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Using primary care data to assess population-level estimates of maternal smoking and nicotine replacement therapy during pregnancy

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ABSTRACT

Background: Smoking in pregnancy is the most significant preventable cause of poor health outcomes for women and their babies and, therefore, is a major public health concern. In the UK there is a wide range of interventions and support for pregnant women who want to quit. One of these is nicotine replacement therapy (NRT) which has been widely available for retail purchase and prescribing to pregnant women since 2005. However, measures of NRT prescribing in pregnant women are scarce. These measures are vital to assess its usefulness in smoking cessation during pregnancy at a population level. Furthermore, evidence of NRT safety in pregnancy for the mother and child's health so far is nebulous, with existing studies being small or using retrospectively reported exposures.

Aims and Objectives: The main aim of this work was to assess population-level estimates of maternal smoking and NRT prescribing in pregnancy and the safety of NRT for both the mother and the child in the UK. Currently, the only population-level data on UK maternal smoking are from repeated cross-sectional surveys or routinely collected maternity data during pregnancy or at delivery. These obtain information at one point in time, and there are no population-level data on NRT use available. As a novel approach, therefore, this thesis used the routinely collected primary care data that are currently available for approximately 6% of the UK population and provide longitudinal/prospectively recorded information throughout pregnancy. The specific objectives for this thesis were:

- To assess the quality of smoking data recorded during pregnancy in primary care
- To quantify annual NRT prescribing trends in and around pregnancy and describe the characteristics of mothers prescribed NRT

- To assess the association between NRT and smoking exposure during pregnancy and major congenital anomalies (MCAs), stillbirth, low birth weight and mode of delivery

Methods: All women aged 15-49 years, with pregnancies ending in live or stillbirth, were identified from The Health Improvement Network (THIN) primary care database (2000-2009). Medical Read codes related to smoking status and Multilex smoking cessation drug prescription codes were used to extract data on women's smoking status and NRT prescriptions. The proportion of pregnancies with a smoking status record was calculated and logistic regression was used to assess how this varied by women's characteristics. Women were categorised as being smokers or non-smokers during pregnancy based on the recorded Read codes. Where smoking data were missing during pregnancy, smoking status recorded before pregnancy (up to 27 months before pregnancy, ever before pregnancy) was used as a proxy for smoking status during pregnancy. Annual smoking measures from THIN were then compared to other national datasets. Pregnancies ending in early fetal losses were not included for calculating smoking prevalence, as these outcomes can go unrecognised or can be the first recognised sign of pregnancy, making early ascertainment of all pregnancies uncomprehensive; this was also broadly in line with pregnancy ascertainment in the other national datasets. Prescribing prevalence of NRT and patterns of prescribing in terms of frequency, timing and different form of NRT were assessed. Logistic regression was used to assess women's likelihood of receiving NRT prescriptions by maternal characteristics. Absolute and relative risks (99% Confidence Interval (CI)) for four birth outcomes (MCAs, stillbirth, low birth weight and mode of delivery) were calculated for women prescribed NRT (defined as the NRT group) and women who continued to smoke during pregnancy (defined as smokers) compared to women who did not smoke during pregnancy (defined as non-smokers) with appropriate adjustments for potential

confounders. To assess MCAs and birth weight in relation to NRT and smoking a restricted cohort of children was used who had maternal-child linked records in THIN.

Results: There were 277,552 pregnancies in 215,703 women, of which 28% had a gestational smoking status record. In 2000, smoking status was recorded in 9% of pregnancies; 43% in 2009. Smoking estimates from THIN data did not completely agree with estimates from other sources. For example, in 2009 smoking prevalence was 12.9% in THIN, compared to 19.5% in Child Health Systems Programme (CHSP) data. However, the use of smoking data recorded up to 27 months before conception increased the THIN prevalence to 22.9%, which was slightly higher, but compared better with the CHSP estimates.

NRT was prescribed in 4,826 pregnancies for an average duration of 2 weeks (Interquartile range 1-2 weeks), which represented 2% of all pregnancies (11% in smokers). NRT prescribing prevalence before and after pregnancy was half the prevalence during pregnancy. NRT prescribing increased with socioeconomic deprivation (Odds Ratio (OR) =1.33, 95% CI 1.14-1.52) for the most compared to the least deprived group). Prescribing was higher in pregnant smokers with asthma (OR=1.34, 95% CI 1.21-1.50) and mental illness (OR=1.29, 95% CI 1.18-1.43) compared to smokers without these diagnoses.

The absolute risk of MCA was 279/10,000 live births. Compared with non-smokers the adjusted OR for MCA in the NRT group was 1.34 (99% CI 0.94-1.91). No statistically significant increase in the risk of MCA for the NRT group was found when the reference group was changed to smokers (OR=1.35, 99% CI 0.94-1.93).The absolute risk of stillbirth was 4/1000 live and stillbirths. Compared with non-smokers the adjusted OR for stillbirth in the NRT group was 1.19 (99% CI 0.47-3.01). In smokers, the risk of stillbirth increased by 27% compared to non-smokers (OR 1.27, 99% CI 1.01-1.60). The mean birth weight

was 3.41kg (standard deviation 0.59) and the absolute risk of low birth weight was 6.4%. Compared to non-smokers, the risk of women having low birth weight babies was 93% higher in the NRT group (OR 1.93, 99% CI 1.48-2.53). However, there was no statistically significant increase in the risk of low birth weight in the NRT group compared with smokers. There was no increased risk of assisted delivery or caesarean section in the NRT group compared to smokers. However the risk of assisted delivery decreased by 25% in the NRT group (Relative Risk Ratio 0.75, 99% CI 0.60-0.93) compared to non-smokers.

Conclusion: The completeness of smoking status recording during pregnancy in primary care data is improving; however, under-recording of smoking status during pregnancy still results in unreliable estimates of the prevalence of smoking in pregnancy and needs improvement. Pre-conception smoking records are reasonably complete and it is possible that low recording in pregnancy is because a woman's smoking status has not changed or that increased interaction with other health services, such as midwifery, during pregnancy means women are less likely to be asked about their smoking by their primary physician and information on their smoking does not get relayed back to their primary care record. Nevertheless records should be updated in pregnancy to ensure comprehensive health care. NRT was most commonly prescribed in pregnancy for about two weeks, which may not be adequate time for effective smoking cessation. Nevertheless, prescribing was higher during pregnancy compared to the nine months before and after pregnancy, which makes establishing its safety during pregnancy even more crucial. The safety studies in this thesis did not find NRT to be any more harmful than smoking during pregnancy if not beneficial. Considering that smoking in pregnancy remains one of the largest public health problems in the UK, improvements of antenatal and postnatal smoking in primary care may not only help identify women for

preventive measures earlier but would be invaluable for safety studies considering the outcomes are rare yet severe.

PUBLICATIONS AND CONFERENCE PRESENTATIONS

PUBLICATIONS FROM THESIS WORK

Dhalwani NN, Tata LJ, Coleman T, Fleming KM, Szatkowski L. Completeness of maternal smoking status recording during pregnancy in United Kingdom primary care data. *PLoS ONE*. 2013; 8(9):e72218.

Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Prescribing of nicotine replacement therapy in and around pregnancy: a population-based study using primary care data. *British Journal of General Practice.* 2014; 64(626): e554-e560

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Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Nicotine replacement therapy in pregnancy and major congenital anomalies in offspring.*Pediatrics* Revision in process

OTHER RELATED PUBLICATIONS

Hardy B, Szatkowski L, Tata LJ, Coleman T, Dhalwani NN. Smoking cessation advice recorded during pregnancy in United Kingdom primary care. *BMC Family Practice.* 2014; *15*(1), 21.

CONFERENCE PRESENTATIONS

Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Maternal smoking, nicotine replacement therapy in pregnancy and stillbirth: A population-based study using the United Kingdom primary care data. 20th IEA World Congress of Epidemiology, Alaska, USA, 17th-21st August (Oral presentation)

Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Maternal smoking, nicotine replacement therapy in pregnancy and congenital malformations in offspring: A population-based study using the United Kingdom primary care data. 20th IEA World Congress of Epidemiology, Alaska, USA, 17th-21st August (Oral presentation)

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comparison with other national datasources. European Congress of Epidemiology 2013, Aarhus, Denmark 11th-14th August 2013 (Poster presentation)

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LIST OF ABBREVIATIONS

AHD	Additional Health Data
AIS	Additional Information Services
BMI	Body Mass Index
BNF	British National Formulary
BP	Blood Pressure
CAs	Congenital Anomalies
CBT	Cognitive Behavioural Therapy
CDC	Center for Disease Control
CHSP-PS/CHSP	Child Health Systems Programme (Pre-school component)
CI	Confidence Interval
CNS	Central Nervous System
CO	Carbon monoxide
COPD	Chronic Obstructive Pulmonary Disease
CPRD	Clinical Practice Research Data link
CSD	Cegedim Strategic Data
DNBC	Danish National Birth Cohort
e-PACT	Electronic Prescribing Analysis and Cost Tool
EPIC	Epidemiology and Pharmacology Information Core
ePROs	electronic Patient-Reported Outcomes
EUROCAT	European Surveillance of Congenital Anomaly
FDC	Full Data Collection
GLF	General Lifestyle Survey
GP	General practitioner
GPRD	General Practice Research Database
HEA	Health Education Authority
HES	Hospital Episodes Statistics

HR	Hazard Ratio
HSE	Health Survey for England
ICD	International Classification of Diseases
IFS	Infant Feeding Survey
IHS	Integrated Household Survey
InPS	InPractice Systems
LRT	Likelihood Ratio Test
MHRA	Medicines and Healthcare products Regulatory Authority
MREC	Multi-centre Research Ethics Committee
MRI	Magnetic Resonance Imaging
NBDPS	National Birth Defects Prevention Study
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NICU	Neonatal Intensive Care Unit
NRT	Nicotine Replacement Therapy
ONS	Office for National Statistics
OR	Odds Ratio
OTC	Over the counter
PAH-SYMPACT	Pulmonary Artery Hypertension Symptoms and Impact
PASS	Power Analysis & Sample Size Software
PHR	Public Health Research Consortium
PPROM	Pre-term premature rupture of membranes
PRAMS	Pregnancy Risk Assessment Monitoring System
QOF	Quality and Outcomes Framework
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RR	Relative Risk/Risk Ratio
RRR	Relative Risk Ratio

SATOD	Smoking at the Time of Delivery
sd	Standard Deviation
SHS	Second hand smoke
SIDS	Sudden Infant Death Syndrome
SMR	Scottish Morbidity Record
SNAP	Smoking Nicotine and Pregnancy Trial
SSS	Stop Smoking Services
SSSP	Stop Smoking Services for Pregnant women
STS	Smoking Toolkit Study
THIN	The Health Improvement Network
TIA	Transient Ischaemic Attack
UK	United Kingdom
USA	United States of America
VAMP	Value Added Medical Products
WHO	World Health Organisation

1 INTRODUCTION

1.1 HEALTH EFFECTS

Smoking in pregnancy is the most significant preventable cause of poor health outcomes for women and their babies.[1,2] Approximately one-third of all perinatal deaths in the United Kingdom (UK) are attributable to smoking.[3] In the United States of America (USA) maternal smoking in pregnancy increases infant mortality by 40% and approximately 5% of infant deaths in the USA have been attributable to maternal smoking.[4] It not only affects perinatal outcomes adversely but has also been related to problems in later childhood as discussed below.

1.1.1 Obstetric and perinatal complications

Maternal smoking during pregnancy causes a myriad of obstetric and perinatal complications. Some of the most important complications are discussed below.

1.1.1.1 Placental complications

Smoking during pregnancy reduces blood flow to the uteroplacental fetal unit and results in higher frequency of placental abruption.[5] Additionally, it has been linked to placental enlargements and increased placental weight consequently increasing the risk of placenta previa.[6] A meta-analysis of 13 published studies presented a pooled odds ratio (OR) of 1.90 (95% Confidence Interval (CI) 1.8-2.0) for placental abruption associated with maternal smoking.[7] Furthermore, data from the Swedish Medical Birth Registry including about 2 million births reported 53% greater risk of placenta previa in smokers compared to non-smokers in a dose-dependent manner.[8] Cigarette smoking during pregnancy is

also an independent risk factor for pre-term premature rupture of membranes (PPROM)[9] with a 70% increase in the risk (OR 1.70, 95% CI 1.18-2.25).[10]

1.1.1.2 Low birth weight

In developed countries, maternal smoking is one of the major risk factors for low birth weight (a birth weight of less than 2500g[11]).[12] A proposed mechanism behind this is the reduced uterine blood flow and fetal hypoxia caused by smoking.[13,14] A study including 5,166 live births occurring in Pelotas, Brazil found an increased risk of low birth weight associated with maternal smoking during pregnancy (OR 1.45, 95% CI 1.30-1.95).[15] A case-control study from Boston based on 207 cases of low birth weight and 534 controls found the risk of having low birth weight babies to be twice as high in smokers compared to non-smokers (OR 2.1, 95% CI 1.2-3.7).[16] Similar effect estimates were found in another study based on 6,284 singleton live births in Switzerland.[17] Another cohort study from the UK using the Millenium Cohort data found similar risk of low birth weight associated with maternal smoking during pregnancy (OR 1.92, 95% CI 1.60-2.29)[18] More recent data from Johannesburg and Soweto report that the birth weight of infants with smoking mothers was 165g less than of infants with non-smoking mothers.[19] Even more recent data from Sweden suggest a dose response relationship between maternal smoking and low birth weight such that for light smokers (1-9 cigarettes per day) the birth weight of infants reduced by 162g and for heavy smokers (> 9 cigarettes per day) birth weight reduced by 226g compared to non-smokers.[20]

1.1.1.3 Preterm birth

In the 2010 report on global, regional and national causes of child mortality 35% of neonatal deaths were attributable to preterm birth,[21] making it one of the most important contributors to infant deaths worldwide.[22] Cigarette smoking during pregnancy is one of the few modifiable risk factors for preterm birth.[23] A

systematic review of 20 prospective studies on maternal cigarette smoking and preterm birth reported 27% increased risk of preterm birth associated with gestational cigarette smoking.[24] A more recent case-control study from Italy based on 299 cases of preterm birth found that the adjusted ORs were 1.54 and 1.69 for preterm babies and 1.90 and 2.46 for early preterm babies for 1–10 and more than 10 cigarettes/day respectively.[25] Another case-control study from 10 European countries found that the odds of preterm birth increased by 40% in smoking mothers (OR 1.39, 95% CI 1.20-1.60).[26]

1.1.1.4 Ectopic pregnancy

Ectopic pregnancy results when the fertilised egg is implanted outside the uterus.[10] A meta-analysis of nine studies assessing adverse pregnancy outcomes in relation to maternal smoking reported a pooled OR of 1.77 (95% CI 1.31-1.22) for ectopic pregnancy among smokers.[10] A more recent case-control study from France including 803 cases of ectopic pregnancy and 1,633 deliveries found a dose response relationship with quadrupling risk in women smoking ≥20 cigarettes per day compared to non-smokers.[27]

1.1.1.5 Birth defects/ congenital anomalies

Literature suggests an association between maternal smoking in pregnancy and several major congenital anomalies (MCAs). A systematic review based on 173,687 congenital anomaly cases and 11.7 million controls demonstrated an increased risk of heart defects (OR 1.09, 95% CI 1.02-1.17), musculoskeletal defects (OR 1.16, 95% CI 1.05-1.27), limb defects (OR 1.26, 95% CI 1.03-1.73), orofacial clefts (OR 1.28, 95% CI 1.20-1.36), gastrointestinal defects (OR 1.27, 95% CI 1.18-1.36) and other defects associated with maternal smoking but no increase in the risk of all major anomalies combined (OR 1.01, 95% CI 0.96-1.07).[28]

1.1.1.6 Stillbirth and miscarriage

Cigarette smoking during pregnancy is known to cause fetal growth restriction leading to stillbirth. A recent meta-analysis of four studies found a 36% increased risk of stillbirth (OR 1.36, 95% CI 1.27-1.46).[29] Another meta-analysis of 25 observational studies reported the risk of miscarriage to be 32% higher in women who smoke during pregnancy compared to non-smokers (pooled O 1.32, 95% CI 1.21-1.44). [30]

1.1.1.7 Caesarean section

Evidence of the relationship between maternal smoking and mode of delivery is inconclusive to date. A cross-sectional analysis of 170,254 pregnancies delivered in Schleswig-Holstein, Germany between 1991 and 1997 reported no statistically significant difference in caesarean delivery between non-smokers and smokers.[31] However, a recent study conducted in Israel, including approximately 6000 pregnancies reported the risk of any operative or instrumental intervention to be higher in smokers compared to non-smokers OR 1.24 (95% CI 1.01–1.52).[32]

1.1.1.8 Sudden infant death syndrome (SIDS)

Published data support a dose-response relationship between maternal smoking during pregnancy and SIDS. A systematic review of 31 studies on maternal smoking and SIDS reported a twofold increase in the risk of SIDS associated with maternal smoking (OR 2.06, 95% CI 1.83-2.38).[33] Additionally, smoking in the postpartum period was also found to double the risk of SIDS (pooled OR 1.94, 95% CI 1.55-2.34). More recent data from another meta-analysis of 35 case-control studies reported similar risks for smoking during pregnancy (OR 2.25, 95% CI 2.03-2.50) and in the postpartum period (OR 1.97, 95% CI 1.77-2.19) .[34] The effects of cigarette smoking on cardiovascular and respiratory systems are said to play a key role in predisposition to SIDS in infants.[13]

1.1.2 Problems in early childhood and adolescence

Maternal smoking in pregnancy has also been linked to several problems for a child's health in early childhood and adolescence. These problems are further aggravated by second hand smoke (SHS) exposure if the mothers continue to smoke or relapse after delivery. Some of these problems are discussed below.

1.1.2.1 Respiratory problems

Smoking during pregnancy has been shown to reduce lung function in children. A cohort study including 58,841 births in Finland reported 35% greater risk of asthma in in children under the age of seven whose mothers smoked more than 10 cigarettes per day during pregnancy (OR 1.35, 95% CI 1.13-1.62) and 23% increased risk in children whose mothers smoked less than 10 cigarettes per day (OR 1.23, 95% CI 1.07-1.42) compared to children of non-smoking mothers.[35] A meta-analysis of 79 observational studies assessing the association between prenatal and passive smoke exposure on asthma and wheezing found that maternal smoking during pregnancy increased the risk of asthma by 85% (pooled OR 1.85, 95% CI 1.35-2.53) and the risk of wheezing by 41% (OR 1.41, 95% CI 1.19-1.67) in children ≤2 years. Exposure to postnatal maternal smoking was also associated with a 70% increased risk of wheezing in children ≤ 2 years (OR 1.70, 95% CI 1.24-2.35) and a 21% increase in the risk of asthma (Hazard Ratio (HR) 1.21, 95% CI 1.01-1.45).[36]

1.1.2.2 Cancer (Leukaemia, Central nervous system tumours, lymphomas)

Leukaemia, central nervous system (CNS) tumours and lymphomas account for more than two-thirds of all cancers diagnosed in children.[37] A meta-analysis of 30 studies on the association between maternal tobacco use during pregnancy and childhood cancer suggested a 10% increase (OR 1.10, 95% CI 1.03-1.19) in all cancers however no significant associations were found for leukaemia and CNS tumours.[38] A more recent meta-analysis including a total of 6,566 patients

from 12 observational studies also did not show a clear association between maternal smoking during pregnancy and development of brain tumours in children (Risk Ratio (RR) 1.05, 95% CI 0.90-1.21).[39] However, another meta-analysis exploring the association between childhood lymphoma and smoking during pregnancy found a 22% increase in the risk of non-Hodgkin lymphoma associated with maternal smoking during pregnancy (OR 1.22, 95% CI 1.03-1.45, n=7 studies).[40]

1.1.2.3 Obesity/ Overweight

Childhood obesity has become a health concern in many countries including the UK and the US.[41] Women who smoke during pregnancy are more likely to have babies with low birth weight. These infants often show greater 'catch-up' growth resulting in childhood obesity.[42] A meta-analysis of 17 observational studies found that babies of mothers who smoked during pregnancy were 64% more likely to develop childhood obesity compared to babies of non-smokers.[43]

1.1.2.4 Ear infections

A prospective study including 8,556 pregnant women and their babies found the prevalence of otitis media to be higher in children of mothers who smoked during pregnancy such that children of mothers who smoked 1-9 cigarettes during pregnancy were 60% more likely to develop acute ear infection in the first five years of life compared to children of non-smoking mothers. In comparison, odds ratio for developing acute ear infection is reported to be 2.6 (95% CI 1.6-4.2) and 3.3 (95% CI 1.9-5.9) in children of mothers who smoked 10-19 and more than 20 cigarettes during pregnancy respectively.[44] Maternal smoking after pregnancy has also been shown to increase the risk of middle ear infections in children by 62% (OR 1.62, 95% CI 1.33-1.97) in a meta-analysis of 20 studies.[45]

1.1.2.5 Cognitive and behavioural problems

Prenatal smoking exposure in children has been associated with reduced cognitive abilities and academic achievements.[46] A Swedish study on over 375,000 adolescents found that children whose mothers smoked during pregnancy had an increased risk of poor school performance after controlling for maternal and birth characteristics (1-9 cigarettes per day OR 1.59, 95% CI 1.55-1.63, ≥10 cigarettes per day OR 1.92, 95% 1.86-1.98).[47] A systematic review of studies conducted over a 30 year period between 1973 and 2002 demonstrated a link between smoking during pregnancy and attention deficit hyperactivity disorder (ADHD) in children.[48] The odds of developing antisocial behaviour in children with prenatal smoking exposure are shown to be 1.5-4 times greater than unexposed children.[49] Furthermore, children with prenatal tobacco exposure have also shown to have 30-40% higher risk of psychiatric hospitalisations for substance abuse.[50]

1.1.2.6 Diabetes

The British National Child Development Study examined the association between maternal smoking during pregnancy and the risk of diabetes in children and found that the risk of type 2 diabetes in children increased by 11% (OR 1.11, 95% CI 0.31-4.04) for light smokers and quadrupled for heavy smokers (OR 4.55, 95% CI 1.82-11.36).[51]

1.2 ECONOMIC BURDEN

Smoking during pregnancy also imposes a substantial economic burden on society. A report by the Public Health Research Consortium (PHR) in 2010 suggested that costs to the UK National Health Services (NHS) related to maternal outcomes associated with smoking are estimated to be between £8 million and £64 million per year based on different costing methodologies. [52]

Furthermore, costs related to infants' increased risk of preterm delivery, low birth weight, SIDS, perinatal mortality, asthma, otitis media, and upper and lower respiratory infections are estimated to be between £12 million and £23.5 million per year.[52] A study conducted by Petrou and colleagues (2005) in the UK looking at the association between maternal smoking and hospital inpatient costs in childhood found that after adjusting for clinical and socio-demographic factors, the mean cost difference when comparing infants born to women who smoked at least 20 cigarettes per day to infants of non-smoking mothers was £462, over the first five years of life. When infants born to women smoking 10-19 cigarettes per day were compared to infants of non-smoking mothers this difference was £307.[53]

1.3 SMOKING IN PREGNANCY – CURRENT PREVALENCE

1.3.1 International picture

Smoking in pregnancy has become a global public health issue, especially in developed countries. Despite the harms associated with maternal smoking during pregnancy the prevalence of smoking during pregnancy across developed countries still remains high with the prevalence ranging between 10-15% in USA, Canada, Australia and Japan.[54-57] Within Europe, the prevalence figures vary from low figures of <5% in Lithuania and Sweden to as high as 17% in France.[58]

1.3.2 National prevalence and trends over time in the UK

1.3.2.1 Trends over time

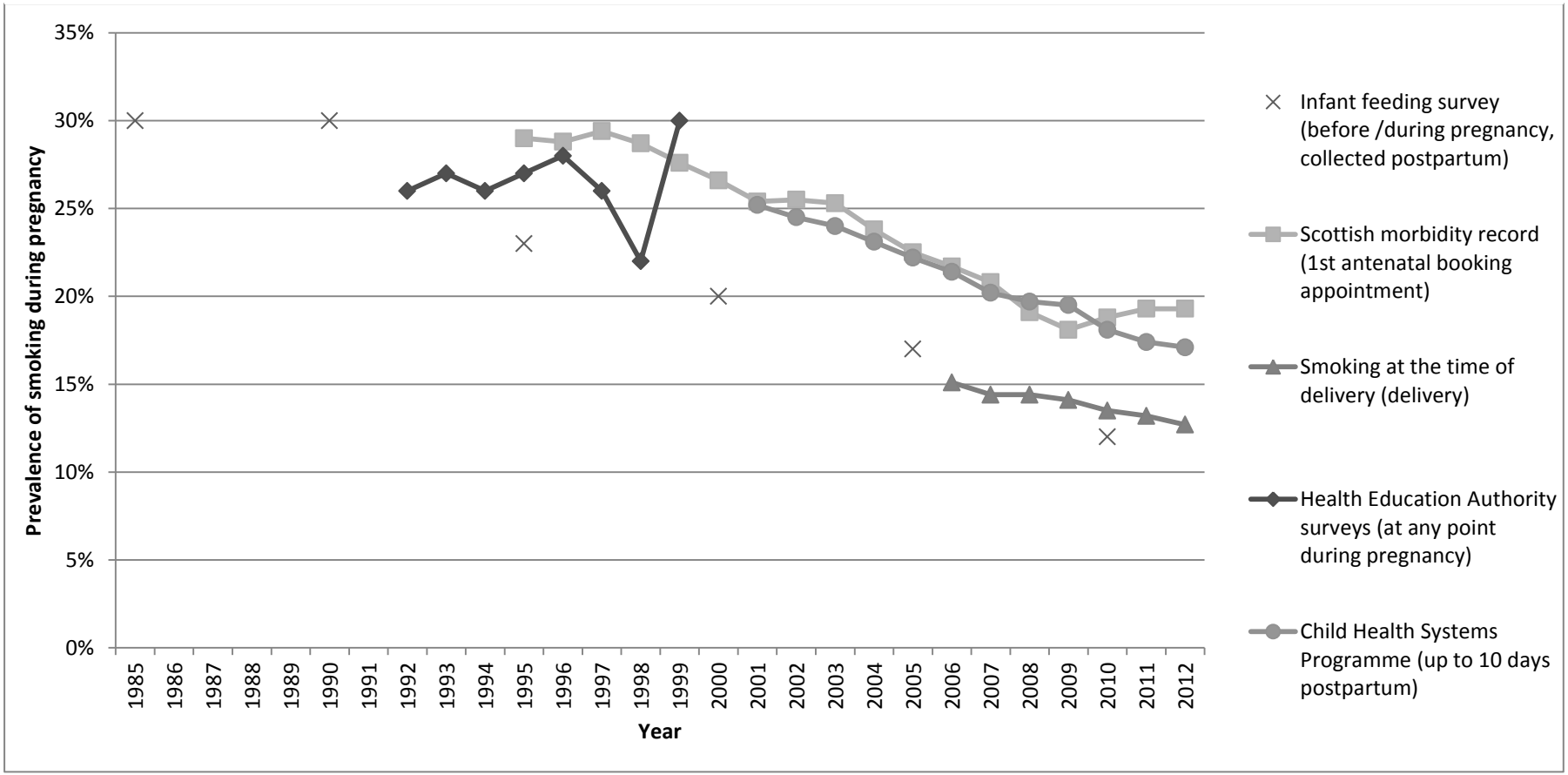
There are four sources in the UK which collect data on smoking in pregnancy. Some of these cover all pregnancies whilst others collect data on a sample of women to capture self-reported smoking status at one or more time points during pregnancy. The Infant Feeding Survey (IFS) 2010, which randomly samples births in the UK every 5 years and measures smoking at delivery

retrospectively at six to eight weeks postpartum in the UK showed that 26% of women smoked before or during pregnancy and 12% smoked throughout pregnancy.[59] The Smoking at the Time of Delivery (SATOD) data, is collected in maternity wards by midwives and measure smoking behaviour at the time of delivery in England, reported 12.6% women to be smoking at the time of delivery in England in 2012.[60] Data from the Scottish Morbidity Records (SMR) collected in antenatal clinics, which measure smoking at the time of first antenatal appointment report slightly higher prevalence compared to the other two data sources (19.3%).[61] The Child Health System Programme Pre-School component (CHSP-PS) data collected by health visitors approximately 10 days postpartum from Scotland report similar prevalence of maternal smoking during pregnancy (17.1%) in 2012.[61]

Figure 1-1 summarises the trends in smoking prevalence during pregnancy in the UK from 1985 to 2012 from the available data sources and the time at which smoking status was assessed in each of these data. Overall there has been a reduction in smoking prevalence during pregnancy in the past two decades and all the data sources reflect a downward trend in maternal smoking during pregnancy. The earliest measures of smoking during pregnancy are obtained from the IFS. According to the IFS, 39% of women smoked before pregnancy and 30% smoked during pregnancy in 1985[62] which has now reduced by over 50% with about 12% women smoking throughout pregnancy.[59] In addition to these routinely collected data and the IFS, the Health Education Authority (HEA), now part of the National Institute for Health and Clinical Excellence (NICE), also conducted a series of small surveys between 1992 and 1999 and found that the prevalence of smoking in pregnancy reduced from 26% in 1992 to 22% in 1998 but then peaked at 30% in 1999 with small fluctuations in the prevalence during the entire seven year period. A potential explanation for this paradoxically high prevalence in 1999 and fluctuations in the prevalence could be the sampling

method for the survey. Women were selected using quota sampling as opposed to probability sampling and also the sample sizes for each of these surveys only ranged from 625-1100 pregnant women,[63,64] which makes the findings less generalisable.

Figure 1-1- Trends in maternal smoking during pregnancy from available data



1.3.2.2 Smoking and socio-demographic characteristics

Maternal smoking prevalence during pregnancy varies by age. According to the IFS 2010 35% of pregnant women in the younger age group (< 20 years) smoked throughout pregnancy compared to 9% of pregnant women in the older age group (> 35 years). Results from SMR data also indicate a similar trend where the prevalence of current smoking in pregnant women younger than 20 years was 38.2% compared to 12.8% in pregnant women over 40 years in 2010.

There is also a marked social gradient in the prevalence of smoking during pregnancy. Data from IFS 2010 showed that 4% of pregnant women in the managerial/ professional group smoked throughout pregnancy in comparison to 20% of pregnant women in the routine/manual group. [59]

1.4 SMOKING CESSATION DURING PREGNANCY

1.4.1 Benefits of smoking cessation during pregnancy

McBride and colleagues suggest that pregnancy may be a teachable moment for smoking cessation where there is an increased perception of risk which prompts strong emotional responses and triggers cessation.[65] Therefore, a higher proportion of women stop smoking during pregnancy than at other times in their lives.[65] Smoking cessation during pregnancy is associated with reductions in various maternal and fetal complications in addition to the general health benefits. A prospective cohort study conducted in New Zealand and Australia on 2,504 pregnant women suggested that women who stopped smoking before 15 weeks of gestation had similar rates of spontaneous preterm birth and small for gestational age infants as those in non-smokers, indicating that these adverse outcomes can be reduced by quitting early in pregnancy.[66] Another study from Sweden using the Swedish Birth Register concluded that stopping smoking

between the first prenatal care visit and the 32nd week of gestation prevented smoking-associated deficits in birth weight, head circumference and brain-to-body weight ratio.[67] These findings are supported by another study from Taiwan using the Pregnancy Risk Assessment Monitoring System (PRAMS) data which found that the babies of mothers who quit smoking during the first trimester weighed 168 g more than the babies born to smokers and there was no difference in birth weight between babies born to women who quit and never smokers (p-value 0.63).[68] A Cochrane review has shown that smoking cessation interventions reduce low birth weight by 17% (RR 0.83, 95% CI 0.73-0.95, n=16 studies) and preterm birth by 14% (RR 0.86, 95% CI 0.74-0.98, n=14 studies).[69] A study based on a USA 1995 birth cohort reported that using smoking cessation interventions to reduce maternal smoking during pregnancy would prevent 108 cases of SIDS annually, which equated to 3.5% of overall SIDS deaths in the USA.[70]

Apart from these health benefits smoking cessation during pregnancy may also generate financial benefits for the NHS. It is estimated that spending between £13.60 and £37 on smoking cessation interventions per pregnant smoker would yield positive cost savings for the NHS.[52] A study conducted in the USA on 227 pregnant smokers found that for every $1 spent on smoking cessation for pregnant women, as estimated $3 in neonatal intensive care costs can be saved.[71] Another American based study found that an annual drop of a single percentage point in maternal smoking prevalence during pregnancy would prevent 1300 low birth weight live births and save $21 million in direct medical costs.[72]

1.4.2 Smoking cessation interventions for pregnant women

Given the harms of maternal smoking during pregnancy and benefits of cessation, the World Health Organization (WHO) recently produced guidelines for

the prevention and management of tobacco use and second-hand smoke exposure during pregnancy. These guidelines recommend all healthcare providers to ask pregnant women about their tobacco use as early as possible in the pregnancy and at every antenatal care visit and to offer advice and psychosocial interventions for tobacco cessation to all pregnant women who are smokers or recent quitters.[73] No recommendations were made on the use of nicotine replacement therapy (NRT) during pregnancy due to the lack of evidence of the safety, efficacy and adherence to the treatments (see Section 1.5 for further details). Other drugs that are licensed as smoking cessation aids for the general population (bupropion and varenicline) are not currently recommended for use during pregnancy. Table 1-1 summarises the different psychosocial interventions currently used/evaluated for smoking cessation in pregnant women and the evidence for effectiveness of each intervention. Currently financial incentivisation, counselling and self-help are shown to be effective for smoking cessation during pregnancy. There is mixed evidence on the effectiveness of other psychological interventions in pregnancy such as feedback and social support.

Table 1-1 – Psychosocial interventions for smoking cessation in pregnant women and evidence for effectiveness

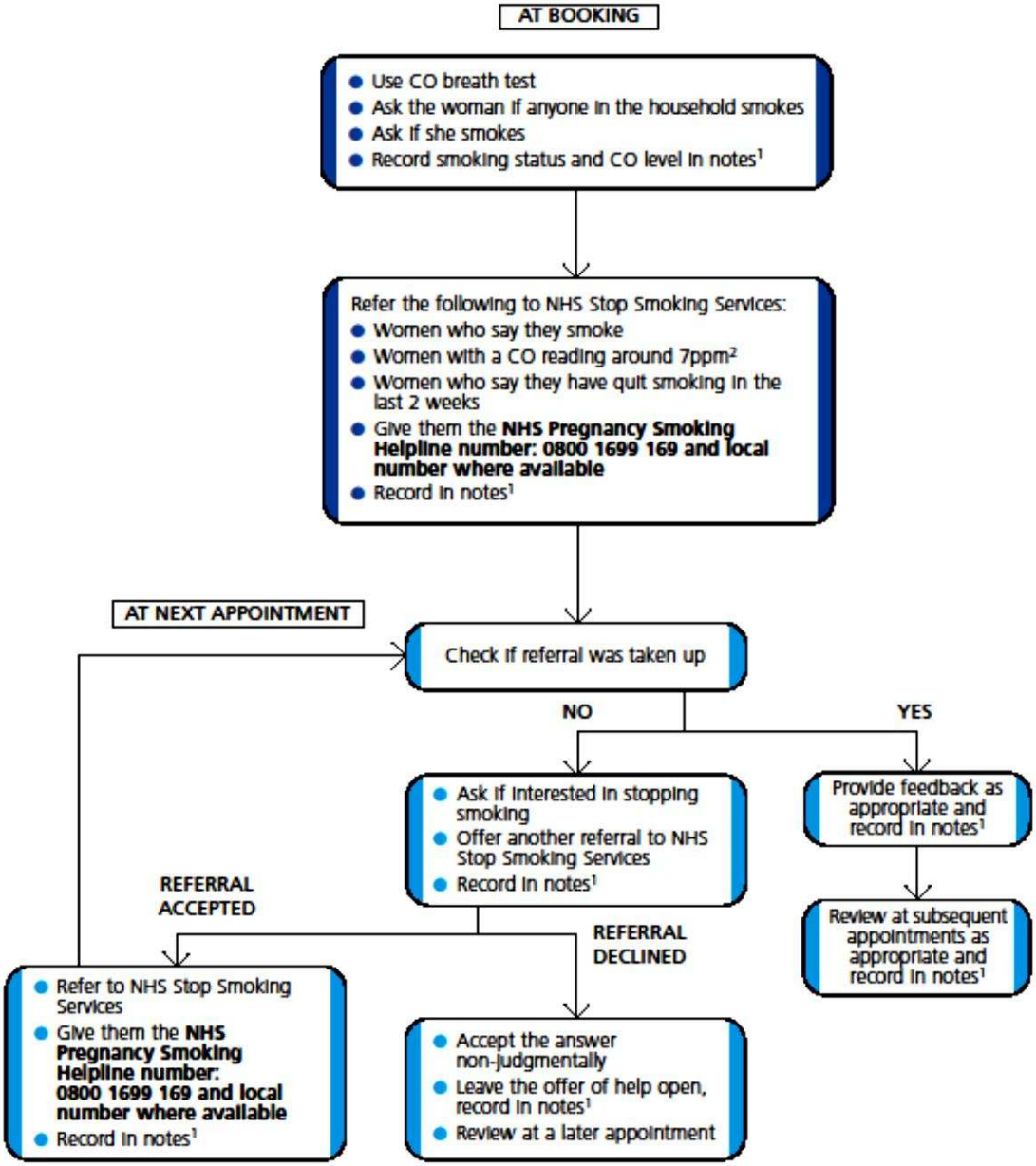
Interventions	Description	Evidence
Cognitive behavioural therapy	• Scheduled face-to-face meetings between pregnant smokers and specialist adviser which may take place individually or in groups typically over a period of at least 4 weeks after the quit date[74]	A systematic review of 86 trials assessing psychosocial interventions for smoking cessation reported that pregnant women provided behavioural counselling such as CBT or MI were 44% more likely to be abstinent in late pregnancy compared to pregnant women given usual care (RR 1.44, 95% CI 1.19-1.75) and women receiving less intensive interventions (RR 1.35, 95% CI 1.00-1.82).[75]
Motivational interviewing	• Directive, client-centred counselling style for eliciting behaviour change, with a focus to help in exploration and resolution of ambivalence regarding smoking cessation.[76] • Aims to increase the likelihood of making an attempt to change a person's harmful behaviour • ranges from brief 20 minutes face to face sessions to telephone and group consultations etc. [77]	
Self-help materials	• Written materials such as booklets but also includes videos or audiotapes[78] • Offered to pregnant women who are referred to Stop Smoking Services (SSS) • Women who opt-out of SSS are also offered these self-help materials[79] • May also be supplemented by telephone counselling or quit lines[74] • Wide-reaching as they can be easily disseminated • Low-cost	A meta-analysis of 12 trials assessing self-help interventions for smoking cessation in pregnant women reported that pregnant women who were given self-help material were 83% more likely to quit compared to women given usual care including brief intervention (pooled OR 1.83, 95% CI 1.23-1.73)[80]
Interventions based on stages of change theory – 'transtheoretical model'	• The core of the transtheoretical model of behaviour change and acts as a basis for behavioural counselling for smoking cessation[81] • Five stages of change i.e. pre-contemplation, contemplation, preparation, action and maintenance.[82] • Tool to develop individually tailored communications for smoking cessation in form of counselling and self-help materials etc.	Mixed evidence regarding the success of interventions based on `stages of change' theory[79] Lumley and colleagues reported a pooled RR of 0.99 (95%CI 0.97-1.00) for smoking cessation in late pregnancy for interventions based on `stages of change' theory [69] Less emphasis was placed on `stages of change' in the updated review and the interventions were broadly categorised as counselling interventions in the new review. [75]
Financial incentivisation	• Thought to influence individual's motivation and self-regulation and also increase health professionals' engagement with patients[83]. These include incentives such as gift and other vouchers	Women who were offered incentives used the services more than women not incentivised. Furthermore, women from the incentivised group reported the experience motivating for their smoking cessation[83]

Interventions	Description	Evidence
	or payments[75]	The four trials with financial incentives as the main intervention compared to usual care showed a three-fold increase in the abstinence in late pregnancy (RR 2.95, 95% CI 1.55-5.63), however the trials included are from the USA[75] A Randomised Controlled Trial (RCT) is in progress in the UK to evaluate the effectiveness of this intervention in the UK[84]
Feedback	• Giving feedback to pregnant women on the effects of smoking on the child and their own health. This includes interventions such as ultrasound monitoring, carbon monoxide or urine cotinine measurements etc.[75]	Chamberlain and colleagues reported a significant effect of feedback on abstinence only when compared with usual care and provided in conjunction with other interventions (RR4.39, 95% CI 1.89-10.21) however no significant effect was found when compared to less intensive interventions (approximate of usual care) (RR 1.19, 95% CI 0.97-2.31).[75]
Social Support	• Including peer/partner support, or support from a healthcare professional [75]	In a recent meta-analysis, social support by peers was reported to increase the abstinence in late pregnancy by 49% (Pooled RR 1.49, 95% CI 1.01-2.19) however social support by partner was not reported to have a significant effect of self-reported abstinence (RR 1.02, 95% CI 0.70-1.50).[75]

Reducing maternal smoking during pregnancy has been an NHS priority since the beginning of the last decade. In March 2011 the government published a white paper titled *"Healthy lives healthy people: A tobacco control plan for England"* which set out how tobacco control would be delivered in the context of new public health systems. One of the aims of this plan is to reduce the rates of smoking throughout pregnancy from 14% to 11% or less by 2015.[2] Currently in the UK there are interventions and support available for pregnant women who want to quit including self-help interventions, pharmacotherapy, specialist support and intensive interventions offered by the NHS Stop Smoking Services (SSS).[85] These services came into place in 2000 following the 1998 tobacco control strategy[86] and since 2001 provide individualised support to pregnant women in clinic settings, home settings and on the phone.[85] Data from the NHS-SSS suggest that about half (46%) of pregnant smokers who use these services quit at the 4 week follow-up.[87] However, less than 14% of pregnant smokers access these services.[88] Therefore, to improve the uptake of these smoking cessation services NICE formulated guidelines on stopping smoking during pregnancy and childbirth in 2010.[79] These guidelines recommend all midwives to assess pregnant women's smoking status at booking, do a carbon monoxide (CO) breath test and refer them to the NHS-SSS. Other healthcare professionals such as general practitioners (GPs), practice nurses, family nurses, obstetricians, paediatricians, sonographers and others are recommended to use any appointment as an opportunity to assess smoking status and offer smoking cessation advice and an NHS-SSS referral to those who want to stop.[79] Similar to the WHO guidelines, bupropion and varenicline are contraindicated for use during pregnancy in the UK. In light of the insufficient data on the safety and effectiveness of NRT, NICE recommends a discussion of the risks and benefits of NRT before prescribing and to only prescribe NRT if cessation without NRT fails.[79]

NICE has also recommended an 'opt out' referral pathway through which the details of all identified pregnant smokers should be passed on to the local smoking cessation service without the need for direct consent.[85] Figure 1-2 explains the detailed pathway for referrals from maternity services to NHS Stop Smoking Services.

Figure 1-2 - Pathway for referrals from maternity to NHS Stop Smoking Services



[1] Preferably the patient handheld record.
[2] Lower level (e.g. 3 ppm) may apply for light/infrequent smokers. Note: higher level might apply if prior exposure to other sources of pollution, e.g. traffic fumes, leaky gas appliances.

Adopted with permission from: National Institute for Health and Clinical Excellence (2010) Quitting smoking in pregnancy and following childbirth PH26. London: National Institute for Health and Clinical Excellence

1.5 NICOTINE REPLACEMENT THERAPY

Nicotine replacement therapy (NRT) contains low doses of nicotine in different medicinal forms. Its use is indicated outside of pregnancy for abrupt cessation of smoking, or to reduce the amount of cigarettes smoked before completely quitting.[89] It can also be used to minimise passive smoking, to treat cravings and reduce compensatory smoking after enforced abstinence in smoke-free environments.[89] The main mode of action of NRT is the stimulation of nicotine receptors in the ventral tegmental area of the brain and the consequent release of dopamine in the nucleus accumbens. This combined with other peripheral actions of nicotine leads to a reduction in nicotine withdrawal symptoms in regular smokers who abstain from smoking.[90] Use for smoking cessation during pregnancy serves two important purposes: firstly, it delivers nicotine without delivering other harmful chemicals and teratogenic products from tobacco smoke to pregnant women and secondly it reduces withdrawal symptoms including cravings.[91]

The use of NRT for smoking cessation during pregnancy is now supported by many countries in the world. The guidelines for smoking cessation in the USA, Australia, and New Zealand recommend that NRT can be used by pregnant women.[92-94] The Ontario Provincial Medical Association in Canada also recommends that NRT should be made available to pregnant women who are unable to quit using non-pharmacological methods.[95] Similar policies are in place for NRT use during pregnancy in European countries like France and Germany.[95]

In the UK, NRT was made available on NHS prescription in 2001; however, its use was contraindicated in pregnancy due to safety fears; for example, concerns about its potential vaso-constrictive properties and potential placental transfer. In 2003 guidance for NRT prescribing was revised such that NRT use in pregnancy was cautioned rather than contra-indicated.[96] In November 2005 the

Medicines and Healthcare products Regulatory Authority (MHRA) conducted a comprehensive review on the safety of NRT during pregnancy and despite a lack of conclusive evidence for efficacy, indicated that NRT use was likely to be less harmful than smoking,[97] consequently broadening the UK licensing arrangements for NRT to include pregnant women in December 2005.[98] As a result NRT can now be prescribed in specialist settings such as the Stop Smoking Services for Pregnant women (SSSPs) as well as in primary care settings. NICE recommends initially prescribing 2 weeks of NRT for use to pregnant women from the day they agree to stop and providing further prescriptions based on re-assessment.[79] NRT is available both on NHS prescription and over-the-counter (OTC) in many different forms and strengths. Table 1-2 presents a detailed description of currently available NRT formulations in the UK which are also available to pregnant women in the UK.

Table 1-2- Nicotine Replacement Therapy formulations currently available in the UK[89,90]

Formulation	Available Strength	Specific side-effects	Maximum recommended daily dose	Additional information
Nicotine chewing gum	2mg, 4mg	Increased salivation, irritation of the throat	60 mg	Treatment to continue for 3 months for smoking cessation
Nicotine inhalation cartridge	10mg, 15mg	Irritation of the throat, reversible atrial fibrillation	12 cartridges of 10mg/ 6 cartridges of 15mg	Single 10mg cartridge lasts for 20 minutes and 15 mg cartridge lasts for 40 minutes
Nicotine lozenge	1 mg, 1.5mg, 2mg, 4mg,	Increased salivation, diarrhoea, constipation, dysphagia, oesophagitis, gastritis, mouth ulcers, bloating, flatulence, taste disturbance, thirst, gingival bleeding, halitosis, chest pain, rash, hot flushes	15 lozenges	Treatment to continue for 6-12 weeks for smoking cessation
Nicotine sublingual tablets	2mg	Dry mouth	40 tablets	Treatment to continue for 3 months for smoking cessation
Nicotine oral spray	1mg/spray	Arrhythmia, hot flushes, sweating, myalgia, chest pain, abdominal pain, flatulence, taste disturbance, dry mouth, paraesthesia, watery eyes, blurred vision	2 sprays per craving episode, 4 sprays every hour and 64 sprays daily	-
Nicotine nasal spray	500 mcg/ spray	Coughing, nasal irritation, epistaxis, sneezing, watery eyes	64 sprays daily, twice every hour for 16 hours	Treatment to continue for 8 weeks for smoking cessation

Nicotine transdermal patches	5mg/16 hrs, 10mg/16 hrs, 25mg/16hrs, 7mg/24hrs, 14mg/24hrs, 21mg/24hrs	Abnormal dreams, sweating, myalgia, arthralgia, arrhythmia, chest pain, dry mouth, minor skin irritation,	25mg/16hrs	>10 cigarettes daily - high-strength patch daily for 6–8 weeks, followed by the medium-strength patch for 2 weeks, and then the low-strength patch for the final 2 weeks <10 cigarettes medium-strength patch for 6–8 weeks, followed by the low-strength patch for 2–4 weeks

1.5.1 Effectiveness of NRT for smoking cessation in pregnant women

In non-pregnant smokers NRT is shown to increase quit rates by 1.5-2.0 times the rate of those trying to quit without NRT[99] however, the evidence of effectiveness of NRT during pregnancy is inconclusive. A recent multicentre, double blinded, randomised, placebo-controlled trial on Smoking, Nicotine and Pregnancy (SNAP) enrolled 1050 pregnant women across England to evaluate the effectiveness of NRT patches for prolonged abstinence and found no significant difference in the rate of abstinence from quit date until delivery between the NRT and placebo group (OR 1.26, 95% CI 0.82-1.96).[100] Furthermore, a systematic review including this trial and five other randomised controlled trials on NRT and smoking cessation in pregnant women, including 1745 women in total, found similar results with no difference for smoking cessation in later pregnancy for NRT in comparison to the placebo group (RR 1.33, 95% CI 0.93-1.91).[101] A potential explanation for reduced effectiveness of NRT during pregnancy is the increased metabolism of nicotine during pregnancy. Several studies have reported higher metabolism of nicotine and cotinine (the primary metabolite of nicotine) in pregnant women compared to non-pregnant population [102,103] such that the half-life of cotinine is reduced to nine hours in pregnancy compared to 17 hours in non-pregnant women.[104] Dempsey and colleagues studied metabolism of nicotine and cotinine in 10 healthy pregnant smokers after intravenous administrations of nicotine and found that both nicotine and cotinine are metabolised more rapidly during pregnancy than in the postpartum period with nicotine clearance being 60% higher during pregnancy compared to outside pregnancy and cotinine clearance being 140% higher. The half-life of cotinine was also significantly higher during pregnancy compared to outside pregnancy (8 hours vs. 16 hours).[104] Another study compared nicotine metabolism using segmental hair analysis during each trimester of pregnancy in a large cohort of pregnant women and observed a significant decrease in hair

nicotine concentrations from the first to third trimester among steady smokers, accompanied by a significant increase in hair cotinine concentrations as nicotine clearance increases during later pregnancy.[105]

Another factor related to the low effectiveness of NRT during pregnancy may be low adherence to the prescribed doses of NRT with a median duration of NRT use to be about two weeks. [100,106-109] In the general population NRT use is recommended for 8-12 weeks for optimal effectiveness therefore two weeks of NRT may be very short to show any effectiveness.[107,110]

1.5.2 Safety of NRT for pregnant women

There is very limited evidence of the safety of NRT during pregnancy and to date the evidence remains inconclusive. A recent systematic review of randomised controlled trials found no differences in the risk of preterm birth (RR=0.85, 95% CI 0.57-1.26), neonatal intensive care unit (NICU) admissions (RR= 0.94, 95% CI 0.64-1.38), miscarriage (RR 1.24, 95% CI 0.37-4.17), and neonatal death (RR 0.28, 95% CI 0.06-1.41) between NRT and placebo groups.[101] Additionally, no increased risk of low birth weight (OR=1.66, 95% CI 0.64-4.27) and stillbirth (RR 1.98, 95% CI 0.55-7.07) was found in the NRT group compared to the placebo group.[101] In contrast, observational data from the PRAMS, USA found that the risk of low birth weight to be twice in mothers who use NRT during pregnancy (OR 1.95, 95% CI 1.10-3.46) compared to non-smokers.[111] Studies using the Danish National Birth Cohort have found no significant association between NRT use and changes in birth weight (β co-efficient=0.25g per week of NRT use) (95% CI -2.31,2.81)[112] or stillbirth (HR) 0.83, 95% CI 0.34-2.00).[113]

Evidence of the association between NRT use and congenital anomalies is also inconclusive. The SNAP trial found no increase in the risk of congenital anomalies associated with NRT use in pregnant women (OR 0.70, 95% CI 0.30-1.66).[100] The Danish National Cohort Data however suggest an increased relative risk for congenital malformations associated with NRT use (RR 1.61, 95% CI 1.01-

2.58).[114] The rate of caesarean section deliveries associated with NRT use has only been assessed in the SNAP trial which found it to be 20.7% which was approximately 45% higher in the NRT group as compared to placebo group (OR 1.45, 95% CI 1.05-2.01).[100]

These studies will be discussed in detail in Chapter 6 and Chapter 7.

1.5.3 Views and attitudes of pregnant women regarding NRT use in pregnancy

The licensing arrangements for NRT have now been broadened to allow use as a smoking cessation medication during pregnancy in the UK. However, as highlighted above, the evidence around its safety and effectiveness is inconclusive. The attitudes and views of pregnant women and care providers vary with some favouring the use of NRT during pregnancy and some being sceptical about it. These views play a key role in the uptake of NRT during pregnancy as the use and uptake of NRT may depend on women's perceptions on the usefulness and safety of the drug. In a small survey of 150 pregnant smokers, identified through antenatal clinics in South West London, approximately half of the pregnant smokers (45%) expressed interest in using NRT. Women who smoked >10 cigarettes per day showed more interest in using NRT than women who smoked <10 cigarettes per day (55.9% vs. 37.4%, p=0.03).[115] Another survey was conducted in the UK after NICE guidelines for smoking cessation supported the use of NRT during pregnancy to aid quit attempts. This survey was based on 145 pregnant women in their third trimester, identified through obstetric case notes. Approximately 70% of these pregnant women expressed interest in using NRT during pregnancy for smoking cessation.[116] Similar figures are reported in an Australian study of 256 pregnant women in an antenatal clinic where 63% of pregnant smokers expressed interest in using NRT if it were provided free of charge.[117] In a qualitative study to investigate the potential barriers to smoking cessation using NRT via focus

groups, the use of patches was considered to be acceptable to most of the women. Some patients with medical problems or history of obstetric complications expressed doubts about using NRT and some were even sceptical of the effectiveness of NRT.[118] However, this study was conducted on a selective sample of women in in Australia therefore the results may not be applicable to other countries like the UK. Additionally, this study was conducted before the guidelines on NRT use in pregnancy were formulated and the licensing arrangements for NRT were broadened, which may have caused a shift in women's perceptions about NRT use during pregnancy. In a more recent qualitative study on 10 pregnant women in a semi-rural area of England, patches were the preferred form of NRT.[119] However, the biggest concern highlighted by these women was that nicotine would harm the baby. Some other concerns related to NRT patch use were the dislike of marks left by the patch and finding a safe unobtrusive place to wear them on the body. Nevertheless, some found the patch to be very discreet with the advantage that once it was worn they forgot about it.[119]

1.5.4 Views and attitudes of health care professionals regarding NRT use in pregnancy

Another important factor in general population prescribing of NRT is the perceptions of health care providers regarding NRT use in pregnancy which may influence their practices and attitudes towards NRT prescribing. In a small survey based on 61 obstetric and paediatric nurses, practitioners and physicians in six community health centres in Boston, USA in 2000, 92% of obstetric providers stated that they would prescribe NRT to pregnant women if safety data were available. However, only 44% of the total sample was prescribing NRT at the time of the study. [120] A more recent study based on 154 obstetricians/ gynaecologists in Ohio, USA reported that only 25% of these specialists prescribed NRT to pregnant women, 32% perceived it as being safe in pregnancy

and only 14% considered it to be effective. Obstetricians/ gynaecologists who perceived NRT to be safe, effective, had confidence in their ability to effectively prescribe NRT and had their colleagues prescribing NRT were more likely to prescribe NRT (OR 20.0, 4.7, 3.9, and 6.7 respectively).[121] In a similar study by the same authors assessing perception of nurses and midwives 74% of the them believed that NRT would reduce the number of pregnant smokers however only 26% were confident in their ability to prescribe/ recommend NRT to pregnant women.[122] A postal survey of 780 health professionals including general practitioners (GPs) and midwives from New Zealand in providing maternity care reported that only 24% of these GPs and midwives perceived NRT to be appropriate to be prescribed to pregnant women.[123] Nevertheless, since NRT is more widely available now and its use is supported by several international guidelines [124-126] this proportion may have increased as a result. In a UK survey of 368 GPs working in four districts of Nottingham, 62% of GPs considered NRT to be effective in pregnancy and 70% considered it to be safer than smoking however only 45% believed NRT to be safe in pregnancy.[127] Even after relaxation of licensing arrangements of NRT in the UK, allowing health professionals to prescribe NRT to pregnant women, NRT in pregnancy was identified as a controversial issue in a qualitative study of midwives and health visitors and midwives expressed concerns in suggesting NRT use to pregnant women.[128] Some of these concerns were related to time-constraints, lack of training and definitive knowledge about the effectiveness of NRT and poor of compliance to NRT during pregnancy.[128]

1.5.5 NRT prescribing and use in pregnant women

Although NRT has been available in different forms for over a decade and pregnant women have been encouraged to use NRT for smoking cessation if smoking cessation without NRT fails, the literature describing trends in NRT prescribing and use by this group is very limited. Studies using the Danish

National Birth Cohort to investigate associations between NRT use and adverse pregnancy outcomes presented self-reported NRT use in pregnant women to be 0.3% in the first 12 weeks of gestation and between 2 to 2.5% when NRT use was assessed until 17-27 weeks of gestation.[112-114,129] A similar study from the USA, using the 2004 PRAMS data reported NRT use to be 4% among pregnant women.[111] A more recent study from the USA based on 296 pregnant smokers enrolled in an RCT reported that 7.4% of these pregnant smokers used NRT during pregnancy.[130] A small study based on 145 pregnant smokers in an antenatal clinic in the UK, before the changes in licensing arrangements took place, found that none of the women in this study were prescribed or counselled about NRT.[116] Another study linking Scottish maternity records with dispensed prescribing data in Tayside, Scotland in 2007 found that 2.4% of the pregnant women were prescribed NRT during pregnancy.[131] In contrast, a recent study conducted in 44 NHS Stop Smoking Services (SSS) across England reported NRT use to be as high as 85% in pregnant smokers attending these services.[132] However, women attending the SSS are more motivated to give up smoking than the general population and therefore these rates may not be true for the whole population.

1.6 SUMMARY AND THESIS OBJECTIVES

Smoking during pregnancy causes significant health and economic burden. Therefore, up-to-date estimates of smoking in pregnancy are not only important for monitoring trends but also important to assess the effectiveness of current interventions and policies to tackle this problem.

Most drugs are contraindicated during pregnancy however NRT is licensed for use in pregnancy in many other countries. In the UK, it is widely available for prescribing for smoking cessation in pregnant women since 2005. However, estimates of the use and prescribing of NRT in pregnant women are scarce.

These measures are vital to assess the utilisation and uptake of NRT which is available on the NHS. Furthermore, evidence of NRT safety in pregnancy is inconclusive with most RCTs being too small to detect an effect and most observational studies using retrospective reporting of exposures making them prone to recall bias.

Therefore, the main aim of the work presented in this thesis was to assess the overall prescribing and safety of NRT in pregnancy. In order to meet this aim, the following objectives were addressed:

1. To assess the completeness of smoking status recording and cessation advice during pregnancy in THIN data
2. To compare the prevalence of maternal smoking in pregnancy from THIN data with other available data sources in the UK
3. To quantify annual trends of NRT prescribing in and around pregnancy in the UK
4. To assess whether NRT prescribing during pregnancy varies with maternal characteristics
5. To investigate the relationship between antenatal exposure to NRT, maternal smoking and major congenital anomalies among children
6. To investigate the relationship between antenatal exposure to NRT, maternal smoking and other birth outcomes (stillbirth, low birth weight and mode of delivery)

1.7 OUTLINE OF THESIS CHAPTERS

Chapter 2 briefly reviews potential data sources to assess the objectives of this thesis and describes in detail the main data source chosen for the studies in this thesis (The Health Improvement Network data).

Chapter 3 assesses the completeness of smoking status recording during pregnancy in primary care data (Objective 1)

Chapter 4 assesses the potential utility of these data to produce population-level estimates of smoking in pregnancy (Objective 2)

Chapter 5 quantifies the prescribing of NRT in and around pregnancy and describes trends and patterns using descriptive statistics as well as poisson models (Objective 3 and 4)

Chapter 6 investigates the association between maternal NRT or smoking exposure and major congenital anomalies in the offspring (Objective 5)

Chapter 7 assess the relationship between maternal NRT or smoking exposure and stillbirth, low birth weight and mode of delivery (Objective 6)

Chapter 8 summarises the main findings of the work presented in this thesis, discusses the public health implications and suggests avenues for future research.

2 POTENTIAL DATA SOURCES AND DESCRIPTION OF THE DATA USED

This chapter briefly presents potential data sources that measure smoking, NRT and other covariates required for the studies in this thesis and then describes in detail the main data source used i.e. The Health Improvement Network primary care data.

In the UK, there are a number of routinely collected data or annual/quarterly/quinquennial surveys which assess different parameters of smoking and NRT use. Table 2-1 compares these data sources on some of the attributes that were essential for the studies in this thesis.

Table 2-1 - Potential data sources in the UK to measure smoking and NRT trends and safety

Data source	Smoking outside pregnancy	Smoking in pregnancy	NRT data	Sociodemographic factors	Birth outcomes*
General Lifestyle Survey (GLF)[133] /Integrated Household Survey (IHS)[134]	Yes	No	No	Yes	No
Health Survey for England (HSE)[135]	Yes	No	No	Yes	No
Office for National Statistics (ONS) Opinions Survey[136]	Yes	No	No	Yes	No
Smoking Toolkit Study (STS)[137]	Yes	No	Yes	Yes	No
Infant Feeding Survey (IFS)[59,138,139]	No	Yes	No	Yes	No
Smoking at Time of Delivery (SATOD)[60]	No	Yes	No	No	No
Child Health Systems Programme (CHSP)[61]	No	Yes	No	Yes	No
Scottish Morbidity Record (SMR) – smoking at booking[61]	No	Yes	No	Yes	No
Commercial over-the-counter NRT data[140]	No	No	Yes	No	No
Electronic Prescribing Analysis and Cost Tool (e-PACT)[141]	No	No	Yes	No	No
Data from the Stop Smoking Services[142]	No	No	Yes	Yes	No
Primary Care Data[143-145]	Yes	Yes	Yes	Yes	Yes

*congenital anomalies, birth weight, stillbirth, mode of delivery

Out of the 12 data sources listed in Table 2-1 only five sources assess smoking status specifically in relation to pregnancy and four sources assess NRT use/prescribing. However, the table above clearly highlights that compared to all the other potential data sources a large dataset of primary care data could potentially provide information on all the attributes required for this thesis including information on smoking status during and outside pregnancy, prescribing of NRT, sociodemographic factors and birth outcomes. In addition, it has other health information on women such as comorbidities. Therefore, these data have the potential to provide detailed information on smoking and NRT use in and around pregnancy, offering a large amount of data for a period of about 20 years, without the costs and time involved in using some other bespoke studies. The Health Improvement Network (THIN) primary care database was chosen as the dataset to be used for this thesis over the Clinical Practice Research Datalink and QRESEARCH it had an established pregnancy cohort with mother-child linkages at the time of the study which is essential for assessing the effects of pregnancy exposures (e.g. smoking, NRT) on birth outcomes (stillbirth, congenital anomalies). Additionally, about half of the general practices that contribute to THIN also contribute to CPRD.[143]

2.1 INTRODUCTION TO THE HEALTH IMPROVEMENT NETWORK DATA

THIN is an electronic primary care database of anonymised patient records from general practices across the UK. It contains medical, prescription, lifestyle and socio-demographic information routinely collected by GPs. THIN was set up in November 2002 following collaboration between the Cegedim Strategic Data (CSD) Medical Research UK, formerly known as the Epidemiology and Pharmacology Information Core (EPIC), part of the group who developed the Clinical Practice Research Database (CPRD) formerly called the General Practice Research Database (GPRD) [146] and InPractice Systems (InPS) who developed the

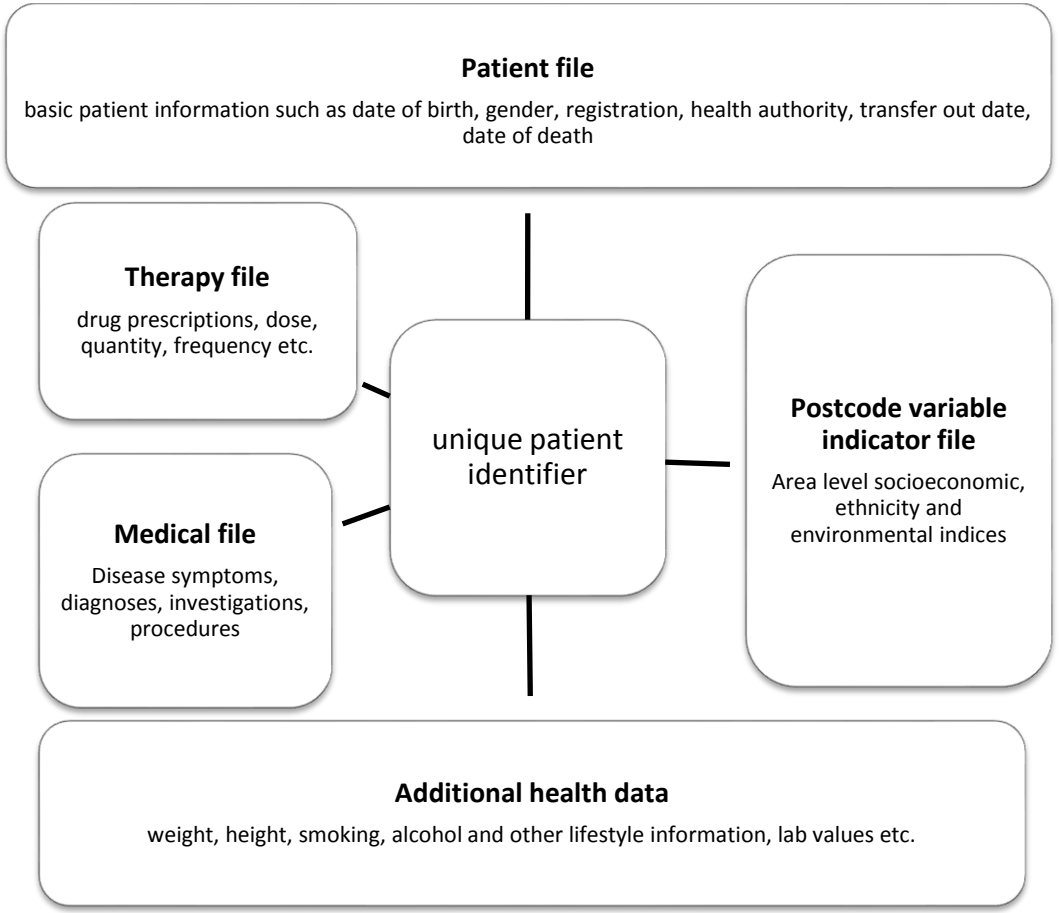
Vision software [143,147] Data are collected prospectively for all the registered patients who are alive. Additionally, historical information is available for patients who have died or transferred out of the practices. All practices participating in THIN use Vision software for their prospective data recording. On joining THIN an initial Full Data Collection (FDC) is conducted where all the retrospective data are collected. [143] Retrospective medical data are also available in each patient's records although general practices may have previously used a number of different software systems to record their data, mostly using the Value Added Medical Products (VAMP) system to enter patient data,[148] which was used in the Clinical Practice Research Data link (CPRD) formerly known as the GPRD.

THIN adds to existing data every quarter to update the dataset with a lag of three to eight months between data being entered and being available for research.[149] With each new release of the dataset the number of practices contributing data to THIN increases as a result of recruitment of new practices, though a small number of practices also leave the scheme.

2.2 DATA FORMAT OF THIN

Information for each patient is split into four main files, which are linked together by a unique patient identification number. Figure 2-1 describes the structure and information contained in each of these files. In addition to these files, there is a Postcode Variable Indicators (PVI) file containing postcode linked area-level socioeconomic, ethnicity and environmental indices however ethnicity information was only available for <15% of the women for the version of data used for this thesis (85% missing, 11% European, 0.6% Asian, 0.6% Black, 1.2% Other White, 1.1% Mixed race) and therefore ethnicity was not included as a covariate in the studies conducted in this thesis[150]

Figure 2-1 - Structure of THIN data



Clinical information in the Medical and Additional Health Data (AHD) file is coded using medical Read codes, a coded thesaurus of clinical terms including signs, symptoms, diagnoses, investigations and procedures etc.[151] The medical Read codes in the file are also complemented by the AHD codes in the AHD file which describe details of lab values and other anthropometric measurements. More detailed clinical information and comments are entered as free text; these data were not available for this work.[150] Prescriptions are entered using multilex drug codes which are linked to the British National Formulary (BNF).

2.3 VERSION USED FOR THIS PHD – THIN 1009

The version of THIN used for the studies conducted as part of this thesis contains anonymised data from 495 practices across England, Scotland, Wales and Northern Ireland with a total of 9.5 million patients and covers approximately 5.7% of the UK population. Of these over 3.46 million patients are currently registered with active practices and can be prospectively followed. Data are available from January 1990 to September 2010.[143] However, data for 2010 were only available for the first nine months of the year and, therefore, all the studies discussed in this thesis have only used data until December 2009.

