

Johanna Mäkinen

SYSTEMATIC SEARCH AND
EVALUATION OF PUBLISHED
SCIENTIFIC RESEARCH

IMPLICATIONS FOR SCHIZOPHRENIA RESEARCH

FACULTY OF MEDICINE,
INSTITUTE OF CLINICAL MEDICINE,
DEPARTMENT OF PSYCHIATRY,
UNIVERSITY OF OULU



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**SYSTEMATIC SEARCH AND
EVALUATION OF PUBLISHED
SCIENTIFIC RESEARCH**

Implications for schizophrenia research

Academic dissertation to be presented with the assent of
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Abstract

The aim of this doctoral thesis is to present methods of search, evaluation and analysis of a specific research domain (schizophrenia) from four perspectives: bibliometric analysis of 1) Finnish doctoral theses and 2) Finnish journal articles on schizophrenia, and meta-analysis to determine the prevalence of 3) alcohol use disorders and 4) cannabis use disorders in schizophrenia.

Over the years, the number of Finnish articles on schizophrenia has increased, as well as the amount of international collaboration. Bibliometric methods were also found to be feasible in the evaluation of psychiatric research. However, the methods should be used with care. Articles written in collaboration with international organisations seem to receive more citations and are published in journals with higher impact factors, which highlights the importance of developing scientific networks. A considerable proportion (20%) of Finnish scientific schizophrenia articles were published in theses consisting of original papers. The current funding system supports the writing of doctoral thesis consisting of original articles and favours epidemiological and biological research over research into medical treatments. This may affect the research culture in Finland and even slow down the development and improvement of the national treatment system.

The reported prevalence of alcohol and cannabis use disorders has differed considerably between studies. No meta-analysis on alcohol or cannabis use disorders in schizophrenia has previously been conducted. In studies ($n = 71$) on schizophrenia patients, the median prevalence was 15% for current and 26% for lifetime alcohol use disorder, and 16% for current and 27% for lifetime cannabis use disorder. Alcohol use disorders are common in schizophrenia patients, although a declining trend was observed when comparing previous reviews. Cannabis use disorders were found to be more common in younger and first-episode patient samples, as well as in samples with a high proportion of males.

Keywords: bibliometrics, information science, meta-analysis, schizophrenia

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Rovaniemi, September 2010

Johanna Mäkinen

Main concepts

Bibliometrics	study of written documents and their citation influence, a subfield of information science and of statistics
Citation	written reference given to previous work
Critical appraisal	the quality assessment of individual studies that are summarized in systematic reviews, the process of assessing and interpreting evidence by systematically considering its validity and relevance to one's own situations
Impact factor	based on two elements: the numerator, which is the number of citations in the current year to any items published in a journal in the previous two years, and the denominator, which is the number of substantive articles (source items) published in the same two years, varies from year to year
Information science	interdisciplinary science primarily concerned with the collection, classification, manipulation, storage, retrieval and dissemination of information
Meta-analysis	mathematical synthesis of the results of two or more primary studies that addressed the same hypothesis in the same way
Review or narrative review	an attempt to synthesize the results and conclusions of two or more publications on a given topic, usually covering broad topics with the aim of giving a qualitative synthesis on the research results.
Systematic search	a repeatable process proceeding from one phase to the next, including a preparatory phase prior to the actual information retrieval
Systematic review	literature review focused on a single question which tries to identify, appraise, select and synthesize all high-quality research evidence relevant to that question

Abbreviations

AUD	alcohol use disorder
CI	confidence interval
CUD	cannabis use disorder
DSM	Diagnostic and Statistical Manual of Mental Disorders
EVO	Research funds from specified government transfers (<i>erityisvaltiosuus</i>)
ICD	International Classification of Diseases
IQR	interquartile range
NPHI	National Public Health Institute

List of original publications

This thesis is based on the following original publications, which are referred to in the text by the Roman numerals I–IV.

- I Koskinen J, Isohanni M, Kotiranta H, Lauronen E, Koponen H, Tienari P & Miettunen J (2004) Finnish doctoral theses on schizophrenic psychoses – descriptive and bibliometric analysis. *Psychiatria Fennica* 35: 46–67.
- II Koskinen J, Isohanni M, Paajala H, Jääskeläinen E, Nieminen P, Koponen H, Tienari P & Miettunen J (2008) How to use bibliometric methods in evaluation of scientific research? An example from Finnish schizophrenia research. *Nord J Psychiatry* 62: 136–43.
- III Koskinen J, Löhönen J, Koponen H, Isohanni M & Miettunen J (2009) Prevalence of alcohol use disorders in schizophrenia – A systematic review and meta-analysis. *Acta Psychiatr Scand* 120: 85–96.
- IV Koskinen J, Löhönen J, Koponen H, Isohanni M & Miettunen J (2009) Rate of cannabis use disorders in clinical samples of schizophrenia patients: a meta-analysis. *Schizophr Bull.* In press. DOI: 10.1093/schbul/sbp031.

In addition, some unpublished data have been included in this thesis.

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1 Introduction

We live in an era of information explosion. The total body of medical information has been doubling every 5 years (Mattox 2000). Not all information that is available is valid or useful for patient care or feasible for research. Therefore, it is important for general practitioners, for instance, to be familiar with efficient search strategies and research evaluation methods to be able to find relevant new information, whereas it is important for researchers and scientists to be familiar with previous research results. Knowing the basics of information science helps in finding accurate information and new research.

Considerable human and economic effort is invested in scientific work. It is important to evaluate its results and output. Evaluation of scientific research and its quality is also needed in many areas of psychiatric research, such as in financial decision-making and funding, in connection with granting awards, applications, selections and appointments to a post and also international evaluations and decisions on science policy. Methods of information science, such as systematic searching and bibliometrics, are used to systematically obtain information.

A systematic search is a repeatable process proceeding from one phase to the next, including a preparatory phase prior to the actual information retrieval (Corrall *et al.* 2002). Bibliometrics is the science of studying written communication by systematically measuring and analyzing research publications. Bibliometric methods can be used to evaluate methodological aspects of reported studies. A citation is a written reference to a previous work. Garfield's impact factor measures the frequency with which an average article in a journal is cited. (Garfield 1986.) The main concepts and abbreviations of information science are presented at the beginning of this summary part of the thesis.

The use of impact factors in assessing scientific research has been criticized in many contexts (Smith 1998, Adam 2002, West & McIlwaine 2002, Berghmans *et al.* 2003, Kurmis 2003). Nevertheless, since 1994, government funding for medical research conducted in universities and hospitals in Finland has partly been based on research points, with a sliding scale corresponding to the impact factor of the journals in which researchers have published their work (Kekomäki 2001, Adam 2002). This makes it especially interesting to perform bibliometric studies on medical research in Finland.

Meta-analysis is a mathematical synthesis of the results of two or more primary studies that have addressed the same hypothesis in the same way. In

addition to synthesizing numerical data, meta-analysis tabulates relevant information on the inclusion criteria, sample size, baseline patient characteristics, withdrawal rate, and results of primary and secondary end points of all the studies included. (Sterne *et al.* 2001.)

Previous reviews have identified a wide range in the prevalence of alcohol use disorder (AUD) and cannabis use disorder (CUD) in schizophrenia (Mueser *et al.* 1990, Cantor-Graae *et al.* 2001). This large variation may be explained by many factors, such as different study designs and sample characteristics. The outcome and prognosis of schizophrenia patients is affected by the comorbidity of substance use disorders. Although systematic reviews have been published considering the prevalence of substance use disorders in schizophrenia patients, no meta-analysis on these topics has yet been conducted.

In this study the aim was to investigate how the methods of information science can be utilized in psychiatric research. A systematic search and critical appraisal were utilized in different ways. One aim was to assess whether bibliometric methods are feasible in the evaluation of Finnish schizophrenia research. Systematic search and statistical methods were utilized to conduct a meta-analysis on the prevalence of alcohol and cannabis use disorders in schizophrenia.

2 Review of the literature

2.1 Information

The terms data, information and knowledge are often used as synonyms. The main difference is in the level of abstraction being considered. The hierarchical explanation for these three concepts is that data is the lowest level of abstraction, information is the next level, and finally, knowledge is the highest level among all three. (Case 2007.) The General Definition of Information states that information is data + meaning; however, it is difficult to give a simple explanation for this concept due to the diversity of meanings (Floridi 2005).

We live in an era of information explosion. The total body of medical information has been doubling every 5 years (Mattox 2000). In a study of global publication trends in biomedicine, it was found that the number of articles in the Medline database had doubled in 10 years. Biomedical articles are published most actively in North America, Australia and Europe. (Rahman *et al.* 2003.) Not all information that is available is valid or useful for patient care or feasible for research. Therefore, it is important for general practitioners, for example, to become familiar with efficient search strategies and research evaluation methods to be able to find relevant new information, whereas it is important for researchers to be familiar with current research results. Knowing the basics of information science helps in finding accurate information and new research.

2.2 Information science

Information science concerns the collection, classification, manipulation, storage, retrieval and dissemination of information. Information science is a relatively new discipline: in Finland, the first professorial chair was founded in 1971 at the University of Tampere. In Germany and the USA, information science has been a university discipline since the end of the 19th century. (Vakkari 2003.)

Information science is an interdisciplinary science, which occupies a minor role in basic medical studies. Teaching focuses on aspects such as introducing medical databases and conducting searches, which are essential in the work of practitioners and researchers today. Medical databases offer a practical everyday tool for clinicians (Romanov & Aarnio 2006) and make (new) research findings more accessible to researchers (Löhönen *et al.* 2009a). Guides on how to use

medical databases have also been published in Finnish (Romanov 2002, Heikkinen *et al.* 2007).

2.2.1 Systematic search

A systematic search is a repeatable process proceeding from one phase to the next, including a preparatory phase prior to the actual information retrieval (Corrall *et al.* 2002). In research methods the criteria for a systematic search, such as key words, databases used, the language of the searched publications and searched publication types should be presented, along with the date on which the search was conducted. The use of several keywords related to the topic of interest as well as keyword synonyms makes the search more comprehensive. In order to achieve more extensive search results, several databases should be used (Löhönen *et al.* 2009b). When combining search results from different databases, duplicated results should be removed. Other factors that should be taken into account are the years from which data are collected and language limitations. In addition, the publication type should be noted; *e.g.* preliminary results are occasionally published in letters and conference abstracts.

2.2.2 Bibliometric methods

In bibliometrics, systematic measurement and analysis of research publications are used to study written communication. In bibliometric evaluation, information such as the number of publications, impact factors (IF) and the number of received citations is utilized. (Garfield 1986.)

Publication analysis is the predominant type of bibliometric method. Scientific publications are measured and grouped to provide information on the proportion and dispersion over time of a researcher's or institution's research activities (Lewison & Dewey. 1998, Debackere & Glänzel 2004). However, publication analysis is not widely used in the evaluation of psychiatric research.

A citation is a written reference to previous work. The references used in scientific publications are one way of linking new information to prior data, and of acknowledging articles published earlier in the field. A quantitative expression of the utilization, acceptance and visibility of published research in international scientific literature and communication can be provided using citation counts. (Garfield 1986.)

An impact factor is based on two elements: the numerator, which is the number of citations in the current year to any items published in a journal in the previous two years, and the denominator, which is the number of substantive articles (source items) published in the same two years (Garfield 1986). The impact factors of journals are published in the Thomson ISI (Institute for Scientific Information) Journal Citation Reports database and they vary from year to year.

Other commonly used bibliometric indexes also exist that were not applied in this research. The h index is a number that aims to characterize the scientific output of researchers. The index is the x number of articles published over the years and which have received x number of citations (Hirsch 2005). Price's law is widely used in analysis of the productivity of science. According to this law, scientific productivity increases exponentially, so that it doubles every 10 to 15 years. Lotka's law also indicates scientific productivity among researchers. It estimates the number of authors who publish a certain number of articles in certain fields and over a certain time span. Bradford's law is used in studying the distribution of articles in publishing journals. According to this law, articles written in a certain scientific field are concentrated in a small number of publishing journals. Detailed explanations of these laws can be found, *for instance*, in Hubert (1981).

Bibliometrics provide tools that can be applied in research evaluation, but it does not aim to replace qualitative methods with quantitative approaches. Bibliometric methods are not designed to evaluate research results. Traditionally, bibliometrics has measured productivity in terms of publication counts and the visibility of published research in terms of citation counts for individual papers. Bibliometric data are not exclusively used for science policy and funding purposes. In various disciplines, publication and citation data may simultaneously serve very different objectives. For example, information scientists may focus on publications in the context of information management and retrieval systems, sociologists of science use them to study the professional and communal behaviour of scientists, and medical researchers rely on bibliometric data for monitoring and mapping the state of the art in their respective and highly diverse fields. Bibliometric indicators can also be used to trace and track the scientific performance of individuals or groups. Bibliometric data are mainly used to support the justification for allocating research funding and to allow the comparison of scientific input and output in science policy and administration. (Debackere & Glänzel 2004).

Since 1994, government funding for medical research at universities and hospitals (*erityisvaltionosuus* (EVO), research funds from specified government transfers) in Finland has been partly (approximately 55% in 1997–99) based on research points, with a sliding scale corresponding to the impact factor of the journals in which researchers have published their work (Kekomäki 2001, Adam 2002). Articles receive 1 research point if published in journals with an impact factor of 0-1, 2 points if the impact factor is 1-3, and the maximum of 3 points if published in journals with an impact factor greater than 4. One point is received from the summary part of a PhD thesis. Monographs receive six research points. In 2008, one research point corresponded to 4.718,15 euros of funding (Ministry of Social Affairs and Health, decree 31/2009). This makes it particularly interesting to perform bibliometric studies on medical research in Finland. In Europe, bibliometric methods are nowadays also used in some form in Germany (Kaltenborn & Kuhn 2004) and Belgium (Debackere & Glänzel 2004) when making decisions on research funding.

Scientific study on the use of bibliometric methods to investigate the visibility and impact of research in psychiatry is scarce. Ingwersen (2002) analysed the number of articles as well as the number of citations received and assessed the differences between Northern European countries and in the EU, US and world contexts. In his study concerning the visibility and impact of research in psychiatry, he found that the number of internationally published Finnish psychiatric articles has steeply increased, whereas the trend has been a decreasing one in Sweden and Denmark. He also reported that Finnish psychiatric articles have improved their position among EU countries in terms of citations and impact factors. In her Master's thesis, Heikkinen (2005) has investigated the development in the number of scientific articles on schizophrenia published in the Nordic countries or the Netherlands. A comprehensive search was made from six databases (Cinahl, Elsevier Science Direct, Ovid, PsycINFO, Pubmed, Web of Science): the included articles were published in English between 1986–2003. Altogether, 3164 articles were included, of which 29.2% were Swedish, 25.0% Danish, 21.1% Dutch, 14.7% Finnish, 8.2% Norwegian and 1.8% Icelandic. The distribution followed that reported by Ingwersen (2002). The number of published schizophrenia articles has increased in all countries. Among the Nordic countries, the number of schizophrenia articles published annually has increased the most in Finland, being ten times higher in 2003 than in 1986. Finnish schizophrenia articles found to be published in journals with the highest impact factor (3.575), although the difference compared to Danish (3.491) and Swedish (3.374) articles

was not large. In all these countries, the mean impact factor of the publishing journals had decreased slightly during the period 1986–2003. When examining the distribution of the articles, Finnish articles were most often published in journals with high impact factors. (Heikkinen 2005.)

López-Muñoz and his team have examined productivity in Spanish psychiatric research and also conducted bibliometric analyses on biomedical publications concerning antidepressants and bipolar disorder (López-Muñoz *et al.* 1995, 2003, 2006). Leta *et al.* (2001) assessed the central international visibility of Brazilian articles on psychiatric research. Another Brazilian study conducted by Figueira *et al.* (2003) compared Brazilian psychiatric articles published in domestic and international journals. Statistical methods have also been evaluated in psychiatric research (Miettunen & Nieminen 2004).

The use of bibliometric methods in research evaluation is briefly summarized below (modified from original paper II, Table 1). In addition, when utilizing databases in scientific searches, one should be aware of the possible selection bias and its effects on the findings of the conducted search. Selection bias is a systematic bias that occurs in selected samples but not in the whole population of interest. For example, European journals (Nieminen & Isohanni 1999) and psychiatric journals (McDonald *et al.* 1999) may be underrepresented in databases, which may cause bias especially when evaluating research articles from different specialities or countries.

1. General instructions

- In article search an impartial source of data should be used: More accurate results can be received by combining results from several databases.
- Be familiar with the search strategy of the search engine to avoid possible sources of error in the search process.
- Informaticians can be consulted for instructions.

2. Publication analysis

- **Impact factor** of the publishing journal should be considered as an estimate of article visibility.
- Impact factors in different years can be reached via Journal Citation Reports (www.scientific.thomson.com/products/jcr). The journals are categorized by subject, publisher and country.

- When analyzing the received **citations** more accurate information can be revealed about the visibility gained and placing within the specific scientific network.
- The number of received citations can be reached via Web of Science (www.scientific.thomson.com/products/wos) by choosing the cited reference search.
- Other databases presenting citations are e.g. SCOPUS (www.scopus.com) and Google Scholar (www.scholar.google.com).
- When analyzing the number of received citations of a single article the time-span for citations should be recognized.
- If possible self-citations, should be excluded and the quality of all citations checked.

Bibliometric methods can be used as an easily available proxy of productivity and visibility when evaluating research. However, objective evaluation of research quality in particular is extremely difficult. Subjecting research to evaluation by expert opinions and panels is one method of evaluating research quality, *e.g.* when making decisions on funding and awards. However, there are certain limitations involved in this method that should be recognized. In addition to being costly and requiring considerable time, expert panels consist of specialists whose expertise is confined to a rather narrowly specified area. Especially in countries with a small population (*e.g.* Finland) and in specified research fields, objective evaluation may therefore be difficult, because there is a high likelihood of collaboration and, on the other hand, competition for the same grants. Impartial and often international evaluation is particularly needed in these circumstances and bibliometric methods provide a tool for this purpose.

2.2.3 Limitations of bibliometric methods in research evaluation

The original intention of impact factors was to allow comparison between the citation rates of journals (Garfield 1999). The impact factor system and its application in the evaluation of scientific research has been criticized in many ways. An impact factor does not measure the visibility of an individual article published in a journal: it simply measures the mean number of citations of an average article appearing in the publishing journal (Smith 1998, Kurmis 2003, Ministry of Social Affairs and Health 2006). There is little correlation between the number of times an individual article may be cited and the impact factor of a

journal (Seglen 1997, Smith 1998). In addition, the articles that are considered in calculating the impact factor of a journal are poorly determined. Journal Citation Reports define source items as being original research papers, technical notes, and reviews and papers presented as proceedings, and the denominator of the impact factor calculation is solely made up by these. Non-source items, including letters, news stories, abstracts, book reviews, and editorials, are not included in the denominator of the impact factor equation but may be included in the numerator. In the calculation of impact factors, reviews and original articles are not separated, although reviews usually receive more citations (Seglen 1997, Bloch & Walter 2001). The impact factor system uses a short citation window that counts received citations from only one year. Many important papers achieve their scientific impact outside of this time frame, and several factors affect the immediate received impact in the scientific world (Kurmis 2003). It has also been noted that impact factors assigned to studies conducted in the United States have been approximately 30% higher than those given to publications in the rest of the world and there was found to be bias towards journals published in English, which received higher impact factors (Seglen 1997). The impact factor system is not applicable in the comparison of different research areas or specialities, and it favours major specialities and rapidly developing research areas (Seglen 1997, Kurmis 2003, Ministry of Social Affairs and Health 2006).

Citation counts have also received their share of criticism. In studies on different fields in medicine it has been reported that a high number of citations seems to reflect the geographical region of the study rather than study quality evaluated by experts (West & McIllwaine 2002). In addition, a journal's authors seem to prefer citations in the national language of the journal (Seglen 1997). American studies as well as trials reporting positive findings were found to receive more citations (Berghmans *et al.* 2003). The database also has an English language bias (Seglen 1997).

Self-citations can be made by journals and authors. Authors' self-citations are assumed as either a neutral form of reporting, not unlike references to others' work, or as an unsavoury kind of academic egotism (Hyland 2003). More sophisticated citation content analysis takes time but also reveals, in addition to self-citations, how frequently authors have cited the article to refute, support, apply, compare or just to make note of a concept (Garfield 1983). Controversial studies may receive a notable number of critical or negative citations. (Garfield 1978).

Journal Citation Reports contains information about the impact and influence of scholarly journals. It has been published by Thomson ISI since 1975. In addition, Journal Citation Reports annually releases the impact factors of scientific journals. Journal Citation Reports also contains information on journals' self-citations. Journals that are leaders in the field publish consistently high quality papers and often have unique subject matter, and self-citations in these journals are therefore not unusual. However, selective journal self-citations have been claimed to be a problem in impact factor-based evaluation. In a study by Thomson Scientific from the Journal Citation Reports data it was found that the self-citation rate shows only a weak correlation with the impact and subject of a journal. The removal of self-citation resulted in significant changes in the quartile rank in only a small proportion of journals, and there was a greater dependence on the contribution of self-citations in some journals with lower impact factors. (www.scientific.thomson.com).

