendation at a time. Physicians and other personnel in the clinic all attended the training. Moreover, the key issues of the treatment recommendations were reviewed and compared with MIKSTRA results at separate sessions in 2001 and 2002. Members of the MIKSTRA working group attended these sessions as outside experts. No local house codes were drawn up. All service points of the health centre participated in collecting the information. Representatives from MM participated in 4 of the 7 instructor training sessions organised.

MIKSTRA was somewhat sidetracked by other projects and by the transfer to population responsibility. Initial complications in instructor training were a disappointment and decreased instructor motivation. Training material and patient instructions would have been needed at an earlier stage and interim results from the programme would have been useful to support the training. Also, a high turnover among physicians made it difficult to organise the training: all incoming physicians would have had to be trained from scratch, and there was no time for this. Some of the treatment recommendations were criticised as being impractical. The health centre's participation in the MIKSTRA programme was covered to some extent in the local media.

PBL: MIKSTRA implementation at the health centre of NN

NN was randomly assigned to group B and thus to use the problem-based learning (PBL) training method. A training session about two hours long was held for each infection, separately for physicians and nurses. The health centre's own patient cases were included in the training material, as well as local bacterial sensitivity data. A local specialist participated in the sessions on sinusitis and skin infection. A local house code was written up on the basis of the treatment recommendations. All service points of the health centre participated in collecting the information. The instructor of NN participated in all instructor training sessions organised.

The PBL method was found to be good and inspiring, and there was willingness to apply it to other matters besides infections. The ground rules drawn up were approved of and considered to promote coping at work. The physicians were generally enthusiastic about MIKSTRA. The health centre's participation in the MIKSTRA programme was covered to some extent in the local media.

SECTION 2: REPORT ON RESULTS

5 Results

A total of 34,300 infection appointments were logged during the MIKSTRA programme, 29,353 at the MIKSTRA health centres and 4,947 at the control health centres. During this time, 27,515 individual patients filled in a patient survey form, and 6,878 of them were interviewed two weeks after their appointment. The patient form had an ID number that was transferred to the indication survey form (CRF). These pairs of forms were correctly matched in about 70% of cases annually.

In 1998, there were on average 15 CRFs filled in per doctor. In the following years, 1999 to 2002, the average number of CRFs filled in by a single physician was 13, 13, 11 and 11; at the control health centres in 2002, the average number was 13. The decline in indication and patient survey forms filled in is probably partly explained by the dropping out of the large centralised emergency clinics in the Turku and Oulu regions from the programme (Turku from 1999 and Oulu from 2000) (Figure 8).

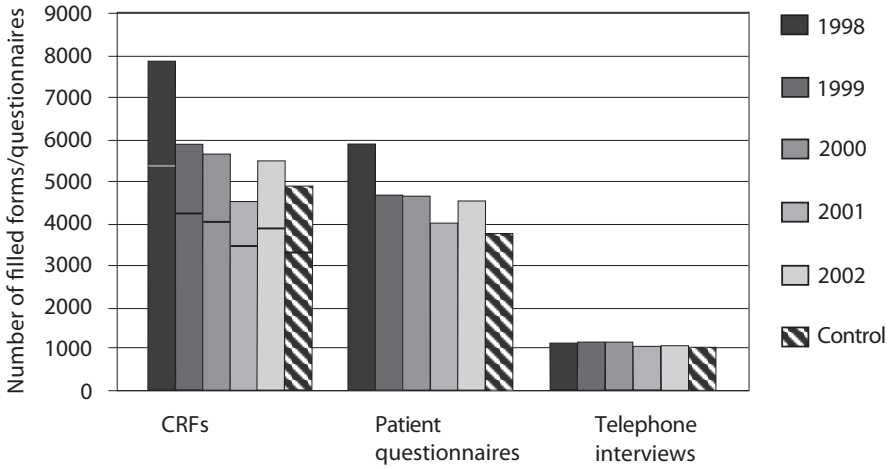


Figure 8. Number of filled forms and questionnaires per year; includes all MIKSTRA study and control health centres. (CRF = case report form; the horizontal line in the CRF bars shows how many matched pairs with patient questionnaires were identified)

The following is a discussion of the key results of the programme by subject area. At the end of each section is a listing of the MIKSTRA publications that contain further information on the points discussed in that section.

5.1 Infection patients

5.1.1 Age distribution

The age distribution of the patients who came to the health centre outpatient clinic because of an infection differed markedly from the age distribution of the general population (Figures 9a and 9b). Children under the age of 5 accounted for one fifth (20.5%) of all infection patients in outpatient care, which is nearly four times higher than their percentage in the general population (5.4%). On the other hand, people aged 65 or older accounted for only 7.7%, about one half of their percentage in the general population (16%).

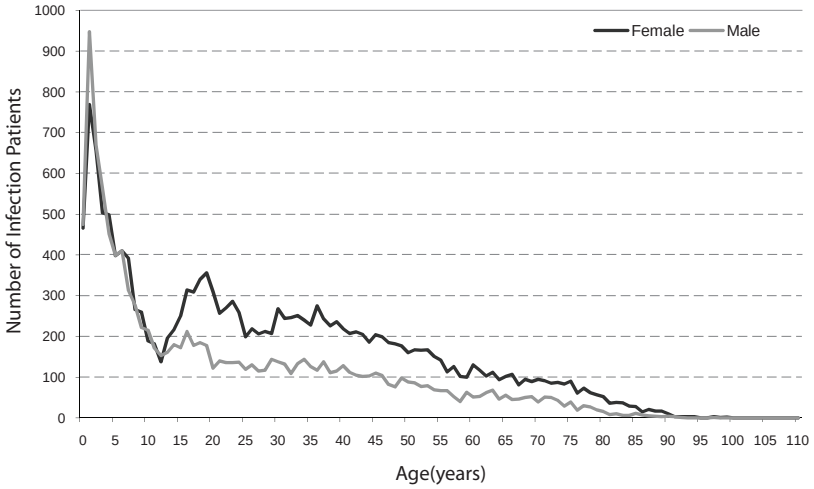


Figure 9a. Age and gender distribution of patients in MIKSTRA data 1998–2002 (N = 29 256).

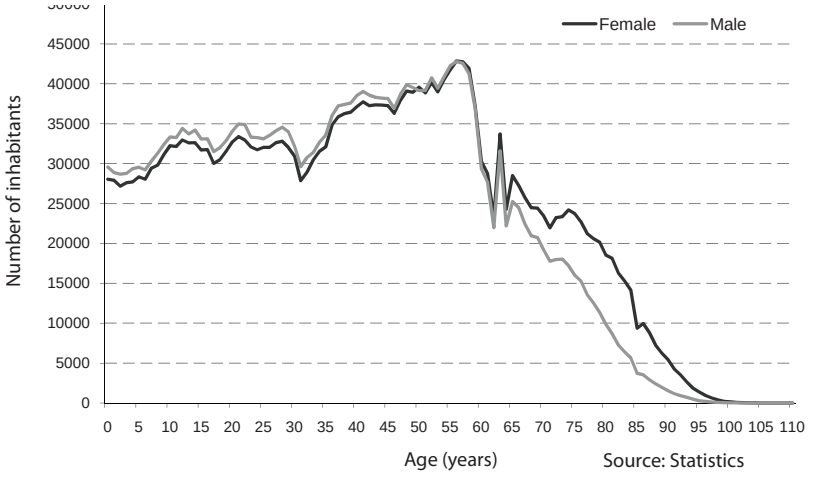


Figure 9b. Age and gender distribution of the Finnish population in 2004.

The percentage of women was slightly higher among infection patients (60%) than in the general population (51%). The only group with more boys than girls was the group of children under the age of 5, whereas in the general population men are in the majority until the age of about 55.

5.1.2 Incidence of infections in different years

On the basis of the Pirkanmaa study it was known that during one week in winter between 0.5% and 1% of the population on average have an appointment at a health centre because of an infection (2). The numbers of appointments recorded in the MIKSTRA programme were on the same order (0.54%–0.95% of the population base, depending on the year). There were no significant differences between the years in the distribution of infection diagnoses (Table 8). Respiratory tract infections accounted for three fourths of all infections. The most common diagnosis was an unspecified upper respiratory tract infection (i.e. common cold), which accounted for about one in four infections, followed by otitis media and sinusitis. Lower respiratory tract infections accounted for about 10%, most of them cases of acute bronchitis. Out of the group of 'other infections', about one half were cases of conjunctivitis.

Table 8. Distribution of infection diagnoses in MIKSTRA study and control health centres (includes all consultations with physicians and nurses).

Diagnosis	MIKSTRA health centres					Control HCs*
	1998	1999	2000	2001	2002	2002
	%	%	%	%	%	%
Unspecified URTI**	25 %	29 %	28 %	27 %	30 %	29 %
Otitis media	16 %	15 %	15 %	16 %	14 %	12 %
Tonsillitis	8 %	7 %	8 %	5 %	6 %	6 %
Pharyngitis	4 %	3 %	3 %	3 %	3 %	3 %
Sinusitis	12 %	12 %	11 %	14 %	12 %	12 %
Acute bronchitis	8 %	8 %	8 %	9 %	8 %	7 %
Pneumonia	1 %	1 %	2 %	2 %	1 %	1 %
Respiratory tract infections total	74 %	74 %	74 %	77 %	74 %	70 %
Skin infections	6 %	5 %	7 %	6 %	6 %	7 %
Urinary tract infections	6 %	6 %	6 %	5 %	5 %	5 %
Intestinal infections	4 %	3 %	2 %	3 %	6 %	7 %
Gynaecological infections and STDs***	2 %	1 %	1 %	1 %	1 %	3 %
Other infection	8 %	11 %	9 %	7 %	7 %	8 %
N Total	7 774	5 796	5 572	4 460	5 441	4 881

*HC = Health Centre

**URTI = Upper Respiratory Tract Infection

***STD = Sexually Transmitted Disease

5.1.3 Infections by age group

The infection distribution differed substantially between age groups (Figure 10). Respiratory tract infections accounted for more than 80% of all infections in patients under the age of 15, but for less than half beyond the age of 70. In the oldest age groups, the most common type of infection was urinary tract infection. With age, especially beyond the age of 40, the percentage of lower respiratory tract infections out of all respiratory tract infections also increased.

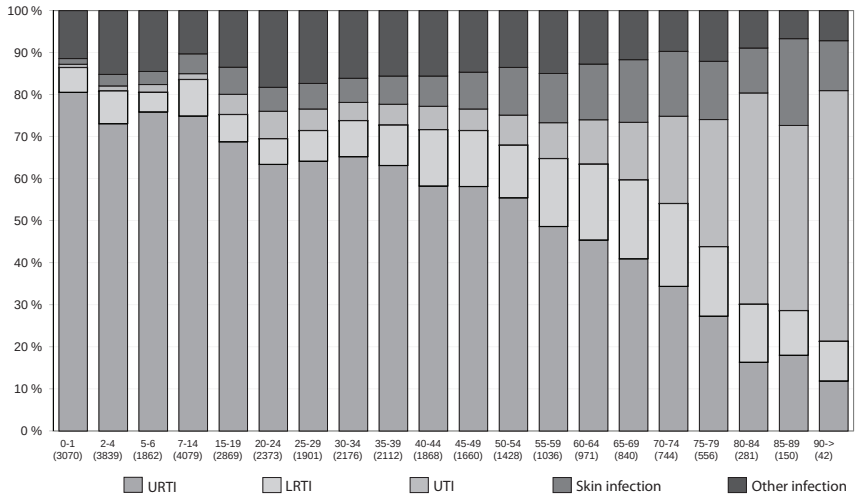


Figure 10. Distribution of diagnoses by age group, all MIKSTRA health centres included (URTI = Upper Respiratory Tract Infection; LRTI = Lower Respiratory Tract Infection; UTI = Urinary Tract Infection).

5.1.4 Patients referred to further treatment

During the MIKSTRA programme monitoring period, a total of 682 infection patients (2.1%) were referred from a health centre to specialist medical care or to a health centre hospital (Table 9). Annual variation in the percentage of patients referred to further treatment was slight (1.9%–2.3%). The highest percentage of referrals was among patients who had pneumonia (15.5% of patients referred to further treatment), deep cellulitis (13.4%) or a chronic pulmonary disease exacerbated by an infection (4.8%). One referral in ten on average was to a health centre inpatient ward and the rest – the overwhelming majority – to specialist medical care. However, about one in three referrals for patients with deep cellulitis, urinary tract infection or chronic pulmonary disease were to a health centre inpatient ward (40%, 35% and 27% of referrals, respectively).

Most of the otitis media, bronchitis and flu patients who were given a referral were children, whereas most of the chronic pulmonary disease and deep cellulitis patients who were given a referral were elderly persons. In urinary tract infections, the distribution of patients receiving a referral was U-shaped: the most referrals went to patients under the age of 10 and over the age of 70.

Table 9. Patients who received a referral by diagnosis (all years and all health centres pooled).

	Total	Received a referral		Of those who received a referral			
				Referred to secondary care	First appointment	Age (median)	Male
	N	n	%	%	%	years	%
Otitis media	4 938	67	1	100	31	2	64
Tonsillitis	2 138	50	2	98	51	20	50
Sinusitis	3 973	40	1	100	25	35	40
Pharyngitis	1 118	7	1	100	50	17	71
Unspecified URTI	9 057	50	1	96	60	7	44
Acute bronchitis	2 252	33	1	100	84	3	52
Infection exacerbating chronic lung disease	459	22	5	73	59	63	64
Pneumonia	456	70	15	81	60	38	50
Skin infection	1 905	61	3	92	52	45	49
Deep cellulitis	224	30	13	60	76	62	50
Urinary tract infection	1 811	54	3	67	72	49	28
Intestinal infection	1 291	53	4	92	67	26	30
Other infection	3 243	155	5	97	64	34	49
All infections	32 865	692	2	90	58	28	46

The majority of respiratory tract infection patients receiving a referral were men, even though women were in a majority (60%) in the patient material overall.

In the case of otitis media and sinusitis, a referral was most commonly (64% to 79%) given at the second appointment, but in the case of unspecified upper respiratory tract infection, acute bronchitis or chronic pulmonary disease exacerbated by an infection, a referral was most commonly (54% to 85%) given at the first appointment.

5.2 Indications for antimicrobial treatment

5.2.1 Percentage of patients given antimicrobials

Although Kela statistics indicate that more than 60% of children aged 1 and 2 are given a prescription for antimicrobials in any one year (Figure 11), the MIKSTRA programme material indicates that the threshold for prescribing antimicrobials is no lower for children than for any other age group (Figure 12). In the MIKSTRA

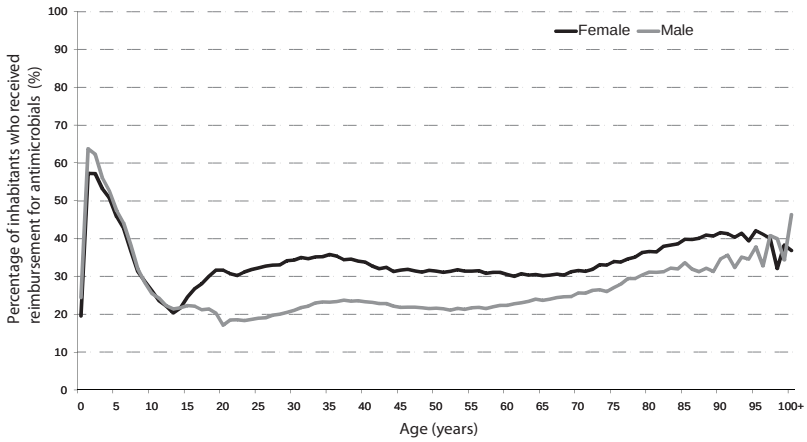


Figure 11. Percentage of inhabitants in each age group who received reimbursement for antimicrobials in 2002. (Source: National Prescription Register of the Social Insurance Institution)

Figure 12. Percentage of patients in each age group who were prescribed antimicrobials at MIKSTRA health centres; all MIKSTRA health centres and all years (includes only patients who consulted a physician).

material, the age group of over 65 was the only age group among infection patients where antimicrobial prescriptions were more common (62%–68% of all infection patients in this age group received an antimicrobial prescription) than in any other age group (patients aged 0 to 4, 40%–49%; 5 to 14, 40%–50%; 15 to 64, 42%–49%). The large number of antimicrobial prescriptions for small children is mainly explained by the fact that very young patients have several cases of upper respiratory tract infection per year and have several appointments.

On average, about half (45%–51%) of all infection patients were prescribed antimicrobials, and no significant changes occurred over the years (Figure 13). There was also no difference between the MIKSTRA health centres and the control health centres in this respect in 2002. Annual variation between health centres, on the other hand, was quite substantial.

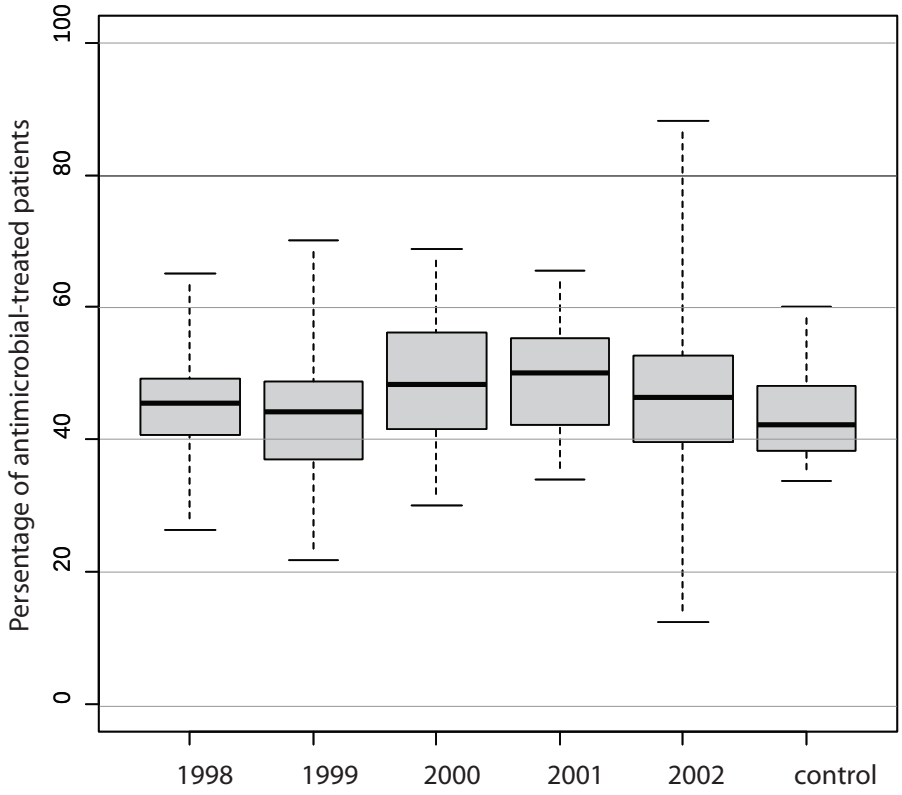


Figure 13. Percentage of patients who were prescribed antimicrobials in MIKSTRA health centres (HCs) annually and in control health centres 2002. (The line inside the box represents median, the lower edge of the box indicates the first quartile and the upper edge the third quartile. The ends of the vertical lines are minimum and maximum values each year.)

Antimicrobials were relatively rarely prescribed for throat infection and unspecified URTI, during the entire monitoring period (Table 10). By contrast, antimicrobials were used to treat nearly all cases of otitis media (82%–91%), sinusitis (83%–89%) and urinary tract infection (88%–92%). Antimicrobials were also relatively frequently prescribed for bronchitis and skin infection (59%–74% and 68%–77%, respectively).

Table 10. Proportion of infection patients by diagnoses who were prescribed antibiotics in MIKSTRA and control health centres in 1998–2002 (only visits to doctors included except for the last row).