2.4 STRENGTHS AND LIMITATIONS OF DATASET IN RELATION TO THE PHD WORK

Electronic primary care data such as THIN are a good resource for descriptive epidemiology. However, there are limitations to its use which are important to consider. The relative strengths and limitations of THIN, particularly with reference to studying smoking and NRT prescribing in pregnancy are discussed below.

2.4.1 Nature of data recording

THIN has information on smoking status, prescriptions, cessation advice and counselling recorded prospectively compared to retrospective data collection in other data sources such as IFS and SATOD, which minimises the potential for misclassification due to recall or reporting errors. In addition to the smoking information, it also contains other clinical information recorded prospectively which may affect the smoking behaviour and other outcomes under study. Furthermore, THIN is based on routinely-collected data and reflects real life situation rather than experimental settings. It is therefore also useful to study the effect of certain policy and guideline changes on patient behaviour in the general population. These data however present a picture of routine UK clinical practice and inevitably lack information on people who did not consult their GPs for medical problems, which needs to be kept in mind while interpreting the findings from any study using primary care data. Additionally, the recording of different covariates will vary in the population as these data are not collected at regular intervals.

2.4.2 Size, representativeness and generalisability

Small sample sizes are one of the biggest drawbacks of many research studies in pregnancy as they result in reduced statistical power and are much less likely to represent the target population. THIN is a large database with information on over nine million patients and approximately two million women in their childbearing years from approximately 500 practices around the UK. Utilising THIN to estimate the prevalence of smoking and NRT prescribing in pregnancy could potentially produce precise estimates based on routine data with no added costs to conduct any surveys.

Most people in the UK are registered with a GP. General practices voluntarily contribute data to THIN and therefore may have a slight under-representation of

the most deprived socioeconomic group compared with the UK as a whole. Nevertheless, electronic primary care data have been shown to be generally representative of the UK population in terms of demographics, prevalence of major conditions and mortality rates.[152] Therefore, estimates of the clinical burden of disease, drug prescribing and the utilisation of primary care resources can be reasonably generalised to the population of the UK.

2.4.3 Validity and data quality of exposures/ outcomes of interest

Independent studies have shown high validity for both common and rare outcomes in THIN, including fertility rates.[152-154] THIN has also been previously validated for recording of smoking status at a national and regional level in the general population[149,155] and prescriptions for smoking cessation medications.[156] Additionally, the prevalence of congenital anomalies in THIN is shown to be consistent with European Surveillance of Congenital Anomalies (EUROCAT) data[157] and has been validated against written GP records.[158] Other pregnancy outcomes, however, have not been validated but show similar estimates to national figures (e.g. stillbirth).[159]

As these data are primarily not collected for research purposes, information on certain exposures and outcomes may be more complete in certain groups compared with the general population. For example, a GP is more likely to ask and update smoking status in smokers as smoking is an important risk factor for many other medical conditions. Additionally, GPs address an average of two to three different medical problems during a single consultation[160,161] however, only the dominant topics of the visit may be coded.[141, 142] Therefore the information contained in these data heavily relies on the GPs' assessment of the extent and importance of the problem. Behavioural factors such as smoking, alcohol, exercise and diet etc. may therefore not always be recorded. Initial inspection of THIN data demonstrated poor recording of smoking status before 2000.

Therefore, for the purposes of this thesis analysis was limited to data from 2000 onwards.

Additionally, some drugs such as NRT are available from multiple sources in the UK for example GPs, SSS and OTC. Therefore, THIN may only be able to give population-based estimates of prescribing in primary care and not from other sources. NRT only became available on NHS prescription in 2001.[162] Therefore, the studies in this thesis assessing NRT prescribing and safety only analyse data from 2001 onwards.

2.4.4 Duration of follow-up

The average follow-up time for each woman in the data is approximately 4.5 years. This may be useful when assessing prevalence of smoking at a population level and comparing trends in smoking prevalence and NRT prescribing over time. Whilst this is a relatively short time in the context of a lifetime, it surpasses other available data where cross-sectional sectional surveys are used.

2.4.5 Contemporaneous

The version of THIN used for this thesis has data up to September 2010. However, THIN data are updated routinely and have a lag of only three to eight months before the data become available for research. Therefore, methods used in this thesis could be utilised to provide contemporaneous and timely estimates of smoking in future.

2.5 MOTHER-CHILD LINK

To assess the health effects of maternal exposures on children, the anonymised primary care records of mothers and their children in THIN version 1009 were linked to form a pregnancy cohort with maternal-child linked records. This was done by Dr Linda Fiaschi and Dr Laila J. Tata using unique household

identification numbers to find mothers and children within the same household and then matching them using the delivery details in the mothers' primary care records and birth details in the children's primary care records. Approximately 87% of the children registered within three months of birth are matched to their mothers' records. This dataset was created independent of the work in this thesis and serves as a resource for several studies within the Division of Epidemiology and Public Health. This mother-child linked data was used for Objectives 5 and 6 (safety of NRT).

2.6 ETHICAL APPROVAL

All data are anonymised before leaving the practice such that individual patient identifiers such as the name, address, date of birth, hospital number and specific location of general practices cannot be identified by researchers. THIN data collection was approved by the NHS South-East Multi-centre Research Ethics Committee (MREC) in 2003.[163] Ethical approval for the use of THIN data for studies on smoking and NRT prescribing prevalence was obtained from THIN Scientific Review Committee (Ref.No 11-047). Ethical approval for the studies on NRT safety in pregnancy was obtained from the Medical Research Ethics Committee, administered and approved by the NHS MREC (REC Ref. 04/MRE01/9).

3 COMPLETENESS OF SMOKING STATUS RECORDING DURING PREGNANCY IN THIN

3.1 INTRODUCTION

Current recommendations in the UK emphasise that all healthcare workers involved in a pregnant woman's care (e.g. midwives, GPs, practice nurses and obstetricians) should assess the woman's smoking status at the earliest possible stage of pregnancy and offer cessation advice and a referral to specialist stop smoking advisers for women who smoke.[74,79,164-166] Documentation of a woman's smoking status in her medical records is recommended to enable her healthcare team to offer appropriate support throughout the pregnancy. [165] Midwives record these data on the handheld maternity records and GPs record this information in the electronic primary care data. In the UK women must be registered with a GP in order to receive antenatal care provided by the NHS and, although most antenatal contacts are with midwives, an estimated 77% of women see their GPs first for confirmation of pregnancy before attending an antenatal booking appointment with a midwife.[167] This visit is therefore an ideal opportunity for the GPs to assess smoking status, communicate it to the healthcare team and provide advice on quitting, given the benefits of quitting early in pregnancy.[66-68] Primary care is the central hub in the current UK health care system and the assessment and complete documentation of smoking status, amongst other health indicators, in primary care is important to increase opportunities for providing smoking cessation advice and interventions during pregnancy. However, the extent to which smoking status is assessed and recorded during pregnancy in primary care is currently unknown. Additionally, there are no measures on whether GPs provide smoking cessation advice to pregnant women and how well it is recorded. These are important questions not only to identify missed opportunities for smoking cessation in primary care but

also to assess the potential utility of these data to generate smoking estimates during pregnancy at a population-level.

This chapter is aimed at addressing the very important questions highlighted above. It begins with a brief overview of the Quality and Outcomes Framework (QOF), a national scheme introduced to increase the recording of medical conditions and lifestyle factors, including smoking, in primary care data. This is followed by an investigation of the completeness of maternal smoking status recording during pregnancy in THIN data, assessing the annual proportion of pregnant women who have a record of their smoking status during pregnancy in their primary care data and how this varies with sociodemographic factors and maternal morbidities. This study was published in *PLOS One* in September 2013 and is attached as Appendix 10.1.

Appendix 10.2 presents the results of a study which assessed the completeness of recording of smoking cessation advice during pregnancy in primary care and variations in completeness with maternal factors. This study was conducted as a BMedSci project undertaken by Bethany Hardy and jointly supervised by myself and Dr Lisa Szatkowski. This paper was published in *BMC Family Practice* in February 2014 and it attached as Appendix 10.2.

3.2 QUALITY AND OUTCOMES FRAMEWORK

In April 2004, a new contract for GPs was implemented which introduced a number of pay-for-performance targets as part of the QOF.[168] A set of indicators was developed under four main domains (clinical, organisational, patient experience and additional service) to measure the performance of GP practices using points. Approximately 7.5-8% of the QOF points (worth around £10,000) per year per practice are related to the recording of smoking status and delivery of smoking cessation advice.[169-171] At the time of its introduction, the QOF required GPs to document the smoking status of patients with hypertension, diabetes, asthma and certain other smoking-related morbidities every 15 months and have at least one record of smoking status in the absence of these morbidities. In 2006, this was slightly changed to require all GPs to document smoking status of all patients at least once every 27 months. The target was then changed in 2013 to every 24 months for the general population and every 12 months for patients with chronic conditions.[171] No rules however have been developed for the recording of smoking status or smoking cessation advice specifically during pregnancy. A detailed explanation of the QOF rules for smoking status recording in the general population from 2004 to date is given in Table 3-1.

Table 3-1 - QOF requirements for recording of smoking status[172,173]

		2004-2005	2005-2006	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014
Recording of smoking status in those with specific conditions	Hypertension	The notes of patients with any one or combination of these conditions should contain a record of smoking status in the previous 15 months, except those who have never smoked where the smoking status need only be recorded once since diagnosis.									The notes of patients with any one or combination of these conditions should contain a record of smoking status in the previous 12 months, except those who have never smoked where the smoking status need only be recorded once since diagnosis.
	Coronary heart disease										
	Diabetes mellitus										
	COPD*										
	TIA** or stroke										
	Asthma										
	Chronic kidney disease										
	Schizophrenia, bipolar disorder or other psychoses										
	Peripheral Artery Disease										

		2004-2005	2005-2006	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014
Recording of smoking status in all registered patients in the general population		The notes of patients aged 15-75 should contain at least one record of smoking status.		The smoking status of patients aged 15+ should be recorded in every 27 months, except those who have never smoked where smoking status need be recorded only once.		The smoking status of patients aged 15+ should be recorded every 27 months, except those who have never smoked where smoking status is to be checked annually until age 25. Ex-smokers are to be asked about smoking status on an annual basis until they have been a non-smoker for 3 years.					The smoking status of patients aged 15+ should be recorded every 24 months, except those who have never smoked where smoking status is to be checked annually until age 25. Ex-smokers are to be asked about smoking status on an annual basis until they have been a non-smoker for 3 years.

Table adapted with permission, and updated from Szatkowski L (2011) PhD Thesis: Can primary care data be used to evaluate the effectiveness of tobacco control policies? Data quality, method developments and assessment of the impact of smokefree legislation using data from The Health Improvement Network. Nottingham: University of Nottingham.
*COPD – Chronic Obstructive Pulmonary Disease, TIA – Transient Ischaemic Attack
Shaded areas represent the time when there are no QOF recording rules in place for specific conditions

The introduction of the QOF led to an improvement in the recording of clinical information in primary care medical records including the data on smoking status and smoking cessation advice. A study examining the impact of the QOF rules on the recording of smoking targets in primary care using THIN found that with the introduction of the QOF in 2004, the recording of smoking status in the general population improved such that the overall proportion of patients with a smoking status record within the last 27 months increased from 30% in 2003 to over 40% in 2004 and increased steadily over time such that in 2008 the proportion of patients with a smoking status record within the last 27 months in THIN was approximately 65%.[174] Similar increases were seen for recording of smoking status in patients with chronic conditions where this proportion increased from 50% in 2003 to over 75% in 2004 and then plateaued.[174] A similar study using the QRESEARCH primary care database, including 525 general practices across the UK, reported similar results with a 33% increase in the recording of smoking status between 2001/2002 and 2006/2007 with large increases in the collection of smoking data after the implementation of the QOF.[175]

3.3 JUSTIFICATION FOR THE STUDY

In the general practice population as a whole the recording of patients' smoking status is more complete after the introduction of the QOF.[149,155] However, as discussed above the QOF set no specific incentives for the recording of smoking status in pregnant women. Having smoking status recorded in a pregnant women's medical records is not only useful for clinical management, but also increases opportunities for health professionals to provide smoking cessation interventions throughout pregnancy and afterwards. Additionally, a cohort of pregnant smokers was required as a denominator to calculate NRT prescribing prevalence and also as a comparison group to compare the safety of NRT in this thesis. Therefore, the primary aim of this study was to assess the completeness

of recording of smoking status during pregnancy in primary care medical records over time and investigate whether completeness varied with women's sociodemographic and health-related characteristics. Additionally, the secondary aim of this work was to investigate whether, despite having no specific targets for pregnancy, there was an increase in the completeness of smoking status recording during pregnancy in UK primary care after the introduction of the QOF.

3.4 METHODS

3.4.1 Study population

For this particular study the population included all pregnancies recorded in THIN between 2000 and 2009 in women of reproductive age (15-49 years), as defined by the WHO,[176] which resulted in either a live birth or a stillbirth. Pregnancies ending in spontaneous abortions and terminations were not included in the study population as these do not have comprehensive information on pregnancy-related exposures and outcomes.

3.4.2 Smoking status records

Records of maternal smoking status during pregnancy were identified using Read codes.[151] These included codes for current, never, and ex-smoking, codes indicating the type or number of cigarettes smoked, and codes indicating smoking cessation interventions delivered to patients. Code lists are attached as Appendix 10.5. Women were also considered to be smokers if they had a prescription for a smoking cessation drug (nicotine replacement therapy, bupropion or varenicline) in their medical records during pregnancy. Code lists are attached as Appendix 10.6. Further information was extracted using the smoking AHD codes in Appendix 10.7. This method of classifying smoking status in electronic primary care data to calculate smoking prevalence has been previously validated in general population.[149]

3.4.3 Maternal characteristics

To investigate the factors that may be associated with the recording of maternal smoking status during pregnancy, data were extracted on the following maternal characteristics. Code lists for the morbidities discussed below are attached as Appendix 10.8.

3.4.3.1 Age and socioeconomic status

Age was considered as a categorical variable with five-year age bands progressing from 15 years through to 49 years with seven categories in total.

Socio-economic status was assessed using quintiles of the Townsend index of material deprivation.[177] The Townsend deprivation index measures area level deprivation based on four indicators: unemployment, house ownership, car ownership and overcrowding. This was derived using the 2001 Census data, converted into five equal quintiles and then matched to UK postcodes to give deprivation quintiles for each postcode, quintile 1 being the least deprived group and quintile 5 being the most deprived group.

3.4.3.2 Diabetes

For each pregnancy, women were said to have diabetes if there was a medical Read code for diabetes or a prescription of insulin or an oral hypoglycaemic agent documented in the therapy file or a diabetes record in the AHD file within 27 months before conception until delivery. Although the QOF required the smoking status of patients to be recorded every 15 months in patients with diabetes and other comorbidities until 2013, for the general population smoking status needed to be recorded every 27 months.[173] Since this thesis is focused around smoking in pregnant women (who represent a fairly healthy group from the general population) the period of 27 months was set as a cut-off point for extraction of diabetes and all other morbidities for consistency purposes.

3.4.3.3 Hypertension

For each pregnancy, a woman was said to have hypertension if there was a Read code for hypertension recorded in the medical file or three or more readings of high blood pressure (BP) (systolic > 140mmHg with/ or diastolic >90mmHg) documented in the AHD file between 27 months before conception until delivery.

3.4.3.4 Asthma

Women were defined as having asthma if they had a medical code for asthma within 27 months before conception until delivery or if they had a medical code for asthma any time in their general practice record before delivery and a drug prescription for asthma within 27 months before conception until delivery to identify if women had active asthma in and around the time of pregnancy

3.4.3.5 Mental illness

This variable included five psychiatric conditions: depression, anxiety, bipolar disorder, schizophrenia and other psychoses. A woman was said to have a mental illness if there was a definitive diagnosis (based on International Classification of Diseases (ICD)-10 codes) of any of the above mental illnesses in a woman's primary care record between 27 months before conception until delivery.

3.4.3.6 Pre-conception body mass index

Body Mass Index (BMI) was extracted from the medical file using Read codes. Information on BMI was also extracted from the AHD file using the AHD information on weight. The most recent recording of BMI within 27 months before conception was considered to keep it consistent with the method of determining all other comorbidities.

BMI was then divided into four categories according to the WHO classification[178]: normal (18.5-24.9 kg/m^2), underweight (<18.5 kg/m^2), overweight (25-29.9 kg/m^2), obese (≥30 kg/m^2). A separate category was created for missing BMI information.

3.4.4 Statistical analysis

The prevalence of smoking status recording during pregnancy was calculated for each year from 2000 to 2009 as the number of pregnancies with at least one recording of smoking status during the gestational period divided by the total number of pregnancies delivered in that year. These data were plotted graphically.

For women who only had records of being a never smoker up to the age of 25 and who did not have a record of smoking during a subsequent pregnancy, a never smoking record was imputed during gestation. Similarly, for women who had no smoking status records during gestation but who were recorded as ex-smokers for three consecutive years before the conception an ex-smoking record was imputed during gestation. The annual proportion of pregnancies with a recording of smoking status during the gestational period was then recalculated. These imputations were based on the QOF rules discussed in Section 3.2. Since April 2006 the QOF has not required GPs to record smoking status of patients after the age of 25 years if they have been a never smoker until that age.[179] After 2008, if a patient who once smoked has been recorded as an ex-smoker for three years, GPs need no longer check and update the patient's smoking status records.

Logistic regression was used to calculate ORs for associations between women's characteristics and the recording of smoking status during pregnancy. All covariates that reached statistical significance ($p<0.05$) in the univariable analysis were initially included in the multivariable analyses and each covariate

was tested sequentially in the multivariable model. Covariates that reached statistical significance ($p<0.05$) in the multivariable analysis were retained in the final model. As some women had more than one pregnancy during the study period that contributed to the analyses, this potential clustering of pregnancies within women was accounted for by calculating robust CIs around the odds ratios using the clustered sandwich estimator. The clustered sandwich estimator allows for intragroup correlation (i.e. more than more pregnancy for each woman).[180,181]

Logistic regression was carried out for two separate time periods: before the implementation of the QOF (January 2000-April 2004) and after the implementation of the QOF (April 2004-December 2009). The introduction of the QOF incentivised the recording of smoking status in patients with smoking-related chronic conditions therefore it was expected to be an effect modifier of the association between recording of smoking status during pregnancy and these morbidities.

Visual comparisons of the magnitude, precision and statistical significance of the odds ratios for each maternal factor in the pre and post-QOF periods were made in order to assess whether the association between maternal factors and the recording of smoking status during pregnancy changed after the QOF was introduced.

3.5 RESULTS

3.5.1 Baseline characteristics

A total of 215,703 women with pregnancies resulting in live births or stillbirths were identified between January 2000 and December 2009. Of these, 162,295 (75.0%) had only one pregnancy, 46,062 (21.5%) had two pregnancies and 7,346 (3.5%) had three or more pregnancies, giving a total of 277,552 pregnancies. The mean age at conception was 29.5 years (standard deviation

(sd) 5.9) and the average length of pregnancy was 39.4 weeks (sd 2.2). Table 3-2 describes the baseline characteristics of the study population in the pre-QOF and post-QOF time periods. The overall prevalence of diagnosed asthma, diabetes, hypertension and mental illness within the study population was approximately 8%, 2%, 2.5% and 9% respectively. Information on socioeconomic status (Townsend index) was missing for 6% of the total pregnancies and information on BMI was missing for 42% of pregnancies.

Table 3-2 - Baseline characteristics of the study population

	Pre-QOF(January 2000- March 2004)			Post-QOF (April 2004- December 2009)		
	Total pregnancies (n=98,373)	**Pregnancies with a gestational smoking record (n=12,381)****		**Total pregnancies (n=179,179)**	**Pregnancies with a gestational smoking record (n=64,188)**	
	n	**n**	**%***	**n**	**n**	**%***
Age at Conception						
15-19 years	5,529	953	(17.2%)	9,854	4,856	(49.3%)
20-24 years	14,809	2,202	(14.9%)	29,323	12,607	(43.0%)
25-29 years	25,732	3,175	(12.3%)	45,416	16,758	(36.9%)
30-34 years	32,621	3,750	(11.5%)	54,574	17,437	(32.0%)
35-39 years	16,614	1,944	(11.7%)	32,778	10,296	(31.4%)
40-44 years	2,907	338	(11.6%)	6,868	2,123	(30.9%)
45-49 years	161	19	(11.8%)	366	111	(30.3%)
Townsend Score in quintiles						
Quintile 1 – least deprived	24,760	2,850	(11.5%)	38,815	11,733	(30.2%)
Quintile 2	19,288	2,277	(11.8%)	32,962	11,025	(33.4%)
Quintile 3	18,592	2,317	(12.5%)	35,209	12,542	(35.6%)
Quintile 4	17,128	2,279	(13.3%)	33,982	13,114	(38.6%)
Quintile 5 - most deprived	13,252	1,964	(14.8%)	25,742	10,915	(42.4%)
Missing	5,353	694	(13.0%)	12,469	4,859	(39.0%)
Pre-conception Body Mass Index (kg/m^2)						
Normal(18.0-24.9)	26,663	3,948	(14.8%)	59,267	21,209	(35.8%)
Underweight(<18.0)	1,968	293	(14.9%)	4,355	1,714	(39.4%)
Overweight(25-29.9)	11,923	1,867	(15.7%)	29,476	10,957	(37.2%)
Obese(>=30)	7,125	1,240	(17.4%)	20,993	8,406	(40.0%)
Missing	50,694	5,033	(9.9%)	65,088	21,902	(33.6%)
Asthma	6,537	1,297	(19.8%)	16,807	8,911	(53.0%)
Hypertension	2,372	377	(15.9%)	4,962	1,959	(39.5%)
Diabetes	1,345	194	(14.4%)	4,864	1,857	(38.2%)
Mental illness	8,717	1,439	(16.5%)	17,294	7,373	(42.6%)

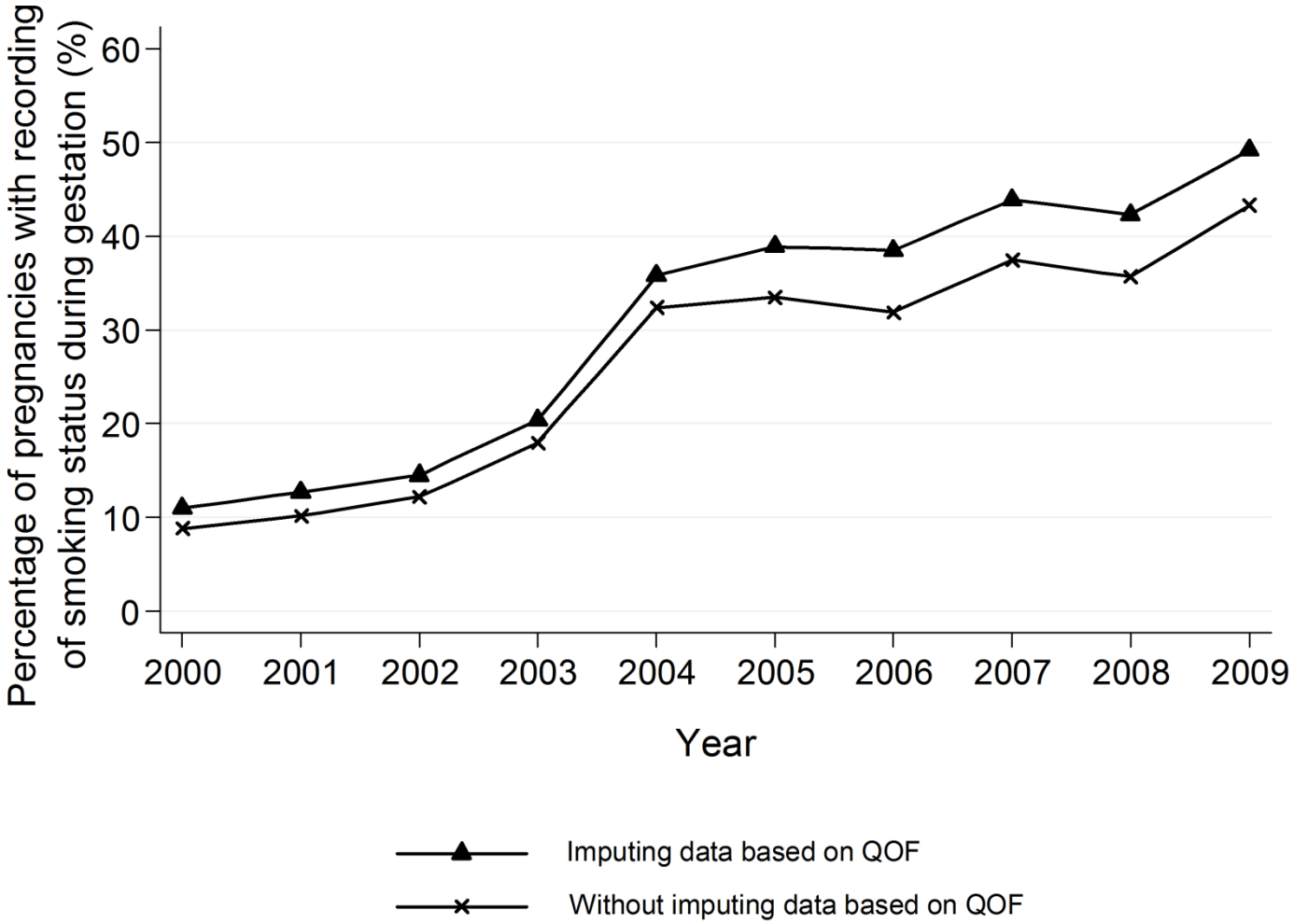
*pregnancies with a gestational smoking record in each sub-category divided by the total number of pregnancies in the respective sub-category
** women had information on whether they were an ex/never/current smokers or had a smoking cessation prescription

3.5.2 Completeness of maternal smoking records

A record of smoking status at any point during gestation was present in 76,569 (28%) of the 277,552 pregnancies. Of the 76,569 pregnancies in which there was smoking status information, 913 (1.2%) only had a recording for smoking cessation drug prescription with no accompanying Read codes indicating smoking status. In 56,605 (73.9%) pregnancies, women had their smoking status recorded only once during the gestational period, whereas in 19,964 (26.1%) pregnancies, smoking status was recorded more than once. Figure 3-1 shows the proportion of pregnancies with smoking status recorded during gestation from 2000 to 2009. In 2000, smoking status was recorded during the gestational period for only 1,943 (8.8%) of the total 22,111 pregnancies. This proportion increased steadily to 18% in 2003, with the proportion rising to 32.3% in 2004. After 2004 it increased steadily on an annual basis such that the proportion of pregnancies with smoking status recorded during gestation in 2009 was 43.3% (13,360 out of 30,880 pregnancies).

When data for never smoking and ex-smoking were imputed based on the QOF rules, the overall proportion of pregnancies with a record of smoking status during gestation increased to 32.1%. In 2000, smoking status was recorded during gestation for only 11.0% of pregnancies which increased to 35.8% in 2004 and 49.2% in 2009.

Figure 3-1 - Annual proportions of pregnancies in THIN with smoking status recorded during gestation (2000-2009)



3.5.3 Factors associated with recording of maternal smoking status during pregnancy

Table 3-3 shows variations in the recording of smoking status during pregnancy by women's sociodemographic characteristics and morbidities in the pre-QOF and post-QOF time periods. Overall, the magnitude of effect of the associations between most maternal characteristics and recording of smoking status during gestation was higher in the post-QOF period compared to the pre-QOF period. The recording of smoking status during pregnancy varied with socioeconomic status such that pregnant women from the most deprived group (quintile 5) were 17% more likely to have their smoking status recorded during pregnancy than pregnant women from the least deprived group (quintile 1) before the implementation of the QOF (OR 1.17, 95% CI 1.10-1.25) and 42% more likely afterwards (OR 1.42, 95% CI 1.37-1.47). Similarly, pre-QOF pregnant women with a diagnosis of asthma were 63% more likely to have their smoking status recorded during pregnancy than pregnant women without asthma (OR 1.63, 95% CI 1.53-1.74) and post-QOF pregnant women with asthma were over twice as likely to have their smoking status recorded during pregnancy (OR 2.08, 95% CI 2.02-2.15). Having a diagnosis of diabetes was not associated with the recording of gestational smoking status pre-QOF (unadjusted OR 1.17, 95% CI 1.00-1.36), (p=0.290). However, post-QOF it was associated with a 12% increase in the odds of recording of gestational smoking status (OR 1.12, 95% CI 1.05-1.19). Recording of smoking status during pregnancy was also related to hypertension and mental illness. In both time periods the odds of a woman having her smoking status recorded during pregnancy were greater at younger ages compared with older ages and also greater in overweight and obese women. However, the magnitude of effects and corresponding CIs in the pre-QOF and post-QOF periods overlapped.

Table 3-3 - Odds of having smoking status recorded during gestation by women's characteristics pre-QOF and post-QOF

	Pre-QOF(January 2000- March 2004)				Post-QOF(April 2004-December 2009)			
	UOR (95% CI)	**p-val**	**AOR (95% CI)**	**p-val**	**UOR (95% CI)**	**p-val**	**AOR (95% CI)**	**p-val**
Age at conception								
15-19 years	1.48 (1.37 - 1.60)		1.56 (1.44 - 1.70)		1.66 (1.59-1.74)		1.62 (1.54 - 1.69)	
20-24 years	1.24 (1.17 - 1.32)		1.22 (1.15 - 1.30)		1.29 (1.25-1.32)		1.24 (1.20 - 1.28)	
25-29 years	1	<0.001	1	<0.001	1	<0.001	1	<0.001
30-34 years	0.92 (0.87 - 0.97)		0.95 (0.91 - 1.00)		0.80 (0.78-0.82)		0.84 (0.82 - 0.86)	
35-39 years	0.94 (0.88 - 0.99)		0.99 (0.93 - 1.05)		0.78 (0.75-0.80)		0.83 (0.80 - 0.85)	
40-44 years	0.93 (0.83 - 1.05)		0.99 (0.88 - 1.12)		0.76 (0.72-0.81)		0.80 (0.76 - 0.85)	
45-49 years	0.95 (0.59 - 1.53)		0.99 (0.61 - 1.60)		0.74 (0.59-0.93)		0.77 (0.61 - 0.97)	
Townsend Score								
Quintile 1 (least deprived)	1		1		1		1	
Quintile 2	1.03 (0.78 - 1.09)		1.01 (0.95 - 1.07)		1.16 (1.12-1.19)		1.12 (1.09 - 1.16)	
Quintile 3	1.09 (1.03 - 1.16)	<0.001	1.03 (0.97 - 1.10)	<0.001	1.28 (1.24-1.32)	<0.001	1.18 (1.14 - 1.21)	<0.001
Quintile 4	1.18 (1.11 - 1.25)		1.07 (1.00 - 1.13)		1.45 (1.40-1.49)		1.26 (1.22 - 1.30)	
Quintile 5 (most deprived)	1.34 (1.25 - 1.42)		1.17 (1.10 - 1.25)		1.69 (1.64-1.75)		1.42 (1.37 - 1.47)	
Missing	1.14 (1.04 - 1.25)		1.06 (0.97 - 1.16)		1.47 (1.41-1.54)		1.34 (1.29 - 1.40)	
Body Mass Index (kg/m^2)								
Underweight(<18.0)	1.01(0.88-1.14)		0.92 (0.81 - 1.05)		1.16 (1.10-1.24)		1.03 (0.97 - 1.10)	
Normal(18.0-24.9)	1		1		1		1	
Overweight(25-29.9)	1.07 (1.01-1.13)	<0.001	1.06 (1.00 - 1.13)	<0.001	1.06 (1.03-1.09)	<0.001	1.05 (1.02 - 1.09)	<0.001
Obese(>=30)	1.21 (1.13-1.30)		1.16 (1.08 - 1.25)		1.19 (1.16-1.23)		1.11 (1.08 - 1.15)	
Missing	0.63 (0.60-0.66)		0.63 (0.60 - 0.66)		0.91 (0.89-0.93)		0.90 (0.88 - 0.92)	
Asthma	1.80 (1.69-1.92)	<0.001	1.63 (1.53 - 1.74)	<0.001	2.19 (2.12-2.25)	<0.001	2.08 (2.02 - 2.15)	<0.001
Hypertension	1.32 (1.18-1.48)	<0.001	1.26 (1.12 - 1.41)	<0.001	1.17 (1.11-1.24)	<0.001	1.19 (1.12 - 1.26)	<0.001
Diabetes	1.17 (1.00-1.36)	0.045	- ǂ	-ǂ	1.11 (1.05-1.18)	<0.001	1.12 (1.05 - 1.19)	<0.001
Mental illness	1.42 (1.34-1.51)	<0.001	1.32 (1.24 - 1.41)	<0.001	1.37 (1.33-1.41)	<0.001	1.26 (1.22 - 1.30)	<0.001

UOR=unadjusted odds ratio, AOR=adjusted odds ratio, CI=confidence interval, QOF=Quality and Outcomes Framework, ǂ Diabetes not significant in the final model

3.6 DISCUSSION

3.6.1 Principal findings

Using a large population-based dataset this study found that the recording of smoking status during pregnancy in primary care has improved with time such that the proportion of pregnancies with a recording of smoking status during gestation was 8.8% in 2000 rising to 43.3% in 2009. The odds of a woman's smoking status being recorded during pregnancy was related to age, socioeconomic deprivation, BMI and QOF-incentivised morbidities such as asthma, diabetes, hypertension and mental illness. This indicates that even though there are no QOF targets specific to pregnancy, the QOF has had an influence on the completeness of smoking status recording during pregnancy.

3.6.2 Strengths and limitations

This is the first study to assess the completeness of recording of smoking status during pregnancy in UK primary care medical records at a national level with over 200,000 pregnancies. The study is also novel in that it assesses the association between maternal characteristics and the recording of smoking status during pregnancy, taking into account the effects that the QOF had on the overall recording trends. Additionally, the code lists used to defined smoking status were quite exhaustive including medical Read codes, smoking cessation drug prescription codes and AHD codes related to smoking cessation advice, increasing the sensitivity to identify any smoking related recording in the women's primary care data. However, only electronically-coded data in primary care records were used and no free-text data (additional uncoded data that the GPs might add in patient notes to elaborate on the patient's condition),[182] which may provide additional information on the smoking status of women , were available.

Due to the infrequency of smoking status recordings during pregnancy the recording of smoking status throughout pregnancy was assessed compared to smaller time windows during pregnancy such as in each trimester, which may be more appropriate given that smoking status can fluctuate during pregnancy.[183] A potential explanation for a high proportion of pregnancies in which smoking status was not recorded could be that although this information is part of the hand-held maternity notes [184] (mandatory paper notes that women carry with them throughout pregnancy) it may not be transcribed onto the GP electronic records. Another reason could be that if a woman's smoking habit did not change after she became pregnant, GPs may be less likely to re-enter this information into medical records as there is no specific financial incentive for assessing and recording smoking status in pregnant women. Furthermore, as the QOF does not require GPs to record the smoking status of 'never smokers' after the age of 25, there is no financial incentive for them to update smoking status in the medical records of women who have never smoked. Similarly, ex-smokers need only be asked about their smoking status annually until they have been a non-smoker for three years. When smoking status was recalculated based on these rules, the annual trends in the completeness of smoking data during pregnancy did not vary much from the trends using the original data, however each woman only had 4.5 years of follow-up so for older women who had been non-smokers for life recording may be especially low.

3.6.3 Comparison with current literature

Overall, a steady improvement has been observed in the recording of smoking status during pregnancy in the primary care data. The proportion of pregnancies with a gestational smoking record in this study increased by approximately 2% per year between 2000 and 2002. Since the late 1990s there has been an increased focus on the harms of tobacco use in the UK, with, for example, the publication of the Government White Paper 'Smoking Kills' in 1998 with a

specific objective of offering help to pregnant women to quit[86] and the establishment of NHS-SSS specifically tailored for pregnant women from 2001 onwards.[185] This changing tobacco control environment may have made these pregnant smokers more willing to approach their GPs for help to quit, and focused GPs' attention on encouraging cessation in their patients, thereby increasing the proportion of pregnant women with a smoking status record in their medical notes. The proportion of pregnancies with a recording of smoking status rose sharply from 18.0% in 2003 to 32.4% in 2004, after which it increased slowly until 2009. The most plausible explanation for this marked increase between 2003 and 2004 is GPs' awareness of the impending introduction of the 2004 GP contract. [186] Similar improvements in the recording of smoking status have been seen in the general population. A study using primary care data for over 300 practices throughout the UK found that, although rates of recording of smoking status in patients' electronic medical records had been increasing gradually since the year 2000, the rate of improvement accelerated from 2003, with an 88% increase observed between the first quarter of 2003 and the same period in 2004, just before the introduction of the QOF.[187] This suggests that the introduction of the QOF resulted in better recording of smoking status in the general population which has spilled over into greater recording in pregnancy observed in this study.

For socioeconomic deprivation, asthma and diabetes the magnitude of effect of the association with smoking status recording was observed to be stronger after the introduction of the QOF. Pre-QOF, pregnant women from the most deprived group were 17% more likely to have their smoking status recorded during gestation compared to 42% post-QOF. Smoking prevalence is generally higher in lower socioeconomic groups in both the general population as well as amongst pregnant women[59] and the smoking status of smokers is more likely to be recorded than that of non-smokers [188-190], which likely explains more complete

recording in pregnant women from lower socioeconomic groups. Furthermore, low socioeconomic status is associated with a higher prevalence of chronic diseases such as hypertension, diabetes, asthma and depression. [191] The QOF encourages improved clinical management of these patients, who post-QOF may have had more frequent contacts with their GP and thus have had more chance of being asked about their smoking behaviour, increasing the gradient of the association between socioeconomic status and smoking status recording, reflecting that recording, and thus hopefully monitoring, is more complete where it is most needed. [192,193] Asthma is the most common pre-existing condition encountered during pregnancy [194] and can be exacerbated by smoking,[195] which may explain the high magnitude of association between asthma and recording of smoking status compared to other conditions like diabetes (which affects approximately 2-5% women of reproductive age)[196] and hypertension (0.6-2.7% during pregnancy).[197] Women with a higher BMI have an increased risk of complications during pregnancy and therefore are more likely to visit their GPs.[198] They are also more likely to be smokers[199] which in turn makes them more likely to have a recording of smoking in their primary care record.

The findings from this work are similar to those from a study in the general population which found that primary care patients with smoking-related chronic medical conditions and greater social deprivation were more likely to have a recent recording of smoking status or cessation advice in their medical records.[174] However, the magnitude of effect in the general population study for all morbidities was much higher than what this study found, possibly because currently pregnancy is not a QOF-incentivised condition for recording of smoking and because the pregnant population are generally healthier and younger on average than the whole population in general practice.

3.7 CONCLUSIONS

In conclusion, smoking status of women during pregnancy was found to be recorded in less than half of the study population. This clearly highlights a missed opportunity in primary care considering that over three-quarters of pregnant women see their GP early in their pregnancy.[167]

In relation to the further work in this thesis, even for women with a recording of smoking status during pregnancy in primary care, data may not capture the changes in their smoking status accurately as over three-quarter of these women only had a single smoking related record during pregnancy. This makes it hard to establish if the women smoked throughout pregnancy or quit during the course of pregnancy. It would also mean that if a cohort of pregnant smokers was to be created using gestational smoking records, it may not include all women who may have smoked during pregnancy simply because no information was recorded. This raises questions on the utility of these data to generate population-level estimates on smoking during pregnancy which will be explored further in the following chapter.

4 COMPARISON OF SMOKING PREVALENCE ESTIMATES FROM THIN DATA TO OTHER DATA SOURCES

4.1 INTRODUCTION

As discussed earlier, reducing smoking in pregnancy to 11% or less by 2015 is one of the national goals set in the 2011 White Paper.[2] Information on maternal smoking is therefore important to monitor the progress towards this national goal and also to assess the effectiveness of the interventions currently in place for smoking cessation (discussed in Section 1.4.2). Electronic primary care data are collected routinely and have the power to provide estimates for the whole of the UK as well as constituent countries.[149] Therefore, these data such as THIN could potentially provide comprehensive and timely population-level data on smoking prevalence during pregnancy. Findings from the previous chapter show that even in recent years, smoking status was recorded in less than 50% of pregnancies. However, the completeness of the smoking data were be improved approximately 8% by making various assumptions based on the QOF recording rules discussed in Section 3.2. The next step in the quality assessment of smoking status data during pregnancy in primary care is to examine whether the prevalence obtained using these recordings in THIN is representative of the population-level prevalence of smoking in pregnancy. This is important firstly to assess the potential utility of primary care data such as THIN in providing population-level estimates of maternal smoking during pregnancy and secondly to establish an appropriate cohort of pregnant smokers which can be used for further analyses in this thesis. Hence, this chapter compares the prevalence of maternal smoking during pregnancy in THIN with the smoking prevalence measures obtained from other available data sources in the UK, with certain

assumptions based on the QOF, to assess the validity of recorded maternal smoking prevalence during pregnancy in THIN.

This study was published in the *Journal of Public Health* in October 2014 and is attached as Appendix 10.3.

4.2 CURRENTLY AVAILABLE DATA SOURCES IN THE UK TO PROVIDE PREVALENCE OF MATERNAL SMOKING DURING PREGNANCY

The UK currently has four data sources that provide population-level estimates of smoking during pregnancy. Each data source measures smoking differently, at different points in and around pregnancy and has its strengths and limitations.

Table 4-1 presents the summary of the important characteristics of these data sources and their strengths and limitations. Annual estimates for maternal smoking during pregnancy, for these data and other individual studies are described in Appendix 10.9 and were shown in Section 1.3.2, Figure 1-1. Annual estimates of maternal smoking in pregnancy from each of these data will be compared to estimates from THIN in this study.

Table 4-1 - Summary of available data sources to measure smoking during pregnancy in the UK

Data source	Data collection interval	Country	Sampling frame and method	Sample size ǂ (% of national births)	Data collection method	Time at which data on smoking in pregnancy are collected	Definition of smoking	Strengths	Limitations
Infant Feeding Survey[59,138,139]	Every 5 years	UK (England, Scotland, Wales, Northern Ireland)	Random sample of live births in England and Scotland and all births in Wales and Northern Ireland in study period	22,400 (2.7% of all births in the UK)[159,200-203]	Postal survey administered by the National Health Service Information Centre	6-8 weeks after birth	Several self-reported measures available: smoking prior to pregnancy; ever smoking during pregnancy; quitting on confirmation of pregnancy; quit/cut down attempts during pregnancy; smoking at delivery.	Smoking estimates for overall UK and each constituent country Smoking status presented by socio-demographic factors Measures smoking cessation during pregnancy	Data only collected at 5 years intervals Retrospective reporting of smoking status Low response rates (approx. 52%) Results published at least a year after survey completion
Smoking Status at Time of Delivery (SATOD)[60]	Collected continually and reported quarterly	England	Aims to capture all live births and stillbirths	359,763 (52.1% of all births in England)[159,200]	Midwife-survey (in hospital maternity units)	At delivery	Self-reported smoking status at delivery	Data collected and reported at a local level	Limited to England Data collected postnatally No assessment of smoking by sociodemographic factors

Smoking Data collected as part of the Scottish Morbidity Record (SMR)[61,203]	Collected continually and reported by financial year	Scotland	All pregnant women attending an antenatal booking appointment (pregnancies may end in live birth or stillbirth)	57,398 (100% of all maternities in Scotland)[201,203]	Midwife survey (in hospital or community)	First antenatal booking appointment (usually between 8-12 weeks gestation)	Self-reported smoking status at the time of booking	Provides measures of never / ex smoking along with current smoking Provides annual rates by age and socio-economic status	Limited to Scotland Does not give estimates for the whole duration of pregnancy
Pre-school component of the Child Health Systems Programme (CHSP)[61]	Collected continually and reported by financial year	Scotland	Aims to capture all live births	51,746 (92% of all live births in Scotland)[201,203]	Survey administered by public health nurse or health visitor	Approximately 10 days after birth	Self-reported smoking status at the time of survey approximately 10 days after delivery	Provides data on smokers and non-smokers by age and socio-economic status	Limited to Scotland Data collected postnatally only Does not specifically ask about smoking during pregnancy

‡Sample sizes for each wave vary therefore sample sizes for 2010 described in the table for reference

4.3 METHODS

The study population included all pregnancies recorded in THIN between 2000 and 2009 in women of reproductive age. To prevent the risk of using the same pre-conception smoking status for women in their subsequent pregnancies if the smoking records were not updated only one random pregnancy per woman was chosen.

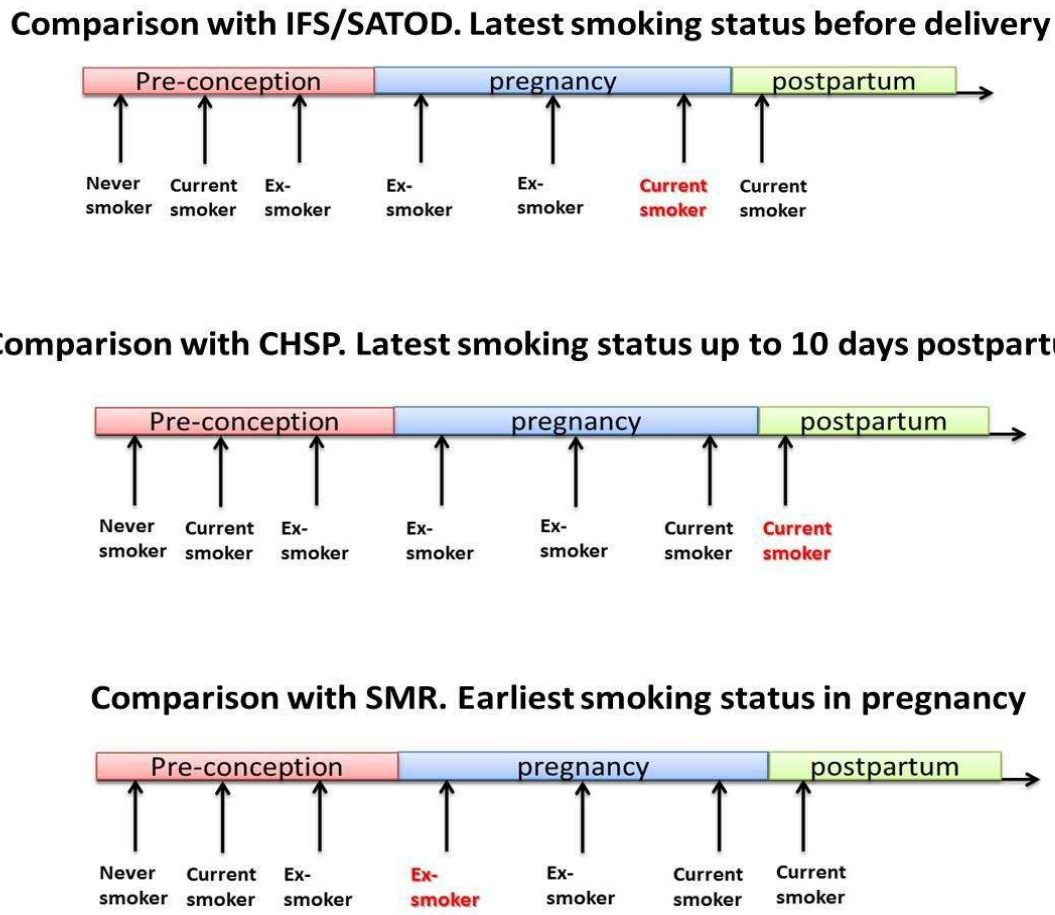
4.3.1 Comparing the prevalence of smoking in pregnancy in THIN with other data sources

For each woman all smoking status records in THIN before and during pregnancy and up to 10 days after delivery were extracted in a similar way as described in Section 3.4.2. A period of 10 days after delivery was included to allow appropriate comparisons with the Child Health Systems Programme (CHSP) data which collects smoking information approximately 10 days postpartum.[61] Where a Read code did not clearly indicate current smoking (e.g. 137X.00 – Cigarette consumption) further information on smoking status was assessed from the AHD and therapy files. This included the number of cigarettes smoked, or presence of prescriptions for smoking cessation medications. If no additional information was found, the recording was labelled as unknown smoking status.

For each comparison, woman's smoking status was determined in a slightly different way (Figure 4-1). The annual prevalence of smoking during pregnancy as recorded in THIN (as a proportion of all births in that year) was then compared against the prevalence measures from the Infant Feeding Survey (IFS), Smoking status at Time of Delivery (SATOD), Scottish Morbidity Record data (SMR) and CHSP data. Each comparison made in the study used a slightly different population of women from THIN and assessed smoking status at a

different point in time in pregnancy to reflect the nature of the data collection in the source being compared (Table 4-2).

Figure 4-1 - Example of a woman's smoking records in primary care and smoking status used for each comparison



Smoking status in red denotes the one used for each comparison

Table 4-2 - THIN comparisons with the currently available data in the UK

Survey	Time at which survey assesses smoking prevalence	Years compared with THIN	THIN population used for comparison	Timing of records considered to define smoking status in THIN
Infant Feeding Survey (IFS)	At delivery	2000, 2005	Data from all UK practices (n=495)	Last smoking status recording between conception and delivery
Smoking Status at Time of Delivery (SATOD)	At delivery	2006-2009	Data from English practices (n=378)	Last smoking status recording between conception and delivery
Scottish Morbidity Record (SMR)	At booking (8-12 weeks gestation)	2000-2009	Data from Scottish practices (n=63)	First smoking status recording between conception and delivery
Child Health Systems Programme (CHSP)	10 days after delivery	2001-2009	Data from Scottish practices (n=63)	Last smoking status recording between conception and 10 days after delivery

Estimates of smoking prevalence from the IFS were derived from the raw datasets of individual women's survey responses, available from the UK Data Service.[204] The IFS only asked about smoking status 6-8 weeks after birth so women were classified as smoking at delivery if they reported that they tried to give up smoking during pregnancy but started again before delivery, if they tried to cut down on the amount smoked during pregnancy, or if they did not try to cut down during pregnancy. Estimates of the prevalence of smoking from SATOD, SMR and CHSP were obtained from the published reports.[60,61,203]

4.3.2 Imputing smoking status where women had no record during the gestational period

Initially, only records of smoking status documented in THIN after the date of conception were used to determine smoking status during pregnancy. However, if a woman's smoking status was not recorded during gestation, pre-conception records of smoking status were assessed to identify women who smoked before pregnancy and may have continued during pregnancy. Based on the QOF rules for the recording of smoking status in the general population, which from April 2004 to March 2006 required the smoking status of patients aged 15 or over to be recorded at least once in primary care records, and since April 2006 have required records to be updated every 27 months, two cut-off points for including pre-conception information were used.[172] Firstly, a cut-off of 27 months before conception was used and women were recoded as smokers if their last smoking record in the 27 months before conception indicated smoking. Finally, if a woman did not have her smoking status recorded either during pregnancy or in the 27 months before conception, any smoking information recorded in their primary care data since registration was included.

4.4 RESULTS

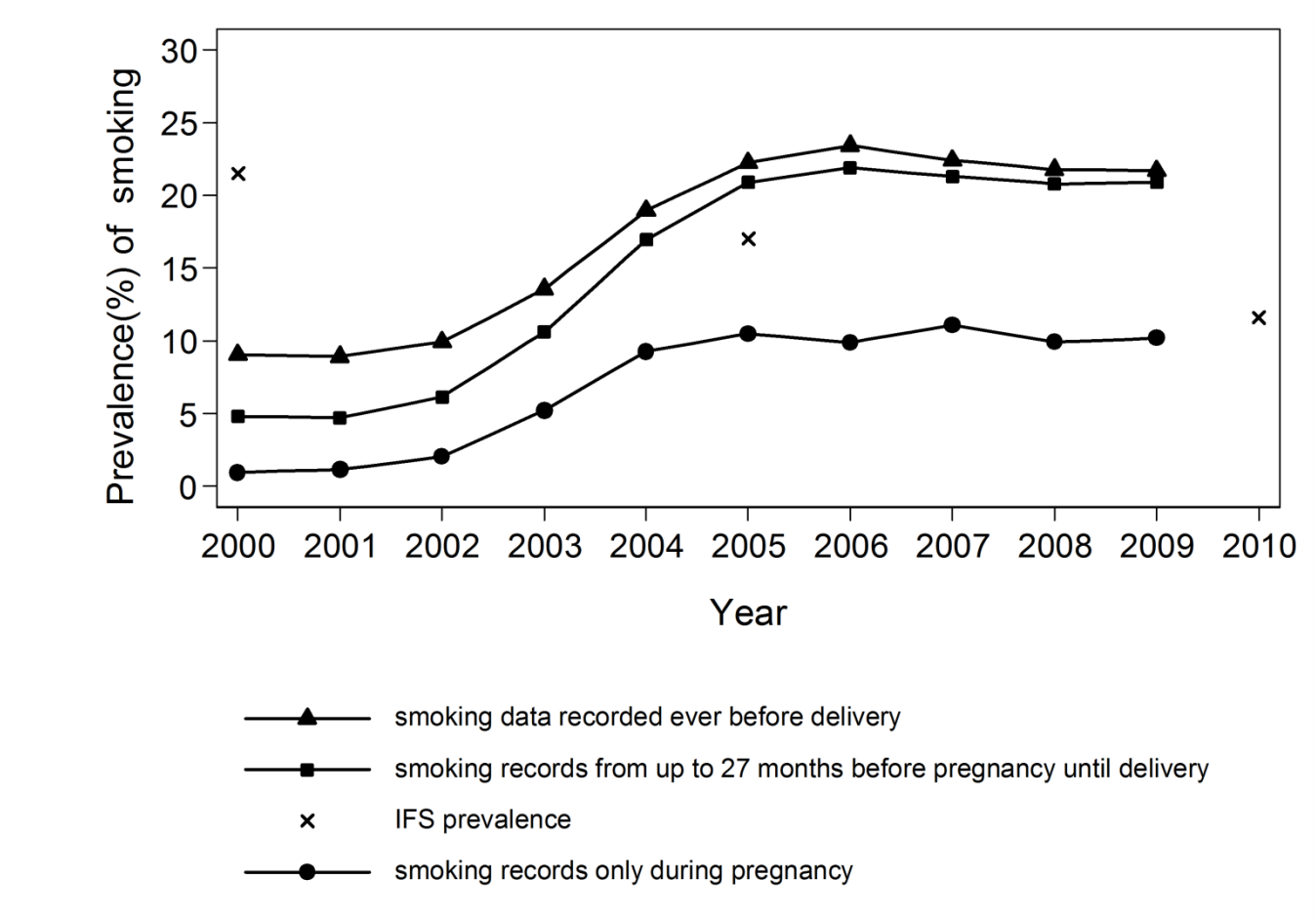
4.4.1 Population of pregnancies in THIN

The total study population consisted of 215,703 pregnancies from 495 practices across the UK; 177,010 of these women were registered with a GP in England and 20,188 were in Scotland. Out of the 495 practices contributing to THIN 378 were from England and 63 were from Scotland. The mean age at conception was 29.5 years (sd 5.9 years).

4.4.2 Comparison with IFS data

Figure 4-2 shows the prevalence of smoking at the time of delivery in women in THIN in relation to the corresponding measures in the IFS. Annual trends could not be compared as there were only two data points available. In 2000, none of the three prevalence estimates using THIN data were comparable to the IFS estimates. In 2005, smoking prevalence including data recorded up to 27 months before conception from THIN was slightly higher than the IFS estimate (17.0% vs. 20.9% respectively) however THIN prevalence using gestational smoking records was approximately seven percentage points lower than the IFS estimate. The THIN estimates were only available until 2009 therefore comparisons for the 2010 estimates were not possible. However, the IFS prevalence of smoking at delivery decreased to 11.6% in 2010 which is in good agreement with the THIN prevalence of (10.2%) in 2009 using gestational smoking records.

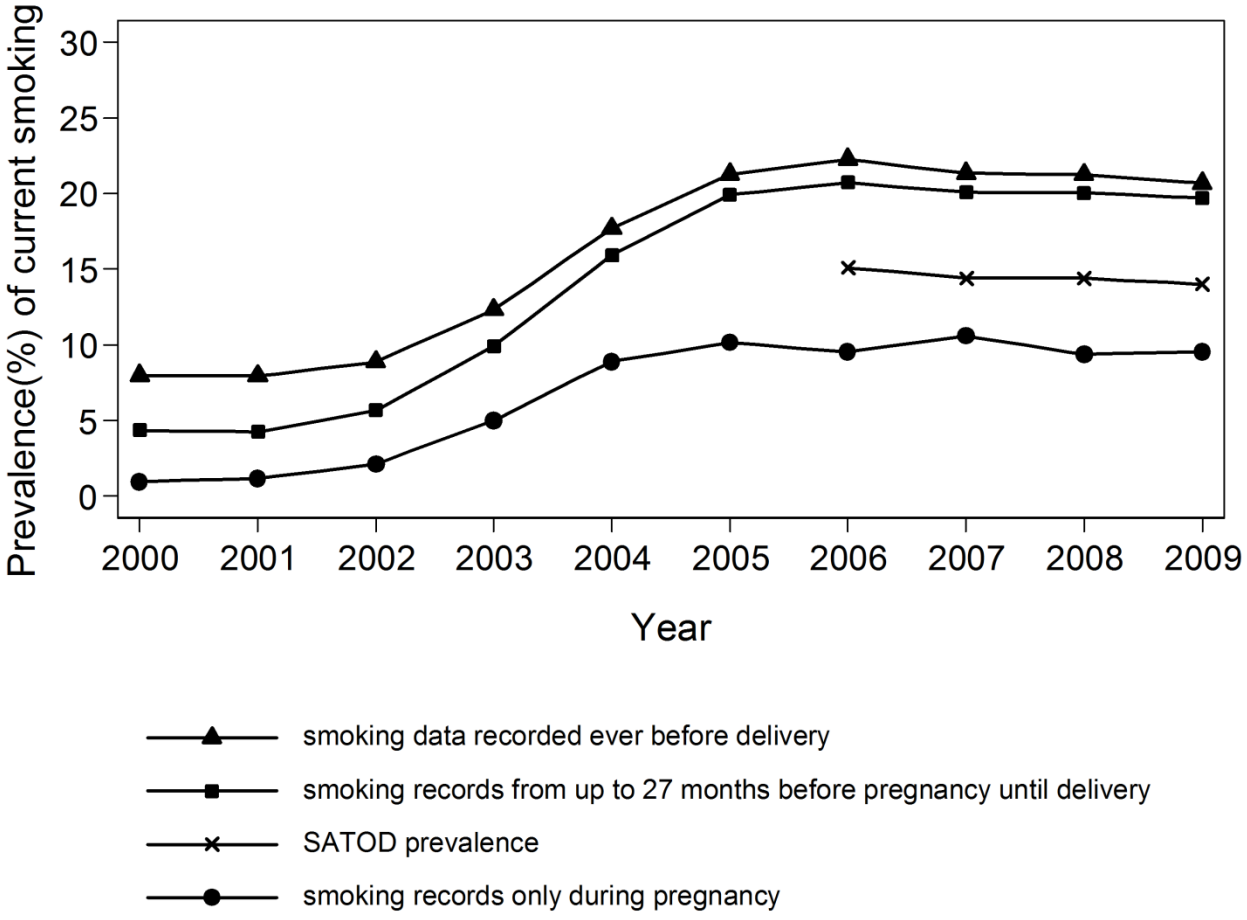
Figure 4-2 - Comparison of maternal smoking prevalence during pregnancy from IFS and THIN



4.4.3 Comparisons with SATOD data

When using smoking data recorded any time before delivery, the prevalence of smoking during pregnancy recorded in THIN was approximately seven percentage points higher than the SATOD estimates from 2006 to 2009. In comparison, the THIN prevalence considering data recorded up to 27 months before conception was approximately four to five percentage points higher over the four years of available data, while the THIN prevalence considering only records of smoking recorded during the gestational period was five percentage points lower than the SATOD estimates (Figure 4-3).

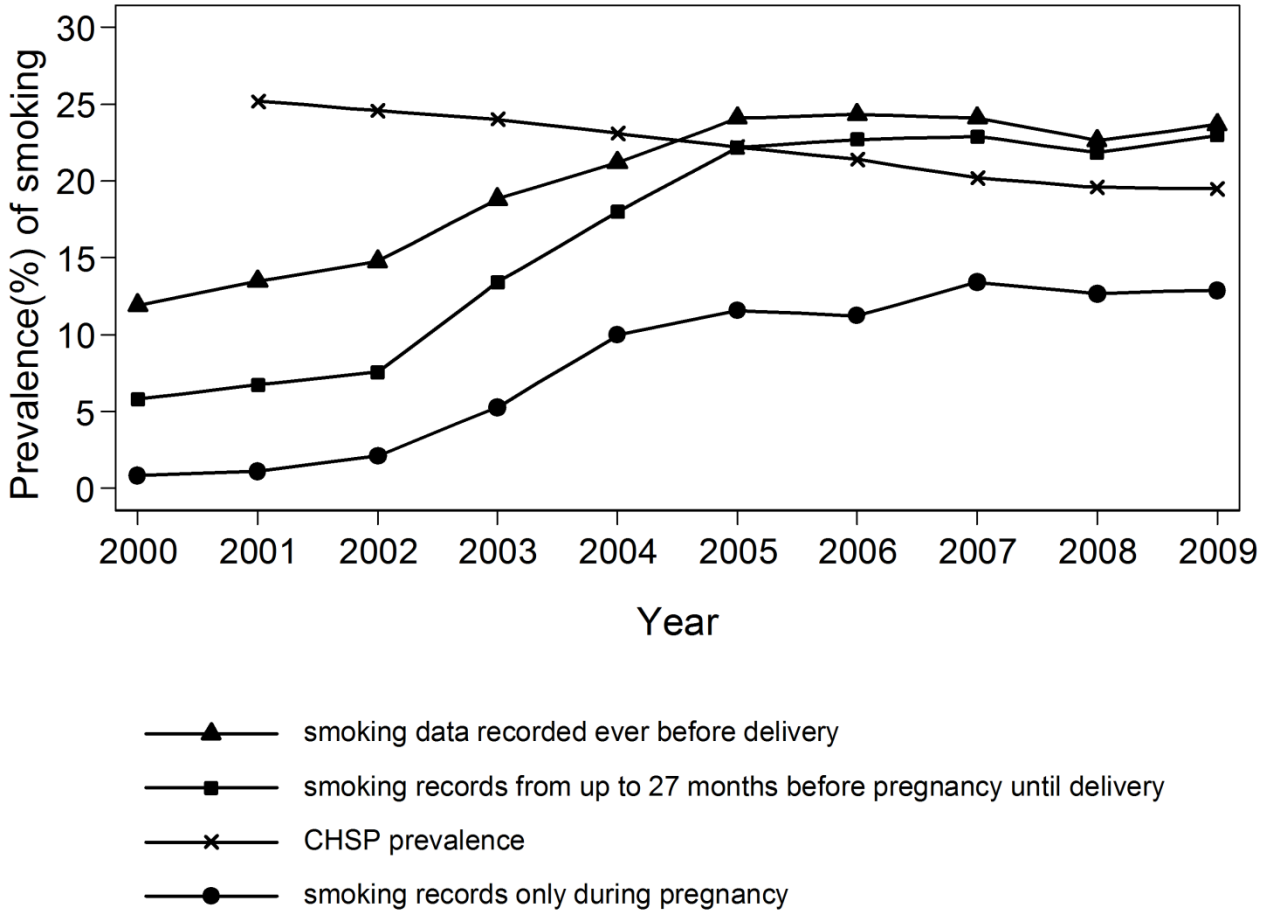
Figure 4-3 - Comparison of maternal smoking prevalence during pregnancy from SATOD and THIN



4.4.4 Comparisons with CHSP data

Using only records of smoking status entered during the gestational period, the THIN prevalence of maternal smoking status was low until 2004 (e.g. 43% of the CHSP prevalence of 23.1% in 2004) (Figure 4-4). It was 12.9% in 2009, approximately seven percentage points lower than the corresponding CHSP prevalence of 19.5%. Using smoking information recorded in the 27 months before pregnancy, the prevalence in CHSP and THIN converged in 2005. After this the THIN estimates were slightly higher than the CHSP estimates, such that in 2009 the THIN prevalence using data recorded up to 27 months before pregnancy was 22.9% compared to the CHSP prevalence of 19.5%. The prevalence estimates using data recorded ever before delivery were only slightly higher than the estimates using the data recorded up to 27 months before conception.

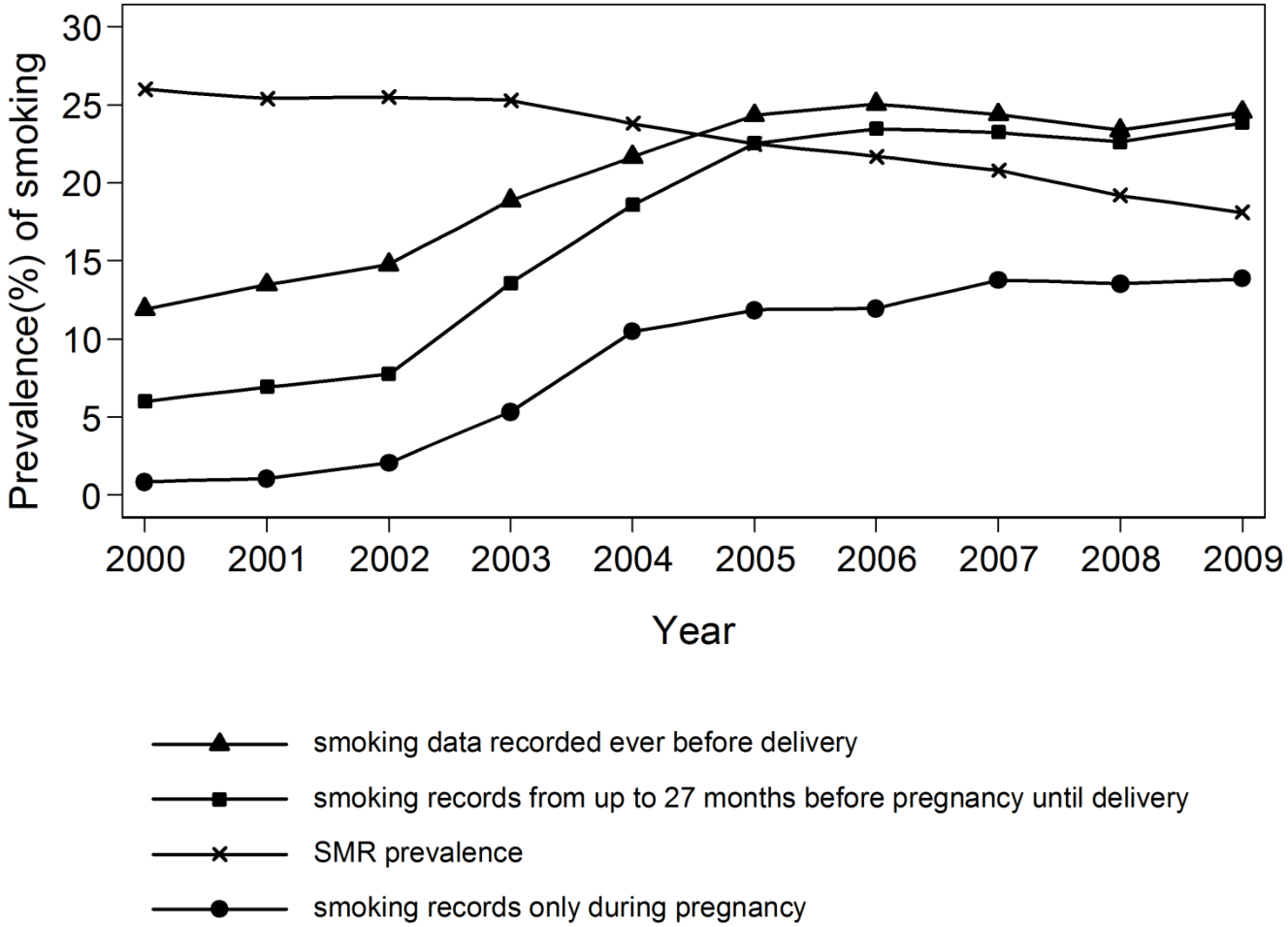
Figure 4-4 - Comparison of maternal smoking prevalence during pregnancy from CHSP and THIN



4.4.5 Comparison with SMR data

Using smoking status data recorded during the gestational period, the THIN prevalence was much lower than the SMR prevalence until 2004 (56% lower than the SMR prevalence of 23.8% in 2004, as shown in Figure 4-5). Prevalence in THIN was 13.8% in 2009 but was still 23% lower than the corresponding SMR prevalence of 18.1%. When including smoking information recorded up to 27 months before conception the two lines converged in 2005; in 2009 smoking prevalence in THIN was 23.8% using data recorded up to 27 months before conception and smoking prevalence using data recorded any time before pregnancy was 24.5% compared to the SMR prevalence of 18.1%.

Figure 4-5 - Comparison of maternal smoking prevalence during pregnancy from SMR and THIN



4.5 DISCUSSION

4.5.1 Principal findings

With current levels of completeness of smoking data in primary care records, it is not possible to produce population level estimates of smoking prevalence during pregnancy that are directly comparable to those derived from the existing data sources. The convergence between THIN estimates and estimates from other data sources has, however, improved over time. The comparability of THIN data to the SMR and CHSP surveys can be improved by the additional use of smoking status data recorded in the 27 months before conception but these to an extent may reflect smoking in general female population.