Although criticism has been levelled against the utilization of bibliometric methods in evaluation of scientific research, such methods are still used in Finland, for instance, when making decisions on research funds from specified government transfers. Concern has been raised about the negative effect of EVO funding on the number of national research projects or the number of articles published in Finnish medical journals, for example (Ministry of Social Affairs and Health 2006). Due to criticism against the current scientific research funding system the Ministry of Social Affairs and Health organised a working group to develop alternative strategies for research funding in 2006. The working group proposed the establishment of a national advisory committee on health science research under the Ministry of Social Affairs and Health. The committee should formulate a strategy for health science research based on the development objectives and guidelines defined for health care by the Government. Eighty per cent of the total amount of funds should be allocated to research centres based on the profitability of their research and 20% based on the plan. The profitability of the research is to be evaluated based on the number and quality of publications, paying particular attention to the effectiveness of the research. In the future, the role of impact factors may not be as marked in Finland as today. (Ministry of Social Affairs and Health 2006.)

2.3 Narrative and systematic review

A review is the generic term for an attempt to synthesize the results and conclusions of two or more publications on a given topic. Narrative reviews often cover broad topics and aim to give a qualitative synthesis of previous research. (Cook *et al.* 1997.) Articles are searched and summarized and clues for practice suggested from the conclusions. However, bias in the collection (collection bias), appraisal and summarizing of information may lead to problems in reviews (Blettner *et al.* 1999). These factors are taken into account in systematic reviews.

Contrary to a narrative review, a systematic review focuses on a single question. It summarises evidence relevant to that question and uses explicit methods to perform a thorough literature search and critical appraisal of individual studies to identify the valid and applicable evidence. Sometimes, statistical methods (meta-analysis, which is presented in detail below) are used in systematic reviews to pool the results of valid studies, or the level of evidence is graded depending on the methodology used. The aim of a systematic review is to minimize bias through an objective and transparent approach to research synthesis, which includes details of the methods used, a reproducible systematic search and critical appraisal (Cook *et al.* 1997.)

Part of a systematic review is critical appraisal, which is the quality assessment of individual studies that are summarized in systematic reviews. In a critical appraisal, evidence is assessed and interpreted systematically and its validity and relevance to the particular question is considered. (Fowkes & Fulton 1991). Checklists in critical appraisal are recommended for evaluating the inclusion of studies and different checklists exist for different study settings and article types (Cook *et al.* 1995, Moher *et al.* 2000, Stroup *et al.* 2000, Altman *et al.* 2001, Vandembroucke *et al.* 2007).

While the number of published scientific research articles is constantly increasing in medicine and there is variation in the quality of research, exhaustive presentation and critical appraisal skills are relevant for all those involved in the process of presenting their own results and transferring research findings into practice, *e.g.* general practitioners and researchers. The number of systematic review articles published in medical journals is constantly increasing, in addition to the number of articles about review methods and empirical studies of the methods used in reviews (Moher *et al.* 2007). The Cochrane Collaboration has also exposed experienced clinicians to the utilization of systematic reviews.

The Cochrane Collaboration (www.cochrane.org) is an international collaboration preparing, maintaining and promoting the accessibility of systematic reviews of the effects of healthcare interventions. Named after the British epidemiologist, Archie Cochrane, the Cochrane Collaboration was founded in 1993. The Cochrane Collaboration has limited its remit to reviews of the effects of health care interventions. The Cochrane Library is the first large-scale, multidisciplinary product of this collaboration, and it is updated quarterly (Cook *et al.* 1997). Each year about 300 new Cochrane reviews are published. (www.cochrane.org). A Canadian research group assessed in their review of 300 studies how well the methods of systematic reviews were reported. The standards varied widely and not all systematic reviews were equally reliable. The authors stated that the situation could be improved by a widely agreed upon set of standards and guidelines. (Moher *et al.* 2007). Some guidelines have already been presented. For example, the Cochrane Handbook for Systematic Reviews of Interventions contains precise methodological guidance for the preparation of a systematic review on intervention studies. Guidance on updating a systematic review is also available (Higgins & Green 2009). It has been found that of 100 guidelines reviewed, 4% required updating within a year and 11% after 2 years. As expected, this need was more prominent in rapidly-changing fields of medicine. At the time of publication as many as 7% of systematic reviews needed updating. (Shojania *et al.* 2007.)

2.4 Meta-analysis

A meta-analysis is a mathematical synthesis of the results of two or more primary studies that addressed the same hypothesis in the same way. Meta-analysis can synthesize numerical data, tabulate relevant information on the inclusion criteria, sample size, baseline patient characteristics, withdrawal rate and the results of primary and secondary end points of all studies. (www.cochrane.org/, Sterne *et al.* 2001.)

Decisions about the utility of an intervention or the validity of a hypothesis should not be based on the results of a single study, because the design, study samples and results typically vary from one study to the next. Rather, a mechanism is needed to synthesize data across studies. Narrative reviews have been used for this purpose with certain difficulties. A narrative review usually covers broad topics and it might be difficult to find the answer to a specific question. The search and study selection is not usually specified, which often

makes a narrative review subjective. Syntheses of narrative reviews are often qualitative summaries. (Cook *et al.* 1997.) In meta-analysis, objective mathematical formulas are applied and the methods can also be used within a small number of studies (www.cochrane.org).

A meta-analysis combines the results of several studies that address a set of related research hypotheses. Karl Pearson introduced meta-analysis for the first time in 1904. It was developed as a statistical method that would overcome the problem of reduced statistical power in studies with small sample sizes. (Pearson *et al.* 1904). The first meta-analysis of a medical treatment was published in 1955. (Bangert-Drowns 1986.)

A weakness of the meta-analytic method is that sources of bias are not controlled by the method. A good meta-analysis of poorly designed studies will still result in poor overall estimates and conclusions (Cochrane Collaboration). Guidelines for conducting meta-analysis have been presented both for interventions (Cook *et al.* 1995) and observational studies (Stroup *et al.* 2000.), which provide checklists in order to improve the quality of included studies. Arguments for including only methodologically sound studies have been presented. (Slavin 1986). However, by using a study-level predictor variable that reflects the methodological quality of the studies, the effect of study quality on the effect size can be investigated. Metaregression is a statistical method that takes into account different study factors (*e.g.* study quality or sample age) in meta-analysis (Sterne *et al.* 2001). Another weakness of meta-analysis is that synthesis is strongly based on published studies. This may increase the effect due to publication bias. As it is more difficult to publish studies that show no results, publication bias should be taken into account when interpreting the outcomes of meta-analysis. (Blettner *et al.* 1999.) So-called funnel plots can be used to estimate possible publication bias (Sterne *et al.* 2001).

Traditionally, meta-analyses have been conducted on clinical trials or interventions. However, meta-analyses are nowadays also conducted on observational studies. Observational meta-analyses can typically concern risk estimations (Moore *et al.* 2007) or prevalence or incidence (McGrath *et al.* 2004, Saha *et al.* 2005). In observational studies, the diversity of studies and study populations may sometimes create a challenge in a meta-analysis. However, these factors can be taken into account by using specially developed methods such as metaregression analysis.

2.5 Publishing forums

2.5.1 Scientific journal articles

Scientific journals are important forums for new information. The most important difference between journals and scientific journals is that articles in scientific journals are peer-reviewed in an attempt to ensure that they meet standards of quality and scientific validity required by the journals and scientific community. The publication of the results of research is an essential part of scientific practice.

2.5.2 Doctoral theses

The role of the doctoral thesis has changed during the history of medicine. In the 19th century it was still compulsory to defend one's thesis to achieve the position of a legalized doctor in Finland. (Ignatius & Nuorteva 1999). Today, the doctoral thesis plays a central part in attaining the doctoral degree in Finnish scientific continuous education; by January 2008, 20.6% (n = 3 859) of Finnish physicians had been awarded a doctoral degree (www.laakariliitto.fi). A considerable proportion of Finnish medical research (including that on schizophrenia) is published in doctoral theses.

The process of preparing and defending a doctoral thesis is nowadays rather structured. Legislation states that to be awarded a doctoral degree a doctoral student must have completed general scientific studies, demonstrate critical and independent scientific thinking, and prepare a doctoral thesis and publicly defend it (Government Decree on University Degrees Chapter 5, Section 22). Two possible forms of doctoral thesis exist: a monograph and a doctoral thesis consisting of a series of papers.

The scientific process is guided by formal supervisors, usually two. The research plan and final phases of the manuscript are evaluated by the faculty in many phases of the process, as described in the instructions for the referees of doctoral dissertations of at the University of Oulu (www.medicine oulu.fi), for example. In Finland, psychiatrists are not very active in scientific continuous education. According to the website of the Finnish Medical Association, in January 2008 only 121 (13%) out of 908 psychiatrists had completed a doctoral degree (www.laakariliitto.fi). The proportion was higher in other major specialities in medicine, being 26% in internal medicine and in 44% neurology, for example.

Monographs

A monograph is a scientific presentation only in the name of the doctoral candidate, which is based on previously unpublished results from independent research. A monograph (a single book) was especially common before the 1990s. Since then the vast majority of theses have consisted of a series of papers. However, the monograph form is still used, especially if the topic is national or the results are otherwise not easy to publish in international scientific publications. The form of a monograph is also used if the topic is difficult to divide into 4-5 original publications dealing with the same topic or problem. Knowledge of the existence of theses is important, as older monographs, in particular, are not usually included in international scientific databases.

Doctoral theses consisting of a series of papers

The Government Decree on University Degrees Chapter 5, Section 22 (Ministry of Social Affairs and Health 2004) states that original publications in a doctoral thesis should be individual scientific publications that consider the same research subject or topic of the doctoral thesis. These publications can include joint publications, provided that the candidate has demonstrably played an independent part in their production. The summary part of the doctoral thesis consisting of a series of papers is always written by the doctoral student. Only publications published in peer-review journals can be part of the doctoral thesis. Although legislation regulates the policy of original publications in doctoral theses in Finland on a general level, there are some minor differences in publication policies between the five universities having a Faculty of Medicine (the Universities of Helsinki, Kuopio, Oulu, Tampere and Turku). However, every application at every university is evaluated by the Faculty Board and its Thesis Subcommittee, although the actual evaluation policy may differ between the universities.

2.6 Schizophrenia

In this study, schizophrenia research was used as an example to present systematic search methods and the utilisation of bibliometric methods in research. Schizophrenia is a severe and actively studied mental illness that still partly remains a scientific mystery. The symptoms of schizophrenia are often

categorized into positive (*e.g.* hallucinations, delusions, bizarre behaviour, derailment, flight of ideas, and illogicality) and negative symptoms (*e.g.* flattened affect, impaired attention, poverty of speech, apathy, and asociality). The highest risk for developing schizophrenia is in early adulthood. Schizophrenia is ranked within the top five causes of disability and it is considered to be one of the leading unsolved disorders affecting humans. (Hirsch & Weinberger 2003.) A considerable amount is presently known about schizophrenia, and the amount of knowledge is constantly increasing, schizophrenia being a central subject of psychiatric study. Schizophrenia is a relatively common illness in Finland: in a register-based study the prevalence was estimated to be 0.7–1.5% (Arajärvi *et al.* 2005), and the lifetime prevalence for schizophrenia in the general population has been found to be 0.87% (Perälä *et al.* 2007). Hence, there is also a long and extensive study culture on schizophrenia. In addition to the author's scientific interest, the extent of schizophrenia research in Finland enabled the presentation of bibliometric methods in research evaluation. Due to limited resources, the evaluation of research conducted in all medical specialities or in the Nordic countries rather than only the main Finnish scientific organizations was not possible at this point, but they do, however, offer new research possibilities for the future.

2.7 Schizophrenia and alcohol use disorders

Disorders associated with alcohol are caused by the consumption of alcohol over a period of time and in ways that lead to problems with health, personal relationships, or work (ICD-10, DSM-IV). In this study, alcohol use disorders were considered to include diagnoses of alcohol abuse and alcohol dependence. However, alcohol intoxication and alcohol withdrawal can also be categorized in these disorders.

In DSM-III-R, the diagnosis of alcohol dependence includes both physiological and behavioural symptoms, whereas alcohol abuse is a residual category for diagnosing those who do not meet the criteria for dependence, but who drink despite alcohol-related physical, social, psychological, or occupational problems, or who drink in dangerous situations. In DSM-IV, alcohol abuse criteria also include drinking despite recurrent social, interpersonal, and legal problems as a result of alcohol use and the criteria for dependence have become stricter. DSM-III and ICD-9 differ greatly, whereas DSM-IV and ICD-10 have been developed into more compatible systems, although differences still exist. ICD-10 does not

differ greatly in terms of dependence diagnosis from DSM-IV diagnostics. Alcohol use that causes either physical or mental damage in the absence of dependence is categorised in ICD-10 as harmful use. This category highlights the somatic problems related to alcohol use more than DSM-IV's abuse diagnosis. These medical conditions usually appear in older age, which may lead to underdiagnosis in younger populations in the case of ICD-10 (Kaczynski Pollock *et al.* 2000, Hiller 1989).

Alcohol use disorders (AUD) are common in patients with schizophrenia. Previous systematic reviews have reported a wide range (12–55%) in the prevalence of AUD in schizophrenia (Mueser *et al.* 1990, Cantor-Graae *et al.* 2001). Previous studies published between 1960–1989 were reviewed by Mueser *et al.* (1990) and those from the period 1990–2001 by Cantor-Graae *et al.* (2001). Both reviews presented results from several substances and the included studies varied greatly in their methodological, diagnostic and sample characteristics. However, it remains unclear how these factors affect the prevalence of AUD in schizophrenia or what is the overall estimate of the AUD prevalence in schizophrenia patients. No meta-analysis on this topic has yet been conducted.

There are several reasons why it is important to examine AUD in schizophrenia. There is strong evidence that comorbid AUD worsens the clinical outcome in schizophrenia patients: they have more psychotic symptoms and more severe depressive symptoms (Potvin *et al.* 2006, 2007), poorer treatment compliance, increased somatic morbidity, a risk of violence, criminality and suicides, more negative psychosocial events such as divorce and unemployment, more admissions and longer hospitalization periods. Taken together, in addition to adding to individual suffering, they also increase the costs of treatment (Drake and Mueser. 1996, Dixon 1999, Gregg *et al.* 2007).

2.8 Schizophrenia and cannabis use disorders

Cannabis use disorders include disorders caused by all substances with psychoactive properties derived from the cannabis plant in addition to chemically similar synthetic substances. A diagnosis of cannabis dependence in the ICD and DSM includes both physiological and behavioural symptoms, whereas cannabis abuse in the DSM and harmful use of cannabis in the ICD indicate cannabis use irrespective of substance-related physical, social, psychological, or occupational problems or cannabis use in risky situations. Cannabis is one of the most commonly used addictive substances among patients with schizophrenia.

Previous systematic reviews have found a wide range (13%-45%) also of cannabis use disorder prevalence in schizophrenia (Mueser *et al.* 1990, Cantor-Graae *et al.* 2001). It remains unclear what the overall estimate of cannabis use disorders prevalence is in schizophrenia patients.

Cannabis use may provoke psychotic symptoms; for example, DSM-IV includes a diagnosis of cannabis-induced psychotic disorder. It has also been found that individuals who have ever used cannabis have an increased risk of any psychotic outcome. However, the role of cannabis use in the onset, course and clinical expression of schizophrenia is not clear (Moore *et al.* 2007). It has been found that schizophrenia patients who use cannabis are younger (Hambrecht & Häfner 2000) and have more psychotic relapses (Dixon 1999). It has also been suggested that schizophrenia patients are more vulnerable to the effects of tetrahydrocannabinoid, which is the CNS-active compound of cannabis (Gregg *et al.* 2007). Cannabis use has been reported to increase positive symptoms in schizophrenia (Gregg *et al.* 2007, Talamo *et al.* 2006, Stefanis *et al.* 2004), while the findings have been contradictory regarding negative symptoms (Gregg *et al.* 2007, Talamo *et al.* 2006, Compton *et al.* 2007). In a recent systematic review, Zammit *et al.* (2008) examined the effects of cannabis use on the outcomes of psychotic disorders. They found an association with increased relapse and non-adherence. The reported findings were more disparate regarding the severity of symptoms.

Only studies reporting the rates of cannabis use disorders according to the DSM (Diagnostic and Statistical Manual of Mental Disorders by the American Psychiatric Association) or ICD (International Classification of Diseases by the World Health Organization) diagnostic systems were included in this meta-analysis. In DSM-III-R, the diagnosis of cannabis dependence includes both physiological and behavioural symptoms, whereas the diagnosis of cannabis abuse is a residual category for diagnosing those who do not meet the criteria for dependence, but who use cannabis despite substance-related physical, social, psychological or occupational problems, or who use cannabis in dangerous situations. In DSM-IV, cannabis abuse criteria also include substance use despite recurrent social, interpersonal and legal problems as a result of cannabis use and the criteria for dependence are stricter. In the diagnostics of substance use disorders, DSM-IV and ICD-10 have been developed into more compatible systems, although differences still exist. ICD-10 does not differ greatly from DSM-IV diagnostics in terms of the dependence diagnosis. Cannabis use that causes either physical or mental damage in the absence of dependence is

categorized in ICD-10 as harmful use. This category highlights the somatic problems related to cannabis use more than the abuse diagnosis of DSM-IV.

2.9 Summary of the literature

The previous literature on the topic of this thesis can be summarized briefly as follows. Knowledge of the basics of information science has become increasingly important in medicine, as the amount of new information is constantly increasing. The methods of information science can help doctors and medical researchers to find relevant information on the current status of research and existing knowledge, although it is important to understand the limitations of certain methods. In medicine, systematic reviews and meta-analyses are particularly used for pooling results and research findings and are considered as a strong form of medical evidence. Bibliometric methods are used in the evaluation of scientific research in Finland especially in medicine. Part of state funding to universities is nowadays also distributed based on impact factors. In meta-analysis, a systematic search is utilized to pool studies on a specific topic. Alcohol use disorders are common in schizophrenia patients. In addition, cannabis is one of the most commonly used addictive substances among patients with schizophrenia. There is strong evidence of the negative effect of AUDs on the outcome of patients, but in CUD the findings have been more disparate. No meta-analysis on the prevalence of AUD and CUD in schizophrenia has previously been conducted and there is no agreement on the overall prevalence.

3 Aims of the study

The overall aim of this study was to present the methods of search, evaluation and analysis in a specific research domain, namely schizophrenia, from two perspectives: bibliometric analysis of Finnish journal articles and doctoral theses on schizophrenia, and meta-analysis of the prevalence of alcohol and cannabis use disorders in schizophrenia. The main contents of the study are presented in four original publications (referred to by the Roman numerals I - IV)

The specific aims of the original articles were to:

1. Study the bibliometric characteristics and form of Finnish theses concerning schizophrenia, and evaluate the proportion of new scientific information on schizophrenic psychoses published in doctoral theses in different Finnish universities (I);
2. Describe bibliometric methods and provide practical clues as to how they can be utilized in evaluation, and discuss whether bibliometric methods are feasible when studying differences in publication profiles between institutions (II);
3. Systematically collect and review studies published in 1996–2008 on AUD in schizophrenia, using meta-analysis to estimate the overall prevalence of AUD in schizophrenia, and assess how study design and sample characteristics affect the prevalence of AUD in schizophrenia patients (III);
4. Systematically collect and review studies published in 1996–2008 on CUD in schizophrenia, estimate the current overall prevalence, and determine how study characteristics affect the prevalence of CUD in schizophrenia (IV).

4 Material and methods

4.1 Systematic searches

4.1.1 Finnish doctoral theses on schizophrenic psychoses: descriptive and bibliometric analysis (I)

One aim of this study was to locate all Finnish doctoral theses on schizophrenic psychoses. Theses presenting specific results on schizophrenia and related psychoses and with the major part of the sample consisting of individuals with a schizophrenia diagnosis were included. The inclusion or exclusion of theses that were difficult to categorize as schizophrenia studies was discussed among the study group. In theses consisting of a series of papers, at least one of the publications had to concern schizophrenic psychoses.

Searches were conducted from Finnish databases (Medic and Finnish University Library Databases). Duplicated references were eliminated manually. A manual search was made from the bibliography (Österman 1989) and from the lists of doctoral theses offered by the websites of Finnish universities. Furthermore, various departments (psychiatry, psychology, nursing sciences) of all Finnish universities were contacted. Finnish doctoral theses on schizophrenia were searched up to May 2005 and for descriptive purposes the search was updated for this summary part in July 2008.

In addition, data were collected from the Web of Science for the years 1994–2005 to examine the proportion of articles published in doctoral theses and their influence on new scientific information. “Schizophrenia” was used as a keyword. All the articles with a Finnish corresponding organization were included.

Finnish theses on schizophrenia were presented divided into monographs and theses consisting of a series of papers. From all the theses, information on the name of the doctoral student, year of publication, publishing university and department, language, title and key results was collected. For original articles, the range of years of original publications was also presented.

4.1.2 Bibliometric analysis of Finnish scientific journal articles on schizophrenia (II)

The articles were collected using the Web of Science database (Thomson ISI). The search was conducted from the abstract, title and keywords. In order to identify Finnish schizophrenia studies, the search term used was the following: “TS = (schizophreni*) AND AD = (Finland)”. The search was limited to English-language journal articles only, published between 1996–2005. The first author and institution of the article was defined by the corresponding address given in the Web of Science database. Altogether, 456 articles were found. In order to specify the search of articles, an impartial search from the title and author-given keywords was conducted, as the original search results also included articles in which, for example, “schizophreni*” was only mentioned as a keyword of the references of the articles (a so-called “Keyword Plus”). “Schizophreni*” had to be mentioned in the article’s title or author-given keywords. Altogether, 265 articles met these additional criteria and were included.