Diagnosis	MIKSTRA health centres					Control HCs*
	1998	1999	2000	2001	2002	2002
	%	%	%	%	%	%
Unspecified URTI** (common cold)	12	9	15	9	9	10
Otitis media	88	82	87	88	91	87
Tonsillitis	57	61	58	59	60	61
Pharyngitis	17	17	22	20	20	20
Sinusitis	83	84	87	89	88	88
Acute bronchitis	70	59	73	69	74	71
Pneumonia	63	71	79	89	79	66
Respiratory tract infections total	57	51	56	56	57	55
Skin infections	71	68	72	75	77	72
Urinary tract infections	90	90	92	91	88	88
Other infections	16	16	13	14	14	16
All infections	55	50	54	56	54	54
Variation between health centres	30–72	27–75	34–73	40–73	38–88	42–76
All infections (including those patients who visited a nurse)	48	45	49	51	46	43

*HC = Health Centre

**URTI = Upper Respiratory Tract Infection

Physician-specific practices

Correlation between the practices of individual physicians in prescribing antimicrobials and the patient diagnosis was studied with regard to respiratory tract infections. The sample for this examination included 198 physicians in the material from the first year of the programme who had each treated at least ten patients with a respiratory tract infection. The patient sample numbered 3,478, including only patients at the first appointment.

The physicians were divided into three categories according to the percentage of antimicrobial prescriptions they had given (high, medium and low) so that each category contained a similar number of physicians. In the 'low' category physicians had given antimicrobial prescriptions to less than half of their patients (average 35%), whereas in the 'high' category the figure was more than two thirds (average 77%). The average in the 'medium' category was 56% (Figure 14).

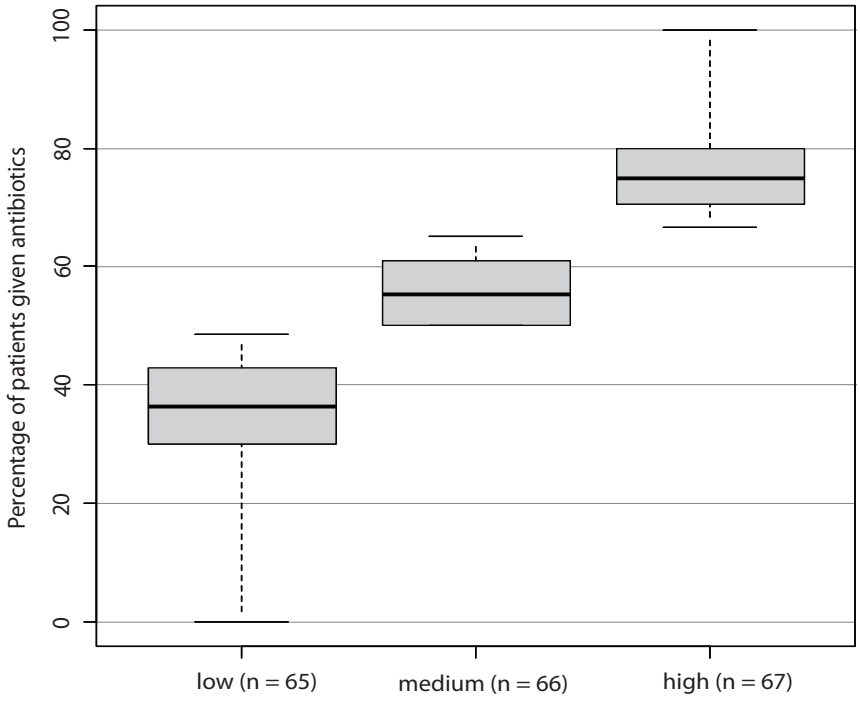


Figure 14. Percentage of respiratory tract infection patients who were prescribed antimicrobials for physicians who were low, medium and high prescribers. (The line inside the box represents median, the lower edge of the box indicates the first quartile and the upper edge the third quartile. The ends of the vertical lines are minimum and maximum values within each group of physicians.)

Physicians in the 'high' and 'medium' categories had made more diagnoses of otitis media, sinusitis and bronchitis and fewer diagnoses of common cold than physicians in the 'low' category (Figure 15).

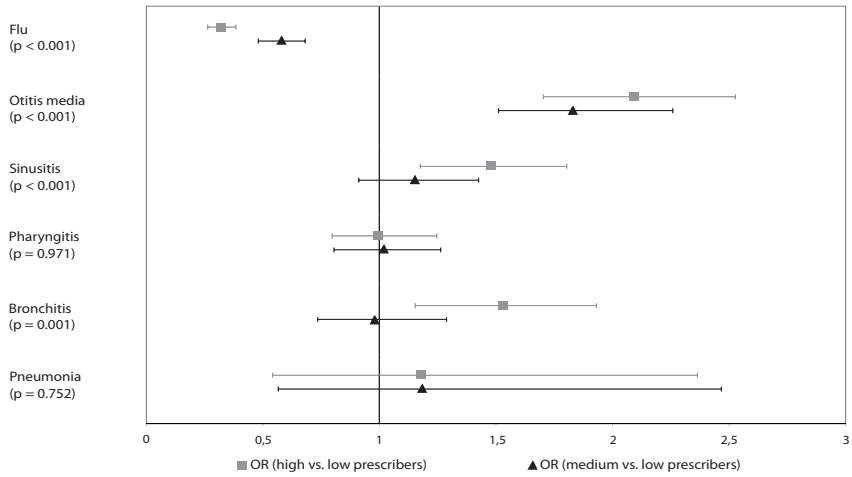


Figure 15. Odds ratio (OR) for selected diagnoses for medium and high prescribing physicians compared to low prescribers. (Dot is the OR-value and the ends of lines represent 95% confidence interval. P-value of the trend-test is given below the name of the diagnosis.)

In examining the percentages of patients who were prescribed antimicrobials by diagnosis, the ranking of the categories remained the same except in the case of pneumonia (Table 11). Not only did the physicians in the 'high' category diagnose bacterial infection more frequently, they were also more likely to prescribe antimicrobials for any respiratory tract infection (including those that were probably viral) than physicians in the 'medium' and 'low' categories. For instance, antimicrobials were prescribed to 68%, 82% and 95% in the 'low', 'medium' and 'high' categories, respectively, of patients with sinusitis, and to 5%, 13% and 21% similarly of patients with a common cold. There was no difference in choice of drugs between the categories, except that physicians in the 'high' and 'medium' categories were less likely to prescribe penicillin-V than those in the 'low' category.

The information collected in the MIKSTRA programme was also compared to data on the same physicians in the Kela register concerning the number of antimicrobial prescriptions given by them in the periods of six months before and after the information collection week. It was found that the physicians ranked similarly into 'high', 'medium' and 'low' categories by the number of antimicrobial prescriptions given even over a longer period of time. This would indicate that each physician has an individual and relatively stable practice in prescribing antimicrobials, depending on their style of diagnosing and their threshold for

Table 11. Percentage of patients with respiratory tract infections prescribed antimicrobials by low (n = 65), medium (n = 66) and high (n = 67) prescribers.

		Unsp. URTI*		Otitis media		Sinusitis		Throat infection***		Acute bronchitis		Pneumonia	
Prescriber group		**Patients**	**Ab + †**	**Patients**	**Ab + †**	**Patients**	**Ab + †**	**Patients**	**Ab + †**	**Patients**	**Ab + †**	**Patients**	**Ab + †**
Low		41 %	5 %	18 %	79 %	15 %	68 %	16 %	27 %	10 %	44 %	1 %	62 %
	n	451	21	194	154	170	116	175	48	107	47	13	8
Mediumt		28 %	13 %	28 %	87 %	17 %	82 %	16 %	46 %	9 %	70 %	1 %	75 %
	n	326	42	326	283	198	163	184	85	109	76	16	12
HIgh		18 %	21 %	31 %	95 %	21 %	95 %	16 %	72 %	14 %	85 %	1 %	63 %
	n	216	45	369	349	252	239	190	137	166	141	16	10
Total	N	993		889		620		549		382		45	

† = Patients who received an antimicrobial precription

*Unspecified Upper Respiratory Tract Infection

**Includes tonsillitis and pharyngitis

prescribing antimicrobials. Those who are the most critical with antimicrobials are perhaps also more conservative than on average in their choice of drugs.

5.2.2 Antimicrobials by indication

During the data collection weeks, more than 16,000 antimicrobial prescriptions were given at MIKSTRA health centres. Nearly half of these (49%) were for otitis media and sinusitis; upper respiratory tract infections altogether accounted for almost two thirds (64%) of all antimicrobial prescriptions (Table 12). One in seven prescriptions was for a lower respiratory tract infection, most of these being cases of acute bronchitis. One in ten prescriptions was for urinary tract infection or for skin infection.

Table 12. Distribution by diagnosis of all patients who were treated with an antimicrobial, MIKSTRA 1998–2002 (N = 16 125).

Diagnosis	n	%
All infections of upper respiratory tract	**10 230**	**64**
Otitis media	4 369	27
Throat infection	1 560	10
Sinusitis	3 535	22
Unspecified URTI	766	5
All infections of lower respiratory tract	**2 289**	**14**
Acute bronchitis	1 624	10
Infection exacerbating chronic lung disease	292	2
Pneumonia	373	2
Urinary tract infections	1 559	10
Skin infections	1 504	9
Other infections	543	3
Total	**16 125**	**100**

One fourth of all antimicrobial prescriptions were given to children under school age, the most common diagnosis here being otitis media (75% of all antimicrobials) (Table 13). In this age group, only 5% of antimicrobial prescriptions were for something other than respiratory tract infections.

In patients of working age (19 to 64), just over half (55%) of all antimicrobial prescriptions were for upper respiratory tract infections, most commonly for sinusitis (33%). Bronchitis, skin infection and urinary tract infection were more or less tied for second place at just over 10% each (Table 13).

In the elderly age group (65 and above), one third (33%) of all antimicrobial prescriptions were for urinary tract infection, slightly over one fourth (28%) for upper respiratory tract infection and one fifth (21%) for lower respiratory tract infection.

Table 13. Distribution (%) by diagnosis of all patients who were treated with an antimicrobial in four age-group, MIKSTRA 1998–2002 (N = 16 151).

Diagnosis	0–6 yrs (n = 3 912)	7–18 yrs (n = 2 901)	19–64 yrs (n = 7 583)	> 65 yrs (n = 1 755)
All infections of upper respiratory tract	87	75	55	28
Otitis media	75	31	6	3
Throat infection	5	19	10	2
Sinusitis	3	21	33	18
Unspecified URTI	4	4	6	4
All infections of lower respiratory tract	8	12	17	21
Acute bronchitis	7	8	12	12
Infection exacerbating chronic lung disease	0,2	1	2	7
Pneumonia	1	3	2	3
Urinary tract infections	1	4	11	33
Skin infections	3	7	12	16
Other infections	1	2	6	3
Proportion of all treated	24	18	47	11

During the first two years of the programme, the percentage of amoxicillin out of all antimicrobials prescribed increased from 25% to 30% and then held stable (Figure 16). At the control health centres in 2002, its percentage was about the same as at MIKSTRA health centres in 1998.

Compound of amoxicillin and clavulanic acid accounted for about 2% of all antimicrobials prescribed in the early years of the MIKSTRA programme (Figure 16). After 2000, this percentage doubled (about 4%), and at the control health centres it was even higher (5%).

The percentage of macrolides initially dropped by a few percentage units but then recovered and exceeded its initial level (Figure 16). The percentages of other antimicrobials declined by a couple of percentage units (sulpha-trimethoprim, penicillin-V, cephalosporins) or remained stable (fluoroquinolones).

Penicillin

Nearly two thirds (63%) of the penicillin-V prescriptions recorded in the MIKSTRA programme were for throat infection, accounting for 71% of the antimicrobials prescribed for this diagnosis (Figure 17). The second most common indication was otitis media (11%), where penicillin-V, however, accounted for less than five per cent of all antimicrobials prescribed (4.5%). The remaining small prescription percentages were mainly for respiratory tract infections.

Parenteral penicillin preparations (procaine penicillin and penicillin G) were used in only 30 cases in the entire material, most of them (20) for skin infection (19 of these were for deep cellulitis, usually erysipelas) and the rest for pneumonia (6) and throat infection (4).

Amoxicillin

About half (54%) of amoxicillin prescriptions were for otitis media and one third (32%) for sinusitis (Figure 18). The percentage of amoxicillin out of all antimicrobial prescriptions for these infections was on the same order (55% of prescriptions for otitis media, 41% of prescriptions for sinusitis). Amoxicillin accounted for a fair amount of antimicrobial prescriptions for common cold and acute bronchitis (25% and 19%, respectively), but these indications only accounted for a small percentage of the overall use of amoxicillin (4% and 7%, respectively).

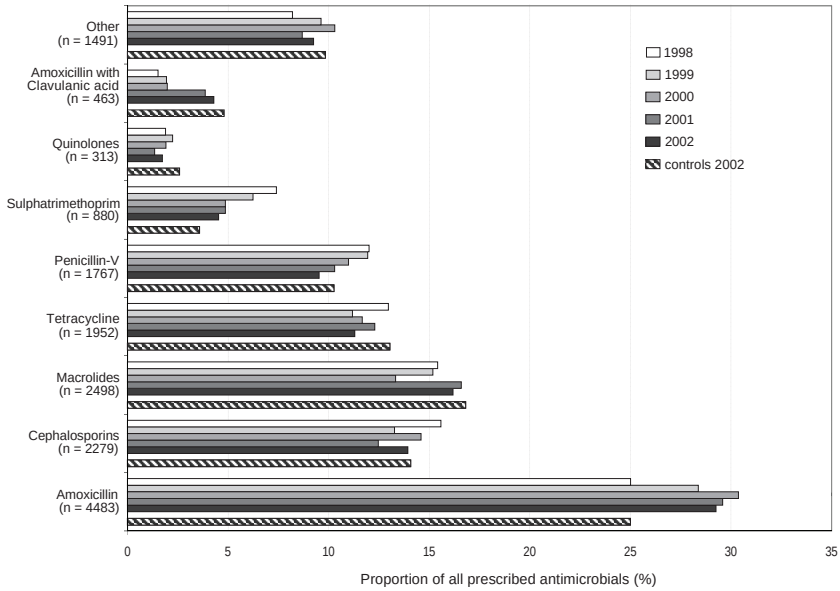


Figure 16. Percentage of the most common antimicrobials (%) out of all antimicrobial prescriptions in MIKSTRA study and control health centres in individual study weeks (N = 16 125).

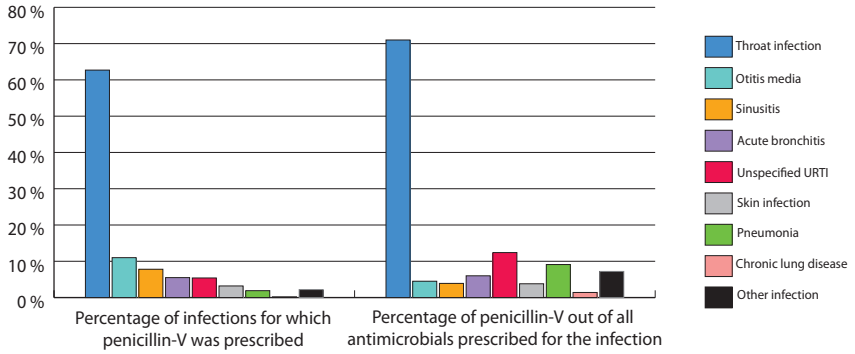


Figure 17. Indications for use of penicillin-V in MIKSTRA 1998–2002 (n = 1767 prescriptions).

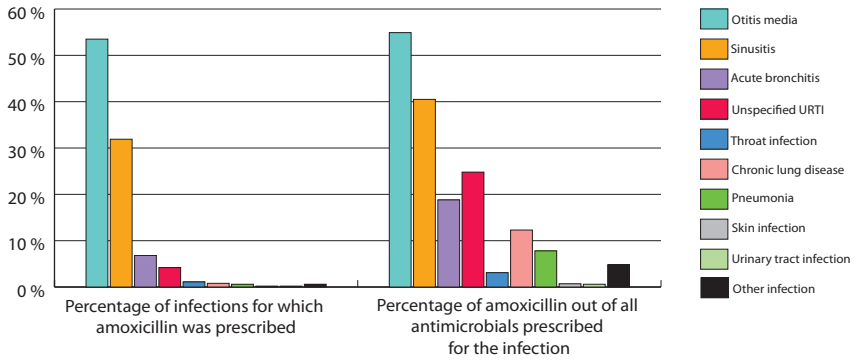


Figure 18. Indications for use of amoxicillin in MIKSTRA 1998–2002 (n = 4483 prescriptions).

Amoxicillin – clavulanic acid

Otitis media and sinusitis accounted for the majority (86% altogether) of prescriptions for the compound of amoxicillin and clavulanic acid (Figure 19). However, this compound was only prescribed in 5% of all antimicrobial prescriptions for these indications.

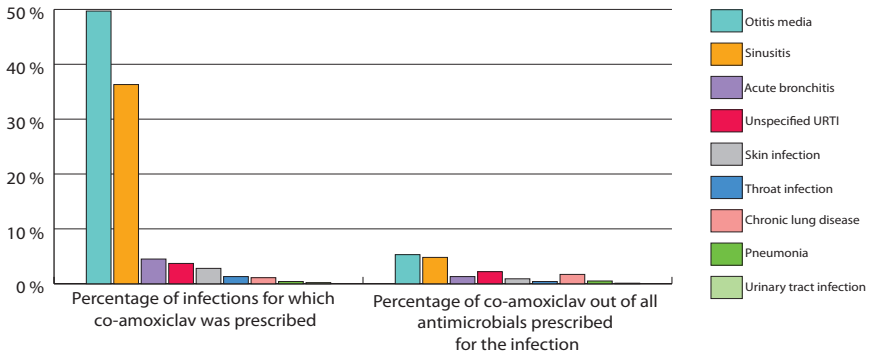


Figure 19. Indications for use of amoxicillin with clavulanic acid in MIKSTRA 1998–2002 (n = 463 prescriptions).

Macrolides

According to recommendations, macrolides are second-line drugs in the treatment of the commonest kinds of infection, such as otitis media and sinusitis, and also acute bronchitis. Despite this, the MIKSTRA programme results show that macrolides were used relatively commonly to treat these infections at health centres, and they accounted for three fourths of all of the use of macrolides (Figure 20).

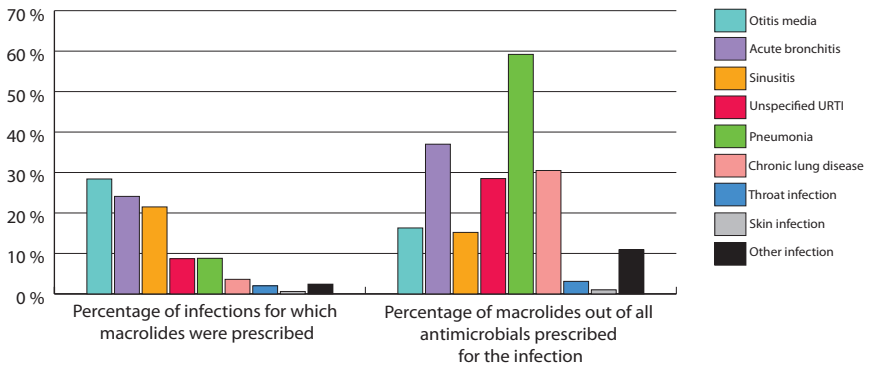


Figure 20. Indications for use of macrolides in MIKSTRA 1998–2002 (n = 2498 prescriptions).

Slightly over half of the macrolide prescriptions involved azithromycin, although its percentage decreased from 65% in 1998 to 55% in 2002, while the percentage of clarithromycin increased by a factor of 2.5 (7% in 1998 and 18% in 2002). The percentage of roxithromycin remained stable at about one fourth of all macrolide prescriptions, while the percentage of erythromycin decreased from a couple of per cent in the early years to less than 1%. Azithromycin was the most commonly prescribed macrolide for upper respiratory tract infections, and roxithromycin for lower respiratory tract infections.

Pneumococcus is a significant pathogen for both otitis media and sinusitis. The sensitivity of pneumococci to macrolides has rapidly declined since the 1990s. Resistance is more common in areas where macrolides are used a lot. The macrolide group has a cross-resistance tendency, i.e. if bacteria are resistant to one drug in this group, they will also be resistant to others.