4.5.2 Strengths and limitations

This is the first study to assess the potential of primary care data to provide population level estimates of smoking during pregnancy and compare it with other current data sources in the UK. As discussed earlier, fertility rates in THIN are comparable to national fertility rates[153] and therefore the ascertainment of pregnancies is reasonably complete. However, like the other data sources under comparison, data on smoking status recorded in THIN are self-reported and women may not accurately report their smoking behaviour, particularly during pregnancy where there may be social stigma attached to smoking.[205] Underreporting of smoking during pregnancy may arguably be a particular problem in the IFS, where women are surveyed six to eight weeks after delivery.

A potential limitation of this work is the inclusion of pre-conception smoking records to predict smoking status during pregnancy, which may not be an accurate reflection of women's smoking status during pregnancy. Studies which have investigated smoking behaviour in early pregnancy indicate that many women attempt to quit when they find out they are pregnant or later during

pregnancy,[206] so it is unlikely that the inclusion of pre-conception records resulted in an under-estimation of smoking prevalence during pregnancy. It could however, lead to misclassification of some ex-smokers as smokers, resulting in an over-estimation of the prevalence of smoking during pregnancy in THIN. A substantial over-estimation is unlikely as approximately 35-50% of pregnancies in the UK are unplanned,[207,208] which means that only some women are likely to make positive behaviour changes such as quitting smoking before attempting to conceive. It may, however, hold true for some women who quit on confirmation of their pregnancy.

Another potential weakness of this study, and of primary care data, is that using primary care records it is difficult to determine the timing of smoking status ascertainment in relation to progress through gestation; this makes direct comparison with other data sources, obtained at booking or delivery, difficult. Lastly, smoking status during pregnancy is a complex and variable behaviour and it may fluctuate throughout pregnancy.[183] Therefore, single measures of smoking such as smoking at booking or smoking at delivery captured in SATOD, SMR and CHSP data are limited in their usefulness. Although these single measures may give a snapshot of smoking behaviour at a certain time, they may not give a complete picture of smoking behaviour throughout pregnancy. Hence, these data sources may provide population-level prevalence of maternal smoking at different points relative to pregnancy but do not contain information on changes in women's smoking status throughout pregnancy or postpartum period. IFS data assess smoking behaviour throughout pregnancy in more detail, albeit collected retrospectively. Nevertheless, these data are collected on a quinquennial basis and thus may become out of date quickly. A study with complete pregnancy follow-up and accurate assessment of smoking status and changes in women's smoking behaviour may be required for this. However, if smoking information was collected and recorded by GPs more frequently

throughout pregnancy, then primary care data may prove to be very useful to assess these changes in the smoking status of women during pregnancy but as shown in this study currently these data are not complete.

4.5.3 Interpretation in light of the current literature

To date, there are no studies assessing the validity of primary care data for quantifying the prevalence of smoking during pregnancy. A study comparing smoking prevalence recorded in THIN to smoking prevalence in the general population (measured by the General Lifestyle Survey (GLF)) found a good agreement between THIN and the GLF after 2008 and concluded that primary care data may provide an alternate means of monitoring national smoking prevalence.[149] Despite the smaller sample sizes at regional level, primary care data have also been shown to be a good means of monitoring regional smoking prevalence in the general population.[155]

The prevalence estimates of smoking during pregnancy from primary care do not accurately converge with other data sources because, at least in part, smoking status recording during pregnancy in primary care is incomplete.[20 209] Potential reasons for this have already been discussed in Section 3.6.3. This was shown in the previous study in this thesis which found that from 2000 to 2009 smoking status was only recorded in primary care for 28% of pregnancies. Nevertheless, this is to an extent similar to conducting a survey on a selected group of pregnant women from the population where smoking information may only be available on the women surveyed out of the whole population, which in this case is only available for women who were asked about their smoking status during pregnancy out of the whole primary care population of pregnant women.

Another possible explanation for the lower THIN prevalence could be that THIN over-represents general practices from more affluent areas of the UK. Since smoking prevalence is lower in women from more affluent groups, this may

slightly under-estimate the smoking prevalence generated using THIN data and account for some of the differences between THIN prevalence estimates and other data sources.

Whilst THIN estimates using only gestational smoking records do not approximate closely to annual prevalence from other data sources, THIN estimates using gestational smoking status show a close converging pattern with the data from SMR (collected at booking) in 2009. This is sensible as women see their GPs for initial care in pregnancy and implies that primary care data may be most useful to provide adequate data on smoking prevalence early in pregnancy, when most women see their GPs for initial care, compared to the time around delivery, when most women will be cared for essentially in secondary care facilities.

4.6 CONCLUSIONS

All existing data sources that measure smoking during pregnancy have their strengths and limitations. Primary care data have a great potential to measure smoking status during pregnancy at a population level. Although recording of gestational smoking status in THIN is improving over time, it is not adequately complete to produce maternal smoking estimates at a population level with most women just having a single record of smoking status throughout the course of pregnancy. Periodic recording of smoking status during pregnancy is important to monitor changes in smoking behaviour throughout pregnancy and to maintain and improve women's care before and after delivery. Although this information may be recorded and updated in hand-held maternity notes, there is currently no centralised recording system and the information in these notes is lost after delivery. Better integration of recording systems in primary care and midwifery services is required to improve communication and relay of relevant medical and lifestyle information including smoking status.

In terms of the further work in this thesis, it means that a cohort of pregnant smokers developed using smoking data recorded during gestation may not be representative of the UK population of pregnant smokers and some assumptions including use of pre-conception smoking records may need to be made in order to capture more women who smoke during pregnancy. Using gestational smoking records to create a cohort of smokers for studying the trends in the epidemiology of NRT prescribing in pregnant women in the later chapters will result in an underestimation of smokers. Therefore, a more exhaustive approach is needed to define the denominator of smokers for further analysis in this thesis. Smoking records from 27 months before conception were therefore included where no gestational smoking records were available. The comparability of THIN measures with prevalence measures from other data sources increased by including smoking information recorded within 27 month before conception and therefore this will provide a more appropriate denominator for further analysis in the thesis especially after 2004 as the recording of smoking status improved after the introduction of QOF. Another important consideration which was highlighted in this chapter was that even when considering the smoking records from 27 months before conception, the comparisons for earlier years i.e. 2000-2003 are not good, so it may be more appropriate to also use all pregnant women as a denominator for the later analysis in addition to pregnant smokers to rule out any bias that may arise due to the changes in smoking data quality over time.

5 PRESCRIBING OF NICOTINE REPLACEMENT THERAPY IN AND AROUND PREGNANCY

5.1 INTRODUCTION

As discussed in Section 1.5, NRT has been available on NHS prescription since 2001; however, it was only in 2003 that the BNF changed its instructions for NRT use in pregnancy to a caution from a contraindication.[96] The 2005 MHRA review concluded that despite a lack of conclusive evidence for efficacy, NRT use was likely to be less harmful than smoking,[97] consequently broadening the UK licensing arrangements for NRT to include pregnant women in December 2005.[98] It is now widely available and recommended for smoking cessation in pregnant women in the UK, based on the theoretical notion that it is safer to use NRT during pregnancy than to smoke. The BNF clearly states that the use of NRT in pregnancy is preferable to the continuation of smoking but should be used only if smoking cessation without NRT fails.[210]

NRT use is also recommended in guidelines for smoking cessation in pregnancy, where cessation without NRT fails.[79,124] However, information on NRT prescribing and use in pregnant women is lacking worldwide. In light of this, the WHO recently recommended an urgent need for studies on surveillance of current use of NRT in pregnancy.[73] Literature describing NRT use in pregnancy is limited to observational studies from the USA and Denmark assessing the association between NRT use during pregnancy and adverse birth outcomes. The prevalence of self-reported NRT used in the first 12 weeks of gestation was 0.3% [114], 2-2.5% in 17-27 weeks of gestation in the Danish National Birth Cohort [112,113] and in the Pregnancy Risk Assessment Monitoring System (PRAMS) from four USA states it was 3.9% (2004).[111] Since then, new NRT products have been introduced and international guidelines on gestational NRT use have changed. Thus far, only a limited number of studies in the UK have assessed prescribing

and uptake of NRT during pregnancy in the UK and these studies are either too small,[116] providing local data [116,131] or only including prescribing taking place in the NHS-SSS.[132] It is also important to know the NRT prescribing trends for pregnant women by different maternal factors as the prevalence of maternal smoking varies by different maternal factors (e.g. age, socioeconomic status etc.[59]). Therefore, investigation of factors related to NRT prescribing may give an insight on the characteristics of women who attempt to quit smoking during pregnancy and whether targeted interventions are needed for women with specific characteristics. However, none of these previous studies have assessed these in detail. The generalisability of the findings from the previous is therefore limited. Furthermore, none of the previous studies have assessed changes in prescribing after the relaxation of the licensing arrangements for NRT which is important to assess the effect of this change on the prescribing rules. Therefore, this chapter aims to assess the prescribing of NRT in and around pregnancy, using the UK primary care data. This will potentially provide population-based estimates for NRT prescribing in pregnant women which can be generalisable to the whole of the UK, which previous studies have failed to do. The specific objectives for the study discussed in this chapter are:

1. To examine patterns of NRT prescribing before, during and after pregnancy
2. To calculate annual prescribing prevalence of NRT before, during and after pregnancy to inform changes in relation to the MHRA relaxation
3. To assess whether and how NRT prescribing varies by maternal characteristics

This study was published in the *British Journal of General Practice* in September 2014 and attached as Appendix 10.4.

5.2 METHODS

5.2.1 Study population

The study population for this analysis was restricted to all pregnancies between January 2001 and September 2009 in women of childbearing age (15-49 years) which resulted in either a live birth or a stillbirth, as NRT only became available on NHS prescription in 2001.

5.2.2 Extracting smoking status, NRT prescribing and other covariates

All prescriptions for NRT were extracted, using multilex drug codes for all the NRT formulations available in the UK according to the BNF (Appendix 10.6) which may be used by the GPs to prescribe NRT in primary care .[210] To investigate the maternal factors that may be associated with NRT prescribing during pregnancy, data were extracted on women's age at conception, socioeconomic deprivation as measured by quintiles of the Townsend Index of deprivation,[177] pre-conception BMI and recorded diagnoses of medical conditions (hypertension, diabetes, asthma, and mental illness) as described in Section 3.4.3. These conditions are most prevalent in women of childbearing age and are closely related to smoking[51,59,195,211,212] and therefore may also influence quit attempts made using NRT.

5.2.3 Statistical analysis

The overall and annual proportions of pregnancies with one or more NRT prescriptions before, during and after pregnancy were determined. This was repeated restricting the denominator to pregnancies in smokers only (making use of gestational smoking data and smoking information from 27 months before conception). A period of nine months before and after pregnancy was used to calculate prescribing prevalence, as this was similar to the average pregnancy length allowing for comparisons of period prevalence. There is no evidence of the time before and after pregnancy during which smokers are more likely to

attempt to quit. However, since nine months is a comparatively long time and smoking behaviours may fluctuate during this time, prescribing prevalence of NRT was also assessed in smaller three month windows before, during and after pregnancy. In addition, the use of different forms of NRT (patches, gum, nasal spray, lozenges, sublingual tablets, and inhalator cartridges) and combination NRT was also assessed. Oromucosal nicotine spray was first authorised for use in November 2010[213] and therefore was not included in this analysis.

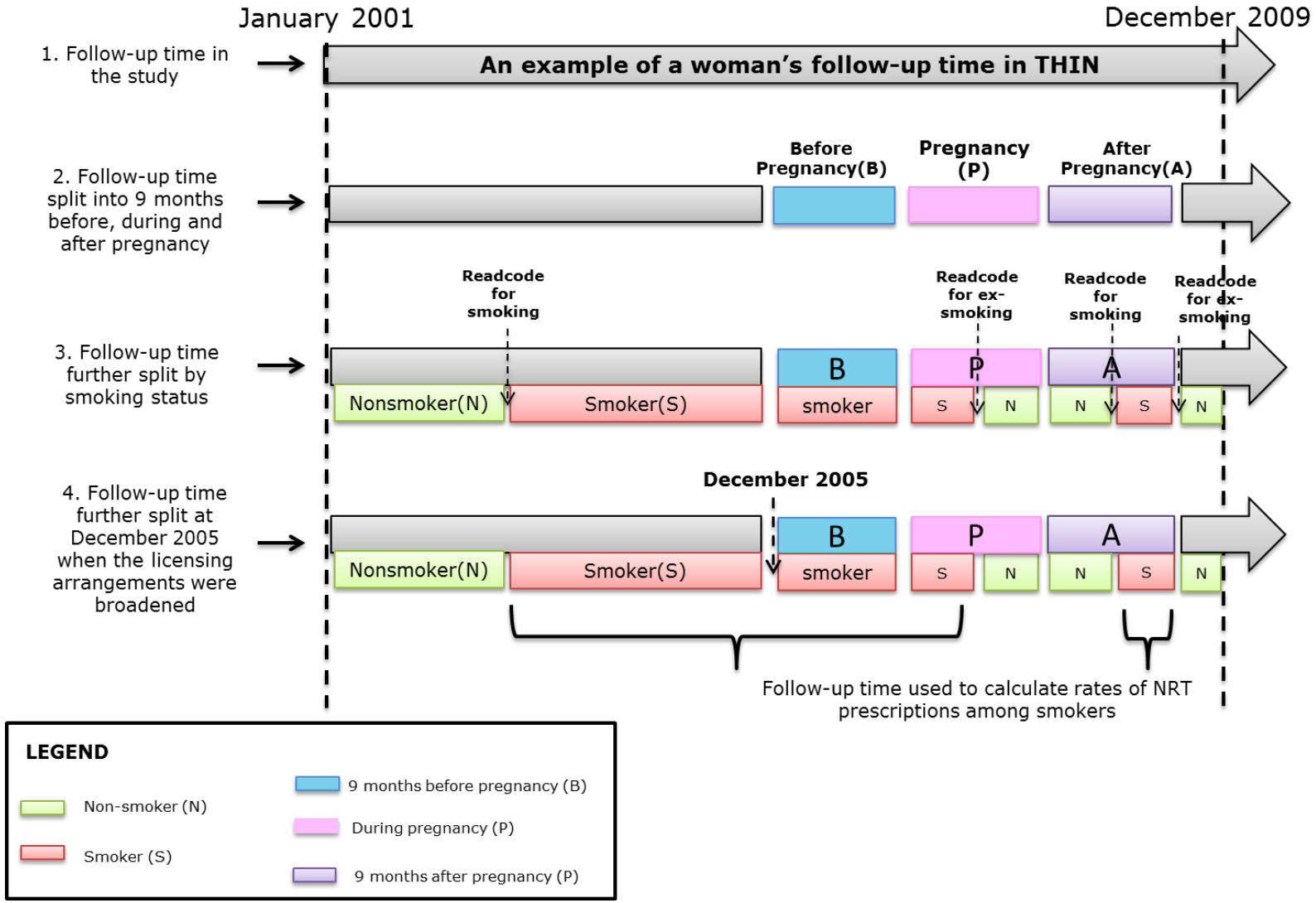
Logistic regression was used to calculate ORs for associations between women's characteristics and NRT prescribing to smokers during pregnancy, restricting the analysis to pregnancies delivered between January 2006 and December 2009 since NRT was not licensed for use in pregnancy until December 2005 and therefore prescribing was not expected to be very frequent. Likelihood ratio tests (LRT) were used to assess the associations with categorical covariates and Wald p-values were used for binary covariates. All covariates that reached statistical significance ($p<0.05$) in the univariable analysis were initially included in the multivariable analyses and each covariate was sequentially dropped from the model to assess whether the associations were still significant. Covariates that reached statistical significance ($p<0.05$) in the multivariable analysis were retained in the final model. As some women had more than one pregnancy during the study period, this potential clustering of pregnancies within women was accounted for by calculating robust CIs around the odds ratios using the clustered sandwich estimator, [180,181] which is explained in Section 3.4.4.

5.2.4 Sensitivity analysis

In addition to calculating overall proportions, rates of prescriptions per 1,000 person-years were also calculated as this allowed for better categorisation of time windows before, during and after pregnancy (nine months), controlling for possible fluctuations in smoking status. The study time was split into times

before, during and after pregnancy to accurately assess the rates of NRT prescribing for smokers in each of the three time periods. Smoking was treated as a time-varying covariate using lexis expansion i.e. women's smoking status was allowed to change at every point of smoking status recording in their primary care data to capture women's smoking episodes more accurately. Figure 5-1 explains the step-by-step splitting of the follow-up time for each woman by pregnancy time and smoking status. The follow-up time was further split into times before and after the relaxation of NRT licensing arrangements in December 2005. The rates of NRT prescriptions per 1,000 person-years were calculated before, during and after pregnancy in two time periods (2001 to 2005 and 2006 to 2009). Finally, rate ratios and 95% CIs were calculated to compare prescribing in smokers before and after the relaxation of licensing arrangements in the three time periods, using poisson regression.

Figure 5-1 - Step-by-step splitting of the study follow-up time by smoking status and pregnancy time



5.3 RESULTS

5.3.1 Baseline characteristics

A total of 201,465 women were identified with 255,411 pregnancies resulting in live births or stillbirths between January 2001 and December 2009, of which 45,045 (18%) were pregnancies of mothers classified as smokers. The mean age at conception was 29.5 years (sd 5.9) and the average length of pregnancy was 39.4 weeks (sd 2.2). Table 5-1 describes women's characteristics for all pregnancies and pregnancies among smokers, and NRT prescribing prevalence according to these characteristics. In the whole population, asthma, diabetes, hypertension and mental illness affected 9%, 2%, 3% and 9% of pregnancies respectively. Only the prevalence of asthma and mental illness were higher in smokers.

Table 5-1 - Baseline characteristics of the study population

	Total pregnancies (n=255,441)	Pregnancies with an NRT prescription (total n=4,826)		Pregnant smokers* (n=45,045)	Pregnant smokers with an NRT prescription (n=4,826)	
Age at Conception						
15-19 years	19,212	636	(3.3%)	6,716	623	(9.3%)
20-24 years	43,569	1,227	(2.8%)	12,300	1196	(9.7%)
25-29 years	69,159	1,237	(1.8%)	11,620	1223	(10.5%)
30-34 years	78,034	1,103	(1.4%)	9,246	1086	(11.7%)
35-39 years	38,764	527	(1.4%)	4,412	523	(11.9%)
40-44 years	6,384	90	(1.4%)	712	89	(12.5%)
45-49 years	319	6	(1.9%)	39	6	(15.4%)
Townsend score in quintiles **						
Quintile 1 – least deprived	57,859	486	(0.8%)	5,339	474	(8.9%)
Quintile 2	47,841	586	(1.2%)	6,118	582	(9.5%)
Quintile 3	49,670	921	(1.9%)	8,797	904	(10.3%)
Quintile 4	47,292	1,315	(2.8%)	11,376	1,295	(11.4%)
Quintile 5 - most deprived	36,103	1,188	(3.3%)	10,515	1,166	(11.1%)
Missing	16,676	330	(2.0%)	2,900	325	(11.2%)
Pre-conception Body Mass Index						
Normal(18.0-24.9)	80,003	1,502	(1.9%)	15,040	1,483	(9.9%)
Underweight(<18.0)	5,871	152	(2.6%)	1,630	151	(9.3%)
Overweight(25-29.9)	38,931	784	(2.0%)	7,306	771	(10.6%)
Obese(>=30)	26,753	617	(2.3%)	5,500	603	(11.0%)
Missing	103,883	1,771	(1.7%)	15,569	1,738	(11.2%)
Asthma	21,884	678	(3.1%)	5,216	670	(12.8%)
Hypertension	6,885	107	(1.6%)	966	107	(11.1%)
Diabetes	5,971	114	(1.9%)	939	114	(12.1%)
Mental illness	24,178	947	(3.9%)	7,166	937	(13.1%)

*recorded as current smoker within 27 months before conception until delivery, **socioeconomic status

5.3.2 Patterns of NRT prescribing in and around pregnancy

NRT was prescribed in a total of 4,826 pregnancies, which represents a prescribing prevalence of approximately 2% of all pregnancies and 11% of pregnancies in smokers. In comparison, the prescribing prevalence was 1% during both the nine months before and after pregnancy and approximately 5% in pregnancies in smokers. Figure 5-2 shows the prescribing prevalence in each three-month period before, during and after pregnancy in all pregnant women and Figure 5-3 shows the prescribing prevalence among pregnant smokers. Among smokers, NRT prescribing was more prevalent during the first and second trimester, with a prescribing prevalence of just over 5% in each compared to approximately 2.5% in the third trimester, which was similar to the periods before and after pregnancy.

Figure 5-2 - Proportion of all pregnancies with NRT prescription in each three month period, between 2001 and 2009

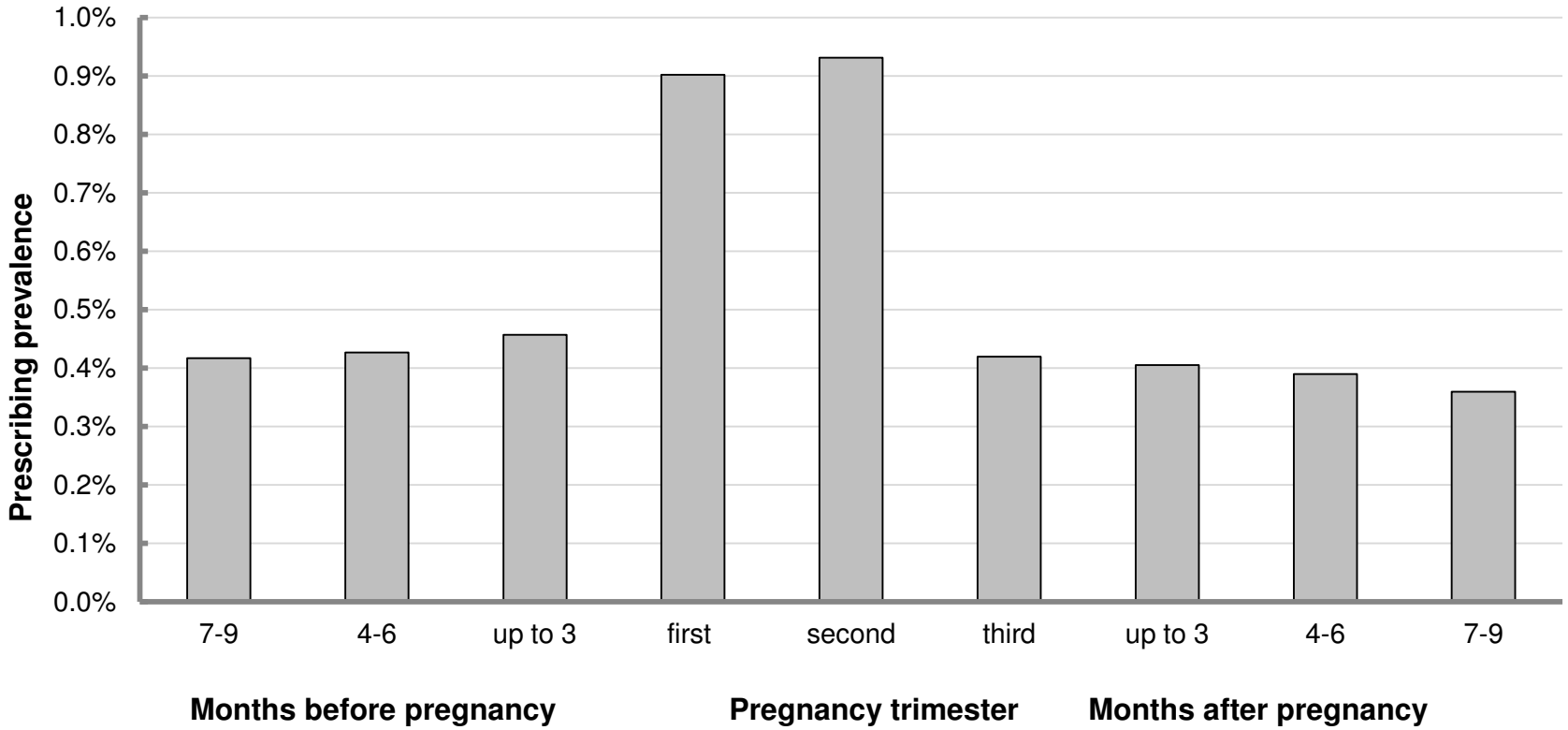
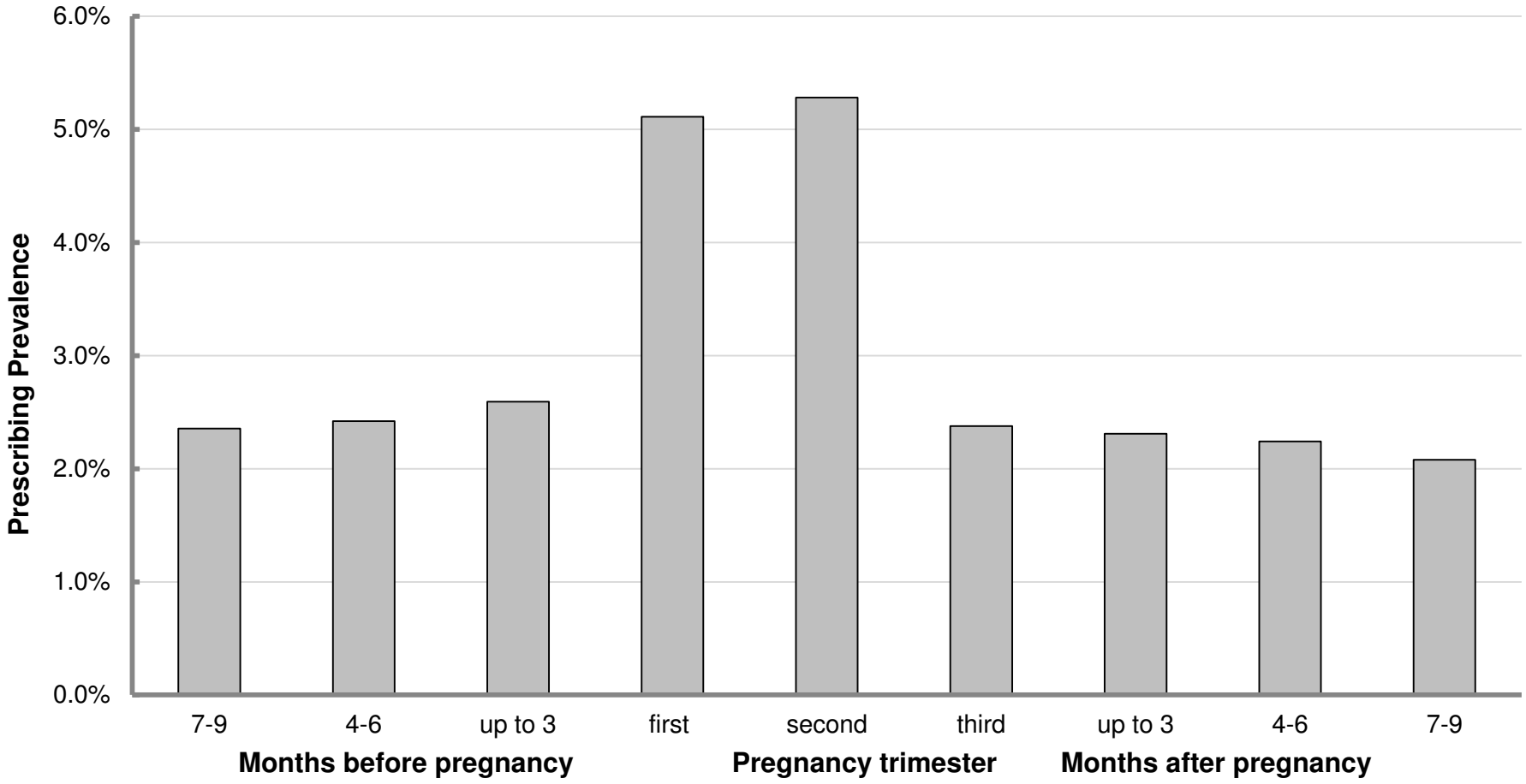
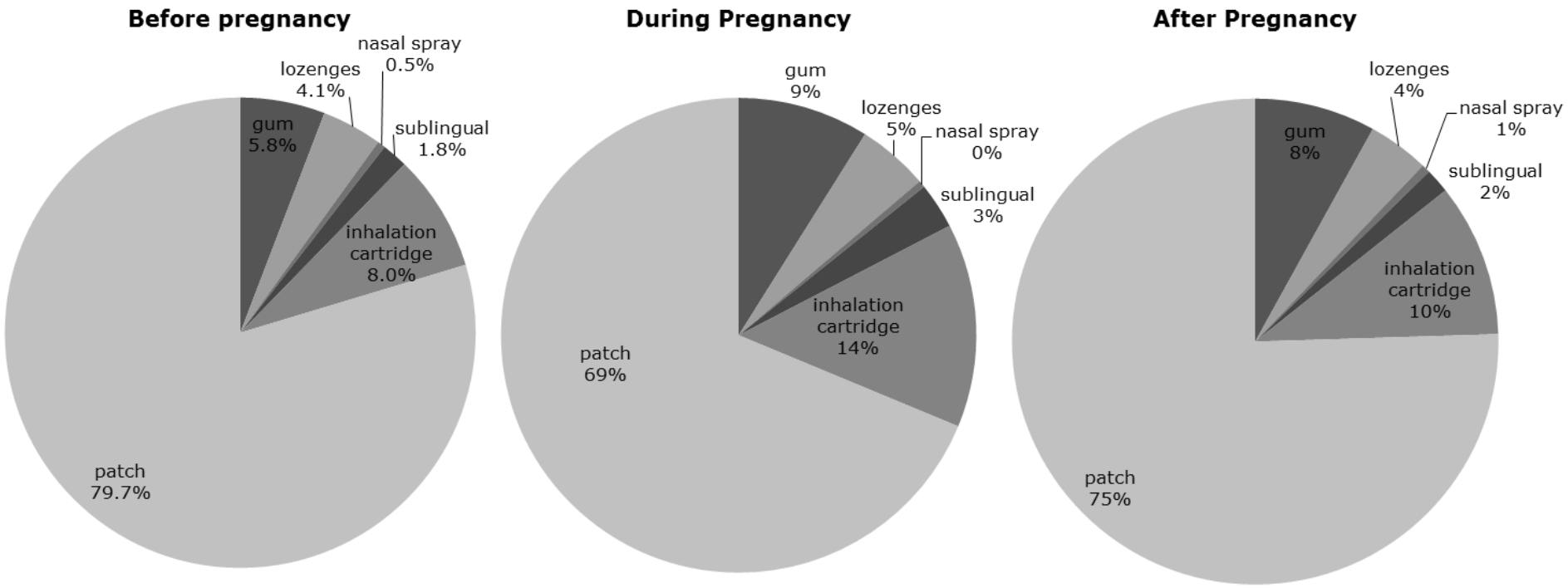


Figure 5-3 - Proportion of pregnant smokers with NRT prescription in each three month time period, between 2001 and 2009



Among the 4,826 women who were prescribed NRT during the nine months of pregnancy, over half of these (56%) were only issued one prescription for NRT. Another quarter of these women were prescribed NRT on two separate occasions. The maximum number of prescriptions issued during pregnancy was 26. On average, women were prescribed a total of 2 weeks' worth of NRT (IQR 1-2 weeks). The frequency of NRT prescribing nine months before and after pregnancy was similar to the pattern within pregnancy, with over half of the women receiving only a single prescription for NRT in each nine month period. In approximately two thirds of the pregnancies in which NRT was prescribed during gestation NRT prescribing was initiated only during pregnancy; there were no records of NRT prescriptions in these women's primary care data prior to the start of pregnancy. The most common form of NRT used during pregnancy was transdermal patches (approximately 70% of all prescriptions), followed by inhalator cartridges (14%), gum (9%), lozenges (5%), sublingual tablets (3%) and nasal spray (0.5%). The distribution of NRT forms prescribed before and after pregnancy was very similar. Figure 5-4 describes the distribution of different forms of NRT prescribed before, during and after pregnancy. Prescribing of combination NRT was observed in 471 (10%) of the 4,826 women where NRT was prescribed during pregnancy, 204 (8%) of 2,645 mothers with NRT prescriptions before pregnancy and 273 (11%) of 2,410 mothers with NRT prescriptions after pregnancy.

Figure 5-4 - Use of different forms of NRT before, during and after pregnancy



5.3.3 Annual prescribing of NRT before, during and after pregnancy

Figure 5-5 shows the annual proportion of pregnancies and Figure 5-6 shows the proportion of pregnancies in smokers between 2001 and 2009 where NRT was prescribed before, during and after pregnancy. In 2001, the prescribing prevalence of NRT during pregnancy, taking all pregnancies as the denominator, was 0.03% (0.7% in pregnancies in smokers). This increased to 2.6% (11.5% in pregnancies in smokers) in 2005 after which it remained stable such that in 2009 the prescribing prevalence of NRT in all pregnancies was 2.6% (11.2% in pregnancies in smokers). The overall prescribing prevalence of NRT during pregnancy between 2001 and 2005 (i.e. before the relaxation of licensing arrangements) was 1.1 %(9.6% in pregnancies in smokers) and increased to 2.5% (11.1% in pregnancies in smokers) for the period of 2006-2009 (time after the relaxation of licensing arrangements). NRT prescribing prevalence in the nine months before and after pregnancy increased until 2005 after which it remained stable at around 1% (6% in smokers), with a slight decline after 2006.

Figure 5-5 - Annual prescribing prevalence of NRT in all pregnancies

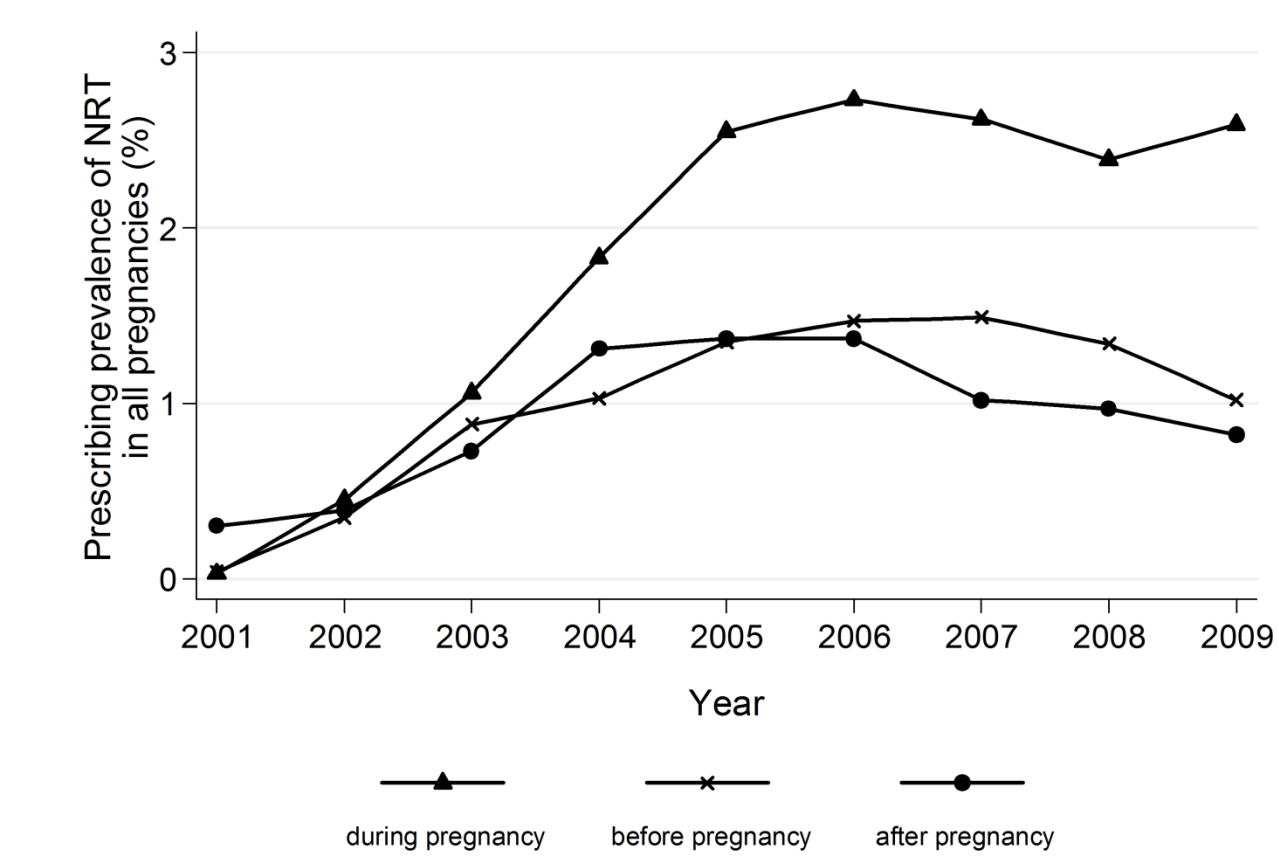
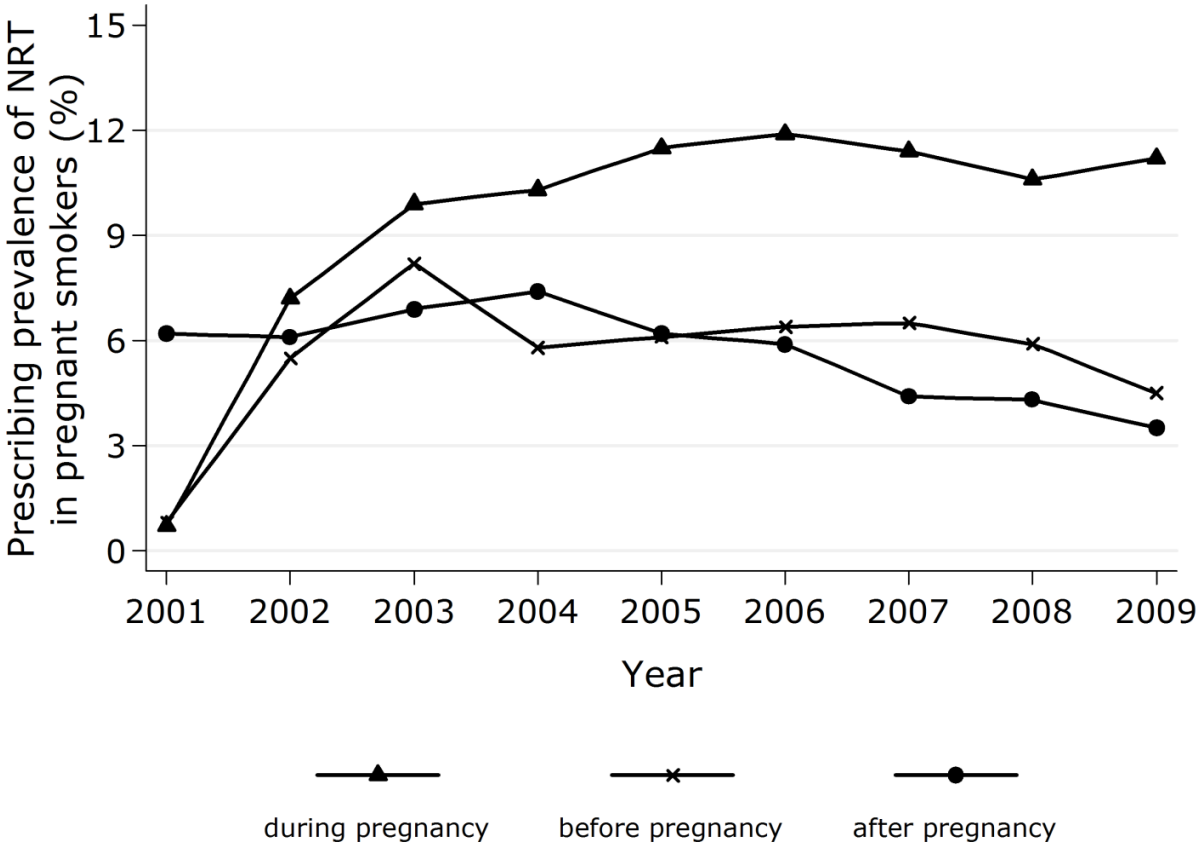


Figure 5-6 - Prescribing prevalence of NRT in pregnant smokers



5.3.4 Prescribing of NRT by maternal characteristics

Table 5-2 shows the maternal characteristics associated with prescribing of NRT within pregnant smokers between 2006 and 2009. Pregnant smokers from more deprived groups were more likely to receive an NRT prescription compared to pregnant smokers from less deprived groups (OR for Quintile 5 compared to Quintile 1= 1.33, 95% CI 1.14-1.52) and older pregnant smokers were more likely to receive NRT than younger smokers (OR for 30-35 years compared to 25-30 = 1.21, 95% CI 1.09-1.35). Pregnant smokers with a diagnosis of asthma were 34% more likely to be issued an NRT prescription in primary care compared to pregnant smokers without asthma (OR 1.34, 95% CI 1.21-1.50). In addition, pregnant smokers with a diagnosis of mental illness were 29% more likely to receive a prescription for NRT during pregnancy compared to pregnant smokers without mental illness (OR 1.29, 95% CI 1.18-1.43).

Table 5-2 - Prescribing of NRT during pregnancy in smokers by maternal characteristics between January 2006 and December 2009

Demographic variables	Pregnant smokers with one or more NRT prescriptions (n=3,160)	Unadjusted Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)**	p-value
Age at conception					
15-20 years	430 (10.1%)	0.91 (0.80-1.02)		0.89 (0.78-1.00)	
20-25 years	833 (10.6%)	0.96 (0.86-1.06)	<0.001	0.94 (0.85-1.04)	<0.001
25-30 years	801 (11.0%)	1		1	
30-35 years	692 (12.8%)	1.19 (1.07-1.32)		1.21 (1.09-1.35)	
35-40 years	337 (12.5%)	1.15 (1.00-1.32)		1.18 (1.03-1.35)	
40-45 years	63 (13.8%)	1.29 (0.98-1.69)		1.28 (0.97-1.69)	
45-49 years	4 (16.7%)	1.61 (0.55-4.73)		1.58 (0.53-4.71)	
Townsend score					
Quintile 1 (least deprived)	285 (9.4%)	1		1	
Quintile 2	384 (10.3%)	1.10 (0.94-1.30)	<0.001	1.11 (0.94-1.31)	<0.001
Quintile 3	611 (11.0%)	1.20 (1.04-1.39)		1.23 (1.05-1.43)	
Quintile 4	880 (12.2%)	1.35 (1.17-1.56)		1.39 (1.20-1.61)	
Quintile 5 (most deprived)	766 (11.6%)	1.28 (1.10-1.47)		1.33 (1.14-1.52)	
Missing	234 (12.6%)	1.39 (1.16-1.67)		1.43 (1.21-1.76)	
Pre-conception Body Mass Index (kg/m^2)					
Normal(18.0-24.9)	1,036 (11.1%)	0.89 (0.2-1.09)			
Underweight(<18.0)	104 (10.0%)	1	0.549	-	-
Overweight(25-29.9)	532 (11.3%)	1.02 (0.91-1.35)			
Obese(>=30)	433 (11.8%)	1.06 (0.94-1.19)			
Missing	1,055 (11.4%)	1.03 (0.94-1.13)			
Diabetes *	86 (13.5%)	1.23 (0.98-1.56)	0.078	-	-
Hypertension*	71 (12.2%)	1.09 (0.85-1.41)	0.476	-	-
Asthma*	477 (14.4%)	1.37 (1.24-1.53)	<0.001	1.34 (1.21-1.50)	<0.001
Mental illness*	612 (13.9%)	1.34 (1.22-1.47)	<0.001	1.29 (1.18-1.43)	<0.001

NRT – Nicotine Replacement Therapy, CI – confidence interval, * compared to women without the condition **all covariates mutually adjusted

5.3.5 Sensitivity analysis

A total of 201,465 women contributed 669,230 person-years before pregnancy, 927,952 person-years during pregnancy and 971,754 person-years after pregnancy giving a total person time of 2,568,936 years. The rate of NRT prescribing during pregnancy in smokers between 2001 and 2005 was 34.1 prescriptions per 1000 person-years (95% CI 34.1-33.0), equating to approximately 3.4% of women annually. The rate of NRT prescribing in the nine months before and after in women during pregnancy was 30% lower than the rates of prescribing during (RR 0.70, 95% CI 0.66-0.73) each. After the relaxation of licensing arrangements in December 2005 this rate of prescribing during pregnancy increased to 68.3 per 1000 person-years equating to approximately 7% of women annually. The gradient between prescribing during pregnancy and outside increased such that women were 45% less likely to receive an NRT prescription before pregnancy (RR 0.55,95% CI 0.52-0.58) and 52% less likely to receive a prescription after pregnancy (RR 0.48, 95% CI 0.46-0.50) compared to during pregnancy.

Table 5-3 - Time specific rates and rate ratios of NRT prescribing

Exposure time	No. of Prescriptions	Person-years	Rate*	95% CI	RR	95% CI
		2001-2005				
9 months before pregnancy	2,535	107,857	23.5	22.5-24.5	0.70	0.66-0.73
During pregnancy	3,701	108,476	34.1	34.1-33.0	Reference	
9 months after pregnancy	1,994	84,671	23.6	22.5-24.6	0.70	0.66-0.73
		2006-2009				
9 months before pregnancy	2,107	561,373	37.5	35.9-39.2	0.55	0.52-0.58
During pregnancy	5,594	819,476	68.3	66.5-70.1	Reference	
9 months after pregnancy	2,892	887,083	32.6	31.4-33.8	0.48	0.46-0.50

*rate of NRT prescribing per 1000 person-years
RR – Rate Ratio, CI – Confidence interval
Total number of women=201,465

5.4 DISCUSSION

5.4.1 Principal findings

After NRT was made available on NHS prescription in 2001 prescribing in and around pregnancy increased; by 2005 prescribing was twice as high during pregnancy as that in the nine months immediately before and after pregnancy, despite it being contraindicated for pregnant women. The December 2005 licence relaxation to allow prescribing in pregnancy did not further increase these trends and the prescribing prevalence during pregnancy has remained stable at 2% (11% in smokers). Women with asthma or mental illness and those from more socio-economically deprived areas were more likely to receive prescriptions during pregnancy. However, 80% women received less than 2 prescriptions, lasting two weeks on average.

5.4.2 Strengths and limitations

This study presents longitudinal and contemporaneous prescribing estimates; it is the first study of NRT prescribing during pregnancy in the UK primary care and the only study internationally to assess NRT prescribing trends. The ascertainment of NRT in this study is based on prescribing data rather than the self-reported NRT use, which women may under-report.[112] Additionally, prescribing in the nine month periods immediately before and after pregnancy has also been assessed in this study, whereas other studies only report NRT use in trimesters 1-2.[112-114,129] Therefore, the findings of this study are novel in that they present the first estimates of NRT prescribing around pregnancy, which provides some information on smoking cessation attempts pre-conception and postpartum.

The data used in this study capture all NRT prescribing to pregnant women in UK primary care in practices registered in THIN. However, this may not include NRT prescribing in other settings such as local NHS Stop Smoking Services for

Pregnant women (SSSP) and NRT purchased over-the-counter or off the shelf. Only 3% of pregnant women use the SSSP on average each year[214,215] and a survey of all SSSPs in England conducted between April 2010 and March 2011 reported that almost half of the NRT provided by these services was issued through GPs.[185] In terms of self-purchased NRT, this is expected to be infrequent for several reasons. Firstly, the prevalence of medication use without health professional consultation is lower during pregnancy than when women are not pregnant.[216] Furthermore, all NRT packaging, clearly instructs women to consult a doctor before using this if they are pregnant. Lastly, in the UK women are entitled to free NHS prescriptions during pregnancy and the first year after delivery[217] so they may be more likely to get free prescriptions through GPs than paying for NRT. Hence, this study is believed to capture the majority of the prescriptions of NRT issued.

Some women may quit or relapse after delivery consequently leading to changes in the denominator of smokers and therefore the NRT estimates could be both over-estimated if more women relapse than are recorded and under-estimated if more women quit. Therefore, prescribing prevalence is also reported in all pregnancies in addition to smokers. Also, in these data over 75% of pregnant women who were classified as smokers during pregnancy and who had a recording of smoking status within the nine months after delivery were still recorded to be smokers. Hence, a substantial over-estimation or under-estimation of NRT prescribing prevalence in smokers is unlikely. The rates of NRT prescribing were also calculated, treating both smoking and pregnancy as time-varying covariates, to take into account the changes in women's smoking status over time. These rates were found to be slightly lower than the calculated NRT prescribing prevalence in smokers (~7% compared to ~11% after 2005). This is because although rates allow for more appropriate categorisation of time and exposure windows, the recording of smoking status during pregnancy is

incomplete as discussed in Chapter 3, masking the true reflection of smoking status changes over time and consequently limiting the advantage of using lexis expansion for this analysis. Nevertheless, the rate ratios using poisson regression were in concordance with the other results reiterating that NRT prescribing during pregnancy was almost double that of the prescribing before and after pregnancy in the post-relaxation period (RR 0.55 before pregnancy and RR 0.48 after pregnancy).

Another potential limitation of the study is that prescriptions provide no measures of actual medication use, compliance to the drug therapy or successful quit attempts made and some of the prescriptions issued may not have been redeemed. However, a validation study comparing the recorded prescriptions for smoking cessation medications in THIN and the NHS dispensing data between January 2004 and December 2005 reported good comparability between the two data sources indicating that prescriptions recorded for smoking cessation medications in primary care data are collected by the patients.[156] The only measures of compliance are available from trials. The SNAP trial reported low compliance rates in both treatment and placebo group (7.2% and 2.8% respectively using NRT for more than a month).[100] However, the reasons for low compliance remain unexplored. A qualitative study conducted on pregnant smokers in Australia explored barriers to NRT use and found that women with medical problems or history of obstetric complications expressed doubts about using NRT and were sceptical about its effectiveness.[118] However, specific reasons for low compliance rates to NRT during pregnancy have not been studied to date. Lastly, there were no measures available for nicotine dependence in the data. Assessing these measures of dependence (e.g. Fagerstrom Test for Nicotine Dependence) is difficult without surveying the study participants which would be limited by potential response biases and are rarely possible on the large population scale presented by the data in this study.

5.4.3 Comparison with current literature

There are no studies internationally which have assessed the annual prescribing prevalence of NRT in pregnant women in detail. However data from nested case-control studies from the USA and Denmark assessing associations between NRT use and adverse pregnancy outcomes report the overall prescribing prevalence of NRT in all pregnancies to range from 0.3 to 4%,[111-113] which is very similar to the findings of this study. The findings of this study closely mirror that of the Scottish data linkage study where NRT was prescribed to 2.4% of all pregnant women[131]. In addition, NRT usage in pregnant smokers attending English SSSPs is reported to be 85%[132] and considering that only 3% of pregnant women attend these services, this also equates to 2.5%. This implies that the uptake of NRT during pregnancy in smokers is quite high (~11% of smokers) despite the lack of evidence of its effectiveness and safety.

The results of this study also demonstrate that the annual prescribing prevalence of NRT has been stable and not increased much since the changes in the licensing arrangements in December 2005, although overall prescribing in the years after the relaxation of licensing arrangements has almost doubled. The difference between the prescribing prevalence in pregnancy and the nine month periods immediately before and after pregnancy started widening after 2003. This may be attributed to the changes in prescribing indications for NRT use implemented in May 2003, when pregnancy was removed from the list of contraindications for NRT use and instead cautious use of NRT products in pregnancy was advised if smoking cessation without NRT failed.[96] After the relaxation of licensing arrangements of NRT in 2005 prescribing of NRT during pregnancy was almost twice as high compared to the prescribing in the nine months immediately before and after pregnancy. This may also be related to the licensing of varenicline for smoking cessation in the general non-pregnant

population in December 2006, after which a reduction in prescribing of NRT and bupropion in the general population was seen.[218] Alternatively, women may be more motivated to quit after finding out they are pregnant or may deliberately wait to quit until they get pregnant as they can get free NRT prescriptions during pregnancy.

The prescribing prevalence of NRT was found to be the highest in the first two trimesters during pregnancy compared to the other time periods under study and the prescribing prevalence within the third trimester was very similar to the prescribing prevalence before and after pregnancy. In a survey of all SSSPs in England between April 2010 and March 2011 assessing delivery of smoking cessation support, 60% of the SSSPs reported that there was a difference in the proportion of pregnant women seeking help by the stage of pregnancy, with the most referrals given in the first two trimesters.[185] This may be related to the level of motivation to quit smoking which has been shown to be higher during early pregnancy compared to late pregnancy resulting in more women seeking help at these times in pregnancy.[219] A study using an online database containing data on 3,880 pregnant smokers supported by one of the 44 regional SSS in England reported that 55% of all pregnant smokers (65% of pregnant NRT users) used combination NRT,[132] which is very high compared of 10% as shown in this work. This is mostly likely related to different baseline populations i.e. data from specialist stop smoking services compared to data from primary care. Women voluntarily attending these specialist services will likely have a higher motivation to quit which may result in more quit attempts and more NRT being prescribed compared to women attending primary care.

NICE recommends that pregnant women should initially be prescribed two weeks of NRT from their agreed stop date, with further NRT after re-assessment.[79] The average duration of prescription for women in this study was two weeks and most women (80%) received two or less prescriptions. One reason for this may

be that compliance was low and women did not quit or use it to quit in which case no further NRT was prescribed. Some women may have bought NRT independently after the first prescription; however, considering that women are entitled to free prescriptions during pregnancy and NRT from retailers is reasonably expensive, this is unlikely. Studies in other populations have not reported the duration of NRT use in pregnancy. However, eight to twelve weeks' use is recommended for optimal effectiveness in the general population[110] so it is unlikely that two weeks' use is effective for smoking cessation in pregnancy.

A study conducted in four states of the USA, in 5,716 pregnant women between the ages of 18-45 years, found NRT prescribing to be lower in pregnant smokers younger than 35 years of age compared to pregnant smokers over the age of 35.[111] In comparison, prescribing was assessed within 5 year age bands between 15-49 years in this study and the results were found to be similar, with NRT prescribing increasing with age; however the confidence intervals between the age categories overlapped. Advancing maternal age is associated with a higher risk for pregnancy complications [220] which may lead women to visit their GPs more often during pregnancy providing more opportunities to provide smoking cessation advice and prescribe NRT which may explain higher prescribing rates in these smokers compared to younger smokers. Low socioeconomic status is associated with a higher prevalence of chronic disease [191] and higher risk of adverse pregnancy outcomes[221], which would explain why pregnant smokers in the deprived group would be prescribed more NRT than affluent groups. Asthma and mental illness are the most common conditions encountered during pregnancy[194,222] and are closely related to smoking, which may explain a significant association with NRT prescribing compared to other conditions.

5.5 CHAPTER CONCLUSIONS

In conclusion, this study shows that the prevalence of prescribing of NRT during pregnancy, especially after the relaxation of licensing arrangements in 2005, was almost twice the prevalence of prescribing in the nine months immediately before and after pregnancy. Although studies on NRT prescribing in pregnancy are lacking worldwide, these findings give insight into prescribing in and around pregnancy and highlight that the prescribing of NRT during pregnancy is quite high. These data also show that NRT was prescribed for an average of only two weeks during pregnancy which is unlikely to be effective.

Prescribing was also found to be relatively lower before and after pregnancy, which are also important times when quitting has significant health benefits for the woman and her child. This is indicative of a possible missed opportunity to assist many young women in quitting smoking. Whilst interactions between health professionals and pregnant women should be used to discuss and offer interventions to promote smoking cessation, greater potential benefit would be derived from starting before pregnancy which should be a focus for women and health care providers.

6 NICOTINE REPLACEMENT THERAPY, MATERNAL SMOKING AND CONGENITAL ANOMALIES

6.1 INTRODUCTION

The findings from the previous chapter report that approximately 11% of pregnant smokers are prescribed NRT in primary care settings annually. In addition, some women may be getting their NRT directly from the SSSP and some, although a small proportion, may be buying it OTC which would make the proportions of pregnant smokers using NRT even higher. Whilst the use of NRT is now recommended for smoking cessation during pregnancy in both UK and European guidelines,[79,124] the evidence concerning its safety in pregnancy is still lacking. Therefore, the WHO has made a strong recommendation for more research on the safety of NRT in pregnant women.[73] This chapter and the following chapter (Chapter 6 and Chapter 7) address this gap in the literature by assessing the safety of NRT use during pregnancy. This chapter focuses on investigating the relationship between antenatal NRT exposure or smoking, as recorded in primary care data, and the presence of congenital anomalies in children born to women exposed to these potential risks in early pregnancy and the following chapter will focus on other birth outcomes.

The association between maternal smoking in pregnancy and congenital anomalies in infants seems to be biologically plausible. Compromised oocyte quality in mothers who smoke may be one of the possible mechanisms by which smoking causes congenital anomalies.[223] Another possible mechanism is the chromosomal damage and epigenetic changes leading to subtle changes in the gene expression in babies of mothers who smoke.[223] However, this association is currently not very clear in the literature. A large systematic review of observational studies published between 1959 to 2010 including 173,687 cases of congenital anomalies and 11,674,332 controls showed an OR of 1.01 (0.96-

1.07) for all malformations combined in relation to maternal smoking during pregnancy. However, significantly increased risks of system-specific anomalies including heart defects (OR 1.09, 95% CI 1.02-1.17), musculoskeletal defects (OR 1.16, 95% CI 1.05-1.27), orofacial clefts (OR 1.28, 95% CI 1.20-1.36), limb defects (OR 1.26, 95% CI 1.15-1.39), eye defects (OR 1.25, 95% CI 1.11-1.40) and gastrointestinal defects (OR 1.27, 95% CI 1.18-1.36) were found.[28] Contrary to the systematic review, a newer study based on 1,676 cases and 3,267 controls from a total of 44,732 live births in Rhode Island between 2007 and 2010 found a significantly increased risk of congenital anomalies associated with maternal smoking (OR 1.27, 95% CI 1.05-1.55).[224] Similarly, a more recent case-control analysis from the Baltimore-Washington Infant Study found no statistically significant association between maternal smoking and congenital heart defects (OR 1.07, 95% CI 0.80-1.45) however an increased risk was reported for specific anomalies e.g. pulmonary valve stenosis (OR 1.35, 95% CI 1.05-1.74), truncus arteriosus (OR 1.90, 95% CI 1.04-3.45).[225] Another study using the PRAMS data from nine states of the USA found no increased risk of congenital heart defects in relation to maternal smoking (OR 0.50, 95% CI 0.22-1.10).[226] In contrast, a study from Greece including 157 infants with congenital heart defects and 208 infant without congenital heart defects born between 2006 and 2009 reported approximately a three-fold increase in the risk of congenital heart defects associated with maternal smoking during pregnancy (OR 2.75, 95% CI 1.66-4.48)[227] and a systematic review including all studies between 1947 to 2011 on maternal smoking and congenital heart defect found the risk of congenital heart defects to be 11% higher in children of mothers who smoked compared to non-smokers (RR 1.11, 95% CI 1.02-1.21).[228] Data from the National Birth Defects Prevention Study (NBDPS), USA showed no significant increase in the risk of neural tube defect in children in relation to active maternal smoking (OR 0.9, 95% CI 0.8-1.1).[229] Hence, to-date the evidence of the association of maternal smoking and congenital anomalies is inconclusive.

The evidence of the teratogenic safety of NRT is only limited to two studies which have assessed the association between maternal use of NRT during pregnancy and congenital anomalies in the offspring. Table 6-1 describes these studies in detail.

Table 6-1 Summary of studies assessing congenital anomalies in relation to NRT use during pregnancy

First author, year and location	Study methodology	Sample size (Inclusion/Exclusion)	Exposure Assessment	Outcome Assessment	Results for NRT safety
Coleman (2012), UK [100]	Large, double-blinded, placebo-controlled multicentre RCT	1050 participants between 16 to 50 years with pregnancies of 12-24 weeks of gestation smoking five or more cigarettes per day	4 weeks supply of Standard nicotine patch (15mg/16 hrs) versus visually identical placebo, started on the quit date	Secondary outcome: Adverse pregnancy and birth outcomes including congenital anomalies	OR for congenital anomalies associated with NRT use = 0.70 (95% CI 0.30-1.66) compared to placebo group. Estimates only based on 9 cases in the treatment group and 13 cases in the placebo group.
Morales-Suarez-Varela (2006), Denmark [114]	Cohort study using Danish National Birth Cohort	76,768 pregnancies between 1996 and 2002	Smoking and NRT during the first 12 weeks of pregnancy	Congenital anomalies diagnosed at birth or during the first year of life, further classified based on EUROCAT criteria[230]	OR 1.61 (95% CI 1.01-2.56) for congenital malformations in children born to non-smokers, who used nicotine substitutes compared to non-smokers who did not use any nicotine substitutes. When restricted to major malformations the odds ratio was 1.13(95% CI 0.62-2.07)

The SNAP trial found no association between the use of NRT during pregnancy and congenital anomalies in the offspring.[100] Although the SNAP trial is the biggest trial of NRT patches in pregnancy conducted so far, the primary end point was abstinence from the date of smoking cessation until delivery and therefore all the safety analyses were underpowered, especially for the more rare outcomes like congenital anomalies. This finding was based on only 22 children with congenital anomalies so this negative finding for the association between NRT use in pregnancy and congenital anomalies could be due to Type 2 error (low statistical power) in the trial to detect any association with congenital anomalies. Another important point to consider is that the mean gestational age at the time of study enrolment in the trial was about 16 weeks indicating that most of the pregnant women in the trial were given NRT after the end of the first trimester, when most of the organ development had already taken place. By contrast, the study using the Danish National Birth Cohort (DNBC) found a 61% (95% CI 1.01-2.58) increase in the risk of congenital anomalies in the babies of mothers using NRT during pregnancy compared to non-smokers but no increased risk was found when restricted to only major congenital anomalies. Although the population-based nature of the study and prospective data collection minimised the potential for ascertainment and selection bias in the study, the data on smoking and NRT use were self-reported. Furthermore, this study was conducted over a decade ago (1997-2003) after which many new forms of NRT have been introduced to the market and the prescribing of NRT in pregnancy has increased. In light of these limitations of the current literature, this chapter describes the relationship between antenatal exposure to NRT or maternal smoking described in primary care data and the presence of MCAs in children born to women exposed to these potential risks in early pregnancy.

6.2 METHODS

6.2.1 Study population

All live born children delivered between January 2001 and December 2009, with linked mother records were included in this analysis. The study population was limited to only live births because stillborn children are generally not registered with the GPs. Data before January 2001 was excluded as NRT only became available on NHS prescription in 2001.

6.2.2 Exposure

A variable indicating NRT exposure in early pregnancy (defined here as one month before conception until the end of the first trimester) and smoking was developed with four categories. The period of four weeks before conception was used to enable inclusion of drug prescriptions received immediately before pregnancy and potentially used around the time of conception. The first trimester of pregnancy is considered the critical period for the developments of congenital anomalies [231,232] and therefore only early pregnancy exposure was considered. The four exposure categories are described below:

- **Non-smoker:** All women with Read codes for never smoking or ex-smoking in their primary care records during the first trimester and within 27 months before pregnancy, with no current smoking codes in this time were classified as non-smokers.
- **NRT group:** All pregnant women with a drug code for NRT prescription during the first trimester of pregnancy or within four weeks before the estimated conception dates in their primary care records were classified as being prescribed NRT during early pregnancy. Similar to other drug safety studies, the period of four weeks before conception was included to enable the inclusion of NRT prescriptions immediately before

pregnancy and potentially used during very early pregnancy and around conception.[233]

- **Smoker:** If any records of current smoking were found during early pregnancy or if the latest smoking status record within 27 months before pregnancy until the end of first trimesters indicated smoking, women were categorised as being smokers during that pregnancy.
- **Unknown:** All women who did not have a recording of smoking status or NRT prescription during early pregnancy or where the smoking status records did not clearly indicate whether they were smokers or non-smokers were included in this category.

6.2.3 Outcome

All information on major congenital anomalies recorded at any age in children's primary care records was extracted using Read codes mapped to the EUROCAT classification system (Code list attached as Appendix 10.10).[230] This system identifies all conditions classified as major congenital disorders coded by the Q chapter of the International Classification of Disease version 10 (ICD-10)[234] and a small number of conditions in the other ICD-10 chapters and categorises them into subgroups.[230] Minor congenital anomalies are not very well recognised and therefore not recorded very well in primary care. Therefore, epidemiological studies only focus on assessing major congenital anomalies and so do registries. Therefore, in line with the EUROCAT classification, minor congenital anomalies (e.g. lip hypertrophy, congenital flat foot etc.) were excluded from the case definition.[230] Children with medical codes for teratogenic anomalies (e.g. PK80.00 – Fetal alcohol syndrome, PK84.00 Fetal valproate syndrome) were also excluded from the study population.

6.2.4 Potential confounders

Maternal age, socioeconomic status and all other maternal morbidities described in Section 3.4.3 were considered to be potential confounders due to the associations of these conditions or their treatments with congenital anomalies and maternal smoking. [51,59,195,199,211,235-244] In addition, epilepsy was also deemed to be an important clinical confounder for this analysis as the medical treatment for epilepsy is strongly related to congenital anomalies[245,246] and studies have shown epilepsy to be associated with smoking as well.[247] Records of diagnosed epilepsy were extracted from both the Medical and AHD files and epilepsy medication prescriptions were extracted from the Therapy file. For the purpose of this study, pregnant women were said to have epilepsy if they had a diagnostic recording of epilepsy ever before delivery and had a recording of epilepsy prescription during pregnancy or within 27 months before conception. Medical code lists and prescription code lists are attached as Appendix 10.8.11 and Appendix 10.8.12.

6.2.5 Statistical analysis

To estimate the disease burden of all major and individual system-specific congenital anomalies, absolute risks (per 10,000 live births) for the total population and each exposure group (i.e. non-smokers, smokers, NRT group and unknown group) were calculated. ORs for any major and each system-specific anomaly group were calculated for the NRT group and smokers using non-smokers as the reference group in a logistic regression model. Some women had more than one pregnancy in the study period; this was accounted for by calculating robust CIs around the OR using the clustered sandwich estimator, [180,181] which is explained in Section 3.4.4. In recognition of the fairly large number of exposure and outcome categories in this analysis, 99% CIs were calculated for each measure of association; exact p-values (to 3 decimal places) have also been presented for more transparent reader assessment of

associations potentially arising by chance. Adjustments were also made for potential confounders discussed above. Chi-squared tests were used to determine whether each of these confounders was associated with the exposure and with the outcome. Covariates with statistically significant associations at 5% level of significance were included in the multivariable model to obtain adjusted ORs. The reference group was then changed to smokers and ORs for MCAs in the NRT group were calculated.

6.2.6 Sensitivity analysis

6.2.6.1 Restricting to only singleton live births

The absolute and relative risks of overall and individual system-specific congenital anomalies were calculated, restricting the study population to only singleton live born babies, as malformations are more likely to occur in multiple births compared to singleton births.[248]

6.2.6.2 Reclassifying smokers and non-smokers based on gestational smoking status recording

The definitions of smokers and non-smokers were restricted to only mothers who had a gestational smoking status record during early pregnancy indicating them to be a smoker or non-smoker respectively. This was done because some women who were documented to be smokers in the 27 months before conception may have given up smoking before pregnancy and therefore the definition of smokers and non-smokers during early pregnancy may result in some misclassification between these two exposure categories. The absolute risks of overall and system-specific MCA groups were calculated using only smokers and non-smokers, based on gestational records and ORs (99% CI) for MCAs in children with maternal NRT exposure during early pregnancy were calculated.

6.2.6.3 Exposure window changed to 2nd/3rd trimester

The exposure period was changed from early pregnancy to 2nd/3rd trimester and all women with NRT prescriptions in early pregnancy were excluded from the analysis. Although most of the organogenesis takes place in the first trimester, consequently increasing the risk of structural defects, some periods in the second and third trimester are also slightly sensitive for the development of congenital anomalies.[249] These include defects of the eye, ear, teeth, central nervous system and genitalia. [250] Therefore, the absolute and relative risks of overall and system-specific MCA groups for NRT group and smokers, compared to non-smokers were calculated based on 2nd/3rd trimester exposure.

6.2.7 Sample size calculation

Previous literature suggests the prevalence of MCAs to be 2.7%[251] and the prescribing prevalence of NRT during pregnancy has been found to be approximately 2%.[252] Based on these numbers, a sample size of 138,064 children with maternal NRT prescriptions in early pregnancy was needed in this study to detect an OR of 1.50 with 80% power at a 1% level of significance. The sample size to achieve this power for system-specific anomalies was much higher (e.g. 301,082 children with maternal NRT prescriptions for heart defects). Similarly, a sample of 19,041 children with smoking mothers was needed to detect an OR of 1.50 for the association between maternal smoking and presence of CAs, with 80% power at a 1% level of significance. Sample size calculations were performed in PASS 12 (Power Analysis & Sample Size Software).[253]

6.3 RESULTS

6.3.1 Baseline characteristics

A total of 232,242 live born children were included in the study population out of whom 6,480 had at least one major congenital anomaly (279 per 10,000 live births). Out of these 232,242 children 0.7% were born to mothers who were prescribed NRT , 16% to mothers who smoked during pregnancy and 49% to mothers who did not smoke during. Table 6-2 shows the baseline maternal characteristics in children with and without MCAs. The distribution of maternal age at conception, socioeconomic status and pre-conception BMI was very similar in women whose children had any MCA and women whose children did not have any MCA. The prevalence of maternal morbidities particularly epilepsy (0.4% vs. 0.7%), was found to be higher in the MCA group. Similarly, multiple births were more common in children with congenital anomalies compared to children without congenital anomalies (3.6% vs. 5.2%).