The usefulness of the Web of Science database was validated, and six other international databases (CINAHL, EBSCOhost, Elsevier, Ovid, PsycINFO, PubMed) and three Finnish databases (Aleksi, Arto, Medic) were also searched for articles using similar criteria. Duplicated references were eliminated manually.

4.1.3 Meta-analysis on the prevalence of alcohol and cannabis use disorders in schizophrenia (III & IV)

The recommendations of Meta-analysis of Observational Studies in Epidemiology (MOOSE) (Stroup *et al.* 2000) were used as guidelines when conducting these studies. In order to find articles reporting the prevalence of AUD and CUD in schizophrenia published in 1996–2008 as extensively as possible a search using three electronic databases (PsycINFO, PubMed and Web of Science) was conducted. Several searches were conducted, the latest in January 2009. The keywords used were “schizophreni*”, “psychosis”, “psychoses” and “psychotic” to locate studies on schizophrenic psychoses and “alcoholism”, “alcohol abuse”, “alcohol dependence”, “alcohol use disorder”, “cannabis abuse”, “cannabis dependence”, “cannabis use disorder”, “substance use disorder”, “substance abuse”, “substance dependence” and “dual diagnosis”. Duplicated references were manually eliminated. Altogether 3,323 articles were retrieved, and their abstracts and titles were analyzed. Of these, 611 were identified as possibly

relevant, and their full texts were analyzed in detail. The inclusion of each article was independently evaluated and agreed upon.

In addition, a manual literature search was performed for the same time period from the journals *Acta Psychiatrica Scandinavica*, *American Journal of Psychiatry*, *Archives of General Psychiatry*, *British Journal of Psychiatry*, *Journal of Clinical Psychiatry*, *Psychiatry Research*, *Schizophrenia Bulletin*, *Schizophrenia Research*, and *Social Psychiatry and Psychiatric Epidemiology*. These journals were selected because they had published a considerable proportion of the articles included (approximately 40%) on this topic based on the systematic database search and they were available for evaluation. Manual search found altogether 6 articles that met the inclusion criteria and were not found in electronic search. Also approximately 30 authors were contacted to obtain unpublished data.

The inclusion criteria published in studies in the collection were that (1) at least 80% of the participants were individuals with a schizophrenia-spectrum diagnosis (schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder). Results from studies reporting findings from several psychiatric classifications were also included if they had determined the prevalence of AUD or CUD in schizophrenia-spectrum patients alone. Other inclusion criteria were the following: (2) the study reported on the prevalence of AUD or CUD, (3) the subjects were older than 16 years, and (4) the study sample included more than 15 participants. Only articles (5) reporting schizophrenia and AUD or CUD diagnoses according to the DSM or ICD criteria and (6) written in English were included. Studies with samples that might have biased the present prevalences of AUD and CUD in the study (eg. samples recruited from prisons, forensic psychiatry units, or homeless shelters) were excluded. Trials and intervention studies were also excluded.

4.2 Variables

4.2.1 Bibliometric analysis of doctoral theses (I)

The number of monographs and theses consisting of a series of papers from seven Finnish universities (Åbo Akademi, Helsinki, Jyväskylä, Kuopio, Oulu, Tampere and Turku) as well as mean impact factors and mean citations of theses consisting of a series of papers were presented. Citations were collected from the Web of

Science database on 2 May 2005 for the original articles and updated for this study on 1 July 2008. The impact factors of the publishing journals of the Finnish articles on schizophrenic psychoses were examined. Impact factors vary from year to year, and we used the impact factor for the specific publication year of the original article. The proportion of Finnish schizophrenia articles published in doctoral theses by the corresponding organization was determined. The organizations were categorized into the seven major universities mentioned above, the National Public Health Institute (NPHI; currently National Institute for Health and Welfare) and other organizations.

4.2.2 Bibliometric analysis of Finnish scientific journal articles on schizophrenia (II)

The articles were retrieved using the Web of Science databases. Citations were collected on 20 December 2006. As the articles were published over a long period of time, the effect of the time taken to receive citations was eliminated by using quartiles of articles determined by the amount of citations for each year of publication. Highly cited articles were defined as those being in the approximate upper quartile in each year of publication. Cut-offs were also determined so that the number of citations required for the highly cited category did not increase on follow-up. The organizations were categorized into the five major universities (Helsinki, Kuopio, Oulu, Tampere and Turku), the NPHI, other Finnish organizations and non-Finnish organizations. Other Finnish organizations included central hospitals, the National Research and Development Center for Welfare and Health and the Finnish Institute of Occupational Health.

The impact factors of the publishing journals were collected from the ISI Journal Citation Reports database. The specific impact factor for the publication year of each article was used. Journals with an impact factor >4 were defined as having a high impact factor. This was based on the research funding system currently used in Finland (Kekomäki 2001). In 2005 there were 11 psychiatric journals in the Web of Science having an impact factor greater than 4.

Psychiatric sub-fields of the studies were determined by the author of this thesis. Each study was exclusively classified into one category that best described the content of the article in question. The following classification was used: clinical-epidemiological, psychopharmacological and biological topics. Clinical-epidemiological articles also included aetiological (non-biological) articles as

well as articles on rehabilitation and treatment, while biological topics included genetic and imaging studies, for example.

4.2.3 Meta-analysis on the prevalence of alcohol and cannabis use disorders in schizophrenia (III & IV)

Information on the diagnostic system used was collected. Studies on AUD and CUD have mainly used the DSM and ICD diagnostic systems and in this study only papers using these diagnostic systems were included. In this study the terminology of AUD and CUD is adopted from the DSM diagnostic system (abuse and dependence). It was compared whether, the diagnostic system (ICD-9, ICD-10, DSM-III-R or DSM-IV in AUD; and ICD-10, DSM-III-R or DSM-IV in CUD) used had an effect on the presented prevalences. For schizophrenia the criteria differ mainly in terms of duration of psychotic symptoms: in ICD the symptoms should last 1 month and in DSM 6 months before the diagnosis is made.

Prevalences between first-episode and long-term patient samples were compared, separately for current and lifetime diagnoses. The average duration of illness was determined from the studies; the minimum average duration reported was 9 years. All these studies were categorized as long-term patient samples. In addition, the study location was determined and whether the sample consisted of inpatients or outpatients. Information on gender distribution, proportion of schizophrenia patients, mean age and age range were collected when reported.

4.3 Statistical methods

4.3.1 Bibliometric analyses (I & II)

The results were presented as frequencies and percentages. The mean value of impact factors and citations was reported from each research organization. In original study III, the articles were categorized into three groups. To estimate the reliability of the classification, two of the researchers (Johanna Mäkinen and Hannu Koponen) independently classified 25 randomly selected articles. Twenty-two (88%, $\kappa = 0.80$) of these 25 articles were classified in the same category by them. In original article III, the annual number of publications for the research

organizations was examined using a three-year median due to the small numbers of publications.

4.3.2 Meta-analysis on the prevalence of alcohol and cannabis use disorders in schizophrenia (III & IV)

The number of studies is presented as well as the mean, standard deviation, median, inter-quartile range (IQR), and range for prevalence estimates of AUD and CUD in each of these variables of interest. The heterogeneity was studied using Cochran Q statistic (Sterne *et al.* 2001). Due to statistically significant heterogeneity random mean estimates, which is a conservative weighting method giving the same weight to all studies, are presented. When evidence is found of heterogeneity in the prevalence estimates between studies, metaregression with z test can be used to analyse the association between prevalences and study characteristics. (Sterne *et al.* 2001.) Metaregression was used to compare the effect of diagnostic systems (DSM vs. ICD), study setting (first episode vs. long-term sample, inpatients vs. outpatients) and location (North America vs. Europe) to prevalence estimates. Both gender distribution (proportion of males) and mean age were studied as continuous variables. For reasons of presentation these were categorized into three groups. The results of metaregression are presented adjusted for the method of AUD and CUD diagnosis, so that variables for abuse (no/yes), dependence (no/yes), and time period (lifetime/current) are included in the metaregression models. In additional analyses the findings in lifetime abuse prevalence were compared to those by Cantor-Graae *et al.* (2001) using meta-regression (z test) in comparison of AUD and CUD prevalence estimates. In the CUD study with smaller amount of studies, bootstrap methods were used instead of meta-regression because they make fewer assumptions about the distribution of the rates (Delucchi & Bostrom 2004). We created 1000 bootstrap samples by randomly resampling with replacement from the original data. The data were analyzed with Stata 9.0 (Stata Corporation 2001).

4.4 Ethical considerations and personal involvement

According to the Act on Medical Research (488/1999, amendment 295/2004) and Decree (986/1999), no formal ethical permission was required for this research, as the sample in this study consisted of articles, not living study subjects. The data used and analyzed in this research have been previously published in scientific

journals or doctoral theses and have been ethically considered in that part of the process.

The author of this thesis participated in the study design, data analysis and reporting of the results in all original studies (I-IV). The author participated actively and independently in designing the search strategy and sample collection, together with informaticians Henna Paajala (née Kotiranta) and Johanna Löhönen (née Heikkinen) in all original studies. The author evaluated all articles together with Adjunct Professor Jouko Miettunen in original publications III and IV. Statistical analyses in this study were conducted together with Jouko Miettunen. The author wrote the first and last versions and acted as a corresponding author in all the original articles.

5 Results

5.1 Finnish doctoral theses on schizophrenic psychoses: descriptive and bibliometric analysis (I)

5.1.1 Monographs

Table 1 presents Finnish doctoral theses concerning schizophrenic psychoses in monograph form. The author, main department and university, publication year, language, title of the thesis and its key results are presented. Most of the articles were published by departments of psychiatry. Before 1977, all published theses were from the University of Helsinki. Most of the theses were written in English or Finnish, except for one in Swedish and one in German.

5.1.2 Doctoral theses consisting of a series of papers

In Table 2, Finnish doctoral theses on schizophrenic psychoses and consisting of a series of papers are presented. The table provides the author, department and university, publication years (for the thesis and original papers), title and key results. The first thesis consisting of a series of papers was published in 1979. Most often, the theses have been published in a department of psychiatry, but the distribution of publishing departments was wider than in the case of monographs. In all theses the original papers were written in English. The summary parts were also written in English, except in one where the language was Finnish (author Leo Heikkilä). Tables 1 and 2 are updated from original paper II and the theses are presented in chronological order.

Table 1. Finnish doctoral theses on schizophrenic psychoses in monograph form by July 2008 (updated from Table 1 in original paper II).

Author	Department (University)	Year (language)	Title	Key Results
Jokivartio Erkki	Medical Chemistry (Helsinki)	1939 (E)	Either-soluble plasma phosphatides in schizophrenia	A relation between the schizophrenic process and the decrease of plasma phosphatides was found.
Alanen Yrjö	Psychiatry (Helsinki)	1958 (E)	Mothers of schizophrenic patients	Among the mothers of schizophrenic patients, personality disorders more severe than neurosis were found. Also their relationship to the child was disordered.
Achte Kalle	Psychiatry (Helsinki)	1961 (G)	Cause, prognosis and rehabilitation of schizophrenia	Prognosis was not essentially better during neuroleptic era as compared to the time of shock treatments.
Tienari Pekka	Psychiatry (Helsinki)	1963 (E)	Psychiatric illnesses in identical twins	First twin-study of schizophrenia by using twin register. Concordance was lower in the monozygotic twins as compared with earlier studies.
Elosuo Reino	Psychiatry (Helsinki)	1966 (F)	Rehabilitation of schizophrenia	Rehabilitation improved the prognosis.
Niskanen Pekka	Psychiatry (Helsinki)	1970 (F)	Home treatment in schizophrenia	Part of patients could be treated in home-like wards in hospital.
Virkkunen Matti	Psychiatry (Helsinki)	1974 (E)	Suicides in schizophrenia and paranoid psychoses	Most schizophrenia patients had intrapsychic and social crisis before suicide.
Ojanen Markku	Psychology (Tampere)	1975 (F)	Reasons for hospitalisation, factors affecting to duration of treatment and adjustment back to society in psychiatric inpatients	Schizophrenic persons (especially hopeless, socially isolated, regressive and paranoid) stayed longer in hospital than non-schizophrenic inpatients. Prediction of rehospitalization was difficult.
Suominen Jaakko	- (Helsinki)	1975 (F)	Psychosis and inability to work	Psychosis and inability to work was not similar in different parts of the country.

Author	Department (University)	Year (language)	Title	Key Results
Räkköläinen	Psychiatry (Turku)	1977 (E)	Onset of psychosis	Onset of psychosis occurred often in transition period of life.
Viljo	Psychiatry (Turku)	1977 (E)	Psychosocial development and prognosis of schizophrenia	Prognosis was better than found earlier although the dependence of patients had increased.
Salokangas	Psychiatry (Turku)	1982 (F)	Development and course of paranoid and nonparanoid schizophrenia	There was differences between paranoid and non-paranoid schizophrenia patients in premorbid development, onset of disease, psychopathology and the need for hospital care.
Pulkkinen	Psychiatry (Helsinki)	1984 (F)	Art therapy in a psychiatric hospital : a study of the psychodynamic content of drawings made by neurotic and schizophrenic patients	The pictures produced during hospital ward art therapy contain unconscious psychic material which suggests that art therapy can be used as a part of inpatient psychotherapy.
Alanko	Psychiatry (Helsinki)	1984 (E)	Onset of functional psychoses in later middle age: a social-psychiatric psychodynamic and family-dynamic study	The psychotic patients had less successful marital status, fewer friendships and leisure activities as well as serious self-esteem problems during the period preceding the psychotic breakdown and poorer mental and social development than the controls.
Mattila	Psychiatry (Turku)	1984 (E)	Vulnerability to schizophrenia: A theoretical and empirical approach	Social adjustment difficulties may be markers of enhanced vulnerability in the children of non-chronically ill schizophrenic mothers with non-paranoid symptoms.
Vilho	Psychology (Helsinki)	1985 (F)	Problem of the analytic psychotherapy of schizophrenia	Analytic psychotherapy was very useful to treat the developmental crisis of schizophrenia. Therapy included developmental crisis, which was essential for recovering.
Wrede	-	1986 (F)	The prognosis of schizophrenic psychoses	In the follow-up 58% were without psychotic symptoms but only 30% recovered socially
Gunnel	(Turku)	1986 (E)	Principles and practices in diagnosing schizophrenia	Hospital diagnoses of schizophrenia were very specific and reliable but were not as sensitive.
Johansson				
Allan	(Turku)			
Kuusi	Psychiatry (Helsinki)			
Katrina	Psychiatry (Helsinki)			
Paksliahti	Psychiatry (Helsinki)			
Antti				

Author	Department (University)	Year (language)	Title	Key Results
Tuori	Psychiatry (Turku)	1987 (F)	Systemic family therapy in schizophrenia	Family therapy was useful and decreased the number of future hospital treatment periods.
Timo	Nursing Science (Tampere)	1990 (F)	The rehabilitation of a long-term patient	The activities of daily life of a long-term psychiatric patient increased when the patient received consistent, long-term support.
Järvinen	Theology (Åbo Akademi)	1991 (S)	Psychosis and religion	Religion and its symbolic systems and roles played an important part in a psychotic person's illness and healing process.
Seikkula	Psychology (Jyväskylä)	1991 (F)	The family-hospital boundary system in the social network	The network-centered treatment style decreased the need for inpatient treatment and the use of the hospital during the one-year follow up period.
Keränen	Psychology (Jyväskylä)	1992 (F)	The choice between outpatient and inpatient treatment in a family centred psychiatric treatment system	The reciprocal interaction between the patient, the family and the admission team in the admission meeting was a crucial factor influencing the choice between outpatient and inpatient treatment.
Larmo	Psychiatry (Turku)	1992 (E)	Parents' psychosis: influence on offspring	Interaction models often transited through generations.
Anneli	Psychiatry (Helsinki)	1993 (E)	Sleep in non-affective psychoses: a polysomnographic study	Shortened rapid eye movement latency correlated to psychotic symptomatology in patients suffering from non-affective psychosis, although this correlation did not seem to be specific for schizophrenia.
Björn	Psychology (Tampere)	1994 (F)	Psychosocial outcome of mental health care and the use of mental health services. A follow-up in the health care district of Peijas	A positive or a negative evolution of the illness of psychiatric patients was found to be the result of connected and cumulating individual and environmental factors.

Author	Department (University)	Year (language)	Title	Key Results
Laitinen Jorma	Psychiatry (Turku)	1994 (F)	Medical models in psychiatry – schizophrenia from a philosophy-of-science viewpoint	Modeling a descriptive general diagnostic concept like schizophrenia was problematic.
Pihlajarinne Marja-Leena	Psychology (Jyväskylä)	1994 (F)	The onset of schizophrenic disorder at a young age. A family therapeutic study.	A failure in individuation and separation at a young age were central problems in falling ill with psychosis and were caused by adolescent's own structural vulnerability but also by conflicts between the parents.
Wahlberg Karl-Erik	Psychiatry (Oulu)	1994 (F)	Parental communication and thought disorders of the offspring. An adoptive study	A vulnerability to thought disorder appeared to be genetically transmitted. Families of high-risk children should be particularly encouraged to aim at unambiguous communication.
Honkonen Teija	Public Health (Tampere)	1995 (E)	Need for care and support in schizophrenia: a follow-up study of discharged schizophrenia patients	There was found to be need for long-term support and rehabilitation for schizophrenia patients.
Kaltiala-Heino Riittakerttu	Public Health (Tampere)	1995 (E)	Involuntary psychiatric hospitalization. A comparison of voluntarily and involuntarily admitted psychotic patients, their experiences of and attitude to coercion in psychiatry	Perceived involuntariness was associated with involuntary legal status, less insight and poorer psychic status. The patients who felt coerced by the admission also felt worse about the treatment and perceived poorer outcome and were assessed to be of worse psychic status in follow-up.
Koistinen Pekka	Psychiatry (Oulu)	1995 (E)	Thought disorder and the Rorschach: A study on psychopathology and vulnerability of adoptees	Adopted-away offspring of schizophrenic mothers had more severe thought disorders than control adoptees. Thought disorder may be a feature of high-risk adoptees.

Author	Department (University)	Year (language)	Title	Key Results
Keskitalo Pirjo	Psychiatry (Oulu)	2000 (E)	Stability of parental communication deviance and the correlation with the development of thinking in adopted children predisposed to schizophrenia and controls	The presence of the children affected parental communication and the presence of the parents altered the children's communication.
Saari Mauno	Psychiatry (Oulu)	2002 (F)	Psychosis team in treatment of severe mental disorders in Kainuu in 1992–1996	The work of the psychosis team was more profitable and economical than conventional psychiatric special treatment
Vuokila-Oikkonen Päivi	Psychiatry (Oulu)	2002 (F)	Narratives unfolding in cooperative team meetings in acute psychiatric care	A psychiatric team meeting could be cooperative or expert-initiative, which had different goals.
Hotti Aira	Psychiatry (Turku)	2004 (F)	What does a psychiatric patient want to know? A study of the knowledge and the needs to know of schizophrenic patients.	According to psychiatric patients they should be informed of the nature of the disorder, treatment, factors affecting the course of the disorder, prognosis, social rights and how the disorder affects their ability to manage in everyday life.
Iso-Koivisto Eeva	Psychiatry (Turku)	2004 (F)	"Away from here, upwards, back again"-meaning given to the experience of first psychotic episode	Patient's narrative of experiencing the psychosis as well as gender should be taken into account when choosing treatment approaches.
Nordling Esa	Psychology (Tampere)	2007 (F)	"Started to treat as a human being"	Patients' experience of adequate social support correlated with subjective well-being as well as good therapeutic relationship in out-patient treatment.

Language: E = English, F = Finnish, G = German, S = Swedish.

Table 2. Finnish doctoral theses on schizophrenic psychoses based on a series of papers by July 2008 (updated from Table 2 in original paper II).