Because prescribing macrolides is justifiable in some cases, the justification for prescribing a macrolide entered by the physician on the CRF was taken into account when analysing the MIKSTRA material between 1999 and 2002. In cases of otitis media and sinusitis, a macrolide prescription was considered justifiable at a first appointment if to the physician's knowledge the patient was allergic to the first-line drugs, or if the drug sensitivity situation in the patient's history or with bacteria in the area motivated the use of a second-line drug. A recurring or chronic infection following a prescription of a first-line drug was also considered an acceptable justification for a macrolide prescription. In cases of common cold and acute bronchitis, there were additional requirements such as a prolonged or severe infection or a high CRP.

By these criteria, macrolide prescriptions were considered justifiable in about half of the cases of otitis media and sinusitis recorded (Figure 21). In cases of acute bronchitis and flu, however, only about 10% of macrolide prescriptions were considered justifiable.

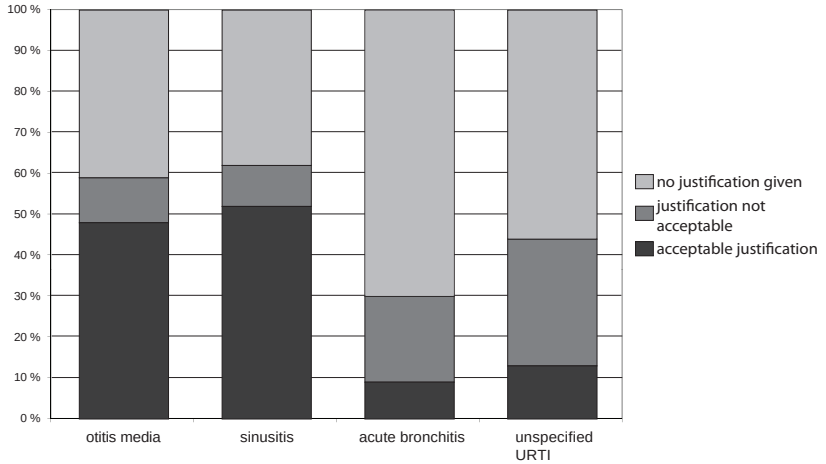


Figure 21. Justifications for use of macrolides as primary option for treatment in four common infections in MIKSTRA health centres in 1999–2002.

According to calculations made in the MIKSTRA programme, the overall use of macrolides could be cut by up to a half from the 2002 level by abandoning macrolides as a first-line drug for treatment of otitis media and sinusitis and by avoiding loosely justified prescriptions of them for treatment of infections such as acute bronchitis and flu.

Tetracyclins

The overwhelming majority (98%) of prescriptions for drugs in the tetracyclin group was for doxicyclin. There were only 49 prescriptions for other tetracyclins in the five-year material, the majority of them (43, or 88%) for treatment of skin infection. Nearly half (48%) of the tetracyclin prescriptions were for sinusitis, and about one fourth (26%) for acute bronchitis (Figure 22). Tetracyclins accounted for about one fourth (24%) of antimicrobial prescriptions for common cold, but flu only accounted for less than 10% of tetracyclin prescriptions.

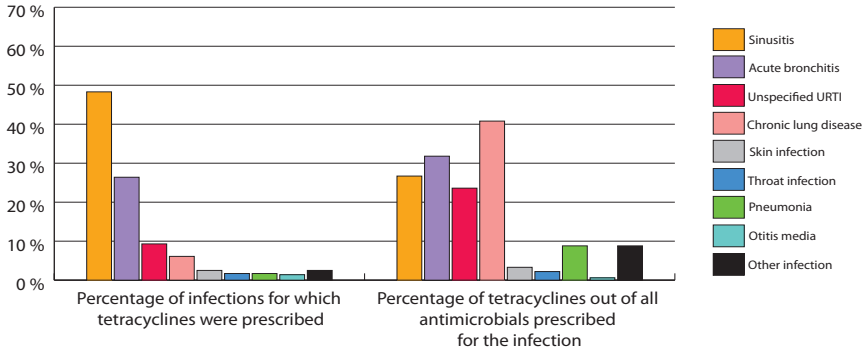


Figure 22. Indications for use of tetracyclines in MIKSTRA 1998–2002 (n = 1952 prescriptions).

Cephalosporins

Out of the cephalosporin prescriptions given at MIKSTRA health centres in 1998, 91% were of first-generation drugs; in 2002, the corresponding figure was 97% at MIKSTRA, and 92% at the control health centres. Half of the cephalosporin prescriptions were for skin infection and just over one third for upper respiratory tract infections (Figure 23).

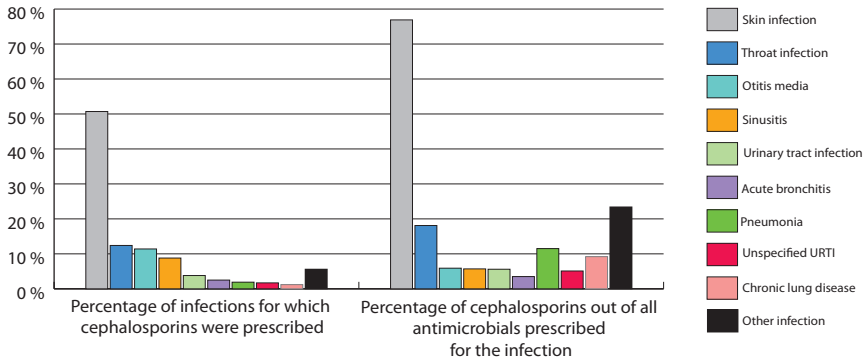


Figure 23. Indications for use of cephalosporins in MIKSTRA 1998–2002 (n = 2279 prescriptions).

Out of the prescriptions of second- and third-generation cephalosporins (n = 143), the largest part (42%) was for otitis media; 12% was for sinusitis, a similar portion for skin infection, and 7% for pneumonia. Patients admitted into an inpatient ward received half of the second- and third-generation cephalosporins prescribed for lower respiratory tract infection, more than one third of those prescribed for urinary tract infection and just under one third of those prescribed for skin infection.

Sulpha-trimethoprim

Finland has traditionally had a higher rate of sulpha-trimethoprim use than other European countries (Figure 4, p. 23). However, it is not used primarily for urinary tract infections in outpatient care as is the case elsewhere in Europe; the MIKSTRA material shows that in 78% of the prescriptions it was prescribed for upper respiratory tract infections, usually otitis media in children (62%) (Figure 24). Sulpha-trimethoprim accounted for about 12% of all antimicrobials prescribed for otitis media, which is clearly more than its 8% share of all antimicrobials prescribed for urinary tract infections.

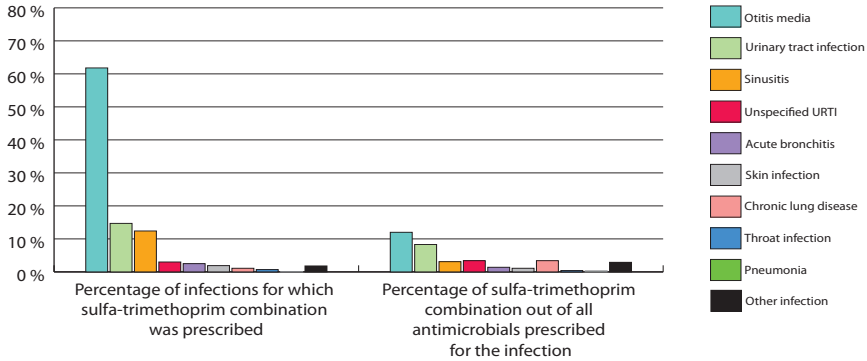


Figure 24. Indications for use of sulfa-trimethoprim combination in MIKSTRA 1998–2002 (n = 880 prescriptions).

Quinolones

All of the quinolone prescriptions recorded at MIKSTRA health centres were for fluoroquinolones. The majority of these (71%) were for urinary tract infections, for which indication they accounted for 14% of all antimicrobial prescriptions (Figure 25). Other indications that accounted for more than 10% of all fluoroquinolone prescriptions were skin infection (10%) and 'other infections' (13%, half of these for intestinal infections).

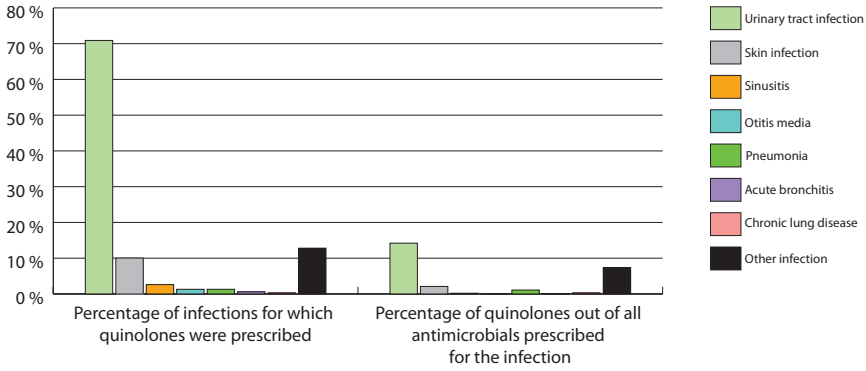


Figure 25. Indications for use of quinolones in MIKSTRA 1998–2002 (n = 313 prescriptions).

Choice of antimicrobials for various infections

In the entire MIKSTRA material for five annual data collection weeks, amoxicillin was the most commonly prescribed treatment for otitis media and sinusitis (55% and 40% of cases, respectively) (Table 14). The next most commonly prescribed treatments were macrolides for children's otitis media (16% of cases) and tetracyclins for adult sinusitis (mostly doxycycline; 27%). In the treatment of throat infection, V-penicillin reigned supreme (71%), although cephalosporins were somewhat more common than assumed (18%). The treatment of choice for lower respiratory tract infections was a macrolide or doxycycline in two thirds of all cases (67%–71%). Cephalosporins were the predominant treatment for skin infection (77%) and 'urinary tract antibiotics' such as mecillinam, nitrofurantoin and trimethoprim for urinary tract infections (71% altogether). For common cold and the 'other infections' category, choices of treatment were more diverse than for other indications.

Changes in indication-specific drug choices as a result of the training intervention are discussed in more detail in section 5.7.

Table 14. Antimicrobials by infection (all years and all MIKSTRA study and control health centres pooled; N = 16, 126 prescriptions).

	Otitis media	Throat infection	Sinusitis	Unsp. URTI*	Acute bronchitis	Infection exacerbating chr. lung disease	Pneumonia	Skin infection	UTI**	Other infection
	(n = 4 369)	(n = 1 560)	(n = 3 535)	(n = 766)	(n = 1 624)	(n = 292)	(n = 373)	(n = 1 505)	(n = 1 559)	(n = 543)
	%	%	%	%	%	%	%	%	%	%
Penicillin-V	4	71	4	12	6	1	9	4	0	7
Amoxisillin	55	3	40	25	19	12	8	1	1	5
Amoxisillin with clavulanic acid	5	0,4	5	2	1	2	1	1	0,1	0
Cephalosporins	6	18	6	5	4	9	12	77	6	23
Tetracyclines	1	2	27	24	32	41	9	3	0,1	9
Macrolides	16	3	15	28	37	30	59	1	0	11
Quinolones	0,1	0	0,2	0	0,1	0,3	1	2	14	7
Sulfa-trimethoprim	12	0,4	3	3	1	3	0,3	1	8	3
UTI-antibiotics †	0	0	0	0	0	0,3	0	0	71	0,2
Parenteral penicillins	0	0,3	0	0	0	0	2	1	0	0
Others	0	1	0,1	0	0,1	0	0	9	0,1	35
Total	100	100	100	100	100	100	100	100	100	100

*Unspecified Upper Respiratory Tract Infection

**Urinary Tract Infection

† includes pivmecillinam, nitrofurantoin and trimethoprim

Related MIKSTRA articles:

Rautakorpi U-M, Klaukka T, Honkanen P, Mäkelä M, Nikkarinen T, Palva E, Roine R, Sarkkinen H, and Huovinen P on behalf of the MIKSTRA Collaborative Study Group. Antibiotic use by indication; a basis for active antibiotic policy in the community. Scand J Infect Dis 2001;33:920-926

Leistevuo J, Huikko S, Rautakorpi U-M, Leistevuo T, Honkanen PO, Klaukka T, Mäkelä M, Palva E, Roine RP, Sarkkinen H, Varonen H, Huovinen P & The MIKSTRA Collaborative Study Group. Prescription rates and diagnostic patterns are stable: A comparison of high- medium- and low-prescribing primary care physicians treating community-acquired respiratory tract infections. Scand J Infect Dis 2005;37:465-470

Rautakorpi U-M, Klaukka T, Huovinen P, Helin-Salmivaara A ja MIKSTRA-työryhmä. Makrolidien kulutus väheni vuonna 2004. Suom Lääkäril 2005;60(25-26):2798-800.

5.3 Symptomatic and topical treatment

About one third of all patients were prescribed or recommended a symptomatic drug or topical treatment preparation – one preparation for 28% and two or more for 4% of patients. These were most commonly prescribed for conjunctivitis (96% of patients), chronic lung disease exacerbated by infection (53%) or acute bronchitis (49%). Symptomatic and topical treatment were prescribed the least for patients who had an appointment because of a urinary tract infection (2%), enteric infection (13%) or STD (sexually transmitted disease) (14%). The four most commonly used groups of preparations (cough medicines, cold medicines, topical treatment preparations for eye diseases, and painkillers) accounted for three fourths of all symptomatic treatment (Table 15).

Table 15. Most commonly prescribed or recommended symptomatic and topical treatment in MIKSTRA 1998–2002.

Preparation group	n	%
Cough medicines	3 369	25
Medicines for rhinitis	2 815	21
Topical eye drops	2 075	16
Non-steroidal anti-inflammatory drugs and analgesics	1 916	14
Asthma medicines	966	7
Topical eardrops	730	5
Others	1 557	12
Total	13 428	

In lower respiratory tract infections, symptomatic treatment was mostly about alleviating the symptoms of the infection in cases of pneumonia and acute bronchitis (cough medicines, cold medicines and analgesics), whereas in cases of chronic pulmonary disease exacerbated by infection the treatment focused on the underlying pulmonary disease (asthma drugs and systemic corticosteroids) (Table 16).

Table 16. Most commonly prescribed or recommended symptomatic and topical treatment in MIKSTRA 1998–2002, in cases where a lower respiratory tract infection was the main diagnosis.

Preparation group	Acute bronchitis		Infection exacerbating a chronic lung-disease		Pneumonia	
	n	%	n	%	n	%
Cough medicines	827	67	80	25	86	69
Asthma medicines	239	19	143	45	14	11
Systemic corticosteroids	24	2	76	24	0	0
Non-steroidal anti-inflammatory drugs	27	2	0	0	8	6
Medicines for rhinitis	67	5	11	3	7	6
Others	60	5	8	3	10	8
Total	1 244	100	318	100	125	100

The use of symptomatic medication was analysed more closely for cases of sinusitis and otitis media.

The Current Care guideline for sinusitis published in 1999 noted:

–"*In treatment to restore normal sinus function, the aim is to normalise the permeability of the ostium by reducing swelling of the mucosa and stimulating the cilia. This may be achieved with nasal saline lavage, drugs to reduce the viscosity of the mucus, nasal decongestants or oral sympathomimetic drugs; the efficacy of the latter, however, has not yet been satisfactorily demonstrated.*

–Corticosteroid nasal sprays have been found to benefit allergy patients.

–Antihistamines, with or without sympathomimetic drugs, are used to reduce swelling of the mucosa. They benefit patients with nasal polyps or allergic rhinitis, but for other patients antihistamin treatment is not indicated in cases of acute sinusitis."

Symptomatic treatment of sinusitis was examined in the cases of the 2,448 patients in the MIKSTRA material who had arrived for their first appointment with sinusitis as the only diagnosis. Symptomatic medication had been prescribed or recommended to 41% of these patients (irrespective of whether they were also

prescribed an antimicrobial); one preparation in 35% of the cases and two or more preparations in 4% of the cases. The most commonly prescribed symptomatic medication (23% of sinusitis patients) was a systemic antihistamin with or without a sympathomimetic drug, mostly a compound of acrivastine and pseudoephedrine (17%). Cough medicine was recommended to about 8% of patients, a local or systemic decongestant to about 6%, and a corticosteroid nasal spray to about 4%. Adults of working age were prescribed symptom-based cold medicine more frequently (35%) than patients aged less than 15 (19%) or more than 65 (26%) years.

The Current Care guideline for otitis media published in 1999 noted:

–"*If a child wakes up in the night with an earache, it is not necessary to see a doctor immediately; as first aid, the child may be given a painkiller and anaesthetic ear drops...*

–*Otalgia may be treated with paracetamol (15–20 mg/kg x 4), ibuprofen (10 mg/kg x 3) or naproxen (5 mg/kg x 2).*

–*There is little evidence as to the efficacy of anaesthetic ear drops to anaesthetise the tympanic membrane, but they may be used for pain medication in the early stages of otitis if the tympanic membrane is intact.*"

The MIKSTRA material contained 3,059 first appointments where the only diagnosis was otitis media. Half of these patients were under 5 years old, and 85% were under 15. Symptomatic or topical treatment was prescribed to one third of the patients over 15 and one fourth of the patients under 15. The medications most commonly prescribed or recommended for patients under 15 were analgesics (10.4% of patients in this group), anaesthetic ear drops (4.4%), cough medicines (3.6%) and antihistamine preparations (3.5%). These four groups of medications accounted for nearly three fourths of all symptomatic treatment in this age group. The low percentage in this material of patients given painkillers may be partly explained by the fact that painkillers are considered 'self-evident', and since most painkillers are over-the-counter drugs and many people have them at home, they did not end up recorded on the study forms. Nevertheless, since the traditional treatment for otitis media in Finland has included antimicrobials, the symptomatic treatment of pain may have received too little attention.

Related MIKSTRA articles:

Pulkki J, Huikko S, Rautakorpi U-M, Honkanen P, Klaukka T, Mäkelä M, Palva E, Roine R, Sarkkinen H, Varonen H & Huovinen P for the MIKSTRA Collaborative Study Group. Management of pain in acute otitis media in Finnish primary care. Scand J Infect Dis 2006;38:265–7

Pulkki J, Rautakorpi U-M, Huikko S, Honkanen P, Klaukka T, Mäkelä M, Palva E, Roine R, Sarkkinen H, Huovinen P and Varonen H for the MIKSTRA Collaborative Study Group. Recommended and prescribed symptomatic treatment for acute maxillary sinusitis in Finnish primary care. Rhinology 2007;45:197–201

5.4 Use of diagnostic aids

Acute respiratory tract infections resemble each other in terms of both their symptoms and their pathogens. Such infections may be caused by viruses or bacteria or a combination of both. It is up to the treating physician to decide when to use antimicrobials to treat an infection.

There are many diagnostic tests that can help specify the diagnosis or estimate the severity of the infection. Differential diagnostics can be further specified by tympanometry in the case of otitis media, ultrasound or X-ray in the case of sinusitis, and throat swabs in the case of throat infection. Pneumonia often shows up on an X-ray, and an elevated CRP particularly in lower respiratory tract infections may indicate a bacterial infection or a severe infection. The Current Care guidelines note that these tests are useful aids to clinical diagnostics and their use contributes to the quality of the treatment decision; therefore, the use of these aids was monitored in the MIKSTRA programme.

In the MIKSTRA study as a whole, 44% of patients on average had at least one diagnostic test performed on them. Patients who received antimicrobials were tested slightly more frequently (48%) than those who did not (42%). Patients at a second appointment were tested more frequently than patients at a first appointment (54% and 42%, respectively).

The rate of test use varied depending on the diagnosis (Table 17). Diagnostic aids were rarely used for otitis media at a first appointment (pneumatic otoscopy was considered a basic diagnostic method and was not listed separately).

Table 17. The use of diagnostic aids at a first appointment for a respiratory or urinary tract infection; percentage of patients tested (all years and all health centres pooled).

