Deregulation of Nicotine Replacement Therapy Products in Finland:
Reasons for Pharmaceutical Policy Changes and Reflections on Smoking Cessation Practices

Terhi Kurko
Main Supervisors  Professor Marja Airaksinen, PhD (Pharm)
Clinical Pharmacy Group
Division of Pharmacology and Pharmacotherapy
Faculty of Pharmacy
University of Helsinki
Helsinki, Finland

Docent Kari Linden, PhD (Pharm), MSc (Econ)
University of Helsinki
and
Sr Scientific Advisor
Pfizer Oy
Helsinki, Finland

Co-Supervisor  Pharmacy Owner Kirsi Pietilä, PhD (Pharm)
Pharmacy of Kontula
Helsinki, Finland

Reviewer  Docent Tellervo Korhonen, PhD (Public Health), MSc (Health Care)
Department of Public Health
University of Helsinki
Helsinki, Finland
and
Institute of Public Health and Clinical Nutrition
University of Eastern Finland
Kuopio, Finland

Director Kenneth Shermock, PharmD, PhD
Center for Medication Quality and Outcomes
The Johns Hopkins Hospital
and
Associate Director, Center for Drug Safety and Effectiveness
The Johns Hopkins Bloomberg School of Public Health
United States of America

Opponent  Professor Pekka Puska, MD, PhD, MPolSc
National Institute for Health and Welfare
Helsinki, Finland

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Abstract

Nicotine Replacement Therapy (NRT) products, having been in the pharmaceutical market for over three decades and sold without prescription for a long period of time in many countries, are the most commonly used smoking cessation (SC) pharmacotherapy.

This study explores the deregulation of NRT products from pharmacy-only distribution to general sales in Finland, which took place in 2006. The overall aim of this study was to assess the reasons for the NRT deregulation and its reflections on SC practices in Finland. NRT deregulation was explored from three perspectives: 1) NRT deregulation as a policy-making process; 2) community pharmacists as health care professionals providing guidance on NRT use; and 3) NRT users’ perceptions of NRT in SC.

This multi-method study applied quantitative and qualitative methods. The study of NRT deregulation from the policy-making perspective was based on an inductive content analysis of all the publicly available documents and interviews of 12 Finnish Members of the Parliament (Study I). A nationwide representative survey of every second pharmacy owner and community pharmacist (n=2 291) was conducted a year after the deregulation in 2006-2007 (Studies II & III). The NRT users’ perspectives of the role of NRT in SC were explored by analysing postings in the national internet-based discussion forum (STUMPPI) supporting SC (Study IV). This study was based on a qualitative analysis of smokers’ and quitters’ postings (n=24 481) in five discussion areas during 2007-2012.

The NRT deregulation was politically communicated as a safe and evidence-informed decision promoting public health by advancing SC in Finland. On the basis of the analysis of all the documents and interviews, the following five themes emerged: 1) how deregulation may influence on SC; 2) appropriate and safe use of NRT products taking into account the characteristics of these products. The debate extended beyond NRT and SC to become 3) a debate of the principles of who is allowed to sell medicines and what is the importance of professional advice for treatment outcomes; 4) debate on how evidence-informed the decision was; and 5) the way the political process was carried out. Finally, the analysis revealed that two of the most important motives for the deregulation, poor NRT availability and NRT’s effectiveness in SC, were largely based on assumptions instead of actual scientific evidence.

At the time of the pharmacy owners’ and community pharmacists’ survey in 2007, half of the respondents reported to be familiar with the Finnish SC Guideline. Guideline familiarity enhanced guideline implementation: in addition to counselling on NRT use, the pharmacists familiar with the SC guideline used other guideline-based SC methods more frequently compared with respondents unfamiliar with the Guideline. According to the survey respondents, (n=2 291), NRT deregulation had sizeably diminished the sales of NRT at pharmacies as well as the contacts between NRT customers and community pharmacists. In particular pharmacy owners’ motivation towards counselling NRT customers had decreased. However, community pharmacists still saw it as their duty to guide and support SC.
The studies conducted in the post-NRT deregulation period among community pharmacists (III), and smokers and quitters (IV) found a great variety of NRT usage patterns. The most common usage pattern was the use of too low a dosage or too short a period compared with the instructions for NRT use. With both community pharmacists and smokers and quitters it was perceived to be possible that the use of NRT products can cause dependence on NRT.

In the analysis of smokers’ and quitters’ internet-based discussions (IV) three major themes emerged related to NRT in SC: 1) distrust and negative attitude towards NRT; 2) neutral acceptance of NRT as a useful SC method; and 3) trust on the crucial role of NRT and other SC medicines. The negative attitude was related to the perceptions that NRT use maintains tobacco dependence, fear of NRT dependence or experience of not gaining help from NRT use. NRT was perceived to be useful particularly in the initiation of SC attempts and in dealing with physiological dependence. The most highlighted factors of successful quitting were quitters’ own psychological empowerment and peer support from the discussion community.

The findings of this study suggest that NRT deregulation was politically presented as a significant promotion of public health. In contrast to this, the findings among smokers and quitters imply that simply the increased access and use of NRT may not be as crucial in SC as suggested by different stakeholders during the deregulation process. Instead, many Finnish smokers and quitters saw NRT as less important in SC or held negative perceptions towards NRT use and feared dependence on NRT. Furthermore, the study provided evidence that in Finland NRT products are often used in a way which may not be optimal for treatment success. These findings suggest that many smokers and quitters could benefit from personalized support for NRT use which would include behavioural components and a plan for NRT use to optimize the treatment and avoid the feared dependence on NRT. Community pharmacists could constitute an important countrywide public health resource to provide such counselling and personalized SC plans. However, their motivation and expertise in NRT counselling decreased after the deregulation which means that health care may have lost one guideline-based resource in SC.

The findings of this study highlight the need to further evaluate the benefits gained from the deregulation. There is also a future need to investigate how deregulation will reflect in the following matters in the long run: 1) the development of the rate of smoking among the Finnish adult population, 2) what will be the role of NRT products in SC in terms of gaining permanent abstinence, 3) which SC services and interventions smokers and quitters prefer, and finally, 4) community pharmacists’ motivation and practices to support SC. These aspects should be taken into account in policy-making when planning future SC services and interventions in Finland.
Acknowledgements

This study was carried out at the University of Helsinki, Faculty of Pharmacy, Division of Social Pharmacy during 2006-2012. The planning of this study started already in the spring 2005 after NRT deregulation was publicly suggested. At this time, I was finalizing my Master’s thesis on pharmacies’ participation in multidisciplinary SC collaboration.

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Contents

Abstract .....................................................................................................................................................3
Acknowledgements ...................................................................................................................................7
List of original publications ..................................................................................................................... 12
Definitions of the key concepts ..............................................................................................................13
Abbreviations ............................................................................................................................................18

1 Introduction .......................................................................................................................................20

2 Smoking from a society and individual smokers’ perspective ............................................. 22
   2.1 Smoking from a society perspective .............................................................................................. 22
   2.2 Smoking from individual smoker’s perspective ............................................................................ 23
      2.2.1 Nicotine as the cause of physiological tobacco dependence .............................................. 23
      2.2.2 Behavioural, psychological and social aspects of tobacco dependence ............................ 24
      2.2.3 Tobacco dependence as a chronic disease .......................................................................... 25
   2.3 Brief overview of the tobacco control policy in Finland ............................................................... 26

3 Description of NRT products’ role in SC and its evolution ................................................... 28
   3.1 Brief description of NRT products’ role in SC ............................................................................... 28
   3.2 Recognition of nicotine addiction and the birth of NRT .............................................................. 29
   3.3 The establishment and implementation of evidence-based SC guidelines ................................ 31
      3.3.1 The establishment of evidence-based SC guidelines ........................................................... 31
      3.3.2 SC guideline implementation and factors associated with it ............................................ 33
   3.4 Community pharmacists’ role in counselling the use of non-prescription NRT .................... 36
      3.4.1 International experiences on pharmacists’ involvement in SC ............................................ 36
      3.4.2 The Finnish experience on pharmacists’ involvement in SC ............................................. 37
   3.5 NRT deregulation to general sales ................................................................................................. 39
3.5.1 International NRT deregulations ........................................................................................ 39
3.5.2 The Finnish NRT deregulation ............................................................................................ 40
3.5.3 The role of NRT after deregulation..................................................................................... 40
3.6 Widening NRT use to new user groups and the introduction of combination therapy .......... 41
3.7 NRT for harm reduction ........................................................................................................... 41
3.8 Advocating for a more liberal nicotine policy and market ....................................................... 43

4 Efficacy and effectiveness of OTC NRT ....................................................................................... 44

4.1 Evidence on NRT efficacy and its generalizability to real life .................................................. 44
   4.1.1 Evidence on NRT efficacy.................................................................................................. 44
   4.1.2 Examples of differences between RCT and real life conditions ...................................... 45
   4.1.2.1 Differences between NRT users in RCTs and real life............................................... 45
   4.1.2.2 Other differences between the two conditions......................................................... 45
4.2 Effectiveness of OTC NRT ............................................................................................................. 46
   4.2.1 Different studies assessing the effectiveness of OTC NRT................................................. 46
   4.2.2 Contradictory evidence of the real life effectiveness of OTC NRT .................................. 47
   4.2.2.1 Studies supporting the effectiveness of OTC NRT....................................................... 47
   4.2.2.2 Studies with mixed or non-supporting evidence on OTC NRT effectiveness .......... 48
   4.2.3 Reasons for contradictory results and conclusions of the chapter .................................. 48

5 Key arguments related to NRT deregulation: what was the expectation and what has
been achieved ....................................................................................................................................50

5.1 Evidence of the development of NRT use after deregulation................................................... 52
5.2 Change in NRT pricing after the Finnish deregulation............................................................... 53
5.3 How NRT use in quitting attempts has developed after deregulations? .................................. 54
5.4 Smoking prevalence after NRT deregulations ......................................................................... 55
   5.4.1 Evidence from the US, Australian and British smoking statistics..................................... 55
   5.4.2 Evidence from the Finnish smoking statistics................................................................... 56
5.5 Safety of OTC NRT ....................................................................................................................... 57
6 Real life NRT use: Why NRT deregulation is not directly reflected in smoking statistics? ........................................ 59

6.1 Smokers’ and quitters’ reasons not to use NRT .................................................................................. 59

6.1.1 Popularity of unassisted quitting .............................................................................................. 59

6.1.2 Unwillingness to use NRT ....................................................................................................... 60

6.2 Concept of NRT adherence ............................................................................................................ 62

6.2.1 What is meant by the concept of adherent NRT use? ............................................................... 62

6.3 Real life NRT use patterns ............................................................................................................. 63

6.3.1 Use for a short period .............................................................................................................. 63

6.3.2 Use of too low a dosage ......................................................................................................... 63

6.3.3 Concurrent smoking and NRT use ....................................................................................... 63

6.3.4 Use of NRT for other purposes than quitting ..................................................................... 64

6.4 Other reasons why the detection of the influence of NRT deregulation on smoking statistics is
difficult ............................................................................................................................................. 64

7 Counselling and NRT: evidence base and practical viewpoints .................................................. 65

7.1 Evidence-base related to the combination of counselling and NRT use ....................................... 65

7.2 What kind of counselling is needed in real life practice? ............................................................... 65

8 Summary of the key findings of the literature review (Chapters 3-7) ........................................... 67

9 Aims of the study ................................................................................................................................... 69

10 Materials and methods .................................................................................................................. 70

10.1 Study context and design .......................................................................................................... 69

10.1.1 Brief description of the operationalization of the theoretical background ......................... 70

10.2 Data sources utilized ................................................................................................................... 70

10.2.1 Policy-making related to NRT deregulation .................................................................... 70

10.2.2 Community pharmacists’ survey .................................................................................... 72
10.2.3 Internet-based discussions on NRT use ................................................................. 73

10.3 Methods .................................................................................................................... 74

10.3.1 Qualitative studies utilizing inductive content analysis ...................................... 74

10.3.1.1 Steps in the data analysis .................................................................................. 74

10.3.1.2 Policy-making related to NRT deregulation .................................................... 74

10.3.1.3 Internet-based discussions on NRT use .......................................................... 75

10.3.2 Nationally representative survey among community pharmacists .................. 75

10.3.2.1 The survey instrument ..................................................................................... 75

10.3.2.2 Statistical analysis .......................................................................................... 79

11 Results ......................................................................................................................... 80

11.1 NRT deregulation from policy-making perspective ............................................... 80

11.1.1 NRT deregulation and public health ................................................................. 81

11.1.2 Extensions of the debate: fundamental change in pharmaceutical policy and structures related to policy-making ...................................................... 81

11.2 Community pharmacists’ involvement in SC ....................................................... 82

11.2.1 Community pharmacists’ familiarity with the Finnish SC Guideline ............... 82

11.2.2 The implementation of the SC Guideline-based actions .................................. 83

11.3 Reflections of NRT deregulation on community pharmacists’ perceptions of NRT sales and their professional role in SC ............................................... 85

11.4 How do Finnish smokers and quitters value NRT in SC? .................................... 87

11.4.1 Key explanations given to distrust and negative attitude towards NRT ............ 87

11.4.2 Neutral acceptance of NRT as a useful SC method .......................................... 89

11.4.3 Trust in the crucial role of SC medicines ......................................................... 89

11.4.4 Components of permanent success in SC ....................................................... 89

11.5 NRT usage patterns in Finland ............................................................................. 90

11.5.1 Community pharmacists’ perceptions of NRT usage patterns ......................... 90

11.5.2 Smokers’ and quitters’ perceptions of NRT usage patterns ............................... 91

11.6 Key findings of the study ....................................................................................... 91
12 Discussion .............................................................................................................................................. 93

12.1 Key findings in relation to earlier literature .......................................................................................... 94

12.1.1 NRT deregulation from the political level .......................................................................................... 94

12.1.1.1 The evidence base for the political decision of NRT deregulation ........................................... 94

12.1.1.2 Evidence-informed decision-making and the NRT deregulation process .............................. 95

12.1.2 NRT deregulation from health service providers’ level .................................................................. 96

12.1.2.1 Community pharmacists’ involvement in SC ............................................................................ 96

12.1.2.2 Community pharmacists’ perceptions of their professional role in SC after NRT deregulation ......................................................................................................................................... 97

12.1.3 NRT deregulation from the customers’ level ..................................................................................... 98

12.1.3.1 Explanation given to the negative attitude towards NRT .......................................................... 99

12.1.3.2 NRT usage patterns in Finland in the post-deregulation period ................................................. 100

12.2 Methodological considerations ............................................................................................................ 100

12.2.1 Qualitative studies ............................................................................................................................ 101

12.2.1.1 Analysis of the political process of NRT deregulation .............................................................. 101

12.2.1.2 Smokers’ and quitters’ perspective .............................................................................................. 102

12.2.2 Community pharmacists’ survey .................................................................................................... 103

13 Conclusions, implications for further evaluation, research and health care services 105

13.1 Conclusions ........................................................................................................................................ 105

13.2 Implications for further research and evaluation .................................................................................. 106

13.3 Implications for health care services .................................................................................................. 107

14 References ......................................................................................................................................... 109

Appendices
List of original publications

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Definitions of the key concepts

Abstinence
According to the Glossary of the Cochrane Tobacco Addiction Group (2014) “Abstinence means period of being quit, i.e., stopping the use of cigarettes or other tobacco products”.

Deregulation of nicotine replacement therapy products
Deregulation of nicotine replacement therapy products means a shift of the products’ sales channels from pharmacy-only to general sales. This means that the products can be purchased in a variety of sales outlets including grocery stores, supermarkets, kiosks and gas stations without the supervision or guidance of any health professional (Larsen et al. 2004). The term ‘deregulation’ is often used as a synonym to OTC Switch which describes the change of the status of prescription (Rx) medicine to non-prescription one (World Health Organization 2000). However, in this thesis the term ‘deregulation’ is used to describe the change from pharmacy-only to general sales. (See also the following definitions: ‘Nicotine replacement therapy products’, ‘Over-the-counter medicine’ and ‘OTC conditions for NRT purchase’).

Efficacy
Efficacy means how the studied treatment works on a controlled environment where the effects of the treatment, the study population and the circumstances are isolated from each other by a well-planned and precise study design, control group, randomization, blinding and analysis (Rush 2009, Saturni et al. 2014). At best, these idealistic circumstances are achieved in randomized controlled trials (RCTs), which are known as the golden standard of studies aiming at investigating the efficacy of treatments (Saturni et al. 2014).

Effectiveness
Effectiveness means the assessment of therapeutic outcomes in conditions presenting real life (Rush 2009, Saturni et al. 2014) i.e., how the therapy works in practice. Studies assessing effectiveness in real life have high external validity, as these study designs can include all kinds of patients and environments and their characteristics may have an influence on the results (Saturni et al. 2014).

Evidence-based intervention
According to The Centre of Evidence-based Intervention of University of Oxford (2015): “Evidence-based interventions or programmes are those which have been proven effective in multiple, high-quality randomised controlled trials”. In this thesis the term ‘evidence-based SC intervention’ refers to those SC interventions which are proven to be effective in SC and recommended in the national treatment guidelines (see also Finnish SC Guideline).
Evidence-informed decision making
Evidence-informed decision-making means a procedure which aims to facilitate well-informed, transparent and systematic processes in decision-making, taking into account the decision-making context (Dobrow et al. 2004, Oxman et al. 2009). Evidence-informed decision-making supports policymakers’ understanding of systematic processes ensuring the identification, appraising and usage of relevant research. Furthermore, if evidence-informed decision-making is followed in the decision-making process, evaluation of the decision is highly important (Jansen et al. 2009, Oxman et al. 2009). In this thesis the term evidence-informed decision making refers to the principles in political decision-making.

Finnish smoking cessation (SC) Guideline
In this thesis, The Finnish smoking cessation, SC, Guideline means the national Current Care Guideline of Tobacco Dependence and Smoking Cessation by the Finnish Medical Society Duodecim (2012). According to the Finnish Medical Society Duodecim (2014), “Current Care Guidelines are independent, evidence-based clinical practice guidelines. These national guidelines cover important issues related to Finnish health, medical treatment as well as prevention of diseases. The guidelines are intended as a basis for treatment decisions and can be used by physicians, healthcare professionals and citizens”.

Harm reduction
According to the Cochrane Tobacco Addiction Group (2014) harm reduction is defined as follows: “Strategies to reduce harm caused by continued tobacco/nicotine use, such as reducing the number of cigarettes smoked, or switching to different brands or products, e.g., potentially reduced exposure products (PREPs) or smokeless tobacco”.

Nicotine dependence
Nicotine is the substance responsible for the physiological dependence on cigarettes (US Department of Health and Human Services 1988, Benowitz 2009). The Expert report of Tobacco Advisory Group of the Royal College of Physicians (2000) has concluded “tobacco use to be self-administration of nicotine”. Therefore, nicotine dependence can be defined as the physiological component of tobacco dependence. According to the Finnish SC Guideline (the Finnish Medical Society Duodecim 2012), nicotine dependence means permanent neurological changes caused by the use of nicotine containing products. Lack of nicotine administration causes withdrawal symptoms (Royal College of Physicians 2000). See also the definitions for ‘Tobacco addiction’ and ‘Tobacco dependence’.

Nicotine Replacement Therapy product (NRT)
Nicotine Replacement Therapy, NRT, products are a group of nicotine containing pharmaceutical products intended to reduce withdrawal symptoms caused by the abstinence of smoking, and thus, support SC (Silagy et al. 2002;2004, Stead et al. 2008; 2012).
Non-prescription medicine
A licensed medicinal product sold without prescription or classification governing such medicines (Medicines Act 395/1987, 57 §, Ministry of Social Affairs and Health 2003, Medicines Act and Statues 2003, European Medicines Agency 2006). In this thesis ‘non-prescription medicine’ means a licensed pharmaceutical product which is sold without prescription only at pharmacies.

Over-the-counter medicine (OTC medicine)
Over-the-counter medicine refers to licensed medicinal products which can be purchased without a prescription (Ministry of Social Affairs and Health 2003, European Medicines Agency 2006, Food and Drug Administration 2014). Traditionally, in the European Union, including Finland, non-prescription medicines are available only at pharmacies (Ministry of Social Affairs and Health 2003, Medicines Act and Statues 2003, European Medicines Agency 2006). In Finland all the over-the-counter medicines are sold at pharmacies with the exception of NRT products. Further according to Finnish medical legislation, community pharmacists have a legislative duty to assure proper and safe use of all non-prescription medicines by counselling (Medicines Act 395/1987, 57 §). Contrast to this in the USA and currently in many European countries OTC medicines are sold in addition to pharmacies in food stores, supermarkets, kiosks and gas stations and without the supervision or guidance of any health care professional (European Medicines Agency 2006, Food and Drug Administration 2014).

Over-the-counter, OTC, conditions for NRT purchase
The definition of over-the-counter conditions used in this theses is adopted from the work of professor Shiffman and his colleagues (Shiffman et al. 2002a,b, Shiffman and Sweeney 2008). Their definition is as follows: “OTC conditions in which smokers self-selected and used the products without any instructions or counselling, relying only on the product labels”. Furthermore, according to them, use under OTC conditions “implies use with no behavioural treatment, and also without personal instruction and structure, which could be seen as important contributions to efficacy”.

OTC paradigm
According to Shiffman and Sweeney (2008), OTC paradigm means “to extend OTC treatments beyond acute use for acute symptomatic conditions to long-term use for treatment of chronic, asymptomatic conditions and for support of preventive lifestyle changes”.

15
**Pharmaceutical policy/medicines policy**

According to Traulsen and Almarsdóttir (2005) “Pharmaceutical policy sets up the principles that guide pharmaceutical policy making. It is plan or course of actions that influence, guide or determine future decision-making in the field of pharmaceuticals”. In the Finnish Medicines Policy 2020 strategy, the “joint objectives of the social and health care authorities and stakeholders in the field of pharmaceuticals are defined”. Most importantly, the strategy defines that “pharmaceutical service is a part of the social and health service system” (Ministry of Social Affairs and Health 2011).

**Public health**

According to World Health Organization, WHO, (2014a) “public health refers to all organized measures (whether public or private) to prevent disease, promote health, and prolong life among the population as a whole. Its activities aim to provide conditions in which people can be healthy and focus on entire populations, not on individual patients or diseases.”

**Self-medication**

Self-medication “involves the use of medicinal products by the consumer to treat self-recognized symptoms or disorders or the intermittent or continued use of medication prescribed by physician for chronic or re-occurring symptoms (World Health Organization 2000). In the Finnish Medicines Policy 2020 strategy the relationship between self-care and self-medication is defined as follows: “Self-care which is done by the use of non-prescription medicine” (The Ministry of Social Affairs and Health 2011).

**Smoking cessation (SC)**

According to WHO (2003): Smoking cessation, synonymous to treatment of tobacco dependence “refers to a range of techniques including motivation, advice and guidance, counselling, telephone and internet support and appropriate pharmaceutical aids. The success of these interventions depends on their synergistic use in a broader context of comprehensive tobacco control programmes“. According the Glossary of the Tobacco Addiction Group of Cochrane Collaboration (2014) SC is synonymous to ‘quitting’ and is defined as follows: “The goal of treatment is to help people achieve abstinence from smoking or other tobacco use, also used to describe the process of changing the behaviour.”

**Tobacco addiction**

According to Grey et al. (2005): “Tobacco addiction is the umbrella term for compulsive, generally harmful pattern of drug self-administration as is characteristics of most cigarette smokers”. It has been suggested that the term tobacco addiction should be used instead of tobacco dependence (Grey et al. 2005, West and Hardy 2006). This is to underline the addiction as a holistic neurobiological condition including behaviour and feelings. However, in this thesis the term tobacco dependence is used, according to the Finnish SC Guideline (The Finnish Medical Society Duodecim 2012).
**Tobacco control**
The umbrella term for all the acts in the battle against the global tobacco epidemic. WHO (2003c) has defined Tobacco control as follows: “a range of supply, demand and harm reduction strategies that aim to improve the health of a population by eliminating or reducing their consumption of tobacco products and exposure to tobacco smoke”.

**Tobacco dependence**
Abbreviations

5A’s    Ask, Assess, Advise, Agree, and Assist
AFP    Association of Finnish Pharmacists
ASH    Action on Smoking and Health
CNS    Central Nervous System
CT     Cold Turkey
DDD    Defined Daily Dose
EMA    European Medicines Agency
FDA    Food and Drug Administration (US)
FIMEA  Finnish Medicines Agency
FCTC   Framework Convention on Tobacco Control
FTND   Fagerström Test for Nicotine Dependence
ICD    International diagnostic classification
HSI    Heaviness of Smoking Index
MP     Member of Parliament
NICE   National Institute for Health and Care Excellence
NRT    Nicotine replacement therapy
OTC    Over-the-Counter
OTC NRT Nicotine replacement therapy products sold in general sales
RCP    Royal College of Physicians
RCT    Randomized Controlled Trial
Rx     Prescription
SAHC   Social Affairs and Health Committee
S&H    Social Affairs and Health (Ministry or Parliamentary Committee)
SC     Smoking Cessation
UK     United Kingdom
USA    United States of America
WHO    World Health Organization
1 Introduction

Tobacco control and promotion of smoking cessation (SC) are key global public health priorities (World Health Organization 2014c, 2015). Globally, the use of tobacco products kills six million people each year prematurely and causes significant humanistic, economic and societal hazards. Actually, the use of tobacco products is the key attribute for most of the serious public health hazards (US Department of Health and Human Services 2014). There is no group of organs for which smoking would not be harmful and the evidence of the harm accumulates continuously. Very recent evidence shows that even two thirds of regular smokers die prematurely due to their smoking (Banks et al. 2015).

Nicotine was publicly recognized by the report of the Surgeon General in 1988 for the first time as the substance responsible for causing tobacco dependence (US Department of Health and Health Behaviour 1988). Since then, a robust evidence-base has been gathered identifying tobacco dependence as a chronic disease which requires several treatment episodes and comprehensive support (World Health Organization 1992, Fiore et al. 2008, Cummings and Mahoney 2008). Promoting different methods for supporting SC has been a central focus of tobacco control policy especially in Western countries.

SC is one of the most effective ways to promote public health and reduce healthcare costs (Cromwell et al. 1997, Parrot and Godfrey 2004, Fiore et 2008, National Institute for Health and Clinical Excellence 2008, World Health Organization 2014d). Traditionally all health care professionals are considered to have a key role in supporting the treatment of tobacco dependence. To increase their participation in SC, evidence-based guidelines have been established in many countries. These guidelines give detailed recommendations of the use of a wide range of evidence-based SC interventions, highlighting pharmacotherapy and behavioural support as the cornerstone of SC treatment (Fiore et al. 2008, Zwar et al. 2011, The Finnish Medical Society Duodecim 2012, National Institute for Health and Care Excellence 2013).

Nicotine replacement therapy (NRT) products, having been in the pharmaceutical market for over three decades and sold without a prescription for a long period of time in many countries, are the most commonly used SC pharmacotherapy (Silagy et al. 2002; 2004, Stead 2008; 2012). Since the very first years in the pharmaceutical market, NRT products’ role in SC has been influenced by the constant increase in information and understanding of tobacco dependence as a chronic condition and nicotine as the key agent causing it. NRT products were the first prescription (Rx) medicines used in SC in addition to behavioural counselling. Their use was highlighted as a part of the comprehensive treatment of tobacco dependence, but their availability was strictly regulated because of the potential risk of nicotine dependence (Elam 2012, Keane 2013).

During the past decades, the body of evidence related to SC and NRT products’ efficacy and safety has increased. This increased evidence has reflected in the changing role of NRT and their accessibility. In many countries, NRT were first released from prescription-only status to non-prescription medicines sold in community pharmacies. For this
reason, amongst various health professional groups, community pharmacists have especially been responsible to take care of supporting rational SC pharmacotherapy. The global role of pharmacists in SC interventions has been acknowledged in the scientific literature and in a few treatment guidelines (Fiore et al. 2008, Zwar et al. 2011, The Finnish Medical Society Duodecim 2012, National Institute for Health and Care Excellence 2013). In Finland, the international development to increase pharmacists’ participation in SC was reflected in the nationwide efforts to increase pharmacist’s involvement in SC in the 1990s and 2000s (Kurko et al. 2011).

In many countries NRT products have been deregulated from pharmacy-only status to general sales, meaning sales at food stores, kiosks and gas stations, during the mid-1990s to mid-2000s. These over-the-counter (OTC) deregulations can be perceived as an important starting point for new NRT usage patterns. Traditionally, non-prescription medicines are indicated for the treatment of minor and temporary conditions and symptoms (World Health Organization 2000, 2003b). After their deregulation, NRT products were the first group of OTC medicines indicated for the support of a behavioural life-style change and their use was recommended to last for several months (Shiffman and Sweeney 2008). For this reason, the NRT deregulation has been used as an example and justification for extending self-medication practices and the paradigm related to OTC medicines.

After NRT deregulation, NRT has assumed more and more consumer product-like characteristics as against a medicinal product intended to be used under the comprehensive SC treatment procedure, including behavioural support from health professionals (Keane 2013). This development has currently accelerated, as many opinion leaders advocate for a more ‘liberal nicotine policy’ (Le Houezcek et al. 2011, Fagerström and Bridgman 2014). This new nicotine policy relies on the principle that all nicotine containing products should be regulated according to the possible harmful health consequences instead of the principle of regulating pharmaceuticals.

This thesis concentrates on the deregulation of NRT products in Finland from pharmacy only status to general sales which took place in the beginning of 2006. This change was principally important in pharmaceutical policy and self-medication practices, as NRTs were and still are the sole group of pharmaceuticals sold outside pharmacies in Finland. Globally the Finnish situation is unique, as specific legislation was created for one special group of pharmaceuticals. The literature provides limited information on the NRT deregulation, and there is no previous work assessing it from multiple aspects. Therefore, the overall aim of this thesis is to provide a comprehensive understanding of NRT deregulation.

This thesis consists of two parts: a literature review and an empirical section. The literature review provides the contextual framework for the empirical part (Chapter 10.1) but also describes the factors related to the NRT deregulation and its’ reflections on public health. It also covers the introduction of the role of smoking from the viewpoint of society and an individual (Chapter 2). Furthermore, it describes NRT products’ role in SC and its evolution (Chapter 3), NRT’s therapeutic value on the basis of its efficacy and real-world effectiveness (Chapter 4), health political argumentation and experience of the NRT deregulation (Chapter 5), evidence on NRT use in real life (Chapter 6) and the rationale for
combining counselling and NRT use (Chapter 7).

The empirical part of the thesis investigates the NRT deregulation from the perspective of policy-making, health professionals and users of NRT products (Chapter 9, Studies I-IV). These perspectives were chosen because they are relevant for understanding the background and consequences of the NRT deregulation. Currently, the literature provides only sparse information on these subjects.
2  Smoking from a society and individual smokers’ perspective

This chapter briefly describes smoking from a society and individual smokers’ perspective, the physiological mechanisms and the complexity of tobacco dependence disease. In addition, the key means of tobacco control in Finland are listed. The information given in this chapter serves as a background to understand the importance of SC from a public health perspective.

2.1  Smoking from a society perspective

Smoking is closely related to the cultural and social environment, which influences remarkably on smoking behaviour (Hakkarainen et al. 2013, US Department of Health and Human Services 2014). A clear indication of this is the change in the general attitude towards smoking, which has altered over the last 60 years in Western society (World Health Organization 2003a, US Department of Health and Human Services 2014). Six decades ago smoking was only seen as a habit and often the prevailing culture supported its spread (World Health Organization 2003a, Hakkarainen 2013, US Department of Health and Human Services 2014). For instance in Finland, it is visible and has been acknowledged that the social status of tobacco products has radically shifted from that of harmless everyday consumption products to very harmful products, which are currently controlled by specific legislation aimed at ending the use of these products (Hakkarainen 2013).

Tobacco dependence is a global epidemic (World Health Organization 2013, 2014d). The World Health Organization, WHO, has described the smoking epidemic as three waves, from the first wave of expansion of smoking in developing countries to the third wave of current decrease in Western countries. Currently, in the European Region the death rate attributable to smoking is globally highest, but WHO estimates that by 2030 nearly 80% of tobacco attributed deaths will take place in low and middle-income countries (World Health Organization 2013). The smoking rate varies significantly between European Countries, and across the population in different countries (World Health Organization 2013, 2014e). According to meta-analysis of WHO (2011) smoking is far more common among people with a low-income than a high-income. Actually, smoking is the key explanation for health inequalities between different social groups, causing a strong socioeconomic gradient between the wealthiest and poorest groups (Marmot et al. 2001, Jha et al. 2006). At least half of the socioeconomic differences in mortality in men aged 35-69 years are explained by smoking (Jha et al. 2006). In Finland, it has been estimated, based on the evidence originating from Finnish population registers, that smoking is still the key reason explaining the difference in life expectancy between the most and least educated socioeconomic groups (Martikainen et al. 2013). Especially the influence of smoking in this difference is increasing among the Finnish women.