Author	Department (University)	Year	Title	Key Results
Salonen	Psychiatry (Turku)	1979 (1971-1979)	Intensive psychotherapy of schizophrenia	Significance of intensive psychotherapy in schizophrenia can be likened to that of extensive intervention in somatic medicine.
Simo	Psychiatry (Turku)	1983 (1976-1983)	The psychiatric ward as a therapeutic community	Therapeutic community model in modified form was possible even for acute psychosis patients.
Ischanni	Psychiatry (Oulu)	1988 (1986-1988)	Dopamine receptors in peripheral tissues and in the central nervous system: pharmacological characterization and adaptations after repeated administration of neuroleptic drugs	When studying drug-induced changes in the DAergic autoregulation in the CNS, the peripheral neuronal DA receptor activation was a useful functional model for the study.
Jarmo	Pharmacology (Turku)	1989 (1985-1987)	A psychoneuroimmunological approach to acute psychiatric disorders.	Viral infections, inflammatory and autoimmune processes were found to have significance in the etiopathogenesis of acute (functional) psychiatric disorders.
Ahokas	Psychiatry (Helsinki)	1992 (1984-1993)	Substance P, opioid peptides, somatostatin, and prolactin in schizophrenia	There was a tolerance phenomenon of prolactin secretion in schizophrenia after long-term treatment with neuroleptics.
Antti	Psychiatry (Helsinki)	1993 (1985-1994)	Family therapy and schizophrenia in public mental health care	Family therapy was an important part of the treatment of schizophrenia. Continuity of the treatment of schizophrenia was important.
Heikkilä	Psychiatry (Helsinki)	1993 (1990-1993)	Suicide among psychiatric inpatients	Schizophrenia was the most common diagnosis among male inpatients committing suicide.
Leo	Psychiatry (Turku)	1994 (1989-1994)	Interferons and interleukins in schizophrenia	Schizophrenia patients showed decreased production of interferons and patients with acute illness showed higher plasma levels of interleukins when compared to controls.
Lehtinen	Psychiatry (Turku)			
Klaus	Psychiatry (Turku)			
Taiminen	Psychiatry (Turku)			
Tero	Psychiatry (Turku)			
Katila	Psychology (Helsinki)			
Heikki	Psychology (Helsinki)			

Author	Department (University)	Year	Title	Key Results
Lillrank Sonja	Biomedical Sciences (Tampere)	1994 (1992-1995)	Dopamine and transmitter amino acids in animal models of drug-induced psychosis	After PCP administration there was a change in the release of D-aspartate and GABA, which may be due to increased dopaminergic activity and alterations in other neurotransmitters.
Nieminen Peniti	Psychiatry (Oulu)	1996 (1990-1996)	Therapeutic community research and statistical data analysis	Some motivated psychosis patients seemed to benefit from an individually timed longer inpatient experience in a therapeutic community setting
Eronen Markku	Psychiatry (Kuopio)	1997 (1993-1996)	Psychiatric disorders and homicidal behavior in Finland	Homicidal crimes were overrepresented among patients with schizophrenia, especially if they had comorbid alcohol use disorder.
Repo Eila	Psychiatry (Helsinki)	1997 (1997)	Finnish pretrial fire-setting offenders: psychiatric characteristics and criminal recidivism	Non-schizophrenic and alcoholic schizophrenic fire-setters generally had high rates of commission of criminal offences.
Wahlbeck Kristian	Psychiatry (Helsinki)	1997 (1993-1997)	The brain renin-angiotensin system in schizophrenia and pain disorder	Chronic schizophrenia patients with neuroleptic treatment had higher levels of angiotensin I-converting enzyme in cerebrospinal fluid than healthy controls.
Hovatta Iiris	Medical Genetics (Helsinki)	1998 (1994-1999)	Molecular genetics of familial schizophrenia and PLO-SL	The PLO-SL gene region did not contain a major gene which predisposes individuals to schizophrenia. There was evidence of involvement of chromosomes 5q, 6p, 8p, 8q and 20p to schizophrenia as well as evidence of 1q, 4q, 9q and Xp being putative schizophrenia susceptibility genes.
Mäkiyö Taru	Psychiatry (Oulu)	1998 (1997-1998)	Schizophrenia: diagnosis, early social factors and comorbidity	Patients experienced overmorbidity and -mortality as well as substance use disorders

Author	Department (University)	Year	Title	Key Results
Heilä Hannele	Psychiatriy (Helsinki)	1999 (1997-)	Suicide and schizophrenia: a nationwide psychological autopsy study in Finland	Drug overdose was the most frequent suicide method among schizophrenia patients: 2% had communicated suicidal intent as often as non-schizophrenic victims, 57% of schizophrenic suicide victims in the active phase were either not prescribed adequate neuroleptic treatment or were not using it, suicide risk factors may vary in different treatment phases among patients with schizophrenia.
Holma Juha	Psychology (Jyväskylä)	1999 (1995-1998)	The search for a narrative: investigating acute psychosis and the need-adapted treatment model from the narrative viewpoint	Early family- and network-centered intervention was of special value in cases of acute psychosis.
Ilonen Tuula	Psychiatriy (Turku)	1999 (1997-2000)	Neuropsychological function in patients with first-episode schizophrenia and severe affective disorders	Patients with first episode schizophrenia achieved significantly lower full-scale IQ and performed systematically worse on neurocognitive measures compared to healthy control group.
Joffe Grigori	Psychiatriy (Helsinki)	1999 (1996-1999)	Difficult-to-treat schizophrenia – a clinical, psychopharmacological, and neuroimmunological study	Clozapine treatment was effective treatment for treatment-resistant schizophrenia and it should be started earlier in the course of schizophrenia than is the general practice today.
Laakso Aki	Pharmacology and Clinical Pharmacology (Turku)	1999 (1996-2001)	Dopamine transporter in schizophrenia: a positron emission tomography study	(18 F)CFT was found to be a useful PET tracer for dopamine transporter in human brain. There was a lack of lateralization of dopaminergic innervation among schizophrenia patients compared to healthy subjects.
Suvisaari Jaana	Psychiatriy (Helsinki)	1999 (1999-2000)	Incidence and risk factors of schizophrenia in Finland	Incidence on schizophrenia and seasonal variation of births among the illness have decreased. Familial and sporadic schizophrenia had a different clinical picture.

Author	Department (University)	Year	Title	Key Results
Isohanni Irene	Psychiatry (Oulu)	2000 (1998-2001)	Education and mental disorders: a 31-year follow-up in the Northern Finland 1966 Birth Cohort	Small pre- and postmorbid educational failures were associated with schizophrenia.
Nikkilä Heikki	Psychiatry (Helsinki)	2000 (1995-2002)	Cerebrospinal fluid cytology in schizophrenia	Schizophrenia patients had increased rates of mononuclear cell and abnormalities in lymphocytes in CSF.
Räsänen Sami	Psychiatry (Oulu)	2000 (1999-2000)	Gender differences in schizophrenia observations from Northern Finland	No gender differences in age of illness onset were found and differences regarding sociodemographic and clinical characteristics were very few.
Ekelund Jesper	Medical Genetics (Helsinki)	2001 (1999-2001)	Molecular genetics of schizophrenia and comorbid and related traits	Several regions in chromosomes 1, 5 and 7 could be linked to schizophrenia.
Kerppainen Liisa	Psychiatry (Oulu)	2001 (2000-2002)	Family predictors of severe mental disorders and criminality in the Northern Finland 1966 Birth Cohort	Some characteristics of the early childhood family environment were associated with severe mental disorders in adulthood and form part of the developmental trajectory of these disorders.
Koskinen Tiina	Pharmacology and Toxicology (Kuopio)	2001 (2000-2003)	The role of 5-HT ₂ receptors in the modulation of premature responding type of impulsivity in rats. Interactions with dopaminergic and noradrenergic systems.	Overactivity of 5-HT _{2a} receptor increased impulsivity, the activation of D ₂ -receptors and α ₁ -adrenoreceptors also seemed to be involved.
Vuoristo Jussi	Medical Biochemistry and Molecular Biology (Oulu)	2002 (1998-2001)	Human GNAL, C18orf2, and MPPE1 genes: Genomic organization of the human GNAL gene and characterization of two novel genes, C18orf2 and MME1, on chromosome 18p11.2, a susceptibility region for schizophrenia and bipolar disorder	The GNAL gene was expressed in various regions of the human brain as approximately 6 kb transcripts; two previously unknown genes were found in chromosome 18p11.2 which is associated with bipolar disorder and schizophrenia.

Author	Department (University)	Year	Title	Key Results
Kampman Olli	Psychiatry (Tampere)	2003 (2000-2004)	Compliance in psychotic disorders	The patients at risk for non-compliance could be identified. An adequate information about possible side-effects of medication should be given to patients and their relatives.
Koivisto Kaisa	Psychiatry (Oulu)	2003 (2001-2003)	Uncontrollable sense of self as the focus while helping psychotic patient	The care of patients with uncontrollable sense of self should involve protection from vulnerability to a more integrated inner world supporting individual empowerment and coping
Kontkanen Outi	Molecular Sciences (Kuopio)	2003 (2000-2002)	Gene expression in rat brain: alterations by antipsychotic drugs	Antipsychotic drug treatments induced alterations in several gene expression (e.g. fos and jun family genes, cytochrome c oxidase, some presynaptic genes) in a cell culture model and in rat brain.
Lindberg Nina	Psychiatry (Helsinki)	2003 (2002-2003)	Sleep in mental and behavioral disorders	Structure and continuity of sleep were unaffected by olanzapine in healthy women and men.
Mäki Piirjo	Psychiatry (Oulu)	2003 (2003-2004)	Parental separation at birth and maternal depressed mood in pregnancy: associations with schizophrenia and criminality in the offspring	Early separation and mother's depressed mood during pregnancy did not increase the risk of schizophrenia.
Putkonen Hanna	Forensic Psychiatry (Helsinki)	2003 (1998-2003)	Homicidal women in Finland 1982-1992	A psychotic disorder was diagnosed in 28% of the homicidal women, 18% of the women who had committed some offence before the index offence had a psychotic disorder.
Raaska Kari	Clinical Pharmacology (Helsinki)	2003 (1998-)	Pharmacokinetic interactions of clozapine in hospitalized patients	Only CYP1A2 inhibition could significantly elevate serum clozapine concentrations.
Valkonen-Korhonen Minna	Psychiatry (Kuopio)	2003 (2001-2005)	Information processing in acute psychosis	Acute early psychosis affected automatic cerebral responses, conscious later components as well as reactivity and timing of autonomic nervous system responses.

Author	Department (University)	Year	Title	Key Results
Anttila Sami	Psychiatry (Tampere)	2004 (2003-2004)	Genetic factors in schizophrenia – studies on treatment response to typical neuroleptics and the age at onset	A predictive effect of the combination of two polymorphisms (NOTCH4: SNP2 and COMT: V108/158M) on treatment response to typical neuroleptics was found. There was also an association with EGF polymorphism and schizophrenia and polymorphisms of NOTCH4, EGF and APOE were associated with age at the onset of schizophrenia.
Haapasalo-Pesu Kirsi-Maria	Psychiatry (Turku)	2004 (2001-)	Studies on the psychopharmacological treatment of adolescents in Finland	Olanzapine showed good response for adolescent patients with psychotic symptoms. The major adverse effect was excessive weight gain.
Niemi Laura	Psychiatry (Helsinki)	2004 (2003-)	Offspring of mothers with psychotic disorder: childhood development and adulthood psychiatric morbidity	The cumulative incidences of schizophrenia were 6.7, 5.0, 6.7 and 0.6% among offspring of mothers with schizophrenia, schizoaffective disorder, other schizophrenia spectrum disorders and controls. Among high-risk offspring, social adjustment problems at pre-school age and severe neurological symptoms predicted future schizophrenia spectrum disorder.
Riiala Kaisa	Psychiatry (Oulu)	2004 (2003-)	Adolescent predictors of adult social and psychiatric adversities. A prospective follow-up study of the Northern Finland 1966 Birth Cohort	The initiation age of regular smoking was closely related to the age of onset of schizophrenia. Adult regular smoking was associated with low overall mean scores and low combined mathematical and natural science scores at the end of compulsory school in schizophrenia patients.
Heikkilä Jyrki	Psychiatry (Turku)	2005 (2002-)	Family functioning and personality profile in first-episode severe mental disorders	Relatives' expressed emotion is not directly related to patient psychopathology. Difference in psychodynamic personality traits between severe mental disorders could not be confirmed.
Hennah William	Medical genetics (Helsinki)	2005 (2003-2005)	Genetics of schizophrenia: the 10q2 locus in Finnish families	Disk1 pathway seemed to be involved in the aetiology of schizophrenia in Finnish population.

Author	Department (University)	Year	Title	Key Results
Hirvonen Jussi	Psychiatry (Turku)	2005 (2001-)	Brain dopamine receptors and genetic risk for schizophrenia	Dopamine dysregulation in schizophrenia may be related to genetic vulnerability rather than being solely associated with phenotypic expression.
Järveläinen Juha	Radiology (Helsinki)	2005 (2001-)	Reactivity of the human primary motor cortex during observation of action	Weakened reactivity of the primary motor cortex suggested a dysfunction of motor cognition in schizophrenia.
Kailla Outi	Psychology (Jyväskylä)	2005 (2002-2004)	Characteristics, course and outcome in first-episode psychosis. A cross-cultural comparison of Finnish and Spanish patient groups.	Finnish and Spanish patients received different treatment and lived in different sociocultural environments, but shared many similarities in illness manifestation, course and outcome.
Murray Graham	Psychiatry (Oulu)	2005 (2003-2006)	Early development and adult cognitive function in schizophrenia and the general population - a longitudinal perspective	In schizophrenia, mild infant motor developmental delay, adolescent scholastic performance and cognitive deficits may be age-dependent manifestations of the same underlying neural process.
Saari Kaisa	Psychiatry (Oulu)	2005 (2002-2005)	Hyperlipidemia and metabolic syndrome in schizophrenia	Persons with schizophrenia or on antipsychotic medication were at risk for hyperlipidemia and metabolic syndrome.
Stengård Eija	Psychology (Tampere)	2005 (1990-2003)	Journey of hope and despair. The short-term outcome in schizophrenia and the experiences of caregivers of people with severe mental disorder.	Service providers and policy makers should be sensitive to the needs of families and involve caregivers in the service planning decisions.
Tuulio-Henriksson Annamari	Psychology (Helsinki)	2005 (2002-2004)	Cognitive dysfunction in schizophrenia: a familial and genetic approach	Cognitive dysfunction observed in schizophrenia patients and their relatives is heritable and shows familial effects.
Väisänen Jussi	Psychiatry (Kuopio)	2005 (1997-2004)	Non-competitive NMDA-receptor antagonist in rodent modelling of schizophrenia	Systemic administration of NMDA-receptor ion channel blockers altered the mRNA expression of several NMDA receptor-associated molecules in the rat entorhinal cortex.

Author	Department (University)	Year	Title	Key Results
Arajärvi Ritva	Psychiatri (Helsinki)	2006 (2004-2006)	Clinical phenotype and genetic epidemiology of schizophrenia in a Finnish isolate	The isolate patients, regardless of their familial loading for schizophrenia, had less delusions and hallucinations than familial patients in the whole country, which may be related to the genetic homogeneity in the isolate.
Janno Sven	Psychiatri (Helsinki)	2006 (2004-2008)	Assessment of neuroleptic-induced movement disorders in a naturalistic schizophrenia population	Neuroleptic-induced movement disorder was found in two-thirds of study population of naturalistic schizophrenia patients.
Siira Virva	Psychiatri (Oulu)	2006 (2004-2008)	Vulnerability signs of mental disorders in adoptees with genetic liability to schizophrenia and their controls measured with Minnesota Multiphasic Personality Inventory	Genetic vulnerability to schizophrenia spectrum disorders, gene-environment interaction and later onset of psychiatric disorders were found to manifest in the adoptees: Minnesota Multiphasic Personality Inventory.
Alanen Hanna-Mari	Psychiatri (Tampere)	2007 (2006-)	Antipsychotic use among older persons in long-term institutional and home care	Approximately 19% of the older residents in long-term institutional care with schizophrenia were not on antipsychotic medication.
Hautala-Jylhä Piijo-Liisa	Psychiatri (Kuopio)	2007 (2005-)	Psychiatric post-ward outpatient services: between hospital and community	Psychiatric post ward services offered versatile care and improved the continuity of treatment.
Lauronen Erika	Psychiatri (Oulu)	2007 (2005-2008)	Course of illness, outcome and their predictors in schizophrenia: The Northern Finland 1966 Birth Cohort study	Both clinical and social outcomes were relatively poor, persons having a family history of psychosis, poor social contacts, poor school performance, early age of illness onset or short first hospitalization seemed to have the worst outcome.
Metsänen Miia	Psychiatri (Oulu)	2007 (2004-)	Thought disorder as a predictive sign of mental disorder. A study of high-risk and low-risk adoptees in the Finnish Adoptive Family Study of Schizophrenia	High scores on several Thought Disorder Index variables at the initial assessment were shown to predict a follow-up diagnosis of a psychiatric disorder among all adoptees.

Author	Department (University)	Year	Title	Key Results
Puukonen Anu	Forensic psychiatry (Kuopio)	2007 (2002-2007)	Mental disorders and violent crime. Epidemiological study on factors associated with severe violent offending	Homicidal behavior of patients with major mental disorder, antisocial personality disorder and substance use disorder was often associated with arguments with non-relatives when intoxicated whereas persons with only major mental disorder more often killed relatives as a result of delusions.
Svirskis Tanja	Psychiatry (Turku)	2007 (2005-)	Clinical characterization of subjects vulnerable to psychosis	Vulnerable to psychosis status was associated with a high number of Axis-I psychiatric disorders, increase in substance use, impaired functioning ability and decreased quality of life.
Turunen Joni	Medical genetics (Helsinki)	2007 (2002-)	Search for susceptibility genes in schizophrenia	The GABA receptor subunit, GABRG2, is significantly associated with schizophrenia and seems to affect the functioning of working memory. The risk of schizophrenia was increased two-fold by an RhD maternal-fetal genotype incompatibility.

Abbreviations in the table: 5-HT2a = serotonin receptor 2a, CNS = central nervous system, CSF= cerebrospinal fluid, DA = dopaminergic, Disk1 = disrupted-in-schizophrenia-1, GABA = Gamma-aminobutyric acid, GABRG2 = gamma-aminobutyric acid A receptor, gamma 2, GNAL = guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type, IQ = intelligence quotient, MPPE1 = metallophosphoesterase 1, mRNA= messenger ribonucleic acid, NMDA = glutamate, PCP = pentachlorophenol, PLO-SL = polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy, RhD = Rhesus D antigen.

Bibliometric analysis

Table 3 presents the number of Finnish theses on schizophrenic psychoses published in different universities. Altogether, 40 monographs and 61 theses consisting of a series of papers were found. The percentage of theses consisting of a series of papers was 22% before and 81% after 1994. A total of 36 theses on schizophrenic psychoses were published at the University of Helsinki, 21 at the University of Turku and at the University of Oulu, 11 at the University of Tampere, 6 at the University of Kuopio, 5 at the University of Jyväskylä, and 1 at Åbo Akademi University.

In addition, bibliometric results are presented: the mean number of citations received and the mean impact factor (June 2008) of original papers by universities in theses are summarized in Table 3. The mean impact factor of all theses based on original publications was 10.20 and the overall mean number of citations was 58.80. Theses published at the University of Kuopio received the most citations, while articles appearing in theses published at the University of Helsinki were most often published in high impact factor journals.

Table 3. Summary of Finnish doctoral theses on schizophrenic psychoses by universities (updated until July 2008 from Table 3 in orig paper II).

University	Total N	Mono-graphs N	Theses with a series of papers		
			N	Mean IF ¹	Mean citations ¹
University of Helsinki	36	15	21	14.26	80.90
University of Jyväskylä	5	3	2	2.26	39.50
University of Kuopio	6	0	6	12.55	83.67
University of Oulu	21	5	16	8.55	41.06
University of Tampere	11	6	5	8.46	56.00
University of Turku	21	10	11	5.80	33.64
Åbo Akademi University	1	1	-	-	-
Total	101	40	61	10.20	58.80

¹Mean Impact factors (IF) and citations for all original papers included in the thesis.

In addition, the proportion of articles published in doctoral theses between 1994–2005 was determined. In total, 20.2% of all Finnish articles on schizophrenic psychoses found in a search of the Web of Science database were published as part of a doctoral thesis based on original papers. There appeared to be differences in publication cultures between universities: at the University of Tampere, a major proportion of articles (54%, n = 14) were published as part of theses based on original articles, while at the University of Jyväskylä (100%, n = 5) and the University of Turku (97%, n = 65), articles on schizophrenic psychoses were mainly not part of a thesis. See also Table 4 in the original article (I).

5.2 Bibliometric analysis of a sample of Finnish schizophrenia studies (II)

5.2.1 The coverage of Web of Science

In a validation study using the same criteria (schizophreni*, Finland, English language, 1996–2005), the Web of Science database included approximately 83% of the 294 articles found when searching a total of seven international databases and three national databases.

5.2.2 The number of annually published articles and sub-fields

The search in the Web of Science yielded 265 articles on schizophrenia that had at least one author whose background institution was Finnish. The number of annually published articles varied quite considerably, but the trend was increasing. Table 4 presents the number of articles published each year during 1996–2005 by the corresponding institution. The bottom lines of the table summarize the number of articles where institutions have participated as other than the corresponding institution, as well as the total number of schizophrenia articles published.

Table 4. Number of schizophrenia articles published in 1994–2005 by year and by institution (based on ISI data base search) (Reproduced from original paper II [Koskinen et al. (2008)]).

As corres- ponding institution	Univ Helsinki	Univ Kuopio	Univ Oulu	Univ Tampere	Univ Turku	NPHI ¹ , Helsinki	Other Finnish ²	Non- Finnish ³	Total
Year									
1996	1	2	1	0	5	0	1	1	11
1997	2	0	4	0	7	2	0	1	16
1998	4	2	3	0	4	3	5	7	28
1999	6	4	3	1	6	4	2	4	30
2000	6	1	4	2	4	2	1	7	27
2001	7	1	2	0	4	3	2	5	24
2002	7	4	0	1	6	2	0	10	30
2003	3	2	4	6	2	6	2	8	33
2004	4	2	5	4	3	7	3	7	35
2005	2	4	7	2	4	4	3	5	31
Total	42	22	33	16	45	33	19	55	265
As other institution	52	15	15	18	23	38	68	59	
As any institution	94	37	48	34	68	71	87	114	

¹NPHI = National Public Health Institute. ²Group "Other Finnish" refers to articles where the correspondence institution is some other Finnish research institute, group ³"Non-Finnish" signifies articles where the address of the corresponding author is not in Finnish. The number of articles where a certain institution is involved as a corresponding institution or as an other institution are mentioned, as well as the total number of articles where the institution is involved as any institution.