	Any test	B-leuk	CRP	Throat-/urine culture	Throat-/urine rapid test	Chest x-ray	Sinus x-ray	Sinus ultrasound
Otitis media	8	1	1	1	1	0,3	0,1	3
Throat infection*	73	3	8	30	40	0,4	1	7
Sinusitis	80	2	3	1	1	1	7	73
Acute bronchitis	36	6	14	1	1	6	1	20
Pneumonia	66	22	41	3	3	53	5	10
Unspesified URTI**	35	5	10	5	7	2	2	17
Urinary tract infectior	87	2	5	56	57	0,3	0,1	0,3

*Includes tonsillitis and pharyngitisi

**Unspesified Upper Respiratory Tract Infection

By contrast, diagnostic testing was used a lot in cases of urinary tract infection and sinusitis; and in cases of throat infection and pneumonia too, at least one diagnostic aid had been used on two thirds of the patients. Although it was found that one in three health centres had a tympanometer, this was used as a diagnostic aid at first appointments for only 46 patients out of 20,179. In about half of these cases (21) the diagnosis was otitis media.

The severity of symptoms seems to have influenced both the use of tests and decisions on drugs, but the nature of this influence varied from one indication to another. Diagnostic tests were more likely to be performed when the initial physician carried out the treatment than when the patient was referred elsewhere. Changes in the use of diagnostic aids over years is discussed in more detail in section 5.7.

Related MIKSTRA articles:

Honkanen P, Rautakorpi U-M, Huovinen P, Klaukka T, Palva E, Roine R, Sarkkinen H, Varonen H, Mäkelä M, and the MIKSTRA Collaborative Study Group. Diagnostic tools in respiratory tract infections: use and comparison to Finnish guidelines. Scand J Infect Dis 2002;34:827–830

MIKSTRA-työryhmä (Huovinen P, Honkanen P, Klaukka T, Mäkelä M, Palva E, Rautakorpi U-M, Roine R, Sarkkinen H, Varonen H). Terveyskeskusten diagnostiset apuvälineet hengitystieinfektioissa. Suom Lääkäril 2003;58:1668–71

5.5 Treatment of infection patients by nurses

On average, 14% of infection patients at the MIKSTRA health centres were treated by nurses (Figure 26a), though the actual percentage varied between 0% and 48% depending on the health centre and the year. At the control health centres, the average percentage of infection patients treated by nurses in 2002 was clearly higher (23%; Figure 26b) than at the MIKSTRA health centres in the same year (18%) or during the programme on average

Patients were assigned to nurses and physicians according to local practices at each health centre, and the MIKSTRA programme did not try to influence this in any way. It is likely that the low percentage of patients treated by nurses at some health centres was caused by nurses not having been sufficiently activated to collect information. This was not studied systematically. The actual variation was probably smaller than the material indicates, and nurses probably actually accounted for a somewhat larger percentage of infection patients treated. Extrapolated to the national level, the observed 14% out of the approximately five million infection cases treated annually would mean about 670,000 patients per year.

Appointments with a nurse were analysed in more detail using the material from the first two years of the MIKSTRA programme. During the information collection weeks in 1998 and 1999, the MIKSTRA health centres treated a total of 13,689 infection patients, 11,772 of whom saw a physician and 1,917 (14%) a nurse. Out of the patients treated by nurses, 81 (4%) also saw a physician, and nurses consulted a physician in 192 cases (10%).

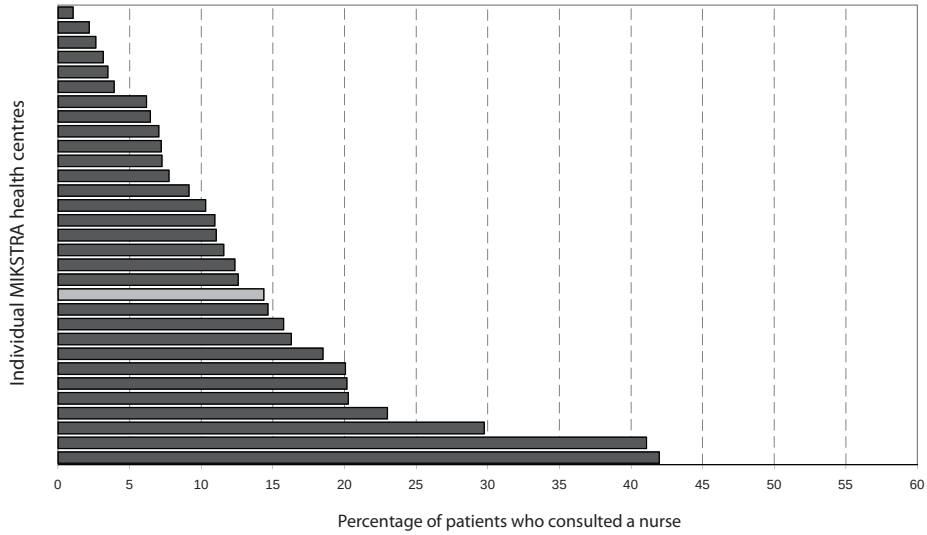


Figure 26a.

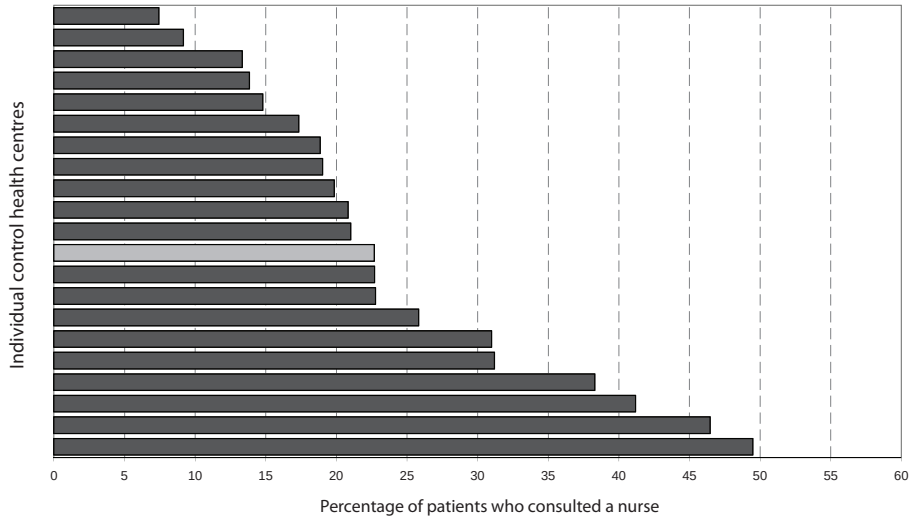


Figure 26b.

Figure 26 a and b. Percentage of patients who consulted a nurse at each health centre in the study (For MIKSTRA health centres, all five data collections are pooled; for the control health centres, figures are for the year 2002 only. Figures include those patients who consulted both a nurse and a physician at the same appointment. Black bars represent each individual health centres. The grey bar illustrates the average of MIKSTRA health centres in Figure 26a and that of the control health centres in Figure 26b).

The most common diagnoses made by nurses were flu (50%), intestinal infection (13%) and throat infection (12%), followed by urinary tract infection (7%) and skin infection (5%). Nurses treated 25% of all flu patients, 54% of the patients with intestinal infections, 15% of the patients with throat infection and 17% of the patients with urinary tract infection. When the health centres were divided into three categories according to how high a percentage of patients was treated by nurses in them, the distribution of diagnoses made by nurses remained more or less the same regardless of the percentage of patients treated by a nurse (Figure 27). Thus, epidemiological reasons would not seem to explain the differences observed between health centres in the percentages of patients treated by a nurse.

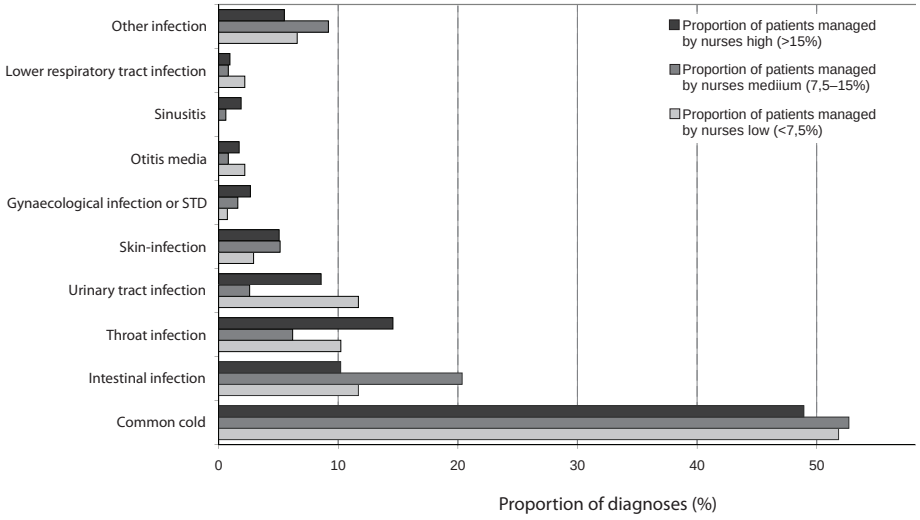


Figure 27. Distribution of diagnoses of patients who consulted a nurse; health centres classified in three groups according to the proportion of the patients managed by nurses in MIKSTRA data (high, medium low)

Having an appointment with a nurse was most frequently explained by needing a medical certificate for sick leave (OR 5.04; 95% confidence interval 4.15–6.12) or a feeling that no medication would be required (OR 4.11; 95% confidence interval 3.36–5.03). Patients also tended to book an appointment with a nurse when they had only had symptoms for a short time (0 to 3 days) (OR 2.21; 95% confidence interval 1.84–2.66). However, patients treated by a nurse considered themselves to be fairly ill or very ill almost as frequently (57%) as those who sought a physician's treatment (60%). In the phone interviews conducted two weeks after their appointment, 95% (n = 118) of the patients treated by a nurse felt themselves to be healthy or their condition to have improved, while the figure for patients treated by a physician was 93% (n = 2.213). Of the patients treated by a nurse 22% and of those treated by a physician 19% sought a second appointment for the

same infection within two weeks of the first appointment. These differences are not statistically significant.

Related MIKSTRA articles:

MIKSTRA-työryhmä (Rautakorpi U-M, Honkanen P, Huikko S, Anttila H, Klaukka T, Laippala P, Leistevuo J, Mäkelä M, Palva E, Roine R, Sarkkinen H, Varonen H, Huovinen P). Hoitajat - liian vähän käytetty voimavara infektioiden hoidossa? Suom Lääkäril 2002;44:4480–83

5.6 Patient attitudes, expectations and treatment compliance

Patient attitudes and expectations were explored using a questionnaire given out to patients when they arrived for their appointment. A total of 23,785 patients at the MIKSTRA health centres and 3,730 patients at the control health centres filled in a questionnaire. A sample of the patients (5,823 from the MIKSTRA health centres and 1,055 from the control health centres) were interviewed by phone 10 to 14 days after their appointment.

The material for 1998 (n = 5,927) shows that about half of the patients hoped to receive medication to alleviate their symptoms and/or information about what is wrong with them; one in three patients wanted information on how severe the illness is and about the need for treatment (Table 18). Just under one third of the patients considered that they needed antimicrobials, and one in five considered that they need sick leave or child care leave.

Table 18. Percentage of patients who selected each of the optional answer to the question ”What kind of help are you hoping to receive from the doctor or nurse at this appointment?” Respondents were allowed to select multiple options and therefore the figures do not add up (MIKSTRA 1998).

Options	Proportion of patients, who selected the option
I want to be given medicine to alleviate my symptoms	56 %
I want to know what is wrong with me / my child	49 %
I want to make sure that my /my child's illness is nothing serious	33 %
I want to know whether my / my child's illness requires treatment	33 %
I feel that I / my child need a course of antibiotics	31 %
I need sick leave or leave to look after my sick child	19 %
I would like to have a referral for further investigations at the health centre	6 %
I would like to have a referral to a specialist	3 %
I would like to have a referral to a hospital	1 %
Something else	6 %

A need for antimicrobials was cited by about one fifth of patients with flu (22%), about one third of patients with bronchitis (33%), two fifth of patients with sinusitis (40%) or urinary tract infection (44%), and about half of patients with otitis media (47%).

When patients were specifically asked about their willingness to have a course of antimicrobial treatment on a scale from 1 to 5 (1 = I want a course of antimicrobial treatment – 5 = I do not want a course of antimicrobial treatment), a slightly larger percentage (40%) than the above wanted or would like to have a course of antimicrobial treatment. Just over one fourth of the patients (28%) were opposed to antimicrobial treatment, and one third (32%) could not state an opinion. The sicker a patient felt when coming to an appointment, the more likely he/she was to want antimicrobial treatment. On the other hand, a patient's desire to receive an antimicrobial prescription correlated with a higher probability of getting one (patients who wanted and got an antimicrobial prescription, 68%; patients who did not want one or did not say so and got one anyway, 37%).

There seemed to be no clear correlation between the fulfilment of patients' expectations regarding antimicrobial treatment and their coming back for a second appointment. Out of the patients who were prescribed an antimicrobial at their first appointment, 21% returned for a second appointment; the figure for those who were not prescribed an antimicrobial was 25% ($p = 0.213$). Out of the patients who at their first appointment wanted antimicrobial treatment, 19% returned for a second appointment regardless of whether they had received antimicrobial treatment or not.

Patients' expectations as described by the patients themselves and as perceived by the physicians were rarely similar (Figure 28). Physicians seemed to be particularly poor at recognising when patients did not want antimicrobial treatment.

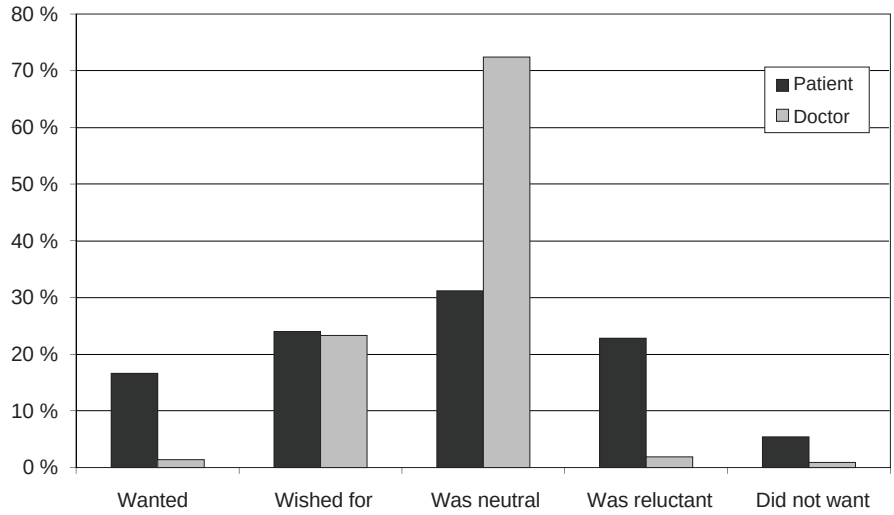


Figure 28. Patient's expectation on receiving antimicrobial for his/her infection (patient survey) and doctor's anticipation of patient's expectation (indication survey) at MIKSTRA health centres in 1998.

Treatment compliance among infection patients was studied using the phone interview material from the first year. The interviewees were a random sample of the patients diagnosed with otitis media, tonsillitis, sinusitis, acute bronchitis, urinary tract infection, skin infection or unspecified upper respiratory tract infection.

Of these, 70% had received an antimicrobial prescription and 27% had received symptomatic medication, with or without antimicrobial treatment, while 19% had received no medication at all. Some of the patients given antimicrobial treatment had used self-medication in addition to the treatment prescribed. More than one in three used an antipyretic self-medication. Cough medicine or cold medicine had been taken by 10% (each). Also, 14% had used natural remedies or alternative treatments.

Out of the patients who were given an antimicrobial prescription, 94% said that they had picked up the drug from the pharmacy. Some 3% said they had not picked up the drug, and for the rest no clear response was received. One in four of those who did not have their prescription filled said that they thought they did not need the drug. Other reasons cited were that the drug was expensive or that the course of treatment had only been prescribed as a precaution.

Out of those who had picked up their antimicrobial at a pharmacy, 8% said that they had discontinued the treatment. On average, they had taken just over half of their course of treatment, and the treatment period was shortened by an average of 3.6 days. Discontinuing was slightly more common with courses of antimicrobial treatment prescribed for bronchitis, otitis media or urinary tract infection. In more than one in four cases of discontinuation, the reason was a side effect of the drug, and in one in five cases the patient felt healthy or otherwise considered that he/she no longer needed the drug. Bad taste was a reason for discontinuation only for child patients; and some patients simply forgot to take their medication.

About one in four patients who received an antimicrobial prescription reported side effects. The most typical of these were digestive symptoms (41% of those reporting side effects) and skin rash (14%).

Related MIKSTRA articles:

Petter Tuderman. MIKSTRA-puhelinhaastattelututkimus infektiotautien lääkinnästä - näkökulmana hoitomyöntyvyys. Sosiaalifarmasian pro-gradu-tutkielma, Helsingin yliopisto, Farmasian laitos, Farmakologian ja toksikologian osasto, kesäkuu 2001

Tuderman P, Klaukka T, Palva E ja MIKSTRA työryhmä (Huovinen P, Honkanen P, Klaukka T, Mäkelä M, Palva E, Rautakorpi U-M, Roine R, Sarkkinen H, Varonen H). Mikrobilääke näyttää menevän hyvin perille. Suom Lääkäril 2001;44:4510-11

Rautakorpi U-M, Honkanen P, Klaukka T, Mäkelä M, Palva E, Roine R, Sarkkinen H, Varonen H, Huovinen P for the MIKSTRA Collaborative Study Group. Patients' expectations and antibiotic prescription in common infections in primary care. WONCA Europe 2002, London, June 2002

5.7 Impact of the training intervention on major diagnoses

The training intervention focused on six major infections: otitis media, throat infection, sinusitis, acute bronchitis, skin infection and urinary tract infection. The main variable in the intervention impact assessment was the percentage of first-line antimicrobials according to the treatment recommendations in treatment choices at first appointments and the duration of treatment relative to the recommendations. Other variables included the use of diagnostic aids as per the recommendations and the percentage of patients who were prescribed antimicrobials. The analyses were conducted using the 'intention to treat' principle.

At the MIKSTRA health centres, the percentage of first-line drugs in accordance with the recommendations in antimicrobials prescribed at first appointments increased between 1998 and 2001 for all infections covered by the intervention (Table 19). The change was significant for sinusitis ($p < 0.001$), acute otitis media ($p = 0.015$) and urinary tract infection ($p = 0.009$).

Table 19. Recommended first-line antimicrobials in the national Current Care guidelines and the percentage of cases where these were used before (1998) and after (2001) the intervention and at the follow-up (2002) (includes first appointments only).