Smoking causes a tremendous economic burden for the society (World Health
Organization 2014f). This burden is explained by a loss of productivity, health care costs and personal suffering. Loss of productivity is explained by premature deaths, health problems and employee abstinence. The World Bank's estimate (2011) suggests that smoking-related health care costs cover between 6% and 15% of all the annual health care costs in high-income countries. Other aspect of this economic burden is that the great majority (80%) of the world's nearly one billion smokers live in low and middle income countries (World Health Organization 2011, 2014c). Further, among the poorest households, the share of families' income spent on tobacco products is the largest, and thus, the use of tobacco products causes a deficiency of necessities (World Health Organization 2011).

2.2 Smoking from individual smoker’s perspective

From individual smoker’s perspective, smoking behaviour and thus SC are influenced by a great diversity of factors (Lerman and Niaura 2002, The Finnish Medical Society Duodecim 2006; 2012). The genetic differences explain a great deal of the variation in smoking behaviour and the development of dependence (Lerman and Niaura 2002, Korhonen and Kaprio 2012). Further, environmental, behavioural and social factors influence significantly on tobacco use initiation and maintenance. For instance, over the past decades, the tobacco industry has in its marketing strategy spread the image of self-selected, independent, enjoyable, adult-like behaviour, which has appealed so many individuals to initiate smoking (World Health Organization 2003d). Many smokers still associate smoking with mostly positive images and tend to underestimate the harmful health effects (McKie et al. 2003, Katainen 2011).

After the initiation, the habituation of smoking behaviour occurs, as it includes the reinforcing and rewarding effects of smoking, both in physiological and psychological sense (Royal College of Physicians 2000). Smoking is often associated with pleasure, a manner of coping in stressful events, social event or as a reward or refreshment (Royal College of Physicians 2000, McKie et al. 2003). Smokers have a great variety of reasons to continue to smoke, despite them knowing about the health hazards (McKie et al. 2003, Katainen 2011). According to the results of the annual Health Behaviour and Health Survey among the Finnish Adult Population, over half of the smoking respondents would like to quit and nearly 40% had seriously attempted to quit (Helldán et al. 2013). However, quitting is very difficult and normally several quit attempts are needed before permanent SC (The Finnish Medical Society Duodecim 2012). This is because of the existence of tobacco dependence.

2.2.1 Nicotine as the cause of physiological tobacco dependence

Nicotine is the substance responsible for the physiological dependence on cigarettes (US Department of Health and Human Services 1988, Benowitz 2009). The Expert report of the Tobacco Advisory Group of the Royal College of Physicians (2000) has concluded “tobacco use to be self-administration of nicotine”. Nicotine inhaled from tobacco smoke is
adsorbed from lungs to blood circulation and administrated to the central nervous system (CNS) in 10 seconds from cigarette smoke (Royal College of Physicians 2000).

Already the very first nicotine-doses bind to nicotine receptors and thus stimulate the release of various neurotransmitters (Royal College of Physicians 2000, Mustonen 2004, Benowitz 2009). Of these the most important is dopamine, which is the key transmitter in producing pleasurable, reinforcing effects and thus maintaining drug dependence. In humans, even short term intake of tobacco products induces pleasure, stimulation, reduces stress and anxiety (Royal College of Physicians 2000, Mustonen 2004, Benowitz 2009, US Department of Health and Human Services 2014). The maintenance of these pleasurable effects is one explanation for the physiological tobacco dependence. There is evidence that even a short-term period of a few weeks of regular smoking increases the amount of nicotine receptors and changes the structure of nicotine receptors (Royal College of Physicians 2000, Benowitz 2009). Furthermore, the continued nicotine administration via smoking causes tolerance (Royal College of Physicians 2000, Mustonen 2004). This means that the smoker must use more cigarettes, or smoke them more intensively, to receive the rewarding effects of nicotine release.

Withdrawal symptoms are experienced when the level of nicotine is lowered in the plasma (Mustonen 2004, Benowitz 2009). These withdrawal symptoms are defined as collection of signs and symptoms caused by the abstinence of the drug of which one's body is physiologically adopted (West and Gossop 1994, Royal College of Physicians 2000, West and Hardy 2006). The most common tobacco withdrawal symptoms include anxiety, restlessness, poor concentration and irritability or aggression, increase in appetite, urge to smoke and night-time awakenings (Royal College of Physicians 2000, Benowitz 2009). Most of these symptoms will disappear after a sustained abstinence of 4 weeks, as the smoker's body reverts to its normal state (Royal College of Physicians 2000). According to current knowledge, relief of withdrawal symptoms caused by nicotine dependence is the key action mechanism for SC pharmacotherapy, including NRT (Henningfield et al. 2009).

A great variety of tests and scales exists for assessing the level of nicotine dependence for clinical practice and research (Royal College of Physicians 2000, DiFranza 2010). Of these, Fagerström Test for Nicotine Dependence (FTND) is the most commonly used scale in clinical practice. (Heatherton 1991, Royal College of Physicians 2000). It measures the consumption of cigarettes and experienced difficulty to tolerate the decrease in the nicotine level (Fagerström et al. 1989). Heaviness of Smoking Index (HSI) is developed on the basis of FTND for clinical screening purposes (Kozlowski et al. 1994). It consists of two questions, which assess daily cigarette consumption and the time of smoking of the very first daily cigarette.

2.2.2 Behavioural, psychological and social aspects of tobacco dependence

At the same time as the physiological nicotine dependence is developing, smoking behaviour becomes more conditioned and associated with the pleasurable physiological effects caused by nicotine (Benowitz 2009). This behavioural dependence is associated with cer-
tain manners, like rolling one’s own cigarettes or associating smoking with certain occasions (Royal College of Physicians 2000, Benowitz 2009).

*Psychological dependence* develops for tobacco and nicotine use (Royal College of Physicians 2000, Mustonen 2004). For most smokers the pattern of cigarette use, in terms of daily consumption, routines related to smoking and amount of inhaled nicotine, remains constant and stable over time (Royal College of Physicians 2000). Part of the psychological dependence, is to continue smoking to avoid withdrawal symptoms related to negative mood (Royal College of Physicians 2000, Benowitz 2009).

*Social dependence* means associating the use of tobacco products with certain company and social events. Social dependence is important especially in the initiation phase of smoking (Royal College of Physicians 2000). Typically smoking starts at a very early age and the social pressure is a key mediator in learning such action (Walsh and Tzelepis 2007, Ollila et al. 2010, Finnish Medical Society Duodecim 2012). Later, smoking is associated with the practices in the workplace and belonging to social group (Katainen 2011). Vice versa, in the cessation phase, belonging to a community supporting SC may be equally important in the initiation of a smoke-free lifestyle (Secker-Walker et al. 2002).

### 2.2.3 Tobacco dependence as a chronic disease

There is robust evidence, that tobacco dependence should be seen as a chronic condition, which requires several treatment episodes and comprehensive support (Sims and Fiore 2002, Etter and Stapleton 2006, Cummings and Mahoney 2008, Fiore and Baker 2011). Nicotine and tobacco dependence and the withdrawal symptoms caused by the abstinence from tobacco use have been classified as chronic diseases by two international diagnostic classification systems for already three decades (World Health Organization 1992, American Psychiatric Association 1996).

Due to the highly addictive nature of tobacco products, tobacco dependence has been assessed decades ago as *“the most addictive and dependence-producing form of self-administered gratification known to man”* (Russell 1978). Later, dependence on tobacco products has been noticed to be equal to that on heroin and cocaine (Royal College of Physicians 2000). As described above, nicotine is the key component of tobacco dependence (US Department of Health and Human Services 1988). However, other substances in the tobacco smoke (Benowitz 2009, US Department of Health and Human Services 2014) and patterns related to smoking and its social position, are important as well (West and Hardy 2006). Tobacco dependence is widely investigated and there is a great variety of models explaining this neurobiological and psychological condition (West and Hardy 2006).

For the reasons described above, also SC is not straightforward. It includes multiple aspects, which should be taken into account in planning supportive structures, suitable for individual smokers (Fiore et al. 2008, Fiore and Baker 2011). Furthermore, no consensus is reached on an exact model or theory explaining overcoming tobacco dependence. Instead, the SC behaviour of an individual smoker has been described by a great variety of different models (West and Hardy 2006). The most commonly and traditionally used one in clinical practise is the transtheoretical model of behavioural change (DiClemente et al.
1991), which characterises smokers and quitters into five different stages of change. The model has been criticized (West 2005) and also it has been as a start point for developing more recent models explaining SC behaviour (Michie et al. 2011). Based on the information on these models and the nature of tobacco dependence, the great challenge in developing SC interventions is due to the relapse causing nature of tobacco dependence.

2.3 Brief overview of the tobacco control policy in Finland

Like any health promotion, the policies guiding tobacco control and SC have expanded to every level in the society (World Health Organization 2003a). Tobacco prevention and SC have been priorities in the Finnish public health policy since 1976 when the Finnish Tobacco Act was enacted (Heloma et al. 2012). Prevention of the inequality between the socioeconomic groups has been the key reason to implement a long term tobacco control policy in Finland. However, the policy has been the most influential among the wealthiest socioeconomic groups but it has been less capable of diminishing smoking among the lower socioeconomic groups (Helakorpi 2008). Finnish tobacco policy has partly succeeded as the smoking prevalence of men has halved over the last 30 years (Heloma et al. 2012). In 2013 only 19% of Finnish men and 13% of women were daily smokers but there exists a strong socioeconomic gradient in smoking prevalence (Helldán et al. 2013).

The Finnish Tobacco Act (1976) has emphasized prevention and restrictions on smoking, banning advertising and support for smoke-free environment. These goals were strengthened in 2005 when Finland ratified the Framework Convention on Tobacco Control public health treaty, FCTC, by WHO (World Health Organization 2014g). During its ten years existence this international treaty has been the key weapon in the battle against the global tobacco epidemic (World Health Organization 2015).

Since October 2010 the Finnish Tobacco Act has aimed to end the use of tobacco products, making it internationally one of the strictest tobacco legislation (World Health Organization 2014g). This Finnish devotion is in accordance with the international aim in tobacco control policy and science to totally end the use of tobacco products (Warner 2013, Malone et al. 2014). These ‘end-game proposals’ give ideas how to expand tobacco control to the broader community, utilize innovative strategies to finally implement a total freedom from tobacco in the society (Warner 2013, Malone et al. 2014). Key means in the Finnish endgame tobacco policy are effective legislation, prevention of tobacco use and intensive SC services (Hara and Simonen 2013, Ministry of Social Affairs and Health 2014).

Over the last decade, several amendments came into force to make the Finnish Tobacco Control stricter (Heloma et al. 2012, Finnish Action on Smoking and Health 2014). These include extending the existence of smoke-free restaurants and other public areas, working places and municipalities, forbidding the visibility of tobacco products in the sale outlets and protection of minors. However, Finnish Tobacco legislation does not give recommendations for organizing SC.

Instead, state and community level health care is responsible for organizing SC services in Finland (Sandström et al. 2009, Heloma et al. 2012). SC has mostly been guided by the
Finnish SC Guideline (The Finnish Medical Society Duodecim 2012). The Guideline was developed by a multidisciplinary expert group and it is based on robust scientific evidence. It provides background information on tobacco and smoking as a health risk. Furthermore, the SC Guideline introduces a wide range of evidence-based SC interventions, which are applicable in various health care settings. The Guideline is distributed nationwide by free internet access along with online education supporting its implementation.

Effective SC services can be produced both in local health care centres, occupational health care settings and in the private sector (Sandström et al. 2009, The Finnish Medical Society Duodecim 2012). The recommendations of the Finnish SC Guideline, are targeted to all health care professionals, but in the most current version (2012) physicians are in key position in encouraging and supporting SC. The key recommendations of the Guideline for all health professionals are the provision of behavioural support, by utilizing the method of 5A’s (6K’s in Finnish practice): Ask, Advice, Assess, Assist, Arrange (Fiore et al. 1996) on SC support and recommending effective pharmacotherapy (See Chapter 3.3). In Finland there are three first-line SC pharmacotherapies, bupropion, NRT products and varenicline.
3 Description of NRT products’ role in SC and its evolution

3.1 Brief description of NRT products’ role in SC

NRT products are a group of nicotine containing pharmaceuticals intended to reduce withdrawal symptoms caused by the abstinence of smoking and thus support SC (Stead et al. 2012). NRT products’ use is based on the idea that it is too difficult for an individual smoker to overcome simultaneously psychological and physiological tobacco dependence (Sees 1990). NRT products’ use can reduce most of the physiological and psychological withdrawal symptoms (Stead et al. 2012).

In the Finnish market, there are currently five different dosage forms of NRT products (Finnish Medical Agency 2015). Of these, the slow-release nicotine patch does not replace any of the behavioural activities related to smoking (Stead et al. 2012). However, the patch keeps nicotine level steadier without peaks, which can help especially in the psychological withdrawal (Fiore et al. 2008). The more rapidly acting forms include nicotine gum, lozenge, oral spray and inhaler, which can release nicotine to the CNS in 20 minutes. If nicotine is swallowed, it passes first pass metabolism in the liver and loses its efficacy. For this reason all oral NRT products are intended to be used so that nicotine is directly adsorbed from the oral mucosa (Elam 2012, Stead et al. 2012). All NRT products release nicotine into the body at a much slower rate and with a lower dosage than smoking does (Fiore et al. 2008, Stead et al. 2012).

NRT products are the most utilized and investigated SC pharmacotherapy (Silagy et al. 2004, Shiffman and Sweeney 2008, Stead et al. 2008; 2012). This is due to their existence in the pharmaceutical market for over three decades, over-the-counter, OTC, status and their proved efficacy and safety profile for various patient groups. SC guidelines in many Western countries recommend NRT use as being the first line gold standard SC treatment (see for example Fiore et al. 2008, National Institute for Health and Clinical Excellence 2008, Zwar et al. 2011, The Finnish Medical Society Duodecim 2012). NRT patch and gum have been added to WHO list of essential medications (World Health Organization 2009a). These recommendations and decisions rely on the robust evidence of NRT products’ efficacy and safety (Fiore et al. 2008, Stead et al. 2012, Cahill et al. 2014).

Over the past decades, the role of NRT products in SC has changed (Figure 1). This chapter describes some key milestones related to NRT’s lifecycle, based on published literature. These milestones are described along with the general development of the understanding and practises related to SC. Therefore also the development of the evidence-based SC guidelines clinical SC practises and the role of health professionals supporting SC is described in the NRT lifecycle context. The key focus of this thesis is on the Finnish experience of NRT. However, as the most comprehensive published data on the lifecycle of NRT is from the United States of America (USA), the United Kingdom (UK) and Australia, experiences from these countries are reviewed.
3.2 Recognition of nicotine addiction and the birth of NRT

Already in the 1960’s reports from the Royal College of Physicians, RCP, in the UK (1962) and the US report from the Surgeon General (the US Department of Health and Human Services 1964) had published the idea of nicotine as the dependence causing agent in tobacco products (Elam 2012, Elam and Gunnarson 2012.) However, most focus was put on the social and psychological dependence whereas physiological dependence was given less attention. At the same time, NRT gum was developed in Sweden (Elam 2012, Elam and Gunnarson 2012). The original first Nicorette® brand name with the connotation of “Nico and Rätt” instead of “Nico ”and “Wrong” of tobacco use, describes well the ideology related to NRT (Elam 2012, Elam and Gunnarson 2012). The first Nicorette® gum was finally registered as a therapeutic drug to treat tobacco dependence in 1978 in Sweden (Table 1).
**Table 1. Some milestones related to the lifecycle of NRT products in SC, modified from the review of Keane (2013) and other cited literature.**

<table>
<thead>
<tr>
<th>NRT’s milestones (time period)</th>
<th>Explanation (References in addition to Keane 2013)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Birth of NRT and pre-market period (1960-1978)</strong></td>
<td>NRT gum was developed in Sweden by Ove Fjörno’s Research Group from the traditional snus. The development was slow and complicated, as no earlier data existed on pharmacokinetics and pharmacodynamics of nicotine. Further challenges were caused by the threat of nicotine poisoning, finding the suitable administration route and the idea of increasing saliva’s pH. The first Nicorette® products were finally registered in 1978 by Leo© (Elam 2012, Elam and Gunnarson 2012).</td>
</tr>
<tr>
<td><strong>NRT was part of SC treatment plan (1978- early 2000’s)</strong></td>
<td>NRT use brought smokers into the medicalized network, which included the help of health professional. Nicotine in NRT products was separated from nicotine in tobacco products. After understanding smoking as a chronic condition, in various countries clinical guidelines for treating tobacco dependence were established. These guidelines highlighted the importance of the combination of behavioural and pharmacological support in SC (Fiore et al. 1996, Commonwealth Department of Health and Aged Care 1999). NRT use was one element of the therapeutic regime recommended in SC guidelines. Like Henningfield (1995) described: “The very first idea of NRT use was associated with diagnosis, rational dosing, appropriate instructions, warnings and follow-up.” In most countries NRT were Rx medicines.</td>
</tr>
<tr>
<td><strong>Establishing the first clinical SC guidelines (1996-1999)</strong></td>
<td>NRT products became non-prescription medicines, sold only at pharmacies in many countries. Pharmacists had a specific role in supporting the rational use of NRT (Brock and Tailor 2007).</td>
</tr>
<tr>
<td><strong>NRT were released to pharmacies (during the 1990’s)</strong></td>
<td>NRT use was one element of the therapeutic regime recommended in SC guidelines. Like Henningfield (1995) described: “The very first idea of NRT use was associated with diagnosis, rational dosing, appropriate instructions, warnings and follow-up.” In most countries NRT were Rx medicines.</td>
</tr>
<tr>
<td><strong>NRT Deregulation</strong></td>
<td>After the deregulation, the use of NRT products solely was highlighted and NRT were seen as the replacement. Due to the NRT deregulation the products’ role changed. In addition to being a pharmaceutical intervention meant for therapy, the products were also a safe consumer product, which use was dependent on consumers’ freedom to choose (Shiffman and Sweeney 2008).</td>
</tr>
<tr>
<td><strong>Denmark 2001</strong></td>
<td><strong>Australia 2005</strong></td>
</tr>
<tr>
<td><strong>Finland 2006</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Expanding NRT use to new indication areas (Harm reduction) and populations (mid 2000’s)</strong></td>
<td>Harm reduction included new strategies for NRT use such as cutting down to quit, reduction of the amount of smoked cigarettes and pre-cessation treatment (Lancaster et al. 2007). Harm reduction has been accepted as an official indication in the UK in 2005, Australia 2007, Finland 2011 and in the US it is under FDA consideration (Raw 2005, Lohi S. Personal information 2014, US Food and Drug Administration 2015). Widening the population of whom to recommend NRT based on increased evidence on the safety of NRT (Britton et al. 2008, Fiore and Baker 2011).</td>
</tr>
<tr>
<td><strong>New nicotine market and new, more appealing NRT products suggested (2010’s-)</strong></td>
<td>More appealing NRT products should be developed to contain more nicotine and release it more rapidly. The development should start from comparing the products to tobacco instead of placebo. Many public health experts yearn for the new nicotine market (Gray et al. 2005; Le Houeczeé et al. 2011, Fageström and Bridgman 2014).</td>
</tr>
</tbody>
</table>
The NRT gum market expanded worldwide at the beginning of 1980’s. NRT gum products have been available on Rx since the early 1980’s in Europe, for instance in Finland since 1983, and in the USA since 1984 (Sees et al. 1990, Amodei and Lamb 2008, Shiffman and Sweeney 2008, Keane 2013). In addition to an increase in neurobiological knowledge of nicotine dependence, the existence of NRT products was one good trigger to finally and publicly announce the addictive nature of nicotine in tobacco products (Elam 2012, US Department of Health and Human Services 1988; 2014). This was done for the first time in the so called White-paper report of the Surgeon General in 1988 (p.9), which described nicotine as “the drug in tobacco that causes addiction.”

In the 1980’s, the body of clinical trials assessing NRT efficacy increased and new NRT formulations were also invented (Jarvis et al. 1987, Buchkremer 1989). Most significantly, the slow-releasing NRT patch was developed in the USA (Rose et al. 1984). In the 1980’s and beginning of the 1990’s NRT products’ role was perceived ambiguous (Elam 2012, Keane 2013). The products were either perceived as therapeutic interventions, supporting SC, as the clean nicotine the products contain helps in overcoming withdrawal symptoms (Russell et al. 1980, Sees 1990, Keane 2013). However, NRT products could also be seen as a change in technology from tobacco products to a pharmaceutical product in delivering nicotine into the body (Keane 2013). These perceptions are still, in the 2010’s, influencing in NRT use among smokers and quitters (see Chapter 6).

### 3.3 The establishment and implementation of evidence-based SC guidelines

At the time NRT use was expanding in Western countries, tobacco dependence was understood to be a complex physiological and psychological condition (Russell et al. 1980, Jarvis et al. 1982). SC was expected to require the treatment of both these components (Table 1). All the very first reviews focusing on the clinical use of NRT highlighted that in any circumstances the sole use of NRT gum only helps overcome withdrawal symptoms and the psychological work to gain SC the quitter must do themselves (Russell et al. 1980, Sees 1990).

At this time West and Scheiders (1987) also noticed that ex-smokers experienced cravings for smoking even years after quitting, when no traces of nicotine were left in their bodies. This finding in addition to the declaration of the Surgeon General (1988) and the recognition of tobacco dependence as a chronic disorder in the international disease classifications highlighted the need to build structures and practices in the health care system to comprehensively support SC.

#### 3.3.1 The establishment of evidence-based SC guidelines

To meet this comprehensive need to support SC, evidence-based clinical guidelines were globally established after the mid 1990’s (see for example: Fiore et al. 1996, Commonwealth Department of Health and Aged Care 1999, McNeill et al. 2005, Raw et al. 2005). The guidelines give detailed instructions on how to organize and provide services meeting
the needs of individual smokers. For instance, in the USA in 1996 the Smoking Cessation Clinical Practise Guideline was published (Fiore et al. 1996). Its’ expert recommendations were based on over 3 000 scientific publications. It highlighted the dependence causing nature of smoking and the existence of effective SC treatments, including NRT.

In the UK, the first SC guideline was published in 1998 (McNeill et al. 2005, Raw et al. 2005). In addition to presenting evidence-based practises, the British guideline was also equipped with the information on the cost-effectiveness of SC. This information supported the establishment of a new treatment service system for SC. In the UK the National Institute of Clinical Excellence (NICE) has later published a detailed cost-effectiveness analysis of NRT products use for the society, which has altered practises of how NRT is distributed and reimbursed (West et al. 2005).

In Australia altogether three clinical guidelines were established during 1996-1999 to increase physicians’ participation in implementing a National Tobacco Strategy (Commonwealth Department of Health and Aged Care 1999).

In Finland, the first Finnish SC Guideline was published in 2002 (The Finnish Medical Society Duodecim 2002). It and its later updates in 2006 and 2012 have been developed from the multidisciplinary viewpoint by the Finnish Medical Society. According to it, all healthcare professionals have specified SC responsibilities, and the local cooperation between them should facilitate SC by increasing and strengthening contacts with patients.

All these guidelines and all their later updated versions in the 2000s and 2010s have underlined the importance of the role of all health care professionals in SC (Fiore et al. 2008, National Institute for Health and Clinical Excellence 2008, Zwar et al. 2011, The Finnish Medical Society Duodecim 2012). Physicians have traditionally been the guidelines’ main target group, but the later versions of the SC guidelines highlight other health professionals and their multidisciplinary co-operation as well.

In the guidelines, the most highlighted interventions for health professionals are proactive assessment of smoking status, forms of behavioural support, different pharmacotherapies and combining these treatments (Fiore et al. 2008, National Institute for Health and Clinical Excellence 2008, Zwar et al. 2011, The Finnish Medical Society Duodecim 2012). As NRT products were the first group of pharmaceuticals for SC, they were found to be a significant part of the treatment tools for health care professionals (Russell 1980, Buchkremer et al. 1989, Keane 2013). This role is reflected also in the recommendations in the guidelines (Table 2).
The existence of NRT as concrete SC supporting tools for health professionals, may also have motivated health care professionals to intervene within smoking and offer help (Russell et al. 1980, Buchkremer et al. 1989). For example, in Australia the implementation of national guidelines was assessed by a survey among physicians (Young and Ward 2001). The most commonly followed, self-reported guideline recommendation was supporting the use of NRT.

### 3.3.2 SC guideline implementation and factors associated with it


### Table 2. Examples of recommendations in the US Smoking Cessation Clinical Practice Guideline 1996 related to behavioural support on NRT use (modified from Fiore et al. 1996).

<table>
<thead>
<tr>
<th>Examples of recommendations</th>
<th>Examples of recommended activities</th>
</tr>
</thead>
</table>
| NRT patch and gum are efficient treatments when used along with psychosocial interventions. | Some examples of psychosocial interventions:  
Offer problem solving, skills facilitating SC treatments  
Include recognition of danger (urges to smoke), coping skills (identification of coping skills and problem solving practices),  
provide basic information on smoking  
Arrange Quit day  
Arrange social support |
| Clinician should tailor the dosage and duration of the NRT treatment to fit patients’ needs and give adequate information. | Notice precautions (pregnancy, cardiovascular diseases, side effects)  
Heaviness of Smoking Index is recommended in assessing the level of nicotine dependence  
Instructions for chewing technique (gum) or placing (patch)  
Instructions for scheduling the dosage  
Information on possible side effects |
| If resources are feasible, clinician should meet the quitter at least four times. Individual SC treatment should last as long as resources are available. | Encourage the patient in the quit attempt  
Encourage the patient to discuss about the quitting process  
Provide basic information on smoking and success on SC |
| OTC NRT* is accepted by FDA | The introduction of OTC NRT does not reduce clinician’s responsibility to intervene with smoking, encourage NRT use or counselling the appropriate usage. |

* In the US OTC NRT refers to general sales and sales from pharmacies as well
Beenstock et al. 2012). There is strong evidence that changing healthcare professionals’ practices requires more effort than solely disseminating the guidelines; systematic efforts are needed to promote their usage (Stone et al. 2002, Francke et al. 2008, Fiore et al. 2008).


In the literature several facilitators of the implementation of SC guidelines are known (Table 3). Based on the systematic meta-review of Francke et al. (2008) these facilitators can be classified into those related to the guideline content, its implementation, patient and health care professional or working environment (Table 3). Examples of all these levels are given in Table 3.
Table 3. Examples of facilitators of SC guideline implementation among health care professionals based on published literature. The classification used is based on the systematic meta-review of Francke et al. (2008).

<table>
<thead>
<tr>
<th>Facilitators of SC guideline implementation (references in addition to Francke et al. 2008)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guideline characteristics</strong></td>
</tr>
<tr>
<td>The aim of SC guidelines is to make SC part of daily practise and adhering their recommendations does not require remarkable additional resources (Fiore et al. 2008, The Finnish Medical Society Duodecim 2012).</td>
</tr>
<tr>
<td><strong>Multifaceted implementation strategy</strong></td>
</tr>
<tr>
<td>Use of peers in dissemination (Smit et al. 2014)</td>
</tr>
<tr>
<td>Examples of educational strategies:</td>
</tr>
<tr>
<td>- Education focusing on motivational interviewing (Rosseel et al. 2011)</td>
</tr>
<tr>
<td>- Education with role plays (Secker-Walker et al. 2000)</td>
</tr>
<tr>
<td>- Education influencing on knowledge and attitudes (Rosseel et al. 2011)</td>
</tr>
<tr>
<td><strong>Smoker (Patient)</strong></td>
</tr>
<tr>
<td>Patients’ motivation (no resistance to SC counselling) (Francke et al. 2008 Fiore and Baker 2011)</td>
</tr>
<tr>
<td>The situation is ideal for SC counselling, for example:</td>
</tr>
<tr>
<td>- Before an operation (Thomsen et al. 2010)</td>
</tr>
<tr>
<td>- During pregnancy (Melvin et al. 2000)</td>
</tr>
<tr>
<td>SC counselling does not affect patients intimacy (Brewster et al. 2005, Beenstock et al. 2012).</td>
</tr>
<tr>
<td><strong>Healthcare professional</strong></td>
</tr>
<tr>
<td>Positive attitude (Smit et al. 2013)</td>
</tr>
<tr>
<td>Professional role and identity (Amemori 2012, Amemori et al. 2013)</td>
</tr>
<tr>
<td>Experience showing that supporting SC is easy to remember or conduct (Amemori 2012, Amemori et al. 2013)</td>
</tr>
<tr>
<td>Confidence in one’s own counselling skills (Vogt et al. 2005)</td>
</tr>
<tr>
<td>Knowledge level (Beenstock et al. 2013)</td>
</tr>
<tr>
<td>Positive belief towards SC (Vogt et al. 2005)</td>
</tr>
<tr>
<td>Health professional being non-smoker (Ratschen et al. 2009, Duaso et al. 2015).</td>
</tr>
<tr>
<td><strong>Working place (environment)</strong></td>
</tr>
<tr>
<td>Positive atmosphere and practice-wide commitment to SC (Pullon et al. 2005, Smit et al. 2013)</td>
</tr>
<tr>
<td>Multidisciplinary collaboration (An et al. 2008,)</td>
</tr>
<tr>
<td>Support from working place such as in daily care and encouragement over-time (Sandström et al. 2009, Rosseel et al. 2012)</td>
</tr>
<tr>
<td>Guarantee of needed resources (financial and other) (Pullon et al. 2005, Stacey et al. 2006)</td>
</tr>
</tbody>
</table>
3.4 Community pharmacists’ role in counselling the use of non-prescription NRT

Together with the development of the SC guidelines, the status of NRT changed over time. In many European countries and in Australia NRT products were gradually released from prescription-only status to pharmacy-only sales, starting mostly from the mildest, 2mg, NRT gum round the 1990s (Paul et al. 2003, Brock et al. 2007). Though, in Switzerland NRT products were directly registered as non-prescription medicines in pharmacies already in the introduction year of NRT gum in 1978 (Elam 2012, Elam and Gunnarson 2012). In Finland the smallest packages of NRT gum were switched to a non-prescription medicine a decade later, in 1988 and followed by larger packages in 1992 (The Finnish Medical Society Duodecim 2002).

The non-prescription status of NRT was expected to facilitate contacts between quitters and pharmacists and provide community pharmacists with a special role in counselling the rational use of NRT (Brock et al. 2007). Pharmacists are easily accessible by the public and they are often the only health care professionals whom the quitter meets (Hudmon et al. 2006, Brock et al. 2007).

3.4.1 International experiences on pharmacists’ involvement in SC

NRT switches to non-prescription-medicines sold at pharmacies prompted the consideration at the highest organisational level to increase pharmacists’ participation in promoting SC. Globally the pharmacists’ role in supporting SC is part of the global health promotion efforts by the WHO, dating back to the 1990’s (World Health Organization and EuroPharm Forum 1998). In the Second Global WHO meeting on the ‘Role of the Pharmacists in the Health Care System’, held in Tokyo in 1992, pharmacists were seen as an important resource for advancing SC (World Health Organization and EuroPharmForum 1998). In Europe the pharmacies’ participation in SC is coordinated by EuroPharmForum, which is a coordination body of WHO Europe Regions and European Pharmacy Associations. In the strategy of Europharm Forum SC has been perceived as one key area in which to develop community pharmacists’ involvement in advancing public health.

According to the systematic reviews conducted, community pharmacists’ support may increase SC rates (Sinclair et al. 2004, Cramp et al. 2007, Dent et al. 2007, Saba et al. 2014). This provides pharmacists with a good opportunity to develop evidence-based SC services for those willing to quit. There is evidence that many customers find the pharmacists’ role in supporting SC suitable (Hudmon et al. 2006). Still, community pharmacists could extent their participation in SC through several alternative actions and strengthen evidence-based practices (Aquilino et al. 2003, Paul et al. 2003, Chiang et al. 2006, Hudmon et al. 2006, Brock et al. 2007, Thannanithisak et al. 2008, Saba et al. 2014).

However, in some countries the NRT switch to non-prescription medicine has been debated because of the possible safety and efficacy concerns. For instance, in Germany the medical authorities were re-considering whether the products should be reeregulated to prescription status, even though German pharmacists were obliged to guide and counsell
the use of NRT (Hasford et al. 2003). According to an Australian survey a significant proportion (40%) of the responding users of non-prescription NRT had not received any instructions from health care professionals (Chiang et al. 2006). Furthermore, a large proportion of the respondents used NRT products in a non-optimal way.