In Table 5 the articles are presented according to psychiatric sub-fields. The number of articles in each sub-field is presented according to the institution. The articles published were mostly clinical-epidemiological (49%) and biological articles (38%). There were differences between institutions in the proportions of various sub-fields.

Table 5. Number of schizophrenia articles by sub-field 1996–2005 from Web of Science (Reproduced from original paper II [Koskinen et al. (2008)]).

Institution of the corresponding author	Sub-field					
	Biological		Pharmacological		Clinical-Epidemiological	
	N	%	N	%	N	%
Univ Helsinki	18	43	15	36	9	21
Univ Kuopio	11	50	3	14	8	36
Univ Oulu	10	30	0	0	23	70
Univ Tampere	9	56	2	13	5	31
Univ Turku	11	24	5	11	29	64
NPHI ¹ , Helsinki	10	30	1	3	22	67
Other Finnish ²	5	26	2	11	12	63
Non-Finnish ³	26	48	7	13	22	40
Total	100	38	35	13	130	49

¹NPHI = National Public Health Institute. ²Other Finnish refers to articles where the correspondence institution is some other Finnish institution than mentioned in the table whereas ³Non-Finnish signifies articles where the correspondence institution is not Finnish.

5.2.3 Publishing journals

The publishing journals were analyzed and compared to determine which journals have published the most Finnish schizophrenia studies. Finnish schizophrenia studies were found to have been published in a total of 78 journals. Table 6 summarises the journals most frequently publishing Finnish schizophrenia research in this data set.

Table 6. The most frequent Finnish schizophrenia research publishing journals in 1996–2005 (Reproduced from original paper II [Koskinen et al. (2008)]).

Journal	Number of articles	Percent (%)	Impact factor ¹
Schizophrenia Research	32	12.0	4.231
Acta Psychiatrica Scandinavica	17	6.4	2.968
American Journal of Psychiatry	17	6.4	8.286
Nordic Journal of Psychiatry	13	4.9	0.964
Schizophrenia Bulletin	12	4.5	2.871
British Journal of Psychiatry	10	3.8	4.956
Archives of General Psychiatry	10	3.8	12.642
Molecular Psychiatry	9	3.4	9.335
Psychiatry Research	9	3.4	1.957
European Psychiatry	8	3.0	1.273

¹Impact factor for 2005

5.2.4 Citations and impact factors

The median number of citations in the total sample was 9, being 13 for biological articles and 6 and 7, respectively, for clinical-epidemiological and pharmacological articles. Table 7 presents the frequency and percentage of highly cited articles as well as articles published in high IF (>4) journals from 1996–2005 according to the research institution. Articles in which the corresponding address was non-Finnish or NPHI received the most citations and were most often published in high IF journals.

Table 7. Number and proportion of highly cited* schizophrenia articles and number of articles published in journals with impact factor over 4 by publishing corresponding institutions in 1996–2005 from Web of Science (Reproduced from original paper II [Koskinen et al. (2008)]).

Institution of the corresponding author	Total	Highly cited ¹	High (>4) Impact Factor
University of Helsinki	42	6 (14 %)	9 (27 %)
University of Kuopio	22	4 (18 %)	9 (41 %)
University of Oulu	33	9 (27 %)	9 (27 %)
University of Tampere	16	0 (0 %)	2 (13 %)
University of Turku	45	3 (6.7 %)	8 (18 %)
NPHI ² , Helsinki	33	10 (30 %)	19 (58 %)
Other Finnish	19	2 (11 %)	3 (16 %)
Non-Finnish	55	30 (55 %)	29 (53 %)

¹Highly cited according to 3-year medians (required number of citations for highly cited articles): 1996: 45 citations, 1997: 42, 1998: 39, 1999: 33, 2000: 32, 2001: 27, 2002: 25, 2003: 15, 2004: 13, 2005: 9).

²NPHI = National Public Health Institute

Table 7 indicates that more than half of the articles written at the NPHI are published in international journals with impact factors greater than 4. A large proportion of articles with the first author from a non-Finnish institution are also published in journals with high impact factors.

The most frequently cited articles were those by Lewis *et al.* (2003) with 245 (biological subfield), Jones *et al.* (1998) with 171 (clinical-epidemiological subfield) and Hovatta *et al.* (1998) with 134 citations (biological subfield). In 8 out of 10 of the most cited articles, the first author's institution was non-Finnish.

The median impact factors for publications according to the institution and year are presented in Figure 1. Annual medians varied considerably, even though the three-year median was used. Articles from the NPHI currently have the highest median impact factors.

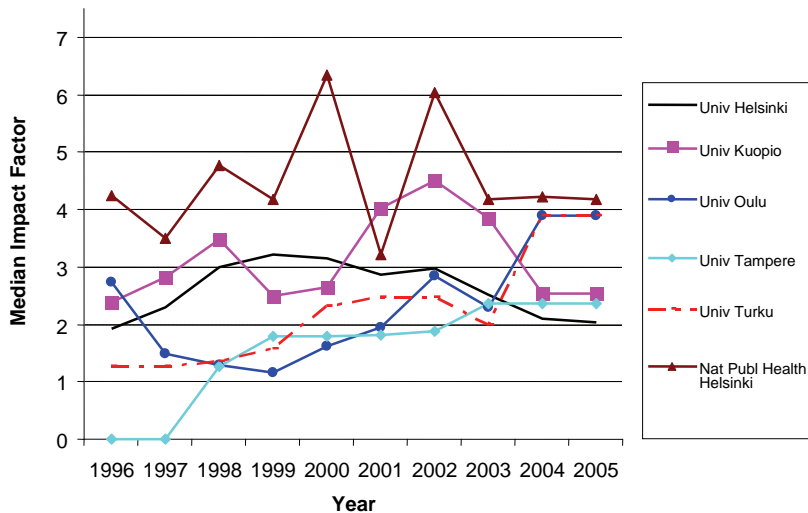


Fig. 1. Median annual 3-year impact factor by publishing institution of the corresponding author of Finnish schizophrenia articles. Other Finnish and Non-Finnish institutions not shown (Reproduced from original paper II [Koskinen et al. (2008)]).

5.2.5 International co-operation

International co-operation was evident in many Finnish schizophrenia articles. In the sample, 114 articles out of 265 (43%) were written in collaboration with an international institution. It appeared that international co-operation has increased over time, from 27% in 1996 to 54% in 2005. Overall, Finnish schizophrenia researchers have had international contacts with 28 countries. International co-operation was most active with the USA (50 articles) and the United Kingdom (39 articles).

5.3 Meta-analysis on the prevalence of alcohol use disorders in schizophrenia (III)

Altogether 60 studies met the inclusion criteria. The studies are summarized in Original paper III (Table 1). From each study the following details are presented where available: first author of the study, publication year, location of the study (country), diagnostic system and distribution of schizophrenia diagnoses (schizophrenia/schizophrenia spectrum), duration of illness/first-episode sample, study setting, mean age and age range, sample size, gender distribution, alcohol use diagnosis (current/lifetime, abuse/dependence) and prevalence (%) of patients with AUD. As seen from the table studies vary greatly by study design and sample characteristics.

Table 8 shows the prevalences in the studies grouped according to type of current/lifetime alcohol use diagnosis. Total median prevalence of AUD in schizophrenia was 17.8% (IQR 9.7–28.6, 60 studies). Median of lifetime AUD prevalence was 20.6% (IQR 12.0–35.9, 47 studies) and median of current AUD prevalence 9.4% (IQR 4.6–19.0, 18 studies).

Table 8. Prevalence of alcohol use disorders in schizophrenia patients by type of alcohol use diagnosis (Table 2 from original paper III).

Alcohol use diagnosis	Number of studies	Mean (%)	Median (IQR)	Range
Lifetime				
abuse	19	17.0	13.5 (5.9-24.0)	1.5-47.1
dependence	10	22.3	18.7 (12.0-32.4)	3.8-46.9
abuse or dependence	29	24.5	20.6 (13.5-35.9)	1.3-57.0
total	47	23.4	20.6 (12.0-35.9)	1.3-57.0
Current				
abuse	9	10.6	4.6 (2.1-14.9)	1.1-38.8
dependence	4	13.0	11.4 (6.4-19.7)	5.9-23.4
abuse or dependence	8	12.8	10.5 (6.3-21.5)	1.1-24.5
total	18	12.4	9.4 (4.6-19.0)	1.1-38.8
Total	60	20.9	17.8 (9.7-28.6)	1.1-57.0

Note: 5 studies reported both lifetime and current AUD. IQR = inter-quartile range. In total, higher prevalence estimates are used from abuse and dependence diagnoses (altogether 11 studies reported both abuse and dependence on lifetime diagnoses and 3 from current diagnoses).

Figure 2 presents the studies categorized by different study characteristics. For each study characteristic mean prevalence estimates (with 95% confidence interval), median and range are shown. The number of articles reporting the information on each study characteristics varies. There were 5 studies using several diagnostic systems and therefore these studies are not included in Figure 2. The studies using DSM-III-R reported substantially higher median prevalence estimates than studies using DSM-IV, ICD-9 or ICD-10 (32.4/17.4/11.4/6.2%). In metaregression, differences between mean prevalences of diagnostic systems were also statistically significant ($z = -4.03$, $p < 0.001$). For mean age and duration of illness current and lifetime diagnoses are presented separately. The median prevalence estimates of current AUD is lower in older (mean age 30 years or more) than in younger patient samples (23.4 vs. 11.0%, however, in metaregression, this difference was not statistically significant ($z = 1.19$, $p = 0.23$)). In lifetime AUD diagnoses the prevalence was significantly higher ($z = 2.46$, $p = 0.01$) in age group 30–39 years compared to other age groups (medians 24% vs. 15%). Other study characteristics did not affect the AUD prevalence.

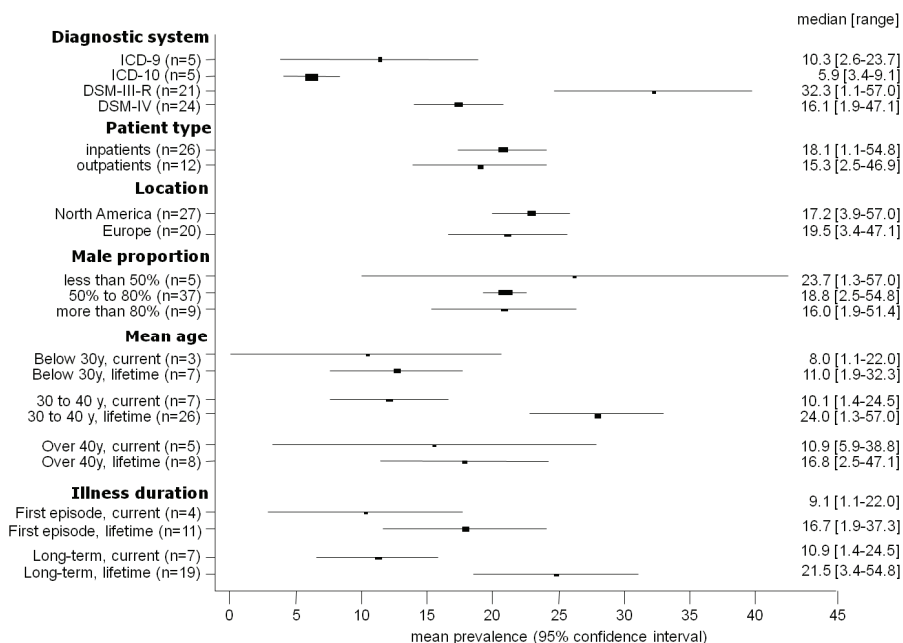


Fig. 2. Prevalence of alcohol use disorders by study characteristics (Figure 1 from original paper III).

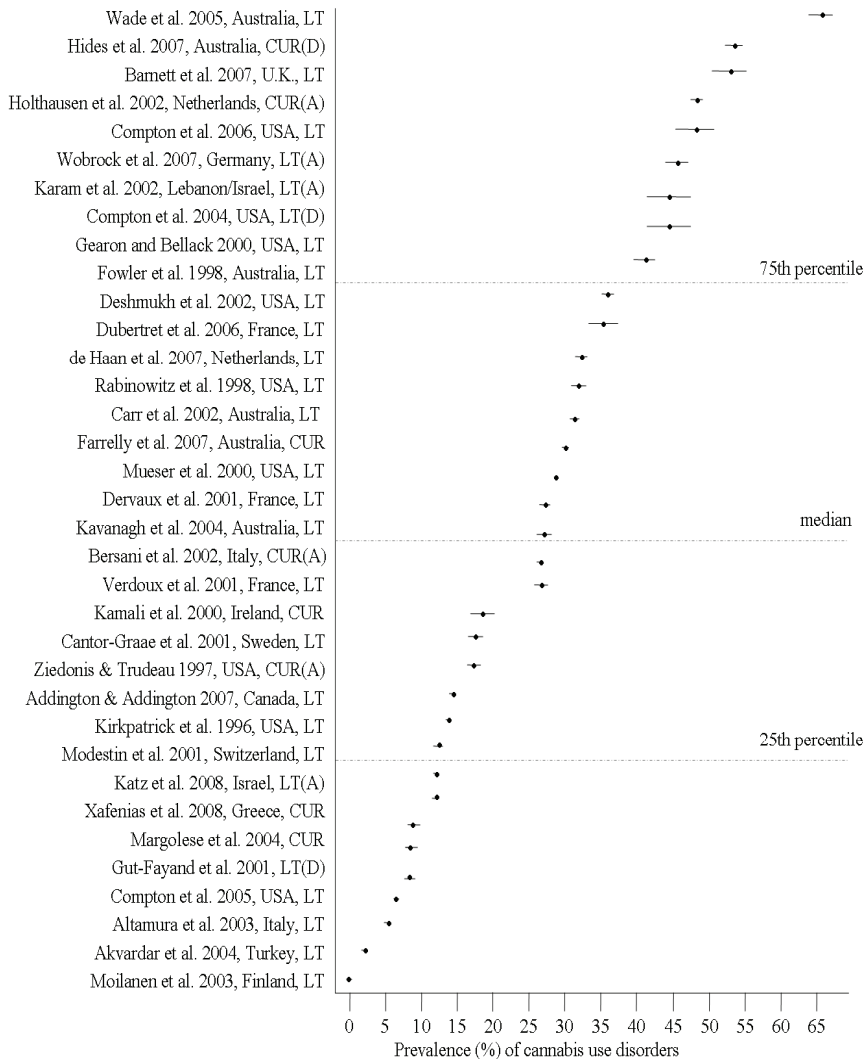
In studies published between 1960–89 (Mueser *et al.* 1990) the median lifetime abuse prevalence was 19% (range 12–30%, $n = 6$), whereas in the studies published in 1990–95 (Cantor-Graae *et al.* 2001) the median of prevalences in lifetime abuse or dependence diagnosis was 36% (range 21–54%, $n = 10$). In this meta-analysis the median of lifetime abuse, 14% (range 2–47%, $n = 19$), and the median of any lifetime AUD diagnosis was 21% (range 1–57%, $n = 47$). The change in AUD prevalences from studies published in 1990–95 to the current study was statistically significant ($z = 2.59$, $p = 0.01$).

5.4 Meta-analysis on the prevalence of cannabis use disorders in schizophrenia (IV)

Of the 611 articles evaluated in detail, 35 studies met the inclusion criteria (Original paper IV, Table 1). These provided data from 16 countries (1 study each from Finland, Germany, Greece, Ireland, Lebanon, Sweden, Switzerland, Turkey,

and the United Kingdom, 2 studies from Canada, Israel, Italy, and the Netherlands, 4 from France, 6 from Australia, and 9 from the USA). The total number of cases was 5540. As can be seen from the table, the characteristics of the studies varied considerably.

The total median rate of cannabis use disorder in schizophrenia was 27.0% (range 0.0–65.6, 35 studies). The median rate of lifetime CUD was 27.1% (IQR 12.2–38.5, 28 studies) and that of current CUD was 16.0% (IQR 8.6–28.6, 10 studies). Figure 3 presents rate estimates for cannabis use disorders in all the samples. The results are presented using forest plots with 95% confidence intervals (CI). The studies are sorted according to the CUD rate estimate, and the median, lower and upper quartiles for the rate estimates are also presented.



Abbreviations: LT = lifetime, CUR = current, A = only abuse, D = only dependence; * Also unpublished data from the authors.

Fig. 3. prevalence of cannabis use disorders in schizophrenia samples (1996–2008). (Figure 1 from original paper IV).

Figure 4 presents the studies categorized according to different study characteristics. Mean CUD rate estimates (with 95% confidence interval), medians and ranges are shown for each study characteristic. For mean age and duration of illness current and lifetime diagnoses are separately presented. The

number of articles reporting the information on each study characteristics varies. There was one study that used several diagnostic systems and therefore this study is not included in Figure 4. Cannabis use disorders were more common in younger (< 30 years) than older (\geq 30 years) patient samples: the median estimated rates of CUD for the two age groups were 38.5% vs. 16.0% for current and 45.0% vs. 17.9% for lifetime schizophrenia diagnoses. In bootstrapped regression analyses, these differences were also statically significant for current ($z = -2.26$, $P = .02$) and lifetime ($z = -2.35$, $P = .02$) schizophrenia diagnoses. The median rate of CUD was also higher in samples in which more than two-thirds of the subjects were males compared to the other samples (33.8% vs. 13.2%). In regression analysis, the finding was also statistically significant ($z = 3.08$, $P = .002$). In studies presenting results from first-episode samples, the median CUD rate was higher than for the others (28.6% vs. 22.0% for current, and 44.4% vs. 12.2% for lifetime diagnoses). However, this difference was only statistically significant in patients with a lifetime diagnosis (current $z = 1.72$, $P = .09$, lifetime $z = 3.46$, $P = .001$). All the statistically significant results remained significant in meta-regression analyses. The rate of CUD was not statistically significantly affected by other study characteristics. The results are presented in Figure 4 with the mean CUD rate (95% confidence interval), as well as the median and range. When comparing studies according to the recruitment strategy, the median estimated CUD rate was 26.7% (range 0–53.5) in studies with consecutive patient samples ($n = 20$) and 12.3% (range 6.3–35.3) in those with convenience samples.

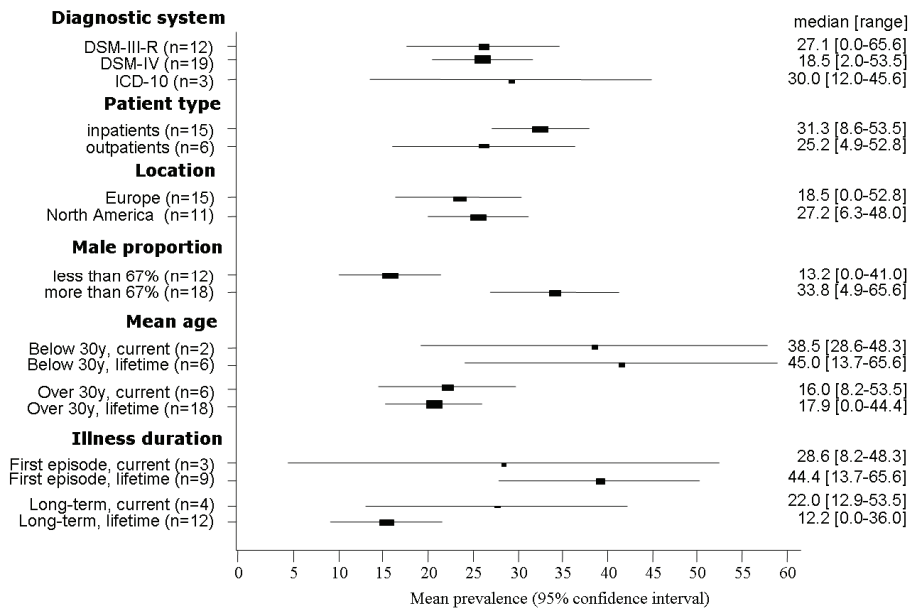


Fig. 4. Prevalence of cannabis use disorders in schizophrenia samples (1996–2008). (Figure 1 from original paper IV).

6 Discussion

6.1 Main findings

The main study findings corresponding to the presented aims are:

1. The number of published monographs has decreased over the years. There are differences in publication policies between the investigated research organizations (I).
2. Bibliometric methods reveal differences between scientific institutions and are feasible when evaluating psychiatric research institutions and utilized with care; international cooperation increased the visibility of research (II).
3. Alcohol use disorders are common in schizophrenia patients although there has been a decreasing trend compared to previously reported prevalences. This may be explained by the changes in diagnostic systems (III).
4. Cannabis use disorders were especially common in younger and first-episode schizophrenia patient samples, as well as in samples with a high proportion of males (IV).

6.2 Discussion of results

6.2.1 *Finnish doctoral theses on schizophrenia (I)*

Psychiatry is a very extensive speciality and includes many possibilities and challenges without scientific orientation. For example, formal psychotherapy training is a long and demanding process, as is also practical orientation to the main clinical duties. Clinical duties and a shortage of psychiatrists may create a conflicting situation if someone tries to combine a scientific and clinical career. Some clinical and most academic posts require a doctoral degree. Economically, a scientific career has not been able to compete with clinical posts.