Table 6-3 presents the maternal and birth characteristics by smoking and NRT exposure. Women in the NRT group and smokers were more likely to be from socioeconomically deprived groups compared to non-smokers. Additionally, the NRT group had a higher prevalence of asthma (14.4%) compared to smokers and non-smokers (11.1% and 10.3% respectively). Similarly, mental illness was found to be most prevalent in the NRT group (20.8%) and epilepsy was found to be the highest in smokers (0.7%), followed by the NRT group (0.6%). The distribution of other morbidities was very similar across the exposure groups.

Table 6-2 - Maternal and birth characteristics of the study population

	All children		Children without MCAs		Children with MCAs	
	N=232,242		n=225,762		n=6,480	
	n	%	n	%	n	%
Age at conception						
15-19 years	12,037	5.2%	11,692	5.2%	345	5.3%
20-24 years	36,003	15.5%	34,999	15.5%	1,004	15.5%
25-29 years	59,203	25.5%	57,624	25.5%	1,579	24.4%
30-34 years	73,844	31.8%	71,822	31.8%	2,022	31.2%
35-39 years	42,477	18.3%	41,262	18.3%	1,215	18.7%
40-44 years	8,341	3.6%	8,046	3.6%	295	4.5%
45-49 years	337	0.1%	317	0.1%	20	0.3%
Townsend score in quintiles						
Quintile 1 (least deprived)	53,916	23.2%	52,430	23.2%	1,486	22.9%
Quintile 2	43,850	18.9%	42,653	18.9%	1,197	18.5%
Quintile 3	45,280	19.5%	43,986	19.5%	1,294	20.0%
Quintile 4	42,696	18.4%	41,490	18.4%	1,206	18.6%
Quintile 5 (most deprived)	31,884	13.7%	30,963	13.7%	921	14.3%
Missing	14,616	6.3%	14,240	6.3%	376	5.8%
Pre-conception Body Mass Index (kg/m^2)						
normal(18.5-24.9)	73,002	31.4%	71,019	31.5%	1,983	30.6%
underweight(<18.5)	5,225	2.2%	5,071	2.2%	154	2.4%
overweight(25-29.9)	35,625	15.3%	34,626	15.3%	999	15.4%
obese(>=30)	24,594	10.6%	23,876	10.6%	718	11.1%
missing	93,796	40.4%	91,170	40.4%	2,626	40.5%
Asthma	19,932	8.6%	19,335	8.6%	597	9.2%
Hypertension	6,392	2.8%	6,165	2.7%	227	3.5%
Diabetes	5,490	2.4%	5,268	2.3%	222	3.4%
Mental illness	22,154	9.5%	21,507	9.5%	647	10.0%
Epilepsy	1,036	0.4%	994	0.4%	42	0.7%
Multiple birth	8,373	3.6%	8,038	3.6%	335	5.2%

MCAs = major congenital anomalies

Table 6-3 - Numbers and proportions of maternal and birth characteristics by NRT exposure and smoking

	NRT group*		Smokers**		Non-smokers***		Unknown	
	n= 1,594		n= 37,141		n=114,254		n= 79,253	
	n	%	n	%	n	%	n	%
Age at conception								
15-19 years	110	6.9%	3,918	10.5%	4,044	3.5%	3,965	5.0%
20-24 years	354	22.2%	9,885	26.6%	14,895	13.0%	10,869	13.7%
25-29 years	443	27.8%	10,005	26.9%	29,888	26.2%	18,867	23.8%
30-34 years	400	25.1%	8,127	21.9%	38,695	33.9%	26,622	33.6%
35-39 years	236	14.8%	4,335	11.7%	22,230	19.5%	15,676	19.8%
40-44 years	49	3.1%	846	2.3%	4,330	3.8%	3,116	3.9%
45-49 years	2	0.1%	25	0.1%	172	0.2%	138	0.2%
Townsend score in quintiles								
Quintile 1 (least deprived)	152	9.5%	4,573	12.3%	29,060	25.4%	20,131	25.4%
Quintile 2	219	13.7%	5,120	13.8%	23,056	20.2%	15,455	19.5%
Quintile 3	339	21.3%	7,281	19.6%	22,382	19.6%	15,278	19.3%
Quintile 4	438	27.5%	9,303	25.0%	19,090	16.7%	13,865	17.5%
Quintile 5 (most deprived)	338	21.2%	8,524	23.0%	12,731	11.1%	10,291	13.0%
Missing	108	6.8%	2,340	6.3%	7,935	6.9%	4,233	5.3%
Pre-conception BMI (kg/m^2)								
Normal (18.5-24.9)	495	31.1%	12,535	33.7%	44,568	39.0%	15,404	19.4%
Underweight (<18.5)	49	3.1%	1,277	3.4%	2,733	2.4%	1,166	1.5%
Overweight (25-29.9)	262	16.4%	6,011	16.2%	21,472	18.8%	7,880	9.9%
Obese (>=30)	223	14.0%	4,553	12.3%	14,369	12.6%	5,449	6.9%
Missing	565	35.4%	12,765	34.4%	31,112	27.2%	49,354	62.3%
Asthma	230	14.4%	4,116	11.1%	11,764	10.3%	3,822	4.8%
Hypertension	36	2.3%	793	2.1%	3,731	3.3%	1,832	2.3%
Diabetes	45	2.8%	746	2.0%	3,324	2.9%	1,375	1.7%
Mental illness	331	20.8%	5,882	15.8%	9,095	8.0%	6,846	8.6%
Epilepsy	9	0.6%	248	0.7%	497	0.4%	282	0.4%
Multiple birth	47	2.9%	1,290	3.5%	4,021	3.5%	3,015	3.8%

*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy, *** No smoking in early pregnancy

6.3.2 Absolute risks of major and system-specific congenital anomalies

Table 6-4 presents the numbers and absolute risks of any major and system-specific congenital anomalies in the total population and also stratified by maternal exposures. The absolute risk of MCAs in the NRT group was higher than non-smokers (364/10,000 live births compared to 273/10,000 live births). Similar increases in the risk were seen in the most common anomaly groups in the NRT group like heart, limb, genital and urinary defects. The absolute risks of MCAs in smokers were found to be very similar to the non-smokers with slightly higher risk in the more rare anomalies such as abdominal anomalies (5/10,000 live births in smoking group compared to 1/10,000 live births in the reference group).

Table 6-4 - Absolute risks of major congenital anomalies by NRT exposure and maternal smoking

	All children		NRT group*		Smokers**		Non-smokers***		Unknown	
	N= 232,242		n= 1,594		n= 37,141		n=114,254		n= 79,253	
	n ǂ	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000
All MCAs combined	6,480	279	58	364	1,009	272	3,121	273	2,292	289
Heart	2,021	87	15	94	327	88	999	87	680	86
Limb	1,243	54	11	69	183	49	623	55	426	54
Genital system	1,077	46	12	75	158	43	507	44	400	50
Urinary system	622	27	6	38	89	24	304	27	223	28
Chromosomal	438	19	3	19	53	14	216	19	166	21
Musculoskeletal	416	18	5	31	64	17	196	17	151	19
Oro-facial cleft	348	15	2	13	57	15	158	14	131	17
Digestive system	347	15	5	31	44	12	174	15	124	16
Nervous system	359	15	3	19	58	16	170	15	128	16
Other malformations[$]	316	14	2	13	45	12	150	13	119	15
Eye	256	11	1	6	32	9	120	11	103	13
Respiratory system	188	8	10	63	32	9	89	8	57	7
Genetic	176	8	0	-	21	6	82	7	73	9
Abdominal wall	61	3	0	-	20	5	17	1	24	3
Ear, face & neck	41	2	0	-	8	2	15	2	18	2

MCA = Major Congenital Anomalies
ǂ each case may have more than one system anomaly, therefore total of all system-specific anomalies may vary
*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy, *** no smoking in early pregnancy
[$] e.g. Asplenia, conjoined twins etc.

6.3.3 Relative risks of major and system specific congenital anomalies

Table 6-5 shows the adjusted ORs for overall and each system specific major congenital anomaly comparing the NRT group and smokers to non-smokers. The OR for MCAs in the NRT group was 1.34 (99% CI 0.94-1.91, p-value 0.034) compared with non-smokers. There was no increased risk of MCAs in smokers compared to non-smokers (OR 0.99, 99% CI 0.89-1.09, p-value 0.819) compared to non-smokers. The ORs for system-specific anomalies were broadly similar to the overall findings. At 99% confidence interval, odds ratios showed no increased risk of any system specific congenital anomaly in the NRT group compared to non-smokers except respiratory system anomalies (OR 7.61, 99% CI 2.93-19.74, p-value <0.001). However, this was based on a very small number of exposed cases (10 cases of respiratory system anomaly) as shown in Table 6-4.

Table 6-6 presents the ORs for major congenital anomalies in the NRT group compared to smokers. The relative risk of major congenital anomalies in NRT group was not appreciably altered when the reference group was changed to smokers (OR 1.35, 99% CI 0.94-1.93 for overall MCAs).

Table 6-5 - Adjusted odds ratio for major congenital anomalies by maternal NRT and smoking exposure

	NRT group*¥		Smokers**¥		Unknown¥	
	n= 1,594		n=37,141		n= 79,253	
	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value
All MCAs combined	1.34 (0.94-1.91)	0.034	0.99 (0.89-1.09)	0.815	1.06 (0.98-1.15)	0.032
Heart	1.08 (0.55-2.13)	0.757	1.02 (0.86-1.21)	0.787	0.99 (0.87-1.13)	0.861
Limb	1.31 (0.59-2.88)	0.380	0.94 (0.75-1.17)	0.487	0.99 (0.84-1.16)	0.847
Genital system	1.66 (0.78-3.55)	0.082	0.92 (0.72-1.18)	0.411	1.14 (0.96-1.36)	0.047
Urinary system	1.43 (0.49-4.16)	0.385	0.92 (0.67-1.26)	0.511	1.05 (0.83-1.34)	0.523
Chromosomal	1.03 (0.23-4.64)	0.961	0.85 (0.56-1.28)	0.313	1.09 (0.83-1.42)	0.424
Musculoskeletal	1.89 (0.58-6.16)	0.166	1.03 (0.70-1.52)	0.826	1.13 (0.85-1.49)	0.268
Oro-facial cleft	0.86 (0.14-5.37)	0.828	1.05 (0.69-1.58)	0.748	1.20 (0.88-1.64)	0.123
Digestive system	2.01 (0.62-6.49)	0.125	0.76 (0.49-1.19)	0.118	1.02 (0.75-1.38)	0.873
Nervous system	1.17 (0.26-5.24)	0.792	0.98 (0.65-1.47)	0.904	1.13 (0.83-1.53)	0.314
Other malformations[$]	0.96 (0.15-6.02)	0.952	0.92 (0.59-1.44)	0.654	1.14 (0.83-1.56)	0.296
Eye	0.56 (0.04-7.47)	0.567	0.77 (0.45-1.30)	0.197	1.23 (0.87-1.75)	0.121
Respiratory system	7.61 (2.93-19.74)	<0.001	1.07 (0.62-1.86)	0.745	0.93 (0.60-1.44)	0.683
Genetic	-	-	0.85 (0.44-1.65)	0.532	1.26 (0.83-1.92)	0.150
Abdominal wall	-	-	2.27 (0.94-5.44)	0.016	1.87 (0.81-4.30)	0.053
Ear, face & neck	-	-	1.62 (0.49-5.37)	0.300	1.68(0.68-4.14)	0.138

*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy, ¥Reference category = non-smokers during early pregnancy, ‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes and epilepsy, [$] e.g. Asplenia, conjoined twins etc. MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence interval

Table 6-6 - Adjusted odds ratio for major congenital anomalies in the NRT group compared to smokers

	NRT group* n=1,594	
	AOR ¥‡ (99% CI)	**p-value**
All MCAs combined	1.35 (0.94-1.93)	0.032
Heart	1.06 (0.54-2.11)	0.813
Limb	1.39 (0.62-3.10)	0.292
Genital system	1.80 (0.83-3.90)	0.051
Urinary system	1.55 (0.52-4.61)	0.297
Chromosomal	1.20 (0.26-5.61)	0.750
Musculoskeletal	1.83 (0.55-6.06)	0.195
Oro-facial cleft	0.81 (0.13-5.18)	0.774
Digestive system	2.63 (0.78-2.11)	0.041
Nervous system	1.19 (0.25-5.47)	0.770
Other malformations[$]	1.04 (0.16-6.68)	0.962
Eye	0.73 (0.05-10.01)	0.759
Respiratory system	7.10 (2.60-19.38)	<0.001
Genetic	-	-
Abdominal wall	-	-
Ear, face & neck	-	-

¥Reference category – smokers during early pregnancy
* NRT=nicotine replacement therapy prescription in early pregnancy
‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes, epilepsy, [$] e.g. Asplenia, conjoined twins etc.
MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence intervals

6.3.4 Sensitivity analysis

6.3.4.1 Restricting to only singleton live births

Table 6-7 shows the absolute risks of all major and system specific congenital anomalies in singleton live-born children by NRT and smoking exposure. Similar to the main results, the absolute risk of MCAs was higher in the NRT group compared with non-smokers (356/10,000 live births compared to 270/10,000 live births). Similar increases in the risk were seen for the most common anomalies in the NRT group like heart, limb, genital and urinary defects but the absolute risk differences were very small.

Table 6-8 shows the adjusted ORs for overall and each system specific major congenital anomaly group in singleton live-born children comparing the NRT group and smokers to non-smokers. The effect estimates remained unaltered with no increased risk of congenital anomalies in the NRT group and smokers compared with non-smokers.

Table 6-7 - Absolute risks of major congenital anomalies by NRT exposure and maternal smoking in singleton live borns

	All children		NRT group*		Smokers**		Non-smokers***		Unknown	
	N= 223,869		n= 1,547		n= 35,851		n=110,233		n= 76,238	
	n ǂ	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000
All MCAs combined	6,145	274	55	356	959	267	2,973	270	2,158	283
Heart	1,868	83	14	90	307	86	927	84	620	81
Limb	1,199	54	11	71	177	49	604	55	407	53
Genital system	1,020	46	12	78	152	42	482	44	374	49
Urinary system	597	27	6	39	85	24	296	27	210	28
Chromosomal	425	19	3	19	51	14	208	19	163	21
Musculoskeletal	398	18	5	32	62	17	187	17	144	19
Oro-facial cleft	333	15	2	13	54	15	149	14	128	17
Digestive system	330	15	5	32	44	12	166	15	115	15
Nervous system	347	16	3	19	56	16	163	15	125	16
Other malformations[$]	306	14	2	13	44	12	144	13	116	15
Eye	241	11	1	6	30	8	114	10	96	13
Respiratory system	176	8	8	52	28	8	86	8	54	7
Genetic	168	8	-	-	19	5	81	7	68	9
Abdominal wall	55	2	0	-	19	5	15	1	21	3
Ear, face & neck	41	2	0	-	8	2	15	1	18	2

MCA = Major Congenital Anomalies, NRT = nicotine replacement therapy
*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy, *** no smoking in early pregnancy
ǂ each case may have more than one system anomaly, therefore total of all system-specific anomalies may vary
[$] e.g. Asplenia, conjoined twins etc.

Table 6-8 - Adjusted odds ratio for major congenital anomalies by maternal NRT and smoking exposure in singleton live-born children

	NRT group*¥		Smokers**¥		Unknown¥	
	n= 1,547		n=35,851		n= 76,238	
	AOR*‡ (99% CI)	p-value	AOR*‡ (99% CI)	p-value	AOR*‡ (99% CI)	p-value
All MCAs combined	1.31 (0.91-1.87)	0.053	0.98 (0.89-1.08)	0.684	1.06 (0.98-1.15)	0.038
Heart	1.07 (0.53-2.15)	0.797	1.02 (0.86-1.22)	0.708	0.98 (0.85-1.12)	0.660
Limb	1.33 (0.61-2.94)	0.340	0.94 (0.75-1.18)	0.465	0.98 (0.83-1.15)	0.699
Genital system	1.73 (0.81-3.68)	0.063	0.93 (0.73-1.19)	0.451	1.13 (0.94-1.35)	0.079
Urinary system	1.46 (0.50-4.24)	0.359	0.90 (0.65-1.25)	0.423	1.03 (0.81-1.29)	0.757
Chromosomal	1.07 (0.24-4.80)	0.909	0.85 (0.56-1.28)	0.312	1.11 (0.85-1.45)	0.319
Musculoskeletal	1.97 (0.611-6.36)	0.135	1.05 (0.71-1.55)	0.742	1.13 (0.85-1.51)	0.265
Oro-facial cleft	0.91 (0.14-5.74)	0.900	1.07 (0.70-1.62)	0.677	1.25 (0.91-1.70)	0.066
Digestive system	2.07 (0.64-6.69)	0.110	0.79 (0.51-1.24)	0.182	0.99 (0.73-1.36)	0.966
Nervous system	1.21 (0.27-5.44)	0.745	0.98 (0.65-1.48)	0.923	1.15 (0.84-1.56)	0.244
Other malformations[$]	0.98 (0.16-6.18)	0.983	0.94 (0.59-1.47)	0.709	1.16 (0.84-1.59)	0.244
Eye	0.59 (0.04-7.81)	0.596	0.76 (0.44-1.30)	0.186	1.21 (0.84-1.73)	0.168
Respiratory system	6.36 (2.43-16.63)	<0.001	0.99 (0.56-1.76)	0.977	0.92 (0.59-1.44)	0.644
Genetic	-	-	0.78 (0.40-1.53)	0.350	1.19 (0.78-1.82)	0.285
Abdominal wall	-	-	2.25 (0.90-5.59)	0.022	1.83 (0.76-4.39)	0.074
Ear, face & neck	-	-	1.75 (0.55-5.60)	0.213	1.69 (0.66-4.40)	0.151

*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy
¥Reference category = non-smokers during early pregnancy, ‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes and epilepsy MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence interval
[$] e.g. Asplenia, conjoined twins etc.

6.3.4.2 Reclassifying smokers and non-smokers based on gestational smoking status recording

When the smoker and non-smoker groups were reclassified to women with a gestational smoking status recording in their primary care data indicating such behaviour only 3% were classified as smokers and 8% as non-smokers. The absolute risk of CAs in smokers was now higher compared to the risk using a broader definition (298/10,000 live births compared to 272/10,000 live births). However, the association between NRT exposure, smoking during early pregnancy and MCAs remained unchanged with no significant association between NRT exposure and smoking compared to non-smokers apart from respiratory anomalies where the risk of MCAs was over six times higher in the NRT group compared to definitive smokers during early pregnancy (OR 6.49, 99% CI 2.35-17.87, p-value <0.001). Table 6-9 presents the absolute risks of congenital anomalies by each exposure group and Table 6-10 presents adjusted ORs for NRT and smoking exposure, based on a restricted definition of smokers and non-smokers.

Table 6-9 - Absolute risks of major congenital anomalies by NRT exposure and maternal smoking, using only gestational smoking records

	All children		NRT group*		Smokers**		Non-smokers***		Unknown	
	N= 232,242		n= 1,594		n= 198		n=547		n= 205,602	
	n ǂ	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000
All MCAs combined	6,480	279	58	364	198	298	547	297	5,677	276
Heart	2,021	87	15	94	116	84	330	91	1,560	86
Limb	1,243	54	11	69	73	53	192	53	967	54
Genital system	1,077	46	12	75	57	41	172	48	836	46
Urinary system	622	27	6	38	31	22	97	27	488	27
Chromosomal	438	19	3	19	21	15	70	19	344	19
Musculoskeletal	416	18	5	31	24	17	59	16	328	18
Oro-facial cleft	348	15	2	13	29	21	50	14	267	15
Digestive system	347	15	5	31	21	15	60	17	261	14
Nervous system	359	15	3	19	27	19	51	14	278	15
Other malformations[$]	316	14	2	13	26	19	35	10	253	14
Eye	256	11	1	6	9	6	42	12	204	11
Respiratory system	188	8	10	63	16	12	33	9	129	7
Genetic	176	8	0	-	7	5	28	8	141	8
Abdominal wall	61	3	0	-	5	4	9	2	47	3
Ear, face & neck	41	2	0	-	2	1	5	3	34	2

MCA = Major Congenital Anomalies, NRT = nicotine replacement therapy
*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy, *** no smoking in early pregnancy
ǂ each case may have more than one system anomaly, therefore total of all system-specific anomalies may vary
[$] e.g. Asplenia, conjoined twins etc.

Table 6-10 - Adjusted odds ratio for major congenital anomalies by maternal NRT and smoking exposure using only gestational smoking records

	NRT exposed group*¥		Smokers**¥		Unknown¥	
	n= 22,814		n=1,113		n= 19,038	
	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value
All MCAs combined	1.22 (0.84-1.77)	0.156	1.00 (0.80-1.25)	0.978	0.93 (0.82-1.04)	0.096
Heart	1.04 (0.52-2.06)	0.886	0.92 (0.69-1.23)	0.485	0.96 (0.81-1.12)	0.506
Limb	1.34 (0.59-2.98)	0.353	1.03 (0.72-1.48)	0.817	1.00 (0.82-1.23)	0.543
Genital system	1.56 (0.72-3.38)	0.138	0.84 (0.56-1.26)	0.265	0.98 (0.79-1.22)	0.788
Urinary system	1.42 (0.48-4.21)	0.408	0.85 (0.49-1.45)	0.435	1.00 (0.76-1.34)	0.951
Chromosomal	1.00 (0.22-4.62)	0.996	0.86 (0.45-1.66)	0.566	0.98 (0.70-1.38)	0.901
Musculoskeletal	1.99 (0.59-6.70)	0.145	1.09 (0.58-2.07)	0.710	1.13 (0.78-1.63)	0.396
Oro-facial cleft	0.86 (0.13-5.57)	0.842	1.44 (0.78-2.68)	0.127	1.07 (0.71-1.62)	0.661
Digestive system	1.85 (0.56-6.18)	0.185	0.90 (0.46-1.75)	0.692	0.86 (0.59-1.25)	0.314
Nervous system	1.26 (0.27-5.81)	0.700	1.30 (0.69-2.44)	0.279	1.12 (0.76-1.66)	0.447
Other malformations[$]	1.31 (0.20-8.61)	0.707	1.95 (0.98-3.92)	0.013	1.45 (0.91-2.30)	0.041
Eye	0.52 (0.04-6.97)	0.512	0.52 (0.20-1.34)	0.075	0.98 (0.63-1.52)	0.907
Respiratory system	6.49 (2.35-17.87)	<0.001	1.22 (0.54-2.78)	0.532	0.78 (0.47-1.29)	0.210
Genetic	-	-	0.70 (0.23-2.09)	0.401	0.99 (0.58-1.68)	0.954
Abdominal wall	-	-	0.89 (0.20-3.85)	0.838	1.07 (0.41-2.75)	0.849
Ear, face & neck	-	-	0.53 (0.05-7.01)	0.391	1.03 (0.26-4.01)	0.957

*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy
¥Reference category = non-smokers during early pregnancy, ‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes and epilepsy MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence interval
[$] e.g. Asplenia, conjoined twins etc.

6.3.4.3 Exposure window changed to 2nd/3rd trimester

When NRT exposure in the 2nd/3rd trimester was assessed the absolute risks of MCAs in the NRT group were lower than the risks in early pregnancy (235/10,000 live births compared to 370/10,000 live births) and also the risk in all live births (279/10,000 live births). However, the association between NRT exposure, smoking during early pregnancy and MCAs remained unchanged with no significant association between NRT exposure and smoking compared to non-smokers. Table 6-11 presents the absolute risks of MCAs by each exposure group in 2nd/3rd trimester and Table 6-12 presents adjusted odds ratio for NRT exposure and smoking in 2nd/3rd trimester.

Table 6-11 - Absolute risks of major congenital anomalies by NRT exposure and maternal smoking during 2nd/3rd trimester

	All children		NRT exposed group*		Smokers**		Non-smokers***		Unknown	
	N=230,648		n= 1,827		n= 37,250		n=112,419		n= 79,152	
	n ǂ	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000
All MCAs combined	6,422	278	43	235	1,024	275	3,070	273	2,285	289
Heart	2,021	87	15	94	327	88	999	87	680	86
Limb	1,243	54	11	69	183	49	623	55	426	54
Genital system	1,077	46	12	75	158	43	507	44	400	50
Urinary system	622	27	6	38	89	24	304	27	223	28
Chromosomal	438	19	3	19	53	14	216	19	166	21
Musculoskeletal	416	18	5	31	64	17	196	17	151	19
Oro-facial cleft	345	15	2	13	57	15	158	14	131	17
Digestive system	347	15	5	31	44	12	174	15	124	16
Nervous system	359	15	3	19	58	16	170	15	128	16
Other malformations[$]	316	14	2	13	45	12	150	13	119	15
Eye	256	11	1	6	32	9	120	11	103	13
Respiratory system	188	8	10	63	32	9	89	8	57	7
Genetic	176	8	-	-	21	6	82	7	73	9
Abdominal wall	61	3	-	-	20	5	17	1	24	3
Ear, face & neck	41	2	-	-	8	2	15	2	18	2

MCA = Major Congenital Anomalies, NRT = nicotine replacement therapy
*NRT=nicotine replacement therapy prescription in late pregnancy, **smoking in pregnancy, *** no smoking in pregnancy
ǂ each case may have more than one system anomaly, therefore total of all system-specific anomalies may vary
[$] e.g. Asplenia, conjoined twins etc.

Table 6-12 - Adjusted odds ratio for major congenital anomalies by maternal NRT and smoking exposure during 2nd/3rd trimester

	NRT exposed group*¥		Smokers**¥		Unknown¥	
	n= 1,827		n= 37,250		n= 79,152	
	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value
All MCAs combined	0.85 (0.57-1.26)	0.285	1.00 (0.91-1.10)	0.936	1.06 (0.99-1.14)	0.041
Heart	1.08 (0.55-2.13)	0.757	1.02 (0.86-1.21)	0.787	0.99 (0.87-1.13)	0.861
Limb	1.31 (0.59-2.88)	0.380	0.94 (0.75-1.17)	0.487	0.99 (0.84-1.16)	0.847
Genital system	1.66 (0.78-3.55)	0.082	0.82 (0.72-1.18)	0.411	1.14 (0.96-1.36)	0.047
Urinary system	1.43 (0.49-4.16)	0.385	0.92 (0.67-1.27)	0.511	1.06 (0.84-1.33)	0.523
Chromosomal	1.02 (0.23-4.65)	0.961	0.85 (0.56-1.28)	0.313	1.09 (0.83-1.41)	0.424
Musculoskeletal	1.89 (0.58-6.16)	0.166	1.03 (0.70-1.52)	0.826	1.13 (0.85-1.49)	0.268
Oro-facial cleft	0.86 (0.14-5.37)	0.828	1.05 (0.69-1.59)	0.748	1.20 (0.88-1.64)	0.123
Digestive system	2.01 (0.62-6.49)	0.125	0.76 (0.49-1.19)	0.118	1.02 (0.75-1.38)	0.873
Nervous system	1.17 (0.26-5.24)	0.792	0.98 (0.65-1.47)	0.904	1.13 (0.83-1.53)	0.314
Other malformations[$]	0.96 (0.15-6.02)	0.952	0.93 (0.59-1.44)	0.654	1.14(0.83-1.56)	0.296
Eye	0.56 (0.04-7.47)	0.567	0.77 (0.45-1.30)	0.197	1.23 (0.87-1.75)	0.121
Respiratory system	7.61 (2.93-19.74)	<0.001	1.07 (0.62-1.86)	0.745	0.93 (0.60-1.44)	0.683
Genetic	-	-	0.85 (0.44-1.66)	0.532	1.26 (0.83-1.92)	0.150
Abdominal wall	-	-	3.62 (1.54-8.47)	<0.001	2.04 (0.89-4.61)	0.025
Ear, face & neck	-	-	1.52 (0.45-5.16)	0.376	1.60 (0.58-4.43)	0.230

*NRT=nicotine replacement therapy prescription in late pregnancy, **smoking in pregnancy
¥Reference category = non-smokers during early pregnancy, ‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes and epilepsy MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence interval
[$] e.g. Asplenia, conjoined twins etc.

6.4 DISCUSSION

6.4.1 Principal findings

This study found that NRT exposure during early pregnancy was not associated with an increased risk of overall and system-specific MCAs in the offspring compared with non-smokers and smokers except for an increased risk of respiratory anomalies; however this finding was based on only 10 cases exposed to NRT. These findings remained unaltered when the population was restricted to only singleton live-borns and to women with a gestational smoking status recording in their primary care data. No increased risks of MCAs were found with $2^{nd}/3^{rd}$ trimester NRT exposure.

6.4.2 Strengths and limitations

This is the largest study to date to investigate the association between NRT prescribing in pregnant women and the presence of MCAs in their offspring. Because the study was based on routinely collected population-based data, the ascertainment of congenital anomaly cases was independent of the exposure variable minimising the potential for selection bias in the study.

Although in the UK congenital anomalies are diagnosed in secondary care, major diagnoses should be communicated to the patients' general practitioners resulting in a primary care record for MCAs. The prevalence of MCAs in THIN has been shown to be highly comparable to EUROCAT data[157]. Furthermore, MCA diagnosis using clinical coding in electronic primary care data has also been validated against doctor-provided written records reported directly from the general practice.[158]

The study was unable to assess MCAs in pregnancies that ended in stillbirth as congenital anomalies are not comprehensively detected and are poorly recorded for stillborn children. Nevertheless, this exclusion of stillborn children is unlikely to cause substantial underestimation of the cases of MCAs or bias the

associations under study because the prevalence of stillbirth in the UK is only 0.6%[254] out of which 8-14% can be attributed to MCAs.[255,256] The study also did not include any miscarriages as most of the miscarriages take place early in pregnancy [257] when women may not know that they are pregnant and therefore it is not possible to ascertain MCAs in these.

Previous studies have used women's self-reports to define NRT exposure which is subject to reporting errors and bias.[100,114] In contrast, the measurement of NRT exposure in this study was based on recorded GP prescribing. As discussed earlier, in the UK women can access NRT in settings other than the GP practice, which means that some women in the smokers /non-smokers category may have received NRT from pharmacies or SSSPs, not documented in the GP records. This may bias the estimates towards null. However, as discussed in Section 5.4, OTC purchasing of NRT is assumed to be infrequent and GP data include SSSP prescribing as well, therefore any misclassification in the exposure will be minimal and non-differential.

Measuring actual drug consumption in any large population-based study is difficult and is a limitation in previous studies.[114] Similarly, in primary care data it is not possible to establish if the women actually used the NRT that was prescribed. However, women are generally more motivated to quit during pregnancy[258] and NRT is only prescribed after a discussion on potential benefits and harms and if the woman agrees to use it.[79] Although data from RCTs show low compliance to NRT especially during pregnancy[100,106] most of these report a median duration of at least two weeks for NRT use.[107-109] The average duration of prescribed NRT was two weeks on average as discussed in Section 5.3.2, therefore it is assumed that women did comply with the NRT prescription. Also, the exposure time of two weeks is fairly short and if there is a higher risk of MCAs with longer NRT exposure this study may not have been able to capture it.

Similarly, ascertaining accurate smoking status is difficult in studies, especially in pregnant women as there is a high potential for misreporting due to the social stigma attached to smoking in pregnancy. All the previous studies investigating the association between maternal smoking and MCAs have relied on self-reported smoking status through interviews or surveys, as biochemical validation is practically difficult and expensive in population-based studies.[28] Similarly, in primary care data it is not possible to be completely certain about the accuracy of the smoking status records in women's electronic notes, as entries are not biochemically validated and are also based on self-reports of women. In this study pre-conception records were also included to ascertain women's smoking status during early pregnancy which may result in misclassification of some non-smokers as smokers and bias the effect estimates towards null. However, a substantial misclassification is unlikely as approximately 35-50% of pregnancies in the UK are unplanned,[31, 32] which means that only some women are likely to make positive behaviour changes such as quitting smoking before attempting to conceive. To address this issue the risks of MCAs were recalculated using only gestational smoking records to define smokers and non-smokers and the findings remained unchanged.

Congenital anomaly is a rare condition and from previous work it is known that NRT prescribing among pregnant women is also rare.[252] Therefore, only 1,594 children had mothers with NRT prescriptions in early pregnancy which although did not provide adequate power (post-hoc power: 60%) but was still about 5 times bigger than the previous study.[114] The number of NRT exposed cases of MCA was also 6 times higher than the Danish study (58 vs 11 cases). Nevertheless, much larger numbers are needed to assess the association between NRT exposure and specific anomaly groups.

6.4.3 Interpretation and conclusion in light of the current literature

In this study the odds of major congenital anomalies in offspring of women prescribed NRT was 34% higher compared to non-smokers, although this finding was not statistically significant. Similarly, the absolute risks of system-specific anomalies were also generally higher than in the overall population and smokers, although these differences were small. A potential explanation for this finding may be that women who were prescribed NRT during pregnancy may be heavier smokers for some part of their pregnancy or immediately before their pregnancy and found it difficult to quit without pharmacotherapy [259,260] leading to confounding by indication. Although data on the exact time of NRT prescription in pregnancy was available, there is still inadequate information in the data regarding the smoking intensity of women before getting an NRT prescription. Therefore, it is difficult to completely separate the effects of smoking for some part of pregnancy from the effects of NRT. Additionally, despite adjustments in the analysis for sociodemographic factors and maternal morbidities, women prescribed NRT may have differed in unrecorded ways. Thus, unmeasured confounding factors may have contributed to the higher OR point estimate for NRT.

The only observational study on NRT and congenital anomalies, using the DNBC, showed that the women who used NRT in the first 12 weeks of pregnancy, but did not smoke, were more likely to have infants with congenital anomalies (OR 1.61, 95% CI 1.01-2.58) compared to non-smokers however when the analysis was only restricted to MCAs no association was found (OR 1.13, 95% CI 0.62-2.07).[114] The exposure time in the DNBC study was very similar to this study (i.e. early pregnancy) and despite the different exposure definition (self-reported NRT use in the DNBC study and GP prescribed NRT in this study) both the studies did not find any significantly increased risk of major congenital anomalies in relation to NRT, which is reassuring. In comparison, the SNAP trial

assessed NRT use at a later stage of pregnancy and reported a 30% lower likelihood of congenital anomalies in the NRT group compared to placebo group; however the results were not statistically significant and based on a very small number of events (9 events in NRT group compared to 13 events in placebo group).[100] When the exposure time in this study was changed to 2nd/3rd trimester NRT exposure the association between NRT and major CAs was did not become statistically significant, which mirrors the findings of the SNAP trial.

For mothers who smoked during early pregnancy this study found no association with congenital anomalies in their infants. This is very similar to the results from a large meta-analysis of 172 observational studies on maternal smoking in pregnancy with a total of 173,687 malformation cases and 11,674,332 controls, which found the OR for all congenital anomalies to be 1.01 (95% CI 0.96-1.07).[28] However, the magnitude of effect for system-specific anomaly groups were slightly different e.g. the systematic review found a significantly increased risk of heart defects associated with maternal smoking (OR 1.09, 95% CI 1.02-1.17).[28] In comparison, this study found an increase of 2% in the risk of heart defects associated with maternal smoking (OR 1.02, 99% CI 0.86-1.21), which was not statistically significant. In line with the findings of this chapter, the Baltimore-Washington Infant Study also did not find a statistically significant association between maternal smoking and congenital heart defects (OR 1.07, 95% CI 0.80-1.45).[225] The meta-analysis also found a higher risk of musculoskeletal defects, orofacial clefts, limb defects, eye defects and gastrointestinal defects[28] contrary to the findings reported here. A potential explanation for the difference in the estimates could be the very large sample size in the meta-analysis compared to this study and the use of 99% confidence intervals compared to the standard 95% CIs presented in the meta-analysis. A recent study on Greece based on 167 children with congenital heart defects found a three-fold increase in the risk of congenital heart defects associated with

maternal smoking[227] which is higher compared to the findings reported in this chapter and other available literature. This study, however, collected smoking exposure in the first trimester retrospectively after the delivery which increases the potential for recall bias. Additionally, no adjustments were made for other maternal co-morbidities (e.g. epilepsy), and socioeconomic status which may be important confounders.[238,246,261] The risk of nervous system anomalies was not found to be higher with maternal smoking (OR 0.98, 95% CI 0.65-1.47). Correspondingly, the OR for neural tube defects, which is the most common nervous system anomaly, in the NBDPS study, a national study from the US, was found to be 0.9 (95% CI 0.8-1.11).[262]

The limited evidence of maternal exposure to NRT during pregnancy and the risk of congenital anomalies in the offspring has not shown any significant associations between these factors. This study with much larger numbers than any other previous study did not find a protective or harmful effect of NRT during pregnancy. Therefore, it may be likely that there is no true association between NRT exposure during pregnancy and congenital anomalies in the offspring. However, it is difficult to be completely certain in the absence of adequate statistical power, for which an even larger study is required. Furthermore, other birth outcomes also need to be assessed in relation to NRT and smoking during pregnancy before making conclusions about the overall safety of the drug during pregnancy.

7 NICOTINE REPLACEMENT THERAPY, MATERNAL SMOKING IN PREGNANCY AND OTHER BIRTH OUTCOMES

7.1 INTRODUCTION

The previous chapter investigated and described the association between exposure to NRT and maternal smoking as recorded in primary care data and congenital anomalies. This chapter focuses on examining the relationship between NRT exposure, maternal smoking and other birth outcomes to comprehensively assess the safety of NRT in pregnancy.

Maternal smoking during pregnancy has been associated with several adverse birth outcomes including stillbirth, low birth weight and other birth outcomes as discussed in Section 1.1.1. Approximately 4-7% of stillbirths in developed countries can be attributed to maternal smoking.[29] A population-based study from Australia with a total sample of 191,941 births reported the risk of stillbirth to be twice as high in smokers compared to non-smokers after 34 weeks of gestation. [263] Similar results were reported by a Danish study assessing the risk of stillbirth in 25,012 singleton children of pregnant women between September 1989 and August 1996.[264] In addition, a meta-analysis of four studies from Australia, Sweden, Canada and the USA found maternal smoking to increase the risk of stillbirth by 36%.[29]

Maternal smoking has also been linked to low birth weight in infants and has been reported as one of the most important preventable causes of low birth weight.[265] A Dutch study from the early 1990s including approximately 800 pregnant women reported a 19g reduction in birth weight for each cigarette smoked in the day while pregnant.[266] As discussed in Section 1.1.1.2 recent data from the developed countries reports a reduction of 165g in birth weight

associated with maternal smoking.[19] This was even greater for heavy smokers where the birth weight reduced by 226g compared to non-smokers.[20]
Whilst there is clear evidence of the association of smoking with outcomes like stillbirth and low birth weight the understanding of the relationship between maternal smoking and the mode of delivery is vague. There are very few studies examining this relationship. A recent study conducted in Germany using a perinatal database including 170,254 singleton pregnancies found no increased risk of caesarean section associated with maternal smoking.[31] Similar results were found in smaller hospital-based studies from Spain and Hong Kong with no statistically significant association between maternal smoking and caesarean section.[267,268] A cross-sectional study from the UK using 15,288 births from the Millenium Cohort Data also did not find any effect of smoking on whether a woman had medical intervention at birth (OR 1.003, 95% CI 0.88-1.44) or caesarean section (OR 1.15,95% CI 0.95-1.39).[269] However, a study conducted in a maternity unit at St. Marys hospital, Portsmouth, UK on 400 smoking mothers and 400 non-smoking mothers showed that the risk of caesarean section was twice as high in smokers compared to non-smokers.[270] Similarly, a recent study conducted in Israel, including approximately 6000 pregnancies, reported the risk of any operative or instrumental intervention to be higher in smokers compared to non-smokers OR 1.24 (95% CI 1.01–1.52).[32]

The studies examining the association between NRT and these birth outcomes are even more limited. To date, there is only one observational study that has assessed the association between maternal NRT use and stillbirth.[113] Other evidence comes from RCTs of NRT patches and gum with inadequate power to assess safety outcomes.[100,107,109] Data from the DNBC suggest no increased risk of stillbirth associated with NRT use in the first 27 weeks of pregnancy (HR = 0.57, 95%CI 0.28-1.16) compared to those who did not use NRT and did not smoke). In comparison, women who both smoked and used NRT had an HR of

0.83 (95%CI 0.34-2.00) compared with non-smoking women who did not use NRT. [113] A meta-analysis of three RCTs assessing stillbirth as a secondary outcome also reported similar findings with no increased risk of stillbirth associated with NRT use compared to placebo (pooled OR 1.98, 95% CI 0.55-7.07).[101] Table 7-1 summarises the studies assessing NRT and birth outcomes including stillbirth, birth weight and mode of delivery.

The few studies assessing the association between NRT and birth weight present mixed evidence. Data from the observational studies report either no association between NRT and birth weight[112] or show an increased risk of low birth weight associated with NRT use.[111] In comparison, data from the trials report either no significant effect of NRT on infant's birth weight[100,107,108] or report higher birth weight in babies born to women randomised to NRT compared to the placebo group (mean difference 337g, ($p<0.01$)[109] (Table 7-1).

The association between NRT and caesarean section has only been investigated in the SNAP trial which found a 45% increased risk of caesarean section associated with NRT use compared to placebo (Table 7-1).

Table 7-1 - Summary of studies assessing the association between NRT use and birth outcomes

First author, year and location	Study methodology	Sample size (Inclusion/Exclusion)	Exposure Assessment	Outcome Assessment	Results for NRT safety
NRT and stillbirth					
Strandberg-Larsen (2008), Denmark [113]	Cohort study using Danish National Birth Cohort	87,032 pregnancies between 1996-2002	NRT self-reported usage, total number of weeks with NRT use during the first 27 weeks of gestation, NRT type used	Stillbirth, defined as any foetus that did not breathe or show any other signs of life at birth after a minimum of 20 weeks of gestation, derived from The Civil Registration System and Danish Medical Birth Registry	Women who used NRT during pregnancy had a HR of 0.57 (95%CI 0.28-1.16) for still birth compared to those who did not use NRT. Women who both smoked and used NRT had a HR of 0.83 (95%CI 0.34-2.00) compared with non-smoking women who did not use NRT
Coleman (2012), UK [100]	Large, double-blinded, placebo-controlled multicentre RCT	1050 participants between 16 to 50 years with pregnancies of 12-24 weeks of gestation smoking five or more cigarettes per day	4 weeks supply of Standard nicotine patch (15mg/16 hrs) versus visually identical placebo, started on the quit date	Secondary outcome: Adverse pregnancy and birth outcomes including stillbirth	5 cases in NRT group and 2 cases in the placebo group. Stillbirth – OR 2.59 (95% CI 0.50-13.4)
Oncken (2008), Connecticut and Massachusetts [109]	Prospective, randomised, double-blind placebo-controlled clinical trial.	100 women randomised to nicotine gum and 94 to placebo	Individualised behavioural counselling and 6 week treatment with 2mg nicotine gum versus placebo	Stillbirth as a secondary outcome	2 cases in the NRT group and 0 cases in the placebo group. Stillbirth – OR 4.55 (0.22- 93.63)

Pollack (2007), North Carolina, USA[107]	An open-labelled non-placebo, randomised trial	Cognitive Behavioural Therapy (CBT)-only (n=59) versus CBT+NRT (n=122) in pregnant women between 13 and 25 weeks of gestation.	Control: received a "Quit kit" (which contained a booklet, water bottle, straws, candy, exercise band, and stress management tape), as well as 3 counselling sessions from a "support specialist" based on motivational interviewing, trans theoretical model and social cognitive theory. Intervention: as above plus an option of NRT by patch, gum or lozenge. Participants could change mode of administration if they wished.	Stillbirth as a secondary outcome	1 cases in the CBT+NRT group and 1 case in the only CBT group. OR 0.49 (0.03- 7.66)
NRT and low birth weight					
Coleman (2012), UK [100]	Large, double-blinded, placebo-controlled multicentre RCT	1050 participants between 16 to 50 years with pregnancies of 12-24 weeks of gestation smoking five or more cigarettes per day	4 weeks supply of Standard nicotine patch (15mg/16 hrs) versus visually identical placebo, started on the quit date	Secondary outcome: Adverse pregnancy and birth outcomes including birth weight	Low birth weight – OR 1.38 (95% CI 0.90-2.09), mean difference in birth weight=-0.05 (95% CI -0.17, 0.08).

Lassen (2010), Denmark[112]	Cohort study using Danish National Birth Cohort, a nationwide study of pregnant women and their offspring including 101,042 pregnancies between 1996 and 2002	72,761 pregnancies between 1996 and 2002	NRT self-reported usage, total number of weeks with NRT use during the first 27 weeks of gestation, NRT type used	Offspring Birth weight in mothers using NRT	Total NRT use not significantly associated with changes in birth weight (b=0.25g per week of NRT use (95%CI -2.31, 2.81)). Simultaneous use of >1 product associated with a statistically insignificant decrease in birth weight (b=-10.73g per week of NRT use (95% CI -26.51,5.05))
Gaither (2009), North Carolina, USA [111]	Cross-sectional study using data from 2004 Phase V Pregnancy Risk Assessment Monitoring System	6,041 women between the ages of 18-45 years out of which 5,716 included in the final analysis	Smoking, NRT prescription Versus Non-smoking women during pregnancy	Low birth weight defined as <2500g at birth)	After the adjustment for age, marital status, education and race/ethnicity women recommended NRT had twice the risk of low birth weight compared to non-smokers (OR=1.95, 95%CI 1.10-3.46)
Oncken (2008), Connecticut and Massachusetts[109]	Prospective, randomised, double-blind placebo-controlled clinical trial.	100 women randomised to nicotine gum and 94 to placebo	Individualised behavioural counselling and 6 week treatment with 2mg nicotine gum versus placebo	Offspring birth weight	Mean difference in the birth weight between offspring of mothers using NRT versus mothers on placebo=337g (p<0.001)

Pollack (2007), North Carolina, USA[107]	An open-labelled non-placebo, randomised trial	Cognitive Behavioural Therapy (CBT)-only (n=59) versus CBT+NRT (n=122) in pregnant women between 13 and 25 weeks of gestation.	Control: received a "Quit kit" (which contained a booklet, water bottle, straws, candy, exercise band, and stress management tape), as well as 3 counselling sessions from a "support specialist" based on motivational interviewing, trans theoretical model and social cognitive theory. Intervention: as above plus an option of NRT by patch, gum or lozenge. Participants could change mode of administration if they wished.	Birth weight	The mean difference between the CBT+NRT and CBT only arm in the birth weight = -71g (p=0.51)
Wisborg (2000), Denmark [108]	Double-blinded, placebo-controlled RCT	Pregnant women who smoked ten or more cigarettes after the first trimester (250) were randomly assigned to receive nicotine patches (124) or placebo patches (126).	Women randomized to nicotine were treated with 15-mg patches (16 hours/day) for 8 weeks, and 10-mg patches (16 hours/day) for 3 weeks.	Birth weight	Mean difference between NRT and placebo group (186 g, 95% CI 35-336 g. RR for low birth weight with NRT use during pregnancy =0.40, (95% CI 0.10-1.10)
NRT and mode of delivery					

Coleman (2012), UK [100]	Large, double-blinded, placebo-controlled multicentre RCT	1050 participants between 16 to 50 years with pregnancies of 12-24 weeks of gestation smoking five or more cigarettes per day	4 weeks supply of Standard nicotine patch (15mg/16 hrs) versus visually identical placebo, started on the quit date	Secondary outcome: Adverse pregnancy and birth outcomes including mode of delivery	Caesarean section delivery – OR 1.45 (95% CI 1.05-2.01)

Given the dearth of information on the safety of NRT use during pregnancy and the inconclusive evidence arising from the limited literature available, this chapter focuses on examining the associations between NRT and smoking exposure during pregnancy as recorded in primary care and adverse birth outcomes. The specific objectives for this chapter are:

1. To examine the risk of stillbirth and fetal death (stillbirth and miscarriage) associated with maternal NRT and smoking exposure during pregnancy as described in primary care data
2. To assess the association between maternal NRT and smoking exposure during pregnancy, as recorded in primary care data, with birth weight
3. To assess the association between maternal NRT and smoking exposure during pregnancy as described in primary care data and mode of delivery

7.2 METHODS

7.2.1 Study population

The study population used for assessing stillbirth and mode of delivery was the same as described in Section 5.2.1 i.e. all pregnancies between January 2001 and September 2009 in women of childbearing age (15-49 years) which resulted in either a live birth or a stillbirth.

For low birth weight all live born children delivered between January 2001 and December 2009 with linked mother records and a recording for birth weight in their primary care records were included in the analysis. Stillborn children only constituted 0.07% of the total population and were excluded from this analysis as there may be higher risks of fetal growth restriction in stillborns compared to liveborns.

7.2.2 Exposure

Two different time windows were used to classify the study population into one of the exposure categories: NRT group, smoker, non-smoker and unknown. Firstly, early pregnancy NRT and smoking exposure (defined as exposure between four weeks before conception until the end of the first trimester), as recorded in primary care data, was assessed as described in Section 6.2.2. Additionally, the exposure window was expanded to the whole course of pregnancy until delivery to assess the effects of NRT or smoking exposure any time during pregnancy on stillbirth. This exposure window was then also used for assessing the risk of low birth weight and the mode of delivery as fetal growth takes place throughout pregnancy.

7.2.3 Outcomes

7.2.3.1 Stillbirth

Stillbirth was defined as a baby born with no signs of life at or after 28 weeks of gestation, in accordance with the WHO definition.[271] Information on stillbirth was extracted from the birth outcome variable pre-defined in the mother-child linked data, which has been described in Section 2.5.

A variable combining both stillbirth and miscarriage was created, called fetal death to assess the effect of NRT and smoking exposure on overall fetal death. It should however be noted that the information on miscarriages in these data is not complete which may have implications on the results.

7.2.3.2 Birth weight

Firstly, birth weight was also used as a continuous variable to examine the change in birth weight by each category of exposure. Then, low birth weight was

defined as a live born baby with a birth weight of less than 2500g (2.5kg) according to the WHO definition of low birth weight.[11]

7.2.3.3 Mode of delivery

Mode of delivery was also pre-defined in the mother-child linked file and categorised as normal delivery, assisted delivery and caesarean section. All pregnancies where there was no record of caesarean delivery or an assisted delivery were categorised as normal deliveries.

7.2.4 Statistical analysis

7.2.4.1 Stillbirth

The absolute risk of stillbirth was calculated by dividing the total number of stillbirths by the number of stillbirths and live births combined. Logistic regression was used to compute ORs and corresponding 99% CIs for stillbirth for the NRT group and smokers, using non-smokers as the reference group. Maternal age, Townsend quintile, maternal diabetes, hypertension, asthma, pre-conception body mass index and mental illnesses were considered as potential confounders based on the previous literature.[195,199,211,242-244,272-274] The covariates which had a significant statistical association with the exposure and the outcomes in chi-squared tests were included in the final model. The potential clustering of pregnancies among mothers was accounted for using the clustered sandwich estimator[180,181] The reference group was then changed to smokers and the ORs were re-calculated. This analysis was then repeated using the entire pregnancy until the outcome as the exposure time for NRT and smoking.

To estimate the association between NRT and smoking exposure during pregnancy with fetal death (defined here as stillbirth and miscarriages) the risk of fetal death was calculated for NRT and smoking exposure during the entire

pregnancy time until the outcome, using the analysis techniques described above.

7.2.4.2 Birth weight

The association between NRT exposure maternal smoking during pregnancy and birth weight was analysed using a multiple linear regression model, treating birth weight as a continuous outcome. Only complete case analysis was conducted i.e. only babies with a recording of birth weight were included in this analysis. Potential confounding factors (described above) and clustering were adjusted for in the analysis. The regression co-efficient (β) represents the average change in birth weight in grams associated with NRT group and smoking in relation to non-smokers. The risk of low birth weight for the NRT group and smokers was calculated in a similar fashion using univariable and multivariable logistic regression models as described above.

7.2.4.3 Mode of delivery

A multinomial logistic regression model (for categorical study outcomes) was used to obtain relative risk ratios (RRR) for assisted delivery and caesarean section relative to normal delivery in the NRT group, smokers and unknown categories compared to non-smokers. This model extends logistic regression by estimating the effect of one or more exposure variables on the probability that the outcome is in a particular category.[275] Robust CIs were calculated and appropriate adjustments in the RRRs for potential confounders were made in the same way as described above.

7.2.5 Sensitivity analysis

7.2.5.1 Reclassifying smokers and non-smokers based on gestational smoking status recording

Similar to the previous chapter, the definition of smokers was restricted to only mothers who had a gestational smoking record during pregnancy and the non-smokers to mothers who had a gestational record in their primary care data indicating them to be non-smokers. This was done for both the early pregnancy exposure and exposure throughout pregnancy. The absolute and relative risks of stillbirth, low birth weight and different modes of delivery were re-calculated using this definition.

7.2.5.2 Risk of low birth weight stratified by pre-term birth

Since birth weight is directly related to gestational age[276] the risk of low birth weight was further stratified by whether the baby was born preterm or not. Preterm birth was defined as babies born alive before 37 weeks of pregnancy in line with the WHO definition [277] and deliveries occurring at or after 37 weeks of gestation were classified as term deliveries for purposes of this analysis. Unadjusted and adjusted ORs and corresponding CIs were calculated separately for preterm and term deliveries.

7.2.6 Sample size calculations

The prevalence of stillbirth in the UK is estimated to be approximately 5/1000 live and stillbirths.[159] Based on the known prescribing prevalence of NRT and maternal smoking during pregnancy from previous chapters, a sample size of 96,641 children with mothers prescribed NRT was needed to detect an OR of 1.50 with 80% power at 1% level of significance. For maternal smoking, a sample size of 12,903 children with mothers who smoked during pregnancy was needed to detect an OR of 1.50, with 80% power at 1% level of significance.

Considering the standard deviation of birth weight in general population to be 466g,[278] a sample size of 7,646 babies will have 80% power to detect a mean difference of 150g with a two-sided level of significance of 5%. The prevalence of low birth weight in the UK in 2009 was approximately 7%.[279] In light of this, and the smoking and NRT prescribing prevalence from the previous chapter, a sample size of 43,029 children with mothers prescribed NRT was needed to detect an OR of 1.50 with 80% power at 1% level of significance. For smoking exposure a sample of 5,907 children with maternal smoking exposure was needed to detect an OR of 1.50 with 80% power at 1% level of significance.

7.3 RESULTS

7.3.1 Stillbirth

7.3.1.1 Baseline characteristics

The study population included 255,441 pregnancies delivered between 2001 and 2009 out of which 1,044 ended in stillbirths, giving a prevalence of 4/1,000 live and stillbirths. Pregnancies that were conceived at later ages (>35 years) resulted in a higher prevalence of stillbirth. The prevalence of stillbirths was also higher in pregnant women with diabetes and mental illness (3.5% and 11.9% respectively). The distribution of socioeconomic status, pre-conception BMI, and the prevalence of chronic illnesses like asthma and hypertension were comparable in women with stillbirth and those with live births.

Table 7-2 - Baseline characteristics for all pregnancies, by live birth and stillbirth

	All pregnancies		Live births		Stillbirths	
	N=255,441		N=254,397		N=1,044	
	n	%	n	%	n	%
Age at conception						
15-19 years	14,141	5.5%	14,066	5.5%	75	7.2%
20-24 years	40,879	16.0%	40,703	16.0%	176	16.9%
25-29 years	65,029	25.5%	64,796	25.5%	233	22.3%
30-34 years	79,959	31.3%	79,683	31.3%	276	26.4%
35-39 years	45,765	17.9%	45,543	17.9%	222	21.3%
40-44 years	9,179	3.6%	9,122	3.6%	57	5.5%
45-49 years	489	0.2%	484	0.2%	5	0.5%
Townsend score in quintiles						
Quintile 1 (least deprived)	57,859	22.7%	57,658	22.7%	201	19.3%
Quintile 2	47,841	18.7%	47,664	18.7%	177	17.0%
Quintile 3	49,670	19.4%	49,465	19.4%	205	19.6%
Quintile 4	47,292	18.5%	47,086	18.5%	206	19.7%
Quintile 5 (most deprived)	36,103	14.1%	35,902	14.1%	201	19.3%
Missing	16,676	6.5%	16,622	6.5%	54	5.2%
Pre-conception Body Mass Index (kg/m^2)						
Normal(18.5-24.9)	80,016	31.3%	79,737	31.3%	279	26.7%
Underweight(<18.5)	5,856	2.3%	5,825	2.3%	31	3.0%
Overweight(25-29.9)	38,945	15.2%	38,785	15.2%	160	15.3%
Obese(>=30)	26,741	10.5%	26,595	10.5%	146	14.0%
Missing	103,883	40.7%	103,455	40.7%	428	41.0%
Asthma	21,884	8.6%	21,802	8.6%	82	7.9%
Hypertension	6,885	2.7%	6,848	2.7%	37	3.5%
Diabetes	5,971	2.3%	5,930	2.3%	41	3.9%
Mental illness	24,178	9.5%	24,054	9.5%	124	11.9%

7.3.1.2 Association between NRT and smoking exposure in early pregnancy and stillbirth

Table 7-3 presents the odds of stillbirth in relation to NRT exposure and maternal smoking during early pregnancy. The prevalence of stillbirth in the study population was found to be 4/1,000 live and stillbirths. The absolute risk of stillbirth was 4/1,000 live and stillbirths amongst the NRT group and 5/1000 live and stillbirths among smokers.

In the unadjusted analysis there was no statistically significant increased risk of stillbirth associated with NRT exposure during early pregnancy. However, women who smoked during early pregnancy were 35% more likely to have stillbirths compared to non-smokers (OR 1.35, 99% CI 1.08-1.68). The association between NRT exposure in early pregnancy and stillbirth did not reach statistical significance when adjusted for the potential confounders (OR 1.19, 99% CI 0.47-3.01). The association between maternal smoking and stillbirth was, however, still significant after adjusting for maternal age at conception, Townsend quintile, pre-conception BMI, diabetes and mental illness, with a 27% increase in the risk of stillbirth associated with maternal smoking during early pregnancy (OR 1.27, 99% CI 1.01-1.60).

When the reference group was changed to smokers, no increased risk of stillbirth was found for NRT exposure in comparison to smoking (OR 0.94, 99% CI 0.36-2.38).

Table 7-3 – Risk of stillbirth by NRT and smoking exposure only during early pregnancy

	Total population N=255,441	Stillbirths n (%)	Unadjusted OR (99% CI)	p-value	Adjusted OR (99%CI)‡	p-value
Non-smoker***	125,261	450 (0.4%)	1		1	
NRT-exposed group *	1,759	8 (0.4%)	1.26 (0.50-3.18)	0.508	1.19 (0.47-3.01)	0.622
Smoker**	41,603	201 (0.5%)	1.35 (1.08-1.68)	<0.001	1.27 (1.01-1.60)	0.007
Unknown	86,818	385 (0.4%)	1.23 (1.03-1.48)	0.002	1.20 (1.00-1.45)	0.010

*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy , ***non-smokers during early pregnancy
‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births
OR=Odds ratio, CI= confidence interval

7.3.1.3 Association between NRT, smoking exposure during the entire pregnancy and stillbirth

When the exposure time was expanded to include any NRT prescribing or smoking until delivery the absolute risks were similar.

No increased risk of stillbirth was found to be associated with NRT exposure (adjusted OR 1.67, 99% CI 0.94-2.99) (Table 7-4). Maternal smoking any time during pregnancy was also not found to be associated with an increased risk of stillbirth (OR 1.19, 99% CI 0.95-1.52).

When the reference group was changed to smokers, no increased risk of stillbirth was found in the NRT group in comparison to smoking (OR 1.39, 99% CI 0.76-2.53).

Table 7-4 – Risk of stillbirth by NRT and smoking exposure throughout pregnancy

	Total population N=255,441	Stillbirths n (%)	Unadjusted OR (99% CI)	p-value	Adjusted OR (99%CI) ‡	p-value
Non-smoker***	123,356	447 (0.4%)	1			
NRT-exposed group *	3,254	21 (0.6%)	1.79 (1.00-3.18)	0.010	1.67 (0.94-2.99)	0.022
Smoker**	42,089	193 (0.5%)	1.26 (1.00-1.58)	0.001	1.19 (0.95-1.52)	0.046
Unknown	86,742	383 (0.4%)	1.22 (1.01-1.45)	0.002	1.18 (0.98-1.43)	0.018

*NRT=nicotine replacement therapy prescription any time during pregnancy, **smoking any time during pregnancy, ***non-smokers during pregnancy ‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births
OR=Odds ratio, CI= confidence interval

7.3.1.4 Association between NRT, smoking exposure and fetal death

Table 7-5 presents the unadjusted and adjusted odds ratios for fetal death in relation to NRT and maternal smoking exposure during pregnancy. The prevalence of stillbirth and miscarriages together was the highest among current smokers (20.8%) and the lowest in the NRT group (9.4%).

NRT exposure during pregnancy was found to have a protective effect on fetal death such that it reduced the risk of fetal death by half (OR 0.44, 99% CI 0.38-0.51) in comparison to non-smokers. Smoking was found to increase the risk of fetal death by 16% (OR 1.16, 99% CI 1.11-1.21) when compared to the risk in non-smokers.

Table 7-5 – Risk of fetal death by NRT and smoking exposure throughout pregnancy

	Total population N=311,802	Fetal death n (%)	Unadjusted OR (99% CI)	p-value	Adjusted OR‡ (99%CI)	p-value
Non-smoker***	150,175	25,962 (17.3%)	1		1	
NRT group *	5,234	491 (9.4%)	0.50 (0.44-0.56)	<0.001	0.44 (0.38-0.50)	<0.001
Smoker**	50,643	10,560 (20.8%)	1.26 (1.22-1.30)	<0.001	1.16 (1.11-1.21)	<0.001
Unknown	105,750	20,392 (19.3%)	1.14 (1.11-1.17)	<0.001	0.95 (0.74-1.21)	0.571

*NRT=nicotine replacement therapy prescription any time during pregnancy, **smoking any time during pregnancy, ***non-smokers during pregnancy ‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births
OR=Odds ratio, CI= confidence interval

7.3.1.5 Sensitivity analysis

The results from the sensitivity analysis were very similar to the main results showing no statistically significant increased risk of stillbirth in the NRT group in both early pregnancy (OR 1.44, 99% CI 0.54-3.82) and throughout pregnancy (OR 1.95, 99% CI 1.00-3.63). Similarly, the risk of stillbirth increased by 78% in mothers who smoked in early pregnancy (OR 1.78, 99% CI 1.04-3.02). This effect decreased when exposure throughout pregnancy was assessed (OR 1.47, 99% CI 0.96-2.25).

Table 7-6 – Risk of stillbirth by NRT and smoking exposure only during early pregnancy, using only gestational smoking records

	Total population N=255,441	Stillbirths n (%)	Unadjusted OR (99% CI)	p-value	Adjusted OR (99%CI)‡	p-value
Non-smoker***	20,068	59 (0.3%)	1		1	
NRT-exposed group *	1,759	8 (0.4%)	1.55 (0.59-4.09)	0.246	1.44 (0.54-3.82)	0.336
Smoker**	7,381	41 (0.6%)	1.89 (1.13-3.20)	0.002	1.78 (1.04-3.02)	0.005
Unknown	226,233	936 (0.4%)	1.41 (0.99-1.99)	0.011	1.37 (0.96-1.93)	0.020

*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy , ***non-smokers during early pregnancy
‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births
OR=Odds ratio, CI= confidence interval

Table 7-7 – Risk of stillbirth by NRT and smoking exposure throughout pregnancy, using only gestational smoking records

	Total population N=255,441	Stillbirths n (%)	Unadjusted OR (99% CI)	p-value	Adjusted OR (99%CI) ‡	p-value
Non-smoker***	32,203	101 (0.3%)	1		1	
NRT-exposed group *	3,254	21 (0.6%)	1.79 (1.00-3.18)	0.010	1.95 (1.00-3.63)	0.006
Smoker**	12,126	60 (0.5%)	1.32 (1.06-1.66)	0.001	1.47 (0.96-2.25)	0.019
Unknown	207,757	862 (0.4%)	1.22 (1.01-1.45)	0.002	1.31 (1.00-1.72)	0.018

*NRT=nicotine replacement therapy prescription any time during pregnancy, **smoking any time during pregnancy , ***non-smokers during pregnancy ‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births
OR=Odds ratio, CI= confidence interval

7.3.2 Low birth weight

7.3.2.1 Baseline characteristics

A total of 96,782 children with linked maternal records had their birth weight recorded in THIN out of a total population of 232,242 live born children. The distribution of maternal characteristics in children with a recording of birth weight and without a recording of birth weight was highly comparable however the proportion of missing maternal BMI data was lower in children with who had a recording of birth weight compared to those without a recording of birth weight (35.4% compared with 44.0%) (Table 7-8).

Table 7-8 - Recording of birth weight and maternal characteristics

	All births (N=232,242)		Birth weight recorded (96,872)		No birth weight recorded (135,370)	
	N	%	n	%	n	%
Age at conception						
15-19 years	12,037	5.2%	4,900	5.1%	7,137	5.3%
20-24 years	36,003	15.5%	15,031	15.5%	20,972	15.5%
25-29 years	59,203	25.5%	24,722	25.5%	34,481	25.5%
30-34 years	73,844	31.8%	30,791	31.8%	43,053	31.8%
35-39 years	42,477	18.3%	17,917	18.5%	24,560	18.1%
40-44 years	8,341	3.6%	3,376	3.5%	4,965	3.7%
45-49 years	337	0.1%	135	0.1%	202	0.1%
Townsend score in quintiles						
Quintile 1 (most affluent)	53,916	23.2%	22,061	22.8%	31,855	23.5%
Quintile 2	43,850	18.9%	17,839	18.4%	26,011	19.2%
Quintile 3	45,280	19.5%	19,390	20.0%	25,890	19.1%
Quintile 4	42,696	18.4%	18,109	18.7%	24,587	18.2%
Quintile 5 (most deprived)	31,884	13.7%	13,053	13.5%	18,831	13.9%
Missing	14,616	6.3%	6,420	6.6%	8,196	6.1%
Pre-conception Body Mass Index						
Normal(18.5-24.9)	73,002	31.4%	32,813	33.9%	40,189	29.7%
Underweight(<18.5)	5,225	2.2%	2,317	2.4%	2,908	2.1%
Overweight(25-29.9)	35,625	15.3%	16,254	16.8%	19,371	14.3%
Obese(>=30)	24,594	10.6%	11,233	11.6%	13,361	9.9%
Missing	93,796	40.4%	34,255	35.4%	59,541	44.0%
Asthma	19,932	8.6%	9,002	9.3%	10,930	8.1%
Hypertension	6,392	2.8%	2,910	3.0%	3,482	2.6%
Diabetes	5,490	2.4%	2,400	2.5%	3,090	2.3%
Mental illness	22,154	9.5%	10,131	10.5%	12,023	8.9%
Multiple births	8,373	3.6%	3,361	3.5%	5,012	3.7%

In the 96,782 children with a recording of birth weight, the mean birth weight was 3.41kgs (sd 0.59) and the mean gestational age was 40 weeks (sd 2.11). Figure 7-1 presents a histogram of the birth weight (in kilograms) of the 96,782 children with a recording of birth weight. Birth weight was normally distributed with no skewing towards high or low birth weight. Table 7-9 presents the maternal characteristics of children with normal and low birth weight.