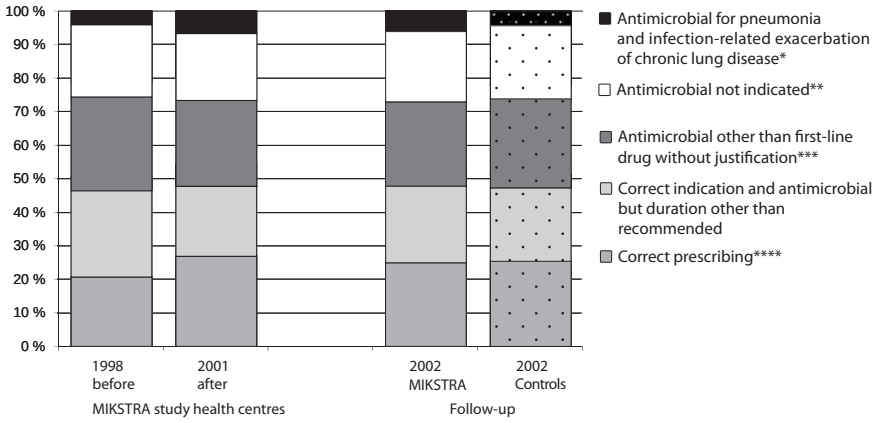
Diagnosis	Recommended first-line drugs in the CC guidelines published 1999-2000	MIKSTRA study HCs*			Follow-up 2002		
		1998	2001	P	MIKSTRA	Control HCs*	P
		%	%		%	%	
Otitis media	amoxicillin or penicillin-V	62	64	0.928	67	67	0.813
Tonsillitis	penicillin-V	77	79	0.612	77	82	0.497
Sinusitis	amoxicillin	35	51	<.001	46	40	0.160
Acute bronchitis	penicillin-V	4	9	0.015	6	6	0.928
Urinary tract infection	trimethoprim, pivmecillinam or nitrofurantoin	66	78	0.009	76	80	0.502
Bacterial skin-infection	1st-generation cephalosporin	86	88	0.579	88	81	0.051

*HC = Health Centre

Except for tonsillitis caused by beta-haemolytic streptococcus, the optimal antimicrobial treatment duration given in the treatment recommendations was shorter than we had been used to in Finland: 5 days for otitis media, 3 to 5 days for urinary tract infection, 5 to 7 days for acute bronchitis and 7 days for sinusitis. After the intervention in 2001, the percentage of shorter treatment periods as per the recommendations had increased significantly at the MIKSTRA health centres compared with the baseline in 1998 for otitis media (2% vs. 21%; $p < 0.001$), sinusitis (32% vs. 46%; $p < 0.001$) and urinary tract infection (55% vs. 64%; $p = 0.042$). The percentage of shorter courses of antimicrobial treatment had also increased for tonsillitis, acute bronchitis and common cold, the latter being examined for comparison purposes although there is no treatment recommendation for it; however, the difference was not statistically significant. In the follow-up in 2002, the percentage of shorter treatment periods was larger for almost all of the aforementioned infections than at the control health centres, but the difference was not statistically significant except for common cold (43% at the MIKSTRA health centres and 27% at the control health centres; $p = 0.045$).

An examination of all respiratory tract infections taken together showed that antimicrobial treatment completely in accordance with the treatment recommendations was only given in one out of five cases at the baseline (21%) (Figure 29). After the intervention, the percentage of treatment periods in compliance with the recommendations increased to about one fourth (27%), and in the follow-up in 2002 it was still higher than the baseline (25%) but not significantly different from the control health centres (25%; $p = 0.732$). Including treatment periods that were otherwise compliant with the treatment recommendations except that they were longer than recommended, the percentage of acceptable treatment choices was almost half already at the baseline in 1998 (47%) and did not increase significantly by 2001 (48%; $p = 0.455$).

In the different study years, about one in five (20%–22%) of the antimicrobial treatments prescribed for respiratory tract infections were prescribed for infections for which antimicrobials are not the first-line recommendation, especially acute bronchitis, and this situation did not change in the course of the MIKSTRA programme (Figure 29). About one in four (25%–28%) of the treatments were aimed at probable or possible bacterial infections (otitis media, tonsillitis or sinusitis), but the treatment chosen was not the first-line drug, even though there was no justification for this such as allergy or a previously noted side effect of the first-line drug. From 1999 onwards, the survey form asked for other justifications for deviating from the treatment recommendation (previous antimicrobial treatment; chronic, recurring or prolonged infection; result of a diagnostic test; or epidemiological information). Taking these other explanatory factors into consideration reduced the percentage of treatment periods not in compliance with the treatment recommendations to just below 40% in 2001 and 2002.



*Not included in the intervention
**Justifications allergy or other previous side-effect
***Prescription of antimicrobials for viral pharyngitis, unspesified URTI and acute bronchitis
****Prescription for middle ear infection, streptococcal tonsillitis and sinusitis of recommended antimicrobial for recommended duration time, or of other than first-line drug if justified by allergy or other previous side effect

Figure 29. Prescription habits for respiratory tract infections compared to the recommendations in the national Current Care guidelines before (1998) and after (2001) the training intervention at MIKSTRA health centres, and compared to the controls in the follow-up year (2002).

The following sections describe the results separately for individual diagnoses, with results tables using the year 1998 as a baseline except for skin infection. The training interim stage years 1999 and 2000 have been combined, as have the post-intervention years 2001 and 2002.

Before each diagnosis-specific results table there is a numbered list of the key points of the relevant Current Care guideline. The results relating to each of these points are numbered correspondingly in the table for ease of reference.

Related MIKSTRA articles:

Rautakorpi U-M, Huikko S, Honkanen P, Klaukka T, Mäkelä M, Palva E, Roine R, Sarkkinen H, Varonen H, and Huovinen P, for the MIKSTRA Collaborative Study Group. The Antimicrobial Treatment Strategies (MIKSTRA) Program: A 5-Year Follow-Up of Infection-Specific Antibiotic Use in Primary Health Care and the Effect of Implementation of Treatment Guidelines. Clin Infect Dis 2006;42:1221-30

5.7.1 Acute otitis media

Some 500,000 cases of acute otitis media in children are diagnosed in Finland each year. About 40% of all children will have had at least one otitis media by the age of one year, and about 70% by the age of two years.

Otitis media accounted for about 16% of all infections treated at the MIKSTRA health centres. Only common cold was more frequent. Of all the antimicrobial treatment prescribed in the course of the MIKSTRA programme, more than one fourth (27%) was for otitis media (Table 12, p. 58).

Of all the appointments for otitis media, three fourths were first appointments, and 5% were agreed follow-up appointments (Table 20). More than a third of the patients (37%–40%) were under 3 years of age. Most of the patients were given an antimicrobial prescription, and their percentage did not change over the years. A follow-up appointment, about one month after the first appointment, was agreed with about half of the patients who were prescribed antimicrobials, and about 1% of the patients were referred to specialist medical care.

Tympanometry was used rarely (1%–4% of appointments) even at health centres that had such a device (Table 20). Although tympanometer use seemed to increase slightly over time, it still remained remarkably underused. Although a tympanometry finding is not in itself sufficient for a diagnosis, it is relevant in ruling out the possibility of otitis media. If the tympanogram is normal, an infection is highly unlikely, and the risk of over-diagnosing a case of flu in a patient with reddened ears as otitis media is reduced. A tympanometer should be standard equipment at every service point where small children are examined at an outpatient clinic.

The percentage of antimicrobial choices in compliance with the recommendation for first-line drugs increased slightly, but in the years following the intervention it was no different than at the control health centres (Table 20). Amoxicillin with clavulanic acid was used very little, although its percentage doubled from 3% to 6%. Macrolides, though defined as second-line drugs, were used relatively often for initial treatment. Despite the recommendations their percentage did not decrease, unlike did the percentage of sulpha-trimethoprim (17% vs. 11%). However, there was a clear change in the length of the courses of antimicrobial treatment prescribed at first appointments towards that specified in the recommendations. Whereas in 1998 these short courses of treatment were only used in a few per cent of cases, after the treatment recommendations their percentage rose to about one fifth.

Table 20. Treatment practices for otitis media and how they changed with the Current Care guideline (numbers refer to the clauses quoted from the recommendation).

Current care recommendations for otitis media 1999:
1. "Diagnosis may be confirmed using tympanometry (or acoustic reflectometry)."
2. "The middle ear secretion observed in acute otitis will disappear without antimicrobial treatment in most children."
3. "Amoxicillin or V-penicillin is recommended as the first-line drug."
4. "Macrolides are second-line drugs."
5. "Five-day courses of treatment have achieved results similar to those of more than seven days."
6. "Ear ache may be treated with paracetamol, ibuprofen, naproxen and/or anaesthetic ear drops."
7. "The best time for a follow-up examination is about one month from the start of treatment."

	MIKSTRA health centres			Controls
Year	**1998**	**1999–2000**	**2001–2002**	**2002**
Total appointments for otitis media	1 230	1 676	1 489	609
First appointments, n (%)	915 (74)	1 214 (72)	1 100 (74)	434 (71)
Agreed follow-up appointments, n (%)	NA	126 (8)	79 (5)	30 (5)
Patients under the age of 3, n (%)	460 (37)	627 (37)	554 (37)	246 (40)
Referred to specialist medical care, n (%)	12 (1)	21 (1)	21 (1)	13 (2)
Prescribed an antimicrobial, all appointments, n (%)	1 066 (87)	1 405 (84)	1 321 (89)	523 (86)
1. Tympanometry performed, n (%)[a)]	8 (1)	5 (1)	16 (2)	15 (4)
2. Prescribed an antimicrobial, first appointments only, n (%)	858 (94)	1 122 (92)	1 053 (96)	403 (93)
3. Antimicrobial prescribed at first appointment compliant with the first-line drug recommendation,n (%) [b)]	535 (62)	795 (71)	691 (66)	269 (67)
4. Antimicrobial prescribed at first appointment was a macrolide, n (%)	113 (13)	126 (11)	143 (14)	55 (14)
5. Course of antimicrobial treatment prescribed at first appointment lasted 5 days, n (%)[c)]	16 (2)	146 (15)	181 (20)	35 (10)
6. Painkillers were prescribed/recommended, n (%)[d)]	159 (13)	230 (14)	147 (10)	84 (14)
7. Prescribed an antimicrobial and follow-up appointment agreed for about 1 month later, n (%)[e)]	NA	629 (45)	618 (47)	246 (47)

a) only the health centres that had a tympanometer are taken into account

b) amoxicillin or V-penicillin; percentage of all antimicrobials prescribed for middle ear infection at first appointment

c) all antimicrobials except azithromycin (Zithromax)

d) painkillers, analgetics and anaesthetic ear drops

e) 4 weeks / 30 days ± 2 days

A cost-benefit analysis was also conducted on the implementation of the Current Care guideline for otitis media. The analysis included all patients aged 0 to 6 who had a first appointment because of otitis media at a MIKSTRA health centre in 1998 (n = 579) and in 2002 (n = 369). The cost-benefit analysis was conducted from the perspective of society at large, ignoring the costs of drawing up the treatment recommendation. The benefit indicators were the number of symptom-free patients in the phone interview and the cost of producing one more symptom-

free child. The analysis found that the percentage of symptom-free patients was 10 percentage points higher after the intervention, while the cost per episode of otitis media was the same or slightly less. However, the analysis only considered short-term impact.

Related MIKSTRA articles:

MIKSTRA-työryhmä (Leistevuo J, Huikko S, Huovinen P, Klaukka T, Mäkelä M, Palva E, Rautakorpi U-M, Roine R P, Sarkkinen H, Varonen H, Honkanen P). Äkillisen välikorvatulehduksen diagnostiikka tarkemmaksi tympanometrillä. Suom Lääkäril 2004;59:4498–4500

Koskinen H, Rautakorpi U-M, Sintonen H, Honkanen P. Huikko S, Huovinen P, Klaukka T, Palva E, Roine R.P, Sarkkinen H, Varonen H, Mäkelä M for the MIKSTRA Collaborative Study Group. Cost-effectiveness of implementing national guidelines in the treatment of acute otitis media in children. Int J Technol Assess Health Care 2006;22:454–9

5.7.2 Throat infection

Throat infection accounted for about 10% of all infections treated at the MIKSTRA health centres, being tied with sinusitis for third place after common cold and otitis media. The majority of the appointments were first appointments. In less than 1% of the cases, a complicating peritonsillar abscess was entered as additional information, and 2% of the patients had been referred to specialist medical care (Table 21).

Throat infection can be caused by a number of pathogens; for treatment purposes, the most important of these are streptococci in groups A, C and G. The leading pathogen is *Streptococcus pyogenes* (a Group A streptococcus), which causes 14%–40% of cases. The purpose of diagnostics is to identify those cases of throat infection that are caused by a Group A streptococcus. In case of an ongoing epidemic, Group C and Group G streptococci are also searched for. Because the symptoms and findings associated with the various pathogens are indistinguishable from one another, and because a clinical examination cannot alone confirm the bacterial etiology, a throat swab or Group A streptococcus antigen test must be performed. In the 1999 Current Care guideline, a throat swab was named as the primary method. Cough and a runny nose make a Group A streptococcus infection unlikely but do not rule it out. It is recommended to take a throat swab from patients who have a sore and/or inflamed throat, but not from patients with a typical cold characterised by coughing and a runny nose.

In 1998, a diagnostic test of some kind was performed on 69% of throat infection patients; after the training intervention, this figure increased to 76% (2001–2002). At the baseline, throat swabs were taken from 57% of throat infection patients; after the training intervention, the figure was 68%, but there was no difference compared with the control health centres (Table 21). Of other tests, only CRP tests and sinus ultrasound scans were performed to any significant extent on

Table 21. Treatment practices for throat infection and how they changed with the Current Care guideline (includes the categories of tonsillitis and pharyngitis on the questionnaire form; numbers refer to the clauses quoted from the recommendation).

Current Care recommendations for pharyngitis 1999:
1. "Antimicrobial treatment for throat infection must be based on the demonstrated presence of beta-haemolytic streptococcus in the throat."
2. "The principal method is a throat swab."
3. "The first-line drug is V-penicillin."
4. "Makrolides (only) if the local resistance situation permits."
5. "The course of treatment shall last 10 days."
6. "Symptomatic treatment for pain must also be included."

	MIKSTRA health centres			Controls
Year	**1998**	**1999–2000**	**2001–2002**	**2002**
Total appointments for throat infection	948	1 150	844	448
First appointments, n (%)	759 (80)	929 (81)	682 (81)	373 (83)
Peritonsillar abscesses, n(%)	5 (1)	6 (0,5)	10 (1)	3 (0,6)
Referred to specialist medical treatment, n (%)	16 (2)	18 (2)	18 (2)	5 (1)
Prescribed an antimicrobial, all appointments, n (%)	413 (44)	536 (47)	376 (45)	204 (46)
1. Throat infection patients prescribed an antimicrobial from whom a throat swab was taken, n (%)	223 (57)	315 (60)	253 (68)	143 (71)
2. Patients prescribed an antimicrobial from whom only a throat culture was taken, n (%)	125 (32)	216 (41)	144 (39)	70 (35)
Prescribed an antimicrobial, first appointments only, n(%)	343 (45)	451 (49)	312 (46)	172 (46)
3. Antimicrobial prescribed at first appointment compliant with the first-line drug recommendation,[a] n (%)	255 (74)	332 (74)	231 (74)	130 (76)
4. Antimicrobial prescribed at first appointment was a macrolide, n (%)	9 (3)	12 (3)	11 (4)	4 (2)
5. Course of antimicrobial treatment prescribed at first appointment lasted 10 days, n (%)	249 (74)	327 (74)	227 (75)	130 (78)
6. 6. Painkillers were prescribed/recommended, n (%)[b]	81 (9)	124 (11)	111 (13)	69 (15)

[a] V-penicillin

[b] Includes painkillers, analgetics and Xylocain gargle

throat infection patients (CRP 5% before and 10% after intervention; ultrasound 7% before and 6% after).

Just under half of the patients were given antimicrobials for their throat infection. The choice of drugs and duration of the course of treatment were fairly well in line with the treatment recommendation even before the intervention (Table 21). Three out of four of those who received antimicrobials received a first-line drug, and the use of first-generation cephalosporins remained stable (15% vs. 16%) as did that of macrolides, which were used very little anyway (3% vs. 4%).

The taking of throat swabs increased somewhat after the treatment recommendation was published. Because the information collection did not

include a question on the results of the throat swab, it is not possible to deduce what the accuracy of the throat swab testing was or whether it guided treatment decisions.

The percentage of cases where first-generation cephalosporins were used as primary treatment for throat infection was considerably higher than the assumed percentage of patients with a penicillin allergy. Some 10% of all patients declare that they have a penicillin allergy, whereas the actual figure suggested in the literature is 0.7%–4%. However, some of the patients may have had a recurring infection caused by beta-haemolytic streptococcus, in which case the prescribing of a first-generation cephalosporin would have been justified.

Related MIKSTRA articles:

MIKSTRA-työryhmä (Leistevuo J, Huikko S, Honkanen P, Huovinen P, Klauk-ka T, Mäkelä M, Palva E, Rautakorpi U-M, Roine R P, Varonen H, Sarkkinen H). Nielutulehduksen hoito terveyskeskuksissa ennen hoitosuositusta ja sen jälkeen. Suom Lääkäril 2005;60:420-2.

Rautakorpi U-M, Huikko S, Honkanen P, Klaukka T, Mäkelä M, Palva E, Roine R, Sarkkinen H, Varonen H, and Huovinen P, for the MIKSTRA Collaborative Study Group. The Antimicrobial Treatment Strategies (MIKSTRA) Program: A 5-Year Follow-Up of Infection-Specific Antibiotic Use in Primary Health Care and the Effect of Implementation of Treatment Guidelines. Clin Infect Dis 2006;42:1221-1230

5.7.3 Acute sinusitis

Sinusitis tied with throat infection as the third most common infection diagnosis (12%) after common cold and otitis media (Table 8, p. 49). Of all the antimicrobial treatment in the MIKSTRA programme, one fifth (22%) was prescribed for sinusitis and it was the second most common indication for antimicrobial treatment after otitis media (Table 12, p. 58). For adults of working age, sinusitis was the most common indication for antimicrobial treatment, accounting for one third of all antimicrobial treatment in this age group. Indeed, the majority of sinusitis patients were adults.

A diagnostic test of some kind was performed on four out of five sinusitis patients, usually an ultrasound examination (75% on average). Sinus imaging was in common use already at the time when the study began and was also in common use at the control health centres (72%; Table 22). A sinus puncture was carried out on 5% of patients on average (annual variation from 4% to 7%). No changes in the use of diagnostic aids happened during the monitoring.

Sinusitis patients sought an appointment at a health centre at a very early stage in their illness. Antimicrobial treatment was often prescribed even when the symptoms had lasted less than a week. A physician diagnosing sinusitis would start the patient on antimicrobials in 80% of the cases even if the symptoms had lasted for less than 4 days. However, the percentage of sinusitis patients receiving antimicrobials whose symptoms had lasted under a week decreased somewhat at the MIKSTRA health centres in the course of the programme (Table 22).

Table 22. Treatment practices for sinusitis and how they changed with the Current Care guideline (numbers refer to the clauses quoted from the recommendation).

Current Care recommendations for acute sinusitis 1999:
1. ″Suspicion of sinusitis prompted by symptoms and findings should be confirmed by other (imaging) examinations.″
2. ″Puncture and lavage are indicated if symptoms are severe or the condition is prolonged.″
3. ″About two thirds of patients will recover without an antimicrobial.″
4. ″Amoxicillin is a suitable first-line drug.″
5. ″Doxicyclin is a second-line drug, and macrolides are third-line.″
6. ″New quinolones should be kept in reserve.″
7. ″Recommended length of a course of treatment is 7 to 10 days.″ (NOTE: This does not apply to azithromycin treatment.)
8. ″During the first week of upper respiratory tract infection symptoms, refrain from prescribing antimicrobials for sinusitis symptoms.″

	MIKSTRA health centres			Controls
Year	**1998**	**1999–2000**	**2001–2002**	**2002**
Total appointments for sinusitis	927	1 311	1 276	563
First appointments, n (%)	670 (72)	940 (72)	926 (73)	415 (74)
Agreed follow-up appointments, n (%)	NA	45 (3)	32 (3)	12 (2)
Referred to specialist medical care, n (%)	9 (1)	14 (1)	13 (1)	4 (1)
Prescribed an antimicrobial, all appointments, n (%)	762 (82)	1 112 (85)	1 116 (87)	486 (86)
1. Sinusitis patients prescribed an antimicrobial on whom an ultrasound or X-ray was performed, n (%)	613 (81)	880 (80)	853 (77)	349 (72)
2. Sinus puncture performed, n (%)	33 (4)	87 (7)	70 (5)	19 (3)
3. Prescribed an antimicrobial, first appointments only, n (%)	596 (89)	876 (93)	885 (96)	378 (91)
4. Antimicrobial prescribed at first appointment compliant with the first-line drug recommendation,[a] n (%)	210 (35)	427 (49)	431 (49)	152 (40)
5. Antimicrobial prescribed at first appointment was a macrolide, n (%)	81 (14)	94 (11)	103 (12)	62 (16)
6. Antimicrobial prescribed at first appointment was a quinolone, n (%)	2 (0,3)	2 (0,2)	1 (0,1)	0
7. Duration of course of antimicrobial treatment prescribed at first appointment compliant with recommendation, n (%)[b]	170 (32)	351 (43)	381 (46)	145 (43)
8. Patients having had symptoms for less than 8 days who were prescribed an antimicrobial at the first appointment, n (%)	270 (45)	385 (44)	334 (38)	152 (40)

[a] Amoxicillin

[b] 7 days; includes all antimicrobials except azithromycin (Zithromax)

The status of amoxicillin, the recommended first-line drug, strengthened as the MIKSTRA programme progressed from about one third at the baseline to about half (Table 22), and also the difference to the control health centres was significant. By the end of the programme, the MIKSTRA health centres were using less macrolides than the control health centres (12% vs. 16%), but the difference was not statistically significant. Treatment periods shortened, and the percentage of 7-day treatments compliant with the recommendations increased significantly as the programme progressed.