A doctoral thesis may fundamentally promote one's career. For most academic posts, and some highly ranked clinical posts a doctoral degree is a prerequisite. A scientific education may help in applying evidence-based medicine, which is increasingly adopted and even required in routine clinical practice. It may increase knowledge, professional qualifications and self-confidence.

Proportion of monographs and theses consisting of a series of papers

At present, doctoral theses are published more actively than before and more doctoral theses consisting of a series of papers are published compared to monographs. Only six monographs have been published within the last decade. This is partly explained by the change in the funding system, which may encourage the writing of a thesis consisting of a series of papers. Articles receive 1 research point if published in journals with an impact factor of 0–1, 2 points if the impact factor is 1–3 yields and the maximum of 3 points if published in journals with an impact factor greater than 4. One point is received from the summary part of a doctoral thesis. In 2008, one research point corresponded to 4 718.15 euros of funding (Ministry of Social Affairs and Health, decree 31/2009). Monographs receive 6 research points. Thus, the topic of the thesis still has an important role when deciding whether to write a monograph or a thesis consisting of a series of papers. Especially if the thesis concerns, for instance, national treatment system issues, it is difficult to attract the interest of international journals. Increased international collaboration is another reason for publishing articles in international journals.

There are probably several reasons why the number of monographs has decreased. The current funding system supports the writing of a doctoral thesis consisting of original articles. In addition, in principle, doctoral students preparing a monograph must adopt an independent working style – perhaps too much alone. In addition, the control and feedback of the scientific community is minimal and not realized until the final phase of the process by the external examiners and the opponent. When the thesis consists of a series of papers there is usually a larger study group that supervises the research and provides support to the doctoral student. The goal is also to produce standard scientific articles in peer-reviewed journals. However, the study group's input may reduce the independent role of a doctoral candidate, who is often the least experienced member of the team, especially at the beginning of the process. However, being an active member of an experienced team provides a very effective scientific education. In addition, passing the publication threshold after the standard control process of the scientific community (peer review, editorial process) usually increases the quality of the articles used as parts of the thesis – and in the case of a doctoral thesis, this makes the roles of the external examiners and the opponent easier.

Language of theses

In Finland, the language of doctoral theses was traditionally Latin until the 17th century, but after that theses were also written in Swedish. The first doctoral thesis written in Finnish was published in 1860. At the end of the 19th century, German and later English were additionally used in doctoral theses (Ignatius & Nuorteva 1999).

Nowadays, the language of doctoral theses is usually English. However, in monographs the culture of publishing the thesis in Finnish is still common. This may be partly explained by the fact that these theses concern national topics targeted at Finnish researchers and clinicians. All theses based on a series of papers in the sample were written in English. As the original articles that are part of the thesis are usually published in English in scientific journals, the threshold to write an English summary might be lower than in the case monographs.

Number of articles

Medical faculties have differed in their policies concerning the required number of articles for doctoral theses. In our sample, the number of original papers included in the thesis varied from 4 to 6. Universities usually allow the inclusion of unpublished submitted manuscripts in the thesis (Helsingin Yliopisto 2008, Kuopion Yliopisto 2007, Oulun Yliopisto 2007, Turun Yliopisto 2007), although the policy differs between universities. For example at the University of Tampere, all original articles have to be accepted or in press at the time the thesis is presented to the Faculty Board (Tampereen Yliopisto 2006).

Sum of impact factors and citations received according to organization

Almost all doctoral theses concerning schizophrenic psychoses were published by medical faculties (87%, n = 84). Most of the theses were published in psychiatry, psychology and nursing sciences. However, doctoral theses on schizophrenia were also published at departments of medical chemistry, radiology, medical genetics, public health, pharmacology and biomedical sciences, as well as from a faculty of theology.

The mean number of citations and mean impact factors of theses consisting of a series of papers and published at different research organizations were compared. Research organizations receiving the most citations had also published

the original articles that were part of doctoral theses in journals with the highest impact factors. However, when interpreting the number of citations received the time-span should be taken into account. In 2005–2008 the proportion of published doctoral theses consisting of a series of papers did not differ between research organizations, and comparison of the number of citations received in this study can be considered relatively reliable.

The sub-fields of schizophrenia research have different citation policies. For example, biological articles receive more citations, and often receive them soon after publication. The journals publishing more biological articles also more often have higher impact factors. This pattern is often seen in rapidly developing fields and in fields where the publication lag is short (Seglen 1997, Kurmis 2003).

6.2.2 Bibliometric analysis of Finnish scientific journal articles on schizophrenia (II)

Number of articles

The annual number of Finnish schizophrenia articles varied quite considerably, with Finnish research groups after all relatively small. However, the general trend has been one of steady growth. The number of Finnish schizophrenia articles published has tripled since 1996. One reason for the recent increase in the number of internationally published Finnish schizophrenia articles may be the fact that the threshold to submit articles to international journals has lowered. This may be partly due to the current funding system based on impact factors with a sliding scale, favouring publication in international journals (Adam 2002, Kekomäki 2001). The increase is in line with the results presented by Ingwersen (2002) regarding all psychiatric publications and by Heikkinen (2005) regarding schizophrenia research.

Sub-fields

Institutions focus on different sub-fields in schizophrenia research, which may partly depend on the study culture, available data and know-how, but may also be affected by collaborating institutions and their interests. In the sample of this study, schizophrenia research seems to have concentrated on the biological subfield at the Universities of Kuopio and Tampere and on the clinical-

epidemiological subfield at the Universities of Oulu and Turku and the NPHI. At the University of Helsinki, schizophrenia research appears to be divided among all three subfields. It should be taken into account that articles included in this sample were only retrieved from the Web of Science database. If the search had been conducted from several databases, the subfield distribution could have been different. The coverage of the Web of Science database is discussed in more detail in chapter 6.3.3.2. The number of articles increased in all three sub-fields during the study period, although the annual number of pharmacological articles is still relatively low.

Impact factors and citations received

The research reports from the NPHI were published in journals with high impact factors. The NPHI has large register data sets that can be utilized in internationally unique, high-quality research. The research reports with a non-Finnish organization or the NPHI as a corresponding institution received the most citations. Again, biological articles received more citations compared to other sub-fields, which is partly explained by the different citation culture in the sub-fields, as discussed before (Seglen 1997, Nieminen & Isohanni 1998, Kurmis 2003). In this study, self-citations were included. However, when using citations specifically as an indicator of the dissemination of research findings, the number of self-citations should be indicated, as discussed earlier.

It seems that when comparing research organizations the impact factors and numbers of citations are comparable, as was also seen in the study of original articles included in doctoral theses. However, when analyzing a relatively small number of studies, *e.g.* the research input of an individual researcher, these indexes may not be as reliable. Moreover, the visibility of research may also be affected by active collaboration with foreign and national institutions. In addition, having a large number of authors has been shown to associate with receiving more citations (Miettunen & Nieminen 2004).

International co-operation

The amount of international co-operation is constantly increasing, which could be seen in the data. For example, the proportion of annually published articles with the involvement of a Finnish organization has doubled since the mid-1990s. One of the reasons for active international co-operation might simply be improved

technology, which makes long distance communication easier. Co-operation also brings new ideas and knowledge and it has an important role in obtaining better funding for research. Multifaceted expertise can nowadays be available in groups that are large enough and have international collaborators. The downside of this is that the ownership of data may be problematic. International collaboration seems to increase the visibility of an article: in 8 out of 10 of the most cited articles published during 1996–2005, the first author’s institution was non-Finnish.

6.2.3 Meta-analysis on the prevalence of alcohol use disorders in schizophrenia (III)

The main results

The results show a descending trend in AUD prevalence compared to the most recent review. However, alcohol use disorders are still common in schizophrenia patients: approximately 10% had current and 20% had lifetime AUD diagnosis. As seen in previous studies as well as in the systematic review, there is great variation in the prevalence of AUD in schizophrenia. The variation may be explained by many factors, such as different study designs and sample characteristics. In the results the diagnostic system affected the prevalence of AUD in schizophrenia, so that the prevalence of AUD was higher especially in studies using DSM-III-R, but also in those using DSM-IV.

Prevalence and time trends of alcohol use disorders in schizophrenia patients

The studies in our sample present mainly results from patient samples that are under treatment. Subjects in clinical studies of schizophrenia are unlikely to be representative of all schizophrenia patients, therefore the prevalence estimate presented in this meta-analysis concern mainly patients under treatment. In our results the prevalence of median current alcohol abuse was 5% and that of dependence 11%. The lifetime prevalences were somewhat higher: 14% for lifetime abuse and 19% for dependence. Some original studies reported markedly higher lifetime dependence than abuse prevalences (Fowler *et al.* 1998, Desmukh *et al.* 2002, Dervaux *et al.* 2006). In two (Dervaux *et al.* 2001, Desmukh *et al.* 2006) of these three studies the prevalence estimates of abuse and dependence are

not overlapping. This could explain the higher prevalence of dependence, which after all is more severe diagnosis. Other original studies reporting both lifetime abuse and dependence prevalences do not show as substantial differences in either way.

To compare our results to previous studies we pooled the prevalences of alcohol use disorders reported in reviews published by Mueser *et al.* (1990) and Cantor-Graae *et al.* (2001). The inclusion criteria in these reviews were comparable to ours: however, there are probably differences in methods as e.g. diagnostic systems have changed during the years. The included studies were published 1960–1989 (Mueser *et al.* 1990) and 1990–1995 (Cantor-Graae *et al.* 2001). These reviews mainly report the prevalence of lifetime alcohol abuse or dependence in patients with schizophrenia, and only these prevalences are therefore compared.

When we compared our results to studies published between 1960–89 (Mueser *et al.* 1990) and 1990–95 (Cantor-Graae *et al.* 2001), our median prevalence in lifetime abuse was statistically significantly lower. This change may be mainly due to variation in diagnostics, sampling and other methodological differences but it may also indicate a descending trend in alcohol use disorders in patients with schizophrenia. Nowadays special treatment strategies including combination treatment and comprehensive care have been developed for schizophrenia patients with comorbid AUD. Although clinicians are trained to recognise dual diagnosis patients, underdiagnosing of AUD still undoubtedly exist (Drake & Mueser 1996, Frances 1996, Buckley 2006). In majority of studies included in our sample the alcohol use disorder diagnoses were ascertained from several sources such as structured or semi-structured interviews, hospital charts, case notes and registers. Only in two studies (Rabinowitz *et al.* 1996, Gråwe *et al.* 1997) the alcohol use diagnosis was based only on clinical diagnosis.

To avoid bias we excluded studies presenting results from samples recruited from prisons, forensic psychiatry units or shelters for the homeless. In these samples substance use disorders tend to be significantly more common than in general population (Drake & Mueser 1996, Shaw *et al.* 2006, Kanato 2008). Our prevalence estimates may therefore underestimate the actual prevalence, as these patient samples are not present in our sample.

Diagnostics

In our data the studies using DSM-III-R diagnostic system reported higher estimates than those studies using DSM-IV, ICD-9 or ICD-10. These differences remained after taking into account other study characteristics (e.g. mean age, gender distribution). Similar results have been reported before: in previous studies comparing alcohol use disorder diagnostics in DSM-III-R, DSM-IV and ICD-10 it has been presented that dependence diagnosis is most common in studies using DSM-III-R (Grant *et al.* 1992, Cottler 1993, Schuckit *et al.* 1994). Previous study has shown that the diagnosis of ICD-10's harmful use is not as common as abuse diagnoses in DSM systems (Grant 1993), which are seen in our results as well.

In our results the prevalence of alcohol abuse and alcohol dependence was rather similar. Therefore we combined these diagnoses when studying covariates. Many original studies have also reported their results combined (see Table 1 in original paper III).

In our data set there are 26 studies reporting results from schizophrenia samples with narrow diagnostic criteria and 21 studies were from schizophrenia spectrum samples with broader criteria. These differences in diagnostic criteria are not likely to affect our findings greatly. Only one study compared the prevalence of alcohol use disorders in patients with schizophrenia and schizoaffective disorder. Mueser *et al.* (2000) studied the prevalence of lifetime alcohol abuse or dependence in inpatient setting. They reported that patients with schizoaffective disorder had 1.4 times more often dual diagnosis.

Location of the study

The substance use profile is greatly affected by cultural factors. Unfortunately, there were only a few non-Western studies in our data set and therefore we were only able to compare North American and (Western) European studies. There were no difference in AUD prevalence between North American and European samples.

In our sample there was only one case-control study reporting the results of alcohol use disorders in in- and outpatients patients with schizophrenia compared to general population written by the Scottish comorbidity study group (McCreadie 2002). They found out that alcohol use disorders were somewhat more common in schizophrenia patients (current abuse 16/9%, current dependence 7/3%, lifetime abuse 39/34% and lifetime dependence 19/8%).

We compared the alcohol use disorder prevalence in schizophrenia to alcohol consumption of in the countries in question reported by World Health Organization (2004). In general, in studies presenting results from countries with high consumption of alcohol, the prevalence of AUD in schizophrenia patients was also higher than in studies from countries with lower alcohol consumption. However, there were some exceptions: e.g. in the United Kingdom alcohol consumption was high but the prevalence of AUD in schizophrenia patients was low, whereas in Sweden alcohol consumption was low in general but AUD prevalence in schizophrenia patients was high. However, alcohol consumption is not directly proportional to alcohol use disorder diagnoses and consumption patterns are strongly associated with culture, which makes this kind of comparison challenging.

Study setting and patient characteristics

In our data the differences between in- and outpatients were not statistically significant. Only in one original study the prevalences between in- and outpatients were compared. In an Australian study by Dawe *et al.* (2000) 57% of inpatients and 46% of outpatients had alcohol use disorder.

There were seven studies reporting current AUD prevalence in long-term patient samples. The duration of illness varied between 7 and 33 years. Current AUD prevalence was presented in four studies from first-episode samples. We found no differences in current AUD prevalences between first-episode and long-term patient samples. As expected in long-term patients, the lifetime AUD prevalence was somewhat higher. In our sample there were only a few studies comparing mean age between the AUD and non-AUD group. Therefore, we compared the reported mean age between the studies, which is not a very efficient method to study the possible effect of age. A better way to study the effects of age to the prevalence of AUD in schizophrenia would be to compare results presented in each study per individual age group (Kraemer *et al.* 2006). However, in lifetime AUD diagnoses the prevalence was higher in older patient samples as expected.

In long-term schizophrenia patient samples discrepant findings have been reported. Desmukh *et al.* (2002) found the AUD group to be somewhat younger (mean age 42.4/46.9) whereas Modestin and his study group (2001) found that comorbid AUD inpatients were older than patients without any substance use

disorder. Dawe *et al.* (2000) reported that the first episode patients with AUD were younger (mean age 23.4/27.5).

Among patients with schizophrenia, AUD is reported to be more common in male patients (Drake & Mueser 1996). In our data set the gender proportion did not show a significant difference, although our method was not very efficient for studying gender differences. There were some studies presenting results on prevalences in males and females. Rabinowitz *et al.* (1996, 1998) reported gender differences in an Israeli and an American sample. In these studies alcohol use disorders were 2 to 4 times more common in male patients with schizophrenia. DeLisi *et al.* (2001) reported that AUD was 7 times more common in male patients with schizophrenia in a Costa Rican and U.S. sample.

6.2.4 Meta-analysis on the prevalence of cannabis use disorders in schizophrenia (IV)

The main results

Cannabis use disorders were found to be common in schizophrenia patients, approximately 16% of whom had a current diagnosis and 27% a lifetime diagnosis of CUD. However, there was wide variation among studies in the rate of CUD. Cannabis use disorders were especially common in younger and first-episode patient samples, as well as in samples with a high proportion of males. The CUD rate was not affected by the study location (Europe vs. North America), classification system used (DSM-III-R vs. DSM-IV vs. ICD-10), or patient type (inpatient vs. outpatient).

Rate of CUD in schizophrenia

Most individuals suffering from schizophrenia undergo treatment (Perälä *et al.* 2007), and the studies in our sample therefore mainly presented results from in- and outpatient samples. The rate of CUD estimated in this meta-analysis therefore mainly relates to these patient groups. In our results, the median rate of current cannabis abuse was 20% and that of cannabis dependence 31%. The lifetime rates were 12% for abuse and 26% for dependence. In general, patients diagnosed with cannabis abuse are not also cannabis dependent, whereas patients with a diagnosis of cannabis dependence may include both those with abuse and dependence. Most

studies reported combined abuse or dependence rates. We combined the rates for studies separately reporting diagnoses of cannabis abuse or dependence.

To avoid bias we excluded studies presenting results solely from samples recruited from prisons, forensic psychiatry units or homeless shelters. In these samples, substance use disorders tend to be significantly more common than in the general population (Shaw *et al.* 2006, Perälä *et al.* 2007, Kanato 2008). A schizophrenia diagnosis is also relatively common in these samples (Folsom & Jeste 2002). However, exclusion of these studies is unlikely to have significantly affected our results. In addition, some studies included in our data set may have included patients from prisons. The fact that cannabis is an illegal substance in most countries may also lead to underreporting of cannabis use. On the other hand, it is also possible that low rates of CUD are not reported. This may especially be the case in papers reporting findings that are not considered to be affected by substance use.

Previous systematic reviews have reported the rate of cannabis use disorder in schizophrenia to vary over a wide range (13%-45%) rate (Mueser *et al.* 1990, Cantor-Graae *et al.* 2001). Studies published from 1960 to 1989 were reviewed by Mueser *et al.* (1990) and those from 1990 to 2001 by Cantor-Graae *et al.* (2001). The median of pooled rates of cannabis abuse or dependence in these reviews were 35.4% (four studies) and 26.0% (six studies), respectively. These rates do not differ markedly from our results, but the relatively small number of studies makes the interpretation of a possible trend difficult.

Classification

A diagnosis of cannabis dependence in the ICD and DSM includes both physiological and behavioral symptoms, whereas cannabis abuse in the DSM and harmful use of cannabis in the ICD indicates cannabis use irrespective of substance-related physical, social, psychological, or occupational problems, or cannabis use in risky situations. In most studies included in our sample, CUD diagnoses were determined from several sources, such as structured or semi-structured interviews, hospital charts, case notes, and registers.

Several articles used the term 'abuse' to indicate heavy or continuous use rather than the definition according to DSM criteria. This confusing use of terminology made it challenging to evaluate the studies. Only articles using DSM or ICD classification criteria were therefore included. In our meta-analysis there was no statistically significant difference in estimated CUD rates between

classification systems. No studies used the ICD-9 classification system, and only three studies used the ICD-10.

Most of the studies in which information about the study sample was available reported results from schizophrenia samples with narrow diagnostic criteria (n = 12), but there were also several studies from schizophrenia spectrum samples with broader criteria, including schizophrenia, schizophreniform disorder, schizoaffective disorder and delusional disorder (n = 16). In the analysis the rate of CUD was similar in both groups: 26% for narrow schizophrenia and 23% for a schizophrenia spectrum.

Patient characteristics

Cannabis use disorders were more common among inpatients than outpatients; however, this difference was not statistically significant. Schizophrenia patients with cannabis use disorders were reported to have more positive symptoms (Addington & Addington 2007) and fewer negative symptoms (Bersani *et al.* 2002, Compton *et al.* 2004). Kirkpatrick *et al.* (1996) recorded no significant difference between deficit and non-deficit groups in current cannabis use, whereas the current use of alcohol or other drugs was less severe in deficit patients.

Substance use disorders have been reported to be more common in male schizophrenia patients than females (Xafenias *et al.* 2008). A significant gender difference was also seen in our data set: the rate of CUD was significantly higher in samples in which more than two-thirds of the subjects were male. All studies comparing CUD in relation to gender reported higher rates among males (Addington & Addington 2007, Dubertret *et al.* 2006, Rabinowitz *et al.* 1998). In addition, several studies reported that schizophrenia patients with cannabis use disorder were younger (Addington & Addington 2007, Barnett *et al.* 2007, Dubertret *et al.* 2006, Modestin *et al.* 2001).

A number of studies reported that alcohol and cannabis were the most commonly abused substances among schizophrenia patients (Karam *et al.* 2002, Margolese *et al.* 2004, Modestin *et al.* 2001, Moilanen *et al.* 2003, Ziedonis & Trudeau 1997). Cannabis-abusing patients also often had co-occurring tobacco use and a lifetime diagnosis of alcohol and other substance abuse or dependence (Kavanagh *et al.* 2004, Wade *et al.* 2006). The presented CUD rates were higher than our unpublished meta-analysis on alcohol use disorders in schizophrenia, in which the median rate of current alcohol use disorder was 9.4% and the median rate of lifetime alcohol use disorder 20.6%. In addition, when comparing the rate

of alcohol use disorders and cannabis use disorders, it seems that younger (< 30 yrs) schizophrenia patient samples (7 studies) more often had CUD, whereas alcohol use disorders were more common in older samples (18 studies).

Studies with consecutive patient samples had higher median rates of CUD (26.7%) compared to convenience samples (12.3%). Consecutive samples may better represent those schizophrenia patients with substance use disorders. However, in our dataset the number of convenience samples was relatively small (n = 5) and comparison with consecutive patient samples was therefore difficult.