3.4.2 The Finnish experience on pharmacists’ involvement in SC

In Finland, pharmacists’ participation in SC originates from the international development, most importantly the initiatives of Europharm Forum, as described above. Especially, the Association of Finnish Pharmacies (AFP), representing Finnish pharmacy owners, has been proactively supporting pharmacists’ involvement in local SC networks and providing SC services since 1995 (Kurko et al. 2011). The SC coordination body within AFP involves representatives from other professional organisations and pharmacy schools to enhance the implementation of evidence-based SC practices and its evaluation. This development was promoted by national training campaigns and SC counselling aid materials (The Association of Finnish Pharmacies 2008).

These systematic efforts to increase pharmacists’ participation in SC in Finland were reflected in the Finnish SC Guideline, published in 2002 (The Finnish Medical Society Duodecim 2002). According to the Guideline, the pharmacists’ role in SC is counsel, support and guide the rational and effective use of NRT in a local multidisciplinary SC team (See Figure 2). This means in practice that pharmacists are expected 1) to assess individual customer’s level of dependence in order to plan the treatment and 2) its follow-up accordingly. 3) They are also expected to recommend the use of non-pharmacological SC aids, such as written materials or internet portals. The SC Guideline was the first Finnish Current Care Guideline, which acknowledged the especial role of Finnish pharmacists in the treatment chain of chronic disease. After the release of the SC Guideline AFP organized country-wide educational campaigns, in nationally, regionally and locally and produced several educational materials supporting the implementation of the SC Guideline (Linden and Korhonen 2005).

In addition to Guideline-based duties and requirements in SC Finnish pharmacies have offered different kinds of proactively developed SC services (Figure 2). For instance nearly all pharmacies have been proactive in recruiting participants to the national Quit and Win contest. Furthermore, in several regions around the Millennium pharmacies participated in multidisciplinary local SC co-operation, which aimed to organize better SC and tobacco prevention in these areas. The most sophisticated service available in Finnish community pharmacies is the individually tailored SC service, which is based on international models (Sinclair et al. 2002).
Though these services are offered by only a minority of pharmacies and they reach fewer customers compared to medication counselling (Figure 2). Furthermore, it is uncommon for community pharmacists to actively give quitting advice. According to the results of the annual survey of the Health and Health Behaviour of the Finnish Adult population by the National Institute for Health and Welfare, less than 2% of the respondents who smoked, had received an advice to quit from community pharmacists (Helldán et al. 2013). In contrast to this, nearly 40% of the smoking survey respondents received quitting advice from a physician and 30% from a public health nurse.

However, compared with other countries the Finnish development of involving pharmacists in SC around the Millennium was advanced. For instance, in the USA similar
kinds of educational activities to increase pharmacists’ activeness and support in SC were established after the mid 2000’s (Hudmon et al. 2006, Hudmon et al. 2007). In Australia, systematic training and pharmacy-based SC programs are just currently being established for the pharmacy profession (Saba et al. 2013). This need is highlighted by the recent evidence of significant gaps in evidence-based SC practice among Australian pharmacists (Saba et al. 2013; 2014). In many European countries it is more common to involve pharmacists in local campaigns, instead of a countrywide dissemination of SC actions (Brock et al. 2007). On the other hand, in Northern Ireland and Denmark, the community pharmacy-based individually tailored SC service was implemented as a countrywide service structure in the mid 2000’s.

### 3.5 NRT deregulation to general sales

Internationally the distribution channels of OTC medicines vary significantly between countries (Mahecha et al. 2006, Mossialos et al. 2008). Key functions influencing on these differences reflect the overall content of pharmaceutical policy, including the values, actors, structures and historical perspective. In this thesis, NRT deregulation means a shift from pharmacy-only distribution to general sales. Further, OTC NRT means NRT products which are sold in general sales. The following paragraphs describe NRT deregulations in different countries in brief.

#### 3.5.1 International NRT deregulations

The first and most investigated NRT deregulation took place in the USA in August 1996, when the FDA approved nicotine gum for OTC sales. This was followed by releasing NRT patches in 1999 and nicotine lozenge in 2002 (Amodei and Lamb 2010, U.S Food and Drug Administration 2013). The US deregulation was justified by the idea of increasing access and utilization of NRT products and thus gaining public health benefits (Shiffman and Sweeney 2008, See Chapter 5). The US pharmaceutical policy has traditionally been very liberal, as all the non-prescription medicines are sold in general sales. NRT deregulation was preceded by the deregulation of many prescription-medicines intended for temporary use (Mahecha 2006).

In the UK, the 2-milligram NRT gum was deregulated from pharmacy-only-status to general sales (equivalent to US OTC) in 1999 (Raw and McNeill 1999). Further, in May 2001 the rest of NRT products were also added to general sales list. This was advocated by various health organizations, with the idea of making NRT products as freely available as cigarettes (See Chapter 5). In the UK, at the same time as NRT deregulation, the world’s most comprehensive national SC policy was implemented (West et al. 2005). This policy consisted of the reimbursement of all prescribed SC medications, widely disseminated clinical guidelines and a nationwide spread of SC clinics, which offer behavioural support and medications.

In the Nordic countries NRT products were deregulated from pharmacy-only to general sales in Iceland in 1999, in Denmark in 2001 and in Norway in 2003 (Morgal and
The NRT deregulation in these countries was a part of a wider deregulation of selected non-prescription medicines. In addition, in Iceland and in Norway the ownership of pharmacies was liberalized. Later, in 2009 in Sweden the pharmacy monopoly (Apoteket Ab) owned by the Government, was dissolved and non-prescription medicines, including NRT products, were deregulated to general sales (Bardage et al. 2013).

3.5.2 The Finnish NRT deregulation

In order to increase the availability and use of NRT products, the Finnish Parliament enacted a change in the prevailing medical legislation extending NRT sales to food stores, kiosks and gas stations from the beginning of February 2006 (Change in Medical Act 2006). At the time of the NRT deregulation process in 2005-2006, none of the strategic pharmaceutical policy documents suggested deregulation of non-prescription medicines. On the contrary, the goal of the Ministry of Social Affairs and Health (S&H) was to include NRTs that were prescribed by the physician, in the reimbursement scheme in autumn of 2004. This was rejected by the Ministry of Finance for monetary reasons. The first time the idea of NRT deregulation was mentioned, was in a speech of the Minister of S&H on March 12, 2005.

Already in May 2005 the Ministry of S&H had prepared the Government Bill (107/2005), which introduced NRT deregulation as a part of a larger package of changes in medical legislation. The Amendment was enacted by the Finnish Parliament in December 2005. The Parliamentary Social Affairs and Health Committee (SAHC) expected the Government to organize monitoring of the NRT deregulation. The monitoring report was completed one year after the deregulation was introduced (Ministry of Social Affairs and Health 2007). The monitoring group suggested further NRT deregulation to restaurants, which became smoke-free in the summer of 2007. This change was enacted, along with the new Tobacco legislation, in the autumn of 2010 (Ministry of Social Affairs and Health 2009).

3.5.3 The role of NRT after deregulation

After the NRT deregulations the products’ role solely in SC has been highlighted (Shiffman et al. 1997, Hughes et al. 2003, Hyland et al. 2005, Shiffman 2007, Shiffman and Sweeney 2008, Hughes et al. 2011). After NRT deregulation, the need for healthcare professionals’ support, which was highlighted in the first clinical trials and guidelines, is given less attention. Instead, smokers’ and quitters’, now self-respondent consumers’, freedom to choose and buy the products independently is highlighted (Shiffman and Sweeney 2008, Keane 2013). Furthermore, quitters do not want to be perceived as patients and they are reluctant to seek help from physicians in SC (Shiffman and Sweeney 2008). Some authors suggest that OTC NRT supports smokers’ and quitters’ self-esteem and capability (McNeill et al. 2001). This is also closely related to general tendency to widen the role of medication users from patients to free consumers (Morgal and Almarsdóttir 1999).
The US deregulation of NRT to OTC has been suggested to present an important example of the new “OTC paradigm” meaning to extend OTC treatments use beyond acute symptomatic conditions to long-term use for treatment of chronic, asymptomatic conditions and for support of preventive lifestyle changes (Shiffman and Sweeney 2008). OTC-NRT has been used as an important landmark on this road to increase the assortment of non-prescription and OTC medicines. In Europe the OTC paradigm has been used to justify the deregulation of orlistat from prescription to non-prescription status in 2008 through a centralized procedure (European Commission 2013). It has also been noticed as a future direction of self-medicine practises (European Commission 2013). It is important to assess how this new paradigm will influence on self-care and non-prescription medicine practices.

3.6 Widening NRT use to new user groups and the introduction of combination therapy

Also during the 2000’s the use of NRT products has expanded into new indication areas and patient groups compared with the first clinical guidelines (see Table 1, Medicines and Healthcare Products regulatory Agency 2005; 2006, Fiore et al. 2008, Keane 2013, U.S Food and Drug Administration 2013). NRT products are recommended to new user groups, for whom NRT use was earlier considered to be contraindicated. These include individuals in the most vulnerable positions, like minors, pregnant and lactating mothers, the elderly and chronically ill (Fiore et al. 2008, Tonstad et al. 2009, Fiore and Baker 2011). This relaxation is related to the increased information on the overall safety related to NRT products compared to the harm associated with continued tobacco use.

Use of stronger NRT doses is also recommended in comparison with earlier advice. For instance, a combination therapy of different NRT products is recommended as a more effective treatment strategy than a single treatment (Fiore et al. 2008, National Institute of Clinical Excellence 2012, Cahill et al. 2013). Efficacy of a combination therapy may be explained by not only higher nicotine concentration but also the timing and form of nicotine delivery (Ebbert et al. 2010, Cahill et al. 2013; 2014).

3.7 NRT for harm reduction

The idea of harm reduction in SC is to minimize the amount of cigarettes smoked and thus the harm of tobacco use by the use of less toxic and carcinogenic nicotine substances (Stead and Lancaster 2007, Le Houezec et al. 2011). Traditionally quitting is perceived as an orthodoxy absence of smoking (abrupt quitting). The instructions for NRT use have warned not to smoke during NRT use (the US Food and Drug Administration 2013).

Significant liberalization of NRT products has taken place during 2005-2013 as many regulatory authorities in different countries have approved more liberal, harm reduction indications for NRT products (Medicines and Healthcare Products regulatory Agency 2006, Royal College of Physicians 2007, National Institute for Health and Care Excellence 2013, the US Food and Drug Administration 2013, Lohi S. /Fimea, personal information 2014).
The ideology of harm reduction is justified by the idea of tobacco dependence as a chronic, relapsing disorder (Le Houezec et al. 2011). In the mid 2010’s harm reduction in SC is probably the hottest topic in tobacco science, accelerated by the radical expansion of the popularity of electronic cigarettes (World Health Organization 2014h). Harm reduction has its powerful supporters and opposites among scientists and stakeholders. SC specialists still differ in their perception on the safety of harm reduction strategies and recommending harm reduction to their patients (Beard et al. 2012).

The most common strategies for harm reduction in relation to NRT use include cutting down before quitting, reduced smoking with NRT use and temporary abstinence (National Institute of Clinical Excellence 2013, see Table 4). These strategies are recommended for smokers, who are either unable or unwilling to quit abruptly. These smokers may be highly dependent on nicotine or suffer from a chronic condition, for instance psychiatric disease, which makes quitting more complicated.

<table>
<thead>
<tr>
<th>Arguments for NRT use in harm reduction (References)</th>
<th>Arguments against NRT use in harm reduction (References)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arguments related to harm reduction strategy generally</strong></td>
<td></td>
</tr>
<tr>
<td>Harm reduction might decrease smoking and harms related to it (Hughes et al. 2006).</td>
<td>The effectiveness and the actual health benefits of harm reduction are still unclear (Hatsukami et al. 2004, Hughes et al. 2006, Stead and Lancaster 2007).</td>
</tr>
<tr>
<td>Too orthodoxical tobacco policy, which only accepts total abstinence from all tobacco and nicotine products as a goal, may judge smokers unable to quit as failures (Gray et al. 2005, Le Houezec et al. 2011).</td>
<td>In a long-term follow-up study of over 20 000 participants only total abstinence was associated with reduced mortality from tobacco related diseases (Godtfredsen et al. 2002).</td>
</tr>
<tr>
<td>A humanistic perspective highlights the need to help those smokers unable to quit, to minimize the health hazards (Le Houezec et al. 2011).</td>
<td>Harm reduction may diminish smokers’ motivation towards quitting if reduction is seen as an alternative to SC (Hughes et al. 2006).</td>
</tr>
<tr>
<td>Harm reduction strategies may increase motivation in future quitting attempts (Hughes et al. 2006).</td>
<td>Harm reduction can benefit the tobacco industry as a means to dialogue with public health experts and also expand its business (Peeters and Gilmore 2015).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Arguments related to specifically on NRT use in harm reduction</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>NRT products are, due to their safety, purity and high standard required by medication regulatory authorities, idealistic harm reduction products (Gray et al. 2005, Le Houezec et al. 2011, Keane 2013).</td>
<td>Originally NRT products were developed from pharmaceutical needs to give therapeutical replacement for nicotine, but not to replace the habits and behaviour related to smoking (Jarvis 1982, Keane 2013).</td>
</tr>
<tr>
<td>Most of the evidence for harm reduction is from NRT studies (Stead and Lancaster 2007).</td>
<td></td>
</tr>
</tbody>
</table>
The evidence for the efficacy of harm reduction and the practises related to it are contradictory (Table 4). According to the systematic Cochrane review on harm reduction, the use of NRT products nearly doubled the odds on reducing the number of smoked cigarettes per day by 50% (Stead and Lancaster 2007). However, only a minority of the study participants were able to maintain this reduction of smoking for a longer period.

### 3.8 Advocating for a more liberal nicotine policy and market

NRT products are currently marketed and regulated as medical products, not as a substitute for cigarette smoking (Le Houezec et al. 2011). However, currently many stakeholders and scientists advocate for a far more liberal nicotine policy (Le Houezec et al. 2011, Fagerström and Brigdman 2014). This sort of policy would relax NRT regulation, change NRT’s status to non-medical products and increase their doses and rates of nicotine delivery to act as a better substitute for tobacco use. Currently better acting NRT products, which would better fit the needs related to smoking behaviour, are already developed and discussed (Shabab et al. 2013, Fagerström and Brigdman 2014).

Furthermore, some stakeholders suggest, that all nicotine containing products should be regulated under the same regulatory authority, which focuses on the harmfulness of nicotine containing products, instead of the current separated regulation for tobacco and nicotine products (Le Houezec et al. 2011, Elam and Gunnarson 2012). This would lead to a new nicotine market, whose regulation would be based on the products’ harmfulness. As a result, the most harmful products would be the most regulated, most unattractive and most inaccessible. These discussions of a new regulation for the nicotine market are also related to recent evolvement and expanding popularity of e-cigarettes (Bell et al. 2012, Etter et al. 2014, World Health Organization 2014h).
4 Efficacy and effectiveness of OTC NRT

During the NRT deregulation debates the concepts of efficacy and effectiveness of OTC NRT were much discussed (see Chapter 5). Therefore it is important to describe what these concepts mean and what the actual evidence-base of the real world effectiveness of OTC NRT is. The aim of this chapter is to describe the differences between these two concepts, their assessment, and report the evidence of OTC NRT efficacy and effectiveness and the aspects related to the generalizability of this evidence in real life.

**Efficacy** means how the treatment studied works on a controlled environment. In this environment the effects of the treatment, the study population and circumstances are isolated from each other by the well planned and precise design, control, randomization, blinding and analysis (Rush 2009, Saturni et al. 2014). Efficacy is associated with high internal validity, as the effects of confounders are controlled. At best, these idealistic circumstances are achieved in randomized controlled trials, RCTs, which are called the golden standard of studies aiming to investigate efficacy of a treatment (Saturni et al. 2014). Traditionally most SC pharmacotherapy investigations have focused on the efficacy in a clinical trial environment (Zhu et al. 2012). This is mostly due to the requirements of medical authorities for gaining marketing permissions.

In contrast to efficacy, effectiveness means the assessment, how therapy works on real life conditions (Rush 2009, Saturni 2014). Studies assessing effectiveness under real life conditions (real life studies) have high external validity, as the study designs permit the inclusion of different kinds of patients and environments allowing their characteristics to influence in the results (Saturni et al. 2014). Real life studies are especially important for assessing the generalizability of findings from RCTs and for locating rare phenomena related to the studied treatment. On the other hand, it is much more difficult to control confounding factors in real life studies than in RCTs’. For this reason, real life studies do not usually have high internal validity and cannot assess causal relationships as rigorously as RCTs can (Rush 2009, Saturni et al. 2014).

4.1 Evidence on NRT efficacy and its generalizability to real life

4.1.1 Evidence on NRT efficacy

Based on the robust scientific evidence on efficacy NRT use is stated as the gold standard in SC treatment (Lemmens et al. 2008, Stead et al. 2012, Cahill et al. 2014). The most cited source of information on NRT efficacy is provided by the high-quality systematic reviews produced by the Cochrane Collaboration. The Cochrane Collaboration is an international, non-profit and independent organization, which produces and disseminates high-quality evidence-based information on different health care interventions (Hartmann-Boyse et al. 2013, The Cochrane Tobacco Addiction Group 2014).
The Cochrane Collaboration has its own, *Cochrane Tobacco Addiction Group* (2014), which assesses the efficacy of different SC interventions, including pharmacotherapy, behavioural methods and society level interventions. The Tobacco Addiction Group has assessed NRT products’ efficacy in altogether four versions of the systematic review during 2000-2012 (Silagy et al. 2002; 2004, Stead et al. 2008; 2012, see Appendix 1). This assessment is based on over 120 RCTs and the confidence intervals of the findings are very narrow, implying high reliability (Lemmens et al. 2008, Stead et al. 2012). All the versions of the Cochrane review have concluded the use of NRT to increase SC rate by 50-70% compared with placebo, regardless of the duration of the therapy, the intensity of additional support provided or setting (Silagy et al. 2002; 2004, Stead et al. 2008; 2012). In the meta-review assessing the efficacy of different SC interventions, NRT efficacy assessment was considered as the strongest (Lemmens et al. 2008).

### 4.1.2 Examples of differences between RCT and real life conditions

Information on NRT efficacy is widely used to justify OTC NRT’s effectiveness in real life (Shiffman and Sweeney 2008, Fiore et al. 2008, National Institute on Clinical Excellence 2012). There are also specific RCTs, mimicking OTC conditions and comparing these to Rx conditions (Shiffman et al. 2002a, Hughes et al. 2003). However, often the RCT results cannot be directly extrapolated to real life due to several differences between RCT and real life conditions (Walsh 2008, Zhu et al. 2012, Saturni et al. 2014).

#### 4.1.2.1 Differences between NRT users in RCTs and real life

Motivation can be expected to be highly essential in lifestyle changes such as SC (Zhu et al. 2012). When NRT trial participants and NRT users in real life are compared, there are differences between their motivations towards behavioural change (Walsh 2008, Zhu et al. 2012). For instance, in many NRT trials mass media advertisements are used in recruitment, though there is evidence that study participants, recruited from advertisement, have better motivation towards quitting compared with all quitters (Silagy et al. 2004, Stead et al. 2008, Walsh 2008). Trial participants have better levels of adherence towards NRT use than the NRT users in real life, partly due to the follow-up and guidance provided in the trial (Walsh 2008, Zhu et al. 2012, Henningfield et al. 2012). In real life poor adherence towards NRT treatment and abrupt discontinuation of the therapy are cited as one key reason for poor real life benefits of NRT use (see Chapter 6.2).

#### 4.1.2.2 Other differences between the two conditions

In most of the trials included in the Cochrane Review on NRT, participants’ rate of initial dependence has been assessed and the treatment has been modified accordingly (Stead et al. 2012). In real life, the OTC NRT users have to choose the treatment option themselves and sometimes they have not taken the level of nicotine dependence into account in that choice (Walsh 2008). For ethical reasons, trial participants have often received NRT free

In addition, due to the trial protocol, even in trials with limited counselling, the study participants in NRT and placebo groups have frequent contacts with the clinical research centre (Stead et al. 2012, see Appendix 1). Although the participants in NRT and placebo groups have received similar counselling, there is evidence, that the number of SC sessions held has an influence on the adherence towards NRT use and the rate of success (Walsh et al. 2008, Stead et al. 2012, Zhu et al. 2012). Furthermore, in many trials NRT use is accompanied by multiple components, such as initial counselling or written NRT use instructions, follow-up visit or audiotapes on SC and self-reflective diaries (Shiffman et al. 2002 Hughes et al. 2003). These components make it difficult to directly compare the effects of NRT use in trials with real life (Hughes et al. 2003, Walsh 2008). This matter also highlights the need for real life effectiveness studies.

4.2 Effectiveness of OTC NRT

Currently, the interest towards and the existence of real life studies is constantly increasing in many therapeutic areas (Rush 2009, Saturni 2014). Studies assessing the effectiveness of OTC NRT have been progressive, as many of these were conducted soon after the US deregulation, near Millennium (Shiffman et al. 1997, Pierce and Gilpin 2002, Thorndike et al. 2002, Hughes et al. 2003, Hyland et al. 2005a). Currently, no study addressing the population based effectiveness of OTC NRT has been conducted in Finland. For this reason, the evidence on effectiveness is based on international evidence in countries, where NRT has been deregulated to general sales.

4.2.1 Different studies assessing the effectiveness of OTC NRT

To gain an understanding of the different studies assessing the effectiveness of OTC NRT, a non-systematic literature search and a narrative literature review was conducted during March-June 2014. Studies were searched from the Scopus database via the University of Helsinki with full coverage for Medline and 98% coverage for Embase.

The studies included in this review (Appendix 2) were chosen to provide either examples of different kinds of study designs or because they were among the most cited ones. When considering the generalizability of this non-systematic review for Finland, it should be noted that none of these studies directly compared the effectiveness of NRT bought from a pharmacy with those from other sales outlets.

Effectiveness of OTC NRT in real life has been investigated through different population-based study designs and data collection methods (Appendix 2). Some of these studies compare data before and after NRT deregulation (Pierce et al. 2002, Thorndike et al. 2002, Hyland et al. 2005a) and some only after deregulation (Alberg et al. 2012, Kazka et al. 2013, Kotz et al. 2014).
In most of the included studies users of OTC NRT are compared with non-users and the key outcome has been tobacco abstinence though some studies have assessed smoking reduction or adherence to NRT as well (Alperg et al. 2005, Balmford et al. 2011, Shabab et al. 2011). Most of the studies are conducted in the USA (Shiffman et al. 1997, Pierce and Gilpin 2002, Thorndike et al. 2002, Hughes et al. 2003, Hyland et al. 2005a, Reed et al. 2005, Shiffman and Sweeney 2008, Henningfield et al. 2009, Hughes et al. 2011). The high number of studies from the USA is because the local pharmaceutical market is the largest and most advanced.

4.2.2 Contradictory evidence of the real life effectiveness of OTC NRT

4.2.2.1 Studies supporting the effectiveness of OTC NRT

There is one meta-analysis assessing the efficacy of NRT in an OTC-like environment (Hughes et al. 2003, Appendix 2). Despite this meta-analysis being based on RCTs assessing efficacy instead of effectiveness, it compared the effects of sole use of NRT and NRT with counselling in mimicked real life conditions. For this reason it was included in this non-systematic literature review. The meta-analysis was based on four studies comparing OTC NRT and Rx NRT patch and it did not include any studies of other dosage forms (Hughes et al. 2003). The meta-analysis showed OTC NRT patch yielding similar six months quit rates compared with Rx-NRT patch. This review is much cited in NRT literature and it has often been used as a justification for the effectiveness of NRT deregulation. However, the conclusions and generalizability of this meta-analysis have been debated (Walsh 2008).

There is also one qualitative review summarizing evidence on OTC-NRT effectiveness from population-based studies (Hughes et al. 2011). It included altogether 11 retrospective cohort studies, in which the cohort members using OTC-NRT were compared with non-NRT users. The authors of the review also located seven pre- and post- OTC-NRT studies. These studies compared the quit rates before and after deregulation. Due to the heterogeneity between the included studies, the authors were unable to conduct a meta-analysis. They summarized the key findings by four different methods and finally, based on their assessment, found OTC NRT to be effective in real life (Appendix 2).

Some prospective cohort studies conducted over the last ten years, have found evidence supporting the real life effectiveness of OTC NRT (Hyland et al. 2005a, West and Zhou 2007, Balmford et al. 2011, Kazka et al. 2013, Appendix 2). These studies have several methodological strengths, including broad and representative data collection and longitudinal analysis. In addition the authors have been able to control many confounding factors in the effectiveness assessment. Furthermore, some US studies based on NRT sales data (Shiffman et al. 1997) or combining sales data to a tobacco survey (Reed et al. 2005) have found evidence supporting the effectiveness of OTC NRT.
4.2.2.2 Studies with mixed or non-supporting evidence on OTC NRT effectiveness

There are mixed results for the effectiveness of different NRT forms (Appendix 2). For instance, the study of Hyland et al. (2004) found that NRT gum was effective but the patch was not. In contrast to this, the study of Kazka and co-authors (2013) found evidence of the effectiveness of the OTC patch but not for any oral NRT dosage forms.

There are also several studies showing no evidence to support the effectiveness of OTC NRT in real life (Pierce and Gilpin 2002, Thorndike et al. 2002, Gilpin et al. 2006, Alberg et al. 2005, Alpert et al. 2012, Kotz et al. 2014, Appendix 2). The most cited ones are the large population-based surveys in California (Pierce and Gilpin 2002) and in Massachusetts (Thorndike et al. 2002) comparing data before and after the US NRT deregulation. Based on their findings, the use of NRT significantly increased after deregulation, but this did not reflect as a reduction in the population-based smoking rate. These studies indicate that OTC NRT use was associated with less successful SC attempts compared to Rx-NRT.

The prospective cohort study of Alpert et al. (2012) found that the likelihood of relapse in SC was most common among study participants who used NRT without any professional support. The study limitations were large loss to follow-up during four years follow-up and possible recall-bias of the study participants. Therefore, the findings of this study, and especially the very critical conclusions drawn by the authors, were debated among the scientific community (Beard 2012, Stapleton 2012).

A recently published retrospective cohort study from the UK (Kotz et al. 2014) assessed the real life effectiveness of different SC pharmacotherapies solely or combined with behavioural support from population based data (See Appendix 2). The authors considered England to be the only country in the world where this kind of study could be conducted. This is because, according to the authors, “England has the most extensive and comprehensive coverage of different SC methods and use of SC medicines is the highest in the whole world” (Kotz et al. 2014). Further, at the time of the data collection, NRT has been OTC medicine in England for a decade, which indicates a stabilized market. NRT products can be purchased by Rx or as an OTC medication, which allowed the authors to compare these two groups of NRT. Based on the results of over 10,000 respondents, OTC NRT was not found effective in SC. In contrast to this, the combination of Rx-NRT with either tobacco specialist’s behavioural support or health professional’s brief advice were associated with an increased success rate compared to no medication use. However, the use of OTC NRT yielded a poorer rate of success than no SC medicine use (Kotz et al. 2014).

4.2.3 Reasons for contradictory results and conclusions of the chapter

The contradictory results on OTC NRT effectiveness can not entirely be explained by study setting, design or methodology used. In addition, the role of confounding factors must also be taken into account. Of these, the most important in population-based retrospective cohort studies is the confounder of respondents’ ability to recall their last quitting attempt (Henningfield et al. 2009, Borland et al. 2012). It is easier to remember quitting at-
tempts in which some form of support, medical or behavioural, was used, compared with attempts without assistance (Borland et al. 2012). The latter ones are more likely to be spontaneous and short, which makes them more difficult to remember. This factor may increase the amount of reported unsuccessful quitting attempts, in which pharmaceutical aids is utilized (Shiffman et al. 2008c).

In addition, the more dependent smokers are on cigarette use, the more likely they are to use pharmacotherapy in their quitting attempts (Cummings et al. 2004, Shiffman et al. 2005, Shiffman et al. 2008c, Hung et al. 2009, Balmford et al. 2009, Borland et al. 2012). This can cause confounding by indication (Shiffman and Sweeney 2008, Borland et al. 2012). This means that as the participants have self-selected their treatment instead of randomized allocation, the proportion of dependent smokers, who are at the highest risk for failure, is over-presented among NRT users. Therefore NRT users do not show a larger success rate than non-users. On the other hand, the motivation towards quitting may be higher among those who decide to use SC treatment (Cummings et al. 2004, Shiffman et al. 2008c).

In conclusion of this chapter, the evidence-base of the effectiveness of OTC NRT is contradictory. As there is a variety of study types, sampling methods and ways to control confounding factors in OTC NRT studies, this is natural. As more studies of OTC NRT effectiveness are published, the knowledge of confounding factors increases and these matters can be better taken into account in future study designs (Shiffman et al. 2005, Rush et al. 2009 Borland et al. 2012, Alpert et al. 2012, Kotz et al. 2014).

Finally, when efficacy and effectiveness are compared, it is important to remember that many SC interventions in real life may have much lower effectiveness than efficacy proven in clinical trials (Curry et al. 2003, Lemmens et al. 2008, Zhu et al. 2012). This degrading of effectiveness in real life compared with a RCT environment is typical for all drug therapies (Saturni et al. 2014, Henningfield et al. 2009).
5  Key arguments related to NRT deregulation: what was the expectation and what has been achieved

Like described in Chapter 3, NRT deregulation took place in many countries during the mid-1990s and the early 2000s (Table 5). The fundamental reason in common with all countries, was to enhance public health by diminishing smoking. It was expected that the wider availability of NRT would significantly increase NRT utilization. This in turn would significantly increase quit attempts, in turn these attempts would increase SC and thus provide significant public health benefits (Shiffman et al. 1997, McNeill and Raw 2002, Shiffman and Sweeney 2008, Government Bill 107/2005). These public health benefits would consist of saved lives, diminished burden of disease and premature deaths and cost savings for the society and for individuals.

Currently over a period of ten to twenty years after the NRT deregulation in various countries, evidence has been gathered from different viewpoints to gain a more comprehensive understanding how OTC NRT has reflected in SC in real life and on the safety of OTC NRT. The aim of this chapter is to describe this evidence. Although NRT deregulations have taken place in many countries, most published evidence originates from the USA following some evidence from the UK and Australia. For this reason, this chapter mostly reports the experiences originating from these countries in addition to Finland.
Table 5: Key arguments supporting the NRT deregulation and a summary of how these arguments are fulfilled in the selected countries based on literature.

<table>
<thead>
<tr>
<th>Key arguments justifying NRT deregulation</th>
<th>Countries in which this argument was presented</th>
<th>How this argument was fulfilled based on published evidence? (Number of the chapter focusing on this matter)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in NRT availability</td>
<td>Australia, Finland, the UK, the USA</td>
<td>YES Number of sales outlets has increased after deregulations (5.1).</td>
<td>Shiffman et al. 1997, McNeill et al. 2001, West and Zhou 2007, Shiffman and Sweeney 2008, Finnish Medical Agency and Social Insurance Institution 2013</td>
</tr>
<tr>
<td>Increased NRT utilization</td>
<td>Australia, Finland, New Zealand, the UK, the USA</td>
<td>YES NRT sales data from different countries suggests that the use of NRT has doubled after deregulation (5.2). The use has significantly increased but it is still considered modest in quit attempts (see 5.3).</td>
<td>Shiffman et al. 1997, Paul et al. 2003, Shiffman et al. 2008c, Shiffman and Sweeney 2008, Scollo et al. 2012, Amodei and Lamb 2008, Heldán et al. 2013, Finnish Medical Agency and Social Insurance Institution 2013</td>
</tr>
<tr>
<td>Deregulation will lower NRT prices</td>
<td>Australia, the UK, the USA</td>
<td>YES Prices have decreased in Finland, but the long term development is unclear (5.2).</td>
<td>Aaltó-Setälä and Alaranta 2009</td>
</tr>
<tr>
<td>Sole use of OTC NRT is effective</td>
<td>Australia, Finland, New Zealand, the UK, the USA</td>
<td>UNCLEAR There is robust evidence on NRT efficacy (4.1). However, population based studies have yielded mixed results of effectiveness (4.2). Counselling is still highlighted in NRT guidelines and SPCs (7.1).</td>
<td>Hughes et al. 2003, Shiffman and Sweeney 2008, Hughes et al. 2011</td>
</tr>
<tr>
<td>Decreased smoking</td>
<td>Australia, the UK, the USA</td>
<td>UNCLEAR NRT Efficacy is considered to remain similar in Rx and OTC conditions. There are mixed results of effectiveness from population based studies (4.2). Smoking statistics are unable to detect remarkable effects of the NRT deregulation to smoking prevalence (5.4).</td>
<td>Shiffman et al. 1997, McNeill et al. 2001, Government Bill 107/2005, Amodei and Lamb 2008, Shiffman and Sweeney 2008, Scollo et al. 2012</td>
</tr>
<tr>
<td>OTC NRT is safe</td>
<td>Worldwide evidence from different studies</td>
<td>YES There is little evidence of serious side effects, dependence on NRT or abuse of NRT (5.5).</td>
<td>Klesges et al. 2003, Johnson et al. 2004, Burton et al. 2006, Rainio et al. 2011, Mills et al. 2013</td>
</tr>
</tbody>
</table>
5.1 Evidence of the development of NRT use after deregulation

Based on evidence from various countries, the use of NRT has sizeably increased after the NRT deregulation (Shiffman et al. 1997, Paul et al. 2003 West et al. 2005, Finnish Medical Agency and Social Insurance Institute 2013). The US sales statistics suggest that after the NRT deregulation, the use of NRT gum and patch has doubled compared with the use before deregulation (Shiffman et al. 1997, Reed et al. 2005, Amodei and Lamb 2008).