Figure 7-1 - Histogram of birth weight in the study population

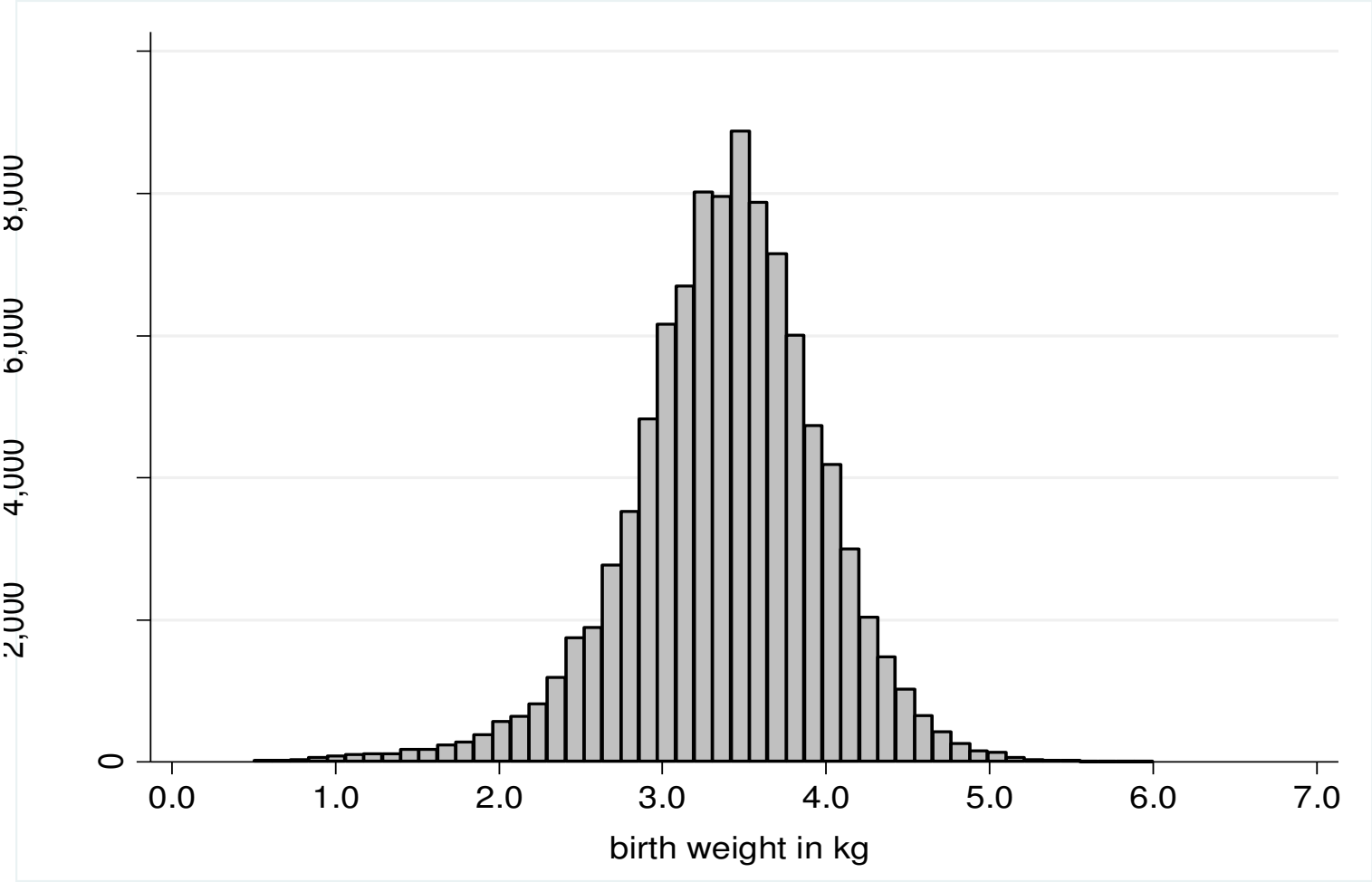


Table 7-9 - Baseline characteristics by birth weight

	All live births (N=96,872)		Normal birth weight (N=90,670)		Low birth weight (N= 6,202)	
	N	%	n	%	n	%
Age at conception						
15-19 years	4,900	5.1%	4,549	5.0%	351	5.7%
20-24 years	15,031	15.5%	14,007	15.4%	1,024	16.5%
25-29 years	24,722	25.5%	23,231	25.6%	1,491	24.0%
30-34 years	30,791	31.8%	28,950	31.9%	1,841	29.7%
35-39 years	17,917	18.5%	16,695	18.4%	1,222	19.7%
40-44 years	3,376	3.5%	3,124	3.4%	252	4.1%
45-49 years	135	0.1%	114	0.1%	21	0.3%
Townsend score in quintiles						
Quintile 1 (least deprived)	22,061	22.8%	20,862	23.0%	1,199	19.4%
Quintile 2	17,839	18.4%	16,791	18.5%	1,048	16.9%
Quintile 3	19,390	20.0%	18,201	20.1%	1,189	19.2%
Quintile 4	18,109	18.7%	16,811	18.5%	1,298	20.9%
Quintile 5 (most deprived)	13,053	13.5%	12,006	13.2%	1,047	16.9%
Missing	6,420	6.6%	5,999	6.6%	421	6.8%
Pre-conception Body Mass Index (kg/m^2)						
Normal(18.5-24.9)	32,813	33.9%	30,667	33.8%	2,146	34.6%
Underweight(<18.5)	2,317	2.4%	2,008	2.2%	309	5.0%
Overweight(25-29.9)	16,254	16.8%	15,310	16.9%	944	15.2%
Obese(>=30)	11,233	11.6%	10,644	11.7%	589	9.5%
Missing	34,255	35.4%	32,041	35.3%	2,214	35.7%
Asthma	9,002	9.3%	8,298	9.2%	704	11.4%
Hypertension	2,910	3.0%	2,501	2.8%	409	6.6%
Diabetes	2,400	2.5%	2,207	2.4%	193	3.1%
Mental illness	10,131	10.5%	9,354	10.3%	777	12.5%
Multiple births	3,361	3.50%	1,823	2.0%	1,538	24.8%

7.3.2.2 Association between maternal NRT and smoking exposure during pregnancy and birth weight

Table 7-10 describes the change in mean birth weight for the NRT group and smokers compared to non-smokers. NRT exposure during pregnancy was associated with a statistically significant decrease in birth weight of 176g compared to non-smokers (β = -176g, 99% CI -221g, -131g). In comparison, smoking during pregnancy was associated with a statistically significant decrease in birth weight of 120g compared to non-smokers (β =-123g, 99% CI -136g,-109g).

When the baseline was changed to smokers, the NRT group was found to have slightly reduced birth weight compared to smokers (β-5g, 99% CI -9g, -0.7g).

Table 7-10 - The association between NRT and smoking exposure during pregnancy and mean birth weight

	Unadjusted change in mean birth weight (g)		Adjusted change in mean birth weight(g)	
	β (99% CI)	**p-value**	**β (99% CI)***	**p-value**
NRT group *	-211 (-258, -164)	<0.001	-176 (-221,-131)	<0.001
Smoker**	-143 (-157, -129)	<0.001	-123 (-136,-109)	<0.001
Unknown	-30 (-41,-19)	<0.001	-28 (-39,-17)	<0.001

Non-smokers during early pregnancy considered as baseline
*NRT=nicotine replacement therapy prescription in pregnancy, **smoking in pregnancy
‡Adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index
CI = confidence interval, OR = Odds ratio

7.3.2.3 Association between NRT exposure, smoking and low birth weight

Table 7-11 presents the prevalence of low birth weight by NRT and smoking exposure in mothers and the corresponding unadjusted and adjusted odds ratios (99% CI). The prevalence of low birth weight was the highest in the NRT group followed by smokers (11.0% and 9.0% respectively). Compared to non-smokers, children born to women in the NRT group were over twice as likely and children born to smokers were 64% more likely to have low birth weight. When adjusted for potential confounders, the risk of low birth weight in the NRT group was 93% higher compared to non-smokers (OR 1.93, 99% CI 1.48-2.53). Similarly, the risk of low birth weight in smokers was 69% higher (OR 1.69, 99% CI 1.53-1.86) compared to non-smoking mothers. When the reference group was changed to smokers, there was no increased risk of low birth weight in the NRT group compared to smokers (OR 1.24, 99% CI 0.97-1.59) (p=0.023).

Table 7-11 – Risk of low birth weight by NRT and smoking exposure during pregnancy

	Total population N=96,872	Low birth weight n (%)	Unadjusted OR (99% CI)	p-value	Adjusted OR (99%CI) ‡	p-value
Non-smoker***	49,452	2,796 (5.6%)	1		1	
NRT group *	1,223	135 (11.0%)	2.07 (1.63-2.63)	<0.001	1.93 (1.48-2.53)	<0.001
Smoker**	16,135	1,445 (9.0%)	1.64 (1.50-1.79)	<0.001	1.69 (1.53-1.86)	<0.001
Unknown	30,062	1,826 (6.1%)	1.08 (0.99-1.16)	0.014	1.09 (0.99-1.18)	0.015

*NRT=nicotine replacement therapy prescription in pregnancy, **smoking in pregnancy, ***non-smokers during pregnancy
‡ Adjusted for maternal age, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index
CI = confidence interval, OR = Odds ratio

7.3.2.4 Sensitivity analysis

7.3.2.4.1 Maternal NRT and smoking during pregnancy and birth weight, using only gestational smoking records

Table 7-12 describes the change in mean birth weight for NRT group and smokers compared to non-smokers, using only gestational smoking records. NRT exposure during pregnancy was still associated with a statistically significant decrease in birth weight of 168g compared to non-smokers (β = -168g, 99% CI -214g, -122g). In comparison, smoking during pregnancy was associated with a statistically significant decrease in birth weight of 139g compared to non-smokers (β =-139g, 99% CI -165g,-113g).

Table 7-12 - The association between NRT and smoking exposure during pregnancy and mean birth weight, using only gestational smoking records

	Unadjusted change in mean birth weight (g)		Adjusted change in mean birth weight(g)	
	β (99% CI)	**p-value**	**β (99% CI)***	**p-value**
NRT group *	-207 (-255, -158)	<0.001	-168 (-214,-122)	<0.001
Smoker**	-168 (-194, -141)	<0.001	-139 (-165,-113)	<0.001
Unknown	-26 (-41,-12)	<0.001	-22 (-35,-8)	<0.001

Non-smokers during early pregnancy considered as baseline
*NRT=nicotine replacement therapy prescription in pregnancy, **smoking in pregnancy
‡Adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index
CI = confidence interval, OR = Odds ratio

7.3.2.4.2 Reclassifying smokers and non-smokers based on gestational smoking status recording

Table 7-13 presents the prevalence of low birth weight by NRT and smoking exposure in mothers and the corresponding unadjusted and adjusted ORs (99% CI) using only gestational smoking status records. The prevalence of low birth weight across the exposure groups was very similar to the main analysis (11.0% in the NRT group and 9.4% in smokers). After adjusting for potential confounders children born to women in the NRT group were 88% more likely (OR 1.88, 99% CI 1.42-2.49) and children born to smokers were 73% more likely (OR 1.73, 99% CI 1.45-2.06) to be of low birth weight compared to children born to non-smokers during pregnancy.

Table 7-13 - Unadjusted and adjusted Odds ratio for low birth weight by NRT and smoking exposure, using only definitive smokers and non-smokers

	Total population N=96,872	Low birth weight n (%)	Unadjusted OR (99% CI)	p-value	Adjusted OR (99%CI) ‡	p-value
Non-smoker***	13,088	740 (5.6%)	1		1	
NRT-exposed group *	1,223	135 (11.0%)	2.07 (1.48-2.03)	<0.001	1.88 (1.42-2.49)	<0.001
Smoker**	4,622	435 (9.4%)	1.73 (1.60-2.67)	<0.001	1.73 (1.45-2.06)	<0.001
Unknown	77,939	4,892 (6.3%)	1.12 (1.00-1.24)	0.006	1.13 (0.99-1.24)	0.012

*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy, ***non-smokers during early pregnancy
‡ Adjusted for maternal age, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index
CI = confidence interval, OR = Odds ratio

7.3.2.4.3 Risk of low birth weight stratified by pre-term birth

Table 7-14 shows the risk of low birth weight by NRT and smoking exposure stratified by preterm birth. Both maternal NRT and smoking exposure during pregnancy were found to be associated with low birth weight in babies in both preterm and term births. However, the risk of low birth weight was slightly higher in term births.

When direct comparisons were made with smokers in both term and pre-term birth, NRT was not found to have any statistically significant increased risk (OR 1.31, 99% CI 0.79-2.20 for pre-term birth and OR 0.99, 99% CI 0.68-1.46 for term births).

Table 7-14 - Unadjusted and adjusted odds ratio for low birth weight by NRT and smoking exposure, stratified by preterm birth

	Unadjusted OR (99% CI)	p-value	Adjusted OR (95% CI) ‡	p-value
		Term birth		
Non-smoker* **	1		1	
NRT group *	2.18 (1.54-3.10)	<0.001	1.82 (1.25-2.66)	<0.001
Smoker**	1.96 (1.73-2.22)	<0.001	1.83 (1.59-2.09)	<0.001
Unknown	1.14 (1.00-1.27)	0.006	1.09 (0.97-1.24)	0.053
		Pre-term birth		
Non-smoker* **	1		1	
NRT group *	1.77 (1.10-2.85)	0.002	2.00 (1.21-3.31)	<0.001
Smoker**	1.28 (1.09-1.51)	<0.001	1.52 (1.27-1.82)	<0.001
Unknown	1.00 (0.87-1.15)	0.972	1.06 (0.91-1.23)	0.354

*NRT=nicotine replacement therapy prescription in early pregnancy, **smoking in early pregnancy, ***non-smokers during early pregnancy
‡Adjusted for maternal age, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index
CI = confidence interval, OR = Odds ratio

7.3.3 Mode of delivery

A total of 255,441 pregnancies among a cohort of 201,465 mothers were identified. Approximately three-quarters of all pregnancies (76.5%) were delivered through normal vaginal delivery, 6.2% through assisted delivery and 17.3% through caesarean section. Compared to the normal and assisted deliveries, women with caesarean sections were older and more obese and had a higher prevalence of hypertension, diabetes and mental illness. Table 7-15 presents the baseline characteristics of women in all three outcome groups. Asthma and mental illness were found to be most common in current smokers and the NRT group. In addition, approximately 50% mothers in smokers group and NRT group were more deprived (Townsend quintile 4 and 5). Table 7-16 presents maternal characteristics by NRT exposure and smoking among the study population. Women prescribed NRT and smokers were more likely to be from younger and more deprived groups. Additionally, the prevalence of asthma and mental illness was the highest among pregnant women who smoked during pregnancy or were prescribed NRT during pregnancy.

The prevalence of assisted delivery was found to be the highest in non-smokers (6.7%) however it wasn't very different in other exposure groups (5.2% in NRT group and 5.7% in smokers and unknown group). Similarly, the prevalence of caesarean section was also found to be the highest in non-smokers (18.3%).

Table 7-15 - Baseline characteristics for all modes of delivery

Baseline characteristics	All N=255,441		Normal delivery n=195,523		Assisted delivery n=15,835		Caesarean delivery n=44,083	
	n	%	n	%	n	%	n	%
Age at conception								
15-19 years	14,141	5.5%	11,776	6.0%	974	6.2%	1,391	3.2%
20-24 years	40,879	16.0%	33,271	17.0%	2,452	15.5%	5,156	11.7%
25-29 years	65,029	25.5%	50,717	25.9%	4,271	27.0%	10,041	22.8%
30-34 years	79,959	31.3%	59,892	30.6%	5,187	32.8%	14,880	33.8%
35-39 years	45,765	17.9%	33,182	17.0%	2,494	15.7%	10,089	22.9%
40-44 years	9,179	3.6%	6,374	3.3%	429	2.7%	2,376	5.4%
45-49 years	489	0.2%	311	0.2%	28	0.2%	150	0.3%
Townsend score in quintiles								
Quintile 1 (least deprived)	57,859	22.7%	43,195	22.1%	4,028	25.4%	10,636	24.1%
Quintile 2	47,841	18.7%	35,996	18.4%	3,274	20.7%	8,571	19.4%
Quintile 3	49,670	19.4%	37,889	19.4%	3,147	19.9%	8,634	19.6%
Quintile 4	47,292	18.5%	36,933	18.9%	2,601	16.4%	7,758	17.6%
Quintile 5 (most deprived)	36,103	14.1%	28,657	14.7%	1,785	11.3%	5,661	12.8%
Missing	16,676	6.5%	12,853	6.6%	1,000	6.3%	2,823	6.4%
Pre-pregnancy Body Mass Index (kg/m$^{2)}$								
Normal(18.5-24.9)	80,016	22.7%	62,131	31.8%	5,724	36.1%	12,161	27.6%
Underweight(<18.5)	5,856	18.7%	4,737	2.4%	391	2.5%	728	1.7%
Overweight(25-29.9)	38,945	19.4%	28,914	14.8%	2,385	15.1%	7,646	17.3%
Obese(>=30)	26,741	18.5%	18,732	9.6%	1,222	7.7%	6,787	15.4%
Missing	103,883	14.1%	81,009	41.4%	6,113	38.6%	16,761	38.0%
Asthma	21,884	22.7%	16,358	8.4%	1,414	8.9%	4,112	9.3%
Hypertension	6,885	18.7%	4,385	2.2%	422	2.7%	2,078	4.7%
Diabetes	5,971	19.4%	3,588	1.8%	356	2.2%	2,027	4.6%
Mental illness	24,178	18.5%	18,338	9.4%	1,385	8.7%	4,455	10.1%

Table 7-16 - Baseline characteristics by NRT and smoking exposure during pregnancy

	All pregnancies		NRT group*		Smokers**		Non-smokers***		Unknown	
	N=255,441		n=3,254		n=42,089		n=123,356		n=86,742	
	n	%	n	%	n	%	n	%	n	%
Age at conception										
15-19 years	14,141	5.5%	306	9.4%	4,649	11.0%	4,558	3.7%	4,628	5.3%
20-24 years	40,879	16.0%	791	24.3%	11,421	27.1%	16,387	13.3%	12,280	14.2%
25-29 years	65,029	25.5%	847	26.0%	11,282	26.8%	32,383	26.3%	20,517	23.7%
30-34 years	79,959	31.3%	773	23.8%	8,980	21.3%	41,389	33.6%	28,817	33.2%
35-39 years	45,765	17.9%	447	13.7%	4,767	11.3%	23,692	19.2%	16,859	19.4%
40-44 years	9,179	3.6%	83	2.6%	944	2.2%	4,717	3.8%	3,435	4.0%
45-49 years	489	0.2%	7	0.2%	46	0.1%	230	0.2%	206	0.2%
Townsend score in quintiles										
Quintile 1 – least deprived	57,859	22.7%	334	10.3%	5,141	12.2%	30,828	25.0%	21,556	24.9%
Quintile 2	47,841	18.7%	381	11.7%	5,886	14.0%	24,779	20.1%	16,795	19.4%
Quintile 3	49,670	19.4%	620	19.1%	8,258	19.6%	24,084	19.5%	16,708	19.3%
Quintile 4	47,292	18.5%	884	27.2%	10,478	24.9%	20,636	16.7%	15,294	17.6%
Quintile 5 - most deprived	36,103	14.1%	804	24.7%	9,624	22.9%	14,068	11.4%	11,607	13.4%
Missing	16,676	6.5%	231	7.1%	2,702	6.4%	8,961	7.3%	4,782	5.5%
Pre-conception Body Mass Index (kg/m^2)										
Normal(18.0-24.9)	80,016	22.7%	1,017	31.3%	14,127	33.6%	48,171	39.1%	16,701	19.3%
Underweight(<18.0)	5,856	18.7%	101	3.1%	1,491	3.5%	2,984	2.4%	1,280	1.5%
Overweight(25-29.9)	38,945	19.4%	515	15.8%	6,860	16.3%	23,060	18.7%	8,510	9.8%
Obese(>=30)	26,741	18.5%	405	12.4%	5,104	12.1%	15,375	12.5%	5,857	6.8%
Missing	103,883	14.1%	1,216	37.4%	14,507	34.5%	33,766	27.4%	54,394	62.7%
Asthma	21,884	22.7%	404	12.4%	4,868	11.5%	12,416	10.1%	4,196	4.9%
Hypertension	6,885	18.7%	70	2.3%	882	2.1%	3,965	3.2%	1,968	2.3%
Diabetes	5,971	19.4%	70	2.6%	865	2.0%	3,548	2.9%	1,488	1.7%
Mental illness	24,178	18.5%	625	19.0%	6,549	15.5%	9,604	7.8%	7,400	8.5%

*NRT=nicotine replacement therapy prescription in pregnancy, **smoking in pregnancy, *** No smoking in pregnancy,

Table 7-17 - Breakdown of mode of deliveries by NRT and smoking exposure

Mode of delivery	Total	NRT group*	Smokers**	Non-smokers***	Unknown
	N=255,441	n=3,254	n=42,089	n=123,356	n=86,742
Normal	195,523 (76.5%)	2,551 (78.4%)	33,019 (78.5%)	92,452 (75%)	67,501 (77.8%)
Assisted	15,835 (6.2%)	159 (4.9%)	2,415 (5.7%)	8,355 (6.8%)	4,909 (5.7%)
C-section	44,083 (17.3%)	544 (16.7%)	6,658 (15.8%)	22,549 (18.3%)	14,332 (16.5%)

*NRT=nicotine replacement therapy prescription in pregnancy, **smoking in pregnancy, *** No smoking in pregnancy

Table 7-18 presents the unadjusted and adjusted RRRs for each mode of delivery for NRT and smoking exposure during pregnancy compared to non-smokers. In the unadjusted analysis pregnant women who were prescribed NRT during pregnancy had a 31% reduced risk of assisted delivery (RRR 0.69, 99% CI 0.55-0.85) and 13% reduced risk of caesarean sections (RRR 0.87, 99% CI 0.77-0.99) compared to non-smokers. Smokers had consistently decreased risks of both assisted delivery and caesarean section compared with women from the referent group (non-smokers). After adjusting for maternal characteristics, NRT exposure during pregnancy was still significantly associated with a 25% reduction in the risk of assisted delivery however the association between NRT exposure and caesarean section was not statistically significant (p=0.566).

When the reference category was changed to current smokers, the relative risk of assisted delivery in the NRT group decreased by 12%, however this was not statistically significant. Similarly, the relative risk of caesarean section in the NRT group compared to smokers was 1.01 (99% CI 0.89-1.16) which indicated no statistically significant association.

Table 7-18 - Unadjusted and adjusted relative risk ratios of each mode of delivery relative to normal delivery by NRT and smoking exposure during pregnancy compared to non-smokers

	Unadjusted				Adjusted ‡			
	Assisted Delivery		C-section		Assisted delivery		C-section	
	RRR (99% CI)	p-value	RRR (99% CI)	p-value	RRR(99% CI)	p-value	RRR(99% CI)	p-value
Non-smoker***	1		1		1		1	
NRT group *	0.69 (0.55-0.85)	<0.001	0.87 (0.77-0.99)	0.005	0.75 (0.60-0.93)	<0.001	0.97 (0.85-1.10)	0.566
Smoker**	0.80 (0.75-0.86)	<0.001	0.83 (0.80-0.86)	<0.001	0.85 (0.80-0.91)	<0.001	0.96 (0.92-1.00)	0.004
Unknown	0.80 (0.77-0.84)	<0.001	0.87 (0.84-0.90)	<0.001	0.84 (0.80-0.88)	<0.001	0.92 (0.89-0.95)	<0.001

*NRT=nicotine replacement therapy prescription in pregnancy, **smoking in pregnancy, *** No smoking in pregnancy, ‡adjusted for maternal age, Townsend score, diabetes, asthma, hypertension, mental illness, RRR= Relative Risk Ratio, CI=Confidence Interval

Table 7-19 - Unadjusted and adjusted relative risk ratios of each mode of delivery relative to normal delivery in non-smokers and the NRT group compared to smokers

	Unadjusted				Adjusted ǂ			
	Assisted Delivery		C-section		Assisted delivery		C-section	
	RRR (95% CI)	p-value	RRR (95% CI)	p-value	RRR(95% CI)	p-value	RRR(95% CI)	p-value
Non-smoker***	1.24 (1.16-1.32)	<0.001	1.21 (1.16-1.26)	<0.001	1.18 (1.10-1.26)	<0.001	1.05 (1.00-1.09)	0.007
NRT group *	0.85 (0.68-1.06)	0.060	1.06 (0.93-1.20)	0.491	0.88 (0.70-1.08)	0.118	1.01 (0.89-1.16)	0.733
Smoker**	1		1		1		1	
Unknown	1.00 (0.93-1.06)	0.864	1.05 (1.00-1.10)	0.002	0.99 (0.92-1.05)	0.599	0.96 (0.92-1.00)	0.016

*NRT=nicotine replacement therapy prescription in pregnancy, **smoking in pregnancy, *** No smoking in pregnancy, ǂadjusted for maternal age, Townsend score, diabetes, asthma, hypertension, mental illness

7.3.3.1 Sensitivity analysis

When smokers and non-smokers were reclassified based on the presence of gestational smoking status records, the proportion of total smokers reduced to 4.8% and non-smokers to 12.6%. However, the distribution of normal, assisted and caesarean deliveries remained similar to the main analysis.

In the unadjusted analysis women in the NRT group had a 31% reduced risk of assisted delivery (RRR 0.69, 99% CI 0.55-0.85) and a 13% reduced risk of caesarean sections (RRR 0.87, 99% CI 0.77-0.99) compared to non-smokers. Smokers had consistently decreased risks of both assisted delivery and caesarean section compared with women from the referent group (non-smokers). After adjusting for maternal characteristics, NRT exposure during pregnancy was significantly associated with a 32% reduction in the risk of assisted delivery, however the association between NRT exposure and caesarean section was not statistically significant anymore (p=0.120).

Table 7-20 - Unadjusted and adjusted relative risk ratios of each mode of delivery relative to normal delivery by NRT and smoking exposure during pregnancy compared to non-smokers, using definitive smokers and non-smokers

	Unadjusted				Adjusted ‡			
	Assisted Delivery		C-section		Assisted delivery		C-section	
	RRR (99% CI)	p-value	RRR (99% CI)	p-value	RRR(99% CI)	p-value	RRR(99% CI)	p-value
Non-smoker***	1		1		1		1	
NRT group *	0.63 (0.51-0.79)	<0.001	0.84 (0.74-0.96)	0.005	0.68 (0.54-0.85)	<0.001	0.92 (0.81-1.05)	0.120
Smoker**	0.71 (0.64-0.80)	<0.001	0.76 (0.70-0.82)	<0.001	0.76 (0.68-0.86)	<0.001	0.88 (0.81-0.95)	<0.001
Unknown	0.81 (0.76-0.86)	<0.001	0.88 (0.85-0.92)	<0.001	0.82 (0.77-0.87)	<0.001	0.91 (0.87-0.95)	<0.001

*NRT=nicotine replacement therapy prescription in pregnancy, **smoking in pregnancy, *** No smoking in pregnancy, ‡adjusted for maternal age, Townsend score, diabetes, asthma, hypertension, mental illness, RRR= relative risk ratio, CI=confidence interval

7.4 DISCUSSION

7.4.1 Principal findings

This study, using a large population based dataset, found no significant association between NRT exposure during the first trimester, and any time during pregnancy, and stillbirth. However, maternal smoking during early pregnancy was found to increase the risk of stillbirth by 27%. In contrast, maternal smoking any time during pregnancy did not significantly increase the risk of stillbirth. Compared to non-smokers, the risk of low birth weight babies was 93% higher in the NRT group and 69% higher in smokers. The mean birth weight in babies in the NRT group was 176g lower than those of non-smoker, and the mean birth weight in the smokers group was 123g lower than those of non-smokers. However, there was no statistically significant difference between the risk of low birth weight in the NRT group and smokers. The study did not find a significantly increased risk of assisted delivery or caesarean section in the NRT group compared to smokers and no significant risk of caesarean section in current smokers compared to non-smokers. However, it found that the risk of assisted delivery decreased by 25% in the NRT group and 15% in smokers compared to non-smokers.

7.4.2 Strengths and limitations

This is the first population-based report to assess the effects of NRT on adverse birth outcomes in the UK and the largest international study conducted thus far. Furthermore, since these data are prospectively recorded the potential for recall bias is greatly minimised. The measurement of drug exposure in the study was based on GP prescribing records rather than self-reports, reducing the potential for recall bias. However, the exposure measurement may still be subject to misclassification, which has been discussed in detail in Section 6.4.2.

Due to the paucity of smoking records during pregnancy, it was not possible to accurately ascertain smoking status at each stage of pregnancy. Therefore if there was any medical record indicating smoking during pregnancy women were assumed to be smoking during that pregnancy. Some of these women may have quit during the course of pregnancy but given the fluctuations of smoking status in pregnancy and the risk of relapse, [183] these women were still categorised as smokers. Therefore, the risk of adverse birth outcomes in relation to maternal smoking during pregnancy may be slightly underestimated. However, the potential for misclassification between the exposure groups cannot be completely eliminated from the previous Danish studies as well because smoking status was self-reported between 12-16 weeks of gestation and was then assumed to be constant until the end of pregnancy. In contrast, the findings reported here are based on the effects of NRT and smoking during the entire pregnancy in addition to early pregnancy as recorded in primary care data. However, for some women there was only a smoking record in the first trimester and therefore the effect estimates may not differ greatly between the two exposure windows. Furthermore, data on intensity of smoking was not complete which limited the ability of the study to examine any dose response effects of maternal smoking on adverse birth outcomes.

Whilst there may be confounding-by-indication by women's smoking intensity in that women who were prescribed NRT may be heavier smokers to start with, pregnant women getting NRT prescriptions could also be the women modifying their potentially harmful exposures for the better health of the baby. These could include smoking, alcohol use, dietary habits or other unmeasured factors. Although the ORs have been adjusted for a number of potential confounders, other unmeasured factors like labour and delivery complications, and household smoking were not adjusted for as enough information was not available in the data. Furthermore, the duration of NRT prescription in these data was relatively

short i.e. two weeks so if there is truly a beneficial or harmful effect of NRT this may be slightly underestimated.

Stillborn babies are usually not registered in primary care. Therefore, the ascertainment of stillbirth in this study is based on the documentation of such events in maternal primary care records. Approximately 97% of deliveries in England and Wales in 2011 took place in the NHS hospitals, maternity units and maternity wings[280] and all the delivery information recorded in the inpatient data should, but may not always, be transferred onto the primary care records. Therefore, this study may have missed cases of stillbirth. Nevertheless, the prevalence of stillbirth in this study was 4/1,000 live and stillbirths, which is comparable to the national prevalence of 5.2/1,000 births in the UK in 2009.[159] A study assessing the completeness of maternity data in UK primary and secondary care between 1998 and 2009 in one general practice found that birth weight and mode of delivery were recorded in only about 14% of 1,212 pregnancies with a linked child record in the primary care data (THIN) compared to 61% of the 3,255 pregnancies in secondary care data (Hospital Episodes Statistics (HES)).[281] The study discussed in this chapter however has data from approximately 500 practices from across the UK and had birth weight recorded for 42% of the babies with linked maternal records in THIN. Nevertheless, using a population of cases with a recording of birth weight, the prevalence of low birth weight was found to be 6.4% which is highly comparable to the national average of about 7%. [279,282] Furthermore, birth weight when plotted graphically was found to be normally distributed indicating that the selected population was broadly representative of the overall population and the presence of birth weight record did not differ by low or high birth weight. Additionally, the maternal characteristics in children with a recording of birth weight were highly comparable to the maternal characteristics in children without a recording of birth weight in primary care again indicating that this selected sample was

representative of the overall population and therefore any selection bias is unlikely to be present.

The prevalence of caesarean sections and assisted deliveries in this study was found to be much lower than the national prevalence of approximately 25% and 12% respectively in 2009.[283,284] All the pregnancies where no caesarean section or assisted delivery was recorded were assumed to be delivered through normal vaginal delivery, over-estimating the proportion of normal deliveries. This in turn may result in non-differential misclassification of the outcome and consequently bias the effect estimate towards null.

7.4.3 Comparison with current literature

7.4.3.1 NRT and stillbirth

NRT exposure during early pregnancy or any time during the entire pregnancy was not found to be associated with an increased risk of stillbirth. The study including 87,032 pregnancies from the DNBC, with information on smoking and NRT use in the first trimester, found that for women who used NRT there was no statistically significant increase in the risk of stillbirth (HR 0.57, 95% CI 0.28-1.16) compared to non-smokers.[113] The non-smoker group in their study included ex-smokers who quit before conception but may be using NRT in pregnancy to avoid a smoking relapse. This may have resulted in misclassification of their exposure variable and under-estimate the effects of NRT use in pregnancy. Despite the differences in the exposure window and definition of stillbirth, the Danish study found very similar results to the ones presented in this chapter. The association between NRT exposure and stillbirth did not reach statistical significance, which is in line with the SNAP trial results[100] and the pooled estimates from the meta-analysis[101] again suggesting that the use of NRT does not significantly increase the risk of stillbirth.

The study found that smoking during early pregnancy increases the risk of stillbirth, which is consistent with the current literature. The study using DNBC found the risk of stillbirth to be 46% higher in smokers (HR 1.46, 95% CI 1.17-1.82) compared to non-smokers using smoking information from the first trimester.[113] Similarly, another Danish study based on a cohort of 25,102 live born singleton children collected smoking data before 30 weeks of gestation and found the risk of stillbirth to be twice as high compared to non-smokers.[264] . These differences could be attributed to the use of slightly different definitions of stillbirth, ascertainment of smoking status, which was mostly self-reported in these studies and also the use of different populations with slightly different prevalence of maternal smoking and stillbirth. In addition, the choice of confounders in each of the previous studies and their definitions and data quality may also contribute to the slight difference in the effect estimates of these studies.

Other studies which assessed smoking at the end of pregnancy or where the exact time of smoking assessment was not specified found the risk of stillbirth in smokers to be 34%[285] to over two fold [29,264,273,286,287] higher compared to non-smokers. In contrast, when the exposure window was expanded to the whole of pregnancy in this study, smoking was not found to be associated with an increase in stillbirth. A population-based cohort study from Sweden reported a significant interaction between gestational age and the effects of smoking; As pregnancy advanced, the risk of stillbirth associated with smoking decreased.[288] This may partly explain the lack of statistically significant association between smoking and stillbirth considering the complete duration of pregnancy.

Smoking reduces fetal oxygenation through increased blood levels of carboxyhaemoglobin and impairment of oxygen unloading.[264] This along with prostacyclin synthesis increases vascular resistance and decreases fetal blood flow. Nicotine in tobacco smoke is also postulated to cause vasoconstriction.[264]

All these effects collectively result in fetal growth restriction and placental complications, which are the most important causes of still birth.[288,289] Thus, this association seems to be biologically plausible. However, from the findings of this study and the previous study it does not seem likely that nicotine alone can result in stillbirth. The study also highlights that the effects of smoking may be more harmful to the immature foetus and placenta.

Although no significant associations were found between NRT and smoking exposure during pregnancy and fetal death, maternal smoking is an important risk factor for miscarriage which may contribute to these fetal deaths. A recent meta-analysis of 98 observational studies concluded that any active smoking during pregnancy was associated with an increased risk of miscarriage (RR 1.23, 95% CI 1.16-1.30).[30] Although the prevalence of smoking may be higher in women having miscarriages, the extent to which details of a miscarriage event is documented in primary care is currently not known. However, many women may not know that they are pregnant at the time of the miscarriage and therefore the recording and ascertainment of such events in the data is not expected to be complete. The reported prevalence of miscarriage in studies is 20%.[290,291] However, only 13% of pregnancies were recorded to end in miscarriage in the primary care data. This may explain the lack of statistically significant associations between smoking and fetal death found in the study.

7.4.3.2 NRT and birth weight

NRT exposure during pregnancy was found to be associated with a reduction in birth weight compared to not smoking with a 74% increased risk of low birth weight in babies of mothers prescribed NRT compared to non-smokers. A study using the PRAMS data to assess the association between NRT use and adverse birth outcomes in approximately 6,000 women in the USA found the risk of having a low birth weight baby in NRT users to be about two fold compared to

non-smokers, [111] which is very similar to the findings of this study. Contrary to the findings reported in this chapter, a study using the DNBC found no significant association between the duration of NRT use, type of NRT product used and offspring birth weight.[112] However, the Danish study primarily assessed NRT use within the first 27 weeks of pregnancy which limits the validity of the findings as fetal weight gain essentially takes place in the second and third trimester and the effects of smoking on fetal growth are more pronounced in the late stages of pregnancy.[292,293] Results from the trials report inconclusive evidence regarding the use of NRT during pregnancy and birth weight with some trials reporting no association between NRT use and birth weight[100,107] and some reporting higher birth weights in the NRT groups compared to placebo groups.[108,109] However, the interpretation of these findings from the trials is complicated by their inadequate power to assess safety outcomes and is highly dependent on compliance and adherence to treatments in both arms.

The study reiterates that smoking during pregnancy has a negative effect on fetal growth such that the risk of low birth weight was 63% higher in smokers compared to non-smokers and babies of smokers weighed 120g less than babies of non-smokers. This is consistent with previous studies which also found a decrease in birth weight of approximately 160g in babies of smokers compared to non-smokers.[19,20]

The risk of low birth weight associated with NRT and smoking were not found to be very different in the pre-term and term babies. This implies that the risk of low birth weight associated with NRT and smoking exposure holds regardless of gestational age. There are several proposed mechanisms by which smoking and NRT may affect birth weight. Nicotine is water soluble and consequently can pass through the placenta into the developing fetal circulation that is unable to metabolise nicotine in the same way as a fully developed adult system. Therefore, the concentration of nicotine builds up over pregnancy in the

placental tissues and amniotic fluids.[294] Nicotine concentrations are reported to be 15% higher in the fetal circulation and 88% higher in the amniotic fluids than in the maternal circulation in smokers.[295] Therefore, although NRT may deliver lower concentrations of nicotine in the blood than smoking the concentrations in fetal circulation will still be higher than the maternal circulation. This may result in poor oxygen and nutrient delivery to the fetus resulting in poor organ development and low birth weight.[294] A case-control study using magnetic resonance imaging (MRI) to assess organ growth and overall fetal growth in 26 pregnant women found lower brain volumes, kidney volumes, impaired lung growth and total fetal volumes in smoking mothers compared to non-smoking mothers, indicating poor organ development.[294] Another study based on 7,098 pregnant women in Rotterdam, the Netherlands found an association between maternal smoking and reduced fetal head circumference, abdominal circumference and femur length.[296] An alternative proposed mechanism could be the suppression of appetite in mothers again leading to poor nutrient intake and inadequate nutrient delivery to the foetus. Lastly, the structure of nicotine is very similar to acetylcholine, which is one of the main enzymes in the nervous system and also regulates cell growth in the developing fetus.[112,297] Hence, it may alter cell growth signalling in the fetus leading to impaired growth and low birth weight. [274] Carbon monoxide in cigarettes may worsen this by causing fetal hypoxia.[294]

This study found no added benefit of using NRT over smoking in relation to birth weight and the risk of low birth weight was slightly higher in the nicotine group in comparison to smokers. This association may be confounded by how nicotine-dependent these women in the NRT group were and how intensely they smoked before NRT prescription, which has been discussed in detail in Section 6.4.2. Also, detailed information on NRT use and compliance was not available and it may be possible that women used NRT and smoked as well, or had periods of

relapses between NRT. These possibilities cannot be completely ruled out. Lastly, there may also be some residual confounding through weight loss during pregnancy as maternal weight changes during pregnancy are directly related to infant birth weight [298]and NRT is known to suppress appetite[299] which may reduce maternal weight or other unmeasured factors, information for which was not available in the current data.

7.4.3.3 NRT and mode of delivery

The SNAP trial found a 45% increase in the risk of caesarean section deliveries with NRT use compared to placebo, however adherence to the therapy was low in both NRT and placebo group and the rate of abstinence from the quit date until delivery was less than 10%.[100] Furthermore, the study was adequately powered to assess abstinence but not the safety of NRT therefore this finding may be solely due to chance as the authors have discussed. In contrast, this study found no increased risk of caesarean section in the NRT group compared to current smokers or non-smokers. Nicotine is postulated to affect the maternal circulation of the placenta which can cause a consequent impairment of oxygen transfer to the fetus leading to an increased need for operative interventions for delivery such as caesarean section or assisted delivery. [32] However, the cardiovascular effects of NRT on both the mother and the fetus are very small [300,301], which is reflected in the study findings. Furthermore, a hospital-based case-control study from France, based on approximately 600 women, aimed to examine the risk factors for caesarean section found similar results with no significant associations between maternal smoking and caesarean section. [302]

The only study to examine the association between smoking and assisted delivery [269] was based on the longitudinal Millennium Cohort from the UK and found no association between maternal smoking during pregnancy and the risk of assisted deliveries (OR 1.003, 95% CI 0.88-1.14). However, the findings from

this chapter paradoxically report a small protective effect of NRT and smoking exposure on assisted deliveries such that the risk of caesarean section reduced by 28% in NRT group and 15% in smokers compared to non-smokers. There may be several explanations for this finding; it may be simply due to the misclassification of some assisted deliveries as normal deliveries in current smokers, due to unmeasured confounding, or smoking may truly reduce the risk of assisted deliveries just like its incongruous protective effect on pre-eclampsia. [10,303]. Nevertheless the absolute risk of assisted deliveries in NRT group, smokers and non-smokers was not very different (4.8%, 5.7% and 6.8% respectively) making this difference in the risk less clinically relevant.

7.5 CHAPTER CONCLUSIONS

This chapter as a whole aimed to assess different birth outcomes in relation to NRT and maternal smoking during pregnancy and found no increased risk of stillbirth in the NRT group compared to non-smokers, which is encouraging. In contrast, maternal smoking during pregnancy was found to increase the risk of stillbirth. Women who were prescribed NRT or smoked during pregnancy had higher risks of having a low birth weight baby compared to non-smokers. Lastly, the risk of caesarean sections in the NRT group and smokers was found to be similar to non-smokers however the risk of assisted deliveries was lower in comparison to non-smokers. Based on these findings it can be said that NRT exposure during pregnancy has no increased risks of stillbirth, low birth weight and caesarean section in comparison to maternal smoking. Nevertheless, these findings represent NRT exposure as recorded in general practice data only and therefore need to be interpreted with caution due to the limitations discussed above. Other immediate and long-term neonatal and paediatric outcomes need to be examined carefully before NRT can be considered to be completely safe during pregnancy.

8 OVERALL CONCLUSIONS, IMPLICATIONS AND FUTURE DIRECTIONS FOR RESEARCH

The overall aims of this thesis were to assess the potential usefulness of primary care data to inform assessment of smoking behaviours in pregnant women at a population level and to investigate the prescribing and safety of NRT among pregnant women. This concluding chapter summarises key findings from the research presented in this thesis, highlights clinical and public health implications and makes recommendations for future public health practice and research areas in relation to maternal smoking ascertainment (Section 8.1) and NRT prescribing and safety (Section 8.2).

8.1 QUALITY OF MATERNAL SMOKING STATUS DATA DURING PREGNANCY IN PRIMARY CARE

8.1.1 Summary of main findings

Having smoking status recorded in a pregnant women's medical records is not only useful for clinical management, but can also increase the potential utility of primary care data in informing national smoking estimates for pregnant women in a cost-effective and timely manner. The studies in this thesis have highlighted several features of the recording of smoking status during pregnancy in primary care data which must be taken into account when using these data to study the trends in the epidemiology of smoking or the provision of smoking cessation treatments. It showed that the recording of smoking status during pregnancy is incomplete and only present in less than 30% of the pregnant population under study. Therefore currently, certain informed assumptions need to be made to enhance the utility of these data for assessing smoking and smoking cessation treatment among pregnant women at a population level. Two such assumptions based on the QOF rules were tested in this thesis i.e. including smoking records

from 27 months before conception and smoking records ever before delivery to determine the smoking status for pregnancies where there was no gestational smoking record available. Smoking estimates using the 27 months assumption were generally found to have better comparability to other available data sources and therefore smoking records from 27 months before conception were considered to determine smoking status during pregnancy where gestational smoking status was missing. At an individual level, however, women do not have enough records of smoking status during pregnancy to assess changes in their smoking status throughout pregnancy.

8.1.2 Implications for further research

Data from this thesis suggest that the completeness of smoking status recording during pregnancy in primary care data is improving over the years with about 40% women with smoking status recorded during pregnancy in 2009. Further research demonstrating this trend in future years may strengthen the utility of THIN for research on smoking in relation to pregnancy.

8.1.2.1 Statistical methods for missing data

In this thesis simple imputations were made for missing smoking data using assumptions based on QOF recording rules to provide an appropriate population of smokers for analysis. An alternative approach could be to use multiple imputation techniques to statistically impute smoking status during pregnancy, for which first the patterns of missing data will need be to be assessed (e.g. missing at random, missing not at random, missing by age, sex, disease or any other factors). Data on smoking could be imputed based on multinomial regression techniques.[304] Finally the results from these multiple imputation techniques can be compared from the results in this thesis to assess the validity of both approaches. This could be done by reviewing the records of a random group of pregnant women from general practices or surveying pregnant women

and comparing the self-reported smoking prevalence in this subgroup to the prevalence using recorded and imputed smoking status to investigate the potential validity of primary care data to predict smoking status during pregnancy. However, data anonymity in THIN may make this difficult and may also require substantial manpower, training and resources. An alternative approach could be to use the Additional Information Services (AIS) offered by THIN to provide more information to researchers which includes anonymised patient or GP questionnaires, copies of patient-related correspondence, laboratory tests etc.[163] This service can be used to collect self-reported smoking information from pregnant women to calculate smoking prevalence and validate the approaches discussed above. However, this may involve payments which may not always be available in projects.

8.1.2.2 Use of free text data

GPs may sometimes record more details on smoking status as free text data, which were not available for use for the purposes of this research. Free-text information from primary care records has been previously used to estimate death rates[305] and the incidence of rheumatoid arthritis[306] previously. However, no studies have assessed the utility of these data to improve estimates of smoking prevalence in pregnancy or wider general population. Nevertheless, researchers in the Division of Epidemiology and Public Health, University of Nottingham are currently analysing free text records in detail and have found that a lot of smoking information is recorded in the free text in primary care data (Vishal Basra, personal communication, 3rd February 2014). Such free text data are available to researchers, subject to relevant payments, and may provide more in-depth data on smoking status and fluctuations occurring during pregnancy and add to the partially incomplete coded information on smoking status during pregnancy.

8.1.2.3 Mixed methods research

This thesis investigated maternal characteristics related to the completeness of maternal smoking status recording in pregnancy. GP characteristics such as gender, training, smoking status may influence the recording of smoking status in the general population.[307,308] Similarly, certain practice characteristics (e.g. location, catchment area and staffing etc.) may also influence the recording and provision of smoking cessation advice.[309] However, more research is needed on the influence of these factors on the recording of smoking status and provision and recording of smoking cessation advice in pregnant women. Therefore mixed-methods research using both qualitative and quantitative studies on the patient, caregiver and practice attributes may provide some valuable insights into how smoking status is recorded during pregnancy.

8.1.2.4 Using other primary care data to answer similar questions

There are other larger primary care datasets available for research purposes in the UK such as QRESEARCH and the Clinical Practice Research Database (CPRD) formerly known as the GPRD, which is also linked to the maternity data from Hospital Episode Statistics (HES), and the Office for National Statistics (ONS) data. The CPRD currently has over 650 practices and data on over 5 million patients[310] and QRESEARCH contains data from over 600 practices.[144] The methods used here to define smoking status and investigate the quality of data can be applied to these other datasets when assessing the trends in maternal smoking prevalence and these larger datasets can be used for external validation of the associations between NRT and birth outcomes in future once pregnancy cohort is established in these data.

8.1.2.5 Potential linkage with midwives notes

Midwives are the main point of contact for women during pregnancy and are also responsible along with other health care team members for assessing and

documenting the smoking status of pregnant women. A recent study assessing the consistency and completeness of maternity hand-held notes in the UK analysed 63 different sets of hand-held notes currently in use in the UK and found that smoking related questions were part of all these notes.[184] Therefore, smoking status recording in the hand-held midwives notes may be more complete than primary care data. However, currently there is no research investigating how complete this information is in the midwives' notes. Also since there is no centralised recording and documenting system for midwives this information is not at hand after delivery. Therefore, electronic linkages between midwives notes and primary care data, or electronic imaging or transmission of midwives notes into the GP data, may be very useful not only to assess smoking and smoking cessation treatments during pregnancy but to also provide a detailed description of other events occurring during pregnancy to supplement and augment the information already present in primary care data. The Maternity Data Set by the Health and Social Care Information Centre[311] could be used as a template for this to extract maternity data, which could then be linked to primary care data.

8.1.3 Implications for clinical practice and policy

Given the detrimental effects of maternal smoking during pregnancy, more accurate and up-to-date recording of smoking status in the pregnant population is vital in planning and delivering health services and other interventions to promote smoking cessation. The antenatal care model in the UK is midwife-led where midwives are responsible for care of women during pregnancy. However, current guidelines recommend that monitoring of smoking status during pregnancy should be a shared responsibility between all healthcare professionals involved in the care of pregnant women, including the GPs and midwives.[74,79,165] The Royal College of Midwives recommends that during pregnancy midwives should have full confidential access to a woman's written and electronic records

and GPs should ensure that all significant and relevant information is copied into women's hand-held maternity records.[166] Similarly, relevant information collected by midwives during pregnancy should also be communicated to the GPs and fed back into the electronic primary care records. Therefore, appropriate methods should be introduced to improve communication and documentation of such information between the midwives and GPs during pregnancy. One such method could be the use of electronic tools, such as digital pens, to complete hand-held maternity records which may then also transmit data to other central sources such as primary care. This will enable continuity of care and better communication between the GPs and midwives without requiring any extra time and effort.

Electronic patient-reported outcomes (e-PROs) is a fairly new concept in e-Health research where patients can report their health outcomes electronically. [312] ePROs are commonly used in clinical trials where patients can report the intensity, frequency, duration of symptoms (e.g. the Pulmonary Artery Hypertension – Symptoms and Impact (PAHSYMPACT) which measures the symptoms and impact of pulmonary artery hypertension using an electronic device), physiological measures (peak expiratory flow using a peak flow meter device which can transmit information directly to a central database).[313] Several modes of data collection can be used for this such as digital pens, smart phones, tablets, mobile applications and web-based responses etc.[313] ePROs are now being integrated into clinical care especially for cancer patients and the compliance to such tools has been reported to be good.[314] This concept could also be integrated in primary care data to obtain a detailed snapshot of several outcomes including smoking behaviour during pregnancy by giving women more control of their data and allowing them to enter their information themselves. This is in the early stages of development in the UK[312] but may be a useful tool in future to monitor patterns and trends of maternal smoking during pregnancy.

Based on the results from this work, it can be observed that the recording of smoking status improved in conditions which were included in the QOF such as diabetes, asthma, hypertension etc. This raises an important issue of whether pregnancy should be included as a condition in the QOF to record smoking status, given the current gaps in the recording of smoking status in pregnant women in primary care. Although some women may go to a midwife directly, according to the National Perinatal Epidemiology Unit 77% of women see their GP first for pregnancy care.[167] This may be an opportune time for the GPs to assess and document women's smoking status and provide brief advice and guidance on the resources available to quit. Therefore, including smoking status and cessation advice in pregnancy as a QOF recording target and linking payments to it may not only increase this recording in primary care data but also make the GPs more vigilant of monitoring smoking during pregnancy and providing referrals to interventions and services that are proven to work, thereby decreasing the overall smoking prevalence a little, if not substantially.

8.2 PRESCRIBING AND SAFETY OF NRT IN PREGNANCY

8.2.1 Summary of main findings

Trends in NRT prescribing, its use and safety were the gaps in the current literature highlighted by the WHO in the recent recommendations for the prevention and management of tobacco use in pregnancy.[73] Three studies in this thesis focused on these highlighted areas and assessed the prescribing of NRT in and around pregnancy across the UK and safety outcomes: major congenital anomalies, stillbirth, birth weight and mode of delivery.

The prescribing of NRT in and around pregnancy has increased substantially following its availability as an NHS prescription; however, the annual prescribing prevalence plateaued after the relaxation of licensing arrangements in 2005. Nevertheless, overall prescribing in the post-relaxation period was found to be

about twice as high compared to prescribing in the pre-relaxation period. The prescribing prevalence of NRT during pregnancy was almost double that of the prescribing prevalence in the nine months immediately before and after pregnancy; however, most women only had a record of single NRT prescription during pregnancy, lasting two weeks on average. Prescribing of NRT was also found to increase with greater socio-economic deprivation and the presence of comorbidities like asthma and mental illness.

No increased risk of congenital anomalies was found in the NRT group compared to smokers or non-smokers except for respiratory anomalies however this estimate was based on only 10 exposed cases. The risk of stillbirth in the NRT group was similar to non-smokers, which is encouraging. In contrast, maternal smoking during pregnancy was found to increase the risk of stillbirth. Contrarily, women who were prescribed NRT or who smoked during pregnancy had higher risks of having a low birth weight baby compared to non-smokers. Lastly, the risk of caesarean sections in the NRT group and current smokers was found to be similar to non-smokers, however the risk of assisted deliveries was lower in comparison to non-smokers.

8.2.2 Implications for further research

8.2.2.1 Potential data linkages

Currently primary care data such as THIN are one of the best available resources in the UK to examine population-level trends and patterns of NRT prescribing during pregnancy. Data from the NHS-SSS may only represent a subgroup of very motivated pregnant women. However, access to these data may provide useful information not only on the patterns and success of NRT use but also on other cessation interventions. A potential-linkage system between primary care and the NHS-SSS data may be useful in describing NRT use during pregnancy throughout the UK. Moreover, it will also give a more detailed account of quit

attempts made by women both during and outside pregnancy and the outcome of those quit attempts. However, no such links exist presently. NRT data can also be obtained from other data sources like OTC sales data which are available commercially (e.g. Electronic Point of Sales scanner data[140]) and the ePACT data which monitor electronic drug prescribing. However, currently these data do not have any specific information on sales and dispensing to pregnant women. Women get free prescriptions during pregnancy as discussed earlier in the thesis and therefore if pregnant women are flagged up in these sales and prescribing data, then these data may be able to supplement the estimates from primary care data and give a more comprehensive picture of NRT prescribing and use during pregnancy in the UK.

Information on birth weight and mode of delivery in this work was missing for a substantial number of pregnancies. As indicated earlier, this information is expected to be more complete in secondary care data. Therefore, potential linkages between primary and secondary data may present more accurate estimates and reduce the proportion of missing data substantially. The CPRD primary care data have now been linked to HES and HES maternity, and HES linkages with THIN data have now been completed for approximately 70 practices with more practices being added with every release. This will not only improve the information on these selected outcomes but will also provide information on a number of labour and delivery events and complications which may be important when assessing the impact of drugs or smoking in future. The completeness and quality of the exposure data (smoking and NRT) can also be improved by potential linkages suggested above.

8.2.2.2 Qualitative research

Apart from these objective measures of NRT prescribing it is also important to combine subjective measures (such as self-reported use of NRT and outcomes of

quit attempts). The only qualitative study assessing women's perspectives on barriers and facilitators of smoking cessation using NRT was conducted on a small selected sample of pregnant smokers in Australia.[118] Therefore, qualitative studies using focus groups of pregnant smokers may therefore help explore the barriers and facilitators that pregnant women experience in using NRT. This may also provide more information on women's choices of NRT forms, as each form has a slightly different dose of NRT and mechanism of action which may have implications for the safety of the drug. It will also be instrumental in exploring the socio-demographic characteristics of women in relation to NRT prescribing in more detail which will help policy makers and public health professionals in tailoring these services and targeting special groups to encourage smoking cessation.

8.2.2.3 Larger studies

Although this was one of the biggest studies to determine the association between NRT, maternal smoking and congenital anomaly a bigger sample size is required to provide more power to the analysis and generate more precise risk estimates associated with smoking and NRT use. Therefore, a study using more recent primary care data, with more practices, more pregnancies and longer follow-up time, using similar methods is warranted. This will improve the precision of the estimates. However, considering the prevalence of congenital anomalies, the statistical power of epidemiological studies may always be limited in assessing the risks for system-specific anomaly groups especially the more rare ones.

8.2.2.4 Other outcomes

In addition to the outcomes assessed in this thesis other immediate and long-term neonatal and paediatric outcomes such as neonatal intensive care admissions, neonatal deaths, respiratory infections in early life etc., need to be

examined carefully before NRT can be deemed to be completely safe during pregnancy. The only available estimates for the association between nicotine replacement therapy and neonatal outcomes comes from trials [100]and currently the evidence is inconclusive. A meta-analysis of three trials of NRT in pregnancy found a pooled OR of 0.94 (95% CI 0.64-1.88) for neonatal intensive care admissions and 0.28 (95% CI 0.06-1.41) for neonatal death.[101]

8.2.3 Implications for clinical practice and policy

Considering that NRT use in the general population for smoking cessation is recommended for at least eight to twelve weeks, two weeks of NRT may not be truly helpful for women to quit smoking. The findings also indicated that only 1% of women of reproductive age who smoke are prescribed NRT before they get pregnant, indicating a missed opportunity to assist many young women in quitting smoking. Whilst interactions between health professionals and women during pregnancy should be used to discuss and offer interventions to promote smoking cessation, greater potential benefit would be derived from starting before pregnancy which should be a focus for women and health care providers.

Currently, NRT use is recommended by the national guidelines for smoking cessation aid during pregnancy, where pregnant women cannot quit without NRT.[79] However, NRT should not be considered as a panacea for smoking cessation during pregnancy and smoking cessation without pharmacotherapy should be encouraged to help pregnant women quit. Health care professionals need to encourage women to quit before pregnancy to reduce the risks associated with any kind of nicotine exposure to the foetus. Also given, the effectiveness of NRT outside pregnancy it's use during postpartum period can be encouraged more to prevent postpartum relapse in women who quit during pregnancy.

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10 APPENDICES

10.1 COMPLETENESS OF MATERNAL SMOKING STATUS RECORDING DURING PREGNANCY IN UNITED KINGDON PRIMARY CARE DATA

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Completeness of Maternal Smoking Status Recording during Pregnancy in United Kingdom Primary Care Data

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Abstract

Background: Given the health impacts of smoking during pregnancy and the opportunity for primary healthcare teams to encourage pregnant smokers to quit, our primary aim was to assess the completeness of gestational smoking status recording in primary care data and investigate whether completeness varied with women's characteristics. As a secondary aim we assessed whether completeness of recording varied before and after the introduction of the Quality and Outcomes Framework (QOF).

Methods: In The Health Improvement Network (THIN) database we calculated the proportion of pregnancies ending in live births or stillbirths where there was a recording of maternal smoking status for each year from 2000 to 2009. Logistic regression was used to assess variation in the completeness of maternal smoking recording by maternal characteristics, before and after the introduction of QOF.

Results: Women had a record of smoking status during the gestational period in 28% of the 277,552 pregnancies identified. In 2000, smoking status was recorded in 9% of pregnancies, rising to 43% in 2009. Pregnant women from the most deprived group were 17% more likely to have their smoking status recorded than pregnant women from the least deprived group before QOF implementation (OR 1.17, 95% CI 1.10–1.25) and 42% more likely afterwards (OR 1.42, 95% CI 1.37–1.47). A diagnosis of asthma was related to recording of smoking status during pregnancy in both the pre-QOF (OR 1.63, 95% CI 1.53–1.74) and post-QOF periods (OR 2.08, 95% CI 2.02–2.15). There was no association between having a diagnosis of diabetes and recording of smoking status during pregnancy pre-QOF however, post-QOF diagnosis of diabetes was associated with a 12% increase in recording of smoking status (OR 1.12, 95% CI 1.05–1.19).

Conclusion: Recording of smoking status during pregnancy in primary care data is incomplete though has improved over time, especially after the implementation of the QOF, and varies by maternal characteristics and QOF-incentivised morbidities.

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Introduction

Smoking during pregnancy has a well-documented negative effect on the health of a mother and her baby [1] and smoking cessation during pregnancy has been linked to a reduction in maternal and fetal complications in addition to its wider health benefits [2,3]. Current recommendations emphasise that all healthcare workers involved in a pregnant woman's care (e.g. midwives, general practitioners (GPs), practice nurses and obstetricians) should assess the woman's smoking status at the earliest possible stage of pregnancy and offer cessation advice and a referral to specialist stop smoking advisers for women who smoke [4–8]. Documentation of a woman's smoking status in her medical records is recommended to enable her healthcare team to offer appropriate support throughout the pregnancy [7].

In the United Kingdom (UK) women must be registered with a GP in order to receive antenatal care and, although most antenatal contacts are with midwives, an estimated 77% of women see their GPs first for confirmation of pregnancy before attending an antenatal booking appointment with a midwife [9]. This first contact with a GP and subsequent visits during pregnancy could potentially be used as an opportunity for assessing and recording the smoking status of pregnant women.

In April 2004, a new contract for GPs was implemented which introduced a number of pay-for-performance targets known as the Quality and Outcomes Framework (QOF) [10]. Approximately 8% of the QOF points (worth around £10,000) per year per

practice are related to the recording of smoking status and delivery of smoking cessation advice [11,12]. GPs are required to document patients' smoking status at least once every 27 months, or every 15 months where the patient has hypertension, diabetes, asthma and certain other smoking-related morbidities. A detailed description of QOF targets is available elsewhere [13].

In the population as a whole the recording of patients' smoking status is more complete after the introduction of QOF [14,15]. However, the QOF sets no specific incentives for the recording of smoking status in pregnant women. Having smoking status recorded in a pregnant women's medical records is not only useful for clinical management, but also increases opportunities for health professionals to provide smoking cessation interventions throughout pregnancy and afterwards. Therefore, our primary aim was to assess the completeness of recording of smoking status during pregnancy in primary care medical records over time and investigate whether completeness varied with women's socio-demographic and health-related characteristics. Additionally, our secondary aim was to investigate whether, despite having no specific targets for pregnancy, there was an increase in the completeness of smoking status recording during pregnancy in UK primary care after the introduction of the QOF.

Methods

Data source and study population

The Health Improvement Network (THIN) is an electronic primary care database containing anonymised patient records from general practices across the UK, covering approximately 5.7% of the UK population [16]. The version of THIN used for this study contains data from 495 practices with a combined total of approximately 9.5 million patients, including approximately 2 million women of reproductive age (defined here as age 15–49 years) [16]. The recorded population prevalence of smoking in THIN has been previously validated at both national and regional levels [14,15] and fertility rates in THIN are highly comparable to national fertility rates [17]. For the work reported here, our study population included all pregnancies recorded in THIN between 2000 and 2009 in women of reproductive age which resulted in either a live birth or a stillbirth.

Smoking status and maternal characteristics

Records of maternal smoking status during pregnancy were identified using Read codes [18]. These included codes for current, never, and ex-smoking, codes indicating the type or number of cigarettes smoked, and codes indicating smoking cessation interventions delivered to patients. Women were also considered to be smokers if they had a prescription for a smoking cessation drug (nicotine replacement therapy, bupropion or varenicline) in their medical records during pregnancy. This method of classifying smoking status in electronic primary care data has been previously validated [14]. Code lists are available from the authors on request.

To investigate the factors that may be associated with the recording of maternal smoking status during pregnancy, data were extracted on women's age at conception, socioeconomic deprivation as measured by quintiles of the Townsend Index of material deprivation [19], body mass index (BMI) before conception and recorded diagnoses, during or before the pregnancy, of morbidities common in pregnancy in which the recording of smoking status has been specifically incentivised by the QOF (hypertension, diabetes, asthma, and mental illness which included depression, anxiety, bipolar disorder, schizophrenia and other psychoses). When extracting data on BMI and maternal morbidities before pregnancy, we only considered recent recordings of BMI and comorbidities before pregnancy (27 months prior to pregnancy, in line with the QOF recording rules). Missing data for Townsend quintile and BMI were included as separate categories in the analyses.

Statistical analyses

The prevalence of smoking status recording during pregnancy was calculated for each year from 2000 to 2009 as the number of pregnancies with at least one recording of smoking status during the gestational period divided by the total number of pregnancies delivered in that year. These data were plotted graphically.

Since April 2006 the QOF has not required GPs to record the smoking status of patients after the age of 25 years if they have been a never smoker until that age [20]. After 2008, if a patient who once smoked has been recorded as an ex-smoker for three years, GPs need no longer check and update the patient's smoking status records. Therefore, we recalculated the proportion of pregnancies with missing gestational smoking status data to take these rules into account. For women who only had records of being a never smoker up to age 25 and who did not have a record of smoking during a subsequent pregnancy we imputed a never smoking record during gestation. Similarly, for women who had no smoking status records during gestation but who were recorded as ex-smokers for three consecutive years before the conception we imputed an ex-smoking record during gestation. We then recalculated the annual proportion of pregnancies with a recording of smoking status during the gestational period.

We used logistic regression to calculate odds ratios (ORs) for associations between women's characteristics and the recording of smoking status during pregnancy. All covariates that reached statistical significance ($p<0.05$) in the univariable analysis were initially included in the multivariable analyses. Covariates that reached statistical significance ($p<0.05$) in the multivariable analysis were retained in the final model. As some women had more than one pregnancy during the study period that contributed to our analyses, we accounted for this potential clustering of pregnancies within women by calculating robust confidence intervals (CIs) around our odds ratios using the clustered sandwich estimator to allow for intragroup correlation [21,22]. As the introduction of the QOF incentivised the recording of smoking status in patients with smoking-related chronic conditions, we expected the QOF to be an effect modifier of the association between recording of smoking status during pregnancy and these morbidities. We therefore carried out logistic regression for two separate time periods: before the implementation of the QOF (January 2000–April 2004) and after the implementation of the QOF (April 2004–December 2009). We visually compared the magnitude, precision and significance of the odds ratios for each maternal factor in the pre and post-QOF periods in order to assess whether the association between maternal factors and the recording of smoking status during pregnancy changed after the QOF was introduced. All analyses were performed using Stata version 12.0 (StataCorp LP, College Station, TX).

Ethics Statement

Ethical approval for use of the THIN data was provided by the THIN Scientific Review Committee (reference number 11-047).

Results

Baseline characteristics

We identified 215,703 women with pregnancies resulting in live births or stillbirths between January 2000 and December 2009. Of

these, 162,295 (75.0%) women had only one pregnancy, 46,062 (21.5%) had two pregnancies and 7,346 (3.5%) had three or more pregnancies, giving a total of 277,552 pregnancies. The mean age at conception was 29.5 years (standard deviation 5.9) and the average length of pregnancy was 39.4 weeks (standard deviation 2.2). Table 1 describes the baseline characteristics of the study population in the pre-QOF and post-QOF time periods. The overall prevalence of diagnosed asthma, diabetes, hypertension and mental illness within the study population was approximately 8%, 2%, 2.5% and 9% respectively. Information on socioeconomic status was missing for 6% of the total pregnancies and information on BMI was missing for 42% of pregnancies.

Completeness of maternal smoking records

A record of smoking status at any point during the gestational period was present in 76,569 (28%) of the 277,552 pregnancies. Of the 76,569 pregnancies in which smoking status was recorded, 913 (1.2%) only had a recording for smoking cessation drug prescription with no accompanying Read codes indicating smoking status. In 56,605 (20.4%) pregnancies, women had their smoking status recorded only once during the gestational period, whereas in 19,964 (7%) pregnancies smoking status was recorded more than once. Figure 1 shows the proportion of pregnancies with smoking status recorded during gestation from 2000 to 2009. In 2000, smoking status was recorded during the gestational period for only 1,943 (8.8%) of the total 22,111 pregnancies. This proportion increased steadily to 18% in 2003 and a steep point change was observed in 2004 with the proportion rising to 32.3%. After 2004 it increased steadily on an annual basis such that the proportion of pregnancies with smoking status recorded during gestation in 2009 was 43.3% (13,360 out of 30,880 pregnancies).

When data for never smoking and ex-smoking were imputed based on QOF rules, the overall proportion of pregnancies with a record of smoking status during gestation increased to 32.1%. In 2000, smoking status was recorded during gestation for only 11.0% of pregnancies which increased to 35.8% in 2004 and 49.2% in 2009 (Figure 1).

Factors associated with recording of maternal smoking status during pregnancy

Table 2 shows variations in the recording of smoking status during pregnancy by women's sociodemographic characteristics and morbidities in the pre-QOF and post-QOF time periods. Overall, the strength of the associations between all maternal characteristics and recording of smoking status during gestation was higher in the post-QOF period compared to pre-QOF period. The recording of smoking status during pregnancy varied with socioeconomic status such that pregnant women from the most

Table 1. Baseline characteristics of the study population.