For sinusitis, the effectiveness of the two training methods in influencing changes in treatment practices was evaluated separately. The use of amoxicillin as a first-line drug increased from 39% to 48% at the AD health centres and from 33% to 45% at the PBL health centres; the figure for the control health centres was 40%. The percentage of treatment periods whose length was compliant with the recommendation increased from 34% to 40% at the AD health centres and from 32% to 47% at the PBL health centres (43% at the control health centres). No statistically significant differences were noted between the AD and PBL methods in this respect.

The treatment practices for sinusitis differed the most from the Current Care recommendations in how the treatment was begun. In cases of suspected sinusitis, 80% to 90% of patients were given an antimicrobial prescription within the first week of infection symptoms presenting, even if the symptoms had lasted for less than 4 days. This is in spite of the known fact that only a small percentage of patients will benefit from antimicrobial treatment in such circumstances and that its disadvantages may outweigh its benefits.

Most patients with sinusitis symptoms seek an appointment early, often simply to be given sick leave. An ordinary viral upper respiratory tract infection presents with some of the same symptoms as sinusitis, and distinguishing between the two is difficult. Accordingly, in the early stages of symptoms imaging should be avoided, because common cold may also cause accumulation of fluid in the sinuses, and imaging may lead to unnecessary antimicrobial treatment. In sinusitis with mild symptoms the recommendation is increasingly that it could be treated with symptomatic treatment only.

Related MIKSTRA articles:

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5.7.4 Adult acute bronchitis

Acute bronchitis is defined as a rapidly developing inflammation of the mucosa of the trachea and bronchial tubes that is of short duration. This infection is usually caused by a virus; bacterial infections are estimated to account for 20% of cases. The condition involves prolonged coughing, lasting usually for about two weeks; one third of patients are still coughing in the third week. The diagnosis is based on the patient history, a clinical examination and monitoring the progress of the symptoms. A CRP test can be helpful in the diagnostics, but there is no unambiguous CRP threshold value that would confirm the aetiology as either bacterial or viral, and the test is not reliable in discovering the origin of symptoms that have begun less than 12 hours earlier. Imaging is used as necessary for differential diagnostics for sinusitis and pneumonia, for instance.

Acute bronchitis was the fifth most common diagnosis (at 8%) after upper respiratory tract infections (common cold, otitis media, throat infection and sinusitis) at the MISKTRA health centres. About one fifth of the patients were aged 60 or over, four fifths of the appointments were first appointments, and only a few patients were referred to specialist medical care (Table 23).

About one in three bronchitis patients had a diagnostic test performed (30% before the training intervention and 37% after it). The most frequently used test was a sinus ultrasound, which was performed on about one fifth of the patients (Table 17, p. 71). The second most frequently used test was a CRP test, the use of which slightly increased in the course of the programme (Table 23).

An antimicrobial prescription was written for three fourths of adult bronchitis patients. Slightly under half of those patients who were given antimicrobials at their first appointment had had symptoms for no more than a week (Table 23). The antimicrobial most commonly prescribed at first appointments was doxycycline; its percentage decreased slightly in the course of the programme. One third of the patients were given macrolides both before and after the training intervention. The use of doxycycline as a first-line drug in suspected cases of mycoplasma and chlamydia infection is probably justifiable, however, considering the increased bacterial resistance to macrolides. The baseline percentage for V-penicillin, the first-line drug in the 1999 Current Care guideline, was low (4%), but this figure doubled in the course of the programme (Table 23). The length of treatment periods, on the other hand, seemed to decrease; the percentage of treatment periods complying with the suggested duration of antimicrobial treatment in the treatment recommendation (5 to 7 days) increased from about one fourth to one third (Table 23).

The large percentage of bronchitis patients who were given antimicrobials is clearly contradictory to the recommendation. However, in an actual clinical situation it is often difficult to make the call between bronchitis and pneumonia. Apparently physicians tend to prescribe antimicrobials to err on the side of caution. Refraining from using antimicrobials requires not only a careful clinical examination but also good communication and monitoring between patient and

Table 23. Treatment practices for acute bronchitis in adults (aged 15 and above) and how they changed with the Current Care guideline (numbers refer to the clauses quoted from the recommendation).

Current Care recommendations for acute bronchitis 1999:
1. "CRP should be taken when antimicrobial treatment is considered based on the clinical situation."
2. "In about 80% of cases the pathogen is a virus and ... antimicrobials are largely unnecessary."
3. "In most patients, coughing lasts for about two weeks / an antimicrobial is indicated if the patient has had a fever for more than a week."
4. "The major target pathogen for antimicrobial treatment is pneumococcus, and a drug potent to cope with it is usually sufficient."
5. Macrolides are only to be used as second-line drugs.
6. "Recommended length of a course of treatment is 7 to 10 days." (NOTE: This does not apply to azithromycin treatment.)

	MIKSTRA health centres			Controls
Year	**1998**	**1999–2000**	**2001–2002**	**2002**
Total appointments for bronchitis	380	496	492	215
First appointments, n (%)	291 (77)	398 (80)	394 (80)	161 (75)
Referred to specialist medical care, n (%)	0	3 (1)	5 (1)	1 (1)
Patients aged 60 or older, n (%)	85 (22)	106 (21)	120 (24)	49 (23)
Prescribed an antimicrobial, all appointments, n (%)	282 (74)	342 (69)	380 (77)	163 (76)
1. Bronchitis patients prescribed an antimicrobial whose CRP was taken, n (%)	24 (9)	45 (14)	53 (14)	27 (18)
2. Prescribed an antimicrobial, first appointments only, n (%)	228 (78)	283 (71)	316 (80)	131 (81)
3. Patients who had had symptoms for less than 8 days who were prescribed an antimicrobial at the first appointment, n (%)	106 (47)	112 (40)	133 (42)	50 (38)
Antimicrobial prescribed at first appointment compliant with the first-line drug recommendation,[a] n (%)	9 (4)	22 (8)	28 (9)	8 (6)
4. Antimicrobial prescribed at first appointment was doxicyclin, n (%)	110 (48)	139 (49)	119 (38)	53 (40)
5. Antimicrobial prescribed at first appointment was a macrolide, n (%)	80 (35)	73 (26)	107 (34)	48 (37)
6. Duration of course of antimicrobial treatment prescribed at first appointment compliant with recommendation, n (%)[b]	56 (27)	81 (30)	105 (36)	36 (29)

a) V-penicillin

b) 5 to 7 days; includes all antimicrobials except azithromycin (Zithromax)

doctor. The number of CRP tests could be increased as an aid for augmenting the diagnostic process. Patient instructions drawn up on the basis of the Current Care guideline (www.duodecim.fi/kh, www.mikstra.fi) may be helpful in patient education.

Related MIKSTRA articles:

MIKSTRA-työryhmä (Leistevuo J, Huikko S, Huovinen P, Klaukka T, Mäkelä M, Palva E, Rautakorpi U-M, Roine R P, Sarkkinen H, Varonen H, Honkanen P). Äkillistä keuhkoputkitulehdusta hoidetaan turhan usein mikrobilääkityksellä. Suom Lääkäril 2004;59:3277–9.

5.7.5 Female uncomplicated urinary tract infections

Urinary tract infections are usually divided into cases of cystitis and pyelonephritis depending on the level of infection. These may be further divided into infections with and without complications. Infections with complications are those urinary tract infections, even in the lower urinary tract, in whose examination and treatment special features are involved, for instance infections in pregnant women, men, children and patients with catheter-associated urinary tract infections.

The Current Care guideline for urinary tract infections published in 2000 noted that in cases where uncomplicated cystitis is suspected in a woman, no urine culture or multi-strip test is required. Cystitis in a woman patient in outpatient care is considered to be uncomplicated when the patient has no underlying illness with potential risks, she is not pregnant and the infection has not recurred more than twice a year.

Urinary tract infections accounted for 5%–6% of all patient appointments leading to an infection diagnosis at the MIKSTRA health centres (Table 8, p. 49). Cases of uncomplicated cystitis in women aged 15 to 55 accounted for an average of 45% of all first appointments where a diagnosis of a urinary tract infection was made between 1998 and 2002 (range 39% to 50%).

The use of urine cultures for diagnosing female uncomplicated cystitis almost halved between 1998 (baseline) and 2002 (from 55% to 32%) (Figure 30), but the difference between this and the control health centres (34%, Table 24) was not statistically significant. The use of multi-strip tests did not significantly decrease from the baseline level; in 2002, they were used in clearly more cases (51%) than urine cultures. However, the percentage of patients on whom neither of these tests was performed more than doubled between 1998 and 2002 (from 15% to 36%), although here too the difference between this and the control health centres (34%) was not statistically significant (Figure 30; Table 24).

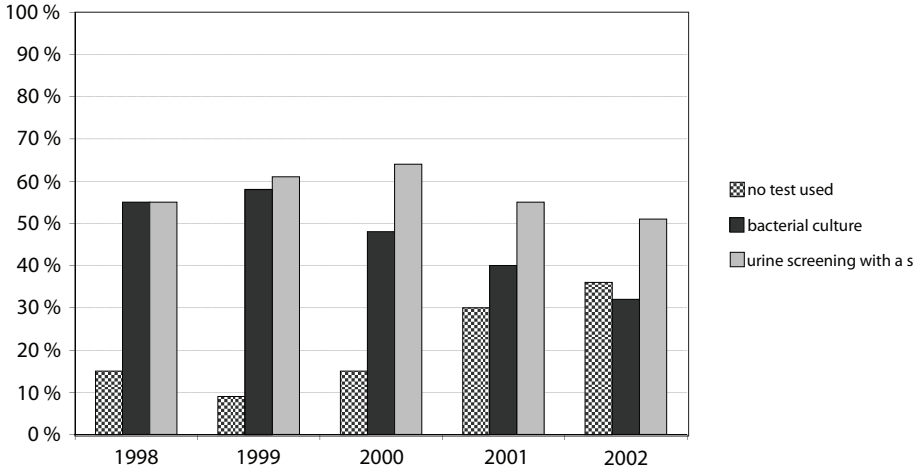


Figure 30. Use of diagnostic aids in uncomplicated cystitis of 15-55 year old females in MIKSTRA study health centres 1998–2002.

The most frequently used first-line drugs (trimethoprim, mecillinam and nitrofurantoine) were options recommended in the Current Care guideline. Actually, these were the most frequently used drugs even before the recommendation was published, but their combined percentage (72%) increased by 14 percentage units after the recommendation was published to 86%; the figure at the control health centres was the same (Table 24). The percentage of sulpha-trimethoprim in the treatment of uncomplicated cystitis halved, while the percentage of quinolones remained low. The percentage of treatment periods whose length conformed to the treatment recommendation also increased (63% to 78%).

Table 24. Treatment practices for female uncomplicated urinary tract infection and how they changed with the Current Care guideline (numbers refer to the clauses quoted from the recommendation).

Current Care recommendations for urinary tract infection 2000:
1. "Diagnosis of women's cystitis without complications is primarily based on symptoms."
2. "In case of atypical symptoms, a strip test may be used as a diagnostic aid ... but the sample must be cultured."
3. "The first-line drugs are trimethoprim, nitrofurantoine and pivmesilliname."
4. Quinolones are second-line drugs.
5. "Drugs to be used (only) for specific reasons (include) sulpha-trimethoprim."
6. The most commonly recommended duration for a course of treatment is 3 to 5 days.

	MIKSTRA health centres			Controls
Year	**1998**	**1999–2000**	**2001–2002**	**2002**
Total appointments for urinary tract infection	437	692	526	238
Women aged 15 to 55 with cystitis without complications, n (%)[a]	207 (47)	277 (40)	209 (40)	88 (37)
...of whom at first appointment, n (%)	167 (81)	243 (88)	184 (88)	79 (90)
1. Women aged 15 to 55 on whom no urine diagnostic was performed, n (%)	32 (15)	37 (13)	75 (36)	30 (34)
2. urine rapid test performed, n (%)	105 (51)	172 (62)	99 (47)	38 (43)
2. urine culture taken, n (%)	120 (58)	144 (52)	78 (37)	43 (49)
Women aged 15 to 55 who were prescribed an antimicrobial at their first appointment, n (%)	149 (89)	219 (90)	167 (91)	66 (84)
3. Antimicrobial prescribed at first appointment compliant with the first-line drug recommendation,[b] n (%)	108 (72)	173 (79)	143 (86)	57 (86)
4. Antimicrobial prescribed at first appointment was a quinolone, n (%)	12 (8)	21 (10)	7 (4)	4 (6)
5. Antimicrobial prescribed at first appointment was sulpha-trimethoprim, n (%)	15 (10)	12 (5)	9 (5)	3 (5)
6. Duration of course of antimicrobial treatment prescribed at first appointment compliant with recommendation, n (%)[c]	94 (63)	156 (71)	131 (78)	49 (74)

[a] For 1998 and 1999, all women aged 15 to 55 with no note on pyelonephritis in their additional information were included. For 2000–2002, all women aged 15 to 55 coded as infections without complications were included.
[b] Trimethoprim, nitrofurantoine or pivmecillinam.
[c] 3 to 5 days

Related MIKSTRA articles:

MIKSTRA-työryhmä (Leistevuo J, Honkanen P, Huikko S, Huovinen P, Klaukka T, Mäkelä M, Palva E, Rautakorpi U-M, Roine R P, Varonen H, Sarkkinen H). Virtsatietulehduksen hoitokäytännön muutokset 1998–2002. Suom Lääkäril 2004;59:2820–22

5.7.6 Primary bacterial infections of the skin

The total percentage of cases of skin infection among all infection cases at the MIKSTRA health centres was about 6% (annual variation 5 to 7%). On average, 10% of these were cases of deep cellulitis (including mastitis, which was not distinguished from other types of deep cellulitis on the survey form until 2000).

A higher percentage of skin infection patients were referred to specialist medical care than of infection patients in general: on average, 4% of all skin infection patients (Table 25) and 13% of deep cellulitis patients (Table 9, p. 51).

Antimicrobials were used to treat just over two thirds of all skin infection patients and most of deep cellulitis patients (Table 25). The material also includes patients who may have been having a follow-up appointment. Drug choices were largely in compliance with the treatment recommendation (in 74% of the cases) already at the baseline, and the situation did not change in the course of the programme.

Table 25. Treatment practices for skin infection and how they changed with the Current Care guideline (numbers refer to the clauses quoted from the recommendation).

Current Care recommendation for bacterial skin infection 2000:

1. First-line drugs for deep cellulitis (erysipelas) are parenteral penicillin and V-penicillin, 1st-generation cephalosporin for all others.
2. "In initial treatment for erysipelas, it is almost always recommended to administer the penicillin parenterally."

	MIKSTRA health centres			Controls
Year	**1998–1999**	**2000**	**2001–2002**	**2002**
Total appointments for skin infection	866	371	616	333
...of which deep cellulitis, n (%)	87 (10)	48 (13)	62 (10)	32 (10)
Referred to specialist medical care, n (%)	33 (4)	18 (5)	25 (4)	15 (5)
Prescribed an antimicrobial, all cases of skin infection, n (%)	549 (63)	251 (68)	439 (71)	211 (63)
Prescribed an antimicrobial, deep cellulitis, n (%)	70 (80)	42 (88)	49 (79)	26 (81)
1. Antimicrobial prescribed at first appointment compliant with the first-line drug recommendation,[a] n (%)	404 (74)	174 (69)	328 (75)	148 (70)
2. 2. Patients with prescriptions who received parenteral penicillin, deep cellulitis only, n (%)	7 (10)	4 (9)	7 (14)	1 (4)

[a] V-penicillin, 1st-generation cephalosporin or parenteral penicillin.

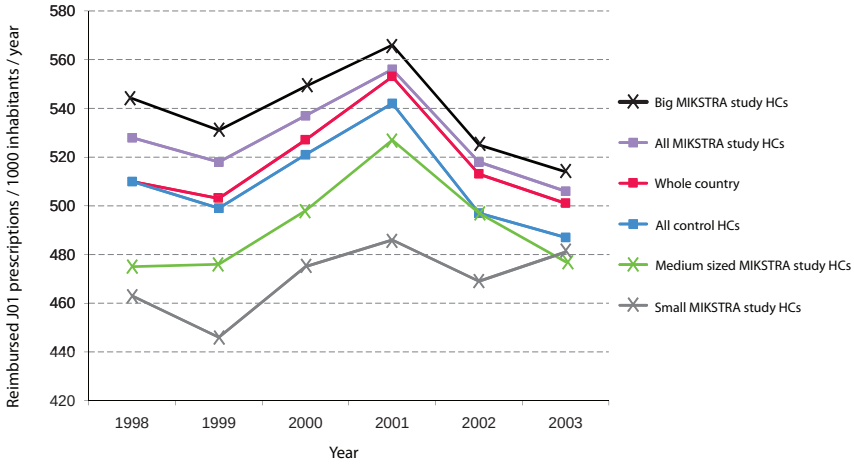
However, with cases of deep cellulitis the use of antimicrobials did not conform to the treatment recommendation as frequently. Parenteral penicillin appeared to have been used much less than indicated in the recommendation. Instead, first-generation cephalosporins were also used generally to treat deep cellulitis (67% of prescriptions on average) even though the treatment recommendation does not really encourage this. The frequent use of first-generation cephalosporins may be explained by the fact that mastitis is included in the deep cellulitis category in this material. Cephalosporin is also recommended as an alternative for patients allergic to penicillin and in cases of erysipelas with a suspicion of staphylococcal complication.

5.7.7 Number of antimicrobial prescriptions at the MIKSTRA health centres and nationwide

Changes in the use of antimicrobials in the catchment areas of the MIKSTRA health centres and nationwide between 1998 and 2003 were compared using Kela prescription databases. It is important to remember that before the compensation policy was revised in 2006, some of the cheapest antimicrobial prescriptions were not included in the prescription statistics. The introduction of generic substitution in spring 2003 and the compensation policy revision at the beginning of 2006 changed the basis for figures entered in the prescription databases so that it is not possible to compare the data directly before and after these changes to each-other. Therefore the comparison was not extended forward beyond 2003.

During the period studied, the annual number of prescriptions decreased slightly nationwide (Figure 31). However, in 2001 the figures were much higher in the catchment areas of all the MIKSTRA health centres and the control health centres, and also nationwide, than in any other year. This spike is probably due more to the respiratory tract infection epidemic situation than to any other factors.

The combined number of antimicrobial prescriptions in all the MIKSTRA health centre catchment areas per 1,000 residents was very similar to the same figure for the entire country. However, this number of prescriptions per 1,000 residents was clearly higher in the catchment areas of large MIKSTRA health centres and lower in those of small and medium-sized ones throughout the period studied compared with the national and MIKSTRA average (Figure 31).



Source: National Prescription Register of the Social Insurance Institution

Figure 31. Number of reimbursed prescriptions of antimicrobials (J01) per one thousand residents at MIKSTRA study and control health centres (HC) and nationwide, 1998–2003.

As the sales statistics for health centre districts are based on the Kela prescription database, the figures include prescriptions written outside the health centres as well, ie. in private sector. In small communities, where other health care services are not so readily available, the figures are probably better indicative of health centre practices than in large communities. On the other hand, the increased centralisation of emergency clinic functions in the final years of the programme was likely to guide an increasing number of antimicrobial prescriptions to be delivered by pharmacies in the communities where the emergency clinics are located rather than in the patients' home communities.