In the UK, NRT gum of 2mg was deregulated to general sales in 1999 and the rest of NRT forms in 2002. In 2001, all SC medications were included in the reimbursement scheme. These changes together resulted in dramatic increased the use of SC medications in the UK from the 28% in 1999 to 61% in 2002, based on sales data and a population based survey (West et al. 2005). However, compared with other regulatory changes leading to the increase in SC medications use, NRT products deregulation was not associated with a statistically significant increase in SC (West et al. 2005).

In Finland, on the basis of the Finnish wholesale statistics of medicines (Finnish Pharmaceutical Data Ltd. /Personal information 2008), the sales of NRT products amounted 26 million Euros in 2005 (retail price including value added tax of 8%). Since 1995, the sales increased approximately by 10% annually. During 2006, the NRT sales increased by 20% compared with the previous year and 30% of the sales occurred outside pharmacies (National Agency of Medicines and Social Insurance Institution 2006). In 2013 the wholesale sales of NRT products amounted to 34 million Euro for other sales outlets and 7 million Euro for pharmacies (Finnish Medicines Agency Fimea and Social Insurance Institution 2014). When measured in wholesale sales NRT products were the most sold group of non-prescription medicines in Finland in 2013.

Defined daily doses (DDD) are the international unit of average medicine consumption (World Health Organization and Norwegian Institute on Public Health 2009). Based on the measurement of DDDs consumed, the use of NRT in Finland has nearly doubled after deregulation (Figure 3). According to sales statistics from 2013, a majority (80%) of the sales are made in the outlets outside pharmacies (Finnish Medicines Agency Fimea and Social Insurance Institution 2014). The most commonly sold product forms are the smallest packages of the mildest NRT gum (Ministry of Social Affairs and Health 2007).
5.2 Change in NRT pricing after the Finnish deregulation

One key argument for NRT deregulation in Finland was the expected decrease in NRT prices, because after deregulation products pricing became free (Government Bill 107/2005). This change was found especially important because of the strong socioeconomic gradient in the smoking behaviour. Before NRT deregulation, NRT products pricing was guided by the Medical legislation, of which one key principle is that all medications have the same...
regulated price in all Finnish pharmacies (Medicines Act 1987). Finnish pharmacies are obliged to pay a pharmacy fee for the sales of all medicines, which on average was 7% of the pharmacy turnover at the time NRT deregulation took place (Act on Pharmacy Fee 1166/2005).

After deregulation NRT products pricing became free and pharmacies were released from the pharmacy fee for the NRT products. According to an analysis of NRT prices, conducted immediately following deregulation in 2006, NRT prices decreased by an average of 15 percent units in all sales outlets in urban areas (Aalto-Setälä and Alaranta 2007). The products were most inexpensive in supermarkets and most expensive in gas stations. The assortment of NRT products was largest at pharmacies and the most modest in kiosks. How much of the development was due to recentness of this change and how the pricing behaviour develops in long turn needs though further investigation.

5.3 How NRT use in quitting attempts has developed after deregulations?

Population-based studies have provided evidence that increased use of NRT products has also increased the number of quit attempts which included NRT use (Shiffman et al. 1997, Pierce and Gilpin 2002, Thorndike et al. 2002, Hyland et al. 2005a, Reed et al. 2005, Amodei and Lamb 2008, Shiffman and Sweeney 2008, Zhu et al. 2012). There are, though, more contradictory findings relating to how much NRT is used in quit attempts and how much for other purposes (Amodei and Lamb 2008). Based on the US sales statistics, Shiffman and his colleges (1997) suggested, that the number of NRT assisted quitting attempts has more than doubled after NRT deregulation (from 2.5 million in 1995 to 5.8 million in 1997).

However, it can be questioned is it a reliable assessment to directly draw the number of quit attempts from sales statistics (Walsh and Penman 2000, Amodei and Lamb 2008). This is because the mere purchase of a product does not guarantee success in quitting or even that the product is used in a quit attempt. On the other hand, West and his colleagues (2005) suggested that, if NRT usage patterns remain stable over the monitored sales period, the assessment from sales data is a valid measure for assessing NRT use in quit attempts.

In Finland, the National Institute for Health and Welfare (2014) conducts an annual representative survey called Health Behaviour and Health among the Finnish Adult Population (AVTK). The surveys, annually conducted, are comparable since 1978 making them the most important follow-up instruments of health behaviour among Finnish adults. According to the results of this survey NRT use in quit attempts has steadily increased during 2005 and 2013 (Figure 4). In 2005, before NRT deregulation, 13.5% of the adult population who smoked during past year, had used NRT for quitting (Helakorpi et al. 2005). In 2013 the corresponding rate was 17.4% (Helldán et al. 2013).
5.4 Smoking prevalence after NRT deregulations

In various countries, it was expected that NRT deregulation will lead to significant reduction in smoking rates (Table 5). However, the evidence from many countries suggests, that NRT deregulation is not directly projected in national smoking statistics (Cummings and Hyland 2005, West et al. 2005, Amodei and Lamb 2008, Wakefield et al. 2008, Zu et al. 2012, see Figure 5).

5.4.1 Evidence from the US, Australian and British smoking statistics

Based on the US smoking statistics, the prevalence of cigarette smoking (24.7%) has remained constant, when comparing the year before the NRT deregulation (1995) and the year after (1997) (Centers for Disease Control and Prevention 2007, Amodei and Lamb 2008). In the USA ten years after the NRT deregulation (in 2006) the smoking rate was 20.8% (Centers for Disease Control and Prevention 2007, US Department of Health and Human Services 2014), with a decline of 3.9% over ten-year period. Compared with the 12.5% drop in the smoking rate over ten-year period of 1974-1985, the increased availability of NRT after deregulation did not significantly reduced smoking.

The nationwide, representative National Health Interview study has collected data on
the US SC rates since 1991 (Zu et al. 2012). According to its findings, the annual SC rate is between 4-5% when measured by abstinence continuing at least three months during past year (Zhu et al. 2012). According to this study, the SC rate varies from year to year with a constant upward trend (Zu et al. 2012). The most positive trend was a reduction in smoking during 1991-1999 but during 1999-2002 there was a significant drop in the SC rate. In 1995, before NRT deregulation, 45.8% of smokers made a quit attempt, whereas in 1997, a year after deregulation, 40.8% of smokers made a quit attempt (Centers for Disease Control and Prevention 1997; 1999, Amodei and Lamb 2008).

The review of Cummings and Hyland (2005) reported a time series analysis of the national US tobacco consumption and NRT sales from the period of 1976 to 1998. The analysis found no statistically significant evidence for the idea that the deregulation of NRT patch and gum products was associated with decreased cigarette consumption. In contrast to this, the introduction of the NRT patch in 1992 was followed by a modest decrease in cigarette consumption.

In Australia NRT product sales were deregulated to supermarket sales in 2005 (Ellerman et al. 2011). The Australian Self-Medication industry (2008) has visibly lobbied for the gradual deregulation of NRT products. According to the Australian National Drug Strategy Household Survey, the prevalence of regular smoking in Australia was 22% in 2004. In 2007, it was 21% and in 2010 it was 20%, indicating of a drop of one percent over a successive three-year period (Winstalley and White 2012).

In the UK smoking has significantly decreased between the 1970s and mid-1990s. After that the decrease in the smoking rate has been much slower. The average annual decline of smoking rate has been 0.4% during 1999-2005 (Cancer Research UK 2014). It has been suggested that the sizeable increase in the use of SC medications during 1999-2002 (soon after NRT deregulation) in the UK has at most optimistically resulted in an annual reduction of smoking prevalence of 0.1% (West et al. 2005). This reduction is considered so marginal, that it is impossible to reliably detect it in annual smoking prevalence surveys.

5.4.2 Evidence from the Finnish smoking statistics

The development of the smoking rate in Finland, originating from the health indicators of the National Institute for Health and Welfare (indicator bank SOTKAnet® 2014), is described in Figure 5. Before NRT deregulation in 2005, the proportion of daily smokers (smoking rate) in Finland was 22.2%. In 2013 the smoking rate was 16.7%. As noticed from the Figure 5, in addition to NRT deregulation, various other changes in the Finnish Tobacco legislation have been enacted after 2006. In addition, in Finland the general attitude against tobacco has been strengthened all the time (Hakkarainen 2014). For these reasons it impossible to directly assess the influence of NRT deregulation on the decline in the smoking rate in Finland. However, there is no compelling evidence supporting the expectation that NRT deregulation will solely lead to a significant reduction in smoking in Finland. Additional reasons why the increased NRT use after deregulation is not directly reflected in smoking statistics are described in Chapter 6.
5.5 Safety of OTC NRT

At the time of NRT deregulation safety concerns were raised (Table 5). As nicotine is a vasocostructive substance, especially the possible existence of serious cardiovascular adverse effects was concerned (Greenland et al. 1998). According to a meta-analysis of 35 studies (Greenland et al. 1998), it is unlikely for NRT to cause cardiac events. Also the results of more recent network meta-analysis suggest that it is unlikely that the use of NRT would cause serious cardiovascular events (Mills et al. 2013).

Further, as nicotine is the key dependence causing agent in tobacco products, it was worried, would OTC NRT cause dependence among the population (Table 5). According to population-based studies the prevalence of dependence on any NRT product is low, approximately 1% of all NRT users (Hughes, et al. 2004, Hughes et al. 2005). On the other hand, it has been suggested that persistent use and dependence on NRT are under-investigated phenomena and therefore, they can be more prevalent than is currently expected (Dome 2011). Less than 10% of smokers use NRT for long-term (> 1 year) (West et al. 2000, Sims and Fiore 2002, Hajek et al. 2007). There is evidence, that the smokers, who are more dependent on tobacco, use NRT for longer periods (Hajek et al. 2007, Shiffman et al. 2008c). The long-term use of NRT is also recommended as a therapeutic option for highly dependent smokers (Fiore and Baker 2011, The Finnish Medical Society Duodecim 2012). The long-term use of NRT is considered as a much safer option compared with tobacco use. However, it has also been stated that long-term use over a number of years may
Possible abuse of NRT products, was presented as a significant safety threat related to NRT deregulation (Table 5). In population-based studies, NRT use among non-smokers, both adult and adolescents, is very rare (Klesges et al. 2003, Etter 2007b, Gerlach et al. 2008, Rainio et al. 2010). For instance, a largely distributed internet-based survey during 2004-2006 was only able to detect five never-smokers, who were using NRT for years (Etter 2007a). Though marginal, these findings imply that nicotine dependence may be initiated from the use of NRT gum as well.

Studies conducted among US and Finnish minors have provided evidence that it is relatively easy for minors to purchase OTC NRT products (Klesges et al. 2003, Johnson et al. 2004, Rainio et al. 2010). Due to the easy access and powerful advertisement of NRT, non-smoking minors may consider NRT as a magic pill for SC (Al-Delaimy et al. 2006). Though, in Finland among adolescents the most common purpose for the use of NRT was just to try (Rainio et al. 2011), there is no compelling evidence, that NRT products are widely abused.

In addition to these worries, the relationship between pure nicotine and cancer has discussed among the scientific community (Dome 2011, Grando 2014). Most recently, the opinion article of Grando (2014) synthetized the preclinical evidence in literature related to this matter. The author suggested that the association between nicotine and cancer could not be excluded. In addition, the individual differences in the expression of nicotine receptors should better be taken in to account. Although these concerns were mostly related to e-cigarettes, Grando (2014) recommended that in future the dose- and time-dependent effects of nicotine and differences between administration routes should be further investigated.
6 Real life NRT use: Why NRT deregulation is not directly reflected in smoking statistics?

As described in Chapter 5, after the NRT deregulations in many countries the radical increase in the use of NRT is not directly reflected in the smoking statistics (Cummings and Hyland 2005, Amodei and Lamb 2008, Henningfield et al. 2009, Zhu et al. 2012). This contradiction between sales data and the development of the smoking rate can be explained by at least four factors related to NRT use in real life. First, despite the deregulation, many individuals are not using NRT in their quit attempts (Shiffman and Sweeney 2008, Amodei and Lamb 2008, Zhu et al. 2012). Secondly, NRT may be used in a suboptimal way in a quitting attempt, making that attempt ineffective (Amodei and Lamb 2008, Zhu et al. 2012). Thirdly, NRT is used in a way that is not related to quitting. Finally there are other reasons for this discrepancy. This chapter describes these reasons in more detail.

6.1 Smokers’ and quitters’ reasons not to use NRT

As described in Chapter 2, nicotine dependence is a chronic condition, requiring comprehensive treatment. Therefore the evidence-based clinical guidelines underline the importance of comprehensive support, which consists of pharmacotherapy and behavioural components (Fiore et al. 2008, The Finnish Medical Society Duodecim 2012). Especially the use of pharmacotherapy is highlighted, because there is such a robust evidence-base for its use (See Chapter 4). Despite this, the use of pharmacotherapy is not the only way to succeed in a SC attempt. Actually at the population level the most common way to quit is to do it unassisted.

6.1.1 Popularity of unassisted quitting

During the period of radical decrease in smoking in the 1970s and 1990s in many Western countries, unassisted quitting synonymous with quitting cold turkey (meaning no use of any evidence-based behavioural or pharmaceutical methods) has been the predominant way to quit (Fiore et al. 2008, US Department of Health and Human Services 2014). Even though during the past twenty years, SC treatments have been greatly developed, unassistant quitting is still the most common way to quit (Cokkinides et al. 2005, Fiore et al. 2008, Gross et al. 2008, Chiang and Chapman 2010, Yeomans et al. 2011, Hung et al. 2011).

There are many reasons for the popularity of unassisted quitting (Table 6). Smokers and quitters may prefer the use of non-traditional SC aids, highlight the importance of their own willpower or are reluctant to seek assistance (Hammond et al. 2004, Gilpin et al. 2006, Gross et al. 2008, Hung et al. 2008, Medbo et al. 2011, Marques-Widall et al. 2011).
Further, according to population-based studies, many quitters just perceive quitting cold turkey far more helpful than other methods (Hammond et al. 2004, Hung et al. 2009). For these reasons, some authors have also suggested that unassisted quitting should be more recognized as an equally good way to quit compared with assisted quitting (Cheong et al. 2007, Chapman and MacKenzie 2010, Alpert et al. 2012). However, this perception is contrasted by the evidence, which suggests that unassisted quitting produces significantly lower permanent abstinence rates compared with assisted quitting (Hughes et al. 2004a, Fiore et al. 2008, National Institute of Clinical Excellence 2012).

6.1.2 Unwillingness to use NRT

The review of Zhu et al. (2012) suggested that the use of SC medicines is influenced by healthcare providers’ interests, costs and marketing efforts. Health care professionals’ proactive role in SC, including the recommending of SC medicines, has been promoted in the great body of SC guidelines (See Chapter 3.3). However, some studies suggest, that health professionals’ false perceptions may still hinder the proper use of NRT (Amodei and Lamb 2008, Beard et al. 2012, Zhu et al. 2012). OTC NRT is widely marketed in most of the Western countries, and there is contradictory evidence, how marketing efforts are reflecting in the actual use (Tauras et al. 2005, Wakefield et al. 2008). NRT products’ price is seen as a significant obstacle to the use and reason to discontinue the use early on. Reimbursement by health insurance increases to some level the use of NRT (West et al. 2005, Kaper et al. 2008).

In addition, NRT users’ perceptions of NRT explain why these products are not used in SC or they are used in a non-optimal way (Table 6). Many smokers and quitters have misinformation or fears towards NRT use, which hinder NRT use.

It has also been questioned, are the current nicotine replacements enough appealing for quitters (Cummings and Mahoney 2008, Shiffman 2010, Caldwell et al. 2012, Fagerström and Bridgman 2014). Because the current NRT products do not sufficiently mimic smoking behaviour, some smokers find NRT unappealing and unrewarding (Caldwell et al. 2012, Fagerström and Bridgman 2014). Further, the current administration routes through oral mucosa or skin, do not release nicotine fast enough to respond to withdrawal symptoms (Caldwell et al. 2012, Ferguson and Shiffman 2014). On the other hand, the key principle in the development of NRT products has been the slow nicotine release rate compared with tobacco products, so avoiding the products ability to maintain nicotine dependence (Elam 2012, Keane 2012).
Table 6. Examples of smokers’ and quitters’ reasons for not using NRT and suboptimal use of NRT.

<table>
<thead>
<tr>
<th>Examples of smokers’ and quitters’ reasons for not using NRT and suboptimal use of NRT (Reference)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reasons related to popularity of quitting without any assistance</strong></td>
</tr>
<tr>
<td>• Cold turkey is effective (Hung et al. 2011, Medbo et al. 2011).</td>
</tr>
<tr>
<td>• Own willpower far more important (Hammond et al. 2004, Vogt et al. 2008).</td>
</tr>
<tr>
<td><strong>Reasons related to perceptions on NRT</strong></td>
</tr>
<tr>
<td>• Lack of awareness (Hammond et al. 2004, Kaper et al. 2005), though in more recent publications, most smokers are aware of NRTs (Bansal et al. 2004, Ferguson et al. 2011).</td>
</tr>
<tr>
<td>• Misunderstanding of treatments action and safety (Etter and Pernager 2001, Bansal et al. 2004; Hammond et al. 2004, Van der Rijt and Westernik 2004, Vogt et al. 2008). Misinformation of safety and/or efficacy may be even more significant barrier to use than cost (Ferguson et al. 2011).</td>
</tr>
<tr>
<td><strong>Reasons related to NRT purchases</strong></td>
</tr>
<tr>
<td>• Access (McNeill et al. 2001, Shiffman and Sweeney 2008, Fiore and Baker 2011). Though very easy access (delivery at home) and possibility to familiarization of NRT forms or NRT free of charge did increase use, but was not associated with quitting (Mooney et al. 2006, Walker et al. 2011).</td>
</tr>
<tr>
<td>• Costs (Cummings and Hyland 2005, Kaper et al. 2005, Hughes et al. 2009). Including SC medications in the reimbursement scheme in the UK significantly increased their use (West et al. 2005). Increase in cost may decrease appropriate use (Sims and Fiore 2002).</td>
</tr>
<tr>
<td>• Relaxed licensing, which allowed the ‘cut down to quit use of NRT’, did not increase significantly OTC NRT use in the UK (Shabab et al. 2009).</td>
</tr>
<tr>
<td><strong>Reasons related to early discontinuation of NRT use</strong></td>
</tr>
<tr>
<td>• Relapse back to smoking (Burns and Levinson 2008, Balmford et al. 2011).</td>
</tr>
<tr>
<td>• Side effects (Burns and Levinson 2008, Balmford et al. 2011).</td>
</tr>
<tr>
<td>• Perception of NRT not helping (Burns and Levinson 2008, Balmford et al. 2011).</td>
</tr>
<tr>
<td>• No longer need for NRT and quitting successfully (Burns and Levinson 2008, Balmford et al. 2011).</td>
</tr>
<tr>
<td>• Low motivation for use, situational or other reasons (Balmford, et al. 2011).</td>
</tr>
<tr>
<td>• Lack of money or NRT cost (Burns and Levinson 2008, Balmford et al. 2011).</td>
</tr>
<tr>
<td>• Purchase by prescription was an important predictor of longer use (Gilpin et al. 2006).</td>
</tr>
<tr>
<td>• Patch is used for longer than gum (Paul et al. 2003).</td>
</tr>
<tr>
<td>• Withdrawal symptoms (Sims and Fiore 2002).</td>
</tr>
<tr>
<td><strong>Examples of use for too a short time</strong></td>
</tr>
<tr>
<td>• In the first population-based study, assessing early discontinuation of NRT use, the median usage period was only 10 days and only 12% of the participants who attempted to quit used NRT for eight weeks or more (Burns and Levinson 2008).</td>
</tr>
<tr>
<td><strong>Examples of use with too a small dosage</strong></td>
</tr>
<tr>
<td>• NRT users typically use only about 50% of recommended doses of SC medicines (Shiffman et al. 2008a,b). Level of adherence is associated with success rate of SC.</td>
</tr>
<tr>
<td>• 19% of quitters who used NRT gum used at least the minimum recommended daily dose (Shiffman et al. 2002a). These quitters were more successful in abstinence in the sixth week compared to those not using the product with the recommended dose.</td>
</tr>
<tr>
<td>• Increased use of nicotine lozenge was associated with a significant increase in SC, so that each additional lozenge used would increase of the likelihood of six weeks abstinence by 10% (Shiffman et al. 2007b).</td>
</tr>
<tr>
<td><strong>Examples of concurrent use of NRT and cigarettes (dual use)</strong></td>
</tr>
<tr>
<td>• NRT is used to temporary replace when smoking is not allowed (Shaw et al. 1998, Sims and Fiore 2002).</td>
</tr>
<tr>
<td>• Concurrent use of NRT inhaler or NRT gum and tobacco is common in population based studies (Hughes et al. 2004,b, Hughes et al. 2005, Beard et al. 2013).</td>
</tr>
<tr>
<td>• NRT use for smoking reduction or temporary abstinence is common. NRT use in these attempts was associated with previous quit attempts (Beard et al. 2012, 2013).</td>
</tr>
<tr>
<td>• Reduction in cigarettes smoked is most common pattern of use for non-cessation reasons (Hughes et al. 2005). This is recommended as cessation strategy for patients unwilling to quit (Fiore and Baker 2011).</td>
</tr>
<tr>
<td>• Although rare, the off-label use of an inhaler is related to a repeatedly concurrent use with tobacco or inhaler use for non-cessation reasons (Hughes et al. 2005).</td>
</tr>
</tbody>
</table>
6.2 Concept of NRT adherence

Adherent use of NRT treatment will significantly increase the likelihood of achieving SC in clinical, hospital-based and community settings (Shiffman et al. 2002, Shiffman et al. 2007a, Burns and Levinson 2008, Shiffman et al. 2008a,b, Raupach et al. 2008). The low rate of adherence partially explains why in many population-based studies OTC NRT use has yielded much lower abstinence rates than could be expected from clinical trials (Curry et al. 2003, Raupach and van Schayck 2011, Raupach et al. 2014). However, while the concept of adherence to NRT is difficult to determine, some background information related to it is given in the next paragraphs.

6.2.1 What is meant by the concept of adherent NRT use?

Increasing adherence to medications has been called the key mediator to improve the effectiveness of all current pharmacological treatments (World Health Organization 2003e). For SC behaviour and NRT use there are some specific characteristics, which make the assessment of adherence and practices improving it more difficult compared with other long-term conditions (Hollands et al. 2011, Raupach et al. 2014). For instance, it can be more difficult to persuade smokers unwilling to use SC medicines to use them compared with medicine users of other therapeutic areas (Hammond et al. 2004, Shiffman et al. 2005, Shiffman et al. 2008c, Hollands et al. 2011).

Currently, there is lack of uniform definition for good adherence of SC medication or measurement of the good adherence (Raupach et al. 2014). There is no consensus on what is the optimum therapeutic period of NRT use (Sims and Fiore 2002, Cummings and Mahoney 2008). The majority of relapses take place either during first eight days or during three first months after a quitting attempt (Hughes et al. 2004a, Cummings and Mahoney 2008, Fiore and Baker 2011). The current recommendations of the optimum treatment period of three months are originating from the RCT’s assessing the efficacy and safety for regulatory purposes (Sims and Fiore 2002, Cummings and Mahoney 2008). In RCT’s NRT efficacy is typically assessed during the period of use for 12 weeks (Cummings and Mahoney 2008, Fiore et al. 2008). On the other hand, some smokers could benefit using oral NRT forms for over six months (Fiore and Baker 2011). Also a great variety of different NRT forms makes it difficult to define the level of optimum dosage. For this reason, most studies have only used post-hoc measurement for adherent dosing (Raupach et al. 2014).
6.3 Real life NRT use patterns

The way NRT products are used in real life can partly explain why their increased use has not been reflected in a sizeable drop on the smoking statistics. Therefore NRT use patterns in real life are described in brief below.

6.3.1 Use for a short period

Despite the lack of consensus of the optimum therapeutic NRT use period, among the most common reasons for relapse in real life NRT studies, is that individuals are not using pharmacotherapy long enough to overcome withdrawal symptoms (Sims and Fiore 2002, Hughes et al. 2004a). In contrast to RCT’s, in population-based studies the majority of the study participants uses OTC NRT for less than four weeks (Etter and Pernager 2001, Thorndike et al. 2002, Hyland et al. 2005a, Pierce et al. 2006, Burns and Levinson 2008, see Table 6). There is also evidence, that OTC NRT is used for a far shorter period than prescription NRTs (Pierce et al. 2006).

6.3.2 Use of too low a dosage

NRT is also used with too low a dosage (See examples in Table 6). NRT users typically use only about 50% of the recommended doses (Shiffman et al. 2008a,b). Especially this is related to all the oral forms of NRT. Sometimes the products are also used with the wrong technique or with refreshments, which hinders the adsorption of nicotine. Furthermore, some NRT users tend to underestimate their level of dependence and use the mildest oral NRT form (Shiffman et al. 2008c).

The same reasons, why NRT is not used at all, also partly explain why many NRT users tend to use NRT for only a very short time or with inadequate dosing (Table 6). In addition to these, in population-based studies a variety of reasons to discontinue use in the early stages have been reported. Of these reasons, the most common one has been the reinitiation of smoking (Burns and Levinson 2008, Balmford et al. 2011).

6.3.3 Concurrent smoking and NRT use

Traditionally the concurrent use of NRT and smoking is forbidden in the instructions for NRT use and it is considered as a reason for NRT treatment failure (Shaw et al. 1998, Sims and Fiore 2002). In population-based studies this concurrent (dual) use of an NRT inhaler or NRT gum and tobacco is common (Thorndike et al. 2002, Hughes, et al. 2004, Hughes et al. 2005, Burns and Levinson 2008 Beard et al. 2010, Balmford et al 2011). Currently smoking reduction with NRT patch as a preceding SC is recommended as a NRT use strategy, especially for patients who otherwise would not be able to quit (Royal College of Physicians 2007, Wang et al. 2008, Sims and Fiore 2011). In Finland, this indication was officially accepted for NRT gum for the first time in August 2011 (Personal information from Lohi S. /Fimea 2014). Some evidence suggests that smoking reduction
can lead to successful SC (Wang et al. 2008, Baker et al. 2010). However, this use should be combined with counselling by a health care professional and a well-planned strategy for how to reduce smoking (Wang et al. 2008, Sims and Fiore 2011).

6.3.4 Use of NRT for other purposes than quitting

There is some evidence, that NRT products are used for other purposes than quitting (Sohlberg et al. 2001, Hammond et al. 2008). In a survey conducted in Minnesota in 1999 about 20% of NRT users did not make a quit attempt while they used NRT (Sohlberg et al. 2001). Similarly, one third of all NRT users in a four-country study used NRT for purposes other than for quitting (Hammond et al. 2008). These purposes were a reduction in the number of cigarettes smoked and temporary abstinence.

In Denmark, after NRT deregulation, NRT use has significantly increased but this has not been associated with a significant decrease in smoking (Laegestyrelsmittelsen 2005). According to a report by the Danish Health Authorities, Sundhetsstyrelssen, (2006) less than half (42%) of the NRT users used products for quitting. Whereas 24% used NRT for smoking reduction and 19% reported being dependent on NRT. According to the survey of the Health and Health Behaviour among Finnish adult population in 2013 (Helldán et al. 2013) 6.5% of the respondents, who smoked during past year, had used NRT other purposes than quitting, whereas in 2005 the corresponding rate was 2.9% (Helakorpi et al. 2005).

6.4 Other reasons why the detection of the influence of NRT deregulation on smoking statistics is difficult

There are also additional reasons why the influence of NRT deregulation is difficult to detect in smoking statistics. Most importantly, SC is a multifaceted phenomenon, which is influenced by several developments taking place in the society. Based on the literature, smoking prevalence among adults has been found to be dependent on the number of adolescent smokers who continue to smoke into their adulthood, the number of smokers who die, the number of quit attempts and on quitters’ ability to remain abstinent (Hatsukami et al. 2008, Hughes 2011, US Department of Health and Human Services 2014). All these factors influence on the smoking rate concurrently, making it hard to detect the influence of one intervention on the overall smoking rate.

Finally, according to the hardening hypothesis, those smokers who are still smoking in the 2010s are those most dependent on tobacco and for them achieving SC is most difficult (Warner and Burns 2003, Hughes 2011). Furthermore, the most dependent smokers are those most likely to use SC pharmacotherapy (Henningfield et al. 2011). This pattern could partly explain why the decline of smoking has been in most Western countries less radical than it was two decades ago. However, the evidence-base on this hypothesis needs more detailed assessment before the impact of more dependent smokers on smoking prevalence can be determined (Hughes 2011).
7 Counselling and NRT: evidence base and practical viewpoints

7.1 Evidence-base related to the combination of counselling and NRT use

All the very first reviews focusing on the clinical use of NRT highlighted that NRT use should be well planned and instructed (Russell et al. 1980, Sees 1990). In addition, behavioural support should be offered. According to these reviews, without behavioural support the treatment would not succeed. These recommendations were based on the addictive nature of nicotine and understanding about the complexity of behavioural change.

Two of the most recent updates of Cochrane review (Stead et al. 2008; 2012) highlighted the beneficial role of sole NRT use in the quitting process independent of any substantial support (Appendix 1). However, the update from 2012 of the review also detected a few studies comparing OTC NRT to placebo. According to the pooled results of these studies the effect of NRT on SC remained positive. However, the authors noted that in those studies the control groups had very low success rates compared with control groups in other settings (Appendix 1). This matter implies the need for counselling related to NRT use.

Similarly, two other Cochrane Reviews have provided evidence supporting the additional effects of NRT use and behavioural support (Stead and Lancaster 2012a,b, see Appendix 1). These reviews focused on the combined effects of behavioural support and SC medications compared with sole medication use. The reviews detected small but statistically significant beneficial effects of increased support in advancing SC.

The current US Clinical Practice Guideline is based on the meta-analyses of over 6 000 scientific publications (Fiore et al. 2008). Based on its evidence NRT efficacy is the best among those smokers who also receive behavioural support in addition to NRT use (Appendix 1). Similarly, the systematic review and meta-analysis assessing long-term (> 2 years) benefits of the use of NRT found the highest quit rates among those smokers, who had received more intensive behavioural support in special SC centres (Etter and Stapleton 2006).

7.2 What kind of counselling is needed in real life practice?

In the scientific literature various aspects are presented why the counselling provided by health professionals for the use of NRT products is important in the real life. These are listed as follows: (1) Nicotine dependence is a chronic condition and its treatment needs comprehensive long-term strategy (Chapter 2). (2) Counselling combined with the use of NRT supports smokers’ motivation towards quitting and remaining abstinent (Fiore et al. 2008). Quitting motivation is highly dependent on cognitive and behavioural components which include perceived self-efficacy and the ability to learn new habits, planning strate-
gies for overcoming temptations to smoke and maintain the decision. Often behavioural support provided in NRT trials and recommended in various clinical guidelines aims to strengthen quitters’ empowerment (Zhu et al. 2012). This comprehensive SC support can help in the prevention of relapses and maintaining the permanent lifestyle change.