	Pre-QOF(January 2000– March 2004)			Post-QOF (April 2004– December 2009)		
	Total pregnancies (n = 98,373)	Pregnancies with a gestational smoking record (n = 12,381)		Total pregnancies (n = 179,179)	Pregnancies with a gestational smoking record (n = 64,188)	
Age at Conception						
15–19 years	5,529	953	(17.2%)	9,854	4,856	(14.8%)
20–24 years	14,809	2,202	(14.9%)	29,323	12,607	(14.9%)
25–29 years	25,732	3,175	(12.3%)	45,416	16,758	(15.7%)
30–34 years	32,621	3,750	(11.5%)	54,574	17,437	(17.4%)
35–39 years	16,614	1,944	(11.7%)	32,778	10,296	(9.9%)
40–44 years	2,907	338	(11.6%)	6,868	2,123	(19.8%)
45–49 years	161	19	(11.8%)	366	111	(15.9%)
Townsend Score in quintiles						(14.4%)
Quintile 1 - most affluent	24,760	2,850	(11.5%)	38,815	11,733	(16.5%)
Quintile 2	19,288	2,277	(11.8%)	32,962	11,025	(14.8%)
Quintile 3	18,592	2,317	(12.5%)	35,209	12,542	(14.9%)
Quintile 4	17,128	2,279	(13.3%)	33,982	13,114	(15.7%)
Quintile 5 - most deprived	13,252	1,964	(14.8%)	25,742	10,915	(17.4%)
Missing	5,353	694	(13.0%)	12,469	4,859	(9.9%)
Pre-conception Body Mass Index						(19.8%)
Normal(18.0–24.9)	26,663	3,948	(14.8%)	59,267	21,209	(15.9%)
Underweight(<18.0)	1,968	293	(14.9%)	4,355	1,714	(14.4%)
Overweight(25–29.9)	11,923	1,867	(15.7%)	29,476	10,957	(16.5%)
Obese(> = 30)	7,125	1,240	(17.4%)	20,993	8,406	(14.8%)
Missing	50,694	5,033	(9.9%)	65,088	21,902	(14.9%)
Asthma	6,537	1,297	(19.8%)	16,807	8,911	(15.7%)
Hypertension	2,372	377	(15.9%)	4,962	1,959	(17.4%)
Diabetes	1,345	194	(14.4%)	4,864	1,857	(9.9%)
Mental illness	8,717	1,439	(16.5%)	17,294	7,373	(19.8%)

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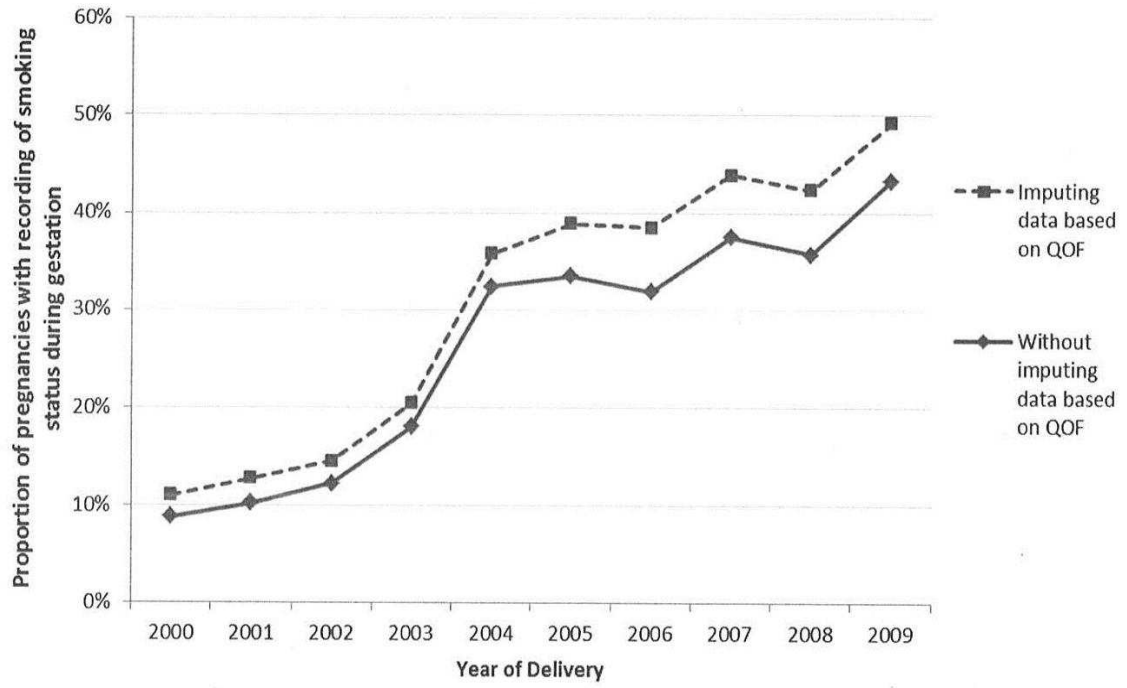

Figure 1. Annual proportion of pregnancies in THIN with smoking status recorded during gestation (2000–2009).
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deprived group (quintile 5) were 17% more likely to have their smoking status recorded during pregnancy than pregnant women from the most affluent group (quintile 1) before the implementation of the QOF (OR 1.17, 95% CI 1.10–1.25) and 42% more likely afterwards (OR 1.42, 95% CI 1.37–1.47). Similarly, pre-QOF pregnant women with a diagnosis of asthma were 63% more likely to have their smoking status recorded during pregnancy than pregnant women without asthma (OR 1.63, 95% CI 1.53–1.74) and post-QOF pregnant women with asthma were over twice as likely to have their smoking status recorded during pregnancy (OR 2.08, 95% CI 2.02–2.15). Having a diagnosis of diabetes was not associated with the recording of gestational smoking status pre-QOF (unadjusted OR 1.17, 95% CI 1.00–1.36), ($p = 0.290$). However, post-QOF it was associated with a 12% increase in the odds of recording of gestational smoking status (OR 1.12, 95% CI 1.05–1.19). Recording of smoking status during pregnancy was also related to hypertension and mental illness. In both time periods the odds of a woman having her smoking status recorded during pregnancy were greater at younger ages compared with older ages and great in overweight and obese women. However, the magnitude of effects and corresponding CIs in the pre-QOF and post-QOF periods overlapped.

Discussion

Using a large population-based dataset we found that the recording of smoking status during pregnancy in primary care has improved with time such that the proportion of pregnancies with a recording of smoking status during gestation was 8.8% in 2000 rising to 43.3% in 2009. The odds of a woman's smoking status being recorded during pregnancy was related to age, socioeconomic deprivation, BMI and QOF-incentivised morbidities such as asthma, diabetes, hypertension and mental illness.

The proportion of pregnancies with a gestational smoking record increased by approximately 2% per year between 2000 and 2002. Since the late 1990s there has been an increased focus on the harms of tobacco use in the UK, with, for example, the publication of the Government white paper 'Smoking Kills' in 1998 [1], the establishment of NHS Stop Smoking Services in 1999 [23], and the availability of smoking cessation medications on NHS prescriptions from 2001 [24]. This changing tobacco control environment may have made these pregnant smokers more willing to approach their GPs for help to quit, and focused GPs' attention on encouraging cessation in their patients, thereby increasing the proportion of pregnant women with a smoking status record in their medical notes. The proportion of pregnancies with a recording of smoking status rose sharply from 18.0% in 2003 to 32.4% in 2004, after which it increased slowly until 2009. The most plausible explanation for this marked increase between 2003 and 2004 is GPs' awareness of the impending introduction of the 2004 GP contract [25]. Similar improvements in the recording of smoking status have been seen in general population. A study using primary care data for over 300 practices throughout the UK found that, although rates of recording of smoking status in patients' electronic medical records had been increasing gradually since the year 2000, the rate of improvement accelerated from 2003, with an 88% increased observed between the first quarter of 2003 and the same period in 2004, just before the introduction of the QOF [26]. This suggests that the introduction of the QOF resulted in better recording of smoking status in the general population which has spilled over into the greater recording in pregnancy observed in our study.

Table 2. Odds of having smoking status recorded during gestation by women's characteristics before and after the QOF implementation.

	Pre-QOF(January 2000–March 2004)				Post-QOF(April 2004–December 2009)			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age								
15–19	1.48 (1.37–1.60)		1.56 (1.44–1.70)		1.66 (1.59–1.74)		1.62 (1.54–1.69)	
20–24	1.24 (1.17–1.32)		1.22 (1.15–1.30)		1.29 (1.25–1.32)		1.24 (1.20–1.28)	
25–29	1	<0.001	1	<0.001	1	<0.001	1	<0.001
30–34	0.92 (0.87–0.97)		0.95 (0.91–1.00)		0.80 (0.78–0.82)		0.84 (0.82–0.86)	
35–39	0.94 (0.88–0.99)		0.99 (0.93–1.05)		0.78 (0.75–0.80)		0.83 (0.80–0.85)	
40–44	0.93 (0.83–1.05)		0.99 (0.88–1.12)		0.76 (0.72–0.81)		0.80 (0.76–0.85)	
45–49	0.95 (0.59–1.53)		0.99 (0.61–1.60)		0.74 (0.59–0.93)		0.77 (0.61–0.97)	
Townsend Score								
Quintile 1 (most affluent)	1		1		1		1	
Quintile 2	1.03 (0.78–1.09)		1.01 (0.95–1.07)		1.16 (1.12–1.19)		1.12 (1.09–1.16)	
Quintile 3	1.09 (1.03–1.16)	<0.001*	1.03 (0.97–1.10)	<0.001*	1.28 (1.24–1.32)	<0.001*	1.18 (1.14–1.21)	<0.001*
Quintile 4	1.18 (1.11–1.25)		1.07 (1.00–1.13)		1.45 (1.40–1.49)		1.26 (1.22–1.30)	
Quintile 5 (most deprived)	1.34 (1.25–1.42)		1.17 (1.10–1.25)		1.69 (1.64–1.75)		1.42 (1.37–1.47)	
Missing	1.14 (1.04–1.25)		1.06 (0.97–1.16)		1.47 (1.41–1.54)		1.34 (1.29–1.40)	
Body Mass Index								
Underweight (<18.0)	1.01(0.88–1.14)		0.92 (0.81–1.05)		1.16 (1.10–1.24)		1.03 (0.97–1.10)	
Normal (18.0–24.9)	1		1		1		1	
Overweight (25.0–29.9)	1.07 (1.01–1.13)	<0.001	1.06 (1.00–1.13)	<0.001	1.06 (1.03–1.09)	<0.001	1.05 (1.02–1.09)	<0.001
Obese (≥30)	1.21 (1.13–1.30)		1.16 (1.08–1.25)		1.19 (1.16–1.23)		1.11 (1.08–1.15)	
Missing	0.63 (0.60–0.66)		0.63 (0.60–0.66)		0.91 (0.89–0.93)		0.90 (0.88–0.92)	
Asthma	1.80 (1.69–1.92)	<0.001	1.63 (1.53–1.74)	<0.001	2.19 (2.12–2.25)	<0.001	2.08 (2.02–2.15)	<0.001
Hypertension	1.32 (1.18–1.48)	<0.001	1.26 (1.12–1.41)	<0.001	1.17 (1.11–1.24)	<0.001	1.19 (1.12–1.26)	<0.001
Diabetes	1.17 (1.00–1.36)	0.045	-‡	-‡	1.11 (1.05–1.18)	<0.001	1.12 (1.05–1.19)	<0.001
Mental illness	1.42 (1.34–1.51)	<0.001	1.32 (1.24–1.41)	<0.001	1.37 (1.33–1.41)	<0.001	1.26 (1.22–1.30)	<0.001

OR = odds ratio, CI = confidence interval, QOF = Quality and Outcomes Framework,
*p-value for trend,
‡Diabetes not significant in the final model.
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For socioeconomic deprivation, asthma and diabetes the magnitude of effect of the association with smoking status recording was observed to be stronger after the introduction of the QOF. Pre-QOF, pregnant women from the most deprived group were 17% more likely to have their smoking status recorded during gestation compared to 42% post-QOF. Smoking prevalence is generally higher in lower socioeconomic groups in both the general population as well as amongst pregnant women [27] and the smoking status of smokers is more likely to be recorded than that of non-smokers [28–30], which likely explains more complete recording in pregnant women from lower socioeconomic groups. Furthermore, low socioeconomic status is associated with a higher prevalence of chronic diseases such as hypertension, diabetes, asthma and depression [31]. The QOF encourages improved clinical management of these patients, who post-QOF may have had more frequent contacts with their GP and thus have had more chance of being asked about their smoking behaviour, increasing the gradient of the association between socioeconomic status and smoking status recording, reflecting that recording, and thus hopefully monitoring, is more complete where it is most needed [32,33]. Asthma is the most common pre-existing condition encountered during pregnancy [34] and is closely related to smoking, which may explain the high magnitude of association between asthma and recording of smoking status compared to other conditions like diabetes (which affects approximately 2–5% in women of reproductive age) [35] and hypertension (0.6–2.7% during pregnancy) [36]. Women with a higher BMI have an increased risk of complications during pregnancy and therefore are more likely to visit their GPs [37]. They are also more likely to be smokers which in turn will affect the completeness of recording of their smoking status. Our findings are similar to those from a study in the general population which found that primary care patients with smoking-related chronic medical conditions and greater social deprivation were more likely to have a recent recording of smoking status or cessation advice in their medical records [38]. However, the magnitude of effect in this general population study for all morbidities much higher than that which we found, presumably because currently pregnancy is not a QOF-incentivised condition for recording of smoking.

To our knowledge this is the first study to assess the completeness of recording of smoking status during pregnancy in UK primary care medical records at a national level, using a large

population-based dataset with over 200,000 pregnancies. A potential limitation of our study is that due to the infrequency of smoking status recordings during pregnancy we did not assess recording of smoking status in smaller windows during pregnancy such as in each trimester, which may be more appropriate given that smoking status fluctuates during pregnancy [39]. Furthermore, we only assessed electronically-coded data in primary care records to examine the recording of smoking status during pregnancy and did not have access to free text or midwives' notes to ascertain smoking status; these may provide additional information on the smoking status of women during pregnancy. A potential explanation for the high proportion of pregnancies in which smoking status was not recorded could be that if a woman's smoking habit did not change after she became pregnant, GPs might be less likely to re-enter this information into medical records as there is no specific financial incentive for recording smoking status in pregnant women. Furthermore, as the QOF does not require GPs to record the smoking status of 'never smokers' after the age of 25, there is no financial incentive for them to update smoking status in the medical records of women who have never smoked. Similarly, ex-smokers need only be asked about their smoking status annually until they have been a non-smoker for three years. However, when we recalculated smoking status based on these rules, the annual trends in the completeness of smoking data during pregnancy did not vary much from the trends using the original data.

The current antenatal model in the UK is a midwife-led care one , where midwives are the main point of contact for women during pregnancy [9,40]. The National Institute for Health and Clinical Excellence (NICE) recommends that all pregnant women should have their smoking status recorded at the first antenatal booking appointment with the midwife and that all smokers should be referred to a stop smoking service and this should be recorded in the hand-held records which women in the UK carry with them throughout their pregnancy [7,41]. Data from a qualitative study of midwives in Glasgow, Scotland, suggested that they view it as part of their role to collect this smoking data at the booking appointment [42]. However, the means of recording of maternity data and provision of smoking cessation information during antenatal visits varies from practice to practice and we do not know whether, or how completely, smoking status data entered onto hand-held records get transferred to a woman's electronic primary care medical record for future reference.

As the current guidelines recommend, monitoring of smoking status during pregnancy should be a shared responsibility between all healthcare professionals involved in the care of pregnant women, including GPs and midwives [4,5,7]. The Royal College of Midwives recommends that during pregnancy midwives should have full confidential access to a woman's written and electronic records and GPs should ensure that all significant and relevant information is copied into a woman's hand-held maternity records [8]. Similarly, relevant information collected by midwives during pregnancy should also be communicated to the GPs and fed back into the electronic primary care records. Therefore, we recommend that appropriate methods should be introduced to improve communication and documentation of such information between the midwives and the GPs during pregnancy. One such strategy could be inclusion of pregnancy in the QOF as a condition where smoking status and smoking cessation advice should be recorded in the electronic primary care record. Primary care is the central hub in the current UK health care system and increasing the assessment and complete documentation of smoking status in primary care will not only increase opportunities for providing smoking cessation advice and interventions during pregnancy, but is also important to maintain continuity of care throughout and beyond pregnancy for both a woman's health and that of her children.

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Author Contributions

Conceived and designed the experiments: LS TC IJT KF. Performed the experiments: NND. Analyzed the data: NND. Contributed reagents/materials/analysis tools: NND LS. Wrote the paper: NND IJT TC KF LS.

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10.2 SMOKING CESSATION ADVICE RECORDED DURING PREGNANCY IN UNITED KINGDOM PRIMARY CARE

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Smoking cessation advice recorded during pregnancy in United Kingdom primary care

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Abstract

Background: United Kingdom (UK) national guidelines recommend that all pregnant women who smoke should be advised to quit at every available opportunity, and brief cessation advice is an efficient and cost-effective means to increase quit rates. The Quality and Outcomes Framework (QOF) implemented in 2004 requires general practitioners to document their delivery of smoking cessation advice in patient records. However, no specific targets have been set in QOF for the recording of this advice in pregnant women. We used a large electronic primary care database from the UK to quantify the pregnancies in which women who smoked were recorded to have been given smoking cessation advice, and the associated maternal characteristics.

Methods: Using The Health Improvement Network database we calculated annual proportions of pregnant smokers between 2000 and 2009 with cessation advice documented in their medical records during pregnancy. Logistic regression was used to assess variation in the recording of cessation advice with maternal characteristics.

Results: Among 45,296 pregnancies in women who smoked, recorded cessation advice increased from 7% in 2000 to 37% in 2004 when the QOF was introduced and reduced slightly to 30% in 2009. Pregnant smokers from the youngest age group (15–19) were 21% more likely to have a record of cessation advice compared to pregnant smokers aged 25–29 (OR 1.21, 95% CI 1.10-1.35) and pregnant smokers from the most deprived group were 38% more likely to have a record for cessation advice compared to pregnant smokers from the least deprived group (OR 1.38, 95% CI 1.14-1.68). Pregnant smokers with asthma were twice as likely to have documentation of cessation advice in their primary care records compared to pregnant smokers without asthma (OR 1.97, 95% CI 1.80-2.16). Presence of comorbidities such as diabetes, hypertension and mental illness also increased the likelihood of having smoking cessation advice recorded. No marked variations were observed in the recording of cessation advice with body mass index.

Conclusion: Recorded delivery of smoking cessation advice for pregnant smokers in primary care has increased with some fluctuation over the years, especially after the implementation of the QOF, and varies with maternal characteristics.

Keywords: Pregnancy, Smoking, Primary care, Smoking cessation advice

Background

Smoking during pregnancy is harmful to both the mother and the unborn child and is associated with substantial morbidities such as ectopic pregnancy, premature rupture of membranes, pre-eclampsia, placental abruption, stillbirth, low birth weight, premature birth and childhood asthma [1-5]. Data from the 2010 Infant Feeding Survey show that 26% of mothers in the United Kingdom (UK) smoked at some point before or during their pregnancy and 12% of women smoked throughout their pregnancy [6]. Given the high proportion of mothers currently smoking during pregnancy and the resulting health impacts, reducing smoking during pregnancy in the UK is a national priority [7].

Offering smokers brief cessation advice lasting no more than five minutes during routine consultations with a general practitioner (GP), during which doctors make clear

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that smoking is harmful and offer help with cessation [8], is one of the simplest and most cost-effective tools to reduce the burden of smoking in the general population and increases rates of quitting by two-thirds compared to unassisted quit rates of 4% (OR 1.66, 95% CI 1.42-1.94) [9]. In pregnant women, cessation rates with brief advice have been low (5-9%) compared with intense advice and counselling (14-17%) [10,11]. However, physician advice to quit has been cited by pregnant women as one of the most important factors which influences their decision to stop smoking [12] and has been recommended in the recent World Health Organsation guidance for the management of tobacco use in pregnancy [13]. Current UK guidelines also recommend that smoking cessation advice should be offered at every available opportunity by health professionals who come into contact with pregnant women, including GPs and midwives, as only after smoking and smoking cessation is raised can it be possible to refer women on for the more intensive behavioural support or other smoking cessation therapies that are known to work [14-17]. The Quality and Outcomes Framework (QOF) introduced in UK primary care in 2004 financially rewards GPs for offering cessation advice to smokers and documenting this advice in the patients' electronic medical records [18]. However, there are no specific QOF targets for offering and recording cessation advice to pregnant women who smoke and little is known about the frequency with which smoking cessation advice is indeed routinely delivered and recorded by primary care health professionals during pregnancy. Data from Health Education Authority (HEA) surveys carried out in the 1990s showed that less than half the women interviewed who were smokers received cessation advice from a health professional [19], and another study conducted in 200 antenatal clinics in Leicester, UK reported that only 34% of current smokers received advice from their GP, 19% from a midwife, 12% from an obstetrician, 9% from family and friends and 26% received no advice at all [20].

Given the national guidelines and the effectiveness of smoking cessation advice in increasing quit rates, we aimed to determine the proportion of pregnant smokers with smoking cessation advice recorded in their electronic primary care records in recent UK data. In addition, we aimed to investigate whether socioeconomic factors and women's existing medical conditions in pregnancy were associated with this recording.

Methods

Data source and study population

The Health Improvement Network (THIN) is an electronic primary care database containing anonymised patient records from general practices across the UK [21]. THIN was set up by Cegedim Strategic Data (CSD) Medical Research UK, formerly known as Epidemiology and Pharmacology Information Core (EPIC) and provides data for research purposes. The University of Nottingham has a license to use data from EPIC, subject to approval from the Scientific Review Committee (SRC) which reviews the ethics and research protocol. Ethical approval for the study was obtained from the THIN Scientific Review Committee (reference number 11–047).

The version of THIN used for this study covered approximately 5.7% of the population and contained data from 495 practices with a nationally representative sample of women of reproductive age (defined here as aged 15–49 years) [21]. Fertility rates in THIN are very similar to national fertility rates [22] and the population prevalence of smoking recorded in THIN has been previously validated at both national and regional levels [23,24]. Our study population included all pregnancies recorded in THIN from 2000 to 2009 in women of reproductive age which resulted in either a live birth or a stillbirth, and where women were considered to be smokers during pregnancy. Women were defined as smokers if they had a Read code [25] indicating smoking recorded in their medical records or a drug code for nicotine replacement therapy (NRT) during their pregnancy, or, in the absence of recording during pregnancy, if their last recorded Read code in the 27 months prior to pregnancy indicated smoking as defined in more detail previously [26].

Recording of smoking cessation and women's characteristics

Our main outcome of interest was whether pregnant women identified as smokers had Read codes [25] for smoking cessation advice recorded in their THIN records during the period of their pregnancy. Code lists are available from the authors on request.

Data were also extracted on women's age at the start of their pregnancy, socioeconomic deprivation as measured by quintiles of the Townsend Index of deprivation [27] based on their home postcode, body mass index (BMI) before their pregnancy and morbidities common in pregnancy for which the recording of smoking status has been specifically incentivised by the QOF (hypertension, diabetes, asthma, and mental illness which included depression, anxiety, bipolar disorder, schizophrenia and other psychoses), during pregnancy or within 27 months before conception in line with the QOF recording rules [28]. A summary variable was also created for the presence of at least one chronic condition out of the morbidities under study. Missing data for Townsend quintile and BMI were included in separate categories in the analyses.

Statistical analysis

Across the whole study period, annual proportions of pregnant smokers with records of smoking cessation advice were calculated as the number of pregnancies

among smokers with recorded smoking cessation advice divided by the total number of pregnancies among smokers who gave birth in that year.

To investigate the factors associated with the recording of smoking cessation advice delivered to pregnant smokers we used data from 2006 to 2009, as the proportion of pregnant smokers given smoking cessation advice in primary care only stablised after 2006 (as seen in Figure 1). Firstly, using univariable logistic regression, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for the association between each variable (age at pregnancy, Townsend quintile, BMI category, asthma, diabetes, hypertension and mental illness) and whether or not smoking cessation advice was recorded during pregnancy. Covariates that were significantly associated with the recording of smoking cessation advice in the univariable model ($p < 0.05$) were considered for inclusion in the final multivariable model. As some women had more than one pregnancy during the study period that contributed to our analyses, we accounted for this potential clustering of pregnancies within women by calculating robust confidence intervals (CIs) around our odds ratios using the clustered sandwich estimator to allow for intragroup correlation [29,30]. All analyses were completed using Stata version 11.0 (StataCorp LP, College Station, TX).

Results

Baseline characteristics

We identified 45,296 pregnancies in 39,781 women resulting in a live birth or stillbirth from 2000 to 2009 and where women were classified as smokers during pregnancy. Of these 4,826 also had NRT prescribed during pregnancy for smoking cessation. The mean age at conception was 27 years (standard deviation 6.17) and 48.6% of the pregnancies included in the study were in women in the two most deprived quintiles of the Townsend Index of deprivation. Smoking cessation advice was recorded in 12,454 (27.5%) of all pregnancies under study and half of the pregnancies (49.5%) where women also received an NRT prescription during pregnancy. Table 1 describes the baseline characteristics of the study population.

Annual trends in recorded smoking cessation advice in primary care

Figure 1 shows the annual proportions of pregnant smokers with smoking cessation advice recorded in their primary care medical records during pregnancy from 2000 to 2009. Overall, there has been an increase in this proportion over time. The proportion of pregnant smokers with recorded smoking cessation advice in 2000 was only 7%. This doubled to 15% in 2003, after which a steep increase was observed in 2004 with the proportion rising to 33%. The proportion of pregnant smokers with recorded smoking cessation advice peaked in 2005 at 37%, after which it stabalised at between 26-29% in the period of 2006–2009.

Factors associated with the recording of smoking cessation advice in pregnancy

Table 2 shows variations in the odds of smoking cessation advice being recorded during pregnancy by women's sociodemographic characteristics and morbidities. Pregnant smokers from the youngest age group (15–19) and the oldest age group (45–49) were more likely to be recorded as having received smoking cessation advice compared to pregnant smokers between the age of 25 and 29 years (OR 1.21 (95% CI 1.10-1.35) and OR 2.37 (95% CI 1.11-5.10) respectively). Recording also varied with socioeconomic status, such that pregnant smokers from the most deprived group (quintile 5) were 38% more likely to have smoking cessation advice recorded in their primary care records than pregnant women from the least deprived quintile (OR 1.38, 95% CI 1.14-1.68). In addition, recorded smoking cessation advice was higher in pregnant smokers with morbidities, such that pregnant smokers with asthma were almost twice as likely to have been recorded as having received smoking cessation advice compared to

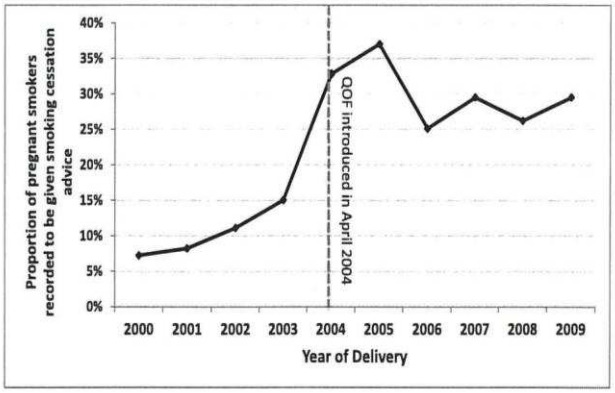

Figure 1 Annual proportions of pregnant smokers with smoking cessation advice recorded in their primary care records (2000–2009).

Table 1 Baseline characteristics of the study population (pregnant smokers)

	Total pregnancies (N = 45,296)	Recorded smoking cessation advice (%*) (N = 12,454)	
Age at conception			
15-19 years	5,019	1,538	(30.6%)
20-24 years	12,180	3,355	(27.5%)
25-29 years	12,005	3,153	(26.3%)
30-34 years	9,736	2,613	(26.8%)
35-39 years	5,254	1,457	(27.7%)
40-44 years	1,048	317	(30.2%)
45-49 years	54	21	(38.9%)
Townsend score in quintiles			
Quintile 1 - most affluent	5,380	1,293	(24.0%)
Quintile 2	6,156	1,625	(26.4%)
Quintile 3	8,842	2,360	(26.7%)
Quintile 4	11,432	3,303	(28.9%)
Quintile 5 - most deprived	10,572	3,141	(29.7%)
Missing	5,380	1,293	(24.0%)
Pre-conception body mass index			
Normal (18.0-24.9)	19,579	5,144	(26.3%)
Underweight (<18.0)	2,106	588	(27.9%)
Overweight (25–29.9)	8,897	2,547	(28.4%)
Obese (> = 30)	6,338	1,874	(29.6%)
Missing	8,302	2,301	(27.7%)
Asthma	5,238	2,102	(40.1%)
Hypertension	969	315	(32.5%)
Diabetes	942	310	(32.9%)
Mental illness	7,193	2,184	(30.4%)
At least one of above morbidities**	12,577	4,177	(33.2%)

*% with recorded smoking cessation advice as a proportion of all pregnancies in smokers within each variable strata.
**Recording of medical conditions including asthma, hypertension, diabetes and mental illness.

pregnant smokers without asthma (OR 1.97, 95% CI 1.80-2.16). Similarly, pregnant smokers with hypertension and diabetes were, respectively, 32% (OR 1.32, 95% CI 1.09-1.60) and 24% (OR 1.24, 95% CI 1.03-1.50) more likely to have smoking cessation advice recorded in their medical records compared to smokers without these morbidities. The presence of at least one of the above morbidities (diabetes, hypertension, asthma, mental illness) increased the likelihood of recording of smoking cessation advice for pregnant smokers by 49% (OR 1.49, 95% CI 1.39-1.60).

Discussion

Using a large population-based dataset, we have shown that the proportion of pregnant smokers recorded as having been advised to quit in primary care increased from 7% in 2000 to 30% in 2009, with substantial increases in the rate of recording around the time of the introduction of the QOF in 2004. We also found smoking cessation advice was more likely to be recorded in pregnant smokers from more deprived socioeconomic groups, among pregnant teenagers and women over age 45 years, and among women with asthma, diabetes, hypertension and mental illness.

Whilst national trends in the delivery of smoking cessation advice have been assessed in the general population [31,32], this is the first study to assess this advice recording during pregnancy in primary care. Our study provides estimates for the delivery of smoking cessation advice during pregnancy in routine GP consultations to complement survey data, which may over-estimate physician behaviours such as delivering smoking cessation advice [33] and may be limited by small sample sizes and non-probability sampling techniques [19,20]. However, we acknowledge that the recording of smoking cessation advice in a pregnant woman's medical records may not always be acknowledged and interpreted as advice to quit by the women, and we do not know whether it was acted upon and resulted in a cessation attempt. The concept of smoking cessation advice is very subjective and different GPs may have different opinions on what constitutes effective advice. This may vary from a detailed discussion on smoking cessation strategies to only a brief mention of smoking during the consultation [34]. Indeed it is possible that in some cases smoking or smoking cessation may not actually have been discussed at all in the consultation and therefore we cannot be completely sure of the degree to which these Read codes represent the nature and extent of the advice delivered to pregnant smokers [32,34]. Additionally, GPs commonly address an average of two to three different medical problems during a single consultation [35,36]. However, the clinical coding does not necessarily reflect the breadth of the consultation and only the dominant topics of the visit may be coded [37]. Therefore, it is possible that smoking cessation advice was provided as part of the consultation yet not recorded electronically in women's primary care notes. Furthermore, defining women as smokers based on NRT prescriptions may result in over-estimation of the cessation advice recording as prescribing of NRT is more likely to be accompanied or preceded by the delivery of smoking cessation advice. However, only 10% of the smokers in our study were identified based on NRT prescriptions. Moreover, only 50% of women who received NRT also had a record of smoking cessation advice, and therefore it would not affect the proportion of smokers with cessation advice substantially.

In the UK health care system midwives are the main point of contact for most women during pregnancy [37,38]

Table 2 Odds ratios of receiving smoking cessation advice by women's characteristics and morbidities between 2006 and 2009

	Pregnant smokers (n = 27,959)	Pregnant smokers with smoking cessation advice (n = 7,716)		Unadjusted		Adjusted	
Age at conception		n	%	OR (95% CI)	p-value	OR (95% CI)	p-value
15–19	3,169	957	30.2	1.19 (1.08-1.32)	0.008	1.21 (1.10-1.35)	0.001
20–24	7,738	2,127	27.5	1.05 (0.96-1.14)		1.04 (0.96-1.13)	
25–29	7,542	2,006	26.6	1		1	
30–34	5,639	1,535	27.2	1.03 (0.95-1.12)		1.05 (0.96-1.14)	
35–39	3,166	872	27.5	1.05 (0.95-1.15)		1.07 (0.97-1.17)	
40–44	671	203	30.3	1.20 (1.00-1.43)		1.18 (0.98-1.41)	
45-49	34	16	47.1	2.45 (1.21-4.98)		2.37 (1.11-5.10)	
Townsend score							
Quintile 1 (most affluent)	3,047	711	23.3	1.00	<0.001*	1.00	<0.001*
Quintile 2	3,745	1,005	26.8	1.21 (1.07-1.35)		1.19 (1.06-1.34)	
Quintile 3	5,532	1,480	26.8	1.20 (1.06-1.36)		1.18 (1.04-1.35)	
Quintile 4	7,191	2,075	28.9	1.33 (1.16-1.53)		1.29 (1.13-1.48)	
Quintile 5 (most deprived)	6,583	1,989	30.2	1.42 (1.17-1.72)		1.38 (1.14-1.68)	
Missing	1,861	456	24.5	1.07 (0.89-1.28)		1.03 (0.85-1.24)	
Body mass index							
Underweight (<18.0)	11,893	3,196	26.9	1.10 (0.97-1.25)	<0.001	1.08 (0.95-1.22)	<0.001
Normal (18.0-24.9)	1,334	385	28.9	1		1	
Overweight (25.0-29.9)	5,689	1,645	28.9	1.11 (1.03-1.19)		1.09 (1.01-1.18)	
Obese (≥30)	4,218	1,252	29.7	1.15 (1.06-1.24)		1.08 (0.99-1.16)	
Missing	4,825	1,238	25.7	0.94 (0.87-1.01)		0.92 (0.83-1.01)	
Asthma	3,317	1,368	41.2	2.02 (1.85-2.2)	<0.001	1.97 (1.80 - 2.16)	<0.001
Hypertension	580	200	34.5	1.39 (1.16-1.67)	<0.001	1.32 (1.09 - 1.60)	<0.001
Diabetes	635	208	32.8	1.29 (1.07-1.55)	0.008	1.24 (1.03 - 1.50)	0.015
Mental illness	4,390	1,314	29.9	1.15 (1.06-1.24)	0.001	1.09 (1.01 - 1.18)	0.019

OR Odds ratio, *CI* Confidence interval, *p-value for trend.

and guidelines indicate that midwives should ask about women's smoking status at the first antenatal booking appointment (usually between 8–12 weeks), and provide smoking cessation advice and referral if warranted [39]. This information should be documented in women's handheld notes (mandatory paper records that women should carry throughout pregnancy as part of the UK's National Health Service antenatal care). However, there are no existing studies to show the extent to which this information is transferred to their electronic primary care records. We may, therefore, have underestimated the proportion of smokers in fact receiving cessation advice.

Our study is novel in that it investigates the maternal characteristics associated with the recording of smoking cessation advice during pregnancy. We found a significant increase in recorded smoking cessation advice with increasing deprivation quintile. A similar trend was seen in a study which examined the impact of the QOF on the recording of smoking advice in the general adult population - smokers from the most deprived quintile were 20% more likely to have a record of smoking cessation advice than smokers in the least deprived quintile [31]. This may be related to a poorer overall health status, higher prevalence of illness in more deprived smokers [40], or generally heavier smoking habits in this group [6], resulting in more GP visits and consequently more opportunities for the delivery and recording of smoking cessation advice. We also found that pregnant smokers in the youngest (15–19 years) and the oldest (45–49 years) age groups were more likely to have smoking cessation advice recorded during pregnancy. Although the latter was only a very small group of women, pregnancies in the 45–49 age groups are generally high-risk, resulting in more GP visits than normal pregnancies, which will make smoking cessation more important and result in more opportunities for providing smoking cessation advice. The prevalence of smoking during pregnancy is generally higher in younger women [6], and teenagers also have generally higher-risk

pregnancies compared with women of average childbearing age [41,42]. According to the Infant Feeding Survey 2010, levels of smoking during pregnancy were the highest among mothers under the age of 20 in England and Scotland [6], which may explain higher smoking cessation advice documentation in this very young group in our study. The presence of comorbidities such as asthma, diabetes, hypertension and mental illness was also related to recording of smoking cessation advice delivery in our study. The effect of asthma was the strongest, such that pregnant smokers with asthma were twice as likely to have cessation advice recorded in their primary care records compared to non-asthmatics. This is consistent with a general population study which showed that presence of comorbidities was strongly related to the recording of cessation advice in primary care in the general population. However, the magnitude of effect for the morbidities was much higher than that found in our study [31], which may be because pregnant women are generally younger and healthier compared to the general adult population.

In our study, the proportion of pregnant smokers with smoking cessation advice recorded in their medical records during their pregnancy doubled between 2003 and 2004 suggesting that, despite having no specific target for recording of smoking cessation advice during pregnancy, the QOF has increased the occurrence of such activity. This marked increase between 2003 and 2004 can be attributed to the introduction of the 2004 GP contract as the negotiations for this contract started between 2002 and 2003 [43]. A general population study using primary care data from over 300 practices throughout the UK to assess the effect of the QOF on recording of smoking status and smoking cessation advice found that although rates of recording of smoking cessation advice in patients' electronic medical records had been increasing gradually since the year 2000, the rate of improvement accelerated from 2003, with a 3-fold increase observed between the first quarter of 2003 and the same period in 2004, just before the introduction of the QOF (Risk Ratio (RR) 3.03, 95% CI 2.98-3.09) [44]. This may be evidence that historically GPs have not documented their delivery of smoking cessation advice in patients' primary care records and after the introduction of QOF in 2004 the documentation of such advice improved. Data collected by semi-structured interviews in antenatal clinics at one UK hospital in the mid-1990s found that 34% of pregnant smokers reported receiving advice to quit from their GP [20]. Similarly, annual surveys between 1992 and 1999 conducted on pregnant women throughout England found that the proportion of pregnant smokers who received advice from a health professional ranged from 38%-55% [19]. Patient recall is known to be biased towards over-reporting in questions about smoking cessation advice [33,45], which may explain why estimates from these surveys are higher than our estimates from THIN data presented here. However, the large difference between the proportion of women with cessation advice recorded in THIN prior to 2004 and these survey estimates suggests that the introduction of the QOF may have resulted in an improvement in the recording of advice, which GPs were already giving but not documenting [34]. Despite these uncertainties in the interpretation of the data presented here, the observation that only approximately one-third of smokers have the delivery of cessation advice recorded in their primary care medical records suggests there is substantial room for improvement in the provision of this important health advice, particularly during pregnancy.

Conclusions

In conclusion, although there are no specific targets to encourage GPs to deliver and document smoking cessation to pregnant women, the effects of smoking-related QOF targets in the general population appear to have increased the overall recording of smoking cessation advice during pregnancy as well with some fluctuations over the years. Pregnancy offers a strategic opportunity for health professionals to promote smoking cessation and motivate women to give up as women are generally more receptive to cessation interventions [46], therefore every opportunity to encourage smoking cessation should be seized by the health care professionals even if it is in the form of brief advice lasting less only a few minutes. The inclusion in the QOF of a target on smoking cessation advice specifically during pregnancy may result in the topic of smoking being raised more frequently, more advice being given and recorded and more pregnant smokers being referred on for specialist support with quitting smoking.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

NND, LJT, TC and LS conceived the idea for the study and analyses, which was conducted using a dataset created under supervision of LJT of women in their potential childbearing years from The Health Improvement Network database. BH carried out the data management and analysis under supervision by NND and LS and wrote the first draft of the manuscript. LJT and TC provided interpretations at different stages of the project and helped to draft the manuscript. All authors read and approved full drafts and the final manuscript.

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10.3 A COMPARISON OF UK PRIMARY CARE DATA WITH OTHER NATIONAL DATA SOURCES FOR MONITORING THE PREVALENCE OF SMOKING DURING PREGNANCY

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A comparison of UK primary care data with other national data sources for monitoring the prevalence of smoking during pregnancy

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ABSTRACT

Background We aimed to assess the potential usefulness of primary care data in the UK for estimating smoking prevalence in pregnancy by comparing the primary care data estimates with those obtained from other data sources.

Methods In The Health Improvement Network (THIN) primary care database, we identified pregnant smokers using smoking information recorded during pregnancy. Where this information was missing, we used smoking information recorded prior to pregnancy. We compared annual smoking prevalence from 2000 to 2012 in THIN with measures from the Infant Feeding Survey (IFS), Smoking At Time of Delivery (SATOD), Child Health Systems Programme (CHSP) and Scottish Morbidity Record (SMR).

Results Smoking estimates from THIN data converged with estimates from other sources after 2004, though still do not agree completely. For example, in 2012 smoking prevalence at booking was 11.6% in THIN using data recorded only during pregnancy, compared with 19.6% in SMR data. However, the use of smoking data recorded up to 27 months before conception increased the THIN prevalence to 20.3%, improving the comparability.

Conclusions Under-recording of smoking status during pregnancy results in unreliable prevalence estimates from primary care data and needs improvement. However, in the absence of gestational smoking data, the inclusion of pre-conception smoking records may increase the utility of primary care data. One strategy to improve gestational smoking status recording in primary care could be the inclusion of pregnancy in the Quality and Outcome's Framework as a condition for which smoking status and smoking cessation advice must be recorded electronically in patient records.

Keywords primary care, pregnancy and childbirth disorders, smoking

Introduction

Smoking in pregnancy is an important preventable cause of poor health outcomes for women and their babies.[1,2] In March 2011, the UK Government white paper entitled 'Healthy lives healthy people: A tobacco control plan for England' set out a national goal to reduce the prevalence of smoking throughout pregnancy to 11% or less by 2015.[3] It is therefore crucial to collect data on maternal smoking to monitor progress towards this national goal. The UK currently has four data sources that provide population-level estimates of smoking during pregnancy. Each measures smoking differently and has its strengths and limitations The Infant Feeding Survey (IFS) measures smoking at

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delivery, retrospectively, at 6–8 weeks postpartum in the UK.[4–6] The smoking at the time of delivery (SATOD) data measure smoking behaviour at the time of delivery,[7] whereas the Child Health Systems Programme (CHSP) Pre-School Component measures maternal smoking around delivery usually within 10 days postpartum.[8] In comparison, data from the Scottish Morbidity Records (SMR) measure smoking at the time of first antenatal appointment. Electronic primary care records contain routinely collected information on medical diagnoses, prescriptions and other data such as patients' smoking status,[9] and thus could potentially provide comprehensive and timely population-level data on smoking prevalence during pregnancy. In April 2004, a contract for UK general practitioners (GPs) (family physicians) was implemented; this introduced pay-for-performance targets known as the Quality and Outcomes Framework (QOF)[10] according to which the recording of smoking status and recorded delivery of smoking cessation advice can generate revenue of up to £10 000 per year per practice.[11,12] Consequently, the recording of smoking status in primary care data has improved such that, outside of pregnancy, UK primary care data are a valid source of data to monitor smoking prevalence at a population level both nationally and regionally.[13,14] However, the potential use of these data for generating estimates of smoking during pregnancy at a population level is yet to be studied. In an earlier study, we found that the recording of smoking status during pregnancy is relatively incomplete; in 2009, only 43% of women had a record for smoking status during pregnancy.[15] However, in this previous work, we found that the utility of incomplete individual-level smoking status data could be improved by making various assumptions which reflected data recording practices encouraged by the QOF.[15] Consequently, in this paper, we test similar assumptions to assess the potential usefulness of primary care data for estimating the population smoking prevalence in pregnancy by comparing estimates from primary care data with those obtained from other available data sources.

Methods

Data source and study population

The Health Improvement Network (THIN) is an electronic primary care database containing anonymized patient records from general practices across the UK. It is representative of the UK population in terms of patient demographics and the prevalence of common illnesses.[16] The version of THIN used for this study contained data from 570 practices, covering ~6% of the UK population.[9] Our study population included all women of reproductive age (defined as 15–49[17]) in THIN with pregnancies ending in live births or stillbirths from 2000 to 2012. Pregnancies ending in miscarriage were not included in the study population as many of these occur early in pregnancy when women may not know they are pregnant. Therefore, they may not be reported to the doctor, or if they are reported, the first consultation indicating the pregnancy may be for reporting the miscarriage, when ascertainment of smoking status would only be retrospective. For women with more than one pregnancy during the study time, one pregnancy was chosen at random for analysis to prevent any clustering effects.

Comparing the prevalence of smoking in pregnancy in THIN with other data sources

For each woman, we extracted all records of smoking status recorded in THIN using Read codes[18] before and during pregnancy and up to 10 days after delivery (e.g. 137R.00—Current smoker). Where a Read code did not clearly indicate current smoking (e.g. 137X.00—Cigarette consumption), we assessed whether smoking status could be derived from any additional information recorded, such as the number of cigarettes smoked, or the presence of prescriptions for smoking cessation medications. If no additional information was found, the recording was labelled as unknown smoking status. Code lists are available from the authors on request.

Using a previously validated algorithm,[13] we used the extracted Read codes to determine each woman's smoking status during their pregnancy. The annual prevalence of smoking during pregnancy as recorded in THIN (as a proportion of all births in that year) was then compared against the prevalence measures from the IFS, SATOD, SMR and CHSP. A detailed description of each of these data sources is provided in Table 1.

Each comparison used a slightly different population of women from THIN and assessed smoking status at a different point in time in pregnancy to reflect the nature of the data collection in the source being compared (see Table 2). Estimates of smoking prevalence from the IFS were derived from the 'raw' data sets of individual women's survey responses, available from the UK Data Service.[24] The IFS only asked about smoking status retrospectively, so women were classified as smoking at delivery if they reported that they tried to give up smoking during pregnancy but started again before delivery, if they tried to cut down on the amount smoked during pregnancy, or if they did not try to cut down during pregnancy. Estimates of the prevalence of smoking from SATOD, SMR and CHSP data were obtained from published reports.

Imputing smoking status where women had no record during the gestational period

Initially, we used only records of smoking status documented in the primary care record after the date of conception to

Table 1 Summary of available data sources to measure smoking during pregnancy in the UK

Data source	*Data collection interval*	*Country*	*Sampling frame and method*	*Sample size* [a] *(% of national births)*	*Data collection method*	*Time at which data on smoking in pregnancy are collected*	*Definition of smoking*	*Strengths*	*Limitations*
Infant Feeding Survey[4–6]	Every 5 years	UK (England, Scotland, Wales, Northern Ireland)	Random sample of live births in England and Scotland and all births in Wales and Northern Ireland in study period	22 400 (2.7% of all births in the UK)[19–23]	Postal survey administered by the National Health Service Information Centre	6–8 weeks after birth	Several self-reported measures available: smoking prior to pregnancy; ever smoking during pregnancy; quitting on confirmation of pregnancy; quit/cut down attempts during pregnancy; smoking at delivery	Smoking estimates for overall UK and each constituent country Smoking status presented by sociodemographic factors Measures smoking cessation during pregnancy	Data only collected at 5 years intervals Retrospective reporting of smoking status Low response rates (~52%) Results published at least a year after survey completion
Smoking Status at Time of Delivery (SATOD)[7]	Collected continually and reported quarterly	England	Aims to capture all live births and stillbirths	359 763 (52.1% of all births in England)[19,22]	Midwife survey (in hospital maternity units)	At delivery	Self-reported smoking status at delivery	Data collected and reported at a local level	Limited to England Data collected postnatally No assessment of smoking by sociodemographic factors
Smoking Data collected as part of the Scottish Morbidity Record (SMR)[8]	Collected continually and reported by financial year	Scotland	All pregnant women attending an antenatal booking appointment (pregnancies may end in live birth or stillbirth)	57 398 (100% of all maternities in Scotland)[20,23]	Midwife survey (in hospital or community)	First antenatal booking appointment (usually between 8–12 weeks gestation)	Self-reported smoking status at the time of booking	Provides measures of never/ex smoking along with current smoking Provides annual rates by age and socio-economic status	Limited to Scotland Does not give estimates for the whole duration of pregnancy
Pre-school component of the Child Health Systems Programme (CHSP)[8]	Collected continually and reported by financial year	Scotland	Aims to capture all live births	51 746 (92% of all live births in Scotland)[20,23]	Survey administered by public health nurse or health visitor	Approximately 10 days after birth	Self-reported smoking status at the time of survey ~10 days after delivery	Provides data on smokers and non-smokers by age and socio-economic status	Limited to Scotland Data collected postnatally only Does not specifically ask about smoking during pregnancy

[a]Sample sizes for each wave vary therefore sample sizes for 2010 described in the table for reference.

Table 2 THIN comparisons with the currently available data in the UK

Survey	*Time at which survey assesses smoking prevalence*	*Years compared with THIN*	*THIN population used for comparison*	*Timing of records considered to define smoking status in THIN*
Infant Feeding Survey (IFS)	At delivery	2000, 2005, 2010	Data from all UK practices ($n = 570$)	Last smoking status recording between conception and delivery
Smoking Status at Time of Delivery (SATOD)	At delivery	2006–2012	Data from English practices ($n = 420$)	Last smoking status recording between conception and delivery
Scottish Morbidity Record (SMR)	At booking (8–12 weeks gestation)	2000–2012	Data from Scottish practices ($n = 85$)	First smoking status recording between conception and delivery
Child Health Systems Programme (CHSP)	10 days after delivery	2001–2012	Data from Scottish practices ($n = 85$)	Last smoking status recording between conception and 10 days after delivery

determine smoking status during pregnancy. However, if a woman's smoking status was not recorded during gestation, we used pre-conception records of smoking status to identify women who might have smoked during pregnancy. Based on the QOF rules for the recording of smoking status in the general population, which from April 2004 to March 2006 required the smoking status of patients aged 15 or over to be recorded at least once in primary care records, and since April 2006 have required records to be updated every 27 months, we used two cut-off points for including information from pre-conception records.[25] Firstly, we used a cut-off of 27 months before conception and recoded women as smokers if their last smoking record in the 27 months before conception indicated smoking. Finally, if a woman did not have her smoking status recorded either during pregnancy or in the 27 months before conception, we included any smoking information recorded in their primary care data since they registered with their practice.

All analyses were conducted in Stata 12.0 (StataCorp LP, College Station, TX, USA). Ethical approval was obtained from the THIN Scientific Review Committee (Reference number 11-047).

Results

Population of pregnancies and smoking in THIN

We identified 310 043 women with one or more pregnancies ending in a live birth or stillbirth from 2000 to 2012; 246 730 of these women were registered with a GP in England and 34 442 were in Scotland. The mean age at conception was 29.5 years (standard deviation 5.9 years). Only 30% of women had their smoking status recorded at least once during pregnancy and of these women 75% only had a single record.

Comparison with IFS data

Figure 1a shows the prevalence of smoking at the time of delivery in women in THIN compared with the prevalence measures in the IFS. Annual trends could not be compared as there were only three data points available. In 2000, none of the three prevalence estimates using THIN data were comparable with the IFS estimates. In 2005, smoking prevalence including data recorded up to 27 months before conception from THIN was slightly higher than the IFS estimate (17.0 versus 20.6%, respectively). In 2010, the IFS prevalence of smoking at the time of delivery decreased further to 11.6%, while the THIN prevalence using data recorded up to 27 months before conception remained similar (19.9%). In comparison, the IFS prevalence for 2010 was ~3 percentage points higher than the THIN prevalence using only smoking data recorded during pregnancy (11.6% in the IFS compared with 9.3% in THIN).

Comparison with SATOD data

When using smoking data recorded any time before delivery, the prevalence of smoking during pregnancy recorded in THIN was ~7 percentage points higher than the SATOD estimates from 2006 to 2012. In comparison, the THIN prevalence considering data recorded up to 27 months before conception was ~4–5 percentage points higher over the 6 years of available data, while the THIN prevalence considering only records of smoking recorded during the gestational period was 4–5 percentage points lower than the SATOD estimates (Fig. 1b).

Comparison with CHSP data

Using only records of smoking status entered during the gestational period, the THIN prevalence of maternal smoking was low until 2004 (e.g. 44% of the CHSP prevalence of 23.1% in

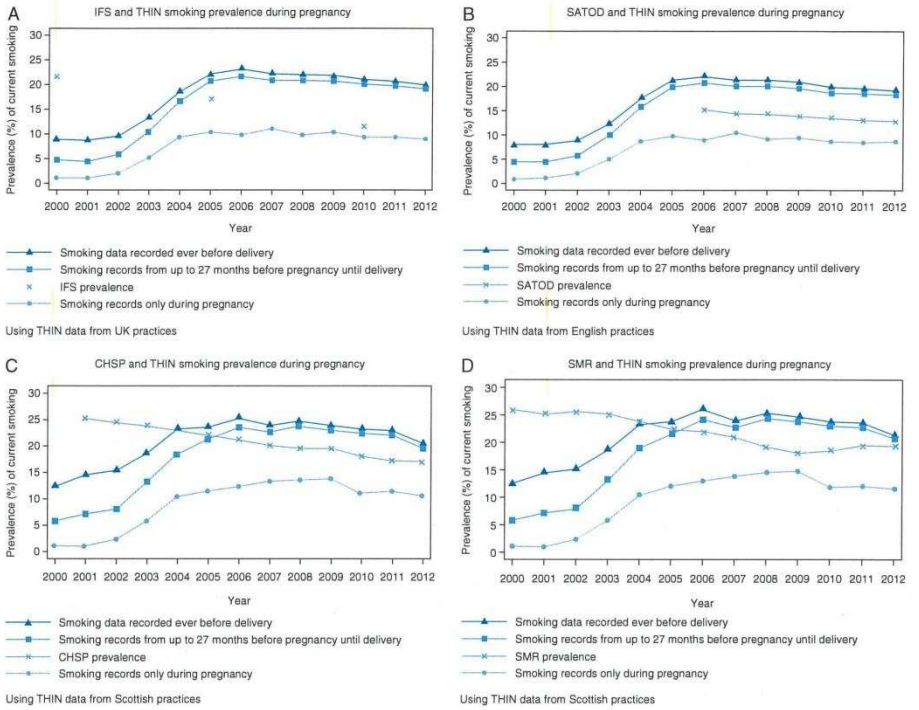

Fig. 1 Comparison of smoking prevalence from currently available data sources and THIN.

2004) (Fig. 1c). It was 10.5% in 2012, ~7 percentage points lower than the corresponding CHSP prevalence of 17.1%. Using smoking information recorded in the 27 months before pregnancy, the prevalence in CHSP and THIN converged in 2005. After this, the THIN estimates were slightly higher than the CHSP estimates, such that in 2012 the THIN prevalence using data recorded up to 27 months before pregnancy was 19.9% compared with the CHSP prevalence of 17.1%. The prevalence estimates using data recorded ever before delivery were only slightly higher than the estimates using data recorded up to 27 months before conception.

Comparison with SMR data

Using smoking status data recorded during the gestational period, the THIN prevalence was much lower than the SMR prevalence until 2004 (THIN prevalence = 10.6% compared with SMR prevalence of 23.8% in 2004, as shown in Fig. 1d). Prevalence in THIN was 11.6% in 2012 but was still 40% lower than the corresponding SMR prevalence of 19.6%. When including smoking information recorded up to 27 months before conception, the two lines converged between 2004 and 2005; in 2012, smoking prevalence in THIN was 20.3% using data recorded up to 27 months before conception and smoking prevalence using data recorded any time before pregnancy was 21.3% compared with the SMR prevalence of 19.3%.

Discussion

Main findings

We found that, with current levels of completeness of smoking data in primary care records, it is not possible to produce population level estimates for smoking prevalence during pregnancy that are directly comparable with those

derived from existing surveys. The convergence between THIN estimates and estimates from other data sources has, however, improved over time especially following the introduction of the QOF. Data from the IFS show good agreement with smoking at delivery in women in 2010 as recorded in THIN based on smoking status records entered in the electronic medical record during pregnancy. THIN data, using smoking data recorded up to 27 months before conception, show good agreement with SMR estimates in the final year of the study period.

What is already known on the topic

To date, there are no studies assessing the validity of primary care data for quantifying the prevalence of smoking during pregnancy. A study comparing smoking prevalence recorded in THIN to smoking prevalence in the general population [measured by the General Lifestyle Survey (GLF)] found a good agreement between THIN and the GLF after 2008 and concluded that primary care data may provide an alternate means of monitoring national smoking prevalence.[18] Despite the smaller sample sizes at regional level, primary care data have also been shown to be a good means of monitoring regional smoking prevalence in the general population.[19]

If primary care data were valid to monitor smoking prevalence during pregnancy, there would be several advantages of using these data to do so. All women in the UK must be registered with a GP in pregnancy to receive free antenatal care, so their records will be available in GP research databases. THIN data are routinely collected, have a lag of only 3–8 months before clinical data become available to researchers, and have the statistical power to provide estimates for the whole UK as well as constituent countries.[18]

What this study adds

The prevalence estimates of smoking during pregnancy from primary care do not accurately converge with other data sources because, at least in part, smoking status recording during pregnancy in primary care is incomplete.[20] If a woman's status did not change after she became pregnant (e.g. a non-smoker before pregnancy remained a non-smoker during pregnancy, or a smoker continued to smoke), GPs might be less likely to re-enter this information, which may account for the low completeness. Furthermore, in the UK, smoking status during pregnancy is primarily ascertained by midwives and recorded in women's handheld maternity records [mandatory paper records that women carry throughout pregnancy as part of the UK's National Health Service (NHS) antenatal care]. While the National Institute for Health and Clinical Excellence (NICE) recommends that midwives and others involved in the care of pregnant women assess and document women's smoking status in their maternity records,[26,27] this information is not routinely entered into primary care records as the documentation in midwives' notes is not usually transcribed onto the electronic primary care records. This was clearly reflected in our previous study which found that from 2000 to 2009 smoking status was only recorded in primary care for 28% of pregnancies.[20] In the current study, smoking status was only recorded for 30% of pregnancies.

Another possible explanation for the lower THIN prevalence could be that THIN over-represents general practices from more affluent areas of the UK. Since smoking prevalence is lower in women from more affluent groups, this may slightly under-estimate the smoking prevalence generated using THIN data and account for some of the differences between THIN prevalence estimates and other data sources.

While THIN estimates using only gestational smoking records do not approximate closely to annual prevalence from other data sources, THIN estimates using smoking data from up to 27 months pre-conception are comparable with the SMR data (smoking status recorded at booking) in 2012. GP data may be most useful to provide adequate data on smoking prevalence early in pregnancy, when most women see their GPs for initial care, compared with the time around delivery, when most women will be cared for essentially in secondary care facilities.

Limitations

This is the first study to assess the potential of primary care data to provide population-level estimates of smoking during pregnancy and compare it with other current data sources in the UK. Fertility rates in THIN are comparable with national fertility rates[28] and therefore our ascertainment of pregnancies is valid. However, like the other data sources under comparison, data on smoking status recorded in THIN are self-reported and women may not accurately report their smoking behaviour, particularly during pregnancy where there may be social stigma attached to smoking.[29]

A potential limitation of our study was the inclusion of pre-conception smoking records to predict smoking status during pregnancy, which may not be an accurate reflection of women's smoking status during pregnancy. Studies which have investigated smoking behaviour in early pregnancy indicate that many women attempt to quit when they find out they are pregnant or later during pregnancy,[30] so it is unlikely that the inclusion of pre-conception records resulted in an under-estimation of smoking prevalence during pregnancy. It could however, lead to misclassification of some ex-smokers

as current smokers, resulting in an over-estimation of the prevalence of current smoking during pregnancy in THIN. We believe that a substantial over-estimation is unlikely as ~35–50% of pregnancies in the UK are unplanned,[31,32] which means that only some women are likely to make positive behaviour changes such as quitting smoking before attempting to conceive. It may, however, hold true for some women who quit on confirmation of their pregnancy.

Another potential weakness of our study, and of primary care data itself, is that it is difficult to determine the timing of smoking status ascertainment in relation to progress through gestation; this makes direct comparison with other data sources, obtained at booking or delivery, difficult. Lastly, smoking status during pregnancy is a complex and variable behaviour and it may fluctuate throughout pregnancy.[33] Therefore, single measures of smoking such as smoking at booking or smoking at delivery captured in SATOD, SMR and CHSP data are limited in their usefulness. Although they may give a snapshot of smoking behaviour at a certain time, they may not give a complete picture of smoking behaviour throughout pregnancy. IFS data assess smoking behaviour throughout pregnancy in more detail, albeit collected retrospectively. However, these data are collected on a quinquennial basis and thus may become out of date quickly. If smoking information was collected and recorded by GPs more frequently throughout pregnancy, then primary care data may prove to be very useful to assess the population-level burden of maternal smoking throughout pregnancy. However, as shown in this study, currently these data are not desirably complete.

Conclusion

All existing data sources that measure smoking during pregnancy have their strengths and limitations. Primary care data have a great potential to measure smoking status during pregnancy at a population level, but this potential appears to be greatest for measuring smoking prevalence in early pregnancy around the time of booking appointments. Although recording of gestational smoking status in THIN is improving over time, it is not adequately complete to produce maternal smoking estimates at a population level with most women just having a single recording of smoking status throughout the course of pregnancy. Periodic recording of smoking status during pregnancy is important to monitor changes in smoking behaviour throughout pregnancy and to maintain and improve women's care before and after delivery. Although this information may be recorded and updated in handheld maternity notes, there is currently no centralized recording system and the information in these notes is lost after delivery. Better integration of recording systems in primary care and midwifery services is required to improve communication and relay of relevant medical and lifestyle information including smoking status. One strategy to improve this recording in primary care may be the inclusion of pregnancy in the QOF as a condition where smoking status and smoking cessation advice should be recorded in the electronic primary care records. This will not only increase opportunities for healthcare professionals to provide smoking cessation advice and interventions, but could also provide valuable data for the evaluation of the effectiveness of these interventions and monitoring progress towards meeting national prevalence targets.

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10.4 PRESCRIBING OF NICOTINE REPLACEMENT THERAPY IN AND AROUND PREGNANCY: A POPULATION-BASED STUDY USING PRIMARY CARE DATA

Research

Nafeesa N Dhalwani, Lisa Szatkowski, Tim Coleman, Linda Fiaschi, and Laila J Tata

Prescribing of nicotine replacement therapy in and around pregnancy:

a population-based study using primary care data

Abstract

Background
Licensing arrangements for nicotine replacement therapy (NRT) in the UK were broadened in 2005 to allow prescribing to pregnant smokers. However, estimates of NRT prescribing in pregnant females in the UK are currently lacking.

Aim
To assess trends in NRT prescribing around pregnancy, and variation in prescribing by maternal characteristics.

Design and setting
Population-based descriptive study using pregnancy data from The Health Improvement Network primary care database, 2001–2012.

Method
NRT prescriptions were identified during pregnancy and in the 9 months before and after. Annual prescribing prevalence was calculated. Logistic regression was used to assess females' likelihood of receiving prescriptions by maternal characteristics.

Results
Of 388 142 pregnancies studied, NRT was prescribed in 7551 for an average duration of 2 weeks. The prescribing prevalence of NRT increased from 0.03% (0.7% in smokers) in 2001 to 2.4% (11.4% in smokers) in 2005, after which it remained stable. Prescribing prevalence of NRT before and after pregnancy was half the prevalence during pregnancy. The odds of prescribing NRT during pregnancy in smokers increased with socioeconomic deprivation (OR = 1.29, 95% CI = 1.15 to 1.45 in the most compared with the least deprived group). Prescribing was 33% higher in pregnant smokers with asthma (OR = 1.33, 95% CI = 1.22 to 1.45) and mental illness (OR = 1.33, 95% CI = 1.23 to 1.44) compared with smokers without these diagnoses.

Conclusion
NRT prescribing is higher during pregnancy compared with before and after, and is higher in smokers from more socioeconomically deprived groups, those with asthma or those diagnosed mental illness.

Keywords
nicotine replacement therapy; pregnancy; prescribing; smoking cessation.

INTRODUCTION

Smoking in pregnancy is related to several adverse outcomes for both mothers and their children.[1,2] In the UK, 26% of mothers smoke directly before or during their pregnancy, and 12% continue to smoke throughout.[3] Similar prevalence has been reported in Australia and the US (11.7% and 10.7% respectively).[4,5] Therefore, reducing smoking in pregnancy is a global public health priority.[6]

Nicotine replacement therapy (NRT) is a pharmacological smoking cessation aid which became available on prescription from the UK NHS in April 2001.[7] It was initially contraindicated during pregnancy because of a lack of evidence for its safety.[8] To date there is no conclusive evidence on its effectiveness during pregnancy,[9] and studies of NRT safety during pregnancy are inconclusive.[9,10-12] Nevertheless, expert consensus is that NRT is likely to be less harmful than smoking during pregnancy and, with various caveats, NRT has been recommended by international guidelines when smoking cessation without NRT is unsuccessful.[13-16]

Literature describing NRT use in pregnancy is limited to observational studies from the US and Denmark assessing the association of NRT use during pregnancy and adverse birth outcomes. The prevalence of self-reported NRT used in the first 12 weeks of gestation was 0.3%,[17] 2–2.5% in 17–27 weeks of gestation in the Danish National Birth Cohort,[18,19] and in the Pregnancy Risk Assessment Monitoring System (PRAMS) from four US states it was 3.9% (2004).[2] Since their publication, new NRT products have been introduced and international guidelines on gestational NRT use have changed. In 2013, the World Health Organization (WHO) recommended an urgent need for studies on the surveillance of current NRT use in pregnancy.[16]

In December 2005, UK licensing arrangements were changed to allow prescribing of NRT to pregnant smokers.[16] As a result, NRT can now be prescribed to pregnant females by GPs, midwives, or other licensed health professionals working in NHS Stop Smoking Services (SSS) after discussing the risks and benefits of using the drug in pregnancy. Although it can also be bought directly from pharmacies or other retailers such as supermarkets, all drug packaging retains warnings against its use in pregnancy without prior GP consultation. Most NRT is probably received via GP prescription, as half of NRT provided by pregnancy SSSs is issued via the patient's GP.[19]

Thus far, only two UK studies have assessed NRT use in pregnancy.[20,21] One of these studies only presents local data from Tayside, Scotland,[21] and the second was only among females attending NHS SSS in England.[20] Given that only 3% of all

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How this fits in

Pregnancy is an opportunistic time to offer smoking cessation interventions to females. This study is the first to quantify prescribing of nicotine replacement therapy before, during, and after pregnancy in the UK. Prescribing prevalence of nicotine replacement therapy during pregnancy was 11% among smokers, double the prescribing prevalence before and after pregnancy. However, most females received only 2 weeks of nicotine replacement therapy during pregnancy. Prescribing was higher in pregnant smokers from more deprived areas and in smokers with diagnoses of asthma or mental illness.

pregnant females attend SSSs, this will have excluded most pregnant smokers.[22,23] In this study, UK prescribing of NRT is quantified before, during, and after pregnancy using a nationally representative sample, and the characteristics of females who receive NRT prescriptions are investigated.

Table 1. Baseline characteristics of the study population

	Total pregnancies, *n* = 388 142	NRT prescribed, total *n* = 7551 (% of pregnancies with NRT prescription)	Pregnancies among smokers,* *n* = 71 685	NRT prescribed, *n* = 7551 (% of pregnancies among smokers with NRT prescription)
Age at conception, years				
5–19	27 365	930 (3.4)	9898	930 (9.4)
20–24	66 486	1962 (3.0)	19 869	1962 (9.9)
25–29	105 967	2004 (1.9)	19 188	2004 (10.4)
30–34	118 031	1664 (1.4)	14 536	1664 (11.4)
35–39	59 561	832 (1.4)	6952	832 (12.0)
40–44	10 222	152 (1.5)	1203	152 (12.6)
45–49	532	7 (1.3)	61	7 (11.5)
Townsend score in quintiles†				
Quintile 1 – most affluent	83 203	722 (0.9)	7970	722 (9.1)
Quintile 2	71 045	925 (1.3)	9511	925 (9.7)
Quintile 3	76 619	1432 (1.9)	14 291	1432 (10.0)
Quintile 4	73 470	2068 (2.8)	18 097	2068 (11.4)
Quintile 5 – most deprived	55 653	1875 (3.4)	16 925	1875 (11.1)
Missing	28 152	529 (1.9)	4891	529 (10.8)
Pre-conception body mass index, kg/m²				
Normal (18.0–24.9)	118 832	2266 (1.9)	22 888	2266 (9.9)
Underweight (<18.0)	8614	256 (3.0)	2353	256 (10.9)
Overweight (25–29.9)	58 693	1237 (2.1)	11 464	1237 (10.8)
Obese (≥30)	42 281	992 (2.3)	9191	992 (10.8)
Missing	159 722	2800 (1.8)	25 789	2800 (10.9)
Asthma	33 724	1061 (3.1)	8188	1061 (13.0)
Hypertension	9992	156 (1.5)	1420	156 (10.8)
Diabetes	10 752	226 (2.1)	1799	226 (12.5)
Mental illness	37 055	1547 (4.2)	11 624	1547 (13.3)

*Smoker classified as those with a record of current smoking at some point within the 27 months before conception until delivery. †Socioeconomic status. NRT = nicotine replacement therapy.

METHOD

Data source and study population

The Health Improvement Network (THIN), an electronic database containing anonymised patient records from general practices across the UK, was used for this study, covering approximately 6% of the population,[24] representative of the UK population in terms of demographics, prevalence of common illnesses, and fertility rates.[25,26] Prevalence of smoking and prescribing of smoking cessation medications in the general population in THIN has been validated against national data.[27,28] The study population included all pregnancies between January 2001 and December 2012 in females of childbearing age (15–49 years), resulting in a live birth or a stillbirth.

Outcome and covariates

The smoking status of females was determined using Read Codes[29] recorded from 27 months before conception up to the end of pregnancy, based on the recording rules in the GP contract,[30] which is described in detail elsewhere.[31] Multilex Drug Codes for all NRT formulations available in the UK according to the *British National Formulary* (*BNF*) were used for NRT prescriptions.[32] Code lists are available from the authors on request.

To investigate factors associated with NRT prescribing, data were extracted on females' age at conception, socioeconomic deprivation (Townsend Index),[33] pre-conception body mass index (BMI), and diagnoses of medical conditions (hypertension, diabetes, asthma, and mental illness, which included depression, anxiety, bipolar disorder, schizophrenia, and other psychoses) during or before pregnancy. These conditions were selected as they are closely related to smoking,[3,34–38] and may influence quit attempts.