6 Discussion

The launching of the MIKSTRA programme in the mid-1990s was largely due to a worldwide realisation of the spreading of bacterial resistance to drugs and thereby the weakening of the efficacy of antimicrobials. While this debate was going on, the use of antimicrobials in Finland was steadily increasing, peaking in 1995. It was therefore only natural to conceive a programme to study the optimum use of antimicrobials and the diagnostics and treatment of infections in outpatient care; this became the MIKSTRA programme.

The MIKSTRA programme has generated nationally (and internationally) unique comprehensive data on issues in the diagnostics and treatment of infections in outpatient care. We used to know what drugs were used and how much. However, only limited indication-specific information on the use of drugs was available, and there was no information at all on situations where antimicrobials were not used, even though information on when and why antimicrobials are not used is also important in governing the use of antimicrobials in medication.

The MIKSTRA programme was a five-year follow-up study in which data were collected on the incidence and distribution of various infections in outpatient care in various age groups. Information was also obtained on the prescription practices of physicians, the contribution of nurses to the treatment of infections, the diagnostics of infections in outpatient care, symptom-based treatment of infections, patients' and physicians' attitudes, and patient recovery. However, the period of one week for collecting information proved to be too short at some health centres for acquiring information on a sufficient number of patients to draw diagnosis-specific conclusions at the local level. Longer-term monitoring of indication-specific use of antimicrobials allowed an evaluation of the impact of the Current Care guidelines published in 1999 and 2000 on treatment practices.

Changes during the MIKSTRA programme

The most significant change for the treatment of several infections was that the courses of antimicrobials prescribed generally became shorter, as was recommended in the treatment guidelines. This change was particularly significant with certain infections that are of prime importance for the overall volume of antimicrobial use, such as otitis media (treatment period length complied with the treatment recommendation in only 2% of cases in 1998, but in 21% of cases in 2001; $p < 0.001$) and sinusitis (32% in 1998 vs. 46% in 2001; $p < 0.001$). This change was in part supported by action taken by the pharmaceutical industry, the packaging sizes of antimicrobials being adapted to conform to the new treatment recommendations.

The drugs recommended as first-line drugs were already the drugs of choice with many infections (otitis media 62%, tonsillitis 77%, urinary tract infection

66% and skin infection 86%). However, with all infections the first-line drug was prescribed more frequently at the end of the MIKSTRA programme than at the baseline. This change was statistically significant however only with some infections, mainly those where the baseline was low, such as sinusitis (35% vs. 51%; $p < 0.001$), bronchitis (4% vs. 9%; $p = 0.015$), but also urinary tract infection (66% vs. 78%; $p = 0.009$).

Some positive trends were also observed in diagnostics in the course of the programme. With sinusitis, the use of diagnostics was already at an appropriate level at the baseline, as 81% of the patients being prescribed antimicrobials had been given a sinus ultrasound or X-ray examination. Throat swabs were underused at the baseline, but the situation improved in the course of the programme (57% vs. 68% of throat infection patients being prescribed antimicrobials had had a throat swab taken). The growth occurred mainly in the use of rapid tests. With female uncomplicated cystitis, the taking of urine samples decreased as per the treatment recommendation (15% vs. 36% of patients were not asked to give a urine sample), but on the other hand the use of strip tests did not decrease as anticipated. The use of CRP as a diagnostic aid with lower respiratory tract infections increased (9% vs. 14% of bronchitis patients being prescribed antimicrobials had had a CRP test taken), but not quite as much as anticipated. Tympanometers at health centres were clearly underused, or else located so that they were not easily available at locations where children with acute otitis media were usually examined.

For many of the aforementioned changes, the difference between the MIKSTRA health centres and the control health centres was not statistically significant. There may be many reasons for this. Because of last-minute cancellations, it may be that the most interested and active health centres on the original shortlist ended up being selected as controls. Also, collecting information on a separate form may have prompted what is known as a Hawthorne effect, i.e. making the participants operate more diligently during the study than they perhaps otherwise would have. It was also clear from the start of the MIKSTRA programme that it would be impossible to avoid contamination of the control health centres, because it would have been unethical not to publish the Current Care guidelines for infections nationwide. The publishing of treatment recommendations generally does not in and of itself lead to changing practices (17–18). The publicity gained by the MIKSTRA programme and the simultaneously started ROHTO workshops may have raised the profile of the new recommendations among physicians and nursing personnel and thereby boosted their introduction in the health care sector in general, not just at the MIKSTRA health centres.

In examining changes in drug prescription practices, it is difficult to avoid impression that shortening a course of treatment or replacing one drug with another is much easier for physicians than refraining from prescribing an antimicrobial at all. Even though efforts were made to support physicians in this through both the media and patient instructions, the action taken may not have been sufficient to

cause real change in the tradition of prescribing antimicrobials, at least not in the short term.

The diagnostic process for infections in outpatient care and the prescribing of antimicrobials are not always rational acts, nor are they based on medical factors alone. Decisions are also governed by the physician's workload, the patient's wishes and the fear of complications. Doctors may do diagnostic tests to avoid prescribing unnecessary antimicrobial drugs as in cases of throat infection or to diagnose a serious illness such as pneumonia as reliably as possible. On the other hand, diagnostic aids can help convince both the physician and the patient that antimicrobials are not needed in a particular case.

Treatment acceptance among patients proved to be very high. Only a few per cent of patients neglected their medication; these figures were much lower than generally reported in treatment acceptance studies. A short course of treatment may increase the motivation to take a prescribed antimicrobial, along with the irritating symptoms of infections that the patient hopes will be removed by the drug. The importance of finishing a course of treatment once started is a message that for decades now has been drilled into patients by health care personnel and pharmacies. We should note, however, that the responses to the survey may be economical with the truth. Not taking one's medication or leaving a course of treatment unfinished are a violation of the instructions given to the patient, who may therefore be tempted to colour the truth in an interview situation.

Experiences of further education in the workplace

The MIKSTRA programme was launched at a time when Current Care guidelines began to be published for the health care sector. MIKSTRA was one of the first national programmes aiming to influence outpatient care practices through treatment recommendations. We rolled out the Current Care guidelines in the field through interactive further education organised in the workplace. It became clear that further education of physicians and nursing personnel was an important factor in the implementation of treatment recommendations and in the updating of knowledge. MIKSTRA was a pioneer in the implementation of Current Care guidelines and paved the way for subsequent recommendations. At the time of this writing, there are some 100 Current Care guidelines, and they have become an essential part of further education at health centres and also an everyday tool. The training tools produced in the MIKSTRA programme have later been used and further developed in the ROHTO workshops.

We encountered some unexpected backlashes during the training intervention, and these had an impact on the training results. The person responsible for the training fell ill just as the training was beginning, which undermined the availability of methodological support to the health centres at the crucial beginning stages of the programme and delayed the production of training materials. This complicated the implementation of the intervention according to the planned randomisation

at least in some way. The project organisation was vulnerable partly because the resources available were very limited. The programme was run on a shoestring budget with no separate funding, and largely on a volunteer basis on part of the organisations and health centres involved. Despite the problems experienced, however, the MIKSTRA health centres were able to perform the information collecting admirably well in all years.

When the MIKSTRA programme began, health centres had enjoyed a good supply of physicians for several years. In the middle of the multi-year programme, this situation suddenly changed, and health centres began to lose physicians. The turnover involved half of the physicians at the MIKSTRA health centres over the five years of the programme. Therefore the MIKSTRA training did not reach all the physicians who participated in the information collecting for the programme. The reported changes have been analysed on the 'intent to treat' principle, and the changes may in fact be even more extensive with regard to permanent personnel at the health centres.

Our experiences show that in aiming for an extensive and permanent change in practices, personnel turnover is a vital factor to take into account through further education in the workplace. If the training is used to agree on common practices particular to that health centre, it is important to record them so that the information can be passed on to new employees. It may also be necessary to revisit the same training theme several times. Training must be extended to all the professional groups that are involved in the patient treatment chain.

Interviews with personnel at the MIKSTRA health centres yielded information on the implementation of the programme and general opinions on the necessity of the programme. The following were cited as strengths of the MIKSTRA programme:

- the programme provided good, concise treatment recommendations with a summary of research-based information,
- the programme had a well-designed information collecting system and feedback process at the health centre level,
- the programme was considered an ambitious research and development project, where documentation and monitoring are used for learning during the programme,
- the physicians appointed as instructors were in many cases local opinion leaders,
- the instructor physicians were motivated, eager to discuss and eager to state their opinion,
- the training project had significant expert input,
- the training project prompted a team spirit, enthusiasm and a network among the instructor physicians,
- the cooperation with the ROHTO network was considered fruitful,

- some of the products of the programme, such as patient instructions, were particularly well received; they inspired personnel to adopt new treatment practices and helped them explain things to patients,
- the programme responded to a key challenge in health care,
- cooperation between programme actors was good, and there was constant dialogue,
- the programme's external relationships and foreign networking were well managed.

Personnel participating in the MIKSTRA programme also submitted development ideas:

- a uniform toolkit for instructor physicians, with the principal instructions and materials related to the programme and the training project,
- more practical support for the training intervention, for instance in communications and paperwork,
- more time for instructor training, and better opportunities for instructor physicians to commit to the programme, for instance through working hours arrangements and compensation,
- clarifications to some of the treatment recommendations that were considered long-winded and difficult to understand,
- closer contact to the Current Care programme through the training intervention and implementation, and thereby a sounding board and critical feedback for ideas.

Changes in the overall sales of antimicrobials during the programme

According to the statistics of the National Agency for Medicines, the sales of antimicrobials for outpatient care have been slowly declining since the early 1990s. There was a decrease of about 13% in sales between 1993 and 1998, before the MIKSTRA programme had even started. During the monitoring period of the programme, 1998 to 2002, sales figures fluctuated slightly but remained essentially stable; since then, they have begun to drop again (Figure 32).

At the same time, big changes have occurred in the choice of individual antimicrobials. Measured in daily doses, the use of penicillin and doxycycline has halved and the use of sulpha-trimethoprim cut by two thirds between 1993 and 2008 (Figure 33). During the same period, the use of cephalosporins has increased by one fifth, the use of amoxicillin by one fourth, and the use of quinolones more than doubled while the use of the compound of amoxicillin and clavulanic acid has increased even sevenfold. In 2008, more than one in four daily doses of amoxicillin (27%) was combined with clavulanic acid without the bacterial sensitivity situation in Finnish outpatient care necessarily having altered so much as to warrant this change in usage.

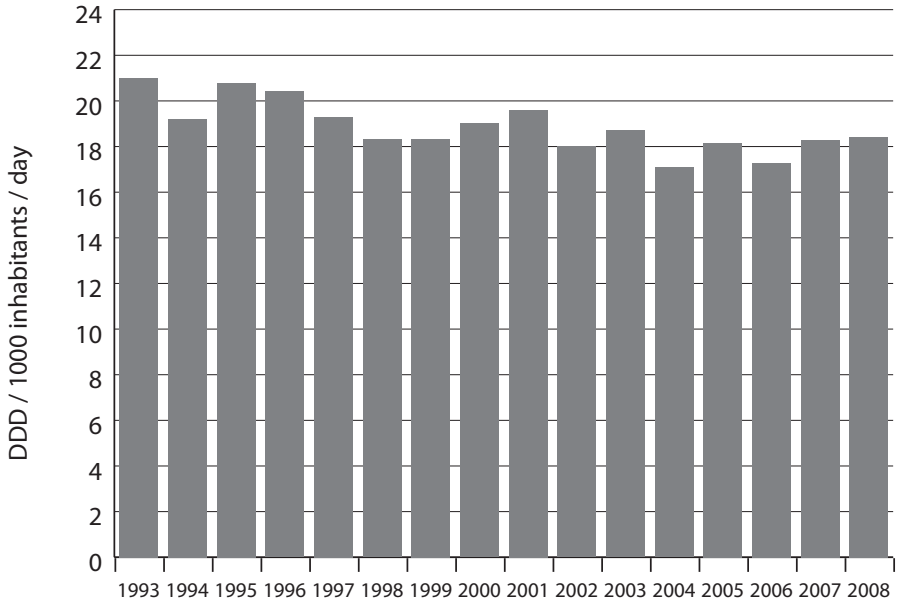


Figure 32. Annual pharmacy sales of antimicrobials (J01) in Finland 1993–2008.

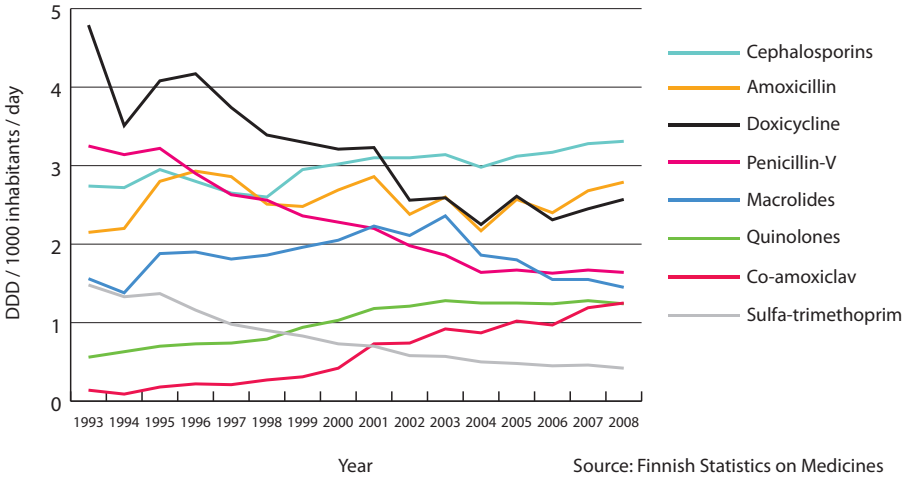


Figure 33. Pharmacy sales of the most common antimicrobials used in outpatient care 1993–2008.

Between 1991 and 1992, the use of macrolides dropped by almost half (from 2.53 to 1.48 daily doses per 1,000 residents per day) as a result of the recommendations published following the increased resistance of Group A streptococcus to macrolides (14). In the early 2000s, the use of macrolides rebounded to almost early 1990s levels, but as the MIKSTRA study shows, the indications for their use tended to be respiratory tract infections other than throat infection (Figure 20, p. 62). The use of macrolides has begun to decrease again after the end of the MIKSTRA programme, possibly because of increased awareness on the worsening of pneumococcal resistance.

Changes in the spectrum of drugs prescribed reflect in part the spirit of the Current Care guidelines. The increased use of amoxicillin is a trend encouraged by the recommendations. The results of MIKSTRA also demonstrate that its use is appropriately targeted. On the other hand, penicillin-V could be just as good in many cases. It is difficult to justify the increased use of the amoxicillin and clavulanic acid compound, however.

The most frequently used cephalosporins in outpatient care were first-generation cephalosporins. This is well justified, as there are scarcely any primary indications for the use of second-generation or third-generation cephalosporins in the Current Care guidelines. Cephalosporins are used as per recommendations in the treatment of skin infection, but their relatively common use for respiratory tract infections is contrary to the spirit of the recommendations. The decrease in the use of penicillin-V can probably be explained by the drug being largely replaced with amoxicillin and cephalosporins.

The decrease in the use of doxycycline is well in tune with the Current Care guidelines. However, the recommendations may have to be revised soon, since the resistance situation with tetracyclines has remained good while it is slowly deteriorating for other drug groups. Therefore the use of tetracyclines (mainly doxycycline) for adult respiratory tract infections may need to be re-evaluated.

The decrease in the use of sulpha-trimethoprim was expected. Bacterial resistance to it was higher than to other drug groups as far back as in the mid-1990s. The potential side-effects of the drug have probably also made it less popular. However, trimethoprim is still a first-line drug for urinary tract infections as per the Current Care guideline. The use of fluoroquinolones has more than doubled, but it seems that in outpatient care they are mainly used for urinary tract infections as per recommendations.

Bacterial resistance to antimicrobials

Over the past 70 years or so, microbes have been subjected to an unprecedented pressure of selection, both by human action and by changes in the environment (19). Under pressure of selection, microbes evolve much more quickly and much more efficiently than human beings. Indeed, the evolution of pathogens is considered an increasing challenge for medicine.

On the other hand, looking back over a perspective of 10 to 15 years, resistance has fortunately been slower to develop than anticipated. Nevertheless, many clinically significant bacterial pathogens, above all pneumococcus, are remarkably resistant now compared with how they were in the early 1990s. Resistance inevitably causes treatmentfailures sometimes. The use of macrolides should continue to decrease markedly so that the rapid increase in pneumococcal resistance to macrolides in recent years could be curbed. There is every possibility for achieving this, as macrolides are only rarely first-line drugs in infection treatment in outpatient care.

In the very recent past, the use of antimicrobials has been associated with changes in the normal human bacterial flora, with potentially significant health impacts. Diarrhoea caused by Clostridium difficile is closely associated with antimicrobial treatment; it spreads in hospitals and has been encountered in outpatient care, too. Studies have been published on links between antimicrobial use and the increasing incidence of allergic symptoms. Now that bacteria have also been associated with obesity and with both type 1 and type 2 diabetes, it is no wonder that the activity that has the greatest impact on the evolution of bacterial flora – the use of antimicrobials – is viewed with keen interest. The pressure to decrease antimicrobial treatment is not going anywhere, and it is no longer motivated just by increased bacterial resistance.

Where do we go from here?

The aim of the MIKSTRA programme was to identify ways of optimising the treatment of infection patients in outpatient care and to curb the development of drug resistance in bacteria. During the programme, and to some extent after it, changes in the right direction were observed in treatment practices, but not as much as was hoped. On the other hand, it is known from literature that it is never easy to change established procedures. Even in more specifically targeted interventions than in MIKSTRA, only changes on the order of 6% to 16% in operating procedures have been achieved (20). Although the average overall shift towards practices outlined in the treatment recommendations of respiratory tract infections was only 6.4% in the MIKSTRA programme, the changes were considerably greater in some individual indicators. Whether MIKSTRA contributed to the decrease in the sales of antimicrobials, particularly macrolides, after the programme ended is impossible to say. The trend is, however, going in the direction pointed by the targets of MIKSTRA, but it requires constant support.

The information generated in the MIKSTRA programme has helped to identify matters in the diagnostics and treatment of infections that should be addressed in the basic and further education of physicians if we want to change practices in the longer term. For example, the overall use of macrolides could be cut by up to a half from the present level by abandoning macrolides as a first-line drug for treatment of otitis media and sinusitis and by avoiding loosely justified prescriptions of

them for treatment of infections such as acute bronchitis and common cold. The unnecessary increase in the use of the amoxicillin and clavulanic acid compound could be curbed through alternative and independent information to balance the information provided by the pharmaceutical industry. After all, it is not a first-line drug in the treatment of normal infections in outpatient care.

The way in which the MIKSTRA study was structured meant that it was not possible to evaluate the correctness of the diagnoses recorded. However, some of our observations led us to suspect that infection diagnoses are sometimes made with deliberate intent, consciously or unconsciously. This is supported in our material for instance by the high cumulative weekly incidence of sinusitis, about 2 to 5 times that which would be expected on the basis of the literature. Similarly, we observed that not only do physicians who prescribe a lot of antimicrobials for their patients have a lower threshold for prescribing antimicrobials in general, they also tend to make diagnoses for which it is acceptable to prescribe antimicrobials. Similar observations have been made elsewhere (21). It is highly likely that cases of otitis media and sinusitis are over-diagnosed and over-treated in Finland. From the literature we know that only a minority of patients with symptoms of otitis media or sinusitis actually benefit from antimicrobial treatment (22–25). The use of antimicrobials for these indications could most probably be decreased by improving diagnostics and the criteria for antimicrobial treatment; by increasing the use of tympanometry in cases of otitis media (26); by daring to adopt a wait-and-see policy more frequently in cases of mild otitis media in children aged over 2, as in the other Nordic countries and the Netherlands (27–29); and by refraining from starting antimicrobial treatment on patients with sinusitis symptoms during the first 7 to 10 days of symptoms if there is no special reason to do so (30).