Location of the study

The substance use profile is greatly affected by cultural factors. Unfortunately, there were only a few non-Western studies in our data set, and we were therefore only able to compare North American and (Western) European studies. There was no significant difference in the rate of CUD between these two sets of samples.

We compared the CUD rate in schizophrenia with cannabis consumption (mainly in the age range 16–65 years) in the respective countries reported by the United Nations (2008). There were examples of countries with a high consumption of cannabis in the general population and in schizophrenia patients (e.g., Australia), as well as those with a low consumption in both the general population and schizophrenia patients (e.g., Finland, Turkey). However, in some countries the consumption in the general population was relatively high compared with that among schizophrenia patients (e.g., Italy, Switzerland), and vice versa (e.g., Germany, the Netherlands). However, general populations in the report of the United Nations and the patient samples in the studies included in our data set differed in factors such as age and gender distribution, which makes the comparison challenging.

Direction of causality of cannabis use and schizophrenia

It is generally accepted that cannabis use can cause different psychotic states, ranging from toxic delirium to acute paranoia. In the DSM-IV classification this is termed cannabis-induced psychosis. However, the role of cannabis use in the onset, course and clinical expressions of schizophrenia is less clear. According to the recent meta-analysis by Moore *et al.* (2007) a study on 50,000 Swedish conscripts is still the only one in which a schizophrenia diagnosis has been used as an outcome for cannabis use (Andréasson *et al.* 1987, Zammit *et al.* 2002). The

authors concluded that “high consumers” (more than 50 occasions) of cannabis had a relative risk of 6.7 (95% confidence interval 2.1–21.7) for inpatient schizophrenia care in a 15-year follow-up period after conscription.

Moore *et al.* (2007) reported in their systematic review that cannabis use increases the incidence of any psychotic outcome; the risk was approximately 40% higher for those who had ever used cannabis. However, a substantial confounding effect was present for psychotic outcomes. No robust evidence was presented indicating that earlier use of cannabis would have more harmful effects. In a recent systematic review, the same research group examined the effects of cannabis use on the outcomes of psychotic disorders (Zammit *et al.* 2008). An association with increased relapse and non-adherence was observed, whereas the reported findings on the severity of symptoms were more variable (Moore *et al.* 2007). On the whole, the direction of causality of cannabis use and schizophrenia needs further studying.

6.3 Strengths and limitations of the study

6.3.1 Finnish doctoral theses on schizophrenic psychoses – descriptive and bibliometric analysis (I)

Strengths of the study

This was the first study to comprehensively present all Finnish doctoral theses on schizophrenia. An exhaustive systematic search was performed from the major psychiatric databases, and to update this information the main research organizations were contacted directly. This was also the first bibliometric analysis on original Finnish papers on schizophrenia that are part of a doctoral thesis. New information was yielded, for instance, on thesis publication activity and at some level on differences in the publication culture between universities.

Limitations of the study

Despite the comprehensive search, some Finnish doctoral theses concerning schizophrenic psychoses may have been missing from the data. In particular, theses published by non-psychiatric departments and older theses may have been missed. The definition of inclusion criteria was challenging and the criteria used

here were rather loose in order to minimize the possibility of missing theses related to schizophrenic psychoses.

Not all of the original papers of the theses necessarily included results on schizophrenic psychoses. The original papers of older theses were often published in journals missing from the Web of Science database. These articles thus lack impact factors and information on citations. Furthermore, some of the original articles were published in books or were originally in submitted form and had not appeared at the time of this study. Therefore, they do not have impact factors or citations, either. When interpreting the sum of citations, the publication years and thereby the time-span over which citations have been received should be taken into account.

In the original article (I), the proportion of Finnish schizophrenia articles that were part of doctoral theses was also estimated. The data were collected up to 2005 (June). However, articles published in recent years may be included in later doctoral theses, so the results are likely to underestimate the proportion of articles in doctoral theses. It usually takes about three to five years to write a doctoral thesis, but as seen in Table 2, it can also take a considerably longer time. The search for this data was based solely on Web of Science search criteria and the results included some non-relevant articles, while some relevant articles may also have been missed. However, the estimate of proportion of Finnish schizophrenia articles that are part of a doctoral theses is probably not affected by the search procedure.

6.3.2 *Bibliometric analysis of Finnish scientific journal articles on schizophrenia (II)*

Strengths of the study

As far as the author is aware, this was the first bibliometric analysis of journal articles on schizophrenia published by Finnish research organizations.

The time taken to receive citations varies for articles published in different years. In this study, in order to avoid this problem, articles were classified annually into highly cited (25%) articles and others. Another solution would be to include only citations in the first two years following publication, for example.

The usefulness of the ISI databases was validated by also searching for articles using several other databases, and it was found to include a large

proportion of all the identified studies, although it was not entirely comprehensive. The search conducted only from the Web of Science included 83% of articles found in the search of seven international databases (CINAHL, EBSCOhost, Elsevier, Ovid, PsycINFO, PubMed, Web of Science) and three national databases (Aleksi, Arto, Medic). The results from searches of other individual databases did not yield such good results. The results regarding the coverage of the Web of Science are even better than those presented by Ingwersen (2002), who reported that approximately 65% of the total journal output indexed in Medline (PubMed) was covered by the ISI databases (Web of Science). In this study the high coverage of the ISI databases may be explained by the Finnish funding system, which encourages researchers to publish their papers in journals with high impact factors. The data do not cover all Finnish schizophrenia articles published between 1996–2005; however, as the search strategy is impartial, it is unlikely that this lack of coverage affected the comparisons between institutions.

In order to specify the search, an impartial search of articles' titles and author-given keywords was conducted, as the original search results also included, for instance, articles where "schizophreni*" was only mentioned as a keyword of the references of the articles (the so-called "Keyword Plus"). "Schizophreni*" had to be mentioned in the title or author-given keywords.

In this study only the Web of Science database was used because it is a multidisciplinary database and also includes information on the citations received as well as the addresses of all the participating institutions. In addition, this method is practical and saves time, because it is not necessary to gain access to the articles in question.

Limitations of the study

In order to investigate the number of articles more profoundly, a search should be conducted using several databases. The Web of Science is a database especially applicable in a citation study. However, the representation of articles from different decades varies greatly. Although the database is constantly updated, a large number of articles are still absent. Citations could additionally be located from other databases (*e.g.* Scopus and Google scholar) (Bakkalbasi *et al.* 2006). In a recent study by Falagas *et al.* (2008), it was found that for citation analysis, Scopus offers about 20% more coverage than the Web of Science, whereas Google Scholar offers results of inconsistent accuracy. Scopus covers a wider

journal range, which is of help both in keyword searching and citation analysis, but it is currently limited to recent articles (published after 1995) compared to the Web of Science. (Falagas *et al.* 2008.)

In this study, selection bias may have existed in the data gathered from the database search. However, this was not likely to have greatly affected the results, since it would not have favoured any particular institution. However, it is possible that institutions have their own policies and culture in selecting the publication forum, which may affect the results. This could be avoided by using several databases when conducting searches. Overall, when utilizing databases in scientific searches, one should be aware of the possible selection bias and its effects on the findings of the conducted search. The limitations of bibliometric methods in scientific research evaluation have been discussed earlier (see chapter 6.2.1.).

6.3.3 Meta-analysis on the prevalence of alcohol use disorders in schizophrenia (III & IV)

Strengths of the study

This is a comprehensive systematic review of recent studies presenting results on AUD and CUD in schizophrenia. These are also first meta-analyses on these topics. The data cover a long time period (1996–2008) and thus it was possible to include a large number of studies (AUD: n = 60; CUD: n = 35) that met our criteria. There was a wide variety of methods and results, and this heterogeneity made it challenging to pool the results. There are certain challenges such as inherent biases and differences in study designs when conducting meta-analyses on observational studies (Stroup *et al.* 2000). In reporting the variation in prevalences, the recommendations of Saha *et al.* (2008) were used. Specific inclusion criteria can be used to exclude studies with methodological problems. For instance, in the current study only articles using the DSM or ICD diagnostic systems were included. Only articles reporting results on diagnoses based on the criteria of ICD-9, ICD-10, DSM-III-R or DSM-IV diagnostic systems (both in schizophrenia and in AUD/CUD) were included. In the majority of the studies the diagnoses of schizophrenia and AUD/CUD were ascertained from several sources.

Limitations of the study

A systematic data base search and extensive manual search from several scientific journals were conducted. In addition, several authors were contacted to receive unpublished data. However, it is possible that some studies presenting results on the prevalences of AUD or CUD in patients with schizophrenia are missing. *E.g.* studies where AUD/CUD is not the main interest of the article may have been missed

Metaregression was used to examine the effect of study characteristics on the prevalence for AUD and CUD. Due to possible differences in other study characteristics metaregression is not a very efficient method. The focus was on estimating the prevalence of AUD or CUD in schizophrenia patients, not on examining specific study characteristics separately. Therefore in the sample there are only a few studies among the original studies looking specifically at study characteristics. These studies are now discussed separately. Study characteristics could be examined more efficiently in a separate meta-analysis with specially developed inclusion and exclusion criteria. These results presented here are generalizable mainly to clinical samples, as original studies included mostly patients under treatment. Another limitation is that the prevalence estimates presented here are mainly from Western samples. Due to limited resources it was possible to include only articles published in English. Without language limitations a more comprehensive view on global AUD and CUD prevalence estimates in schizophrenia patients could perhaps be achieved.

7 Conclusions

7.1 Main conclusions

International cooperation as well as the number of theses consisting of a series of papers has increased, although there are differences in publication culture between scientific organizations. The international visibility of Finnish schizophrenia research has increased in terms of citations received and publication in journals with higher impact factors .

The current funding system emphasizes rapidly developing research areas and articles written in English, perhaps at the expense of national and treatment studies. This may affect the research culture and even slow down the development and improvement of the national treatment system. One of the aims of medical faculties is to produce new information that can be utilized in improving treatment systems and patient care. At present, the state's funding system for research does not support this task.

Bibliometric methods are feasible in research evaluation. However, the methods should be used with care. This study used schizophrenia research as an example and differences were found between research subfields. These differences may be even greater when evaluating psychiatric research as a whole, not to mention evaluation across different specialities. More sophisticated and specially developed bibliometric indicators or indexes should be developed in order to improve the comparison of separate research areas.

Alcohol use disorders are common in schizophrenia patients, although a decreasing trend in AUD in schizophrenia was observed. The decrease may be explained by changes in diagnostic systems, even though it is also possible that other addictive substances, such as cannabis, have replaced alcohol in some countries. However, this hypothesis needs further investigation.

Cannabis use disorders are rather common in schizophrenia patients and especially common among young, male and first-episode patients. Our results indicate that cannabis may nowadays be a more commonly abused substance among young schizophrenia patients than alcohol. However, this hypothesis needs further research. It is important to report information on substance use disorders in schizophrenia patient samples, since it may affect the findings of studies in various research areas.

7.2 Implications of the study

The aim of this research was to present information science and bibliometrics as one of its methods for finding and analyzing published studies. Especially in those fields of science in which the amount of new information is rapidly increasing, the methods of information science presented in this study can help individual researchers and general practitioners to find essential information. In addition, by utilizing the methods of information sciences, it is possible to conduct extensive and impartial systematic searches, which are essential in many scientific evaluation processes.

Bibliometric methods were also feasible in the evaluation of psychiatric research. However, it was found in this study that even within a single research topic (schizophrenia), evaluation based on the impact factors of publishing journals emphasizes certain subfields. These findings should be taken account in research evaluation processes and may help research evaluators in their work.

Articles written in collaboration with international organizations seemed to receive more citations and were published in journals with higher impact factors, which highlights the importance of developing scientific networks. In doctoral theses, the number of monographs has decreased. The current funding system supports the writing of doctoral theses consisting of a series of original papers and favours epidemiological and biological research rather than treatment topics. This may affect the research culture and even slow down the development and improvement of the national treatment system. The partitioning of funding in medical faculties between different specialities is also strongly based on the number doctoral degrees. The findings of this study support previous concerns about the negative effect of the current funding system on clinically oriented studies and studies on the national treatment system. These findings may help in designing a more equal funding system for medical research in the future.

Meta-analysis has not previously been conducted on alcohol or cannabis use disorders in schizophrenia. In previous reviews, the range of prevalence of AUD or CUD has been wide. A pooled estimate of the prevalence was presented, in addition to reviewing recent studies from different countries and patient samples. Alcohol and cannabis use disorders are common in schizophrenia patients. Recognizing substance use disorders as a significant comorbidity in schizophrenia patients that negatively affects the patients' outcome is relevant in order to offer better care and develop new treatment strategies.

7.3 Future research

The Ministry of Social Affairs and Health has proposed a change to the current system of funding scientific research at universities and university hospitals. In the future, it would be interesting to investigate and analyse the effects of this possible change using the methods of information science. It would also be interesting to examine whether the current focus on epidemiology, imaging and genetic research persists and how the number of national treatment system studies and studies published in Finnish medical journals develops. In addition, international networking and its effect on the Finnish research culture is an important research topic. It would be relevant to expand this research in the future and investigate, for instance, research on psychiatry instead of only schizophrenia.

In the meta-analysis the study characteristics affecting the prevalence of AUD and CUD were examined by utilizing metaregression methods. However, these characteristics could be more efficiently studied in a separate meta-analysis with special inclusion criteria. This will be one of the topics of future research.

The most commonly abused substances among schizophrenia patients are nicotine, alcohol and cannabis (Drake & Mueser 1996). In the future, one aim is to consider the possible change in substance use profiles between cannabis and alcohol over the years. Substance use habits are greatly affected by cultural factors. Only a few studies on substance use disorders in schizophrenia patients have recently been conducted in Finland and on Finnish patient samples. Therefore, one aim of future research is to further study substance use disorders in a Finnish schizophrenia patient sample (Northern Finland 1966 Birth Cohort study).

Bibliometric methods, *e.g.* the number of citations and impact factors, currently play an important role in the evaluation of scientific research in medicine. However, new and more feasible methods are needed, such as in the comparison of research published in different specialties, and specially developed indexes could be used. This development will be challenging and could be a topic for future research.

References

- Achte KA (1961) Der Verlauf der Schizophrenie und der schizophreniformen Psychosen. *Acta Psychiatr Scand* 36 (suppl 155): 1–273. (History of schizophrenia and schizophreniform psychoses, in German).
- Adam D (2002) The counting house. *Nature* 415: 726–729.
- Addington J & Addington D (2007) Patterns, predictors and impact of substance use in early psychosis: a longitudinal study. *Acta Psychiatr Scand* 115: 304–309.
- Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, Gøtzsche PC, Lang T & CONSORT GROUP (Consolidated Standards of Reporting Trials) (2001) The revised CONSORT statement for reporting randomized trials: Explanation and elaboration. *Ann Intern Med* 134: 663–694.
- Andréasson S, Allebeck P, Engström A, Rydberg U. (1987) Cannabis and schizophrenia. A longitudinal study of Swedish conscripts. *Lancet* 2: 1483–1486.
- Bakkalbasi N, Bauer K, Glover J & Wang L (2006) Three options for citation tracking: Google Scholar, Scopus and Web of Science. *Biomed Digit Libr.*3: 7.
- Bangert-Drowns RL (1986) Review of Developments in Meta-Analytic Method. *Psychol Bull* 99: 388–399.
- Barnett JH, Werners U, Secher SM, Hill KE, Brazil R, Masson K, Pernet DE, Kirkbride JB, Murray GK, Bullmore ET & Jones PB (2007) Substance use in a population-based clinic sample of people with first-episode psychosis. *Br J Psychiatry* 190: 515–520.
- Berghmans T, Meert AP, Mascaux C, Paesmans M, Lafitte JJ & Sculier JP (2003) Citation indexes do not reflect methodological quality in lung cancer randomised trials. *Ann Oncol* 14: 715–721.
- Blettner M, Sauerbrei W, Schlehofer B, Scheuchenpflug T & Friedenreich C (1999) Traditional reviews, meta-analyses and pooled analyses in epidemiology. *Int J Epidemiol* 28: 1–9.
- Bloch S & Walter G (2001) The Impact Factor: time for change. *Aust NZ J Psychiatry* 35: 563–568.
- Buckley P (2006) Prevalence and consequences of the dual diagnosis of substance abuse and severe mental illness. *J Clin Psychiatry* 67 Suppl.7: 5–9.
- Cantor-Graae E, Nordström LG & McNeil TF (2001) Substance abuse in schizophrenia: a review of the literature and a study of correlates in Sweden. *Schizophr Res* 48: 69–82.
- Case DO. The concept of information (2007) In: *Looking for information: A survey of research on information seeking, needs and behaviour* (2nd edition). United Kingdom, Academic Press: 39–67.
- Compton MT, Furman AC & Kaslow NJ (2004) Lower negative symptom scores among cannabis-dependent patients with schizophrenia-spectrum disorders: preliminary evidence from an African American first-episode sample. *Schizophr Res* 71: 61–64.
- Compton MT, Whicker NE, Hochman KM. Alcohol and cannabis use in Urban, African American, first-episode schizophrenia-spectrum patients: associations with positive and negative symptoms. *J. Clin Psychiatry* 2007;68: 1939–1945.

- Cook DJ, Sackett DL & Spitzer WO (1995) Methodologic guidelines for systematic reviews of randomized control trials in health care from the Potsdam consultation on meta-analysis. *J Clin Epidemiol* 48: 167–171.
- Cook DJ, Mulrow CD & Haynes RB (1997) Systematic reviews: synthesis of best evidence for clinical decisions. *Ann Intern Med* 126: 376–380.
- Corrall C, Wyer P, Zick L & Bockrath C (2002) How to Find Evidence When You Need It, Part 1: Databases, Search Programs, and Strategies. *Ann Emerg Med* 39: 302–306.
- Cottler LB (1993) Comparing DSM-III-R and ICD-10 substance use disorders. *Addiction* 88: 689–696.
- Dawe S, Seinen A & Kavanagh D (2000) An Examination of the Utility of the AUDIT in People with Schizophrenia. *J Stud Alcohol* 61: 744–750.
- Debackere K & Glänzel W (2004) Using a bibliometric approach to support research policy making: the case of the Flemish BOF-key. *Scientometrics* 59: 253–276.
- DeLisi L, Mesen A, Rodriguez C Bertheau A, LaPrade B, Llach M, Riondet S & Razi K (2001) Clinical characteristics of schizophrenia in multiply affected Spanish origin families from Costa Rica. *Psychiatr Genet* 11: 145–152.
- Delucchi KL & Bostrom A. (2004) Methods for analysis of skewed data distributions in psychiatric clinical studies: working with many zero values. *Am J Psychiatry* 161:1159–1168.
- Dervaux A, Bayle FJ, Laqueille X, Bourdel MC, Le Borgne MH, Olié JP & Krebs MO (2001) Is substance abuse in schizophrenia related to impulsivity, sensation seeking, or anhedonia? *Am J Psychiatry* 158: 492–494.
- Dervaux A, Bayle FJ, Laqueille X, Bourdel MC, Leborgne M, Olié JP & Krebs MO (2006) Validity of the CAGE questionnaire in schizophrenic patients with alcohol abuse and dependence. *Schizophr Res* 81: 151–155.
- Deshmukh A, Rosenbloom MJ, Pfefferbaum A & Sullivan EV (2002) Clinical signs of cerebellar dysfunction in schizophrenia, alcoholism, and their comorbidity. *Schizophr Res* 57: 281–291.
- Dixon L (1999) Dual diagnosis of substance abuse in schizophrenia: prevalence and impact on outcomes. *Schizophr Res* 35(Suppl): 93–100.
- Drake RE & Mueser KT (1996) Alcohol-use disorder and severe mental illness. *Alcohol Health Res World* 20: 87–93.
- Dubertret, C, Bidard I, Ades J & Gorwood P (2006) Lifetime positive symptoms in patients with schizophrenia and cannabis abuse are partially explained by co-morbid addiction. *Schizophr Res* 86: 284–290.
- Falagas ME, Pitsouni EI, Malietzis GA & Pappas G (2008) Comparison of PubMed, Scopus, Web of Science, and Google Scholar: strengths and weaknesses. *FASEB J* 22: 338–342.
- Figueira I, Jacques R & Leta J (2003) A comparison between domestic and international publications in Brazilian psychiatry. *Scientometrics* 56: 317–327.
- Floridi L (2005) 'Semantic Conceptions of Information', *The Stanford Encyclopedia of Philosophy* (Winter 2005 Edition), Edward N. Zalta (ed.). Available online at Stanford University.