Statistical analysis

Overall and annual proportions of pregnancies, and pregnancies among smokers, with one or more NRT prescriptions before, during and after pregnancy were determined. There is no evidence of the time before and after pregnancy during which smokers are more likely to attempt to quit, therefore the 9 months before and after pregnancy were used to calculate prescribing prevalence, as these were similar to the average pregnancy length, allowing for comparisons of period

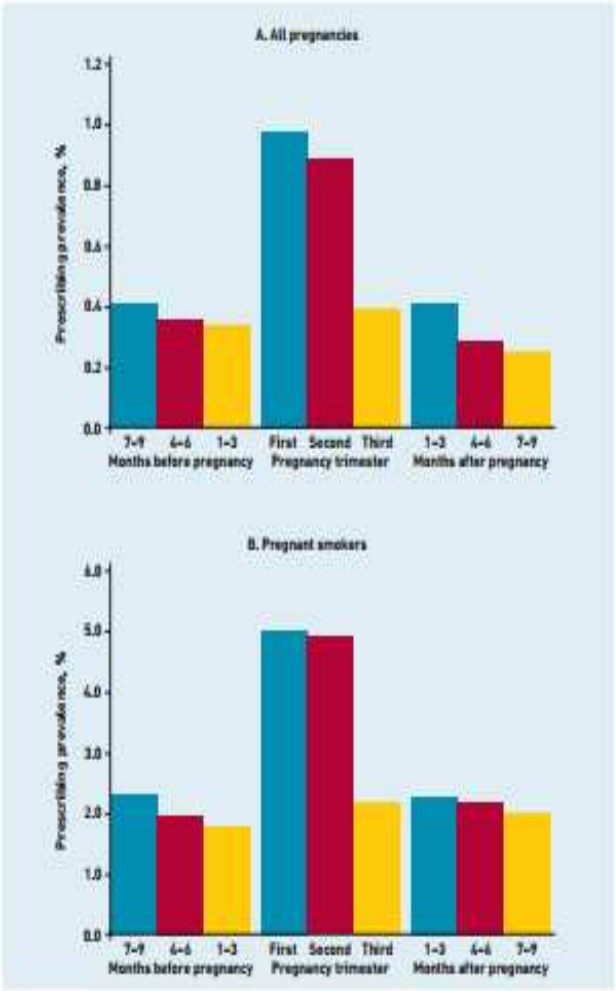

Figure 1. Proportion of overall pregnancies and smokers with NRT prescriptions in each 3-month time period, between 2001 and 2012.

prevalence. As smoking behaviours may fluctuate during a 9-month period, 3-month windows were also assessed during and around pregnancy. The use of different forms of NRT (patches, gum, nasal spray, lozenges, sublingual tablets, inhalator cartridges, and combination) was assessed.

Logistic regression was used to calculate ORs for associations between females' characteristics and prescribing of NRT to smokers during pregnancy, restricting to pregnancies delivered from January 2006, after relaxation of licensing arrangements.[18] All covariates reaching statistical significance at the 5% level in univariable models were included in the multivariable analysis and each covariate was sequentially dropped from the model to assess whether it remained statistically significant, retaining only those that were. Some females had more than one pregnancy during the study period and there may be potential clustering of females within practices; this was accounted for by using generalised estimating equations (GEE) with an exchangeable correlation structure which provided best estimates of the population-level associations with maternal characteristics despite potential dependence between pregnancy, that is accounting for clustered data.[19] Analyses were performed using Stata (version 12.0).

RESULTS

Baseline characteristics

Between 2001 and 2012, 388 142 pregnancies were identified resulting in live births or stillbirths, of which 71 685 (18.5%) were in smokers. Mean age at conception was 29.6 years (SD 5.9). Table 1 describes females' characteristics for all pregnancies and pregnancies among smokers, and NRT prescribing according to these characteristics.

Patterns of NRT prescribing in and around pregnancy

NRT was prescribed in 7551 pregnancies, which represented a prescribing prevalence of 2% of all pregnancies and 11% of pregnancies in smokers. In comparison, the prescribing prevalence was 1% during the 9 months before and after pregnancy overall, and 5% in smokers. Figure 1 shows the prescribing prevalence in 3-month periods outside pregnancy and by trimester. NRT prescribing among smokers was most frequent during the first and second trimesters at just over 5%, compared with 2% in the third trimester.

Among the pregnancies where NRT was prescribed, over half (55%) had only one prescription issued, 25% had two prescriptions, and 20% had three or more prescriptions. The maximum number of prescriptions issued during pregnancy was 26. On average, females were prescribed a total of 2 weeks' worth of NRT (interquartile range 1–2 weeks). The prescription frequency and length of NRT issued in the 9 months before and after pregnancy was similar to pregnancy time.

In two-thirds of the pregnancies in which NRT was prescribed, it was initiated only during pregnancy, with no evidence of NRT prescribing prior to the start of pregnancy. The most common form of NRT used during pregnancy was transdermal patches (65% of all prescriptions), followed by inhalator cartridges (17%), gum (8%), lozenges (6%), sublingual tablets (2%), oromucosal spray (0.7%), and nasal spray (0.3%). Combination NRT was used in 14% of pregnancies where

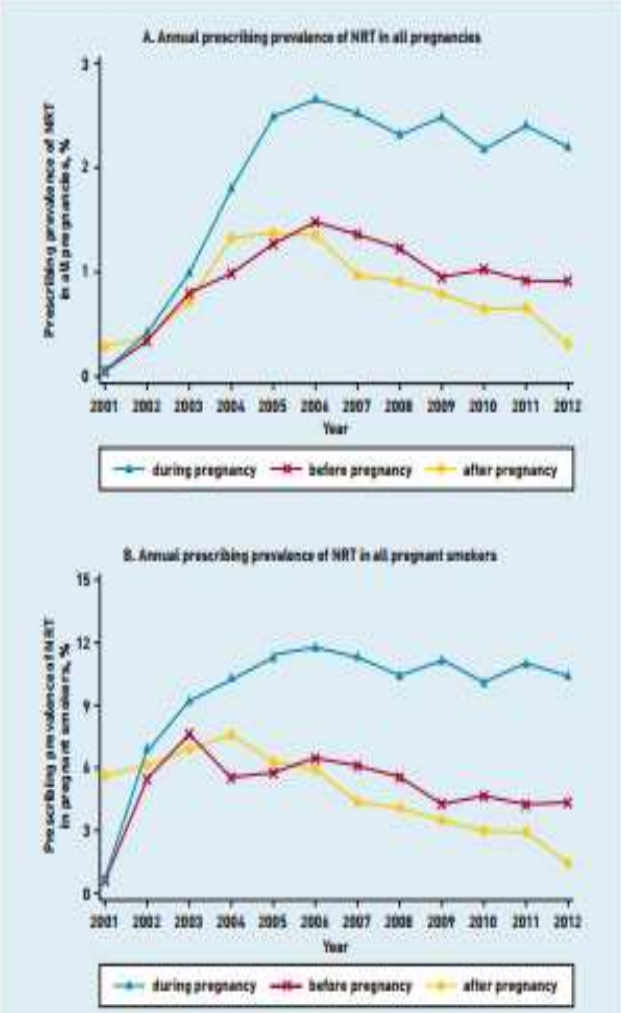

Figure 2. Annual prescribing prevalence of NRT between 2001 and 2012.

NRT was prescribed. The distribution of NRT forms prescribed before and after pregnancy was very similar.

Annual prescribing of NRT before, during, and after pregnancy

Figure 2 shows the proportion of pregnancies between 2001 and 2012 in which NRT was prescribed before, during, and after pregnancy. In 2001, the prescribing prevalence of NRT in all pregnancies during gestation was 0.03% (0.7% of pregnancies among smokers). This increased to 2.6% (11.4% among smokers) in 2005, after which it remained stable. The proportion of pregnancies with NRT prescriptions issued in the 9 months before and after pregnancy increased until 2004, after which it remained stable at around 1% (6% among smokers) with a gradual decline in prescribing prevalence after 2006.

Prescribing of NRT by maternal characteristics

Table 2 shows the maternal characteristics associated with prescribing in pregnant smokers between 2006 and 2012. Prescribing was higher in older compared with younger age groups (OR for 40–44 years = 1.27, 95% CI = 1.03 to 1.58, compared with the 25–29-year age group). Pregnant smokers from more socioeconomically deprived groups were more likely to receive prescriptions compared with less deprived groups (OR for quintile 5 compared with quintile 1 = 1.29, 95% CI = 1.15 to 1.45). Pregnant smokers with a diagnosis of asthma or mental illness were 33% more likely to be prescribed compared with pregnant smokers without these morbidities.

DISCUSSION

Summary

After NRT was made available on NHS prescription in 2001, prescribing in and around pregnancy increased; by 2005 prescribing was twice as high during pregnancy as in the 9 months immediately before and after pregnancy, despite being contraindicated for pregnant females. The December 2005 licence relaxation to allow prescribing in pregnancy did not further increase these trends and the prescribing prevalence during pregnancy has remained stable at 2% (11% in smokers). Females with asthma or mental illnesses and those from more socioeconomically-deprived areas were more likely to receive prescriptions during pregnancy. Eighty per cent of females received ≤2 prescriptions.

Strengths and limitations

Using a large population-based data source, longitudinal and contemporaneous prescribing estimates are presented; this is the first study of NRT prescribing during pregnancy in the UK and the only study internationally that has assessed prescribing trends. Ascertainment of NRT use is based on prescribing data rather than self-reported NRT use, which females may under-report.[11] Prescribing in 9-month periods immediately before and after pregnancy was also assessed, whereas other studies only report NRT use in trimesters one and two.[9,10,12] Therefore, the present estimates of NRT prescribing around pregnancy are novel in providing population-level information on smoking cessation attempts pre-conception and postpartum for the first time.

The present study data capture all NRT prescribing to pregnant females in UK primary care in practices registered

Table 2. Prescribing of NRT in pregnant smokers by maternal characteristics between January 2006 and December 2012

Demographic variables	Pregnancies among smokers with one or more NRT prescriptions, *n* = 5756,* *n* (%)	Unadjusted odds ratio (95% CI)	*P*-value	Adjusted odds ratio (95% CI)†	*P*-value
Age at conception, years					
15–19	721 (9.9)	0.92 (0.84 to 1.01)		0.93 (0.84 to 1.03)	
20–24	1533 (10.2)	0.94 (0.88 to 1.02)	<0.001	0.93 (0.86 to 1.00)	<0.001
25–29	1537 (10.7)	1.00		1.00	
30–34	1222 (11.9)	1.12 (1.06 to 1.22)		1.13 (1.06 to 1.23)	
35–39	616 (12.2)	1.16 (1.05 to 1.28)		1.17 (1.05 to 1.30)	
40–44	122 (13.3)	1.28 (1.05 to 1.56)		1.27 (1.03 to 1.58)	
45–49	5 (10.9)	1.01 (0.40 to 2.58)		1.12 (0.43 to 2.96)	
Townsend score					
Quintile 1 (least deprived)	505 (9.2)	1.00		1.00	
Quintile 2	696 (10.1)	1.10 (0.98 to 1.25)	<0.001*	1.09 (0.96 to 1.24)	<0.001*
Quintile 3	1101 (10.3)	1.14 (1.01 to 1.27)		1.19 (1.05 to 1.34)	
Quintile 4	1605 (11.8)	1.35 (1.19 to 1.48)		1.27 (1.22 to 1.54)	
Quintile 5 (most deprived)	1428 (11.3)	1.25 (1.13 to 1.39)		1.29 (1.15 to 1.45)	
Missing	421 (11.4)	1.27 (1.10 to 1.45)		1.33 (1.15 to 1.54)	
Pre-conception body mass index, kg/m²					
Underweight	206 (11.0)	1.12 (0.96 to 1.30)			
Normal	1786 (10.6)	1.00	0.414	-	-
Overweight	976 (11.2)	1.06 (0.97 to 1.14)			
Obese	806 (11.1)	1.06 (0.96 to 1.15)			
Missing	1982 (10.6)	1.02 (0.95 to 1.09)			
Diabetes	193 (12.2)	1.26 (1.08 to 1.47)	0.075	-	-
Hypertension	114 (11.3)	1.04 (0.86 to 1.27)	0.660	-	-
Asthma	845 (13.8)	1.36 (1.26 to 1.48)	<0.001	1.33 (1.22 to 1.45)	<0.001
Mental illness	1181 (13.7)	1.38 (1.29 to 1.48)	<0.001	1.33 (1.23 to 1.44)	<0.001

*NRT = nicotine replacement therapy. *Percentages of pregnancies in smokers with NRT prescription. †All covariates mutually adjusted. ‡P-value for trend.*

in THIN. These data may not include NRT prescribing in other settings such as local NHS Stop Smoking Services for Pregnant females (SSSP) and NRT purchased in pharmacies or retailers. A survey of all SSSPs in England conducted between April 2010 and March 2011 reported that almost half of the NRT provided by these services was issued through GPs.[38] In terms of self-purchased NRT, the authors believe this will be infrequent for several reasons. Firstly, the prevalence of medication use without health professional consultation is lower during pregnancy than when females are not pregnant.[41] Furthermore, all packages of NRT clearly instruct females to consult a doctor before using them if they are pregnant. Lastly, in the UK females are entitled to free NHS prescriptions during pregnancy,[42] so they are more likely to get free prescriptions through GPs than paying for NRT. Hence, the authors believe that this study captures most prescriptions of NRT issued and provides valuable information on prescribing patterns during pregnancy.

Potential changes in smoking habits were not accounted for over the study, and therefore this study has also presented proportions for all pregnancies. Some females may quit or relapse after delivery consequently leading to changes in the baseline smokers; NRT estimates could therefore be overestimated if more females relapse than are recorded, and underestimated if more females quit. In the present data, however, over 75% of pregnant females who were classified as smokers during pregnancy and who had a recording of smoking status within the 9 months after delivery were still recorded as smokers. Therefore, a substantial overestimation or underestimation is unlikely.

Comparison with existing literature

The present study data suggest that UK prescribing of NRT during pregnancy increased between 2001 and 2005, after which it plateaued. Despite NRT use being recommended in smoking cessation guidelines for pregnant females in several

countries,[14,15,18] no other studies thus far have assessed the annual prescribing prevalence of NRT during pregnancy for comparison. Studies from the US, Denmark, and Scotland report an overall prescribing prevalence of between 0.3% and 4%.[2,16,17,21] NRT use in pregnant smokers attending English SSSs is reported to be 85%[18] and considering that only 3% of pregnant females attend these services, this equates to 2.5%, which is similar to the present findings.

The National Institute for Health and Care Excellence (NICE) recommends that pregnant females should initially be prescribed 2 weeks of NRT from their agreed stop date with further NRT after re-assessment.[3] The average duration of prescription for females in the present study was 2 weeks and most females (80%) received two or fewer prescriptions. One reason for this may be that compliance was low and females did not quit or use it to quit, in which case no further NRT was prescribed. Some females may have bought NRT independently after the first prescription; however, considering that females are entitled to free prescriptions during pregnancy and NRT from retailers is reasonably expensive, this is unlikely. Studies in other populations have not reported the duration of NRT use in pregnancy. However, 8–12 weeks' use is recommended for optimal effectiveness in the general population,[43] so it is unlikely that 2 weeks' use is effective for smoking cessation in pregnancy.

A study including 5716 pregnant females from the US showed NRT prescribing to be lower in pregnant smokers aged <35 years compared with pregnant smokers aged ≥35 years,[2] which is similar to the present findings. Low socioeconomic status is associated with a higher prevalence of chronic disease[44] and higher risk of adverse pregnancy outcomes,[45] which could explain why pregnant smokers in the deprived group in this study were prescribed NRT more often than affluent groups. Asthma and mental illness are the most common medical conditions encountered during pregnancy,[46,47] and are closely related to smoking, which may explain the significant association with NRT prescribing compared with other conditions.

The English SSSPs study reported that 55% of all pregnant smokers (65% of pregnant NRT users) used combination NRT,[18] which is high compared with the present estimate of 14%. This is mostly likely related to different baseline populations. Females voluntarily attending these specialist services likely have a higher motivation to quit, which may result in more quit attempts and more NRT being prescribed compared with females attending primary care.

It is unfortunate that NRT prescribing prevalence outside pregnancy began to decline considering the demonstrated effectiveness of NRT;[48] however, this may be related to the licensing of varenicline for smoking cessation in the non-pregnant population in December 2006, after which a reduction in NRT and bupropion prescribing was seen in the general population.[49]

Implications for practice

Pregnancy offers a strategic opportunity for health professionals to promote smoking cessation as females are generally more receptive to cessation interventions and are more likely to attempt to quit smoking because of the potential foetal harm associated with smoking during pregnancy.[50] The study findings give insight into the prescribing in and around pregnancy, which is important for policy makers and GPs to monitor and promote smoking cessation in females of childbearing age. The study shows that NRT was prescribed for an average of only 2 weeks during pregnancy, which is unlikely to be effective considering that NRT use in the general population for smoking cessation is recommended for at least 8–12 weeks. It is also highlighted that only 1% of smokers who are not yet pregnant receive NRT, which indicates missed opportunities to assist young females to quit, despite the reported effectiveness of NRT outside pregnancy. Although interactions between health professionals and females during pregnancy should be used to discuss and offer interventions to promote smoking cessation, greater potential benefit would result from starting before pregnancy which should be a prioritised focus for females and healthcare providers.

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Ethical approval

Ethical approval for this study was obtained from the THIN Scientific Review Committee (reference number 11-047).

Provenance

Freely submitted; externally peer reviewed.

Competing interests

Tim Coleman was paid to attend a symposium arranged by Pierre Fabre Laboratories, France in 2012. The other authors have declared no competing interests.

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10.5 MEDICAL READ CODES FOR SMOKING

Medcode	Description
137L.00	Current non-smoker
1371.11	Non-smoker
63C5.00	Maternal tobacco abuse
137a.00	Pipe tobacco consumption
137..00	Tobacco consumption
137X.00	Cigarette consumption
6893.00	Tobacco usage screen
68T..00	Tobacco usage screen
137Y.00	Cigar consumption
137Z.00	Tobacco consumption NOS
ZV4K000	[V]Tobacco use
745H000	Nicotine replacement therapy using nicotine patches
8H7i.00	Referral to smoking cessation advisor
6791.00	Health ed. - smoking
E251.00	Tobacco dependence
137Q.00	Smoking started
137H.00	Pipe smoker
137M.00	Rolls own cigarettes
1372.11	Occasional smoker
137h.00	Minutes from waking to first tobacco consumption
137c.00	Thinking about stopping smoking
E251200	Tobacco dependence, episodic
137d.00	Not interested in stopping smoking
E251z00	Tobacco dependence NOS
745H100	Nicotine replacement therapy using nicotine gum
1374.00	Moderate smoker - 10-19 cigs/d
8HTK.00	Referral to stop-smoking clinic
9OO7.00	Stop smoking monitor verb.inv.
137f.00	Reason for restarting smoking
ZRBm211	FTND - Fagerstrom test for nicotine dependence
8I39.00	Nicotine replacement therapy refused
137b.00	Ready to stop smoking
137e.00	Smoking restarted
745Hy00	Other specified smoking cessation therapy
8CAg.00	Smoking cessation advice provided by community pharmacist
1373.00	Light smoker - 1-9 cigs/day
13p5.00	Smoking cessation programme start date
38DH.00	Fagerstr test for nicotine dep
E251000	Tobacco dependence, unspecified
8B3Y.00	Over the counter nicotine replacement therapy
745H200	Nicotine replacement therapy using nicotine inhalator
137J.00	Cigar smoker
67A3.00	Pregnancy smoking advice
137R.00	Current smoker
ZV6D800	[V]Tobacco abuse counselling
8BP3.00	Nicotine replacement therapy provided by community pharmacis
E251100	Tobacco dependence, continuous
8B3f.00	Nicotine replacement therapy provided free
8B2B.00	Nicotine replacement therapy
8I2I.00	Nicotine replacement therapy contraindicated
13p0.00	Negotiated date for cessation of smoking
ZRaM.11	MFS - Motives for smoking scale
8HkQ.00	Referral to NHS stop smoking service
ZRao.11	OFS - Occasions for smoking scale
67H6.00	Brief intervention for smoking cessation
)ZRao.00	Occasions for smoking scale
8CAL.00	Smoking cessation advice
137..11	Smoker - amount smoked
137P.11	Smoker
ZRBm200	Fagerstrom test for nicotine dependence
137V.00	Smoking reduced
137C.00	Keeps trying to stop smoking
13p5000	Practice based smoking cessation programme start date
ZRh4.00	Reasons for smoking scale
1372.00	Trivial smoker - < 1 cig/day
8IAj.00	Smoking cessation advice declined
745H300	Nicotine replacement therapy using nicotine lozenges
137m.00	Failed attempt to stop smoking
1376.00	Very heavy smoker - 40+cigs/d
137Q.11	Smoking restarted
137P.00	Cigarette smoker
ZRaM.00	Motives for smoking scale
ZG23300	Advice on smoking
9OO8.00	Stop smoking monitor phone inv
ZRh4.11	RFS - Reasons for smoking scale
137G.00	Trying to give up smoking
67H1.00	Lifestyle advice regarding smoking
745H400	Smoking cessation drug therapy
1375.00	Heavy smoker - 20-39 cigs/day
ZRao.00	Occasions for smoking scale
E251300	Tobacco dependence in remission
1378.00	Ex-light smoker (1-9/day)
137A.00	Ex-heavy smoker (20-39/day)

137S.00	Ex smoker
137l.00	Ex roll-up cigarette smoker
137j.00	Ex-cigarette smoker
1379.00	Ex-moderate smoker (10-19/day)
137N.00	Ex pipe smoker
137B.00	Ex-very heavy smoker (40+/day)
137K.00	Stopped smoking
1377.00	Ex-trivial smoker (<1/day)
137T.00	Date ceased smoking
137F.00	Ex-smoker - amount unknown
137K000	Recently stopped smoking
137O.00	Ex cigar smoker
1371.00	Never smoked tobacco
13p4.00	Smoking free weeks
9N4M.00	DNA - Did not attend smoking cessation clinic
9OO5.00	Stop smoking monitor 2nd lettr
13p2.00	Smoking status between 4 and 52 weeks
9OO3.00	Stop smoking monitor default
9OOA.00	Stop smoking monitor.chck done
9OO..12	Stop smoking monitoring admin.
E023.00	Nicotine withdrawal
ZV11600	[V]Personal history of tobacco abuse
13p6.00	Carbon monoxide reading at 4 weeks
9OOZ.00	Stop smoking monitor admin.NOS
13p..00	Smoking cessation milestones
137g.00	Cigarette pack-years
9OO..11	Stop smoking clinic admin.
9OO1.00	Attends stop smoking monitor.
13p3.00	Smoking status at 52 weeks
9N2k.00	Seen by smoking cessation advisor
9OO6.00	Stop smoking monitor 3rd lettr
9OO2.00	Refuses stop smoking monitor
9OO..00	Anti-smoking monitoring admin.
4I90.00	Expired carbon monoxide concentration
8HBM.00	Stop smoking face to face follow-up
745H.00	Smoking cessation therapy
745Hz00	Smoking cessation therapy NOS
137D.00	Admitted tobacco cons untrue ?
13p1.00	Smoking status at 4 weeks
9OO4.00	Stop smoking monitor 1st lettr
137E.00	Tobacco consumption unknown
9OO9.00	Stop smoking monitoring delete

10.6 MULTILEX DRUG CODES FOR SMOKING CESSATION MEDICATIONS

Drugcode	Generic name
92309998	BUPROPION mr tab 150mg
92311998	BUPROPION mr tab 150mg
93447992	NICONIL
96930992	NICONIL PATCH 15 MG
96924992	NICONIL PATCH 30 MG
83326998	NICOTINE BITARTRATE sf loz 1mg
82527998	NICOTINE BITARTRATE sf loz 1mg
87922998	NICOTINE BITARTRATE sf loz 2mg
82526998	NICOTINE BITARTRATE sf loz 2mg
82603998	NICOTINE BITARTRATE sublingual tab 2mg
82604998	NICOTINE BITARTRATE sublingual tab 2mg
96845992	NICOTINE TRANSDERMAL PATCH 20CM
96844992	NICOTINE TRANSDERMAL PATCH 30CM
82473998	NICOTINE chewing gum 2mg
82506998	NICOTINE chewing gum 2mg
89112998	NICOTINE chewing gum 2mg
82502998	NICOTINE chewing gum 2mg
82475998	NICOTINE chewing gum 2mg
95727998	NICOTINE chewing gum 2mg
82504998	NICOTINE chewing gum 2mg
98904998	NICOTINE chewing gum 2mg
82476998	NICOTINE chewing gum 2mg
82503998	NICOTINE chewing gum 2mg
91248998	NICOTINE chewing gum 2mg
82505998	NICOTINE chewing gum 2mg
82474998	NICOTINE chewing gum 2mg
82498998	NICOTINE chewing gum 4mg
82472998	NICOTINE chewing gum 4mg
82469998	NICOTINE chewing gum 4mg
82499998	NICOTINE chewing gum 4mg
82497998	NICOTINE chewing gum 4mg
95727997	NICOTINE chewing gum 4mg
91248997	NICOTINE chewing gum 4mg
82496998	NICOTINE chewing gum 4mg
98904997	NICOTINE chewing gum 4mg
82470998	NICOTINE chewing gum 4mg
82471998	NICOTINE chewing gum 4mg
89110998	NICOTINE chewing gum 4mg
82501998	NICOTINE chewing gum 4mg

88291998	NICOTINE inh cartridge 10mg
88288998	NICOTINE inh cartridge 10mg
89863998	NICOTINE loz 0.35mg
92840997	NICOTINE loz 0.35mg
92840998	NICOTINE mint flav chew gum 2mg
92841998	NICOTINE mint flav chew gum 2mg
95727996	NICOTINE mint flav chew gum 4mg
98904996	NICOTINE mint flav chew gum 4mg
82490998	NICOTINE nasal spray 10mg/ml
92657998	NICOTINE nasal spray 10mg/ml
92836998	NICOTINE nasal spray 10mg/ml
83272998	NICOTINE patch 10mg
97739997	NICOTINE patch 10mg
82494998	NICOTINE patch 10mg
97763997	NICOTINE patch 10mg
98581997	NICOTINE patch 11mg/24 hr
92892997	NICOTINE patch 11mg/24 hr
97673997	NICOTINE patch 14mg
82510998	NICOTINE patch 14mg
82771998	NICOTINE patch 14mg
88005997	NICOTINE patch 14mg
82509998	NICOTINE patch 14mg
97737997	NICOTINE patch 14mg
97740997	NICOTINE patch 14mg
84468998	NICOTINE patch 14mg
97763996	NICOTINE patch 15mg
83271998	NICOTINE patch 15mg
82492998	NICOTINE patch 15mg
97739996	NICOTINE patch 15mg
82770998	NICOTINE patch 21mg
97737996	NICOTINE patch 21mg
84466998	NICOTINE patch 21mg
88005996	NICOTINE patch 21mg
82508998	NICOTINE patch 21mg
82507998	NICOTINE patch 21mg
97673996	NICOTINE patch 21mg
97740996	NICOTINE patch 21mg
98581998	NICOTINE patch 22mg/24 hr
92892998	NICOTINE patch 22mg/24 hr
83270998	NICOTINE patch 25mg
83273998	NICOTINE patch 25mg
97763998	NICOTINE patch 5mg
97739998	NICOTINE patch 5mg
82495998	NICOTINE patch 5mg
82723998	NICOTINE patch 7mg
97673998	NICOTINE patch 7mg
97740998	NICOTINE patch 7mg
82511998	NICOTINE patch 7mg
84469998	NICOTINE patch 7mg
97737998	NICOTINE patch 7mg
82512998	NICOTINE patch 7mg
88005998	NICOTINE patch 7mg
82429998	NICOTINE patch+gum 15mg + 2mg
82428998	NICOTINE patch+gum 15mg + 2mg
84442998	NICOTINE sf loz 1.5mg
84443998	NICOTINE sf loz 1.5mg
81928998	NICOTINE sf loz 1.5mg
82707998	NICOTINE sf loz 1.5mg
91248996	NICOTINE sf loz 1mg
98430998	NICOTINE sf loz 1mg
91162998	NICOTINE sf loz 2mg
92889990	NICOTINE sf loz 2mg
87920998	NICOTINE sf loz 2mg
91384998	NICOTINE sf loz 2mg
83301998	NICOTINE sf loz 4mg
82706998	NICOTINE sf loz 4mg
87919998	NICOTINE sf loz 4mg
92888990	NICOTINE sf loz 4mg
98082998	NICOTINE sf loz 4mg
91848998	NICOTINE sf loz 4mg
92840996	NICOTINE sublingual tab 2mg
82500998	NICOTINE sublingual tab 2mg
92841997	NICOTINE sublingual tab 2mg
85397998	VARENICLINE tabs 1mg
85400998	VARENICLINE tabs 1mg
85401998	VARENICLINE tabs 500 micrograms
85398998	VARENICLINE tabs 500 micrograms
85403998	VARENICLINE tabs 500micrograms + 1mg
85399998	VARENICLINE tabs 500micrograms + 1mg

10.7 AHD CODES FOR SMOKING

Ahd code	Description
1003040000	Smoking
1064100000	Advice given

10.8 CODE LISTS FOR COMORBIDITIES

10.8.1 Medical READ codes for Diabetes Mellitus

Medcode	Description
C101000	Diabetes mellitus, juvenile type, with ketoacidosis
C108311	Type I diabetes mellitus with multiple complications
C108600	Insulin dependent diabetes mellitus with gangrene
C10E311	Type I diabetes mellitus with multiple complications
C108112	Type 1 diabetes mellitus with ophthalmic complications
C108300	Insulin dependent diabetes mellitus with multiple complicatn
C108F11	Type I diabetes mellitus with diabetic cataract
C108E00	Insulin dependent diabetes mellitus with hypoglycaemic coma
C108012	Type 1 diabetes mellitus with renal complications
C10EJ11	Type I diabetes mellitus with neuropathic arthropathy
C108912	Type 1 diabetes mellitus maturity onset
C10E800	Type 1 diabetes mellitus - poor control
C10EM00	Type 1 diabetes mellitus with ketoacidosis
C10E700	Type 1 diabetes mellitus with retinopathy
C108D00	Insulin dependent diabetes mellitus with nephropathy
C10EH00	Type 1 diabetes mellitus with arthropathy
C10EA00	Type 1 diabetes mellitus without complication
C107000	Diabetes mellitus, juvenile +peripheral circulatory disorder
C101y00	Other specified diabetes mellitus with ketoacidosis
C100011	Insulin dependent diabetes mellitus
C108.00	Insulin dependent diabetes mellitus
C108F12	Type 1 diabetes mellitus with diabetic cataract
C10EA12	Insulin-dependent diabetes without complication
C10EB11	Type I diabetes mellitus with mononeuropathy
C10EP11	Type I diabetes mellitus with exudative maculopathy
C108512	Type 1 diabetes mellitus with ulcer
C108D12	Type 1 diabetes mellitus with nephropathy
C101.00	Diabetes mellitus with ketoacidosis
C108C12	Type 1 diabetes mellitus with polyneuropathy
C102.00	Diabetes mellitus with hyperosmolar coma
C10C.00	Diabetes mellitus autosomal dominant
C10E712	Insulin dependent diabetes mellitus with retinopathy
C10E612	Insulin dependent diabetes mellitus with gangrene
C108100	Insulin-dependent diabetes mellitus with ophthalmic comps
C108312	Type 1 diabetes mellitus with multiple complications
C108411	Unstable type I diabetes mellitus
C108.13	Type I diabetes mellitus
C10ED11	Type I diabetes mellitus with nephropathy
C108111	Type I diabetes mellitus with ophthalmic complications
C108712	Type 1 diabetes mellitus with retinopathy
C108F00	Insulin dependent diabetes mellitus with diabetic cataract
C108H12	Type 1 diabetes mellitus with arthropathy
C108A11	Type I diabetes mellitus without complication
C108000	Insulin-dependent diabetes mellitus with renal complications
C108B00	Insulin dependent diabetes mellitus with mononeuropathy
C108C00	Insulin dependent diabetes mellitus with polyneuropathy
C108C11	Type I diabetes mellitus with polyneuropathy
K081.00	Nephrogenic diabetes insipidus
C10E211	Type I diabetes mellitus with neurological complications
C10EP00	Type 1 diabetes mellitus with exudative maculopathy
C10EK11	Type I diabetes mellitus with persistent proteinuria
C10EC00	Type 1 diabetes mellitus with polyneuropathy
C10E412	Unstable insulin dependent diabetes mellitus
C10EN11	Type I diabetes mellitus with ketoacidotic coma
C10EB12	Insulin dependent diabetes mellitus with mononeuropathy
C10E212	Insulin-dependent diabetes mellitus with neurological comps
C108812	Type 1 diabetes mellitus - poor control
C108G11	Type I diabetes mellitus with peripheral angiopathy
C10EE00	Type 1 diabetes mellitus with hypoglycaemic coma
C108J12	Type 1 diabetes mellitus with neuropathic arthropathy
C10E511	Type I diabetes mellitus with ulcer
C10E.12	Insulin dependent diabetes mellitus
C108500	Insulin dependent diabetes mellitus with ulcer
C108E12	Type 1 diabetes mellitus with hypoglycaemic coma
C108212	Type 1 diabetes mellitus with neurological complications
C10EC12	Insulin dependent diabetes mellitus with polyneuropathy
C108911	Type I diabetes mellitus maturity onset
C108B12	Type 1 diabetes mellitus with mononeuropathy
C108E11	Type I diabetes mellitus with hypoglycaemic coma
C10E300	Type 1 diabetes mellitus with multiple complications
C10E600	Type 1 diabetes mellitus with gangrene
C108700	Insulin dependent diabetes mellitus with retinopathy

C10z000	Diabetes mellitus, juvenile type, + unspecified complication
C108800	Insulin dependent diabetes mellitus - poor control
C10E200	Type 1 diabetes mellitus with neurological complications
C10E112	Insulin-dependent diabetes mellitus with ophthalmic comps
C108900	Insulin dependent diabetes maturity onset
C10E011	Type I diabetes mellitus with renal complications
ZRbH.00	Perceived control of insulin-dependent diabetes
C10EH12	Insulin dependent diabetes mellitus with arthropathy
C10E400	Unstable type 1 diabetes mellitus
C10E.11	Type I diabetes mellitus
C10E611	Type I diabetes mellitus with gangrene
ZC2C900	Dietary advice for type I diabetes
C108200	Insulin-dependent diabetes mellitus with neurological comps
C10E812	Insulin dependent diabetes mellitus - poor control
C108D11	Type I diabetes mellitus with nephropathy
C10EK00	Type 1 diabetes mellitus with persistent proteinuria
C108H00	Insulin dependent diabetes mellitus with arthropathy
C108811	Type I diabetes mellitus - poor control
C10EQ00	Type 1 diabetes mellitus with gastroparesis
C10E111	Type I diabetes mellitus with ophthalmic complications
C10EL00	Type 1 diabetes mellitus with persistent microalbuminuria
C10EE12	Insulin dependent diabetes mellitus with hypoglycaemic coma
C108211	Type I diabetes mellitus with neurological complications
C108.11	IDDM-Insulin dependent diabetes mellitus
C10E100	Type 1 diabetes mellitus with ophthalmic complications
C108A12	Type 1 diabetes mellitus without complication
C10E012	Insulin-dependent diabetes mellitus with renal complications
C106000	Diabetes mellitus, juvenile, + neurological manifestation
C10FS00	Maternally inherited diabetes mellitus
C10E911	Type I diabetes mellitus maturity onset
C108711	Type I diabetes mellitus with retinopathy
C108J11	Type I diabetes mellitus with neuropathic arthropathy
C108511	Type I diabetes mellitus with ulcer
C101100	Diabetes mellitus, adult onset, with ketoacidosis
C10EA11	Type I diabetes mellitus without complication
C10E811	Type I diabetes mellitus - poor control
C108011	Type I diabetes mellitus with renal complications
C10E912	Insulin dependent diabetes maturity onset
C10E000	Type 1 diabetes mellitus with renal complications
C10EF11	Type I diabetes mellitus with diabetic cataract

C10EE11	Type I diabetes mellitus with hypoglycaemic coma
C108G12	Type 1 diabetes mellitus with peripheral angiopathy
C10EF12	Insulin dependent diabetes mellitus with diabetic cataract
C10ED00	Type 1 diabetes mellitus with nephropathy
C10EL11	Type I diabetes mellitus with persistent microalbuminuria
C10EC11	Type I diabetes mellitus with polyneuropathy
C104000	Diabetes mellitus, juvenile type, with renal manifestation
C10ED12	Insulin dependent diabetes mellitus with nephropathy
C10E411	Unstable type I diabetes mellitus
C108611	Type I diabetes mellitus with gangrene
C10E711	Type I diabetes mellitus with retinopathy
C10EB00	Type 1 diabetes mellitus with mononeuropathy
C10EH11	Type I diabetes mellitus with arthropathy
C10EG11	Type I diabetes mellitus with peripheral angiopathy
C10G000	Secondary pancreatic diabetes mellitus without complication
66An.00	Diabetes type 1 review
C10E312	Insulin dependent diabetes mellitus with multiple complicat
C10EF00	Type 1 diabetes mellitus with diabetic cataract
C108.12	Type 1 diabetes mellitus
C10G.00	Secondary pancreatic diabetes mellitus
C10EJ00	Type 1 diabetes mellitus with neuropathic arthropathy
C10E512	Insulin dependent diabetes mellitus with ulcer
C108H11	Type I diabetes mellitus with arthropathy
C108400	Unstable insulin dependent diabetes mellitus
C10EM11	Type I diabetes mellitus with ketoacidosis
C10EN00	Type 1 diabetes mellitus with ketoacidotic coma
C10E.00	Type 1 diabetes mellitus
C105000	Diabetes mellitus, juvenile type, + ophthalmic manifestation
C101z00	Diabetes mellitus NOS with ketoacidosis
C10y000	Diabetes mellitus, juvenile, + other specified manifestation
C10EG00	Type 1 diabetes mellitus with peripheral angiopathy
C10E900	Type 1 diabetes mellitus maturity onset
C108412	Unstable type 1 diabetes mellitus
C108B11	Type I diabetes mellitus with mononeuropathy
ZC2C911	Diet advice for insulin-dependent diabetes
C108A00	Insulin-dependent diabetes without complication
C10E500	Type 1 diabetes mellitus with ulcer
C108612	Type 1 diabetes mellitus with gangrene
C102000	Diabetes mellitus, juvenile type, with hyperosmolar coma
C109700	Non-insulin dependent diabetes mellitus - poor control
C109300	Non-insulin-dependent diabetes mellitus with multiple comps

C10FF11	Type II diabetes mellitus with peripheral angiopathy
C104100	Diabetes mellitus, adult onset, with renal manifestation
C109E11	Type II diabetes mellitus with diabetic cataract
C109111	Type II diabetes mellitus with ophthalmic complications
C109411	Type II diabetes mellitus with ulcer
C109E12	Type 2 diabetes mellitus with diabetic cataract
C10ER00	Latent autoimmune diabetes mellitus in adult
C10F111	Type II diabetes mellitus with ophthalmic complications
C109312	Type 2 diabetes mellitus with multiple complications
C10F611	Type II diabetes mellitus with retinopathy
C10F211	Type II diabetes mellitus with neurological complications
C10FP00	Type 2 diabetes mellitus with ketoacidotic coma
C109H11	Type II diabetes mellitus with neuropathic arthropathy
C109C11	Type II diabetes mellitus with nephropathy
C109900	Non-insulin-dependent diabetes mellitus without complication
ZC2CA11	Dietary advice non-insulin-dependent diabetes
C105100	Diabetes mellitus, adult onset, + ophthalmic manifestation
C109C00	Non-insulin dependent diabetes mellitus with nephropathy
C10F600	Type 2 diabetes mellitus with retinopathy
C109A11	Type II diabetes mellitus with mononeuropathy
C10F011	Type II diabetes mellitus with renal complications
C100112	Non-insulin dependent diabetes mellitus
C109200	Non-insulin-dependent diabetes mellitus with neuro comps
C10FQ00	Type 2 diabetes mellitus with exudative maculopathy
C10F400	Type 2 diabetes mellitus with ulcer
C10FL11	Type II diabetes mellitus with persistent proteinuria
C109712	Type 2 diabetes mellitus - poor control
C109B00	Non-insulin dependent diabetes mellitus with polyneuropathy
C10FE11	Type II diabetes mellitus with diabetic cataract
C109100	Non-insulin-dependent diabetes mellitus with ophthalm comps
C109112	Type 2 diabetes mellitus with ophthalmic complications
C10F100	Type 2 diabetes mellitus with ophthalmic complications
C10FG00	Type 2 diabetes mellitus with arthropathy
C100111	Maturity onset diabetes
C10FM11	Type II diabetes mellitus with persistent microalbuminuria
C10FR00	Type 2 diabetes mellitus with gastroparesis
C109212	Type 2 diabetes mellitus with neurological complications
C109612	Type 2 diabetes mellitus with retinopathy
C10F511	Type II diabetes mellitus with gangrene
C109G12	Type 2 diabetes mellitus with arthropathy

C107200	Diabetes mellitus, adult with gangrene
C109400	Non-insulin dependent diabetes mellitus with ulcer
C109F12	Type 2 diabetes mellitus with peripheral angiopathy
C10C.11	Maturity onset diabetes in youth
C109J00	Insulin treated Type 2 diabetes mellitus
C109.11	NIDDM - Non-insulin dependent diabetes mellitus
C109E00	Non-insulin depend diabetes mellitus with diabetic cataract
C109511	Type II diabetes mellitus with gangrene
C10FK00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10FF00	Type 2 diabetes mellitus with peripheral angiopathy
C109.13	Type II diabetes mellitus
C109600	Non-insulin-dependent diabetes mellitus with retinopathy
C109G00	Non-insulin dependent diabetes mellitus with arthropathy
C109012	Type 2 diabetes mellitus with renal complications
C10F911	Type II diabetes mellitus without complication
C107100	Diabetes mellitus, adult, + peripheral circulatory disorder
C109D00	Non-insulin dependent diabetes mellitus with hypoglyca coma
C109000	Non-insulin-dependent diabetes mellitus with renal comps
C10F500	Type 2 diabetes mellitus with gangrene
66Ao.00	Diabetes type 2 review
C109D12	Type 2 diabetes mellitus with hypoglycaemic coma
C109412	Type 2 diabetes mellitus with ulcer
C10FQ11	Type II diabetes mellitus with exudative maculopathy
C10FG11	Type II diabetes mellitus with arthropathy
C10F900	Type 2 diabetes mellitus without complication
C109.12	Type 2 diabetes mellitus
C109.00	Non-insulin dependent diabetes mellitus
C10FN00	Type 2 diabetes mellitus with ketoacidosis
C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy
C109G11	Type II diabetes mellitus with arthropathy
C109500	Non-insulin dependent diabetes mellitus with gangrene
C10FC00	Type 2 diabetes mellitus with nephropathy
C10F.11	Type II diabetes mellitus
C10F711	Type II diabetes mellitus - poor control
C10F300	Type 2 diabetes mellitus with multiple complications
C10FE00	Type 2 diabetes mellitus with diabetic cataract
C10F311	Type II diabetes mellitus with multiple complications
C106100	Diabetes mellitus, adult onset, + neurological manifestation
C10D.11	Maturity onset diabetes in youth type 2
C10z100	Diabetes mellitus, adult onset, + unspecified complication
C109J11	Insulin treated non-insulin dependent diabetes mellitus

C109J12	Insulin treated Type II diabetes mellitus
C10F000	Type 2 diabetes mellitus with renal complications
ZC2CA00	Dietary advice for type II diabetes
C10y100	Diabetes mellitus, adult, + other specified manifestation
C109211	Type II diabetes mellitus with neurological complications
C109C12	Type 2 diabetes mellitus with nephropathy
C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria
C109F11	Type II diabetes mellitus with peripheral angiopathy
C109912	Type 2 diabetes mellitus without complication
C10C.12	Maturity onset diabetes in youth type 1
C10D.00	Diabetes mellitus autosomal dominant type 2
C109512	Type 2 diabetes mellitus with gangrene
C109A00	Non-insulin dependent diabetes mellitus with mononeuropathy
C109611	Type II diabetes mellitus with retinopathy
C10FN11	Type II diabetes mellitus with ketoacidosis
C109B12	Type 2 diabetes mellitus with polyneuropathy
C109H12	Type 2 diabetes mellitus with neuropathic arthropathy
C10FH11	Type II diabetes mellitus with neuropathic arthropathy
C109911	Type II diabetes mellitus without complication
C10FD11	Type II diabetes mellitus with hypoglycaemic coma
C10FA11	Type II diabetes mellitus with mononeuropathy
C10F411	Type II diabetes mellitus with ulcer
C109711	Type II diabetes mellitus - poor control
C109B11	Type II diabetes mellitus with polyneuropathy
C109K00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10FB11	Type II diabetes mellitus with polyneuropathy
C10F200	Type 2 diabetes mellitus with neurological complications
C109D11	Type II diabetes mellitus with hypoglycaemic coma
C10F.00	Type 2 diabetes mellitus
C109311	Type II diabetes mellitus with multiple complications
C10FJ00	Insulin treated Type 2 diabetes mellitus
C10FL00	Type 2 diabetes mellitus with persistent proteinuria
C109A12	Type 2 diabetes mellitus with mononeuropathy
C10FD00	Type 2 diabetes mellitus with hypoglycaemic coma
C10FB00	Type 2 diabetes mellitus with polyneuropathy
C109011	Type II diabetes mellitus with renal complications
C10FA00	Type 2 diabetes mellitus with mononeuropathy
C10FC11	Type II diabetes mellitus with nephropathy
C10FJ11	Insulin treated Type II diabetes mellitus
ZC2C800	Dietary advice for diabetes mellitus
C10F700	Type 2 diabetes mellitus - poor control

C10FP11	Type II diabetes mellitus with ketoacidotic coma
C106.13	Diabetes mellitus with polyneuropathy
C10N000	Secondary diabetes mellitus without complication
C100.00	Diabetes mellitus with no mention of complication
C107z00	Diabetes mellitus NOS with peripheral circulatory disorder
C10zz00	Diabetes mellitus NOS with unspecified complication
2G5C.00	Foot abnormality - diabetes related
66AJ100	Brittle diabetes
8I84.00	Did not complete XPERT diabetes structured education program
L180100	Diabetes mellitus during pregnancy - baby delivered
9OLL.00	XPERT diabetes structured education programme completed
66AQ.00	Diabetes: shared care programme
C350011	Bronzed diabetes
C10N100	Cystic fibrosis related diabetes mellitus
9NM0.00	Attending diabetes clinic
C103000	Diabetes mellitus, juvenile type, with ketoacidotic coma
2G51100	Foot abnormality - non-diabetes
2G5D.00	Foot abnormality - non-diabetes
9OLZ.00	Diabetes monitoring admin.NOS
L180200	Diabetes mellitus in puerperium - baby delivered
8CR2.00	Diabetes clinical management plan
C105y00	Other specified diabetes mellitus with ophthalmic complicatn
9NiD.00	Did not attend DESMOND diabetes structured education program
9h41.00	Excepted from diabetes qual indicators: Patient unsuitable
679L.00	Health education - diabetes
8I82.00	Did not complete DAFNE diabetes structured education program
918T.00	Diabetes key contact
2126300	Diabetes resolved
C104y00	Other specified diabetes mellitus with renal complications
9OL1.00	Attends diabetes monitoring
9OL2.00	Refuses diabetes monitoring
8H4e.00	Referral to diabetes special interest general practitioner
9N0n.00	Seen in community diabetes specialist clinic
8Hj5.00	Referral to XPERT diabetes structured education programme
8H7f.00	Referral to diabetes nurse
8Hj0.00	Referral to diabetes structured education programme
9OL7.00	Diabetes monitor.verbal invite
ZRBa.00	Education score - diabetes
66AP.00	Diabetes: practice programme
9OLB.00	Attended diabetes structured education programme
9OLF.00	Diabetes structured education programme completed
9OL3.00	Diabetes monitoring default

9OL9.00	Diabetes monitoring deleted
8HTe.00	Referral to diabetes preconception counselling clinic
ZL62500	Referral to diabetes nurse
8Hj3.00	Referral to DAFNE diabetes structured education programme
8I83.00	Did not complete DESMOND diabetes structured educat program
C100100	Diabetes mellitus, adult onset, no mention of complication
C107.00	Diabetes mellitus with peripheral circulatory disorder
8I81.00	Did not complete diabetes structured education programme
8Hj1.00	Family/carer referral to diabetes structured education prog
C100000	Diabetes mellitus, juvenile type, no mention of complication
66AU.00	Diabetes care by hospital only
L180000	Diabetes mellitus - unspec whether in pregnancy/puerperium
9M00.00	Informed consent for diabetes national audit
9NiE.00	Did not attend XPERT diabetes structured education programme
C106.00	Diabetes mellitus with neurological manifestation
C104.00	Diabetes mellitus with renal manifestation
C103z00	Diabetes mellitus NOS with ketoacidotic coma
9OL..00	Diabetes monitoring admin.
C105.00	Diabetes mellitus with ophthalmic manifestation
Cyu2.00	[X]Diabetes mellitus
9OLC.00	Family/carer attended diabetes structured education prog
L180.00	Diabetes mellitus during pregnancy/childbirth/puerperium
212H.00	Diabetes resolved
C135.00	Diabetes insipidus
C106z00	Diabetes mellitus NOS with neurological manifestation
C106.12	Diabetes mellitus with neuropathy
C107.12	Diabetes with gangrene
9OLG.00	Attended XPERT diabetes structured education programme
9OLH.00	Attended DAFNE diabetes structured education programme
3881.00	Education score - diabetes
66A8.00	Has seen dietician - diabetes
9OL4.00	Diabetes monitoring 1st letter
Kyu0300	[X]Glomerular disorders in diabetes mellitus
C103y00	Other specified diabetes mellitus with coma
9Nl4.00	Seen by general practitioner special interest in diabetes
C10yz00	Diabetes mellitus NOS with other specified manifestation
C10z.00	Diabetes mellitus with unspecified complication
C103100	Diabetes mellitus, adult onset, with ketoacidotic coma
9OLM.00	Diabetes structured education programme declined
C108z00	Unspecified diabetes mellitus with multiple complications
8Hg4.00	Discharged from care of diabetes specialist nurse

8Hl4.00	Referral to community diabetes specialist nurse
C104z00	Diabetes mellitis with nephropathy NOS
9OL5.00	Diabetes monitoring 2nd letter
F372.00	Polyneuropathy in diabetes
Cyu2300	[X]Unspecified diabetes mellitus with renal complications
3882.00	Diabetes well being questionnaire
C10y.00	Diabetes mellitus with other specified manifestation
C10..00	Diabetes mellitus
7276.00	Pan retinal photocoagulation for diabetes
9OLJ.00	DAFNE diabetes structured education programme completed
ZRB6.00	Diabetes wellbeing questionnaire
C106y00	Other specified diabetes mellitus with neurological comps
C10M000	Lipoatrophic diabetes mellitus without complication
3883.00	Diabetes treatment satisfaction questionnaire
8CS0.00	Diabetes care plan agreed
C103.00	Diabetes mellitus with ketoacidotic coma
C108y00	Other specified diabetes mellitus with multiple comps
2BBF.00	Retinal abnormality - diabetes related
C314.11	Renal diabetes
9OL6.00	Diabetes monitoring 3rd letter
66AJ.11	Unstable diabetes
9OL8.00	Diabetes monitor.phone invite
C10yy00	Other specified diabetes mellitus with other spec comps
ZRB4.00	Diabetes clinic satisfaction questionnaire
F171100	Autonomic neuropathy due to diabetes
ZRB5.11	DTSQ - Diabetes treatment satisfaction questionnaire
8B3l.00	Diabetes medication review
9OLA.11	Diabetes monitored
9NN9.00	Under care of diabetes specialist nurse
9NiA.00	Did not attend diabetes structured education programme
C135.12	Diabetes insipidus - pituitary
R102.11	[D]Prediabetes
K01x100	Nephrotic syndrome in diabetes mellitus
C102z00	Diabetes mellitus NOS with hyperosmolar coma
66AX.00	Diabetes: shared care in pregnancy - diabetol and obstet
9h4..00	Exception reporting: diabetes quality indicators
L180400	Diabetes mellitus in pueperium - baby previously delivered
ZRB5.00	Diabetes treatment satisfaction questionnaire
8Hj4.00	Referral to DESMOND diabetes structured education programme
9OLA.00	Diabetes monitor. check done
ZV65312	[V]Dietary counselling in diabetes mellitus
ZRB6.11	DWBQ - Diabetes wellbeing questionnaire

679R.00	Patient offered diabetes structured education programme
9OLK.00	DESMOND diabetes structured education programme completed
C10N.00	Secondary diabetes mellitus
8BL2.00	Patient on maximal tolerated therapy for diabetes
Cyu2000	[X]Other specified diabetes mellitus
C10zy00	Other specified diabetes mellitus with unspecified comps
C105z00	Diabetes mellitus NOS with ophthalmic manifestation
C100z00	Diabetes mellitus NOS with no mention of complication
C107y00	Other specified diabetes mellitus with periph circ comps
66Af.00	Patient diabetes education review
C102100	Diabetes mellitus, adult onset, with hyperosmolar coma
C10M.00	Lipoatrophic diabetes mellitus
66AR.00	Diabetes management plan given
L180300	Diabetes mellitus during pregnancy - baby not yet delivered
C107.11	Diabetes mellitus with gangrene
9M10.00	Informed dissent for diabetes national audit
9OL..11	Diabetes clinic administration
2G51000	Foot abnormality - diabetes related
66A9.00	Understands diet - diabetes
L180z00	Diabetes mellitus in pregnancy/childbirth/puerperium NOS
9h42.00	Excepted from diabetes quality indicators: Informed dissent
8CP2.00	Transition of diabetes care options discussed
ZRB4.11	CSQ - Diabetes clinic satisfaction questionnaire
9NiC.00	Did not attend DAFNE diabetes structured education programme
L180800	Diabetes mellitus arising in pregnancy
L180900	Gestational diabetes mellitus
Q44B.00	Syndrome of infant of mother with gestational diabetes
ZC2CB00	Dietary advice for gestational diabetes
L180811	Gestational diabetes mellitus
14F4.00	H/O: Admission in last year for diabetes foot problem
Lyu2900	[X]Pre-existing diabetes mellitus, unspecified
1434.00	H/O: diabetes mellitus
L180700	Pre-existing malnutrition-related diabetes mellitus
L180500	Pre-existing diabetes mellitus, insulin-dependent
L180X00	Pre-existing diabetes mellitus, unspecified
ZV13F00	[V]Personal history of gestational diabetes mellitus
L180600	Pre-existing diabetes mellitus, non-insulin-dependent
C10AX00	Malnutrit-relat diabetes mellitus with other spec comps
Cyu2100	[X]Malnutrit-relat diabetes mellitus with other spec comps
C10A200	Malnutrition-related diabetes mellitus with renal complicatn
C10A300	Malnutrit-related diabetes mellitus wth ophthalmic complicat
C10A100	Malnutrition-related diabetes mellitus with ketoacidosis
C10A000	Malnutrition-related diabetes mellitus with coma
C10A500	Malnutritn-relat diabetes melitus wth periph circul complctn
C10A700	Malnutrition-related diabetes mellitus without complications
C10A.00	Malnutrition-related diabetes mellitus
Cyu2200	[X]Malnutrit-related diabetes mellitus with unspec complics
C10AW00	Malnutrit-related diabetes mellitus with unspec complics
C10A600	Malnutrition-related diabetes mellitus with multiple comps
C10A400	Malnutrition-related diabetes mellitus wth neuro complicatns

10.8.2Multilex drug codes for Diabetes Mellitus

Drugcode	Generic name
86177998	INSULIN ISOPHANE BOVINE CARTRIDGE inj susp 100 units/ml
90683997	Biphasic isophane insulin product
92376997	Biphasic isophane insulin product
86249998	Insulin biphasic lispro disposable pen inj susp 25:75; 100 units/ml 3ml disposable pen(s) 5
96047998	INSULIN NEUTRAL HUMAN inj 100 units/ml
94322998	Insulin isophane human crb inj 100 iu/ml 3ml disposable pen(s) 5
97524998	INSULIN SOLUBLE BOVINE inj 100 units/ml
98227998	INSULIN SOLUBLE HUMAN VIAL inj soln 100 units/ml
98228998	INSULIN ISOPHANE HUMAN EMP inj 100 units/ml
91295998	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
96053997	ISOPHANE INSULIN 100iu/mL 10m
86243998	Insulin glargine vial inj soln 100 units/ml 1 10ml vial(s)
86237998	Insulin glulisine vial inj soln 100 units/ml 1 10ml vial(s)
86303998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 30:70; 100 units/ml
92940994	INSULIN 1mL syrg+12mm(29G) ndl
90012998	Insulin lispro human prb inj 100 iu/ml 3ml disposable pen(s) 5
91777994	NovoPenclassic
97598992	Insulin isophane (nph) 40 i/u 0
98225998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 50:50; 100 units/ml
96283992	Insulin isophane (nph) 100 i/u inj 0
86269998	INSULIN ISOPHANE HUMAN DISPOSABLE PEN inj susp 100 units/ml
96292992	Insulin isophane (highly purified) 100 i/u inj 0
96076992	Insulin bovine protamine zinc 100 i/u inj 0
90681998	Biphasic isophane insulin product
86284998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp

	15:85; 100 units/ml
86254998	Insulin lispro disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)
91275998	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 10:90; 100 units/ml
97601992	Insulin zinc semilente susp bp 100 i/u inj 0
86308998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 20:80; 100 units/ml
97322997	INSULIN SOLUBLE HUMAN PYR inj 100 units/ml
96061998	Insulin zinc mixed bovine vial inj susp 100 units/ml 10ml vial(s) 1
89555998	Insulin biphasic aspart human pyr inj 30:70; 100 units/ml 3ml disposable pen(s) 5
86253998	INSULIN LISPRO VIAL inj soln 100 units/ml
91505998	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
86250998	Insulin biphasic lispro cartridge inj susp 25:75; 100 units/ml 3ml cartridge(s) 5
94292998	INSULIN SOLUBLE HUMAN EMP inj 100 units/ml
91293997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 20:80; 100 units/ml
97854998	INSULIN ISOPHANE HUMAN CRB inj 100 iu/ml
88973994	Autopen Junior
94296998	INSULIN ISOPHANE HUMAN EMP inj 100 units/ml
96794992	Biphasic isophane insulin product
86186998	INSULIN BIPHASIC ISOPHANE PORCINE CARTRIDGE inj susp 30:70; 100 units/ml
86191998	INSULIN ISOPHANE PORCINE VIAL inj susp 100 units/ml
91276998	INSULIN ISOPHANE HUMAN PRB inj 100 iu/ml
90681996	Biphasic isophane insulin product
86266998	INSULIN ISOPHANE HUMAN DISPOSABLE PEN inj susp 100 units/ml
90817994	BD Ultra Pen
96291992	ISOPHANE INSULIN 100iu/mL 10m
84779998	INSULIN DETEMIR DISPOSABLE PEN inj soln 100 units/ml
91292997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
90697997	Biphasic isophane insulin product
91294997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 10:90; 100 units/ml
92376998	Biphasic isophane insulin product
96053996	Biphasic isophane insulin product
86288998	Biphasic isophane insulin product
96792992	Biphasic isophane insulin product
86256998	Insulin lispro vial inj soln 100 units/ml 1 10ml vial(s)
86189998	ISOPHANE INSULIN 100iu/mL 10m
86242998	Insulin glargine disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)
91292996	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
95162992	NEUTRAL INSULIN 100iu/mL 10mL
92908998	INSULIN BIPHASIC ISOPHANE

	HUMAN PYR inj 20:80; 100 units/ml
98239994	U100 insulin syringe 0.5ml syringe(s) 100
86260998	INSULIN BIPHASIC ASPART CARTRIDGE inj susp 30:70; 100 units/ml
86182998	INSULIN SOLUBLE PORCINE CARTRIDGE inj soln 100 units/ml
86193998	Insulin isophane porcine cartridge inj susp 100 units/ml 3ml cartridge(s) 5
86314998	INSULIN SOLUBLE HUMAN CARTRIDGE inj soln 100 units/ml
94319998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 10:90; 100 units/ml
90689998	Insulin soluble human prb inj 100 units/ml 5ml vial(s) 1
88210994	Autopen Special Edition
97527998	INSULIN ZINC MIXED BOVINE VIAL inj susp 100 units/ml
91274998	INSULIN SOLUBLE HUMAN DISPOSABLE PEN inj soln 100 units/ml
92906998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml
86274998	Insulin isophane human disposable pen inj susp 100 units/ml 5 3ml disposable pen(s)
95168992	Insulin zinc suspension amorphous product
98505998	INSULIN ZINC MIXED BOVINE VIAL inj susp 100 units/ml
99480998	INSULIN ZINC susp MIXED BOVINE & PORCINE inj 100 units/ml
86549998	INSULIN GLULISINE CARTRIDGE inj soln 100 units/ml
87415994	Humapen Ergoburgundy
88413998	INSULIN SOLUBLE PORCINE VIAL inj soln 100 units/ml
94298998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 25:75; 100 units/ml
85591998	INSULIN GLULISINE CARTRIDGE inj soln 100 units/ml
86305998	Biphasic isophane insulin product
97600992	Insulin bovine protamine zinc 40 i/u inj 0
86080998	INSULIN ISOPHANE HUMAN DISPOSABLE PEN inj susp 100 units/ml
90684997	Biphasic isophane insulin product
88995998	INSULIN ISOPHANE PORCINE inj 100 units/ml
96052998	Insulin isophane mixed human inj 100 units/ml 3ml cartridge(s) 5
86315998	INSULIN SOLUBLE HUMAN CARTRIDGE inj soln 100 units/ml
86313998	INSULIN SOLUBLE HUMAN DISPOSABLE PEN inj soln 100 units/ml
86185998	Insulin soluble porcine vial inj soln 100 units/ml 10ml vial(s) 1
86298998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 30:70; 100 units/ml
96045998	Isophane insulin inj 100 iu/ml 10ml vial(s) 1
88974994	Autopen Junior
90169998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 30:70; 100 units/ml
94299998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 50:50; 100 units/ml
86267998	INSULIN ISOPHANE HUMAN VIAL inj susp 100 units/ml
86282998	Biphasic isophane insulin product

99532998	INSULIN ISOPHANE PORCINE VIAL inj susp 100 units/ml
86169998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 50:50; 100 units/ml
94297998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 15:85; 100 units/ml
91273998	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 40:60; 100 units/ml
96281992	Insulin soluble 320 i/u inj 0
96284992	Isophane insulin product
86310998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 10:90; 100 units/ml
98817998	INSULIN ZINC susp CRYSTALLINE HUMAN PRB - INTERMEDIATE ACTING inj 100 units/ml
88211994	Autopen Special Edition
99356998	INSULIN SOLUBLE BOVINE inj 100 units/ml
91293998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 20:80; 100 units/ml
86214998	Insulin glulisine disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)
90690998	Insulin soluble human emp inj 100 units/ml 10ml vial(s) 1
98238994	U100 pre-set insulin syringe 1ml sp.36 [2a] 1 syringe(s)
94477992	NEUTRAL INSULIN 100iu/mL 10mL
97322998	INSULIN SOLUBLE HUMAN PYR inj 100 units/ml
86252998	INSULIN LISPRO CARTRIDGE inj soln 100 units/ml
86179998	Insulin isophane bovine cartridge inj susp 100 units/ml 3ml cartridge(s) 5
97244992	INSULIN/DEPOT
86278998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 25:75; 100 units/ml
90697996	Biphasic isophane insulin product
99359998	INSULIN ISOPHANE BOVINE inj 100 units/ml
91758998	Insulin glargine inj 100 iu/ml 3ml cartridge(s) 5
86271998	INSULIN ISOPHANE HUMAN VIAL inj susp 100 units/ml
96561992	INSULIN SYRINGE
99976992	Insulin soluble 100 i/u inj 0
86176998	Insulin soluble bovine vial inj soln 100 units/ml 10ml vial(s) 1
86264998	Insulin aspart cartridge inj soln 100 units/ml 5 3ml cartridge(s)
96290992	Insulin neutral (purified) 100 i/u inj 0
86180998	Insulin isophane bovine vial inj susp 100 units/ml 10ml vial(s) 1
83405998	INSULIN BIPHASIC LISPRO DISPOSABLE PEN inj susp 50:50; 100 units/ml
99556998	INSULIN ZINC susp MIXED HUMAN PYR inj 100 units/ml
99048992	Syringe insulin (bs1619/1) 2ml 0
83403998	INSULIN LISPRO DISPOSABLE PEN inj soln 100 units/ml
89990998	Insulin biphasic lispro human prb inj 25:75; 100 units/ml 3ml disposable pen(s) 5
86247998	INSULIN BIPHASIC LISPRO DISPOSABLE PEN inj susp 25:75; 100 units/ml
97268994	U100 insulin syringe 1ml 100
	syringe(s)
90682998	Biphasic isophane insulin product
99401998	INSULIN ZINC susp MIXED PORCINE inj 100 units/ml
97323998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
97526998	INSULIN ISOPHANE BOVINE inj 100 units/ml
89685994	U100 insulin syringe 0.5ml
97639992	INSULIN/COMBINATION
91289998	INSULIN BIPHASIC ISOPHANE HUMAN CRB inj 15:85; 100 units/ml
90015998	INSULIN LISPRO HUMAN PRB inj 100 iu/ml
98474990	INSULIN SOLUBLE BOVINE inj 100 units/ml
96286992	NEUTRAL INSULIN 100iu/mL 10mL
86301998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 30:70; 100 units/ml
86251998	INSULIN LISPRO DISPOSABLE PEN inj soln 100 units/ml
96050998	Neutral insulin bovine inj 100 iu/ml 3ml cartridge(s) 5
86241998	Insulin glargine cartridge inj soln 100 units/ml 5 3ml cartridge(s)
96688992	Insulin neutral (human) 100 i/u inj 0
86077998	Insulin biphasic lispro disposable pen inj susp 50:50; 100 units/ml 3ml disposable pen(s) 5
88297994	One Touch Ultra
86265998	Insulin aspart vial inj soln 100 units/ml 1 10ml vial(s)
96063998	Insulin neutral human inj 100 units/ml 10ml vial(s) 1
86175998	Insulin soluble bovine cartridge inj soln 100 units/ml 3ml cartridge(s) 5
90682996	Biphasic isophane insulin product
89554998	INSULIN BIPHASIC ASPART HUMAN PYR inj 30:70; 100 units/ml
87471998	INSULIN DETEMIR DISPOSABLE PEN inj soln 100 units/ml
93137992	Insulin isophane (human) 100 i/u inj 0
90682997	Biphasic isophane insulin product
97053998	INSULIN ZINC susp MIXED HUMAN PRB inj 100 units/ml
86248998	INSULIN BIPHASIC LISPRO CARTRIDGE inj susp 25:75; 100 units/ml
86081998	INSULIN ISOPHANE HUMAN VIAL inj susp 100 units/ml
96787992	Soluble neutral insulin product
91509998	INSULIN ASPART DISPOSABLE PEN inj soln 100 units/ml
86272998	INSULIN GLARGINE CARTRIDGE inj soln 100 units/ml
98198998	INSULIN ASPART CARTRIDGE inj soln 100 units/ml
96294992	Insulin zinc bovine susp 100 i/u inj 0
86281998	Biphasic isophane insulin product
87967998	Biphasic isophane insulin product
86285998	Biphasic isophane insulin product
92555998	INSULIN GLARGINE inj 100 iu/ml
98480998	INSULIN SOLUBLE PORCINE inj 100 units/ml