(3) Counselling of NRT use increases smokers’ and quitters’ understanding how NRT works and how to use it properly (Fiore et al. 2000, Cummings and Hyland 2005, Fiore et al. 2008, Raupach and van Schayck 2011). As described in Table 6, there is a great body of evidence suggesting that many NRT users have inadequate information about the products, which hinders NRT use. It has been suggested that NRT users would benefit from receiving customized medicine information which addresses their perceptions related to NRT (Vogt et al. 2008, Amodei and Lamb 2008, Fiore and Baker 2011, Raupach and van Schayck 2011). (4) Health professionals’ counselling is also needed to increase quitters’ interests towards NRT use (Amodei and Lamb 2008, Amodei and Lamb 2010, Raupach and van Schayck 2011). (5) Further, among NRT users there is a need to increase adherence towards NRT by different methods (Amodei and Lamb 2008, Holland et al. 2011, Raupach and van Schayck 2011). (6) For NRT products, there are many dosage forms and administration routes. For this reason NRT users can benefit from the help of health professionals, who can tailor the most suitable form of NRT therapy and give practical instructions on the use of the different drug forms. (7) The use of NRT for pre-cessation and planned smoking reduction with NRT use should be combined with the counselling from health care professionals (Wang et al. 2008). Otherwise there is a great probability that these strategies do not succeed.

(8) Finally, there are individual differences in the duration of withdrawal symptoms. This matter can notably influence on treatment success (Sims and Fiore 2002). For this reason the therapy of physiological dependence must be treated individually instead of one size fits all considerations (Sims and Fiore 2002, Fiore et al. 2008, National Institute on Clinical Excellence 2012, Raupach and van Schayck 2011).
8 Summary of the key findings of the literature review (Chapters 3-7)

NRT products have been on the market for over three decades. During this time the role of NRT has significantly altered as the evidence-base of the products has steadily increased. NRT deregulations, having taken place in several countries during mid-1990s to mid-2000s, can be perceived as a starting point for a new pattern of NRT use. The deregulation changed NRT products’ role from medicines towards consumer products (Shiffman and Sweeney 2008, Keane 2013). This development is currently accelerated, as many stakeholders advocate for a far more liberal nicotine policy. NRT deregulation has also been used as a successful example for extending self-medicine practices and the paradigm related to OTC use towards the treatment of long-term conditions (Shiffman and Sweeney 2008).

There is compelling evidence of NRT efficacy. However, several factors may hinder generalizing this information to real life, especially in terms of the use of OTC NRT. The effectiveness of OTC NRT in SC has been investigated and debated even very recently (Albert et al. 2012, Kaszka et al. 2012, Kotz et al. 2014). Currently, the evidence-base of the effectiveness of OTC NRT in real life is contradictory.

In Finland, based on the data of the Finnish Statistics on Medicines, during the post NRT deregulation period, NRT products’ sales have nearly doubled and the great majority of NRT purchases are made through other sales channels rather than from pharmacies (Figure 3). This dramatic increase in NRT sales after deregulation is similar to international experiences (Shiffman et al. 1997, West et al. 2005, Laegestrylmittelsen 2005). However, in Finland, according to the annually conducted survey of the Health and Health Behaviour among the Adult Population, NRT use in quit attempts has increased by 3.9% units during the post-deregulation period 2005-2013 (Helakorpi et al. 2005, Helldán et al. 2013, Chapter 5.3). This increase is not so sizeable compared with the dramatic increase in NRT sales.

The most important reason for NRT deregulations worldwide has been the expectation that NRT deregulation would lead to a significant reduction in the prevalence of smoking. Currently however, there is no compelling evidence supporting that expectation (see Chapter 5.4). In Finland, according to the SOTKANET® database by the National Institute for Health and Welfare, the smoking rate among the Finnish adult population has decreased by 5.7% units during the period of 2005-2013 (Figure 5, Chapter 5.4). During the post-deregulation period, several amendments in the Finnish Tobacco legislation have taken place, making the Finnish legislation globally one of the strictest. The introduction of these new norms makes it difficult to directly estimate the effects of NRT deregulation on smoking prevalence in Finland. However, the smoking prevalence has been steadily decreasing during the past decades and there has not been any detectable acceleration of that development after NRT deregulation.

According to the literature there are several reasons why the NRT deregulation has not resulted directly in a sizeable decrease in the smoking rate. For example, the NRT usage patterns in real life are not always optimal. To illustrate, the use of too low a dosage or too short a treatment period compared with the instructions, is common. Finally there are several reasons why health care professionals’ counselling of the use of NRT products remains important.
The overall objective of this study was to explore reasons for the NRT deregulation to general sales in Finland in 2006 and the reflections of this change on SC practices. This study concentrates on exploring NRT deregulation from three perspectives: 1) NRT deregulation as a political process, 2) community pharmacists as health care professionals guiding NRT use, and 3) NRT users’ perceptions of NRT in SC.

The specific study aims are the following:

1) To identify and describe the key dimensions of the political argumentation in the debate leading up to the NRT deregulation in Finland (I).
2) To explore the familiarity and implementation of the Finnish SC Guideline in Finnish community pharmacies, factors relating to Guideline familiarity, implementation and provision of SC services (II).
3) To assess the Finnish pharmacy owners’ and staff pharmacists’ perceptions on the role and usage patterns of NRT products about one year after the deregulation (III).
4) To gain an understanding how smokers and quitters value NRT in SC (IV).
5) To explore what kind of NRT usage patterns existed in Finland in the post-NRT deregulation period (2006-) (III, IV).
10 Materials and methods

10.1 Study context and design

This study applied both qualitative and quantitative methods (Table 7). As NRT deregulation is a relatively new and widely debated phenomenon in Finland, it was explored from three selected perspectives. These perspectives were chosen because they are relevant to understand the background and consequences of the NRT deregulation. In addition, previous literature provides only sparse information on these subjects. Therefore, this study aims to describe the reason for the change and its reflections, instead of assessing the possible causal relationship related to public health.

Various data sources and methods were utilized in this study (Table 7). This triangulation of different study settings, multiple data sources and methods is conducted to provide a more comprehensive and deeper understanding of the investigated phenomenon (Smith 2002).

Table 7. Methods used in the substudies (I-IV).

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Data sources utilized</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Document analysis and twelve personal, open-ended theme interviews in spring 2006.</td>
<td>All publicly available documents of the legislative process introducing NRT deregulation. Interviews of Members of the Finnish Parliament.</td>
<td>Qualitative analysis: Inductive content analysis of the arguments related to NRT deregulation. Two independent analysis, which were compared and merged were conducted during 2011.</td>
</tr>
<tr>
<td>II, III</td>
<td>Nationally representative postal survey among a random sample of Finnish community pharmacists (including pharmacy owners and staff pharmacists) conducted in November 2006- April 2007.</td>
<td>Responses of the Finnish community pharmacists including staff pharmacists and pharmacy owners. Response rate 54% 50% for pharmacy owners, 53% for staff pharmacists</td>
<td>Quantitative analysis: Descriptive statistics, Ohi-Square, Logistic Regression analysis were conducted during 2007-2009.</td>
</tr>
<tr>
<td>IV</td>
<td>Analysis of internet-based postings made by smokers and quitters on NRT products in the period of January 2007-January 2012 in the Finnish national SC supporting Stumppi Forum.</td>
<td>The postings made by Stumppi Forum participants on the five selected internet discussion areas in the Forum. Altogether the data collection and analysis was based on 24,481 postings in these areas.</td>
<td>Qualitative analysis: Inductive content analysis of the postings, concerning NRT use or comparing NRT to other SC methods, was conducted during October 2011- March 2012.</td>
</tr>
</tbody>
</table>

69
10.1.1 Brief description of the operationalization of the theoretical background

Especially in the first study the principle of evidence-informed decision-making was utilized as a theoretical background. It means a procedure, which aims to facilitate well-informed, transparent and systematic processes in decision-making, taking into account the decision-making context (Dobrow et al. 2004, Oxman et al. 2009). As this qualitative study was inductive in its nature, the conceptual background helped to choose the unit of analysis, category building, and grouping but also in the abstraction phase (Elo and Kyngäs 2008, Appendix 3). This study also served as a framework for the later studies (III, IV).

The studies II and III focused on community pharmacists’ involvement in SC and their perceptions of NRT use and deregulation. In the study (II) the concept and the literature of SC guideline implementation among health professionals was used as the theoretical background (See Chapters 3.3, 3.4). This theoretical framework was operationalized in the study by assessing the concepts of guideline familiarity and implementation. More detailed description of the operationalization of the key concepts to measured variables is given in Appendix 3 and in Chapter 10.3.2.

For the studies (III, IV) the literature on real life NRT use (Chapter 6) was used as the conceptual framework. This literature was used as one starting point for developing the survey instrument utilized (III). This concept was operationalized to concrete variables in the forms of statements regarding pharmacists’ perceptions on real life NRT use. In addition, key concepts related to the political debate on NRT deregulation (analysed in Study I) were operationalized in this study as the concrete statements concerning pharmacists’ perceptions on deregulation (see Appendix 3 and Chapter 10.3.2).

In the last study (IV) among Finnish smokers and quitters, the literature on NRT use patterns and on different internet communities and facilities supporting participants’ empowerment and self-management was used as a background for the idea of the study (van Udel-Kraan et al. 2008, Armstrong et al. 2009, Seale et al. 2012). These concepts also helped to understand the topics covered within smokers’ and quitters’ discussions.

10.2 Data sources utilized

10.2.1 Policy-making related to NRT deregulation

All the official, publicly available documents relating to the Amendment of Medicines Act on presenting NRT deregulation were analysed (Figure 6, phases 4-9, 11). Most of them can be accessed online via the Finnish Parliament’s homepage, from which they were downloaded verbatim. The Statements of Interest Groups were received from the Ministry of S&H in February 2010. Altogether the documents consisted of 402 pages (Figure 6).
1. Minister of Social Affairs and Health introduced the idea of reimbursement for NRT (August 31st, 2004)

2. NRT reimbursement is rejected by Ministry of Finance. Reason: lack of money (Autumn 2004)

3. The Speech of Minister of Health: NRT deregulation (March 12th, 2005)


5. The Statements of Interest Groups (n=33, altogether 179 pages) (by May 18th, 2005)


7. The Bill to the Handling of Committee of Social Affairs and Health (SAHC) (September 8th, 2005). The Hearings of the Stakeholders' statements (n=27 altogether 123 pages). The Bill to the Handling of the Constitutional Law Committee

8. The Statement of the Parliamentary SAHC (19 pages) (December 2nd, 2005)

9. The general debate in the plenary sessions (December 7-8th, 2005) (altogether 25 pages)
   I Vote (December 8th)
   II Vote (December 12th)


12. Amendment of Medicines Act: Widening the sales of NRT products to restaurants. (September 29th, 2010)

Figure 6. The legislative process of introducing NRT deregulation, and the documents analysed in the study (bolded).
The main focus of the analysis was on the official documents, but to obtain additional information and enrich viewpoints, personal, open-ended theme interviews of twelve Members of Parliament (MPs) were made shortly after the deregulation was enacted in February-May 2006. The recruitment criterion for the interview was that the representative had a clear interest in health policy (e.g., background as a health professional or membership of the Parliamentary SAHC). The number of interviewees was balanced according to the size of each Parliament Group. Altogether 20 MPs were sent an e-mail request and 12 MPs accepted it. Six of them had voted for and six against the deregulation. The interviews took place in the Parliament Building and lasted between 25 to 90 minutes. All the interviews were conducted by the same researcher (TK). The interview discussions saturated after the ninth interview. More detailed description is given in the original publication I.

### 10.2.2 Community pharmacists’ survey

The survey questionnaire was mailed to a national, random sample of every second Finnish community pharmacist (n=2291), including pharmacy owners (n=289) and staff pharmacists (n=2002) in November 2006. The sample was drawn from the member registers of the three national pharmacists’ professional associations (Table 8). At the time of the survey, these registers covered 100% of the Finnish pharmacy owners and 93% of the staff pharmacists with B.Sc. (Pharm.) and M.Sc. (Pharm.) degrees. Because 7% of the staff pharmacists did not belong to a professional organization, they were not contacted.

The respondents were drawn randomly by choosing every second pharmacist, who were not refusing to give their contact information for research purposes, from a list in which they were presented in an alphabetic order based on their surnames. All the respondents had equally good chances to be chosen as a study participant. For the statistical analysis all the received responses were combined (see also Chapter 10.3.2 and the original publications II and III for a more detailed description).
10.2.3 Internet-based discussions on NRT use

Since 2004, The Organisation for Respiratory Health in Finland has maintained an Internet portal called STUMPP, financed by the government-based Slot Machine Association of Finland (RAY). The STUMPP website (2014) is constantly updated and it contains a lot of current information on tobacco consumption and SC. The website provides free services for registered and unregistered quitters and health professionals. Among the services included are ten discussion areas, each with a different focus. The five most popular discussion areas were selected for this study. These were SC Medications and Replacement Therapies; Pre-Contemplators; Contemplators; Action; and Maintenance. The selected discussion areas were those concentrating most clearly on the role of NRT in different stages of SC process. More detailed description of the selection of these areas is given in the original publication IV.
10.3 Methods

10.3.1 Qualitative studies utilizing inductive content analysis

While assessing the perspective of pharmaceutical policy-making (I) and NRT users (IV), inductive content analysis was utilized. This method pays special attention to the crucial aspects of the textual material and produces classifications based on the content of the material (Sandelowski 1993, Graneheim and Lundman 2004, Elo and Kyngäs 2008). This study investigated rarely explored phenomena and the aim was to gain authentic insights into studied perspectives. Therefore, inductive content analysis was the most suitable analysis method.

10.3.1.1 Steps in the data analysis

Before conducting the analysis the unit of analysis was fixed (see also Appendix 3). In the study of the NRT deregulation as a political process, it was one or more sentences containing one policy argument for or against NRT deregulation. A policy argument was defined as an oral or written statement that advocates the adoption of a policy or justifies decision to adopt a policy (Ball 1995). In assessing the STUMPPI Forum participants’ perceptions unit of analysis was one or more sentences concerning opinions, perceptions, experiences or expectations related to NRT use or comparing NRT with other SC methods (Rx medicines or non-pharmaceutical methods, including cold turkey).

In both studies, the materials were carefully read through several times to ensure the comprehension of their fundamental features. Then all the materials were re-read. For each sentence, relevant to research questions, a short code, true to its original expression, was created. The codes covering similar or nearly similar meaning were combined. These were grouped again to form categories, which were named according to their overall content (Graneheim and Lundman 2004, Elo and Kyngäs 2008). Later, the categories were again grouped to form broader categories, and finally, preliminary themes.

10.3.1.2 Policy-making related to NRT deregulation

The analysis of the political documents was started from the first draft of the Government Bill and continued to further documents in chronological order (Analysis 1). The debates held in the Parliament and the 12 interviews were analysed in a similar way to the documents (Analysis 2). The analysis was started with the documents of the Parliamentary debates in chronological order and followed by the interviews of the MP’s in the order in which they were conducted. Finally, the two analyses (1&2) were compared and merged. In doing so, it was noted that both the analysis resulted in similar themes. More detailed description of the analysis is given in the original publication I, Figure 2.
10.3.1.3 Internet-based discussions on NRT use

In the internet-discussions-based study of smokers’ and quitters’ perceptions on NRT use the data collection and analysis took place simultaneously. It was started by reading systematically through all the postings made during January 2007 and January 2012 in the discussion areas of SC Medications and Replacement Therapies and Pre-Contemplators. All the postings relevant to the research question were copied verbatim onto two specific MS-Word files. For each posting only one code per viewpoint was created, but one posting could include several viewpoints and yield several codes. On basis of these postings on the two areas, the first coding scheme was created. The data collection continued to the three further areas and 20% of the discussions were read. The data saturated in the Maintenance area after 8% of the threats were read. More detailed description of the analysis is given in the original publication IV.

10.3.2 Nationally representative survey among community pharmacists

10.3.2.1 The survey instrument

The survey instrument was designed to cover several aspects of SC practices in community pharmacies, the implementation of the national Finnish SC Guideline and pharmacists’ perceptions on NRT deregulation. The survey instrument was based on an earlier Finnish survey conducted among physicians and nurses to assess their attitude towards smoking and actions taken in SC (Jormanainen et al. 1997, Barengo et al. 2004). The instrument was modified to include community pharmacists. Figure 7 describes the development and conduction of the survey. In Appendix 4 the questions used in the studies II&III are translated into English.
Figure 7. Outline of the national survey among community pharmacists.

Development of the survey instrument
A Finnish nationwide survey for physicians and nurses as a basis (Barengo et al. 1997, Jormanainen et al. 1997); modification to pharmacy context based on the literature review

Pre-testing
two pharmacies
(2 pharmacy owners and 10 staff pharmacists)
Assuring face-validity

Phase 1
November 2006: Mailing of the survey to 2291 participants, (289 pharmacy owners; 2002 staff pharmacists, of which 1628 B.Sc. and 374 M.Sc.)

Phase 1b
December 2006: An electronic reminder via the national pharmacy intranet to every Finnish pharmacy. 827 responses obtained (response rate 36%), of which 126 from pharmacy owners and 701 from staff pharmacists

Phase 2
January 2007: A reminder with a repeat questionnaire sent to all the respondents. 409 additional responses received, of which 17 from pharmacy owners, 392 from staff pharmacists. Cumulatively 1236 responses (response rate 54%)

Phase 2b
March 2007: A reminder via the national pharmacy intranet: 19 additional responses received, of which 1 from a pharmacy owner and 18 from staff pharmacists

Total of 1255 responses received (response rate 55%)

12 recipients were not reached:
The surveys of 12 recipients were returned by the postal service because addresses of the recipients were unknown.

65 responses excluded:
36 of respondents not working in a community pharmacy, 29 empty or inadequate responses.

1190 responses included in the analysis.
Response rate 54%
Operationalization of the key concepts to variables used in the survey instrument


As the familiarity with a guideline is the first step in implementation (Francke et al. 2008) the structured key question of the implementation of the Finnish SC Guideline (the original publication II) was as follows: “How familiar are you with the SC Guideline”. The duties expected by the SC guideline for community pharmacists were used as a basis for the measuring of SC actions taken at community pharmacies. These actions were operationalized in a set of questions assessing the frequency of recommending guideline-based pharmacological and non-pharmacological SC treatment options to the smoking pharmacy customers and respondents’ participation in continuing SC education (see Appendix 3&4). In addition to these variables, participation in local SC multidisciplinary teamwork was used as a background variable (see original publication II) for familiarity with the guideline and measuring its implementation.

In addition the Likert-type of statements on NRT usage patterns were based on a literature review of the topic (See the original publication III, Table 1). Another set of statements concerning the influence of deregulation on pharmacy owners’ and staff pharmacists’ motivation to serve and counsel customers purchasing NRT products was based on the political debate on the possible effects of the deregulation. The conceptualization of these literature reviews and the operationalization of the key outcome variables is described in Appendix 3.

Modifications of the key variables for the analysis

The background variables utilized in the study are presented in Table 9. All the background variables were used in their original format, with two exceptions. The variable related to pharmacist’s participation in continuing SC education was reclassified as a dichotomous variable (yes/no) for the statistical analysis. In addition the pharmacy’s location by province was re-classified to four regions: Southern, Eastern, Western and Northern (combination of options Oulu and Lapland) Finland. Before conducting the statistical analysis, the background variables were categorized to characteristics of the responding pharmacist; characteristics of his/her workplace; and SC actions that have taken place at his/her workplace according to the systematic meta-review of Francke et al. (2008).
Table 9. Characteristics of the respondents (n= 1190) and all Finnish community pharmacists in 2006 (n= 5053).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Respondents (n=1190)</th>
<th>All community pharmacists (n= 5053)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td><strong>Variables associated with the respondent</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Professional status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B.Sc. Pharmacist (Staff pharmacist)</td>
<td>70</td>
<td>833</td>
</tr>
<tr>
<td>M.Sc. Pharmacist (Staff pharmacist)</td>
<td>18</td>
<td>217</td>
</tr>
<tr>
<td>Pharmacy owner (M.Sc. degree or higher)</td>
<td>12</td>
<td>140</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>1190</td>
</tr>
<tr>
<td><strong>Specialization of the respondent</strong>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>25</td>
<td>272</td>
</tr>
<tr>
<td>Diabetes</td>
<td>21</td>
<td>230</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>20</td>
<td>221</td>
</tr>
<tr>
<td><strong>Participation in continuing education in SC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-house training</td>
<td>48</td>
<td>568</td>
</tr>
<tr>
<td>Continuing education (CE)</td>
<td>25</td>
<td>302</td>
</tr>
<tr>
<td>In-house training by a drug company</td>
<td>40</td>
<td>477</td>
</tr>
<tr>
<td>CE by a drug company</td>
<td>33</td>
<td>398</td>
</tr>
<tr>
<td>Not participated</td>
<td>20</td>
<td>229</td>
</tr>
<tr>
<td><strong>Variables associated with the respondent’s working pharmacy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Location by province</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southern Finland</td>
<td>39</td>
<td>459</td>
</tr>
<tr>
<td>Western Finland</td>
<td>33</td>
<td>392</td>
</tr>
<tr>
<td>Eastern Finland</td>
<td>15</td>
<td>174</td>
</tr>
<tr>
<td>Northern Finland</td>
<td>13</td>
<td>157</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>1182</td>
</tr>
<tr>
<td><strong>Annual prescription volume</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40 000</td>
<td>21</td>
<td>252</td>
</tr>
<tr>
<td>40 000–80 000</td>
<td>38</td>
<td>452</td>
</tr>
<tr>
<td>80 001 ≥</td>
<td>41</td>
<td>475</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>1179</td>
</tr>
<tr>
<td><strong>Ownership</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Privately owned</td>
<td>94</td>
<td>1108</td>
</tr>
<tr>
<td>University owned</td>
<td>6</td>
<td>75</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>1183</td>
</tr>
</tbody>
</table>

* Based on the professional programs run by the AFP since late 1990’s to assure community pharmacies’ contribution to the national public health goals. Information available on pharmacists working in privately owned community pharmacies (missing data from the two university owned pharmacies covering about 11% of the total prescription volume).

na = not available
In the question assessing the SC Guideline familiarity for the analysis the options “I have read the Guideline carefully through” and “I am familiar with its main principles “were combined to make up a group of respondents ”Familiar with the Guideline.” The remainder of the respondents were categorized as ”Unfamiliar with the Guideline”.

In the Likert–type statements measuring respondents’ perceptions of the importance of SC and healthcare’s role in it, assessing pharmacists’ perceptions on NRT role or NRT deregulation the options “Always” and “Almost always” were reclassified as “Always”; options “Strongly agree” and “Agree” to “Agree”; and correspondingly “Disagree” and “Strongly disagree” to “Disagree”.

In all statements of the study, B.Sc. and M.Sc. pharmacists shared similar views and thus their responses were combined. The same applied to in the case of pharmacy owners and staff pharmacists with the exception of the set of statements covering how extending NRT sales has influenced on their perceptions. More detailed descriptions of the evidence-base for the key questions, its operationalization to concrete variables and the modification of the variables for analysis is given in original publications (II&III).

10.3.2.2 Statistical analysis

The statistical analysis of the studies was based on bivariate (original publications II, III) and multivariate analysis (II). The statistical significance in the bivariate analysis was tested by Chi Square test. P-value of <0.05 was considered statistically significant in study II and p-value of < 0.01 in study III.

In assessing the factors associated with the guideline familiarity (II), the multivariable analysis, logistic regression was applied to control for a concomitant effect of the background variables selected for the analysis on the basis of the bivariate analysis (Hidalgo and Goodman 2013). The main outcome variable measuring respondents’ familiarity with the SC Guideline was dichotomized (1=Respondent familiar with the Guideline; 0=Unfamiliar). The Spearman’s correlations between the background variables were calculated to avoid possible multicollinearity. Of the two variable pairs with a correlation coefficient of 0.6 or more, (respondent’s age and graduation year; and ”Smoking pass in use” and ”Pocket card to support SC counselling in use”), respondent’s age and use of a SC pocket card were included in the regression analysis. A backward step-wise logistic regression analysis was conducted. The final model did not include interaction terms. The associations between the outcome and background variables were described by Odds Ratios calculated from the B-estimates, and p-values (see Table 3 in the original publication II).

All the statistical analyses were conducted by the SPSS analytical software, version 15 (SPSS Inc., Chicago, IL). More detailed description of the statistical analysis is given in original publications II and III.
11 Results

This chapter summarizes the key findings of the original studies (I-IV). They are also summarized in Figure 12 (Chapter 11.6).

11.1 NRT deregulation from policy-making perspective

Key arguments for the NRT deregulation were assessed by using the analysis of political documents and MP’s interviews of the NRT deregulation as a political process. According to the Interest groups’ statements given for the Ministry S&H and for the Finnish Parliament, NRT deregulation was widely supported. However, most of the Interest Groups’ statements contained several arguments against deregulation. The Head of the Parliamentary Committee of Social Affairs and Health characterized the political process of NRT deregulation as a colourful debate. This debate is analysed in depth in this study. As result of the analysis, the debate comprised of five central themes, which are conceptualized in Figure 8. Key findings related to each theme are described in the following paragraphs.

Figure 8. Key themes of the political debate leading to NRT deregulation emerged from analysis of the documents and interviews. Reproduced with the kind permission of Elsevier (originally published in I).
11.1.1 NRT deregulation and public health

Throughout the debate on NRT deregulation, there was a broad consensus that smoking is a major public health hazard. Protection of public health was used as a starting point for arguments both for and against NRT deregulation (Themes I&II, Figure 8). The objective of the deregulation was to significantly improve access to NRT products, decrease prices, and thus, increase their use (Theme I, Figure 8). This was justified by inadequate NRT access and use, when the number and opening hours of food stores and community pharmacies, i.e., the availability of NRT products and tobacco, were compared. In the debate the argument of poor NRT availability was questioned, because the pharmacy network was regarded as extensive enough to provide NRT for SC.

Increased access to NRT products was expected to increase the number of NRT purchases and quitting attempts, and to make quitting easier, more impulsive and straightforward. The significance of increasing NRT purchases and their use in cessation was highlighted but also criticized, because of the nature of SC as a long-term process. It was also brought up that only succeeded SC attempts were crucial for public health.

Furthermore, the appropriate and safe use of NRT products, when taking into account special characteristics of NRT products, was highlighted in the debate (Theme II, Figure 8). A key part of this was the debate on the effectiveness of sole NRT use without any behavioural components or counselling. It was also discussed whether the information on NRT efficacy from RCTs is equivalent to effectiveness in real life. The Government Bill stated that NRT is safe and the deregulation would not create any safety risks. On the other hand, deregulation was seen as a remarkable threat to drug safety. Possible misuse and abuse of NRT products, especially by minors and athletes, were the most debated safety concerns.

11.1.2 Extensions of the debate: fundamental change in pharmaceutical policy and structures related to policy-making

The political debate extended beyond NRT and SC to become a debate on the principles of pharmaceutical policy and structures guiding the policy-making process. An important part of the debate was, who is allowed to sell medicines and what is the importance of professional advice to treatment outcomes. NRT deregulation was initiated as a fundamental change in Finnish pharmaceutical legislation because NRTs were the first and sole medicinal products intended to be sold outside pharmacies and, as such, without professional advice. Furthermore, the general principle in deregulating the distribution of non-prescription medicines, instead of enacting specific legislation for one medicine group, was raised. In addition, due to the required license system for the sales of NRT, the deregulation made the sales of NRT products more regulated than the sales of tobacco (Theme IV, Figure 8).

The NRT deregulation proposal was strongly presented as a part of the health and tobacco legislation, supporting public health. It was, however, criticized as being a commercial policy, separate from prevailing health and pharmaceutical policy, deliberately
aiming to increase the commercial aspect of medicine use. It was even stated to be an attempt to weaken health care’s role in SC by losing NRT as a resource if sold outside pharmacies.

The proposal for deregulating NRT was equipped with evidence on NRT efficacy and foreign experiences on NRT deregulation. However, two of the key arguments supporting deregulation, the poor NRT availability and the effectiveness NRT deregulation in SC, were not justified by any evidence. Instead both the key reasons were based on an assumption in the Government Bill. Furthermore, the influence of NRT deregulation on SC was seen to be impossible to evaluate. These matters raised questions of how evidence-informed the decision was (Theme IV, Figure 8).

The way the political decision-making process was carried out was also debated from several aspects (Theme V, Figure 8). The Government Bill was criticized because it was prepared in only one ministry, so lacking wider collaboration. Further, the claims of the key authority of medicines regulation, National Agency for Medicines, were not given any attention. It was debated that the change in legislation should have been processed at a slower pace because it contained so many proposals which were changing principles in the prevailing legislation.

Party discipline was seen as the central force supporting the deregulation and according to some interviewed MPs the decision personalized to the Minister of S&H. The process was also seen as very contradictory, as some evidence was interpreted differently by different stakeholders. A more detailed description of the analysis of the NRT deregulation as a political process and examples of original citations is given in original publication I.

11.2 Community pharmacists’ involvement in SC

11.2.1 Community pharmacists’ familiarity with the Finnish SC Guideline

In this study almost half (47%) of the responding pharmacists (n=1190) were familiar with the Finnish SC Guideline (Table 2, original publication II). Based on the bivariate analysis conducted, the following variables related to individual pharmacists’ characteristics positively influenced the familiarity with the SC Guideline: specialization in asthma, ever smoked 100 or more cigarettes, participation in continuing SC education, being a pharmacy owner, and being older and pharmacists’ positive perceptions of SC (Table 2, original publication II). Of the background variables related to respondent’s working pharmacy, its location by province and dispensing counter design were associated with the Guideline familiarity (Table 2, original publication II). All the variables measuring availability of SC services at the respondent’s working pharmacy, such as offering individually tailored SC service, having a guideline on NRT dispensing, participating in local multidisciplinary SC collaboration, were associated with the Guideline familiarity (Table 2, original publication II).

In the multivariate analysis, nine out of the 21 variables were found to have a statistically significant association with the SC Guideline familiarity. The highest ORs were found
in the variables related to respondents’ own perceptions of the personal skills and knowledge in SC (OR 3.8); perceptions of customers value NRT counselling (OR 3.3); and regular use of the pocket card in SC counselling (OR 3.0; all variables, p≤0.001) (Table 3, the original publication II). However no characteristics related to pharmacists’ work place, like geographical location or dispensing design, influenced on Guideline familiarity.

11.2.2 The implementation of the SC Guideline-based actions

Implementation of the guideline-based SC actions and services were more common among the respondents familiar with the SC Guideline (Table 10). The familiarity with the Guideline was strongly associated with respondents’ working pharmacy’s participation in local multidisciplinary SC actions, the frequency of applying the 5A’s Intervention with smoking customers and the discussion about SC with customers who have higher risk factors or buy SC medicines. These actions were not so commonly taken compared with recommending NRT gum or patch, which were reported by almost all respondents despite their Guideline familiarity (Table 10). Similarly, nearly all the respondents reported that they always discuss SC with customers who spontaneously refer to his/her smoking. The same applies to supporting smoker’s own quitting decision which was made by more than 60% of the respondents.
Table 10. Implementation of the Finnish SC Guideline-based SC actions/services among the pharmacists familiar and unfamiliar with the Finnish SC Guideline.

<table>
<thead>
<tr>
<th>The Finnish SC Guideline based actions and services</th>
<th>Familiar with the Finnish SC Guideline (n=512)</th>
<th>Unfamiliar with the Finnish SC Guideline (n=625)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workplace involvement in local multidisciplinary SC actions</td>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Participation in a joint training</td>
<td>15</td>
<td>5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Considered joint practices</td>
<td>12</td>
<td>5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Have joint practices</td>
<td>5</td>
<td>2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Recommends SC Guideline based pharmacological treatment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nicotine gum</td>
<td>94</td>
<td>96</td>
<td>0.450</td>
</tr>
<tr>
<td>Nicotine patch</td>
<td>86</td>
<td>80</td>
<td>0.01</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>22</td>
<td>20</td>
<td>0.345</td>
</tr>
<tr>
<td>Bupropion (Zyban®)</td>
<td>15</td>
<td>10</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Recommends SC Guideline based non-pharmacological tools</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Own quitting decision</td>
<td>68</td>
<td>62</td>
<td>0.020</td>
</tr>
<tr>
<td>Written SC support material</td>
<td>56</td>
<td>41</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Participation in the &quot;Quit and Win&quot; competition</td>
<td>26</td>
<td>23</td>
<td>0.242</td>
</tr>
<tr>
<td>Social support of family and/or friends</td>
<td>17</td>
<td>14</td>
<td>0.120</td>
</tr>
<tr>
<td>Telephone-based SC support</td>
<td>12</td>
<td>8</td>
<td>0.09</td>
</tr>
<tr>
<td>Pharmacy’s individually tailored SC service</td>
<td>10</td>
<td>6</td>
<td>0.006</td>
</tr>
<tr>
<td>Group therapy</td>
<td>9</td>
<td>5</td>
<td>0.027</td>
</tr>
<tr>
<td>Internet-based SC support</td>
<td>7</td>
<td>4</td>
<td>0.080</td>
</tr>
<tr>
<td>Advise to see a public health nurse</td>
<td>4</td>
<td>3</td>
<td>0.104</td>
</tr>
<tr>
<td><strong>Follows at “least often”</strong> the 5A’s Intervention with smoking customers**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Advised to quit during the month prior the survey</td>
<td>12</td>
<td>3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Told about how smoking effects medication during past month</td>
<td>10</td>
<td>2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Asked about smoking during past week</td>
<td>9</td>
<td>2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Assessed quitting date during past month</td>
<td>2</td>
<td>1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Discusses always</strong> about smoking with customers who..</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>self-refer to their smoking</td>
<td>94</td>
<td>91</td>
<td>0.101</td>
</tr>
<tr>
<td>are pregnant</td>
<td>45</td>
<td>32</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>buy SC medicines</td>
<td>35</td>
<td>17</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>suffer from a smoking-related disease</td>
<td>18</td>
<td>7</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

* Between the groups familiar and unfamiliar with the SC Guideline
** Reclassified from the options: “always”, “often”, “at least with every second customer”, “sometimes, never”.
“Often” was considered as option “often or more frequently”
*** “Always” from the original answering options: “always”, “sometimes”, “never”
11.3 Reflections of NRT deregulation on community pharmacists’ perceptions of NRT sales and their professional role in SC

The responding pharmacy owners (n=140) and staff pharmacists (n=1050) had different views on the influence of the deregulation on the sales of NRT products and on counselling customers on the use of these products, one year after the deregulation (Figure 9). Of the pharmacy owners, 30% and 17% of the staff pharmacists saw that their own motivation to counsel clients buying NRT products had diminished. Respectively, 19% of the owners and 5% of the staff pharmacists saw the importance of the NRT products in SC had diminished. The majority (83%) of the pharmacy owners agreed that the sales of NRT products had decreased at their pharmacy after the deregulation (Figure 9). 54% of the owners had also noticed that clients came to the pharmacy for advice on NRT use, but bought the products elsewhere.