- Folsom D, Jeste DV (2002) Schizophrenia in homeless persons: a systematic review of the literature. *Acta Psychiatr Scand* 105:404–413.
- Fowkes F & Fulton P (1991) Critical appraisal of published research: introductory guidelines. *BMJ* 302 (6785): 1136–1140.
- Fowler IL, Carr VJ, Carter NT & Lewin TJ (1998) Patterns of current and lifetime substance use in schizophrenia. *Schizophr Bull* 24: 443–455.
- Frances RJ (1996) Schizophrenia and substance abuse. *Psychiatr Ann* 26: 523–527.
- Garfield E (1978) High impact science and the case of Arthur Jensen. *Essays of an Information Scientist* 3: 652–662.
- Garfield E (1983) How to use citation analysis for faculty evaluations, and when it is relevant? Part 2. *Essays of an Information Scientist* 6: 363–372.
- Garfield E (1986) Which medical journals have the greatest impact? *Ann Intern Med* 105: 313–320.
- Garfield E (1999) Journal impact factor: a brief review. *CMAJ* 161: 979–980.
- Grant BF, Harford TC, Hasin DS, Chou P & Pickering R (1992) DSM-III-R and the proposed DSM-IV alcohol use disorders, United States 1988: A nosological comparison. *Alcohol Clin Exp Res* 16: 215–221.
- Grant BF (1993) ICD-10 and proposed DSM-IV harmful use of alcohol/ alcohol abuse and dependence, United States 1988: Nosological comparison. *Alcohol Clin Exp Res* 17: 1093–1101.
- Gråwe RW, Pedersen PB & Widen JH (1997) Changes in prevalence and comorbidity in a total population of patients with psychotic disorders in Norwegian psychiatric hospitals. *Nord J Psychiatry* 51: 127–132.
- Gregg L, Barrowclough C & Haddock G (2007) Reasons for increased substance use in psychosis. *Clin Psychol Rev* 27: 494–510.
- Hambrecht M, Häfner H (2000) Cannabis, vulnerability, and the onset of schizophrenia: an epidemiological perspective. *Aust N Z J Psychiatry* 34:468–475.
- Heikkinen J, Isohanni M, & Miettunen J (2007) Lääketieteen kirjallisuustietokannat ja tiedonhaku. *Suom Laakaril* 22: 2165–2170. (Searching for information in medical databases, in Finnish).
- Heikkinen A (2005) Pohjoismaiden ja alankomaiden englanninkielisten skitsofrenia - aiheisten artikkelien määrällinen kehitys ja kansainvälinen näkyvyys vuosina 1986–2003. MA thesis, Univ Oulu, Dept Information Science. (Quantitative trend and international visibility of Nordic and Dutch schizophrenia research articles published in English between 1986 to 2003, in Finnish).
- Heikkinen M (1996) Psychiatric research in Finland: alive and well, but in need of money and independence. *International evaluation of psychiatric research in Finland 1994–95. Psychiatria Fennica* 27: 9–18.
- Helsingin yliopisto (2008) Tieteellinen jatkokoulutus. Opinto-opas 2007–2008. Helsinki, Helsingin yliopisto, Lääketieteellinen tiedekunta (Study guide for postgraduate studies 2007–2008. University of Helsinki, in Finnish).
- Higgins JPT, Green S (2009). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.2. The Cochrane Collaboration.

- Hiller W (1989) Alcohol dependence in ICD-9 and DSM-III-R: a comparative polydiagnostic study. *Eur Arch Psychiatr Neurol Sci* 239: 101–108.
- Hirsch J (2005) An index to quantify an individual's scientific research output. *PNAS* 102: 16569–16572.
- Hirsch SR & Weinberger DR (2003). *Schizophrenia*. 2nd edition. Bath, UK, Blackwell Publishing.
- Hovatta I, Lichtermann D, Juvonen H, Suvisaari J, Terwilliger JD, Arajärvi R, Kokko-Sahin ML, Ekelund J, Lönnqvist J & Peltonen L (1998) Linkage analysis of putative schizophrenia gene candidate regions on chromosomes 3p, 5q, 6p, 8p, 20p and 22q in a population-based sampled Finnish family set. *Mol Psychiatry* 3: 452–457.
- Hubert JJ (1981) General Bibliometric Models. *Libr Trends* 30: 65–79.
- Hyland K (2003) Self-citation and self-reference: Credibility and promotion in academic publication. *Journal of the American Society for Information Science and Technology* 54:251–259.
- Ignatius J & Nuorteva J (1999) Väittelystä väitöskirjaan – lääketieteellisen väitöskirjan historia. In: Patja K, Huhtaniemi I, Ikonen E & Kontula K (eds). *Kohti karonkkaa*. Jyväskylä, Gummerus Kirjapaino Oy: 58–82. (From defending a thesis to a doctoral thesis – A history of doctoral thesis in Medicine. In: Towards Defencing of Doctoral Thesis, In Finnish).
- Ingwersen P (2002) Visibility and impact of research in psychiatry for Northern European countries in EU, US and world contexts. *Scientometrics* 54: 131–144.
- Jones PB, Rantakallio P, Hartikainen AL, Isohanni M & Sipilä P (1998) Schizophrenia as a long-term outcome of pregnancy, delivery, and perinatal complications: A 28-year follow-up of the 1966 North Finland general population birth cohort. *Am J Psychiatry* 155: 355–364.
- Kaczynski Pollock N, Martin CS & Langenbucher JW (2000) Diagnostic concordance of DSM-III, DSM-III-R, DSM-IV and ICD-10 alcohol diagnoses in adolescents. *J Stud Alcohol* 61: 439–446.
- Kaltenborn K-F & Kuhn K (2004) The journal Impact Factor as a parameter for the evaluation of researchers and research. *Rev Esp Enferm Dig* 96: 460–476.
- Kanato M (2008) Drug use and health among prison inmates. *Curr Opin Psychiatry* 21: 252–254.
- Karam EG, Yabroudi PF & Melhem NM (2002) Comorbidity of substance abuse and other psychiatric disorders in acute general psychiatric admissions: a study from Lebanon. *Compr Psychiatry* 43: 463–468.
- Kavanagh DJ, Waghorn G, Jenner L, Chant DC, Carr V, Evans M, Hemnan H, Jablensky A & McGrath JJ (2004) Demographic and clinical correlates of comorbid substance use disorders in psychosis: multivariate analyses from an epidemiological sample. *Schizophr Res* 66: 115–124.
- Kekomäki M (2001) State grants for health science research. Evaluation of uses and proposals for a steering system. Working Group Memorandums of the Ministry of Social Affairs and Health 3. (In Finnish).

- Kirkpatrick B, Amador XF, Flaum M, Yale SA, Gorman JM, Carpenter WT Jr, Tohen M & McGlashan T (1996) The deficit syndrome in the DMS-IV Field Trial: I. Alcohol and other drug abuse. *Schizophr Res* 20: 69–77.
- Kuopion yliopisto (2007) Tieteellinen jatkokoulutus. Opinto-opas 2007–2008. Kuopio, Kuopion yliopisto, Opintoasioiden toimisto (Study guide for postgraduate studies 2007–2008, University of Kuopio, in Finnish).
- Kurmis A (2003) Understanding the Limitations of the Journal Impact Factor. *J Bone Joint Surg Am* 85: 2449–2454.
- Leta J, Jacques R, Figueira I & de Meis L (2001) Central international visibility of Brazilian psychiatric publications from 1981 to 1995. *Scientometrics* 50: 241–254.
- Lewis CM, Levinson DF, Wise LH, DeLisi LE, Straub RE, Hovatta I, Williams NM, Schwab SG, Pulver AE, Faraone SV, Brzustowicz LM, Kaufmann CA, Garver DL, Gurling HM, Lindholm E, Coon H, Moises HW, Byerley W, Shaw SH, Mesen A, Sherrington R, O'Neill FA, Walsh D, Kendler KS, Ekelund J, Paunio T, Lönngqvist J, Peltonen L, O'Donovan MC, Owen MJ, Wildenauer DB, Maier W, Nestadt G, Blouin JL, Antonarakis SE, Mowry BJ, Silverman JM, Crowe RR, Cloninger CR, Tsuang MT, Malaspina D, Harkavy-Friedman JM, Svrakic DM, Bassett AS, Holcomb J, Kalsi G, McQuillin A, Brynjolfson J, Sigmundsson T, Petursson H, Jazin E, Zoëga T & Helgason T (2003) Genome scan meta-analysis of schizophrenia and bipolar disorder, part II: Schizophrenia. *Am J Hum Genet* 73: 34–48.
- Lewis G & Devey ME (1998) Bibliometric methods for the evaluation of arthritis research. *Rheumatology* 38: 13–20.
- Löhönen J, Isohanni M, Nieminen P & Miettunen J (2009a) A guide for medical information searches of bibliographic databases – psychiatric research as an example. *Int J Circumpolar Health* 68: 394–404.
- Löhönen J, Isohanni M, Nieminen P & Miettunen J (2009b) Coverage of the bibliographic databases in mental health research. *Nord J Psychiatry*, in press.
- López-Muñoz F & Rubio G (1995) Spanish scientific production in psychiatry: Bibliometric study of the publications with international circulation during the period 1980–1993. *An Psiquiatr* 11: 68–75. (in Spanish)
- López-Muñoz F, Alamo C, Rubio G, García-García P, Martín-Agueda B & Cuenca E (2003) Bibliometric analysis of biomedical publications on SSRIs during the period 1980–2000. *Depress Anxiety* 18: 95–103.
- López-Muñoz F, Vieta E, Rubio G, García-García P & Alamo C (2006) Bipolar disorder as an emerging pathology in the scientific literature: a bibliometric approach. *J Affect Dis* 92: 161–170.
- Margolese HC, Malchy L, Negrete JC, Tempier R & Gill K (2004) Drug and alcohol use among patients with schizophrenia and related psychoses: levels and consequences. *Schizophr Res* 67: 157–166.
- Mattox DE (2000) Welcome to ARCHIVES CME. *Arch Otolaryngol Head Neck Surg*. 126:914.
- McCreadie RG (2002) Use of drugs, alcohol and tobacco by people with schizophrenia: case-control study. *Br J Psychiatry* 181: 321–325.

- McDonald S, Taylor L, Adams C (1999) Searching the right database. A comparison of four databases for psychiatry journals. *Health Libraries Review* 16: 151–156.
- McGrath J, Saha S, Welham J, El Saadi O, MacCauley C & Chant D (2004) A systematic review of the incidence of schizophrenia: the distribution of rates and the influence of sex, urbanicity, migrant status and methodology. *BMC Med* 2: 13.
- Miettunen J & Nieminen P (2004) The effect of statistical methods and study reporting characteristics on the number of citations: a study of four general psychiatric journals. *Scientometrics* 57: 379–390.
- Ministry of Social Affairs and Health (2004) Government Decree on University Degrees Chapter 5, Section 22. (In Finnish).
- Ministry of Social Affairs and Health (2006) Working Group Memorandum. Revision of the criteria for allocation of research funds from specified government transfers. (In Finnish, abstract in English).
- Modestin J, Gladen C & Christen S (2001) A Comparative Study on Schizophrenic Patients with Dual Diagnosis. *J Addict Dis* 29: 41–51.
- Moher D, Tetzlaff J, Tricco AC, Sampson M & Altman DG (2007) Epidemiology and Reporting Characteristics of Systematic Reviews. *PLoS Med* 4: e78.
- Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF & QUOROM Grp (2000) Improving the quality of reports of meta-analyses of randomised controlled trials: The QUOROM statement. *Onkologie* 23: 597–602.
- Moilanen K, Veijola J, Läksy K, Mäkikyrö T, Miettunen J, Kantojärvi L, Kokkonen P, Karvonen JT, Herva A, Joukamaa M, Järvelin MR, Moring J, Jones PB & Isohanni M (2003) Reasons for the diagnostic discordance between clinicians and researchers in schizophrenia in the Northern Finland 1966 Birth Cohort. *Soc Psychiatry Psychiatr Epidemiol* 38: 305–310.
- Moore THM, Zammit S, Lingford-Hughes A, Barnes TRE, Jones PB, Burke M & Lewis G (2007) Cannabis use and risk of psychosis or affective mental health outcomes: a systematic review. *Lancet* 370: 319–328.
- Mueser KT, Yarnold PR, Levinson HS, Singh H, Bellack AS, Kee K, Morrison RL & Yadam KG (1990) Prevalence of substance abuse in schizophrenia: demographic and clinical correlates. *Schizophr Bull* 16: 31–55.
- Mueser KT, Yarnold PR, Rosenberg SD, Swett C, Miles KM & Hill D (2000) Substance use disorder in hospitalized severely mentally ill psychiatric patients: prevalence, correlates, and subgroups. *Schizophr Bull* 26: 179–192.
- Nieminen P & Isohanni M (1998) Bibliometric analysis on Finnish psychiatric research in years 1994–1997. *Sos Laaketiet Aikak* 35: 152–162. (In Finnish)
- Nieminen P & Isohanni M (1999) Bias against European journals in medical publication databases. *Lancet* 8;353:1592.
- Österman B (1989) Suomalaisen psykiatrian ja lastenpsykiatrian bibliografia – Finlands psykiatriska och barnpsykiatriska bibliografi 1762–1988. Uudenmaan mielisairaanhoitopiirin julkaisuja I. Kellokoski: Kellokosken sairaala. (Bibliography of Finnish psychiatry and child psychiatry 1762–1988, in Finnish and Swedish).

- University of Oulu (2007) Study guide for postgraduate studies 2007–2008. Oulu, University of Oulu, Medical faculty.
- Pearson K (1904) Report on certain enteric fever inoculation statistics. *BMJ* 3: 1243–1246.
- Perälä J, Suvisaari J, Saarni SI, Kuoppasalmi K, Isometsä E, Pirkola S, Partonen T, Tuulio-Henriksson A, Hintikka J, Kieseppä T, Härkänen T, Koskinen S & Lönqvist J (2007) Lifetime prevalence of psychotic and bipolar I disorders in a general population. *Arch Gen Psychiatry* 64: 19–28.
- Potvin S, Sepehry AA & Stip E (2006) A meta-analysis of negative symptoms in dual diagnosis schizophrenia. *Psychol Med* 36: 431–440.
- Potvin S, Sepehry A & Stip E (2007) Meta-analysis of depressive symptoms in dual-diagnosis schizophrenia. *Aust N Z J Psychiatry* 41: 792–799.
- Rabinowitz J, Mark M, Popper M & Slyuzberg M (1996) Reported comorbidity of mental disorders with substance abuse among psychiatric inpatients in Israel. *J Ment Health Adm* 23: 471–478.
- Rabinowitz J, Bromet EJ, Lavelle J, Carlson G, Kovasznay B & Schwartz JE (1998) Prevalence and severity of substance use disorders and onset of psychosis in first-admission psychotic patients. *Psychol Med* 28: 1411–1419.
- Rahman M & Fukui T (2003) Biomedical publication—global profile and trend. *Public Health* 117: 274–280.
- Romanov K (2002) Tietoverkon lääketieteelliset tietolähteet kliinikon apuna. *Suom Laakaril* 57: 2419–2422. (How clinicians can utilize medical information resources, in Finnish)
- Romanov K & Aarnio M (2006) A survey of the use of electronic scientific information resources among medical and dental students. *BMC Med Educ* 6: 28.
- Saha S, Chant D, Welham J & McGrath J (2005) A systematic review of the prevalence of schizophrenia. *PLoS Med* 2: e141.
- Saha S, Chant D, McGrath J (2008) Meta-analyses of the incidence and prevalence of schizophrenia: conceptual and methodological issues. *Int J Meth Psychiatr Res* 17:55–61.
- Schuckit MA, Hesselbrock V, Tipp J, Anthenelli R, Bucholz K & Radziminski S (1994) A comparison of DSM-III-R, DSM-IV and ICD-10 substance use disorders diagnoses in 1922 men and women subjects in the COGA study. *Addiction* 89: 1629–1638.
- Seglen PO (1997) Why the impact factor of journals should not be used for evaluating research. *BMJ* 314: 498–502.
- Shaw J, Hunt IM, Flynn S, Amos T, Meehan J, Robinson J, Bickley H, Parsons R, McCann K, Burns J, Kapur N & Appley L (2006) The role of alcohol and drugs in homicides in England and Wales. *Addiction* 101: 1117–1124.
- Shojania KG, Sampson M, Ansari MT, Ji J, Doucette S & Moher D (2007) How quickly do systematic reviews go out of date? A survival analysis. *Ann Intern Med* 147: 224–233.
- Slavin R (1986) Best-Evidence Synthesis: An Alternative to Meta-Analytic and Traditional Reviews. *Educational Researcher* 15: 5–11.

- Smith R (1998) Unscientific practice flourishes in science. Impact factors of journals should not be used in research assessment. *BMJ* 316:1036–1040.
- Stata Corporation (2001) *Stata User's Guide*. College Station, Texas, USA, Stata Press.
- Stefanis NC, Delespaul P, Henquet C, Bakoula C, Stefanis CN, Van Os J (2004) Early adolescent cannabis exposure and positive and negative dimensions of psychosis. *Addiction* 99: 1333–1341.
- Sterne JAC, Bradburn MJ & Egger D (2001) Meta-analysis in Stata. In: Egger M, Smith G, Davey & Altman D (eds). *Systematic reviews in health care: meta-analysis in context*. London: BMJ Publishing Group.
- Stroup D, Berlin J, Morton S, Olkin I, Williamson GD, Rennie D, Moher D, Becker B, Sipe T & Thacker S (2000) Meta-analysis of Observational Studies in Epidemiology A Proposal for Reporting. *JAMA* 283: 2008–2012.
- Svirskis T, Korkeila J, Heinimaa M, Huttunen J, Ilonen T, Ristkari T, Hietala J, Syvälahti E, McGlashan T, Vahlberg T & Salokangas RK (2007) Quality of life and functioning ability in subjects vulnerable to psychosis. *Compr Psychiatry* 48: 155–160.
- Talamo A, Centorrino F, Tondo L, Dimitri A, Hennen J, Baldessarini RJ. (2006) Comorbid substance-use in schizophrenia: relation to positive and negative symptoms. *Schizophr Res*;86: 251–255.
- Tampereen yliopisto (2006) Tieteellinen jatkokoulutus. Opinto-opas. Tampere, Tampereen yliopisto, Lääketieteellinen tiedekunta. (Study guide for postgraduate studies. University of Tampere 2006, in Finnish).
- Turun yliopisto (2007) Tieteellinen jatkokoulutus. Opinto-opas 2007–2008. Turku, Turun yliopisto, Lääketieteellinen tiedekunta (Study guide for postgraduate studies 2007–2008. Medical faculty, University of Turku, in Finnish).
- United Nations. World Drug Report 2008 (2008) Office on Drugs and Crime, United Nations.
- Vakkari P (2003) Mitä on informaatiotutkimus? In: Mäkinen I (ed) *Tiedon tie. Johdatus informaatiotutkimukseen*. Jyväskylä, Gummerus Kirjapaino: 27–30. (What is information science, in Finnish)
- Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, & Egger M & STROBE Initiative (2007) Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). Explanation and Elaboration. *Epidemiology* 18: 805–835.
- Wade D, Harrigan S, Harris MG, Edwards J & McGorry PD (2006) Pattern and correlates of inpatient admission during the initial acute phase of first-episode psychosis. *Aust N Z J Psychiatry* 40: 429–36.
- West R & McIlwaine A (2002) What do citation counts count for in the field of addiction? An empirical evaluation of citation counts and their link with peer ratings of quality. *Addiction* 97: 501–504.
- World Health Organization (2004) *Global status report on alcohol 2004*. World Health Organization, Geneva.

- Zammit S, Allebeck P, Andréasson S, Lundberg I, Lewis G. (2002) Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. *BMJ* 325:1199.
- Zammit S, Moore THM, Lingford-Hughes A, Barnes TR, Jones PB, Burke M, Lewis G (2008) Effects of cannabis use on outcomes of psychotic disorders: systematic review. *Br J Psychiatry* 193:357–363.
- Xafenias A, Diakogiannis I, Iacovides A, Fokas K, Kaprinis G (2008) Factors affecting hospital length of stay: Is substance use disorder one of them? A study in a Greek public psychiatric hospital. *Am J Addict* 17: 447–451.
- Ziedonis M & Trudeau K (1997) Motivation to Quit Using Substances Among Individuals With Schizophrenia: Implications for a Motivation-Based Treatment Model. *Schizophr Bull* 23: 229–238.

Original publications

This thesis is based on the following original publications, which are referred to in the text by the Roman numerals I–IV.

- I Koskinen J, Isohanni M, Kotiranta H, Lauronen E, Koponen H, Tienari P & Miettunen J (2004) Finnish doctoral theses on schizophrenic psychoses – descriptive and bibliometric analysis. *Psychiatria Fennica* 35: 46–67.
- II Koskinen J, Isohanni M, Paajala H, Jääskeläinen E, Nieminen P, Koponen H, Tienari P & Miettunen J (2008) How to use bibliometric methods in evaluation of scientific research? An example from Finnish schizophrenia research. *Nord J Psychiatry* 62: 136–43.
- III Koskinen J, Löhönen J, Koponen H, Isohanni M & Miettunen J (2009) Prevalence of alcohol use disorders in schizophrenia – A systematic review and meta-analysis. *Acta Psychiatr Scand* 120: 85–96.
- IV Koskinen J, Löhönen J, Koponen H, Isohanni M & Miettunen J (2009) Rate of cannabis use disorders in clinical samples of schizophrenia patients: a meta-analysis. *Schizophr Bull.* In press. DOI: 10.1093/schbul/sbp031.

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Original publications are not included in the electronic version of the dissertation.

- I051. Ojala, Kati (2010) Modern methods in the prevention and management of complications in labor
- I052. Auvinen, Juha (2010) Neck, shoulder, and low back pain in adolescence
- I053. Pirkola, Jatta (2010) Gestational diabetes. Long-term, metabolic consequences for the mother and child
- I054. Santaniemi, Merja (2010) Genetic and epidemiological studies on the role of adiponectin and PTP1B in the metabolic syndrome
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- I064. Alaräsänen, Antti (2010) Risk factors and pathways leading to suicide with special focus in schizophrenia. The Northern Finland 1966 Birth Cohort Study
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