The unfounded use of antimicrobials to treat acute bronchitis is not a new phenomenon, and certainly not exclusive to Finland (31). This is probably partly due to the difficulty of distinguishing bronchitis from pneumonia, but partly also due to a lack of awareness on the aetiology of bronchitis and the normal progress of the disease. According to our surveys, health centre patients seem to be quite well informed of the fact that antimicrobials are of no help with viral diseases. This argument should be employed when explaining to a patient why a course of antimicrobial treatment will not be necessary for a case of viral bronchitis. However, it will probably take time and determined, focused efforts to break the deep-seated belief that bronchitis requires antimicrobials. But it is time for both physicians and patients to face the facts: the majority of cases of bronchitis are caused by ordinary viruses in the upper respiratory tract; antimicrobials only help a fraction of these patients; and it is part of the normal progress of bronchitis that the cough lasts for 2 to 3 weeks and that one in ten patients will still be coughing in the fourth week (32). Patients may be aware and demanding these days, but they are also educated and in most cases willing to accept treatment options that go against their preconceptions if they are well explained and justified (33–34). However, refraining

from prescribing an antimicrobial in a case of lower respiratory tract infection will require a thorough clinical examination, considered use of CRP and lung X-rays, good communication between physician and patient, and the possibility of follow-up. These should be allowed for in health care.

For all this, antimicrobials are still miracle drugs, and we could not do without them. There are no foreseeable inventions in the near future that would replace antimicrobials in the treatment of bacterial infections. Therefore our only option is to aim for optimum use of antimicrobials: always when needed, but never when unnecessary. Indeed, clinical practitioners increasingly bear responsibility not just for the infection patient they are currently dealing with but for future patients, too.

The MIKSTRA programme collected a large amount of information on the use of antimicrobials in outpatient treatment. It also succeeded in guiding the use of antimicrobials towards a more appropriate practice. But there is a lot of work still to do. We must all continue to strive in our everyday jobs and in the areas of drug policy, education and research to promote the optimal use of antimicrobials. We hope that the experiences gained and the knowledge produced in the MIKSTRA programme, including this final report and its online appendices, will help clinical practitioners, researchers, medical teachers, and policymakers in these efforts.

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Appendix 1 MIKSTRA study health centres and their contacts

Health centre	Contact persons and instructor physicians
Asikkalan terveyskeskus	Irja Laaksonen, Urpo Halonen, Marja-Liisa Lehtinen
Espoo, Tapiolan terveysasema	Markku Kanerva, Paula Kohonen-Jalonen, Martti Varimo
Haapaveden terveyskeskus	Anne Niemelä, Terttu Piippo
Haminan seudun ktt. ky.	Anna-Riitta Nummi, Timo Virtanen, Arto Junttila
Helsingin kaupunki: Alppiharjun terveysasema	Liisa Toppila, Jaana Söder, Esa Saarelainen
Helsingin kaupunki: Pihlajamäki-Viikin (e. Latokartanon) terveysasema	Camilla Mårtenson, Tarja Parkkila
Inarin terveyskeskus	Kari Penttilä, Pirkko Muotkajärvi
Joutsenon terveyskeskus	Marjatta Kaitila, Pekka Keränen
Juvan, Puumalan, Sulkavan tk. ky.	Jarmo Lappalainen, Matti Rossi
Jyväskylän kaupungin terveyskeskus	Nils Mirsch, Anneli Kuusinen, Ritva Renko
Kannuksen terveyskeskus	Esa Jaakkola, Sirpa Riihola, Anu Kurikkala
Korpilahden-Muuramen ktt.ky.	Timo Kankaanpää, Ulla Häikiö
Kyrönmaan terveyskeskus ky.	Matti Norja, Raimo Paldanius
Lammin-Tuuloksen ktt. ky.	Markku Helko, Pia Nynäs
Maskun ktt. ky.	Esa Mäkinen, Sirkka-Liisa Hiltunen
Mäntsälän terveyskeskus	Pertti Sopanen, Maarit Nevalainen, Esko Nukari
Mäntän seudun ktt.ky.	Kauko Koivisto, Heini Keinänen
Nilsiän terveyskeskus	Outi Peltola, Heikki Väänänen, Esa Asikainen
Oulun terveyskeskus	Olli Sipilä, Eero Kallio, Leena Korpi
Pirkkalan terveyskeskus	Helena Kallunki, Tiina Salminen, Maire Sonninen, Jouko Hietala
Rovaniemen kaupungin terveyskeskus	Arja Mustamo, Lempi Kukkola, Antti Piiroinen
Rovaniemen mlk:n terveyskeskus	Pasi Tonteri, Anna-Maija Kämä
Salon seudun ktt. ky.	Seppo Junnila, Päivi Salomaa
Seinäjoen seudun terveysyhtymä	Markku Valli, Sirpa Reinilä
Suomussalmen terveyskeskus	Marja-Liisa Laitinen, Tuomo Pääkkönen
Tohmajärven terveyskeskus	Martti Tolvanen, Pirjo Rinne, Markku Savola
Turun terveyskeskus	Pekka Kirstilä, Eero Kitinoja, Eero Vaissi
Ulvilan ktt. ky.	Kyösti Lemmetty, Terttu Hällfors, Tuija Haapaniemi
Valkeakosken terveyskeskus	Marketta Klemola, Paavo Rasilainen
Varpaisjärven terveyskeskus	Anne Behm, Risto Kettunen

Appendix 2 Control health centres and their contacts

Health centre	Contact persons
Alahärmän terveyskeskus	Raimo Rasivirta, Elsi Mäki
Alavuden seudun th.ky.	Vilho Vuotari, Satu Mäkelä
Espoo; Viherlaakson terveysasema	Tuula Arvonen, Eila Erola
Etelä-Pirkanmaan th. ky.	Maarit Varjonen-Toivonen, Tuomo Heinonen
Forssan seudun th. ky.	Eeva Kankaanpää, Aulikki Viljanen
Heinolan terveyskeskus	Tuula Korhonen, Taina Sopanen
Joensuun terveyskeskus	Risto Tillikainen, Irja Kolehmainen
Lahden terveyskeskus	Päivi Visakorpi, Risto Savilahti
Kaakkois-Savon tk.ky.	Anneli Silvennoinen, Timo Virtanen
Kemin terveyskeskus	Erkki Kaukoniemi, Leila Arstio
Keminmaan terveyskeskus	Paula Vuollo, Pertti Sakaranaho
Kiimingin terveyskeskus	Jukka Ulkuniemi, Eeva-Liisa Keskisarja
Kirkkonummen ja Siuntion tk.ky.	Jaana Santaholma, Maisa Liimatainen
Loimaan seudun terveyskeskus	Lari Janatuinen, Maire Toivonen
Luoteis-Satakunnan tk.ky.	Anne Ruusuvuori, Pekka Jaatinen
Porvoon terveyskeskus	Lars Rosenberg, Carola Blommendahl
Raahen seudun terveyskeskus	Liisa Rasi, Antti Hynninen
Saarijärven-Karstulan seudun ktt.ky.	Matti Honkimäki, Pirjo Viitasalo
Sallan terveyskeskus	Paula Narkilahti, Mervi Virkkula
Ylöjärven terveyskeskus	Ulla Mattelmäki, Birgitta Vaittinen

Appendix 3 Indication questionnaire 1998

MIKSTRA – Diagnosis and treatment of infections in primary care 1998

(to be filled in for all patients with infection, independent of therapy decisions)

1. Year of birth _____

2. Gender

[1] female [2] male

3. The consultation is…

[1] an acute consultation (at an outpatient clinic or patient's home)
[2] a scheduled consultation (at an outpatient clinic or patient's home)
[3] a telephone contact

4. Main diagnosis (only the most important one)

[1] otitis media
[2] tonsillitis
[3] sinusitis
[4] pharyngitis
[5] unspecified upper respiratory tract infection (URTI)
[6] acute bronchitis
[7] acute infection exacerbating a chronic pulmonary disease
[8] pneumonia
[9] conjunctivitis
[10] skin/wound infection (incl. abscess, acne, and new contaminated wound)
[11] erysipelas, mastitis or other deep cellulitis
[12] urinary tract infection
[13] helicobacter infection
[14] gastrointestinal infection
[15] sexually transmitted disease (STD)
[16] gynaecological infection
[17] other infection, which _____

5. Duration of the patient's symptoms at the time of consultation

[1] 0 - 3 days
[2] 4 - 7 days
[3] 8 - 14 days
[4] 15 days or more

6. Please tick all diagnostic tests which you prescribed for the patient

[1] only clinical examination
[2] sinus ultrasound
[3] thorax X-ray
[4] sinus X-ray
[5] other X-ray, which? _____
[6] throat/urine rapid test
[7] throat/urine culture
[8] nasopharyngeal culture
[9] other microbiological sample, which? _____
[10] CRP
[11] leucocyte count
[12] other haematological test
[13] serological test
[14] other exams, which? _____

7. Did you refer the patient to hospital or for a consultation?

[1] neither
[2] referred to hospital
[3] admitted to health centre bed ward
[4] referred to a specialist
[5] consulted a GP
[6] consulted a specialist

patient code number _____

8. Did the patient need sick-leave / child care-leave because of the infection?

[1] no [2] yes _____ days (including self-reported sick-leave)

9. Did you prescribe an antibiotic to the patient?
(If you make the decision later, i.e. after the arrival of lab results, please complete this paper then)

[1] no [2] yes [3] the patient already had an antibiotic

10. What kind of expectations did the patient have on antibiotic prescribing?
(Please tick the number that in your opinion best illustrates the patient's expectations)

demanded	wished for	was neutral	was reluctant	resisted
1	2	3	4	5

11. Prescribed antibiotic drug(s) (If duration of treatment differs from that counted from the package size, please indicate also the recommended duration in days)

name of the preparation	strength	dosage	package size	(duration, days)
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____

12. Did any of the following factors influence the choice of the preparation?

[1] (suspected) allergy
[2] previous side-effect
[3] pregnancy/breast feeding
[4] patient's demand

13. Prescribed/recommended other (symptomatic) medication for this infection? (If prescribed, give both package size and duration in days, if only recommended, give duration)

name of the preparation	strength	package size	duration, days
_____	_____	_____	_____
_____	_____	_____	_____

14. Was this consultation…

[1] the first one for this episode of illness?
[2] a later one, how many consultations all together? _____

15. This consultation was provided by

[1] Doctor (identification number) _____ [2] Nurse (initials) _____

Stamp of the health centre

Appendix 4 Indication questionnaire 2002

MIKSTRA – Diagnosis and treatment of infections in primary care 2002

(to be filled in for all patients with infection, independent of therapy decisions)

1. Year of birth _____

2. Gender

[1] female [2] male

3. Does the patient (or a child's parents) smoke?

[1] no [2] yes _____ cigarettes /day

4. The consultation is…

[1] an acute consultation (at an outpatient clinic or patient's home)
[2] a scheduled consultation (at an outpatient clinic or patient's home)
[3] a telephone contact
[4] a scheduled follow-up visit

5. Main diagnosis (only the most important one)

[1] otitis media
[2] tonsillitis
[3] sinusitis
[4] pharyngitis
[5] unspecified upper respiratory tract infection (URTI / common cold))
[6] acute bronchitis
[7] acute infection exacerbating a chronic pulmonary disease
[8] pneumonia
[9] conjunctivitis
[10] skin/wound infection (incl. abscess and new contaminated wound)
[10a] acne
[11] erysipelas or other deep cellulitis
[11a] mastitis
[12] UTI: female uncomplicated cystitis
[12a] UTI: other / complicated
[13] helicobacter infection
[14] gastro-enteritis
[15] sexually transmitted disease (STD)
[16] gynaecological infection
[17] other infection, please specify _____

6. Duration of the patient's symptoms at the time of consultation

[1] 0-3 days
[2] 4-7 days
[3] 8-14 days
[4] 15 days or more

7. Please tick all diagnostic tests and interventions which you did or prescribed for the patient

[1] only clinical examination
[2] sinus ultrasound
[3] thorax X-ray
[4] sinus X-ray
[5] other X-ray, please specify _____
[6] throat/urine rapid test
[7] throat/urine culture
[8] nasopharyngeal culture
[9] other microbiological sample, please specify _____
[10] CRP
[11] leucocyte count
[12] other haematological test
[13] serological test
[14] other tests, please specify _____

8. Did you refer the patient to hospital or for a consultation?

[1] neither
[2] referred to hospital
[4] referred to a specialist
[5] consulted a GP

patient code number _____

9. Did the patient need sick-leave / child care-leave because of the infection?

[1] no [2] yes _____ days (including self-reported sick-leave)

10. What kind of expectations did the patient have on antibiotic prescribing?
(Please tick the number that in your opinion best illustrates the patient's expectations)

demanded	wished for	was neutral	was reluctant	resisted
1	2	3	4	5

11. Did you prescribe an antibiotic to the patient?

[1] no [2] yes [3] the patient already had an antibiotic [4] prescription 'in case'

12. Prescribed antibiotic drug(s) (If duration of treatment differs from that counted from the package size, please indicate also the recommended duration in days)

name of the preparation	strength	dosage	package size	(duration, days)
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____

13. Did any of the following factors influence the choice of the preparation?

[1] (suspected) allergy
[2] previous side-effect
[3] pregnancy/breast feeding
[4] patient's request
[5] re-infection/chronic infection
[6] other, please specify_____

14. Prescribed/recommended other (symptomatic) medication for this infection

name of the preparation	strength	dosage	package size	(duration, days)
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____

15. Was this consultation…

[1] the first one for this episode of illness?
[2] a re-consultation; how many consultations all together? _____

16. Was a follow-up visit recommended?

[1] no
[2] yes, in _____ days
[3] yes, if needed
[4] yes, a telephone contact

17. This consultation was provided by

[1] Doctor (identification number) _____ [2] Nurse (initials) _____
[3] Health assistant (initials) _____

18. Have you participated in MIKSTRA-training? [1] no [2] yes _____ times

Appendix 5 Patient questionnaire

DEAR HEALTH CENTRE PATIENT

We are currently conducting a national study into the treatment of common infectious diseases at Finnish health centres. From this study we aim to gather information which will assist doctors in providing patients with even safer and more efficient treatment.

The opinions and expectations of patients play a significant role in the treatment of common infectious diseases. Therefore, we would like to ask you to tell us, by completing this form, about your views relating to certain aspects of the treatment of common infectious diseases in general, and about your expectations relating to your present appointment at the health centre. If the patient is a child, we would like to ask that his/her parent, or the person accompanying him/her, would reply to the questions. The completion of the form will take less than five minutes.

Any information submitted to us, at the National Agency for Medicines, will be treated in confidence. Your individual replies will not be disclosed to anyone else.

Would you kindly return your completed form to the reply box situated in the reception area.

We would like to telephone some patients 10–14 days after the current appointment to ask about matters relating to their recovery and the treatment episode as a whole. Should you be willing to participate in this follow-up, would you kindly give us your contact information on the enclosed consent form. Your personal data and telephone numbers will be destroyed after the telephone interview, or if you are not chosen to be interviewed, and they will not be disclosed to anyone else.

Thank you for your participation! You are contributing towards making the Finnish health service even better.

Ulla-Maija Rautakorpi
MD, Reseacher in charge
MIKSTRA Project Manager

Erkki Palva
MD, PhD, Research Director
National Agency for Medicines

Health centre stamp _____
October 2000

Date of appointment _____/_____ 2000
In what year were you, or the child attending as the patient, born _____
Are you /is your child? 1 female 2 male

PLEASE REPLY TO THE FOLLOWING QUESTIONS BY DRAWING A CIRCLE AROUND THE MOST APPROPRIATE REPLY/REPLIES.

1. Which of the following symptoms of infection are you, or your child, currently suffering from (you may choose one or more options)?

1. temperature	9. cough
2. muscle pains	10. sharp pain, or other pain, on chest (lungs)
3. ear ache	11. urinary complaint
4. sore throat	12. stomach ache
5. pain or pressure in sinuses	13. ripuli
(on cheeks or forehead)	13. diarrhoea
6. runny nose	14. nausea and/or vomiting
7. stinging/redness of eyes	15. rash
8. discharge from eyes	16. other symptom, please specify _____

2. Which of the above symptoms was/were the main reason for you to seek medical help today? You may choose up to two options. Please indicate your choice(s) by using the numbers from the above list or write down your symptoms.

_____

3. For how long have you, or your child, had these symptoms during this particular illness?

1 0 - 3 days
2 4 - 7 days
3 8 - 14 days
4 15 days or more

4. Have you had previous appointment(s) during this episode of illness and if so, how many appointments have you had before this visit?

1 I have not had any appointment
2 I have had an appointment to see a doctor _____ times
3 I have had an appointment to see a health visitor or a nurse _____ times

5. How ill do you feel that you are at the moment, or how ill do you assess your child to be?

1 very ill
2 quite ill
3 only slightly ill
4 I am /my child is almost or totally symptomless

6. What are your expectations regarding antibiotic treatment for your, or your child's, current infection? (circle the number that best corresponds to your expectation)

I want to have an antibiotic	I would prefer to have an antibiotic	I don't know	I would prefer not to have an antibiotic	I don't want to have an antibiotic
1	2	3	4	5

7. What kind of help are you hoping to receive from the doctor or nurse during this appointment? (one or more options)

1 I need sick leave or leave to look after my child
2 I want to know what is wrong with me / my child
3 I want to have medicine to alleviate the symptoms
4 I want to know whether my / my child's illness needs to be treated at all
5 I would like to have a referral for further investigations at the health centre
6 I would like to have a referral to a hospital
7 I would like to have a referral to a specialist
8 I want to make sure that my /my child's illness is nothing serious
9 I feel that I / my child will need a course of antibiotics

Other, please specify _____

8. WHAT IS YOUR OPINION ON THE FOLLOWING STATEMENTS?

Please circle the reply that best corresponds to your opinion, as follows:

1= fully agree 2 = agree to some extent 3 = don't know
4 = disagree to some extent 5 = fully disagree

Statement	Fully agree	Agree to some extent	Don't know	Disagree to some extent	Fully disagree
One recovers from a cold more quickly with antibiotics.	1	2	3	4	5
Penicillin is just as efficient as other antibiotics.	1	2	3	4	5
Antibiotics become less effective if you take them frequently.	1	2	3	4	5
Antibiotics are not effective against infections caused by viruses.	1	2	3	4	5
Doctors prescribe antibiotics too readily.	1	2	3	4	5
Bronchitis needs always to be treated with antibiotics.	1	2	3	4	5
Unnecessary course of antibiotics will not cause any harm.	1	2	3	4	5
One can prevent himself catching a cold by washing hands well.	1	2	3	4	5

THANK YOU FOR YOUR REPLIES!

CONSENT

I accept that the study personnel may telephone me in order to conduct a telephone interview regarding the success of my treatment.

1 I was the patient myself 2 I was accompanying a child patient

Name _____
in block capitals, please

I can be reached most likely:

during the week at _____a.m. / p.m. Tel: _____-_____
or at _____a.m. / p.m. Tel: _____-_____

at the weekend at _____a.m. / p.m. Tel: _____-_____
or at _____a.m. / p.m. Tel: _____-_____

Date _____/_____ 2000

Signature _____

Please return this form to the reply box situated in the reception area or hand it to the receptionist.

This form with all your personal data will be destroyed after the telephone interview, or if you are not chosen to be interviewed!

Appendix 7 MIKSTRA publications

Articles

International:

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(All-together 50 reports, one for each health centre that participated in the programme, each reporting health centres own results compared to all MIKSTRA and all control health centres)

Conflict of interests

Honkanen, Pekka	No conflict of interests.
Huovinen, Pentti	No conflict of interests.
Klaukka, Timo†	No conflict of interests.
Liira, Helena	No conflict of interests.
Mäkelä,Marjukka	Chief editor of International Journal of Technology Assessment in Health Care and thereby annual funding to Finohta from Cambridge University Press.
Nyberg, Solja	No conflict of interests.
Palva, Erkki	No conflict of interests.
Rautakorpi, Ulla-Maija	Since June 2009 20% work contribution to a pneumococcal vaccination study funded by THL and GlaxoSmithKline.
Roine, Risto	Participated in planning of health economic symposium arranged by Abbot.
Sarkkinen, Hannu	No conflict of interests.