Despite the decreasing sales, the pharmacy owners and staff pharmacists shared the opinion that it is their duty to support SC and that the clients valued the NRT counselling provided by pharmacists. They also considered professional service as a more important means of competition than the price competition with the stores. A sizeable proportion of the owners (44%) reported devotion to training in their pharmacy to support SC counselling, and almost a quarter (23%) of staff pharmacists indicated this devotion at their pharmacy in the recent past.
The sales of the NRT products have diminished in my working place \( p < 0.001 \)

- Pharmacists (n=1033)
  - Agree: 45
  - No opinion: 25
  - Disagree: 30

- Owners (n=138)
  - Agree: 83
  - No opinion: 4
  - Disagree: 14

Clients obtain the medical counselling of NRT from pharmacy, but buy the products elsewhere \( p < 0.001 \)

- Pharmacists (n=1033)
  - Agree: 29
  - No opinion: 31
  - Disagree: 40

- Owners (n=138)
  - Agree: 54
  - No opinion: 25
  - Disagree: 20

In my working place there has lately been devotion to education supporting SC counselling \( p = 0.001 \)

- Pharmacists (n=1032)
  - Agree: 23
  - No opinion: 12
  - Disagree: 65

- Owners (n=139)
  - Agree: 44
  - No opinion: 9
  - Disagree: 47

Because of the deregulation of NRT products, their role in SC has diminished \( p < 0.001 \)

- Pharmacists (n=1032)
  - Agree: 5
  - No opinion: 18
  - Disagree: 77

- Owners (n=139)
  - Agree: 19
  - No opinion: 22
  - Disagree: 58

Because of the deregulation of NRT products, my motivation towards the medication counselling of NRT use has diminished \( p = 0.002 \)

- Pharmacists (n=1035)
  - Agree: 17
  - No opinion: 8
  - Disagree: 74

- Owners (n=139)
  - Agree: 30
  - No opinion: 12
  - Disagree: 58

The counselling of NRT use is more important in the competition in their markets than the possible cheaper prices in other sale channels \( p = 0.001 \)

- Pharmacists (n=1033)
  - Agree: 79
  - No opinion: 12
  - Disagree: 9

- Owners (n=139)
  - Agree: 70
  - No opinion: 12
  - Disagree: 18

It is pharmacists’ duty to offer SC support \( p = 0.131 \)

- Pharmacists (n=1041)
  - Agree: 95
  - No opinion: 32

- Owners (n=139)
  - Agree: 93
  - No opinion: 6

Clients value the counselling related to the NRT products \( p = 0.478 \)

- Pharmacists (n=1030)
  - Agree: 89
  - No opinion: 7
  - Disagree: 4

- Owners (n=139)
  - Agree: 86
  - No opinion: 8
  - Disagree: 6

Figure 9. The influence of the NRT deregulation on staff pharmacists’ and pharmacy owners’ perceptions on NRT sales and their professional role in SC. Reproduced with the kind permission of Elsevier (originally published in III).
11.4 How do Finnish smokers and quitters value NRT in SC?

The NRT users’ perceptions of NRT were assessed by analysing smokers’ and quitters’ internet-discussions in the national STUMPPI Forum in the period 2007-2012. As result three major themes explaining how NRT is perceived as a SC method emerged. These themes are conceptualized in Figure 10. Authentic examples of the postings are given in original publication IV, Supplementary Table 1. At the time of NRT deregulation (Chapter 11.1) the NRT role was highlighted. However, in the smokers’ and quitters’ discussions the most common theme that emerged was a negative attitude towards NRT use (Theme 1, Figure 10), offset by acceptance of NRT use early on as a necessary aid in SC (Theme II, Figure 10).

11.4.1 Key explanations given to distrust and negative attitude towards NRT

The frequently emerged explanation for the negative attitude towards NRT use was the fear of NRT use either maintaining tobacco dependence or causing NRT dependence. In the postings, nicotine was suggested as the substance responsible for dependence on tobacco products. For this reason several posters even saw NRT use as equal to smoking. Total freedom from nicotine was highlighted in the postings as the ultimate goal of all SC attempts and this freedom should be achieved at an early stage.

In the postings, the more beneficial effects and successful use of prescription SC medicines (bupropion and varenicline) over NRT were partly explained by the absence of nicotine while using these medications. Similarly the cold turkey quitting (CT), was partly explained by the abstinence of nicotine. Among the posters this culminated in the idea of NRT use in quitting as a less right way, and thus, NRT users are not real quitters as long as they continue to use NRT.

In the analysed discussions, the use of NRT products was found unhelpful and unnecessary for several other reasons. These include discussion participants’ self-reported experiences of not gaining help from NRT use or of adverse effects caused by NRT, general aversion towards medicines and sometimes high prices. Further, a few participants even saw, that the need for NRT has been misinterpreted because of the overestimated physiological nicotine dependence. NRT products were also seen as a business and usage instructions with high doses and long-term use only as pharmaceutical manufacturers’ attempt to gain more financial profit.
### I Distrust and Negative Attitude towards NRT (n=428)

- NRT use maintains dependence on nicotine (n=227)
  - Image: NRT use maintains tobacco dependence (n=54)
  - Experiences and fears of dependence on NRT (n=87)
    - Related to NRT form (n=126)
    - Even stronger than tobacco dependence (n=17)
  - Aim: freedom from nicotine (n=86)
    - NRT use maintains withdrawal symptoms making SC even more difficult (n=37)
    - Allen Carr’s book supports the image of total freedom from nicotine (n=31)
    - Image of SC Rx medicines: freedom from nicotine (n=18)

- Other, commonly emerged, reasons to distrust NRT (n=125)
  - No need for NRT (n=19)
  - Experience: no help on NRT (n=36)
  - Adverse effects (n=21)
    - Use despite these
  - General aversion to medication or toxicity of NRT (n=20)
    - It is easier to win physiological dependence than was assumed (n=13)
    - Price of NRT and other medication (n=16)
    - Seen as moneymaking by manufacturers

### II Neutral Acceptance of NRT as a Useful SC Method (n=404)

- No medication is the guarantee of success (n=87)
  - Need for a permanent lifestyle change (n=42)
  - All the ways are equally good to gain SC (n=45)

- NRT use is especially needed in the beginning of SC (n=121)
  - NRT purchase is a part of the preparation for SC (n=27)
  - Important to have the right form of NRT (n=25)
  - It is meaningful to use NRT for the first time (n=33)
  - Important in the very first days and help in the difficult times (n=36)

- NRT helps to manage physiological dependence and to deal with psychological dependence (n=51)
  - Battle of two frontiers: psychological and physiological (n=11)
  - NRT helps to concentrate on SC and thus NRT use gives time to learn new skills and habits (n=40)

- Relief of worries and acceptance of NRT use (n=95)
  - NRT vs. Tobacco: always better than smoking (n=47)
    - NRT is intended for SC
    - Rely on research and health professionals’ recommendation
  - No reason to fear dependence on NRT (n=36)
    - Experience of sudden quitting of NRT use by itself
  - NRT is a safer and more natural option than Rx medicines (n=12)

- Positive experiences on NRT use (n=50)
  - Has got help from NRT use (n=32)
    - NRT use gives encouragement to try
  - CT quitting too hard or impossible (n=18)

### III Trust on the Crucial Role of NRT and Other SC Medicines (n=211)

- Trust on medication in SC (n=96)
  - Rx medicines: easy CS, no cravings, no nicotine (n=34)
  - Medication helps even without own motivation (n=14)
  - Could not have succeeded without medication (n=48)

- Sharing experiences on medicine use (n=44)
  - Asking to share experiences of different medications (25)
  - Personal experience: Has got help from a SC medication → encouragement for others to try it (n=19)

- Experimental medicine use (n=77)
  - Difference between a try and a true decision (n=38)
  - SC is tried by the use of the first and then the second medication (n=27)
  - Impulsive NRT purchase instead of tobacco (n=12)

### The most Important components of permanent SC (themes I&II) (n=466)

- Own motivation (n=148)
- Own decision and its continuance (n=96)
- Behavioral support, especially peer support in STUMPP (n=88)
- Learning new lifestyle in small steps (n=47)
- All the ways in the beginning are equally good for SC. The most important matter is maintaining the decision in the long run (n=87)
11.4.2 Neutral acceptance of NRT as a useful SC method

Posters having a neutral attitude towards NRT use found this therapy helpful. Though, it was highlighted that no medication guarantees successful quitting, and the actual work to maintain SC should be done by the quitters themselves. In this approach, the importance of NRT use in the beginning of the SC process was highlighted.

In the discussions, the most common justification for NRT use was the perception that NRT use is always a better option than continuing smoking and NRT products are medicines intended for SC. Therefore, their use is highly recommendable. Several posters, including those with self-reported heavy tobacco dependence and long tobacco history, reported how they had gained help from NRT use and NRT use had encouraged them to try. Also health professionals’ recommendations and research results were presented as a justification for NRT use, though these were not as prominent justifications as participants’ personal experiences.

Several participants gave advice to others to relieve their fear of possible NRT dependence. They recommended first to concentrate on mastering tobacco dependence. Later, there would be time to quit NRT use in small steps. NRT was found to be a safer and more natural option compared with prescription SC medicines.

11.4.3 Trust in the crucial role of SC medicines

Though, the idea of medication use to achieve SC was mainly balanced, some posters highlighted the crucial role of medication in SC. These perceptions were especially associated with prescription medicines though trust on NRT was expressed but less frequently. Sharing information on the characteristics and recommending medicines to other participants was the way this perception emerged. Medicine use in quitting was also reported being experimental and difference between true decision and medication use attempts was established. Experimental NRT purchases were one example of this behaviour.

11.4.4 Components of permanent success in SC

In the discussions the most highlighted component of successful quitting was quitters’ psychological empowerment. This included one’s own decisiveness and motivation to maintain a new smoke-free lifestyle. A clear difference was made between physiological nicotine dependence and psychological dependence as the components of tobacco dependence. Psychological dependence was admitted to be the hardest part of SC. To concentrate on its management, one needed relief from physiological withdrawal symptoms, which NRT use could make tolerable. The concentration on psychological dependence included building up new smoke-free self-image, learning a totally new lifestyle, daily habits, and mentally making a permanent change. More detailed description of the results of the study is given in original publication IV.
11.5  NRT usage patterns in Finland

The data describing different usage patterns in Finland is gathered from two studies, with quantitative (III) and qualitative approach (IV).

11.5.1 Community pharmacists’ perceptions of NRT usage patterns

Of NRT usage patterns, almost all, 98%, of the responding pharmacists agreed that it is possible to get addicted to NRT products (Figure 11). A high proportion (86%) of the respondents indicated that NRT products have been misused, misuse meaning use for too

![Figure 11. Pharmacists’ perceptions of the usage patterns of NRT products (all the respondents n=1190). Reproduced with the kind permission of Elsevier (originally published in III).]
short a time or too low a dosage. Furthermore, three quarters of the respondents agreed that the products are used with the wrong technique. One reflection of deregulation was that a majority of the respondents perceived that NRT products could be used for harm reduction purposes though these were not official indications of NRT at the time of the survey was conducted. More detailed description of the findings is given in the original publication III.

11.5.2 Smokers’ and quitters’ perceptions of NRT usage patterns

From the discussions of smokers and quitters a great variety of NRT usage patterns emerged, with the emphasis on avoiding NRT use or at least minimizing the dose and treatment period. Though the importance of sufficient dosage and treatment period were also highlighted (Study IV).

The negative perceptions (Chapter 11.4.1) towards NRT were reflected in the aim of avoiding NRT use in SC. If this was the case, use of NRT products should be intentionally restricted to as short a time and as little a dosage as possible, limiting the use only to the worst moments. Strict control of the use was perceived as a way to avoid the feared NRT dependence.

On the other hand, in the discussions, it was highlighted that it is important to use NRT as long as recommended in the instructions for use and with a sufficient dosage. The sufficient treatment period and dosage were considered crucial in learning to cope with the psychological tobacco dependence. It was also highlighted that the low dosage may have been the reason for failure in previous quitting attempts.

In contrast to this, some participants perceived based on their own self-reported experience, that very low dosage and a short treatment period are enough to overcome physiological dependence. In the discussions, a detailed NRT treatment plan, which included an individualized and decreasing dosage regimen, was recommended to gain SC. It was also seen to help in avoiding the feared NRT dependence. More detailed description of the usage patterns from smokers’ and quitters’ perspective is given in the original publication IV, Table 1 and Supplementary Table 1.

11.6 Key findings of the study

Key findings of this study are presented in Figure 12.
(I) Principles of evidence-informed decision-making were not followed in NRT deregulation:

- Five central themes emerged from the analysis of the political debate: 1) how deregulation may influence on SC, 2) appropriate and safe use of NRT when taking into account the special characteristics of these products, 3) the principle of who is allowed to sell medicines, 4) how evidence-informed the decision was, and 5) the way the political decision-making process was carried out.
- Key reasons: poor NRT availability and the positive influence of NRT deregulation in SC in real life conditions were based on assumptions, though throughout the policy-making process much evidence was brought up.

Summary of studies I-IV: NRT Deregulation is a contradictory phenomenon

Deregulation was presented as a significant, evidence-informed public health policy. Public health was presented as a start-point for deregulation but the key justifications, expected increase in SC and public health benefits of NRT deregulation were based on assumptions instead of evidence (I).

Familiarity with the Finnish SC Guideline and its implementation among community pharmacists had proceeded to some extent. Familiarity reflected directly on the level of SC actions taken by pharmacist. NRT deregulation was contradictory to this development as the deregulation diminished, especially pharmacy owners’ motivation towards SC counselling (III), Still, a majority of all the community pharmacists perceived SC and NRT counselling as important (II,III).

The role of NRT in SC was much highlighted during deregulation (I). Consumers’ best was used as one justification for deregulation (I). However, among smokers and quitters neutral or negative perceptions on NRT are far more predominant than the perception that NRT is crucial for SC (IV).

There exist a great variety of NRT usage patterns in Finland, underuse use being most predominant. Aim of deregulation was to increase NRT use. The existing negative perceptions of NRT may at least partly explain why NRT is little utilized in SC attempts (III,IV).

(II, III) NRT deregulation reflected negatively, especially on pharmacy owners’ motivation to be involved in SC

- Nearly half (47%) of the pharmacists were familiar with the Finnish SC Guideline.
- Familiarity was significantly associated with the level of implementation of more sophisticated SC services. The actual level of implementation was still low.
- One year after NRT deregulation NRT sales at pharmacies had diminished but still clients came often at pharmacy for an advice.
- The motivation towards SC had diminished especially among pharmacy owners.

(IV) Smokers and quitters had mostly either negative or neutral perceptions of NRT:

- Distrust and negative attitude on NRT were explained by fear of NRT dependence, the aim to be totally free from nicotine and own negative experiences of NRT use.
- Neutral acceptance of NRT as part of SC treatment: medication was needed, but quitter must do the work him/herself. Psychological dependence is worst to over-come, but NRT was needed to give peace to concentrate on overcoming psychological dependence.
- Trust on critical role of NRT and other SC medicines was less common and mostly associated with prescription SC medicines.

(III, IV) Different NRT usage patterns, underuse was the most common:

- Underuse, use intentionally or unintentionally, for a lower dosage or shorter time compared to usage instructions, were the most commonly emerged usage pattern among Finnish NRT users (III, IV).
- Fears and true existence of dependence on NRT products in addition to negative perceptions associated with nicotine may partly explain NRT underuse (IV).
- Smokers and quitters perceived NRT as one part of a comprehensive SC strategy, which was needed for permanent SC. However, the role of sole NRT use was not highlighted (IV).

Figure 12. Summary of the key findings of the study.
12 Discussion

This thesis investigated the reasons for the deregulation of NRT products from pharmacy only distribution to general sales in Finland and the reflections of this change on SC practises. This work consisted of two parts: the literature review and the empirical part.

In the literature review of this thesis, evidence related to NRT deregulation was synthetized from various viewpoints. The effectiveness and usage patterns of OTC NRT and the reflections of NRT deregulation on smoking prevalence have been widely studied especially in the USA (see Chapters 4,5,6). Also some perspectives related to the Finnish deregulation have been previously investigated (Alaranta and Aalto-Setälä 2007, Rainio et al. 2010, Rainio et al. 2011). However, all these reflections of NRT deregulation were combined for the first time in the literature review of this thesis. Furthermore, at the time this thesis was written, nine years after the Finnish NRT deregulation, there was sufficient data to assess what were the reflections of the NRT deregulation on the development of NRT sales and Finnish tobacco prevalence (see Chapter 5). Therefore the literature review of this thesis also provided additional evidence related to a less investigated phenomenon from various viewpoints. Thus the literature review complemented the empirical part.

The empirical part (later study) of this thesis focused on three levels of the deregulation: 1) political (NRT deregulation as a political process) level, 2) Health service providers’ (community pharmacists’) level, and 3) customers’ (smokers’ and quitters’) level.

At the political level this study provides new information on the principles of how and why NRT deregulation as a political process took place, based on the analysis of the political debate during the deregulation process. Internationally it is still less known whether the principles of evidence-informed policymaking apply to pharmaceutical policy-making (Maynard and Bloor 2003, Lyles 2004, Fox 2005, Aaserud et al. 2006).

This study also provides new information on the reflections of NRT deregulation on SC practises from the health service providers’ level. According to the Finnish SC Guideline (The Finnish Medical Society Duodecim 2002, 2006, 2012), community pharmacists are the health professional group expected to be most involved in guiding the rational use of NRT. For this reason their involvement in SC and how deregulation had influenced in their practises were assessed one year after the deregulation took place. Although, there are some systematic reviews assessing the effectiveness of community pharmacist-based SC interventions (Cramp et al. 2007, Saba et al. 2013), this study was the first to assess the nationwide implementation of a SC guideline among community pharmacists. In addition, although some non-prescription medicines were switched to general sales in several countries, little is known about community pharmacists’ attitudes to this change. There is some evidence of the effects of NRT products OTC availability on health care providers’ practises (Shiffman et al. 2007c). However it appears that this is the first study assessing pharmacists’ perceptions of the use of NRT products and of the deregulation of non-prescription medicines to general sales.
This study also provides new information at the customers’ level on how NRT is valued in SC. This is important because one key question in planning SC services is what kind of assistance quitters actually want in SC. The literature on SC is predominantly produced by scientists investigating tobacco dependence and SC pharmacotherapy, clinicians and public health experts supporting evidence-based SC practices and stakeholders of tobacco control. There are some studies assessing quitters’ preferences, but their numbers are minimal compared with studies assessing the efficacy and effectiveness of SC interventions.

Finally, this study provides new information on what kinds of NRT usage patterns exist in Finland. The evidence on this matter in Finland was only limited before this study. The following paragraphs compare the key findings of the study with previous literature and the methodological quality of the study is discussed.

12.1 Key findings in relation to earlier literature

12.1.1 NRT deregulation from the political level

From the political level, the Finnish NRT deregulation is an example of decision-making which is influenced by various features other than the sole evidence-informed decision advancing public health, though it was presented as such. Public health provides a widely accepted motive and goal for many kinds of political initiatives even though the scientific evidence of their effectiveness can be missing or weak. This pattern can also be seen in the NRT deregulation case: two of the most important motives for deregulation, namely poor NRT availability and NRT’s effectiveness in SC, were mostly based on assumption instead of actual scientific evidence.

12.1.1.1 The evidence base for the political decision of NRT deregulation

In the political debate on NRT deregulation, efficacy of NRT in SC was highlighted but less attention was given to NRT products’ effectiveness in real-life. Furthermore, the concepts of efficacy and effectiveness were discussed synonymously in the Finnish debate on NRT deregulation, though there are several reasons why information on efficacy cannot directly be generalized to real life conditions (see Chapter 4).

There is some previous evidence that the concept of effectiveness can be used to justify decision-making though it can be misunderstood by its users (Simonen et al. 2009). Authorities using effectiveness data should better understand the concept itself, methodology and limitations of the studies (Simonen et al. 2009, Lyles 2011, Patten et al. 2011). Since information on effectiveness is often used to guide decision-making, there also is a need for better quality information on effectiveness. Poor information at worst can result in misleading and biased decisions (Cochrane 1972, Lyles 2004, Oxman et al. 2009, McCaughey et al. 2010). Decision-makers should be aware of the influence of imperfect information on decision-making and its consequences.

Though the evidence base of NRT deregulation has developed during the years after
NRT deregulation, a great body of evidence was available at the time NRT deregulation was conducted in Finland. For instance the US and British smoking statistics had provided evidence that NRT deregulation in these countries did not lead to a remarkable decrease in smoking prevalence as it was expected to do in Finland (see Chapter 5.4, Hyland et al. 2004, West et al. 2005). Also some population-based effectiveness studies were published already at this time (Thorndike et al. 2002, Pierce and Gilpin 2002). This raises the question, why this information was not utilized in the decision-making at the time of NRT deregulation? Though scientific evidence is only one form of knowledge in political decision-making, more discussion is needed why policy-based evidence, personal experience, opinions and political ideologies are still a common base in decision-making, instead of evidence-informed public health priorities (Dobrow et al. 2004, Lyles 2004, Aaserud et al. 2006, Brownson et al. 2009, Jansen et al. 2010).

Another widely accepted motive and goal for political initiatives is “consumer’s best”, i.e., stating that the proposed political changes will benefit consumers (Noerreslet et al. 2005). During the NRT deregulation process, medicine-users’ possibilities to purchase and try NRT were introduced as ways to support the empowerment consumers by those supporting the deregulation. On the other hand, those against it highlighted the safe and effective use of medicines and consumers’ needs for counselling to guide the rational use of pharmaceuticals. They also emphasized that consumers should be protected from medicalization. However, these arguments were based on limited evidence, because authentic consumers’ perceptions were not assessed.

According to the previous literature and the results of this study on consumers’ level, there are several reasons why NRT is little utilized (see Chapters 6 and 11.4). Less actual evidence exists of the poor availability for these products compared with the other reasons hindering the use of NRT among smokers and quitters.

12.1.1.2 Evidence-informed decision-making and the NRT deregulation process

In decision-making it is highly recommended to compare the beneficial and harmful effects and the health outcomes of different policies to assess the superiority of one policy over another (Oxman et al. 2009, Jansen et al. 2010, Nutley et al. 2010, Lyles 2011). Also the measured outcomes should be agreed in advance (Lyles 2011). Despite these recommendations, the decision on NRT deregulation was not compared with any other tobacco policy options. Furthermore, the key health outcome, an increase in SC, was considered impossible to estimate beforehand. Likewise, the authorities stated that the decision on deregulation was impossible to evaluate. The Parliamentary Social Affairs and Health Committee expected the decision to be monitored. The monitoring was prepared by a special monitoring group, which gave its report less than a year after the deregulation was enacted (Ministry of Social Affairs and Health 2007). The decision and its outcomes have not been reevaluated since then. In the Memorandum of the monitoring group (2007) it was stated that it will be impossible to evaluate the influence of the decision on public health because smoking is influenced by several factors taking place at the same time. However, it would have been important to assess how the decision influences on SC rates
and practises related to NRT use in SC over the longer term.

Similar to the NRT deregulation process, it is still common to consider monitoring and evaluation unimportant (Simonen et al. 2009, Jansen et al. 2010, McCaughey et al. 2010). Collaboration between researchers and decision-makers in all stages of decision-making (preparation, deciding, implementation and evaluation) is needed to alter the culture of policy-making (Brownson et al. 2009, Jansen et al. 2010, Nutley et al. 2010). In the case of NRT deregulation, all key stakeholders gave their statements, but these were used only selectively to justify decisions already made in the preparation stage. In the future all the stages of the decision-making processes should be made more systematic, transparent and informed through the best evidence available, to allocate the scarce resources most efficiently (Apollonio and Bero 2009, Brownson et al. 2009, Oxman et al. 2009, Jansen et al. 2010, Nutley et al. 2010). It is important to separate scientific facts from political goals in the decision-making processes. This is extremely important in public health questions.

12.1.2 NRT deregulation from health service providers’ level

From the health service providers’ level, the aim of this study was to gain an understanding how the policy change in NRT access is influencing on the structures of service provision within health care. This was measured by assessing pharmacists’ commitment to keep up their professional skills and motivation to support SC. In addition, to understand the context of service-provision related to NRT the level of community pharmacists’ involvement in SC was investigated.

12.1.2.1 Community pharmacists’ involvement in SC

One year after the NRT deregulation, this countrywide study on community pharmacists showed that approximately half (47%) of the Finnish pharmacists were familiar with the Finnish SC Guideline i.e., they reported knowing its main principles or having even better knowledge of it.

In an earlier survey conducted among community pharmacists in Iowa in 2002, only 10% of the respondents were familiar with the US SC guideline (Aquillino et al. 2003). At the time of this study, similar nationwide surveys were conducted among Finnish general practitioners and public health nurses assessing the familiarity of the Finnish SC Guideline by similar self-reported measurement than among community pharmacists (Sandström et al. 2007, Kurko et al. 2010). The result showed that 36% of the public health nurses and 25% of the general practitioners were familiar with the Finnish SC Guideline. Compared with these findings, the level of the SC Guideline familiarity was relatively high among Finnish community pharmacists a year after deregulation.

In this study the SC Guideline familiarity was positively associated with the pharmacist’s positive perception towards SC and SC actions taken in their workplace. These findings of the facilitators of SC Guideline familiarity were in line with previous ones (See Chapter 3.3, Table 3). No variables related to the characteristics of the working pharmacy, such as pharmacy’s size, ownership or geographical location influenced SC Guideline fa-
familiarity. This suggests that at the time this study was conducted (2006-2007) all Finns had equal access to SC services provided by community pharmacies regardless of where they lived. This is important from a public health viewpoint, and opposite to the findings from the USA; the study conducted in the pharmacies of New York City area found better availability and lower prices of NRT products in the pharmacies in the wealthiest living areas (Bernstein et al. 2009).

According to this study community pharmacists’ guideline familiarity was associated with the use of more sophisticated SC methods, such as recommending non-pharmacological methods, use of 5A’s Intervention and participation in local multidisciplinary SC actions. However, the SC Guideline familiarity did not influence on the recommendation of NRT products to smoking customers, which clearly was the most common SC action taken among the pharmacists. Similarly, a survey among Australian physicians found a high rate of NRT recommendation, whereas behavioural quitting advice or quit date setting were far rarer (Young and Ward 2001).

However, it is important to notice that still a majority (53%) of the Finnish community pharmacists were unfamiliar with the Finnish SC Guideline. In addition, only a minority of the Finnish pharmacists took other SC actions in addition to counselling on the use of NRT or offered more sophisticated SC services (see Figure 2, Table 10). These actions were offered disappointingly rarely, although the AFP (2008) had, over several years, systematically promoted pharmacists’ involvement in SC. Although SC guideline implementation among health professionals (Chapter 3.3) is challenging, the reasons for this discrepancy need further discussion.

According to the results of this study and the previous literature on pharmacists’ SC practises, the customers’ degree of initiative significantly influences on community pharmacists’ SC counselling activity (Aquilino et al. 2003, Brewster et al. 2005). As health care service providers, community pharmacists must find a balance in their daily practise between the aims of health promotion and the principles of customer service. They do not prefer taking a proactive role to SC, because they fear affecting customers’ intimacy (Brewster et al. 2005). In addition, community pharmacists’ traditional role in customer service used to have less emphasis on life-style counselling. This may partly explain these findings.

12.1.2.2 Community pharmacists’ perceptions of their professional role in SC after NRT deregulation

According to the most recent evaluation, only 20% of NRT products are bought from pharmacies in Finland (Finnish Agency for Medicines and Social Insurance Institution 2014). At the time of this study, nearly all pharmacy owners saw that their sales of NRT products had decreased. Despite this community pharmacy owners’ and staff pharmacists’ commitment to SC was strong one year after the deregulation. Nearly all the staff pharmacists and pharmacy owners saw their participation in supporting SC as their duty and counseling of NRT products highly important. However, it was also noteworthy that even a third (30%) of the pharmacy owners and 17% of staff pharmacists claimed that their motivation
towards counselling of NRT use had decreased due to the deregulation.

Information is only limited on how the deregulation of non-prescription medicines to general sales influences on pharmacists’ perceptions and practises. Evidence of a pseudo patron study from Sweden suggests that, after the deregulation of all non-prescription medicines to general sales, Swedish community pharmacists are becoming more commercial and putting less effort on systematic counselling of their customers (Bardage et al. 2013). It would be worthwhile to assess how pharmacists’ NRT counselling practises have developed in Finland after the NRT deregulation.

Because of the limited information on pharmacists’ attitudes towards the deregulation of a non-prescription medicine, the only data on which to compare pharmacists’ perceptions originates from the studies of physicians’ perceptions of the switch of prescription medicines to OTC (Rosenau 1994). Similar to pharmacy owners in this study, the physicians found the switch to OTC influencing on them economically and professionally, although they considered it inappropriate to admit the economic effect (Rosenau 1994). On the other hand, the review of Shiffman and Sweeney (2008) suggested that physician’s involvement in supporting SC had not changed because of the US NRT deregulation.

At the time of this study 80% of Finnish pharmacists had participated in SC related continuing education while the corresponding rate, for example, among US pharmacists was 8% (Aquilina et al. 2003, Zillich et al. 2004, Hudmon et al. 2006). Furthermore, at the time of this survey 23% of the staff pharmacists and 44% of pharmacy owners saw that their working place had focused recently on education supporting SC. These findings suggest that the systematic efforts by the AFP, including the nationwide educational campaigns and provision of materials to support SC, had succeeded to some extent (Chapter 3.4). However, based on the more recent results of the Annual Review Questionnaire for Pharmacies by the AFP it seems that a few years after NRT deregulation, only a minority of pharmacies are organizing SC related in-house training (Kurko et al. 2011).

In summary, the findings of this study at a service providers’ level indicate that the systematic, nationwide efforts conducted at the beginning of the 2000’s to increase Finnish community pharmacists’ involvement in the treatment chain of SC were adopted in community pharmacies to some extent. NRT deregulation has negatively influenced on this development in pharmacies. The development of community pharmacists’ involvement in SC originates from long-term, international programs, which have been systematically implemented in Finnish community pharmacies (See Chapter 3.4). In contrast to this, the NRT deregulation as a political process was rapid, involving an ad hoc policy with a limited evidence-base. Findings of this study and later evidence from AFP indicate that the NRT deregulation may have stopped the development of implementing countrywide evidence-based SC practises among community pharmacists.

12.1.3 NRT deregulation from the customers’ level

The NRT deregulation from the customers’ level was assessed by analysing the authentic perceptions related to NRT use in SC of Finnish smokers and quitters in the nationwide internet-discussion forum STUMPPI over a five year period immediately after NRT de-
regulation (2007-2012). The most commonly emerged perceptions were a negative attitude towards NRT use offset by acceptance of NRT use as a necessary SC aid in a SC attempt. NRT was only seen as one form of support which was needed in maintaining SC. This indicates that in customers’ level NRT deregulation may not be that crucial in SC as suggested during the political deregulation debate.

According to smokers’ and quitters’ viewpoint, the most important component of permanent SC is the psychological empowerment, which included quitter’s own decision-making and ability to maintain abstinence, in other words the capability to maintain a new smoke-free lifestyle. These perceptions of Finnish smokers’ and quitters’ found in this study are in contrast to the idea that after NRT deregulation sole NRT product use guarantees successful quitting (Shiffman and Sweeney 2008). In addition, the findings of this study indicate that among a reasonable proportion of smokers and quitters there is a comprehensive understanding of the SC process which is less dependent on one pharmaceutical. At the same time the NRT sales have almost doubled but this development is not reflecting in the smoking statistics (See Chapter 5). This discrepancy merits further investigation on the real life NRT use in Finland.

12.1.3.1 Explanation given to the negative attitude towards NRT

Surprisingly many STUMPPI discussion forum participants had a negative attitude towards or experiences of NRT use. The key explanation that emerged from the postings to this was the fear or experience of dependence to NRT. This is in line with previous findings (Etter and Pernager 2001, Bansal et al. 2004, Vogt et al. 2008, Chapter 6). Smokers and quitters fear dependence on NRT and perceive NRT use only as a change of nicotine delivery from tobacco to NRT and maintenance of their nicotine dependence (see Chapters 6 & 11.4).

This perception was obvious in this study although NRT deregulation was proposed to make NRT more an everyday consumer product and convenient to use (see Chapters 3.5, 11.1). During the NRT deregulation process also the possible dependence on NRT was discussed. In this study, nearly all the community pharmacists perceived that it was possible that their customers could become dependent on NRT products. Similarly, in a qualitative study among British physicians it was considered that mere NRT without behavioural support was quite ineffective and smokers without additional counselling might transmit their dependence on cigarettes to NRT (Vogt et al. 2006).

Although population based studies suggest that NRT dependence is rare (Hughes et al. 2004b, Hughes et al. 2005) the fear of NRT dependence is true among smokers and quitters and it hinders appropriate NRT use. On the other hand, health professionals should be better aware of the group of NRT users who have become dependent on these products and need help in a planned withdrawal.
Based on data collected by two methods, this study found that there is a great variety of NRT usage patterns in Finland. The most common one seems to be the use of NRT for a minimal usage period or dosage, which is too low compared with the instructions for use (underuse or suboptimal use). This finding was consistent in the results of the pharmacists’ survey and the analysis of smokers’ and quitters’ discussions. The overall key findings on NRT usage patterns are also in line with the usage patterns widely reported in the literature (Chapter 6).

As described in Chapter 6 it is common that NRT is used in a suboptimal way in a quitting attempt, making that attempt ineffective (Amodei and Lamb 2008, Zhu et al. 2012). This underuse can partly explain why the increased NRT use has not been followed by a sizeable reduction in the smoking prevalence in Finland. On the other hand, consistent with previous findings (Burns and Levinson 2008, Balmford et al. 2011), the qualitative findings of this study imply that sometimes the use of minimal dosage and treatment period may be enough to gain SC. This matter highlights the individuality of SC pharmacotherapy.

This study (III) also found evidence, that NRT use for harm reduction was common in Finland, even before it became an official indication of NRT use in August 2011 (Lohi S, Personal Information from Fimea, June 16th 2014). On the other hand, smokers and quitters especially emphasized that NRT use should be restricted to only supporting total abstinence from tobacco use, not for diminishing the number of smoked cigarettes. However it seems that NRT use for other purposes than quitting has increased during 2005-2013 (Helakorpi et al. 2005, Hélldan et al. 2013).

### 12.2 Methodological considerations

This study focused on the Finnish NRT deregulation from three selected levels. In assessing these levels, *method triangulation* was utilized (Smith 2002). Method triangulation means combining different methodological approaches (Smith 2002, Kemper et al. 2003, Guion et al. 2014). Triangulation increases the overall validity of this study. This is because, the qualitative studies on the political (I) and customers’ (IV) level provided deeper explaining information of less studied phenomena. On the other hand, the quantitative studies based on a nationwide, representative sample of community pharmacists (II,III) provided the more generalizable data of the investigated perspective.

Method triangulation made it also possible to compare the findings from these studies and thus gain a more comprehensive understanding of NRT deregulation. However the results of this study related to the role of NRT in SC were contradictory. This inconsistency may be explained by the different studied levels (political versus health care professionals and customers) rather than as a sign related to the lack of validity of this study. On the other hand, the findings related to NRT products’ real life usage patterns, originating from the community pharmacists’ survey and from the qualitative study on smokers’ and quitters’ perspectives, were in line and the findings complemented each other. This
in turn supports the reliability of this study. The following paragraphs will discuss some methodological considerations crucial for each study. Special attention is paid to the validity and reliability.

12.2.1 Qualitative studies

In both the qualitative studies (I&IV) inductive content analysis was utilized as the most suitable analysis method (Graneheim and Lund 2004, Elo and Kyngäs 2008). The objectives of these studies were to gain genuine insights into phenomena, which were not previously (I) or less studied (IV) (Elo and Kyngäs 2008). Inductive content analysis made it possible to gain a rich overview, true to the original data.

For qualitative studies the concepts of validity and reliability need to be operationalized in a different manner compared with quantitative research (Mayes and Pope 2000). For this reason, for the two qualitative studies, the evaluation criteria for qualitative studies of trustworthiness by Lincoln and Guba (1985) were utilized. The evaluation criteria are 1) credibility, which refers to the confidence and truthfulness of data and how well the data and analysis process address the intended focus of the study. 2) Dependability, which refers to stability of data over time and conditions. 3) Conformability, which means objectivity and neutrality of the data so that two or more people can reach an agreement on the data’s relevance and meaning. 4) Transfermability, which refers to generalizability of the data, meaning to what extent the findings can be applied to other settings and populations in addition to the investigated ones. The further paragraphs describe the key components of the evaluation criteria of trustworthiness related to each study (I&IV).

12.2.1.1 Analysis of the political process of NRT deregulation

This study was based on the analysis of all the publicly available documents on the political process in NRT deregulation. Utilizing written sources of information and analysing all the documents increases the credibility and dependability of the data and further analysis (Lincoln and Guba 1987, Im and Chee 2006). Additional information was received by interviewing MPs, and the information from documents and interviews was triangulated. The data triangulation increased the credibility of the analysis as two data sources were complementary to each other’s.

The analysis of the NRT deregulation as a political process was conducted five years after the deregulation took place, which helped to give distance to the actual lively debate proceeding NRT deregulation in the autumn of 2005 and thus increase the credibility of the analysis. During the data collection and analysis the data saturated, which is highly important for the conformability of the study.

On the other hand, the data analysis was conducted by only one investigator, which can influence on the credibility and conformability of the analysis. There are several opinions on using multiple investigators in the data analysis and seeking agreement, as each researcher interprets the data according to their subjective perspective (Graneheim and Lundman 2004). For instance Sandelowski (1993) states that it is questionable to use
multiple researchers for achieving agreement, as each interpretation is subjective. This matter was taken into account by using the following procedures: Most importantly, during the entire research process, several methodological and data analysis sessions were held within the research group. Secondly, the emerged results were critically discussed with some key participants involved in the decision-making. Finally, the results were controlled for materials outside the analysis. No data was found outside the themes, which is a sign of increased conformability.

Though this study and its findings focused on the Finnish deregulation case, the transformability of the findings can be discussed from the following viewpoints. First, the principle of evidence-informed decision making (Lomas et al. 2000), was the theoretical background of this study. Secondly, utilizing this principle in decision-making was one key finding emerging from the analysis. This finding can be transformed to other legislative procedures related to pharmaceuticals. Further, the key arguments supporting Finnish NRT deregulation are in line with international experiences (Table 5).

12.2.1.2 Smokers’ and quitters’ perspective

In this study the evaluation criteria of the rigour of qualitative analysis (Lincoln and Guba 1985), modified suitably for internet-based research by Im and Chee (2006), were applied. The automatic transcripts provided by the Stumppi forum discussions increase credibility and dependability.

There are several perspectives related to the credibility of this study. The analysis of 3152 postings over a 5-year period (2007-2012) was selected for this study, to give longitudinal data and an understanding of smokers’ perceptions on SC. This unique material provided genuine insights into smokers’ and quitters’ thoughts and behaviours without the interference of a researcher. On the other hand, internet-discussion-based data must be interpreted cautiously (Rollman et al. 2000, Im and Chee 2006, Seale et al. 2010). The analysis of internet discussions is based on what the posters on the forums ‘said’, rather than on their interpretation of what happened. The investigator must rely on postings without verifying these interpretations i.e. by further questions, as could be done in an interview setting (Seale et al. 2010). Furthermore, there is evidence that proactive postings in the threads may receive the greatest diversity of responses, which can highlight the most critical viewpoints (Rollman et al. 2000). Further, due to the anonymity in the discussion forums, it is possible to express fabricated comments. Perhaps, especially too positive comments on any medicine use could be motivated by financial interests. However, it was noticed that the most positive or highly critical comments were balanced by other discussion participants and as such the discussion chains presented mostly balanced opinions. Furthermore, the vast amount of material assessed offered a great variety of aspects of NRT use, which was balanced by different viewpoints.

Saturation point is crucial for reaching the conformability of the analysis. Especially in an internet-based study, it can be difficult to estimate (Im and Chee 2006, Seale 2010). However, in this study a balance between estimating theoretical saturation by researchers’ real time participation (Im and Chee 2006, Seale et al. 2010) and appreciation of the
natural occurrence of postings was achieved. Only five discussion areas were analysed because most of the postings in Stumppi Forum were made in these five areas. These discussion areas were systematically analysed and the data collection continued until no new viewpoints emerged. By doing this a saturated, rich and full overview of different aspects was gained.

The emerged results were discussed with the professionals in the STUMPPI organization who daily follow the virtual discussions. This increased dependability. However in terms of dependability and transferability, it must be borne in mind that this study did not include those smokers and quitters who do not use the internet. In addition, it may be possible that the participants in the STUMPPI Forum may be more aware of SC and NRT use compared with all Finnish smokers and quitters. This matter must be taken into account when interpreting these findings.

This is the first study in Finland assessing NRT use from the smokers’ and quitters’ perspective. As these findings on NRT usage patterns were in line with the ones previously reported in the international literature (Table 6), it can be expected that these findings give genuine insights into the smokers’ and quitters’ perceptions.

12.2.2 Community pharmacists’ survey

In this countrywide representative study, the overall response rate was 54% which is in accordance with (or better than) earlier surveys among pharmacists (Aquilina et al. 2003, Hudmon et al. 2006a). As the original survey questionnaire was six-paged with 62 sets of questions, acknowledging the findings on the effects of the length of a survey instrument affecting the response rate (Jepson et al. 2005) the response rate was relatively high.

The respondents represented well all Finnish community pharmacists at the time of the survey, in terms of academic degree, geographical location, the size of the pharmacy and ownership of the pharmacy (public vs. private, see Table 9). Because more than 90% of Finnish pharmacies have a specialized pharmacist for asthma, diabetes and cardiovascular diseases through the professional programs of the AFP (Association of Finnish Pharmacies 2007), these specialized pharmacists answered more readily compared with other pharmacists (Table 9). This is quite understandable because pharmacists with a specialization can be expected to be more interested in SC. This may though magnify the positive attitude towards SC and its importance with all the pharmacists.

Instead of analysing the characteristics of non-respondents, respondents in different phases were compared. A higher proportion of pharmacy owners responded in phase I compared with staff pharmacists who responded more commonly in phase II (Chi Square test, p < 0.001). No other statistically significant differences were found between the respondents in the two phase. This suggests that the bias of non-responses is minimal (Brenner 1995).

In assessing the familiarity and implementation of the Finnish SC Guideline, respondents’ familiarity with the Finnish SC Guideline was chosen to be the main outcome measure. It was considered more reliable for the respondents to assess their own familiarity with the Guideline than the actual level of implementation, which can be biased by lim-
ited ability to recall or by self-perceptions. However, the level of actual implementation can be more reliably assessed by population based intervention studies or pseudo patron studies.

The role of NRT was studied from the pharmacists’ viewpoint which does not illustrate the perceptions of other health care professionals or quitters or smokers on NRT and its use. This information was, however complemented by the qualitative study among Stumppi participants (Study IV) and in the literature review section of this thesis.

In assessing the reflections of NRT deregulation, the operationalized concepts (see Appendix 3) were designed for assessing pharmacy practitioners’ perceptions on the issue based on their daily contacts with customers buying NRT products and needing their advice in SC. Most of the customer service work is done by staff pharmacists. On the contrary, pharmacy owners deal more with management and planning the services. This can be seen for example, in the “no opinion” responses to the question related to the development of NRT sales, (owners 4% no opinion vs. staff pharmacists no opinion 25%). These “no opinion” responses can be considered as a reflection of these different roles and truthful answers based on their knowledge, experiences and understanding.

This study was conducted during a lively public debate on the delivery routes of NRT and other OTC medicines and on the importance of pharmacists’ advice in general, which may have influenced on respondents’ opinions. However, the main findings are in accordance with the earlier studies on NRT. This increases the reliability of the study.

Although the survey instrument was developed in cooperation with SC experts and pre-tested at pharmacies, some statements and concepts may have been difficult to understand. For example, the statement regarding the use of NRT on smoking reduction may have caused confusion due to the recent discussion on harm reduction and its role in SC. Finally, to note, this cross-sectional study conducted a year after the launch of the deregulation does not allow to draw causal-relationship conclusions between the outcomes variables and the deregulation.
13 Conclusions, implications for further evaluation, research and health care services

13.1 Conclusions

This study found that NRT deregulation from pharmacy-only to general sales was a principally significant but contradictory change in the pharmaceutical legislation. According to this study, at the time of the NRT deregulation was carried out in the Finnish Parliament, it was politically communicated as a straightforward and significant intervention to increase SC among the Finnish population and thus promote public health. Based on the literature review of this thesis and the key findings of this study it can be concluded that NRT deregulation did not directly benefit public health as remarkably as suggested during the policy-making process. The deregulation has reflected negatively on community pharmacists’ involvement in SC, making one health care resource in SC less available. More detailed conclusions of this study, on the key reasons of the Finnish NRT deregulation and its reflections on SC practises, are as follows:

- The politically presented key public health goal of the deregulation, an increase in SC, was supported by only limited evidence. Actually, it was mostly based on the assumptions of poor availability and OTC NRT effectiveness. Furthermore, during the policy-making process of NRT deregulation, several aspects related to the principle in the way the decision-making process was carried out and the fundamental change the deregulation caused in the Finnish pharmaceutical policy were debated. The findings of this study address the need for policy-makers to critically evaluate the evidence and its suitability in the decision-making context.

- This study indicates that community pharmacists could constitute a potential public health resource in SC, which is easily accessible throughout the whole country. One year after the NRT deregulation the development to involve Finnish community pharmacists in the treatment chain of SC had advanced to some extent, measured by the familiarity with and the implementation of the Finnish SC Guideline. NRT deregulation influenced negatively on this development among community pharmacists. This is because the NRT deregulation diminished community pharmacists’ and especially pharmacy owners, motivation to serve and counsel customers buying NRT. If community pharmacists’ motivation and expertise in supporting SC and counselling NRT use are further diminished due to the deregulation, one health care resource in SC may be lost instead of the expected public health benefits of the NRT deregulation.

- Based on the analysis of internet-based discussions, among smokers and quitters NRT products were seen as a less important component of gaining permanent abstinence. More importantly from their viewpoint was their own psychological empower-
ment and the learning of a new smoke-free lifestyle. These findings were in opposition to the importance of the sole NRT in SC, highlighted during the decision-making leading up to the deregulation. Furthermore, a negative attitude towards NRT was the most commonly emerged theme in the analysed smokers’ and quitters’ postings. This was mostly explained by the fear and experiences of dependence towards NRT use.

- Based on qualitative and quantative findings, this study indicates that among Finnish smokers and quitters there are NRT usage patterns which may be suboptimal. Especially underuse, use with too small a dosage, or too short a time, emerged often from the qualitative analysis among Finnish smokers and quitters. It was also the most often reported usage pattern in the community pharmacists’ survey. This finding may at least partly explain why the increase in NRT use after deregulation, based on the Finnish national sales data, may not have been clearly reflected in the Finnish smoking statistics.

13.2 Implications for further research and evaluation

Although the Parliamentary Social Affairs and Health Committee expected the monitoring of NRT deregulation, only very short-term influences were evaluated by the Working Group Monitoring the Sales of Nicotine Preparations in 2007 (Ministry of Social Affairs and Health 2007). The findings of this study suggest, that this evaluation should be repeated to assess the real life benefits of NRT deregulation. Based on this study the following points are suggested as implications for further research and evaluation:

- It is important to assess what is the role for NRT products in SC -will they turn out to be less important tools for health care professionals’ work and less important in SC? Also the pharmacoeconomical aspect of the NRT deregulation should be assessed. We have some evidence of the pricing of NRT after the deregulation (Aalto-Setälä and Alaranta 2008), but it is important to assess how the availability and prices of the products have developed during the nearly ten year period after NRT deregulation and how they will develop in the future.

- There is a need for more research from the smokers’ and quitters’ perspective to assess the real value of NRT compared with other methods in SC. Also smokers’ and quitters’ preferences in SC in general should be further assessed. This information could be used in planning service structures which would be most suitable for their needs in SC. There is also a need to investigate the possible existence of dependence on NRT products from the smokers’ and quitters’ perspective. In recent years, there has been a radical increase in the popularity of e-cigarettes. Therefore it should also be assessed how smokers and quitters perceive e-cigarettes in comparison with NRT as a SC method.
The survey among community pharmacists was conducted in 2006 – 2007, i.e., about nine years ago. This study should be revised in order to find out the long-term effects of the deregulation on pharmacists’ attitudes, motivation, participation in SC and practises to counsel NRT use. This is especially important as the NRT sales and contacts with customers at pharmacies have constantly decreased. Furthermore, there is a need to assess the value of counselling provided by pharmacists in the SC drug use. For instance, could the suboptimal usage patterns of NRT be avoided through pharmacists’ or other health care professionals’ support and guidance?

Since the NRT deregulation, several new tobacco control initiatives have been implemented in Finland (Chapter 5.4). Also a new prescription medicine was launched for SC in 2006 and it was included under the national health insurance scheme in 2014. Despite these significant changes, the real life effectiveness of SC interventions has not been studied in Finland. This kind of study would be important to evaluate the real life importance of different SC interventions and practises in Finland.

13.3 Implications for health care services

Based on the findings of this study and the literature review of this thesis the following implications for the health care services are suggested:

- Many smokers and quitters have several reasons why they use SC medications in a suboptimal way. Therefore, customized medicine information, which addresses their perceptions related to SC, including SC medication use, could support optimal SC medication use. In addition, some smokers and quitters could benefit from even a more comprehensive approach; an individually tailored SC plan (Raupach and van Schayck 2011). This plan could take advantage of the smoker’s own willingness to quit and make lifestyle changes. This kind of individualized SC plan could support optimal SC pharmacotherapy and among NRT users it could prevent the feared NRT dependence. However, support of optimal SC medication use is only one part of the individualized plan. Instead the SC plan should also include non-medical methods supporting SC. This would be in line with STUMPPPI Forum participants’ perceptions, which highlighted the importance of empowerment and quitter’s own decision-making to maintain a new smoke-free lifestyle in gaining permanent abstinence. This kind of plan has been offered in some Finnish health care practises including community pharmacies, but this plan should be made more readily available for smokers and quitters.

- It is also important to discuss the ways of how to support community pharmacists’ involvement in SC, despite their diminished motivation towards SC after NRT deregulation. All health care professionals’, including community pharmacists’, professional role and knowledge-base in SC could be strengthened by educational activities (Table 3). These activities should focus on supporting communication skills and understand-
ing of the importance of empowerment in SC. Also participation in a well-organized multidisciplinary education can support pharmacists’ understanding of the overall importance of the SC treatment chain and their own professional role in a wider context. This kind of education is already available for most of the Finnish pharmacy students. Like the Finnish SC Guideline suggests, all health care professionals benefit from local multidisciplinary SC practices (The Finnish Medical Society Duodecim 2012). This kind of collaboration and local practise could also support pharmacists’ motivation towards SC. Finally, based on the British and Danish experience financial support for more sophisticated SC services provided by community pharmacists has increased the utilization these SC services among their users (Bradley et al. 2006, Association of Danish Pharmacies 2008). This matter should also be discussed in Finland in the wider context of organizing local health care services.

- Finally, all health professionals should find new innovative and customized ways of being involved in the SC process in partnership with smokers and quitters. This is especially important as the ultimate goal of the Finnish Tobacco Control Policy is to end the use of tobacco products in Finland.
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Appendix 1: Summary of key findings related to efficacy of NRT product in relation to behavioral support in SC drawn from the systematic reviews of Cochrane Tobacco Addiction Group, meta-analysis of the US Clinical Practice Guideline and the meta-analysis assessing the long-term effect of NRT use.

<table>
<thead>
<tr>
<th>Name (citation) and objective of the review</th>
<th>Number of trials included, medication and control groups, intervention, other requirements</th>
<th>Evidence supporting sole use of NRT (OTC NRT)</th>
<th>Evidence supporting the combination of behavioural support and NRT use</th>
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<tr>
<td>Nicotine replacement therapy for smoking cessation (Stead et al. 2012): To determine the effect of NRT compared to placebo in aiding smoking cessation and to “Determine whether the effect on SC is influenced by the dosage, form and timing of use of NRT; the intensity of additional advice and support offered to the smoker; or the clinical setting in which the smoker is recruited and treated.”</td>
<td>150 placebo-controlled trials, with &gt; 50 000 smokers. The participants were motivated to quit and smoked &gt; 15 cigarettes a day. Medication group received NRT Control group placebo. Almost all trials provided similar behavioral support, advice, counseling and number of follow-up visits, for the NRT and control groups. Between different trials there were differences in the amount of support. In some analyses the amount of behavioral support was categorized to low and high. Low meant a visit in usual care and high if the duration exceeded 30 minutes or included several visits to the clinic or trial center.</td>
<td>Risk Ratio (RR) for abstinence for any NRT form compared to placebo is 1.60 (CL 95% 1.53-1.69). The RR's for different NRT formulations varied between 1.49 (gum) to 2.02 (nasal spray). NRT use increases the quitting rate by 50 -70%. The results remained similar regardless of the setting, including OTC NRT vs. prescription NRT, duration of the therapy or additional support provided. According to the meta-regression conducted there was no evidence that the relative effect differed by the type of support.</td>
<td>Results of five trials in community volunteers in OTC setting were pooled. The RR (2.71, 95% CI 2.11 to 3.43) was significantly higher than in other settings. This was explained by the most lowest quit rate of control group in OTC studies (2.1%) and the highest smoking clinics (12.1%). For this reason, the authors suggested, that absolute increase in quit rates in OTC setting may be small. The authors discussed that the absolute increase in SC rates related to NRT use will be larger if the baseline chance of success is already raised by the provision of intensive behavioral support.</td>
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<td>Behavioral interventions as adjuncts to pharmacotherapy for smoking cessation (Stead and Lancaster 2012a): “To evaluate the effect of increasing the intensity of behavioral support for people using smoking cessation medications, and to assess whether there are different effects depending on the type of pharmacotherapy, or the amount of support in each condition.”</td>
<td>38 RCTs or quasi-randomized controlled trials, of which 35 examined NRT use. The studies included 15 000 participants, who were expected to have the same level of motivation towards quitting, though the motivation was not assessed. In the SC medication group the participants received similar medication, but different amounts of behavioral support varying from minimal (e.g. written information) to intensive multi-session counselling. Controls could receive any level of support (from intensive personal contact to written information) but they always received lower intensity support than the medication group. Point prevalence at 12 months was used, instead of sustained abstinence. The review focused on the amount, not on the components or the quality of the support.</td>
<td>The review detected a small but statistically significant benefit from more intensive support (RR 1.16, 95% CI 1.09 to 1.24) for abstinence at longest, 12 months, follow-up. Increasing the amount of behavioral support is likely to increase the chance of success by about 10 to 25%, based on a pooled estimate from 38 trials. The authors concluded that providing more intense behavioral support for people making a cessation attempt with the aid of pharmacotherapy will increase the success rates by about 16%.</td>
<td></td>
</tr>
<tr>
<td>Name (citation) and objective of the review</td>
<td>Number of trials included, medication and control groups, intervention, other requirements</td>
<td>Evidence supporting sole use of NRT (OTC NRT)</td>
<td>Evidence supporting the combination of behavioural support and NRT use</td>
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<td>Combined pharmacotherapy and behavioral interventions for smoking cessation (Stead and Lancaster 2012b): “Assess the effect of combining behavioral support and SC medication, compared to a minimal intervention or usual care. To assess are there differences between characteristics of the treatment setting, intervention, population treated, or take-up of treatment.”</td>
<td>42 trials of which the results of 40 trials were included in the pooled results. The studies included &gt; 20 000 patients. Behavioral support was typically provided by SC specialists, who offered between four and eight contact sessions. Medication group: SC medication with behavioral support (tailored materials, brief advice, in person or telephone counselling). Most of the trials in this review offered one or more types of NRT or bupropion. Control group members received either usual care or a brief cessation component (i.e. advice to quit) but no other behavioral support or medication.</td>
<td>The pooled estimate for the remaining 40 trials (RR 1.82, 95%CI 1.66 to 2.00) suggests that a combined intervention might typically increase the SC rate between 70- 100%. One trial, The Lung Health Study, demonstrated a large benefit of a multimodal therapy. At one year follow-up SC rate was 35% in the intervention group and 9% in the control. Sustained benefits after five years and reduced mortality in the intervention group were reported.</td>
<td>Compared to the estimates from the Cochrane reviews of the effects for NRT (50-70%) or bupropione alone, the additional benefit from the behavioral component might seem small. No formal statistical comparison between medication use and behavioral support is conducted and thus the effects cannot be compared directly.</td>
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<td>Treating Tobacco Use and Dependence update 2008 (Fiore et al. 2008 pages 101-103) “Whether combining counseling and medication improved SC rates compared to either of these alone.”</td>
<td>The effect of adding counseling to medication was based on a meta-analysis of 18 studies comparing either medication alone or medication with counseling. The effect of adding medication to counseling was based on meta-analysis of 9 studies, which provided 24 arms to compare medication and counseling alone.</td>
<td>Medication and counseling both are effective and should be provided as stand-alone interventions when it is not feasible to do the both.</td>
<td>The combination of medication and counseling is more effective for SC than either component alone. Therefore, combining medication and counseling should both be provided to patients trying to quit smoking (page 101). There is a strong relationship between the number of counseling sessions when combined with medication and the likelihood of a successful SC (page 103). OR for combining counseling to medication was 1.4 (1.2-1.6) and the OR for combining medication to counseling was 1.7 (1.3-2.1).</td>
</tr>
<tr>
<td>Nicotine replacement therapy for long-term smoking cessation: a meta-analysis (Etter and Stapleton 2006): “To assess if the effect of a single treatment episode with NRT enhances SC over many years. This was the first systematic review of the long-term effects of NRT in the treatment of tobacco dependence. The authors suggest it provides the most reliable evidence that NRT aids in achieving permanent SC.”</td>
<td>Meta-analysis of all randomized trials of NRT with final follow-up of more than one year after the start of the treatment (n= 12). The authors also expected that treatment and controls only differed by the inclusion of an active NRT product in the treatment arm. The most stringent definition of abstinence was used (prolonged abstinence). The follow-up periods varied between 2-8 years. All the studies provided SC rates at 12 months and later follow-up points. The effect of any advice or behavioral counselling was also given. Medication group: received different NRT products and different dosages (n= 2 408). Controls: placebo (n = 2 384) Most of the trials allowed to use NRT for three months but four trials allowed the use for four months. In addition, in all the trials supportive advice or counselling was given to some extent. All the trials were conducted in clinical settings instead of “self-help” settings where NRT is bought (at pharmacies or supermarkets).</td>
<td>Of the 12 trials included, six provided statistical evidence on the effect of NRT at the final follow-up and six gave null results. The combined data from all the trials provided good evidence for the efficacy of NRT beyond 12 months.</td>
<td>The use of NRT in addition to brief advice or behavioral support offered in the included studies gave and odds ratio 2 and suggests 70-90% increase in the SC rate achieved without NRT. The long term success rate of NRT use is extremely modest, representing success in SC of about only 9% of those initially treated by NRT. These results suggest, that nicotine addiction should be treated as a chronic recurring disease in the brain. Its treatment should be planned on a long term basis. The quit rates remained long term among those quitters, who had received more intensive and experienced behavioral support as part of the trial. This finding suggests that NRT use is more effective in SC, when used in addition to counselling.</td>
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</table>
Appendix 2: Examples of studies showing contradictory evidence on the effectiveness of OTC NRT for smoking cessation.

<table>
<thead>
<tr>
<th>Study design/ key characteristics</th>
<th>Participants / How abstinence is defined</th>
<th>Key Findings related to the effectiveness of OTC NRT</th>
<th>To notice (key points in discussion, limitations and strengths of the study)</th>
<th>Supports the effectiveness of OTC NRT?</th>
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<tbody>
<tr>
<td><strong>Systematic reviews and meta-analysis</strong></td>
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</table>
| Hughes et al. 2003:  
To assess whether OTC-NRT is pharmacologically efficacious, whether it produces abstinence rates similar to those in prescription settings, and to estimate the long term (>six month) abstinence rate with OTC NRT.  
All the included studies were conducted in the US.  
Systematic literature review of studies assessing efficacy of OTC NRT.  
All prospective trials were included, which assessed either OTC NRT versus placebo or OTC NRT versus prescription NRT and that reported abstinence rates and the results reported.  
The included studies, assessing the efficacy of OTC NRT vs placebo included altogether nearly 2,500 smokers.  
The included studies assessed the efficacy of OTC NRT vs prescription (Rx) NRT including altogether nearly 9,000 smokers.  
In the OTC NRT vs prescription NRT trials for the meta-analysis the prolonged abstinence of 6 months was used. All included studies used biochemical verification of abstinence.  
This systematic review was able to locate totally 9 eligible studies. All OTC NRT versus OTC placebo trials were randomised, parallel groups studies. Altogether 4 trials were included in the final analysis. In 75% of the studies the follow-up period was 6 months. When the results of these studies were combined in a meta-analysis, the overall OR was 2.5 (95% CI 1.8 to 3.6).  
There were 4 studies comparing OTC NRT to Rx NRT. The OR's varied between the studies from 0.3-3.6 (OR <1 indicating OTC NRT not efficient). In the meta-analysis the final, combined OR was 1.4 (95% CI 0.6 to 3.3)  
The absolute quit rate, including all the studies with 6 months follow-up was 7% (CI 95% 4% to 11%)  
In some OTC trials the participants visited the study centre at various times. In each placebo versus NRT trial, participants received OTC-NRT free of charge.  
Based on their findings the authors concluded, that OTC NRT and prescription NRT yielded similar quit rates.  
The authors recommended that the requirement of simultaneous counseling related to NRT, demanded in many SC programs, should be relaxed. | | YES |
| Hughes et al. 2011:  
To review non-randomized tests to assess effectiveness of OTC NRT  
Most included studies were conducted in the US.  
Literature review including retrospective cohort studies comparing NRT users and non-users and studies comparing quit rates before and after OTC switch.  
Studies were included if they reported abstinence rates and were assessing effectiveness, not efficacy.  
The authors were able to detect 11 retrospective cohort studies, including 14 comparisons of the quit rates of OTC NRT users versus non-users and comparing effectiveness of OTC-NRT and Rx- NRT including counseling  
The authors included studies, which either were retrospective, population-based cohort studies (n=4, all conducted in the US), retrospective cohort convenience samples (n=3, conducted in the US, Canada and UK) or retrospective cohort treatment studies (n=3, all conducted in the US).  
The results of the studies are summarized by four methods for each study type. Retrospective studies:  
- Experimental replication: the authors calculated quit rates for NRT and non-NRT users: NRT use was beneficial  
- Proportion of studies, finding statistically significant evidence supporting NRT use compared to not use: NRT use was more beneficial  
- Assessment of the most internally and externally rigorous study and its results: NRT was not effective  
- Specificity: instances which OTC NRT use did not increase quit rates but other effective methods did: NRT was effective  
- Compliance to OTC NRT was weak. The authors located seven pre- and post OTC NRT- studies: Three used a retrospective population-based sample and four a convenience sample.  
- Experimental replication: NRT use was more beneficial than non-use  
- Fraction of studies: only in 1 out of the 4 studies found NRT use more beneficial  
- Assessment of the most rigorous study: NRT was not effective  
- Specificity: could not be tested  
The included studies were far too heterogeneous for meta-analysis.  
OTC NRT appeared to be less effective in retrospective studies.  
Based on the mixed results it is impossible to draw any further conclusions on the effectiveness of OTC NRT.  
The authors highlight the need for a further, high-quality retrospective, population based study. | | UNCLEAR |
<table>
<thead>
<tr>
<th>Reference, objective and setting</th>
<th>Study design/ key characteristics</th>
<th>Participants / How abstinence is defined</th>
<th>Key Findings related to the effectiveness of OTC NRT</th>
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<tr>
<td>Kotz et al. 2014; Smoking ToolKit Study</td>
<td>Nationally representative survey conducted among those over 16 years by face-to-face with computer-assisted methods every month. This study included aggregated data from November 2006 to May 2012. England is the country with the highest rate of SC medicines use, as these are reimbursed under the national health insurance. NRT is available both by prescription (reimbursed) or OTC in general sales. The aids have been available over 10 years.</td>
<td>Study population: Those respondents, who either were smoking at the time of survey or had smoked for at least 12 months before the survey and had made at least one quit attempt in the proceeding 12 months before the survey but had quit. Self-reported abstinence was key outcome. There is evidence that self-reported abstinence is a reliable measurement in survey setting. Data for the most recent quit attempt was assessed.</td>
<td>Study population (n = 10 335) consisted of 8 932 smokers and 1403 quitters. Half of the study population (51.3%) had not used any pharmacotherapy, a third had used OTC-NRT, 16.5% had received prescription and brief counseling, and 2% had received medication by prescription and specialist counseling. Of the prescription medication users, the majority had used NRT by prescription. According to the final analysis the OR's for quitting were for whole study population: among those respondents who had received medication by prescription and specialist counseling the 3.25 (95% CI [2.05-5.15]); prescription and brief counseling OR: 1.61 (95% CI[1.33-1.94]); NRT-OTC OR: 0.96 (95% CI[0.86-1.31] compared to no use of pharmacotherapy. There existed no sources of recall bias related to use of OTC-NRT.</td>
<td>The key outcome was adjusted to main potential confounders, which were assessed beforehand. Of these the most important was the level of tobacco dependence, which was assessed by urges to smoke. Also demographics and number of quit attempts proceeding the most recent one and time when the most recent quit attempt was initiated were taken into account. These possible confounders were included in the final regression analysis as interaction terms. Also possible recall bias was taken into account in the final analysis. The study did not assess level of medication adherence.</td>
<td>NO These findings question the effectiveness of OTC NRT among English smokers.</td>
</tr>
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</table>
### Prospective cohort studies

#### Kasza et al. 2013:

**Objective and Setting**
- **International Tobacco Control Four Country Survey, ICT**
- Evaluate the population effectiveness of SC medications and accounting for potential recall bias by controlling the recency of the quit attempt.
- Four country survey study: the UK, Canada, Australia and the US.

**Study Design/Key Characteristics**
- Since the 2002 representative samples of smokers from all four countries are interviewed by the random-digit-dialing technique.
- Earlier analysis of this survey has proven these samples representative and that non-response is not a source of systematic bias in this study.
- This study includes data collected between 2002-2009 (eight first survey waves).
- Analysis was restricted to those participants, who participated in at least two consecutive waves and had made their last quit attempt between two survey waves. (n= 7436)
- Survey participants were re-contacted approximately annually to complete the follow-up. Those lost-to-follow-up are replaced by new participants.
- **Abstinence:** Self-reported continues abstinence, 1 months/6 months was assessed in the follow-up interview by different questions.

**Key Findings related to the effectiveness of OTC NRT**
- Based on logistic regression analysis, use of NRT patch, (like varenicline and bupropion as well) was significantly associated with obtaining one month (OR's 1.19- 2.35) and six month (OR 1.15- 4.09) abstinence compared with no medication use.
- Among those, who had been abstinent for one month or six months at the time of the survey this association was most robust, indicating that recall bias may explain to some extent the poor real life effectiveness reported in the literature.
- The evidence of real life effectiveness was not found for oral NRT products.
- As the investigators tightened the control over recall bias, the beneficial effects of medication use increased.

**Strengths of this study** were broad representative sample, large sample size, balance of recall bias, cohort design, repeated longitudinal analysis and adjustment of potential confounders.

#### Alpert et al. 2012:

**Objective**
- To examine the population effectiveness of NRT, with or without professional counselling
- The US, Massachusetts

**Study Design/Key Characteristics**
- Prospective cohort study with a probability sample was conducted by re-interviewing the respondents in three waves.
- Between January 2001 and June 2002 professional telephone interviewers at the Center for Survey Research, University of Massachusetts Boston obtained a probability sample of 6739 Massachusetts adults with oversampling of adult smokers and recent quitters (during past 2 years). At first wave finally eligible responses were received from 46% (n= 4991) of the original sample.
- The analytic sample finally consisted of 787 adult smokers, who had quit during last 2 years prior the first wave. Of these 480 completed the second wave and of these two thirds (n=248) completed the third wave.
- Among the participant A total of 364 completing the second wave had completely quit, but almost one third had relapsed by the time of the second wave and a third of those completing the third wave interview had relapsed.
- Self-reported and recalled abstinence

**Key Findings related to the effectiveness of OTC NRT**
- About one in five of the participants at waves 1&2 had used NRT.
- Though only 7.5% had used it for more than 6 weeks at wave 1 and 13.3% at wave 2.
- The odds for smoking relapse was highest (OR 2.68) for high-dependent smokers, who reported use of NRT for any length without professional advice.
- The odds for relapse were lowest among persons who reported abstinence > 6 months

**Strengths of this study** were broad representative sample, large sample size, balance of recall bias, cohort design, repeated longitudinal analysis and adjustment of potential confounders.

**To notice (key points in discussion, limitations and strengths of the study)**
- The authors discussed selection criteria in trials and the generalizability of the findings from trials to real-life.
- The authors also concluded that those heavily dependent smokers using NRT without support may have unrealistic expectations for the therapy and thus they relapse.
- The authors discussed the loss to follow-up during the four years follow-up period to be the most important possibility of bias
- To note! This study and especially conclusion made has been debated among the scientific community.
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<tr>
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<td><strong>Prospective cohort studies</strong></td>
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<td>Balmford et al. 2011:</td>
<td>The four country cohort survey</td>
<td>The survey included only current, adult smokers. The data of smokers was collected only from one wave, either 5 or 6 in relation to their medication use during last year. Only information on the use of one medication, either NRT or Rx medication was included into the final sample. Abstinence: 6 months abstinence, self reported</td>
<td>A majority (n=981) had used NRT, either OTC (n=670) or by Rx (n=311). In the UK the majority obtained NRT by Rx. A third (30.9%, n=345) used medication at least for 8 weeks and 63.4% (n=773) stopped the use prematurely. 101 persons (5.7%) continued the use beyond 8 weeks. 23% of those who purchased OTC NRT had discontinued use in the first week. A minority, 5.5% used the medication beyond 6 months. Among OTC NRT purchasers there were significantly more premature discontinuations and early relapses than among those who purchased NRT by prescription. There were no differences achieving 6 months abstinence between OTC and prescription NRT users. Of the 1020 included smokers, 548 persons SC outcomes were able to be detected after 6 months. Of these 22.6% achieved six months abstinence. This was more common among prescription medication than NRT users.</td>
<td>The authors discuss that only a quarter of SC medication users are likely to complete the recommended 8 weeks treatment course. Main reason was relapse back smoking. This was especially in the case of NRT users and those with higher dependence. Likelihood of success was increased by duration of the medication use. Though, those who discontinued the treatment because they did not need it any longer a significant proportion was abstinent in six months follow-up. Over two thirds of those who believed the medication had worked and thus discontinued were abstinent in six months follow-up.</td>
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<td>Four Countries</td>
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<td>The UK, US, Canada and Australia</td>
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<td>West and Zhou 2007:</td>
<td>Prospective, longitudinal cohort study</td>
<td>Internet users between 35-65 years, smoking ≥5 cigarettes a day. Only participants with a quit attempt, were used in the analysis (phase 1, n=1578; phase 2, n=983). Self-reported abstinence, assessed at 3 months and 6 months periods. Only continues abstinence throughout the whole 3 months in both follow-up periods was accepted. Participants were asked to list methods they used in their quitting attempt Those, who had received behavioral support or used bupropion, were excluded from the analysis.</td>
<td>A total of 357 participants from phase 1 and 732 from phase 2 were followed the six months period. Of these participants 127 from phase 1 used NRT and 230 did not. 217 from phase 2 used NRT and 535 did not. According to logistic regression analysis conducted NRT use was associated with significant likelihood of achieving six months abstinence compared to non-use. Among Phase 1 participants OR was 3.0 (CI 95% 1.2-7.5), among phase 2 participants OR was 2.1 (CI 95% 1.0-4.1) and combined OR was 2.2 (CI 95% 1.3-3.9). The results were controlled for nicotine dependence.</td>
<td>The finding supporting OTC-NRT effectiveness was replicated in the both separate cohort samples and study participants were frequently followed. Loss to follow-up was considered problematic and the samples were recruited from the internet and the sample consisted of persons intending to quit during the following three months of their enrolment.</td>
<td>YES</td>
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</table>
### Prospective cohort studies

<table>
<thead>
<tr>
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<td>Hyland et al. 2004a: National Cancer Institute’s evaluation of the Community Intervention Trial for SC (COMMIT), The US</td>
<td>Randomized community-based cessation study. The original cohort was identified by a random-digit-dialed telephone survey in 1988 and this original sample of smokers has been followed annually. (loss of follow-up each year 8%).</td>
<td>In 1993 altogether 12,435 smokers were interviewed and 5,778 (35%) were completely re-interviewed in 2001. Of these 15,979 were NRT users. There were 519 pre-OTC NRT users and 878 post-OTC users in the analysis. There were no great differences between the socio-economic or smoking characteristics of these groups with the exception of desire to quit. Self-reported abstinence following each NRT assisted quit attempt or long-term cessation among NRT users. Six months abstinence.</td>
<td>Use of NRT patch decreased from 22.5% in the pre-OTC period to 18.3% in the post-OTC period. After OTC switch the duration of patch use decreased.</td>
<td>Only few smokers used NRT in any quit attempt. Advantages of this study were large sample size, duration of NRT use assessed and geographic diversity.</td>
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</table>

### Population-based cross-sectional surveys

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<tr>
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<th>To notice (key points in discussion, limitations and strengths of the study)</th>
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<tr>
<td>Gilpin et al. 2006: California Tobacco Surveys</td>
<td>Population-based cross-sectional, surveys in 1999 (n=14,739 / 21,657, 68.4% completed) and in 2002 (20,525/ 32,654, 62.8% completed). The surveys were combined to provide adequate statistical power to investigate factors supporting increase in abstinence duration.</td>
<td>Participants: moderate to heavy dependent, adult smokers, consuming at least 15 cigarettes a day prior to the survey. In 1999 there were 3,367 and in 2002 altogether 3,096 recent quitters. Participants were randomly selected for an external interview. Abstinence: Self-reported</td>
<td>Use of NRT or bupropion was more common among moderate to heavy smokers than among light non-daily smokers. There appeared to be a slight short-term benefit from pharmaceutical aid use, which disappeared rapidly over time from the cessation, when followed for up to 180 days.</td>
<td>The authors concluded that after the NRT deregulation the messages regarding cessation had changed and led to less motivated and less prepared smokers to make a quit attempt.</td>
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<td>Pierce and Gilpin 2002: California Tobacco Surveys, CTS conducted in 1992, 1996, and 1999.</td>
<td>The large population-based California Tobacco Surveys, CTS conducted in 1992, 1996, and 1999. A random-digit-dialed telephone interview method was used. Completed interviews were received from 71.3% of adults (n=5,427) in 1992; 72.9% (n=5,973) in 1996 and 68.4% (n=6,412) in 1999. CTS are weighted to make the data representative of the California population and to account for the oversampling of smokers. Population: Recent former smokers (12 months ago but not currently) undergoing SC</td>
<td>Use of pharmaceutical aids (mostly OTC since 1996), and cessation success were also assessed. Between 1992 and 1999, SC attempts among California smokers increased 61.4% (from 38.1% to 61.5%). NRT use in the most recent SC attempt increased significantly (50.5%) from 9.3% in 1992 to 12.7% in 1996, and to 14.0% in 1999. An estimated 3.6-fold growth in NRT use took place between 1992-1999. There was an 85% increase in the proportion of quitters using pharmaceutical aid from 1992 to 1999 among the California quitters for their most recent SC attempt. In 1996 and 1999, the median duration of aid use was only 14 days. To assess quitting success and use of NRT the study utilized regression model. According to its results in contrast with 1992 and 1996, the beneficial effect of NRT use for SC in 1999 was only short-term; after about 3 months the success for NRT users and non-NRT users the rates were similar.</td>
<td>The survey assessed local SC practises, which can also be influenced by other social, environmental or political tendencies. Differences in participant selection criteria can explain why different survey studies have different findings.</td>
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The cessation and abstinence observations are based on self-reported recall of cessation events from a cross-sectional survey not from a longitudinal follow-up of individuals who quitted.
<table>
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<tr>
<th>Reference, objective and setting</th>
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<tr>
<td>Reed et al. 2005:</td>
<td>See description above of Californian Tobacco Survey. The quit attempts were calculated for each month. The attempts were divided according to the use of NRT. The results are based on the regression models of the survey data.</td>
<td>Study population was drawn from the 1996 Californian Tobacco Survey. The analysis concentrated on current and former smokers, aged &gt;25, who reported being a daily smoker 12 months prior to the survey (n=888). Abstinence: Self-reported abstinence (response not at all smoking at the time of survey). Most recent abstinence, lasting at least one month.</td>
<td>8.77 ± 0.96% were abstinent at the time of the survey. This translates into 24.8% of those who reported an attempt to quit being abstinent for months. Results from the regression analysis conducted showed a significant increase in the proportion of smokers using the patch (p &lt; 0.01) and gum (p &lt; 0.05) immediately following their OTC availability. There was also a significantly higher proportion of smokers reporting abstinence with gum use (p &lt; 0.01) and a significant increase in reported abstinence with patch use (p &lt; 0.05) following OTC availability.</td>
<td>The study used cohort data, but its findings were based on future estimations of NRT use.</td>
<td>NO</td>
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<td>Thomdike et al. 2002:</td>
<td>The analysis compared data collected by two comparable surveys: In the pre-deregulation Pre-NRT deregulation period data was collected from the Massachusetts Tobacco Survey (from October 1993 through February 1994, n=1764) by a random-digit-dialed telephone survey. In the post- NRT deregulation NRT period data was collected from the Massachusetts Adult Tobacco random-digit-dialed Survey (from August 1997 to June 1999, n=1420). The sample was limited to those participants, who made a quit attempt after the deregulation (i.e., after July 1996).</td>
<td>Participants: Survey respondents who made at least 1 quit attempt in the past year including those that were unsuccessful (i.e., who were smokers at the time of the survey) and quitters (a person, who reports having smoked at least 100 cigarettes in his/her lifetime and currently smokes &quot;not at all.&quot;). The analysis was limited to respondents either who smoked at the time of the interview or who had quit within the past year (past-year quitters). Abstinence: Self-reported, at least one day abstinence. Past-year quitter was defined self-reported quitting during the past year.</td>
<td>Overall, the rate of successful quitting increased from 17.1% pre-OTC to 24.7% post-OTC, though not statistically significant (P=0.10). Successful quitting increased among NRT users from 18.7% to 31.1% (P=0.28) and among non-NRT users from 16.7% to 23.0% (P=0.22). The increase in quit rates between the pre and the post-OTC-NRT periods was higher for NRT users than non-users (12.4% vs 6.3%), though not statistically significant. Almost half of smokers made quit attempt before and after NRT deregulation and this pattern had not changed. After NRT deregulation the use increased among higher income households and decreased among lower income households.</td>
<td>A subgroup of current smokers were interviewed during the post-OTC period (n=512). In this sample, 28.1% of the current smokers had never used NRT.</td>
<td>NO</td>
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<td>Shiffman et al. 1997:</td>
<td>Sales and marketing data were used to compare use of NRT before and after the deregulation and to estimate the effects of OTC sales on quit rates. This electronic database gathers daily data of prescriptions filled in pharmacies and it represents well the actual situation.</td>
<td>Pre-deregulation data was received from the Walsh America database provided in the Scott-Levin Source Prescription Audit database, to gain representative data on prescription medicines use. Data of the calendar year 1995 was used. Post-OTC data was received from AC Nielsen, collecting electronic data from purchases in merchandisers and balances the existence of outlets not collecting the electronic data. AC Nielsen also gathers data from a representative panel of 40,000 households, which scan their purchases. Data was used during the period March – May 1997.</td>
<td>In 1995 the authors estimated there to be 2.5 million quit attempts with the use of Rx NRT. In the OTC period, based on the estimation, there were 5.8 million quit attempts with OTC NRT in 1997. In addition to this 900,000 new NRT prescriptions were prescribed in 1997. The authors conservatively estimated that there were between 114,000 - 304,000 incremental quit attempts attributed to OTC NRT. This means those quit attempts, which would not have occurred without OTC NRT. The authors estimated that OTC NRT may have increased SC in American population by 10 - 29%.</td>
<td>The authors concluded that OTC NRT has shown a great public health benefit. The results are based on estimates of sales data and extrapolations of this data on quit rates.</td>
<td>YES</td>
</tr>
<tr>
<td>Reference, objective and setting</td>
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<td>Participants / How abstinence is defined</td>
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<td>Open-label RCT with Simulated OTC environment</td>
<td>Separate open-label studies in OTC and Rx environment. OTC environment was simulated so, that the participants choose themselves the NRT product they used. The NRT s were provided with product labels with product information, dosage, usage instructions and contraindications in a pharmacy of in a food store. Participants paid themselves for the products. They were given written product label and directions and audiotape with quitting tips but no other guidance. They visited the study centre for outcomes assessment, in which their smoking status was assessed, they reported their product use and adverse effects. If participants did not appear to follow-up visit, they were contacted and invited.</td>
<td>All participants were smokers. They received active nicotine replacement. OTC gum n=2981, OTC patch 2367, Rx gum n=324, Rx patch n=669. No intervention was provided in OTC setting but physicians prescribed the Rx medications. OTC participants were recruited by advertisement and Rx participants by their prescription records of pharmacy chain. Only participants who were prescribed new NRT Rx were included. They were sent an invitation letter and those who decided to participate were interviewed at the pharmacy. Abstinence: Biochemically validated abstinence at 6 weeks and 6 months. Only those participants who were abstinent at the 6 weeks (end of treatment) were asked to consent to a follow-up of 6 months.</td>
<td>Separate analysis for the OTC and Rx participants were conducted and results were compared. The OTC patch users received abstinence rate 19.0% at 6 weeks and 9.2% at 6 months. The Rx patch users’ abstinence rate was 16.0% at 6 weeks and 3% at 6 months. The OTC gum users received abstinence rate 16.1% at 6 weeks and 8.4% at 6 months. The Rx gum users’ abstinence rate was 7.7% at 6 weeks and 7.7% at 6 months. The outcomes were adjusted for individual differences among study participants and after this adjustment, OTC NRT was found to be more beneficial. Based on study participants’ interviews the authors discussed that the more beneficial effects of OTC NRT were explained by the lack of physician instruction and guidance of prescription NRT users. Conversely, the audiotape and use instructions given to OTC participants may have given stronger instructions than the physicians’ actions.</td>
<td>Participants who did not complete CO monitoring were considered smokers. All participants were included in the analysis as intent-to-treat approach was used and non-respondents were considered smokers. Due to the multiple ways to gathering information, there are potential sources of bias in terms of recruiting Rx participants. In addition, OTC participants were recruited, not gained in natural buying of NRT as the products were not sold as OTC at the time of the study.</td>
<td>YES</td>
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<td>Shiffman et al. 2002a: To assess SC rates achieved by NRT gum and patch in simulated OTC and actual prescription environment (Rx)</td>
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Appendix 3:
Theoretical framework of the study, its operationalization and key outcome indicators (variables/indicators) utilized in the sub-studies (I-IV).

<table>
<thead>
<tr>
<th>Study</th>
<th>Theoretical framework</th>
<th>Key operationalized concepts</th>
<th>Measured indicators</th>
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<tbody>
<tr>
<td>I</td>
<td>Evidence-informed policy-making (Dobrow et al. 2004, Oxman et al. 2009) was the theoretical and conceptual background.</td>
<td>This qualitative study was inductive in its nature, therefore there are no concepts to directly operationalize. However concepts such as the use of evidence, structures and rules of political decision making, adopted from the theoretical framework were used to guide the inductive analysis.</td>
<td>The arguments related to NRT deregulation were analyzed. The unit of analysis was set as a policy argument, which was defined as an oral or written statement that advocates the adoption of a policy or justifies a decision to adopt a policy (Ball 1995). Using this unit of analysis made it possible to gain a perspective of the key attributes of the decision-making context in a wider scope.</td>
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<td>II</td>
<td>Literature on Guideline implementation among healthcare professionals and systematic meta-review of Francke et al. (2008).</td>
<td>According to Francke (2008) the familiarity with a guideline is the first step in guideline implementation. The key operationalized concepts were related to the characteristics of pharmacists’ guideline dissemination and the characteristics of the working place. SC activities provided by pharmacists were based on the Finnish SC Guidelines and recommendations given by AFP, which were measured by pharmacists’ self-reporting.</td>
<td>This was operationalized in the key outcome variable, which assessed the familiarity with the Finnish SC Guideline (Appendix 4 Survey instrument, question number 39). The key variables were classified into those which related to the pharmacist and those relating to the working pharmacy. The variables measuring community pharmacists’ involvement in SC were the variables, which assessed community pharmacists’ self-perception of the following key Finnish SC Guideline based activities and the more sophisticated ones according to the strategy of the AFP (see Appendix 4, Survey instrument questions number 16-18,23-30).</td>
</tr>
<tr>
<td>III</td>
<td>Literature on NRT usage patterns (see Chapter 6, Table 6). Ideology of harm reduction (see Chapter 3.7) Political debate related to NRT deregulation, which was analysed in detail in study I.</td>
<td>These were conceptualized as NRT use patterns most commonly reported in the literature. Professional role, competition with food stores, experience of customer service with smoking customers.</td>
<td>Set of Likert-scale statements concerning pharmacists’ perceptions on most common NRT use patterns (Appendix 4, Survey instrument, Statements 34). Set of Likert-scale statements concerning the influence of deregulation on pharmacy owners’ and staff pharmacists’ motivation to serve and counsel customers purchasing NRT products (Appendix 4, Survey instrument, Statements 34).</td>
</tr>
<tr>
<td>IV</td>
<td>The literature on: NRT usage patterns (Table 6), internet communities and facilities supporting participants’ empowerment and self-management (Van Uden-Kraan et al. 2008, Armstrong et al. 2009) were used as background. The theories of empowerment and self-management (Routasalo et al. 2009) were guiding the analysis to help to understand the participants’ needs for permanent lifestyle change.</td>
<td>This qualitative study was inductive in its nature, therefore there are no concepts to directly operationalize. However concepts such as perception of medication, experience, peer support and empowerment were guiding the analysis.</td>
<td>Unit of analysis was one or more sentences dealing with opinions, perceptions, experiences or expectations related to NRT use or comparing NRT to other SC methods (prescription medicines or non-pharmaceutical methods, including cold turkey).</td>
</tr>
</tbody>
</table>
Appendix 4:
The questions utilized in sub-studies II & III from the original PHARMACIST AND TOBACCO 2006-2007 - survey instrument (in English).

BACKGROUND INFORMATION

1. Current working place
   1 Community pharmacy
   2 Hospital
   3 Pharmaceutical company
   4 Elsewhere, where?

2. Are you
   1 B.Sc. Pharmacist
   2 M.Sc. Pharmacist
   3 Pharmacy owner

3. Geographical location by province of your working pharmacy?
   1 Southern Finland
   2 Eastern Finland
   3 Western Finland
   4 Oulu
   5 Lapland
   6 Åhvenanmaa

4. Where you have worked most of time as pharmacist?
   1 Community pharmacy
   2 Hospital pharmacy
   3 Pharmaceutical company
   4 Elsewhere, where

5. Are you?
   1 Female
   2 Male

6. Your age? __________ years

7. What is your most previous degree in pharmaceutical science?
   1 B.Sc. Pharmacist
   2 M.Sc. Pharmacist
   3 Licenciate or Ph.D.

8. Place of this degree?
   1 University of Helsinki
   2 University of Kuopio
   3 Åbo Akademi

9. Graduation date?
   1 In the 2000’s
   2 In the 1990’s
   3 In the 1980’s
   4 In the 1970’s or before

10. Have you participated in education supporting smoking cessation counselling?
    TO NOTE: It is possible to choose several options.
    1 Yes, in-house training
    2 Yes, continuing education
    3 Yes, in-house training by a pharmaceutical company
    4 Yes, continuing education by a pharmaceutical company
    5 Not participated

11. Have you specialized in the treatment of public health conditions at your working place?
    TO NOTE: It is possible to choose several options.
    1 Yes, asthma
    2 Yes, diabetes
    3 Yes, cardiovascular diseases
    4 Yes, other, what
    5 No

12. Dispensing counter design of your workplace
    1 Traditional counter
    2 Sit-down counseling station
    3 Both in use

13. Is your workplace
    1 Privately owned, not belonging to a pharmacy chain
    2 Privately owned, belongs to a pharmacy chain
    3 University owned

14. What was the annual prescription volume of your workplace in 2005?
    1 Less than 20 000
    2 20 001–40 000
    3 40 001–60 000
    4 60 001–80 000
    5 80 001–100 000
    6 More than 100 000
SITUATIONS AT CUSTOMER SERVICE

15. How often you discuss about smoking with the following customers?

<table>
<thead>
<tr>
<th>Customer who buy smoking cessation medicines</th>
<th>Always</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Customer who suffers from smoking-related disease</th>
<th>Always</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Customer who self-refers to his/her smoking</th>
<th>Always</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Customer who smokes and is pregnant</th>
<th>Always</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

16. Which tools do you recommend to your customers to use in smoking cessation?

TO NOTE: It is possible to choose several options.

1. Nicotine patch (Nicorette®, Nicotinell®)
2. Nicotine gum (Nicorette®, Nicotinell®)
3. Nicotine inhaler (Nicorette®)
4. Nicotine losange (Nicorette®)
5. Bupropion (Zyban®)
6. Other pharmacotherapy, what? _______________
7. Advice to see public health nurse
8. Pharmacy’s own individually tailored smoking cessation service
9. Group therapy
10. Internet-based smoking cessation support
11. Telephone-based smoking cessation support
12. Participation in “Quit and Win” competition
13. Support of family or friends
14. Written SC support material
15. Support of own quitting decision

17. Are there local smoking cessation groups organized by the health care of your area?

TO NOTE: It is possible to choose several options.

1. Yes, we have organized a cessation group in my working place
2. Yes, I have guided customers to a cessation group
3. Yes, but I have not guided customers to a cessation group
4. No, there is no group
5. I do not know

18. Has your working place participated in local multidisciplinary SC actions?

TO NOTE: It is possible to choose several options.

1. Yes, we have participated in joint training
2. Yes, we have considered joint practices
3. Yes, we have joint practices
4. No, we do not have any collaboration
23. Following statements describe customer service situations. Please, choose the most suitable number in each

<table>
<thead>
<tr>
<th>How often have you asked about smoking during the past week (7 days) from smoking customers?</th>
<th>Always</th>
<th>Often</th>
<th>With every second customer</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How often you have advised customers you recognized to smoke, to quit during the past month prior survey?</th>
<th>Always</th>
<th>Often</th>
<th>With every second customer</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How often you have assessed quitting date with your smoking customers during the past month prior survey?</th>
<th>Always</th>
<th>Often</th>
<th>With every second customer</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How often you have told to smoking customers about how smoking effects on medication during the past month prior survey?</th>
<th>Always</th>
<th>Often</th>
<th>With every second customer</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

24. Have you organized an individually tailored smoking cessation service at your work place?
   1. Yes
   2. No (if no, continue from question 29)

25. Have you advertised your individually tailored smoking cessation service?
   1. Yes, to customers, how?
   2. Yes, to other health care, how?
   3. No

26. Have you yourself guided an individually tailored smoking cessation service during the past year?
   1. Yes
   2. No

27. Have you had any customers in your individually tailored smoking cessation service?
   1. Yes
   2. No

28. Do you use smoking pass supporting smoking cessation at your pharmacy?
   1. Yes, we use it always
   2. Yes, we use it sometimes
   3. No

29. Do you use pocket card supporting smoking cessation counseling at your pharmacy?
   1. Yes, we use it always
   2. Yes, we use it sometimes
   3. No
30. How the following statements related to smoking cessation apply to your customers:

<table>
<thead>
<tr>
<th></th>
<th>Always</th>
<th>Almost always</th>
<th>Seldom</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker willing to quit needs nicotine replacement therapy (Nicorette®, Nicotinell®) in quitting</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Smoker willing to quit needs prescription medicine for example bupropion (Zyban®) or varenicline (Champix®) for supporting quitting</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Group counseling suits well with smoking cessation treatment</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Health care professionals support is needed in smoking cessation</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

**PHARMACOTHERAPY SUPPORTING SMOKING CESSATION**

26. How you based your recommendation on the use of certain nicotine replacement therapy product (NRT)?
   1 By Fagerström test of nicotine dependence
   2 According to customers wishes
   3 Recommending a product, which I personally consider effective
   4 Other way, how ______________________________

27. Do you have an in-house guideline on NRT dispensing
   1 Yes, written guideline available
   2 Yes, oral guideline available
   3 No
34. Next, we ask you to answer the following statements related to nicotine replacement therapy products (NRT) based on your perceptions:

**TO NOTE:** Circle the option most suitable for your perceptions

<table>
<thead>
<tr>
<th>Education, skills and tasks</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>No opinion</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>My current personal skills and knowledge are adequate to support smoking cessation</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>It is a pharmacists’ duty to support smoking cessation</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>I would like additional education in supporting smoking cessation</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>NRT-products’ characteristics and use</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>No opinion</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is possible to get addicted to NRT products</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>I have noticed that minors have abused NRT products</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Mere NRT products are not enough for quitting</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>I have noticed that NRT products have been misused (use for too short a time or too low a dosage)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>I have noticed that NRT products have been used with the wrong technique (for instance chewing gum is chewed incorrectly)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>I have noticed that customers use cigarettes and NRT products concurrently</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>NRT products can be used to replace cigarettes when smoking is not allowed</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>NRT products can be used to diminish the adverse effects smoking causes on ones’ health</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Deregulation of NRT products to food stores, kiosks and gas stations</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>No opinion</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>The sales of NRT products have diminished in my working place</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Clients obtain medical counselling of NRT products from pharmacy but buy the products elsewhere</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Because of the deregulation of NRT products my motivation towards the medical counselling of NRT has diminished</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Clients value the counselling related to NRT products</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Because of the deregulation of NRT products, their role in smoking cessation has diminished</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>In my working place there has been devotion to education supporting SC counselling</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>The medical counselling of NRT is more important in the competition of their markets than the possible cheaper prices in other sales channels</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
CURRENT CARE GUIDELINE

Following questions are related “Tobacco Dependence and Cessation” Current Care Guideline. Please: Circle the option most well describing yourself

39. How familiar you are with the Current Care Guideline?
   1 I have read the Guideline through carefully
   2 I am familiar with its main principles
   3 I have skimmed through it
   4 I have heard about it
   5 I am not familiar with it

40. Use of the Current Care Guideline?
   1 I have participated in education related to the Guideline
   2 At my working place it has been encouraged to use the guideline
   3 I have used the Guideline
   4 I have used the Guideline during the last six months
   5 The Guideline has changed my daily practice with customers
   6 I have given the patients’ version of the Guideline to my customers
   7 I do not use the Guideline

41. Your opinion of the Current Care Guideline?
   TO NOTE: It is possible to choose several options.
   1 I have noticed the Guideline to be practical
   2 The Guideline has made my work faster
   3 The Guideline is difficult to use
   4 The Guideline is not suitable for daily practice in the pharmacy
   5 Other opinion

42. Your opinion, how the Current Care Guideline is followed at your working place?
   1 The Guideline is followed at my working place
   2 The Guideline is followed at my working place to some extent
   3 The Guideline is not followed at my working place
   4 No opinion

OWN SMOKING

43. Have you ever smoked at least 100 cigarettes (cigars or pipe) up to date?
   1 Yes
   2 No (continue to question number 52)

53. What is your perception of how harmful tobacco is to health?

<table>
<thead>
<tr>
<th></th>
<th>Not at all</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>How detrimental is smoking to health?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>How detrimental is cigarette smoke to health?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
</tr>
</tbody>
</table>