92909998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 10:90; 100 units/ml
86316998	INSULIN SOLUBLE HUMAN VIAL inj soln 100 units/ml
94337998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
89888998	Biphasic isophane insulin product
99553998	INSULIN SOLUBLE HUMAN PRB inj 100 units/ml
90168998	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
90697998	Biphasic isophane insulin product
93713998	Insulin disp 1ml syringe appliance(s) 1
91294998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 10:90; 100 units/ml
94413998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 40:60; 100 units/ml
97052996	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 30:70; 100 units/ml
88978998	INSULIN BIPHASIC ISOPHANE PORCINE inj 30:70; 100 units/ml
92323998	INSULIN BIPHASIC LISPRO DISPOSABLE PEN inj susp 50:50; 100 units/ml
91291997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 40:60; 100 units/ml
86044998	INSULIN HUMAN inhalation pwdr 3mg
96064992	Insulin zinc suspension amorphous product
96057998	Insulin zinc susp crystalline human prb - intermediate acting inj 100 units/ml 10ml vial(s) 1
91290996	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml
96289992	Insulin zinc suspension crystalline product
86295998	Biphasic isophane insulin product
90828994	Novopen 3fun-blue
98507998	INSULIN SOLUBLE BOVINE inj 100 units/ml
97602992	Insulin soluble 40 i/u inj 0
92649994	Novofine
97528998	INSULIN PROTAMINE ZINC BOVINE VIAL inj susp 100 units/ml
98895998	INSULIN BIPHASIC LISPRO HUMAN PRB inj 25:75; 100 units/ml
90684998	Biphasic isophane insulin product
86553998	Insulin glulisine inj soln 100 units/ml 3ml disposable pen(s) 5
90685998	Insulin zinc susp mixed human prb inj 100 units/ml 10ml vial(s) 1
97051997	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 50:50; 100 units/ml
94328998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 20:80; 100 units/ml
98982998	INSULIN SOLUBLE PORCINE inj 100 units/ml
99402998	INSULIN ASPART VIAL inj soln 100 units/ml
94948998	Insulin soluble porcine inj 100 units/ml 3ml cartridge(s) 5
99144998	INSULIN ZINC susp AMORPHOUS PORCINE inj 100 units/ml
86183998	INSULIN SOLUBLE PORCINE VIAL inj soln 100 units/ml
91275996	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 30:70; 100 units/ml
95165992	Biphasic isophane insulin product
86275998	Insulin isophane human cartridge inj susp 100 units/ml 5 3ml cartridge(s)
86240998	INSULIN GLARGINE VIAL inj soln 100 units/ml
90688998	Insulin isophane human pyr inj 100 iu/ml 3ml pre-filled syringe 5
86255998	Insulin lispro cartridge inj soln 100 units/ml 5 3ml cartridge(s)
91292998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
86268998	INSULIN ISOPHANE HUMAN CARTRIDGE inj susp 100 units/ml
86168998	INSULIN ISOPHANE HUMAN CARTRIDGE inj susp 100 units/ml
90508994	Novopen 3demi
91291998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 40:60; 100 units/ml
86291998	Biphasic isophane insulin product
98506998	INSULIN ISOPHANE BOVINE inj 100 units/ml
86246998	Insulin detemir cartridge inj soln 100 units/ml 5 3ml cartridge(s)
96056998	INSULINISOPHANE BOVINE
99196998	INSULIN BIPHASIC inj 100 units/ml
96044992	Insulin bp 100 i/u 0
94202992	Soluble neutral insulin product
86317998	Insulin soluble human cartridge inj soln 100 units/ml 5 3ml cartridge(s)
90829994	Novopen 3fun-red
96049998	INSULIN SOLUBLE PORCINE inj 100 units/ml
86261998	Insulin biphasic aspart disposable pen inj susp 30:70; 100 units/ml 3ml disposable pen(s) 5
86174998	INSULIN SOLUBLE BOVINE CARTRIDGE inj soln 100 units/ml
86215998	INSULIN GLULISINE DISPOSABLE PEN inj soln 100 units/ml
92456994	Novofine
92907998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 40:60; 100 units/ml
95150997	TOLAZAMIDE
99415998	INSULIN BIPHASIC ISOPHANE PORCINE VIAL inj susp 30:70; 100 units/ml
91933994	NovoPen
91612998	INSULIN ASPART HUMAN PYR inj 100 iu/ml
96295992	Soluble neutral insulin product
86551998	INSULIN GLULISINE VIAL inj soln 100 units/ml
96795992	Isophane insulin product
93467992	Insulin soluble inj i/u^2 0
99047992	Syringe pre-set insulin for blind 2ml 0
86046998	Insulin human inhalation pwdr 3mg 90 blisters
96046998	Insulin zinc lente bovine vial inj susp 100 units/ml 1 10ml vial(s)
87008994	Optipen Pro 1
87967997	Biphasic isophane insulin product
96059998	Insulin zinc susp amorphous porcine inj 100 units/ml 10ml vial(s) 1
99554998	INSULIN ISOPHANE HUMAN PRB inj 100 iu/ml
86270998	INSULIN ISOPHANE HUMAN CARTRIDGE inj susp 100 units/ml
90379998	Insulin aspart human pyr inj 100 iu/ml 3ml disposable pen(s) 5

96058998	Insulin zinc susp crystalline human pyr - long acting inj 100 units/ml 10ml vial(s) 1
98481997	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
96282992	Biphasic isophane insulin product
96293992	Insulin zinc semilente susp 80 i/u inj 0
86259998	INSULIN BIPHASIC ASPART DISPOSABLE PEN inj susp 30:70; 100 units/ml
91700998	INSULIN BIPHASIC ISOPHANE HUMAN CRB inj 50:50; 100 units/ml
89990997	Insulin biphasic lispro human prb inj 50:50; 100 units/ml 3ml disposable pen(s) 5
86318998	Biphasic isophane insulin product
93714996	Insulin 1 ml syringe appliance(s) 1
86029998	Insulin biphasic lispro cartridge inj susp 50:50; 100 units/ml 3ml cartridge(s) 5
98228997	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
93713997	Insulin 2 ml syringe appliance(s) 1
98268998	INSULIN ZINC susp CRYSTALLINE HUMAN PYR - LONG ACTING inj 100 units/ml
86194998	Insulin isophane porcine vial inj susp 100 units/ml 10ml vial(s) 1
86188998	Biphasic isophane insulin product
86306998	Biphasic isophane insulin product
86286998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 50:50; 100 units/ml
93713996	Insulin pre-set 1 ml syringe appliance(s) 1
96055998	Insulin isophane porcine inj 100 units/ml 10ml vial(s) 1
99977992	Biphasic insulin product
86028998	INSULIN BIPHASIC LISPRO CARTRIDGE inj susp 50:50; 100 units/ml
96065998	Human insulin 100u/mL inj cart
86184998	Insulin soluble porcine cartridge inj soln 100 units/ml 3ml cartridge(s) 5
96287992	ISOPHANE INSULIN 100iu/mL 10m
95846992	ZINC BOVINE & PORCINE INSULIN SUSPENSION
89684994	U100 insulin syringe 1ml
84421998	INSULIN GLULISINE DISPOSABLE PEN inj soln 100 units/ml
96054998	Insulin isophane human inj 100 iu/ml 3ml cartridge(s) 5
91767994	NovoPenfun
90698998	Insulin zinc susp mixed bovine & porcine inj 100 units/ml 10ml vial(s) 1
86047998	Insulin human inhalation pwdr 1mg 90 blisters
98525990	INSULIN ZINC MIXED BOVINE VIAL inj susp 100 units/ml
96060998	Insulin zinc susp mixed human pyr inj 100 units/ml 10ml vial(s) 1
98228996	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
96285992	Protamine zinc insulin product
95158992	NEUTRAL INSULIN 100iu/mL 10mL
88851998	INSULIN SOLUBLE HUMAN CRB inj 100 iu/ml

91701998	INSULIN BIPHASIC ISOPHANE HUMAN CRB inj 25:75; 100 units/ml
96046992	Biphasic isophane insulin product
86245998	Insulin detemir disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)
86262998	Insulin biphasic aspart cartridge inj susp 30:70; 100 units/ml 3ml cartridge(s) 5
92932998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
93714997	Insulin disp 0.5ml syringe appliance(s) 1
86312998	INSULIN SOLUBLE HUMAN VIAL inj soln 100 units/ml
86190998	INSULIN ISOPHANE PORCINE CARTRIDGE inj susp 100 units/ml
86173998	INSULIN SOLUBLE BOVINE VIAL inj soln 100 units/ml
89082994	Novopen Juniorgreen
96053998	Biphasic isophane insulin product
90684996	Biphasic isophane insulin product
88999998	INSULIN SOLUBLE PORCINE inj 100 units/ml
99533998	INSULIN BIPHASIC ISOPHANE PORCINE inj 50:50; 100 units/ml
86187998	INSULIN BIPHASIC ISOPHANE PORCINE VIAL inj susp 30:70; 100 units/ml
86287998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 50:50; 100 units/ml
90686998	Insulin isophane human emp inj 100 units/ml 3ml cartridge(s) 5
86283998	Biphasic isophane insulin product
95163992	ISOPHANE INSULIN 100iu/mL 10m
90691998	Insulin soluble human pyr inj 100 units/ml 3ml cartridge(s) 5
88003998	Insulin soluble human crb inj 100 iu/ml 3ml disposable pen(s) 5
87416994	Humapen Ergoteal
94436998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml
99360998	INSULIN ZINC MIXED BOVINE VIAL inj susp 100 units/ml
91160998	Insulin zinc susp mixed porcine inj 100 units/ml 10ml vial(s) 1
98226998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 30:70; 100 units/ml
86319998	Insulin soluble human vial inj soln 100 units/ml 1 10ml vial(s)
90681997	Biphasic isophane insulin product
83404998	INSULIN BIPHASIC LISPRO DISPOSABLE PEN inj susp 25:75; 100 units/ml
86078998	INSULIN BIPHASIC ISOPHANE HUMAN VIAL inj susp 30:70; 100 units/ml
86276998	Insulin isophane human vial inj susp 100 units/ml 1 5ml vial(s)
91275997	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 20:80; 100 units/ml
89081994	Novopen Junioryellow
96689992	Insulin zinc crystalline susp 100 i/u inj 0
96062998	Insulin biphasic inj 100 units/ml 10ml vial(s) 1
97599992	ISOPHANE INSULIN 100iu/mL 10m
86239998	INSULIN GLARGINE DISPOSABLE PEN inj soln 100 units/ml
90683998	Biphasic isophane insulin product

99978992	Insulin isophane (purified) 100 i/u inj 0
90830994	Novopen 3classic
98481998	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
86280998	INSULIN BIPHASIC ISOPHANE HUMAN VIAL inj susp 25:75; 100 units/ml
97051998	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 40:60; 100 units/ml
92376996	Biphasic isophane insulin product
95164992	INSULIN/BOVINE INSULIN ZINC SUSPN/PURE
96048998	INSULIN NEUTRAL HUMAN inj 100 units/ml
96064998	Insulin neutral bovine inj 100 units/ml 10ml vial(s) 1
93714998	Insulin 0.5 ml syringe appliance(s) 1
91290997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml
86238998	INSULIN GLARGINE CARTRIDGE inj soln 100 units/ml
97525998	INSULIN SOLUBLE BOVINE inj 100 units/ml
84422998	INSULIN GLARGINE DISPOSABLE PEN inj soln 100 units/ml
91641994	Humapen
96548992	Biphasic isophane insulin product
93139992	Insulin isophane 100 i/u 0
91273997	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 50:50; 100 units/ml
97052998	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 10:90; 100 units/ml
96051998	Insulin protamine zinc bovine vial inj susp 100 units/ml 10ml vial(s) 1
86178998.00	INSULIN ISOPHANE BOVINE VIAL inj susp 100 units/ml
90687998	Insulin isophane human prb inj 100 iu/ml 5ml vial(s) 1
98048990	INSULIN ISOPHANE BOVINE inj 100 units/ml
87472998	INSULIN DETEMIR CARTRIDGE inj soln 100 units/ml
86294998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 40:60; 100 units/ml
86309998	Biphasic isophane insulin product
97052997	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 20:80; 100 units/ml
86300998	INSULIN BIPHASIC ISOPHANE HUMAN VIAL inj susp 30:70; 100 units/ml
86263998	Insulin aspart disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)
86279998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 25:75; 100 units/ml
91290998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml
99557998	INSULIN SOLUBLE HUMAN PYR inj 100 units/ml
86236998	Insulin glulisine cartridge inj soln 100 units/ml 5 3ml cartridge(s)
86311998	Biphasic isophane insulin product
86304998	Biphasic isophane insulin product
87473998	Insulin detemir inj soln 100 iu/ml 3ml disposable pen(s) 5
86045998	INSULIN HUMAN inhalation pwdr 1mg
97834990.00	GLIPIZIDE tabs 5mg

97026990	GLICLAZIDE tabs 80mg
88449997	Glimepiride tabs 1mg 30 tablet(s)
97146990.00	GLIPIZIDE tabs 5mg
97537997	GLIBENCLAMIDE tabs 5mg
93781990	GLICLAZIDE tabs 80mg
93542990	GLIMEPIRIDE tabs 4mg
93562990	GLIMEPIRIDE tabs 3mg
95025990.00	GLICLAZIDE tabs 80mg
97303998	GLICLAZIDE tabs 80mg
96280998	GLIQUIDONE
98643990	GLIBENCLAMIDE tabs 5mg
91407998	GLICLAZIDE mr tab 30mg
93372990	GLIMEPIRIDE tabs 2mg
98418989	GLIBENCLAMIDE tabs 5mg
95403990	TOLBUTAMIDE tabs 500mg
99349990	TOLBUTAMIDE tabs 500mg
83838998	GLIMEPIRIDE tabs 2mg
99754998	ACETOHEXAMIDE
98418990	GLIBENCLAMIDE tabs 2.5mg
93373990	GLIMEPIRIDE tabs 1mg
96427990	GLICLAZIDE tabs 80mg
99582989	GLIBENCLAMIDE tabs 2.5mg
93095990	GLIMEPIRIDE tabs 2mg
83410998	GLICLAZIDE mr tab 30mg
97590990	GLICLAZIDE tabs 80mg
98664990	GLIBENCLAMIDE tabs 5mg
88447997	GLIMEPIRIDE tabs 1mg
97202990	GLIPIZIDE tabs 5mg
88355998	Glimepiride tabs 4mg 30 tablet(s)
93096990	GLIMEPIRIDE tabs 1mg
83916998	GLICLAZIDE mr tab 30mg
88528998	TROGLITAZONE
97089998	TOLBUTAMIDE tabs 500mg
99195998	TOLBUTAMIDE tabs 500mg
83836998	GLIMEPIRIDE tabs 4mg
95672992	TOLBUTAMIDE
97057998	GLIBENCLAMIDE tabs 5mg
97775989	CHLORPROPAMIDE tabs 250mg
99582990	GLIBENCLAMIDE tabs 5mg
96495990	GLICLAZIDE tabs 80mg
95898990	GLICLAZIDE tabs 80mg
93322990	GLIMEPIRIDE tabs 3mg
97751990	GLIBENCLAMIDE tabs 2.5mg
95255992	CHLORPROPAMIDE

96687998	CHLORPROPAMIDE tabs 250mg
95288990	TOLBUTAMIDE tabs 500mg
99246990	CHLORPROPAMIDE tabs 100mg
96795990	GLIPIZIDE tabs 5mg
96893990	GLIPIZIDE tabs 5mg
93545990	GLIMEPIRIDE tabs 1mg
96755997	Chlorpropamide tabs 250mg 28 tablet(s)
99764998	CHLORPROPAMIDE tabs 100mg
97537998	GLIBENCLAMIDE tabs 2.5mg
96615989	CHLORPROPAMIDE tabs 250mg
97583997	GLIBENCLAMIDE tabs 5mg
96559990	GLIBENCLAMIDE tabs 2.5mg
86018998	GLICLAZIDE
93323990	GLIMEPIRIDE tabs 2mg
97097998	GLIBENCLAMIDE tabs 2.5mg
88334998	GLIMEPIRIDE tabs 4mg
96221990	GLIBENCLAMIDE tabs 2.5mg
93371990	GLIMEPIRIDE tabs 3mg
84783998	Tolbutamide oral liq
93126990	GLIMEPIRIDE tabs 3mg
93564990	GLIMEPIRIDE tabs 1mg
97236992	GLIBENCLAMIDE
99581989	GLIBENCLAMIDE tabs 5mg
96282997.00	Glipizide tabs 5mg 60 tablet(s)
88447996	GLIMEPIRIDE tabs 3mg
99668997	GLIBENCLAMIDE tabs 5mg
97097997	GLIBENCLAMIDE tabs 5mg
96281998	GLIPIZIDE tabs 2.5mg
83887998	Chlorpropamide oral liq
97552990	GLIBENCLAMIDE tabs 2.5mg
97166990	GLICLAZIDE tabs 80mg
94333992	TOLBUTAMIDE I/V
98643989	GLIBENCLAMIDE tabs 2.5mg
99247990	CHLORPROPAMIDE tabs 100mg
93119990	GLIMEPIRIDE tabs 3mg
95446990	GLICLAZIDE tabs 80mg
95601990	GLIBENCLAMIDE tabs 5mg
98188989	CHLORPROPAMIDE tabs 250mg
97133992	CHLORPROPAMIDE
85003998	Gliclazide oral liq
99246989	CHLORPROPAMIDE tabs 250mg
93901990	GLICLAZIDE tabs 80mg
93125990	GLIMEPIRIDE tabs 4mg
88447998	GLIMEPIRIDE tabs 2mg

97109998	Tolbutamide tabs 500mg 28 tablet(s)
97889990	GLICLAZIDE tabs 80mg
97938990	GLICLAZIDE tabs 80mg
98188990	CHLORPROPAMIDE tabs 100mg
96220990	GLIBENCLAMIDE tabs 5mg
99348990	TOLBUTAMIDE tabs 500mg
99668998	GLIBENCLAMIDE tabs 2.5mg
97775990	CHLORPROPAMIDE tabs 100mg
97538990	GLICLAZIDE tabs 80mg
99764997	CHLORPROPAMIDE tabs 250mg
93561990	GLIMEPIRIDE tabs 4mg
93118990	GLIMEPIRIDE tabs 4mg
93544990	GLIMEPIRIDE tabs 2mg
93867990	TOLBUTAMIDE tabs 500mg
93370990	GLIMEPIRIDE tabs 4mg
93128990	GLIMEPIRIDE tabs 1mg
99580990	GLIBENCLAMIDE tabs 5mg
88449998	Glimepiride tabs 2mg 30 tablet(s)
97717998	GLICLAZIDE tabs 80mg
99247989	CHLORPROPAMIDE tabs 250mg
97158990	GLIPIZIDE tabs 5mg
99347990	TOLBUTAMIDE tabs 500mg
93121990	GLIMEPIRIDE tabs 1mg
97127998	Glibenclamide tabs 2.5mg 28 tablet blister pack
96707990	GLICLAZIDE tabs 80mg
95422990	TOLBUTAMIDE tabs 500mg
96699990	GLIPIZIDE tabs 5mg
97127997	Glibenclamide tabs 5mg 28 tablet blister pack
97751989	GLIBENCLAMIDE tabs 5mg
96615990	CHLORPROPAMIDE tabs 100mg
85901998	GLIBENCLAMIDE
97032990	GLICLAZIDE tabs 80mg
83837998	GLIMEPIRIDE tabs 3mg
93324990	GLIMEPIRIDE tabs 1mg
93094990	GLIMEPIRIDE tabs 3mg
99580989	GLIBENCLAMIDE tabs 2.5mg
96282998	Glipizide tabs 2.5mg 28 tablet(s)
99041990	TOLBUTAMIDE tabs 500mg
99787998	GLIBENCLAMIDE tabs 5mg
99230998	TOLBUTAMIDE tabs 500mg
99588998	GLIBORNURIDE
96283997	Gliclazide mr tab 30mg 112 tablet(s)
91247998	GLICLAZIDE tabs 80mg
98133990	GLICLAZIDE tabs 80mg

99419998	GLIPIZIDE tabs 5mg
85265998	Glibenclamide oral liq
84684998	Rosiglitazone + glimepiride (ipu) tabs 8mg + 4mg
95149998	TOLAZAMIDE
98053990	TOLBUTAMIDE tabs 500mg
88135998	GLICLAZIDE tabs 80mg
98548990	GLIBENCLAMIDE tabs 5mg
97154990	GLICLAZIDE tabs 80mg
99145998	GLIBENCLAMIDE tabs 2.5mg
93127990	GLIMEPIRIDE tabs 2mg
96755998	Chlorpropamide tabs 100mg 250 tablet(s)
84685998	Rosiglitazone + glimepiride (ipu) tabs 4mg + 4mg
99591998	GLIPIZIDE tabs 5mg
97552989	GLIBENCLAMIDE tabs 5mg
95148998	TOLBUTAMIDE
97057997	GLIBENCLAMIDE tabs 2.5mg
99581990	GLIBENCLAMIDE tabs 2.5mg
88449996	Glimepiride tabs 3mg 30 tablet(s)
83949998	GLICLAZIDE mr tab 30mg
96981998	ACETOHEXAMIDE
92518997	GLIBENCLAMIDE tabs 5mg
96283998	Gliclazide tabs 80mg 120 tablet(s)
99589998	GLIQUIDONE
98664989	GLIBENCLAMIDE tabs 2.5mg
83839998	GLIMEPIRIDE tabs 1mg
93120990	GLIMEPIRIDE tabs 2mg
97583998	GLIBENCLAMIDE tabs 2.5mg
95150998	TOLAZAMIDE
93563990	GLIMEPIRIDE tabs 2mg
95256992	CHLORPROPAMIDE
94371992	TOLBUTAMIDE
93093990	GLIMEPIRIDE tabs 4mg
95674992	TOLBUTAMIDE
92518998	GLIBENCLAMIDE tabs 2.5mg
93543990	GLIMEPIRIDE tabs 3mg
92831990	GLICLAZIDE mr tab 30mg
96296990	METFORMIN tabs 500mg
84009998	VILDAGLIPTIN + METFORMIN tabs 50mg + 850mg
85622998	PIOGLITAZONE + METFORMIN tabs 15mg + 850mg
99590998	METFORMIN tabs 500mg
96270989	METFORMIN tabs 850mg
94248990	METFORMIN tabs 500mg
84011998	Vildagliptin + metformin tabs 50mg + 850mg tablet(s) 60
99514989	METFORMIN tabs 850mg
99514990	METFORMIN tabs 500mg
92983990	METFORMIN oral soln 500mg/5ml
97087998	Metformin tabs 500mg 30 tablet(s)
95600990	METFORMIN tabs 500mg
99590997	METFORMIN tabs 850mg
95272992	METFORMIN
94246990	METFORMIN tabs 850mg
87180998	ROSIGLITAZONE + METFORMIN tabs 2mg + 1000mg
96850990	METFORMIN tabs 500mg
87773998	Rosiglitazone + metformin tabs 2mg + 500mg 112 tablet(s)
98494990	METFORMIN tabs 500mg
91221997	METFORMIN tabs 850mg
83733998	Metformin mr tab 750mg tablet(s) 28
98654989	METFORMIN tabs 500mg
91221998	METFORMIN tabs 500mg
99513989	METFORMIN tabs 850mg
87054998	Metformin mr tab 500mg 56 tablet(s)
99149990	METFORMIN tabs 500mg
96296989	METFORMIN tabs 850mg
98125989	METFORMIN tabs 850mg
84008998	VILDAGLIPTIN + METFORMIN tabs 50mg + 1000mg
94280992	PHENFORMIN HYDROCHLORIDE S/R
87536998	Metformin oral susp 100mg/ml mls 150
97110990	METFORMIN tabs 500mg
95381990	METFORMIN tabs 500mg
87182998	Rosiglitazone + metformin tabs 2mg + 1000mg 56 tablet(s)
98493989	METFORMIN tabs 500mg
85406998	Metformin (ipu) tabs 1000mg
95239990	METFORMIN tabs 850mg
99149989	METFORMIN tabs 850mg
87053998	METFORMIN mr tab 500mg
95228990	METFORMIN tabs 500mg
97087997	Metformin tabs 850mg 28 tablet(s)
94978990	METFORMIN oral susp 100mg/ml
87772998	Metformin + rosiglitazone tabs 500mg + 2mg 112 tablet(s)
95880997	METFORMIN tabs 850mg
93167990	METFORMIN oral soln 500mg/5ml
87774998	Metformin + rosiglitazone tabs 500mg + 1mg 112 tablet(s)
94518990	METFORMIN tabs 850mg
85673998	METFORMIN oral soln 500mg/5ml
85554998	Metformin caps
95298990	METFORMIN tabs 850mg
87181998	Rosiglitazone + metformin tabs 4mg + 1000mg 56 tablet(s)

83732998	METFORMIN mr tab 750mg
95271992	Metformin hcl 850 mg tab 0
85624998	Metformin + pioglitazone tabs 850mg + 15mg 56 tablet(s)
99513990	METFORMIN tabs 500mg
94235992	Metformin hcl 500 mg tab 0
85625998	Pioglitazone + metformin tabs 15mg + 850mg tablet(s) 56
83401998	Sitagliptin + metformin (ipu) tabs 50mg + 1000mg
85555998	Metformin oral liq
83619998	METFORMIN mr tab 500mg
87165998	Metformin + rosiglitazone tabs 1000mg + 4mg 56 tablet(s)
98654990	METFORMIN tabs 850mg
95599990	METFORMIN tabs 850mg
96270990	METFORMIN tabs 500mg
87770998	ROSIGLITAZONE + METFORMIN tabs 2mg + 500mg
87166998	Metformin + rosiglitazone tabs 1000mg + 2mg 56 tablet(s)
95380990	METFORMIN tabs 850mg
87775998	Rosiglitazone + metformin tabs 1mg + 500mg 112 tablet(s)
98125990	METFORMIN tabs 500mg
95270992	METFORMIN
89155998	METFORMIN tabs 500mg
87882998	METFORMIN tabs 850mg
95299990	METFORMIN tabs 500mg
89155997	METFORMIN tabs 850mg
95880998	METFORMIN tabs 500mg
97110989	METFORMIN tabs 850mg
87883998	METFORMIN tabs 500mg
87771998	ROSIGLITAZONE + METFORMIN tabs 1mg + 500mg
94473990	METFORMIN tabs 850mg
87179998	ROSIGLITAZONE + METFORMIN tabs 4mg + 1000mg
85674998	Metformin oral soln 500mg/5ml 150 mls
96850989	METFORMIN tabs 850mg
94519990	METFORMIN tabs 500mg
98493990	METFORMIN tabs 850mg
94474990	METFORMIN tabs 500mg
83402998	Sitagliptin + metformin (ipu) tabs 50mg + 850mg
84010998	Vildagliptin + metformin tabs 50mg + 1000mg tablet(s) 60
96110990	METFORMIN tabs 850mg
96111990	METFORMIN tabs 500mg
92238997	PIOGLITAZONE tabs 30mg
88131997	NATEGLINIDE tabs 120mg
84338998	VILDAGLIPTIN tabs 50mg
88132996	Nateglinide tabs 180mg 84 tablet(s)
90048996	ROSIGLITAZONE tabs 8mg

88131996	NATEGLINIDE tabs 180mg
89763996	Rosiglitazone tabs 8mg 28 tablet(s)
84694998	EXENATIDE inj 5 micrograms
84696998	Exenatide inj 10micrograms 1 pre-filled pen
84693998	EXENATIDE inj 10micrograms
92237997	Pioglitazone tabs 30mg 28 tablet(s)
92238998	PIOGLITAZONE tabs 15mg
89763997	Rosiglitazone tabs 4mg 56 tablet(s)
98915998	Acarbose tabs 50mg 90 tablet(s)
92237998	Pioglitazone tabs 15mg 28 tablet(s)
85267998	REPAGLINIDE tabs 1mg
85266998	REPAGLINIDE tabs 2mg
99587998	GLYMIDINE SODIUM
88132997	Nateglinide tabs 120mg 84 tablet(s)
88528996	TROGLITAZONE
90048998	ROSIGLITAZONE tabs 2mg
90048997	ROSIGLITAZONE tabs 4mg
88131998	NATEGLINIDE tabs 60mg
91924997	Repaglinide tabs 1mg 90 tablet(s)
91924998	Repaglinide tabs 500 micrograms 90 tablet(s)
91923997	REPAGLINIDE tabs 1mg
89763998	ROSIGLITAZONE
97800994	Dextrostix
87884998	PIOGLITAZONE tabs 45mg
84697998	Exenatide inj 5 micrograms 1 pre-filled pen
91924996	Repaglinide tabs 2mg 90 tablet(s)
88528997	TROGLITAZONE
98475997	ACARBOSE tabs 100mg
87885998	Pioglitazone tabs 45mg 28 tablet(s)
84639998	SITAGLIPTIN tabs 100mg
85268998	REPAGLINIDE tabs 500 micrograms
88523996	TROGLITAZONE
98475998	ACARBOSE tabs 50mg
83830998	Pioglitazone oral liq
95752990	DEXTROSE INTRAVENOUSHUDDERSFIELD R.I.
91923998	REPAGLINIDE tabs 500 micrograms
91559998	GLIBORNURIDE
84341998	Vildagliptin tabs 50mg tablet(s) 56
95149997	TOLAZAMIDE
91923996	REPAGLINIDE tabs 2mg
98333994	Clinitest
88132998	Nateglinide tabs 60mg 84 tablet(s)
98915997	Acarbose tabs 100mg 90 tablet(s)
95130994	Glucotide

88523998	TROGLITAZONE
96262989	GLUCOSE
99261998	GLUCOSE
94470992	GLYMIDINE
84640998	Sitagliptin tabs 100mg 28 tablet(s)
96406998	Diazoxide tabs 50mg 100 tablet(s)
87537998	DIAZOXIDE
85521998	Diazoxide oral liq
85412998	DIAZOXIDE
94581998	Glucagon inj 1mg 1mg vial + pre-filled syringe 1
96406997	Diazoxide inj 300mg/20ml 5 ampoule(s)
99670998	DIAZOXIDE tabs 50mg
93176990	DIAZOXIDE oral susp 50mg/5ml
96638992	DIAZOXIDE
92061998	GLUCAGON inj 1mg
98896998	GLUCAGON inj 1mg
94582998	GLUCAGON inj 1mg
99669998	DIAZOXIDE inj 300mg/20ml
94581997	Glucagon inj 10mg 1 10mg vial + diluent
87184998	DIAZOXIDE BCM
94582997	GLUCAGON inj 10mg
85496994	U100 SINGLE USE INS SYR+12MM NDL30G
95414992	PHENFORMIN HYDROCHLORIDE S/R
86862994	Ascensia Autodisc
90168994	U100single use
89909994	Advantage II
93078992	BLOOD GLUCOSE TEST STRIPS
94064994	Cleanlet 25type A
97723994	Monolet Extratype A
90165994	U100single use
87322994	mhi-500
88310994	Glucoflex-R
90411994	Vitrex Gentle
90435994	U100single use
98877992	LANCET
98861992	INSULIN NEEDLES
98329994	Ketur Test
96262988	GLUCOSE
87320994	mhi-500
90147994	U100single use
90271994	U100single use
94192994	Unilet Superlitetype B
88473994	U100single use
89346998	GLUCOSE10% + KCL (HRI)

97281992	DIAGNOSTIC SOLUTION-TABLETS OF COPPER
90430994	U100single use
96253998	GUAR GUM
96253997	GUAR GUM
91577994	Medi-Test Protein 2
85888994	U100 SINGLE USE INS SYR+8MM NDLE30G 1ML
90434994	U100single use
97778994	Albym Test
90282994	Labstix
99648989	DEXTROSE
95843990	GLUCOSE10% + KCL (HRI)
97948996	GLUCOSE
85557994	MHI-500 3 MONTH CONSUMABLE KIT SIZE 7 NOZZLE
89897994	Unilet GPtype A
88219994	Medisense Soft-Sense
85560994	MHI-500 NEEDLE FREE STARTER KIT
90412994	Vitrex Softtype A
96686992	BLOOD GLUCOSE REAGENT STRIPS 1-22MMOL/L
93489994	Unilet Universal Comfortouchtype B
86574994	U100single use
87512994	Medisense Optium Plus
90429994	U100single use
94226994	Unilet Universal Comfortouchtype A&B
88370994	Syringeord purp spec16[2A]
98331994	Acetest
89661994	MicroletType A ster sgle use
96252998	GUAR GUM
88371994	Syringeord purp spec16[2A]
90148994	U100single use
90274994	U100single use
92813994	Ascensia Glucodisc
90818994	BD Ultra Pen
90169994	U100single use
98332994	Clinistix
97323994	Diabur Test 5000
88523997	TROGLITAZONE
93543992	LANCETS
90109994	Glucotrendplus
98219994	U100single use
98227994	Micro-Fine
90098994	Autopen
89760994	U100single use
85499994	Omnican 100 ins
91179994	Pocket Scan

85546994	Medisense Optium Beta-Ketone test strips
90232994	GlucoTip (Fine)type A
88218994	One Touch Ultrasofttype A
99336994	BM-Accutest
87885994	U100single use
98189994	Syringeord purp spec16[2A]
99268994	BM-Test 1-44
99733994	Syringeord purp spec16[2A]
93067992	URINE GLUCOSE TEST STRIPS
94201992	ZINC HUMAN INSULIN SUSPENSION
98229994	Unilettype B
94191994	Unilet G Superlitetype A
85889994	U100 SINGLE USE INS SYR+8MM NDLE29G 1ML
95084992	GUAR GUM
98313994	GA
87411994	mhi-5003 month
90119994	GlucoMen Sensors
97899998	GUAR GUM
88474994	U100single use
95693994	Supreme
92949994	B-D U-100single use
85558994	MHI-500 3 MONTH CONSUMABLE KIT SIZE 6 NOZZLE
85497994	U100 SINGLE USE INS SYR+12MM NDL30G
95186994	Medi-Test Glucose
92925994	U100single use
94225994	Unilet Universal Comfortouchtype A
90163994	U100single use
86020994	Softclix XLtype C
87494994	GlucoMen (Fine)type A
91326994	Fine Pointtype A
90273994	U100single use
89799994	Unilet General Purposetype A
98334994	Albustix
90444994	U100single use
93836998	DEXTROSE
87321994	mhi-500
98993990	DEXTROSE
91943994	U100single use
90819994	Autopen
90432994	U100single use
90270994	U100single use
95125994	Unilet G Superlitetype A
90164994	U100single use
98330994	Ketostix

86086994	Ascensia Microfill
93070992	BLOOD LANCETS
85498994	Omnican 50 ins
95377994	Monolettype A
87909994	Unilet Comfortouchtype A&B
87317994	Autopen 24
94063994	Cleanlet 25 XLtype B
90820994	Autopen
97322994	Glucostix
92627994	Glucotrend
89842994	Prestige Smart System
89800994	Unilet General Purposetype A
89759994	U100single use
95653992	REAGENT
92924994	U100single use
87412994	mhi-500needle free
96251998	GUAR GUM
90431994	U100single use
90166994	U100single use
92948994	B-D U-100single use
94190994	Unilet G Superlitetype A
98312994	ExacTech
96920992	REAGENT STRIPS
96051992	GUAR GUM
88227994	Freestyletype A
90272994	U100single use
98237994	Hypoguard U100click/count
96264998	GLYMIDINE SODIUM
99391994	U100single use
95305994	Diastix
95413992	PHENFORMIN HYDROCHLORIDE
85559994	MHI-500
88278994	Compact Colorimetric
90167994	U100single use
90428994	U100single use
87410994	mhi-5003 month
85851994	TrueTrack Smart System biosensor strips
95217994	Glucose VT
90332994	Supreme Spectrum
91778998	DEXTROSE INTRAVENOUSHUDDERSFIELD R.I.
95124994	Unilet G Superlitetype A
91942994	U100single use
92950994	B-D U-100single use
89801994	Unilet General PurposeSuperlite type A

90433994	U100single use
99592994	One Touch
90622994	Unilet GPtype A
94193994	Unilet Superlitetype B
98218994	U100single use
90161994	Medisense Optium
98803998	GUAR GUM
93477994	Unilet Universal Comfortouchtype B
96253996	GUAR GUM
95185994	Medi-Test Glycaemie C
90821994	Autopen
89094994	Active
90146994	U100single use
95200994	Medisense G2
95194994	Micro-Fine Plustype A
87319994	Autopen 24

10.8.3AHD codes for Diabetes Mellitus

Ahd code	Description
1009100000	Diabetes Annual Check

10.8.4Medical codes for Hypertension

Medcode	Description
14A2.00	H/O: hypertension
2126100	Hypertension resolved
212K.00	Hypertension resolved
246M.00	White coat hypertension
6146200	Hypertension induced by oral contraceptive pill
662..12	Hypertension monitoring
6627	Good hypertension control
6628	Poor hypertension control
6629	Hypertension:follow-up default
662b.00	Moderate hypertension control
662c.00	Hypertension six month review
662d.00	Hypertension annual review
662F.00	Hypertension treatm. started
662H.00	Hypertension treatm.stopped
662O.00	On treatment for hypertension
662P.00	Hypertension monitoring
7Q01.00	High cost hypertension drugs
7Q01000	Primary pulmonary hypertension drugs band 1
7Q01100	Primary pulmonary hypertension drugs band 2
7Q01200	Primary pulmonary hypertension drugs band 3
7Q01300	Primary pulmonary hypertension drugs band 4
7Q01y00	Other specified high cost hypertension drugs
7Q01z00	High cost hypertension drugs NOS
8CR4.00	Hypertension clinical management plan
8HT5.00	Referral to hypertension clinic
8I3N.00	Hypertension treatment refused
9h3..00	Exception reporting: hypertension quality indicators
9h31.00	Excepted from hypertension qual indicators: Patient unsuit
9h32.00	Excepted from hypertension qual indicators: Informed dissent
9N03.00	Seen in hypertension clinic
9N1y200	Seen in hypertension clinic
9N4L.00	DNA - Did not attend hypertension clinic
9OD..00	Hypertension screen admin.
9ODZ.00	Hypertension screen admin. NOS
9OI..00	Hypertension monitoring admin.
9OI..11	Hypertension clinic admin.
9OI1.00	Attends hypertension monitor.
9OI2.00	Refuses hypertension monitor.
9OIA.00	Hypertension monitor.chck done
9OIA.11	Hypertension monitored
F450400	Ocular hypertension
G20..00	Essential hypertension
G200.00	Malignant essential hypertension
G201.00	Benign essential hypertension
G202.00	Systolic hypertension
G203.00	Diastolic hypertension
G20z.00	Essential hypertension NOS
G20z.11	Hypertension NOS
G22z.11	Renal hypertension
G24..00	Secondary hypertension
G240.00	Secondary malignant hypertension
G240000	Secondary malignant renovascular hypertension
G240z00	Secondary malignant hypertension NOS
G241.00	Secondary benign hypertension
G241000	Secondary benign renovascular hypertension
G241z00	Secondary benign hypertension NOS
G244.00	Hypertension secondary to endocrine disorders
G24z.00	Secondary hypertension NOS
G24z000	Secondary renovascular hypertension NOS

G24z100	Hypertension secondary to drug
G24zz00	Secondary hypertension NOS
G410.00	Primary pulmonary hypertension
G41y000	Secondary pulmonary hypertension
G8y3.00	Chronic peripheral venous hypertension
Gyu2000	[X]Other secondary hypertension
Gyu2100	[X]Hypertension secondary to other renal disorders
J623.00	Portal hypertension
L12..00	Hypertension complicating pregnancy/childbirth/puerperium
L120.00	Benign essential hypertension in pregnancy/childbirth/puerp
L120000	Benign essential hypertension in preg/childb/puerp unspec
L120100	Benign essential hypertension in preg/childb/puerp - deliv
L120300	Benign essential hypertension in preg/childb/puerp-not deliv
L120400	Benign essential hypertension in preg/childb/puerp +p/n comp
L120z00	Benign essential hypertension in preg/childb/puerp NOS
L121.00	Renal hypertension in pregnancy/childbirth/puerperium
L121000	Renal hypertension in pregnancy/childbirth/puerp unspecified
L121100	Renal hypertension in pregnancy/childbirth/puerp - delivered
L121200	Renal hypertension in preg/childb/puerp -deliv with p/n comp
L121300	Renal hypertension in preg/childbirth/puerp - not delivered
L121400	Renal hypertension in preg/childb/puerp + p/n complication
L121z00	Renal hypertension in pregnancy/childbirth/puerperium NOS
L122.00	Other pre-existing hypertension in preg/childbirth/puerp
L122000	Other pre-existing hypertension in preg/childb/puerp unspec
L122100	Other pre-existing hypertension in preg/childb/puerp - deliv
L122300	Other pre-exist hypertension in preg/childb/puerp-not deliv
L122400	Other pre-exist hypertension in preg/childb/puerp + p/n comp
L122z00	Other pre-existing hypertension in preg/childb/puerp NOS
L123.00	Transient hypertension of pregnancy
L123000	Transient hypertension of pregnancy unspecified
L123100	Transient hypertension of pregnancy - delivered
L123200	Transient hypertension of pregnancy - deliv with p/n comp
L123300	Transient hypertension of pregnancy - not delivered
L123400	Transient hypertension of pregnancy + postnatal complication
L123500	Gestational hypertension
L123600	Transient hypertension of pregnancy
L123z00	Transient hypertension of pregnancy NOS
L127.00	Pre-eclampsia or eclampsia with pre-existing hypertension
L127000	Pre-eclampsia or eclampsia with hypertension unspecified
L127100	Pre-eclampsia or eclampsia with hypertension - delivered
L127200	Pre-eclampsia or eclampsia with hypertension - del+p/n comp
L127300	Pre-eclampsia or eclampsia with hypertension - not delivered
L127400	Pre-eclampsia or eclampsia with hypertension + p/n comp
L127z00	Pre-eclampsia or eclampsia + pre-existing hypertension NOS
L128.00	Pre-exist hypertension compl preg childbirth and puerperium
L12B.00	Proteinuric hypertension of pregnancy
L12z.00	Unspecified hypertension in pregnancy/childbirth/puerperium
L12z000	Unspecified hypertension in preg/childb/puerp unspecified
L12z100	Unspecified hypertension in preg/childb/puerp - delivered
L12z200	Unspecified hypertension in preg/childb/puerp -del +p/n comp
L12z300	Unspecified hypertension in preg/childb/puerp - not deliv
L12z400	Unspecified hypertension in preg/childb/puerp with p/n comp
L12zz00	Unspecified hypertension in preg/childb/puerp NOS

10.8.5AHD codes for hypertension

Ahdcode	Description
1005010500	Blood Pressure
1009315000	Target Blood pressure

10.8.6Medical Codes for BMI

Medcode	Description
22K1.00	Body Mass Index normal K/M2
22K2.00	Body Mass Index high K/M2
22K3.00	Body Mass Index low K/M2
22K4.00	Body mass index index 25-29 - overweight
22K5.00	Body mass index 30+ - obesity
22K6.00	Body mass index less than 20
22K7.00	Body mass index 40+ - severely obese
22K8.00	Body mass index 20-24 – normal

10.8.7AHD codes for BMI

1005010200	Weight

10.8.8 Medical codes for asthma

Medcode	Description
14B4.00	H/O: asthma
173A.00	Exercise induced asthma
1780.00	Aspirin induced asthma
1O2..00	Asthma confirmed
2126200	Asthma resolved
663..11	Asthma monitoring
663N.00	Asthma disturbing sleep
663N000	Asthma causing night waking
663N100	Asthma disturbs sleep weekly
663N200	Asthma disturbs sleep frequently
663O.00	Asthma not disturbing sleep
663O000	Asthma never disturbs sleep
663P.00	Asthma limiting activities
663Q.00	Asthma not limiting activities
663U.00	Asthma management plan given
663V.00	Asthma severity
663V000	Occasional asthma
663V100	Mild asthma
663V200	Moderate asthma
663V300	Severe asthma
663W.00	Asthma prophylactic medication used
663d.00	Emergency asthma admission since last appointment
663e.00	Asthma restricts exercise
663e000	Asthma sometimes restricts exercise
663e100	Asthma severely restricts exercise
663f.00	Asthma never restricts exercise
663h.00	Asthma - currently dormant
663j.00	Asthma - currently active
663m.00	Asthma accident and emergency attendance since last visit
663n.00	Asthma treatment compliance satisfactory
663p.00	Asthma treatment compliance unsatisfactory
663q.00	Asthma daytime symptoms
663r.00	Asthma causes night symptoms 1 to 2 times per month
663s.00	Asthma never causes daytime symptoms
663t.00	Asthma causes daytime symptoms 1 to 2 times per month
663u.00	Asthma causes daytime symptoms 1 to 2 times per week
663v.00	Asthma causes daytime symptoms most days
663w.00	Asthma limits walking up hills or stairs
663x.00	Asthma limits walking on the flat
663y.00	Number of asthma exacerbations in past year
66Y5.00	Change in asthma management plan
66Y9.00	Step up change in asthma management plan
66YA.00	Step down change in asthma management plan
66YC.00	Absent from work or school due to asthma
66YE.00	Asthma monitoring due
66YJ.00	Asthma annual review
66YK.00	Asthma follow-up
66YP.00	Asthma night-time symptoms
66YQ.00	Asthma monitoring by nurse
66YR.00	Asthma monitoring by doctor
8791.00	Further asthma - drug prevent.
8793.00	Asthma control step 0
8794.00	Asthma control step 1
8795.00	Asthma control step 2
8796.00	Asthma control step 3
8797.00	Asthma control step 4
8798.00	Asthma control step 5
8B3j.00	Asthma medication review
8H2P.00	Emergency admission, asthma
9OJA.11	Asthma monitored
H312000	Chronic asthmatic bronchitis
H33..00	Asthma
H33..11	Bronchial asthma
H330.00	Extrinsic (atopic) asthma
H330.11	Allergic asthma
H330.12	Childhood asthma
H330.13	Hay fever with asthma
H330.14	Pollen asthma
H330000	Extrinsic asthma without status asthmaticus
H330011	Hay fever with asthma
H330100	Extrinsic asthma with status asthmaticus
H330111	Extrinsic asthma with asthma attack
H330z00	Extrinsic asthma NOS
H331.00	Intrinsic asthma
H331.11	Late onset asthma
H331000	Intrinsic asthma without status asthmaticus
H331100	Intrinsic asthma with status asthmaticus
H331111	Intrinsic asthma with asthma attack
H331z00	Intrinsic asthma NOS
H332.00	Mixed asthma
H333.00	Acute exacerbation of asthma
H33z.00	Asthma unspecified
H33z000	Status asthmaticus NOS
H33z011	Severe asthma attack
H33z100	Asthma attack

H33z111	Asthma attack NOS
H33z200	Late-onset asthma
H33zz00	Asthma NOS
H33zz11	Exercise induced asthma
H33zz12	Allergic asthma NEC
H35y600	Sequoiosis (red-cedar asthma)
H35y700	Wood asthma
H47y000	Detergent asthma

10.8.9 Multilex drug codes for Asthma

MULTILEX EID	GENERIC NAME
87105998	IPRATROPIUM BROMIDE
87107998	IPRATROPIUM BROMIDE
87108998	IPRATROPIUM BROMIDE
87109998	IPRATROPIUM BROMIDE
87125998	IPRATROPIUM BROMIDE
87126998	IPRATROPIUM BROMIDE
87127998	IPRATROPIUM BROMIDE
87128998	IPRATROPIUM BROMIDE
87173998	BECLOMETASONE
87174998	BECLOMETASONE
87275998	SALBUTAMOL
87276998	SALBUTAMOL
87277998	SALBUTAMOL
87438998	BUDESONIDE
87439998	BUDESONIDE REFILLABLE
87513998	IPRATROPIUM BROMIDE
87514998	IPRATROPIUM BROMIDE
87597998	MONTELUKAST(AS SODIUM SALT)
87601998	MONTELUKAST(AS SODIUM SALT)
87704998	CORTISONE ACETATE
87878998	TERBUTALINE
87928998	THEOPHYLLINE
87929998	THEOPHYLLINE
87930998	THEOPHYLLINE
87950998	HYDROCORTISONE
87979998	SALMETEROL+ FLUTICASONE
87980996	SALMETEROL+ FLUTICASONE
87980997	SALMETEROL+ FLUTICASONE
87980998	SALMETEROL+ FLUTICASONE
87986997	BECLOMETASONEEXTRAFINE PARTICLE
87986998	BECLOMETASONEEXTRAFINE PARTICLE
87988997	BECLOMETASONEEXTRAFINE PARTICLE
87988998	BECLOMETASONEEXTRAFINE PARTICLE
87990997	BECLOMETASONEEXTRAFINE PARTICLE
87990998	BECLOMETASONEEXTRAFINE PARTICLE
87991997	BECLOMETASONEEXTRAFINE PARTICLE
87991998	BECLOMETASONEEXTRAFINE PARTICLE
88004998	SALBUTAMOL
88095998	ZAFIRLUKAST
88102998	ZAFIRLUKAST

88156998	BUDESONIDE
88262998	SALBUTAMOL
88273998	IPRATROPIUM BROMIDE
88299998	IPRATROPIUM BROMIDE
88305997	BUDESONIDEWITH FORMOTEROL
88305998	BUDESONIDEWITH FORMOTEROL
88342998	MONTELUKAST(AS SODIUM SALT)
88351996	MONTELUKAST(AS SODIUM SALT)
88351997	MONTELUKAST(AS SODIUM SALT)
88351998	MONTELUKAST(AS SODIUM SALT)
88352997	MONTELUKAST(AS SODIUM SALT)
88352998	MONTELUKAST(AS SODIUM SALT)
88357998	SALBUTAMOL
88434996	BECLOMETASONE
88434997	BECLOMETASONE
88434998	BECLOMETASONE
88469996	BECLOMETASONE
88469997	BECLOMETASONE
88469998	BECLOMETASONE
88470998	SALBUTAMOL
88480997	SALBUTAMOL
88480998	SALBUTAMOL
88487998	FORMOTEROL FUMARATE
88488998	FORMOTEROL FUMARATE
88490997	FORMOTEROL FUMARATE
88490998	FORMOTEROL FUMARATE
88522998	SALMETEROL+ FLUTICASONE
88524996	FLUTICASONE+ SALMETEROL
88524997	FLUTICASONE+ SALMETEROL
88524998	FLUTICASONE+ SALMETEROL
88525996	SALMETEROL+ FLUTICASONE
88525997	SALMETEROL+ FLUTICASONE
88525998	SALMETEROL+ FLUTICASONE
88706997	EPHEDRINE
88706998	EPHEDRINE
88727998	MOMETASONE FUROATE
88832998	BECLOMETASONE
88833997	BECLOMETASONE
88833998	BECLOMETASONE
88834998	SALBUTAMOL
89060998	SALBUTAMOL
89121998	BUDESONIDE
89178998	SALBUTAMOL
89229998	MOMETASONE FUROATE
89235998	TIOTROPIUM
89275998	SALBUTAMOL
89276996	BECLOMETASONE
89276997	BECLOMETASONE
89276998	BECLOMETASONE
89286998	SODIUM CROMOGLICATE
89347998	SALBUTAMOL
89443996	DEFLAZACORT
89443997	DEFLAZACORT
89443998	DEFLAZACORT
89446996	DEFLAZACORT
89446997	DEFLAZACORT
89446998	DEFLAZACORT
89862996	BECLOMETASONE
89862997	BECLOMETASONE
89862998	BECLOMETASONE
90394997	BUDESONIDEWITH FORMOTEROL
90394998	BUDESONIDEWITH FORMOTEROL
90416996	BECLOMETASONE
90416997	BECLOMETASONE
90416998	BECLOMETASONE
90417996	BECLOMETASONE
90417997	BECLOMETASONE
90417998	BECLOMETASONE
90418998	SALBUTAMOL
90419998	SALBUTAMOL
90587998	SALBUTAMOL
90588998	BECLOMETASONE
90680998	SALBUTAMOL+ IPRATROPIUM BR
90758998	MOMETASONE FUROATE
90927998	THEOPHYLLINE+GUAIFEN &EPHEDRINE
90929998	THEOPHYLLINE+GUAIFEN &EPHEDRINE
90942998	FORMOTEROL FUMARATE
90943998	FORMOTEROL FUMARATE
90968998	MOMETASONE FUROATE
91078998	FENOTEROL+ IPRATROPIUM BR
91088996	BECLOMETASONE
91088997	BECLOMETASONE
91088998	BECLOMETASONE
91107998	SALBUTAMOL+ IPRATROPIUM BR
91272998	SALBUTAMOL
91284997	SALBUTAMOL
91284998	SALBUTAMOL
91285998	AMINOPHYLLINE

91310998	IPRATROPIUM BROMIDE+ SALBUTAMOL
91311998	IPRATROPIUM BROMIDE+ SALBUTAMOL
91320998	SALBUTAMOL
91322997	FLUTICASONE
91322998	FLUTICASONE
91334997	FLUTICASONE
91334998	FLUTICASONE
91335998	SALBUTAMOL
91345998	SALBUTAMOL
91348998	SALMETEROL+ FLUTICASONE
91363996	BECLOMETASONE
91363997	BECLOMETASONE
91363998	BECLOMETASONE
91387998	BECLOMETASONE
91390997	AMINOPHYLLINE
91390998	AMINOPHYLLINE
91397998	SALBUTAMOL
91403996	BECLOMETASONE
91403997	BECLOMETASONE
91403998	BECLOMETASONE
91417998	SALBUTAMOL
91493998	BUDESONIDEWITH FORMOTEROL
91547998	SALMETEROL+ FLUTICASONE
91570997	SALBUTAMOL
91570998	SALBUTAMOL
91619996	FLUTICASONE
91619997	FLUTICASONE
91619998	FLUTICASONE
91646998	DEXAMETHASONE
92199998	SALMETEROL+ FLUTICASONE
92285996	BECLOMETASONE
92285997	BECLOMETASONE
92285998	BECLOMETASONE
92411998	BUDESONIDEWITH FORMOTEROL
92412998	HYDROCORTISONE
92473996	FLUTICASONE
92473997	FLUTICASONE
92473998	FLUTICASONE
92665998	IPRATROPIUM BROMIDE
92755998	IPRATROPIUM BROMIDE+ SALBUTAMOL
92756998	IPRATROPIUM BROMIDE+ SALBUTAMOL
92810997	DEXAMETHASONE
92810998	DEXAMETHASONE
92842996	FLUTICASONE
92842997	FLUTICASONE
92842998	FLUTICASONE
92843998	FLUTICASONE
92844998	FLUTICASONE
92845996	FLUTICASONE
92845997	FLUTICASONE
92845998	FLUTICASONE
92861998	BETAMETHASONE SODIUM PHOSPHATE
92894998	FENOTEROL+ IPRATROPIUM BR
92895998	IPRATROPIUM BROMIDE
92899996	FLUTICASONE
92899997	FLUTICASONE
92899998	FLUTICASONE
92900996	FLUTICASONE
92900997	FLUTICASONE
92900998	FLUTICASONE
93017992	SODIUM CROMOGLYCATE
93035992	SODIUM CROMOGLYCATE NEBULISER SOLUTION
93056996	FLUTICASONE
93056997	FLUTICASONE
93056998	FLUTICASONE
93057996	FLUTICASONE
93057997	FLUTICASONE
93057998	FLUTICASONE
93065998	SODIUM CROMOGLICATE
93066996	BECLOMETASONE
93066997	BECLOMETASONE
93066998	BECLOMETASONE
93075998	PREDNISOLONE SODIUM PHOSPHATE
93083997	BAMBUTEROL
93083998	BAMBUTEROL
93084997	BAMBUTEROL
93084998	BAMBUTEROL
93086992	SALBUTAMOL (ALBUTEROL)
93123992	SALBUTAMOL (ALBUTEROL) SULPHATE
93154998	TERBUTALINE
93181996	SALMETEROL
93181997	SALMETEROL
93181998	SALMETEROL
93182996	SALMETEROL
93182997	SALMETEROL
93182998	SALMETEROL
93264998	THEOPHYLLINE+ EPHEDRINE
93302996	BUDESONIDE

93302997	BUDESONIDE
93302998	BUDESONIDE
93303996	BUDESONIDE
93303997	BUDESONIDE
93303998	BUDESONIDE
93326992	BECLOMETHASONE/SALBUTAMOL(ALBUT)100/400
93350998	THEOPHYLLINE+ EPHEDRINE
93411992	AMINOPHYLLINE
93439998	TERBUTALINE
93440998	TERBUTALINE
93457998	TIOTROPIUM
93584998	THEOPHYLLINE
93588998	HYDROCORTISONE NA SUCCINATE
93620992	BECLOMETHASONE DIPROPRIONATE CARTRIDGE
93621992	BECLOMETHASONE DIPROPRIONATE CARTRIDGE
93643992	BETAMETHASONE VALERATE
93645992	BETAMETHASONE
93646992	BETAMETHASONE
93647992	BETAMETHASONE
93650992	BETAMETHASONE VALERATE
93684997	IPRATROPIUM BROMIDE
93684998	IPRATROPIUM BROMIDE
93685997	IPRATROPIUM BROMIDE
93685998	IPRATROPIUM BROMIDE
93697997	ORCIPRENALINE
93697998	ORCIPRENALINE
93731997	SODIUM CROMOGLICATE+ SALBUTAMOL
93731998	SODIUM CROMOGLICATE+ SALBUTAMOL
93732997	SODIUM CROMOGLICATE+ SALBUTAMOL
93732998	SODIUM CROMOGLICATE+ SALBUTAMOL
93754992	AMINOPHYLLINE
93783998	EPHEDRINE
93912996	PREDNISOLONE
93912997	PREDNISOLONE
93912998	PREDNISOLONE
93941996	TERBUTALINE
93941997	TERBUTALINE
93941998	TERBUTALINE
93983996	FLUTICASONE+ SALMETEROL
93983997	FLUTICASONE+ SALMETEROL
93983998	FLUTICASONE+ SALMETEROL
94002992	TERBUTALINE SULPHATE NEBULE
94023998	EPHEDRINE HYDROCHLORIDE
94024996	EPHEDRINE HYDROCHLORIDE
94024997	EPHEDRINE HYDROCHLORIDE
94024998	EPHEDRINE HYDROCHLORIDE
94027992	EPHEDRINE HCL/THEOPHYLLINE
94041997	AMINOPHYLLINE
94041998	AMINOPHYLLINE
94063992	AMINOPHYLLINE
94066992	AMINOPHYLLINE
94134992	DEXAMETHASONE
94199998	SALBUTAMOL
94251994	Salbutamol Cyclohalertype 5
94259998	SALBUTAMOL
94260996	SALBUTAMOL
94260997	SALBUTAMOL
94260998	SALBUTAMOL
94324992	BUDESONIDE REFILL
94334992	CHOLINE THEOPHYLLINATE
94343992	SODIUM CROMOGLYCATE
94373992	TRIAMCINOLONE
94383996	SALBUTAMOL
94383997	SALBUTAMOL
94383998	SALBUTAMOL
94405992	AMINOPHYLLINE
94406992	AMINOPHYLLINE
94407997	SALBUTAMOL
94407998	SALBUTAMOL
94435998	AMINOPHYLLINE
94442992	CORTISONE ACETATE
94442996	SALBUTAMOL
94442997	SALBUTAMOL
94442998	SALBUTAMOL
94455997	SALBUTAMOL
94455998	SALBUTAMOL
94456996	BECLOMETASONE
94456997	BECLOMETASONE
94456998	BECLOMETASONE
94491997	IPRATROPIUM BROMIDE
94491998	IPRATROPIUM BROMIDE
94492997	IPRATROPIUM BROMIDE
94492998	IPRATROPIUM BROMIDE
94529998	SALBUTAMOL
94532996	SALBUTAMOL
94532997	SALBUTAMOL
94532998	SALBUTAMOL
94533996	SALBUTAMOL

94533997	SALBUTAMOL
94533998	SALBUTAMOL
94534998	SALBUTAMOLRONDO
94544992	SALBUTAMOL (ALBUTEROL) INHALER
94557996	BECLOMETASONE
94557997	BECLOMETASONE
94557998	BECLOMETASONE
94558996	BECLOMETASONE
94558997	BECLOMETASONE
94558998	BECLOMETASONE
94559996	BECLOMETASONE
94559997	BECLOMETASONE
94559998	BECLOMETASONE
94585990	IPRATROPIUM BROMIDE
94586990	IPRATROPIUM BROMIDE
94587990	IPRATROPIUM BROMIDE
94587992	SALBUTAMOL (ALBUTEROL) REFILL
94588990	IPRATROPIUM BROMIDE
94597992	SALBUTAMOL (ALBUTEROL)
94624992	ORCIPRENALINE SULPHATE
94624998	THEOPHYLLINE+ LYSINE
94625998	SALMETEROL+ FLUTICASONE
94627997	THEOPHYLLINE+ EPHEDRINE HCL
94627998	THEOPHYLLINE+ EPHEDRINE HCL
94628992	AMINOPHYLLINE/EPHEDRINE/AMYLOBARBITONE
94628998	THEOPHYLLINE+ LYSINE
94630992	AMINOPHYLLINE
94632992	AMINOPHYLLINE
94633992	AMINOPHYLLINE
94634992	AMINOPHYLLINE
94635992	AMINOPHYLLINE
94658992	EPHEDRINE RESINATE/THEOPHYLLINE
94736992	TERBUTALINE SULPHATE/GUAPHENESIN
94833998	SALBUTAMOL
94840997	SALBUTAMOL
94840998	SALBUTAMOL
94846997	SALBUTAMOL
94846998	SALBUTAMOL
94847996	BECLOMETASONE
94847997	BECLOMETASONE
94847998	BECLOMETASONE
94849997	SALBUTAMOL+BECLOMETASONE
94849998	SALBUTAMOL+BECLOMETASONE
94853992	SALBUTAMOL (ALBUTEROL)

94861997	SALBUTAMOL
94861998	SALBUTAMOL
94862998	SALBUTAMOL
94870992	CORTISONE ACETATE
94908992	DEXAMETHASONE
94909992	DEXAMETHASONE
94941996	SALBUTAMOL+BECLOMETASONE
94941997	SALBUTAMOL+BECLOMETASONE
94941998	SALBUTAMOL+BECLOMETASONE
94943996	SALBUTAMOL
94943997	SALBUTAMOL
94943998	SALBUTAMOL
94944997	SALBUTAMOL
94944998	SALBUTAMOL
94963992	EPHEDRINE HCL 24MG/THEOPHYLLINE 120MG
94969992	EPHEDRINE HCL/THEOPHYLLINE 48/180MG S/R
95036992	EPHEDRINE/THEOPHYLLINE
95062998	AMINOPHYLLINE+DRIED AL HYDROX GEL
95063997	AMINOPHYLLINE
95063998	AMINOPHYLLINE
95111998	BECLOMETASONE
95124992	HYDROCORTISONE
95139997	TRIAMCINOLONE
95139998	TRIAMCINOLONE
95140990	CORTISONE ACETATE
95162990	BECLOMETASONE
95163990	BECLOMETASONE
95164990	BECLOMETASONE
95179998	THEOPHYLLINE
95180998	THEOPHYLLINE+PHENOBARB &GUAIFEN
95181998	THEOPHYLLINE+ EPHEDRINE SULPHATE
95182998	THEOPHYLLINE+ EPHEDRINE HCL
95183998	THEOPHYLLINE
95184996	THEOPHYLLINE
95184997	THEOPHYLLINE
95184998	THEOPHYLLINE
95185996	THEOPHYLLINE
95185997	THEOPHYLLINE
95185998	THEOPHYLLINE
95186996	THEOPHYLLINE
95186997	THEOPHYLLINE
95186998	THEOPHYLLINE
95187996	THEOPHYLLINE
95187997	THEOPHYLLINE

95187998	THEOPHYLLINE
95188998	THEOPHYLLINE
95195992	THEOPHYLLINE/ LYSINE
95210998	TERBUTALINE
95211997	TERBUTALINE+ GUAIFENESIN
95211998	TERBUTALINE+ GUAIFENESIN
95212997	TERBUTALINE
95212998	TERBUTALINE
95213997	TERBUTALINE
95213998	TERBUTALINE
95214996	TERBUTALINE
95214997	TERBUTALINE
95214998	TERBUTALINE
95243990	SALBUTAMOL
95306998	SALBUTAMOL
95357992	DEXAMETHASONE
95416998	PREDNISOLONESTEAGLATE
95417996	PREDNISOLONE
95417997	PREDNISOLONE
95417998	PREDNISOLONE
95441992	AMINOPHYLLINE
95484992	PREDNISOLONE E/C
95487992	PREDNISOLONE
95492992	PREDNISOLONE
95492997	BUDESONIDE
95492998	BUDESONIDE
95493992	PREDNISOLONE
95493997	BUDESONIDE
95493998	BUDESONIDE
95526992	BUDESONIDE
95527992	BUDESONIDE REFILL
95528992	BUDESONIDE
95536990	BECLOMETASONE
95571990	IPRATROPIUM BROMIDE
95593990	PREDNISOLONE
95594990	PREDNISOLONE
95651992	EPHEDRINE HC/THEOPHYLLINE/PHENOBARBITONE
95652992	EPHEDRINE HYDROCHLORIDE/THEOPHYLLINE
95658992	TERBUTALINE SULPHATE/GUAIPHENESIN
95676998	ORCIPRENALINE
95677997	ORCIPRENALINE
95677998	ORCIPRENALINE
95722992	SALBUTAMOL (ALBUTEROL) S/R
95750998	NEDOCROMIL SODIUM

95812992	SODIUM CROMOGLYCATE
95847996	METHYLPREDNISOLONE
95847997	METHYLPREDNISOLONE
95847998	METHYLPREDNISOLONE
95851996	METHYLPREDNISOLONE
95851997	METHYLPREDNISOLONE
95851998	METHYLPREDNISOLONE
95912990	PREDNISOLONE
95913990	CORTISONE ACETATE
95938996	BUDESONIDE
95938997	BUDESONIDE
95938998	BUDESONIDE
95967998	BETAMETHASONE
95982990	BUDESONIDE
95983990	BUDESONIDE
95983996	BECLOMETASONE+ SALBUTAMOL
95983997	BECLOMETASONE+ SALBUTAMOL
95983998	BECLOMETASONE+ SALBUTAMOL
95998992	SODIUM CROMOGLYCATE COMPLETE UNIT
96025990	SALBUTAMOL
96026990	SALBUTAMOL
96027990	BECLOMETASONE
96028990	BECLOMETASONE
96029990	BECLOMETASONE
96041992	FLUTICASONE PROPIONATE DISCS
96089992	SALBUTAMOL (ALBUTEROL)
96089998	ISOPRENALINE SULPHATE+SODIUM CROMOGLICATE
96101992	EPHEDRINE HYDROCHLORIDE S/F
96102990	SALBUTAMOL
96108992	AMINOPHYLLINE
96110997	IPRATROPIUM BROMIDE+FENOTEROL HYDROBROM
96110998	IPRATROPIUM BROMIDE+FENOTEROL HYDROBROM
96111996	IPRATROPIUM BROMIDE
96111997	IPRATROPIUM BROMIDE
96111998	IPRATROPIUM BROMIDE
96112998	IPRATROPIUM BROMIDE
96113997	IPRATROPIUM BROMIDE
96113998	IPRATROPIUM BROMIDE
96130990	BECLOMETASONE
96131990	BECLOMETASONE
96132990	BECLOMETASONE
96143997	HYDROCORTISONE
96143998	HYDROCORTISONE
96146990	TERBUTALINE

96165990	SALBUTAMOL
96177992	PREDNISONE
96181992	DEXAMETHASONE
96182992	DEXAMETHASONE
96219992	EPHEDRINE
96222992	EPHEDRINE 15MG/THEOPHYLLINE 120MG
96223992	EPHEDRINE HCL/AMINOPHYLLINE 25/130/MG
96224992	EPHEDRINE
96226992	EPHEDRINE HCL 50MG/THEOPHYLLINE 65MG
96269992	HYDROCORTISONE PELLETS
96361989	PREDNISOLONE
96361990	PREDNISOLONE
96372992	ORCIPRENALINE SULPHATE
96402990	PREDNISOLONE
96403997	AMINOPHYLLINE
96403998	AMINOPHYLLINE
96409992	PREDNISOLONE
96410992	PREDNISONE
96411992	PREDNISOLONE
96425990	SALBUTAMOL
96431997	DEXAMETHASONE
96431998	DEXAMETHASONE
96488992	THEOPHYLLINE
96489992	THEOPHYLLINE
96490992	THEOPHYLLINE
96506992	SALBUTAMOL (ALBUTEROL)
96507992	SALBUTAMOL (ALBUTEROL)
96553997	FENOTEROL+ IPRATROPIUM BR
96553998	FENOTEROL+ IPRATROPIUM BR
96554996	FENOTEROL
96554997	FENOTEROL
96554998	FENOTEROL
96557992	SALBUTAMOL (ALBUTEROL)
96564990	SALBUTAMOL
96577990	PREDNISOLONE SODIUM PHOSPHATE
96578992	TRIAMCINOLONE ACETONIDE
96580992	AMINOPHYLLINE
96581992	AMINOPHYLLINE
96603997	CORTISONE ACETATE
96603998	CORTISONE ACETATE
96626988	BECLOMETASONE
96626989	BECLOMETASONE
96626990	BECLOMETASONE
96628990	SALBUTAMOL
96629992	PREDNISOLONE
96631992	PREDNISONE
96642989	AMINOPHYLLINE
96642990	AMINOPHYLLINE
96675998	CHOLINE THEOPHYLLINATE
96676998	CHOLINE THEOPHYLLINATE
96677996	CHOLINE THEOPHYLLINATE
96677997	CHOLINE THEOPHYLLINATE
96677998	CHOLINE THEOPHYLLINATE
96692990	SALBUTAMOL
96733996	SODIUM CROMOGLICATE
96733997	SODIUM CROMOGLICATE
96733998	SODIUM CROMOGLICATE
96734996	SODIUM CROMOGLICATE
96734997	SODIUM CROMOGLICATE
96734998	SODIUM CROMOGLICATE
96735998	SODIUM CROMOGLICATE+ ISOPRENALINE
96736998	SODIUM CROMOGLICATE
96743992	PREDNISONE
96744992	PREDNISOLONE
96765990	IPRATROPIUM BROMIDE
96766992	SODIUM CROMOGLYCATE INSUF CARTRIDGES
96792990	SALBUTAMOL
96798992	CHOLINE THEOPHYLLINATE
96804992	TERBUTALINE RESPULES FOR NEBULISATION
96835988	SALBUTAMOL
96835989	SALBUTAMOL
96835990	SALBUTAMOL
96842992	SALBUTAMOL (ALBUTEROL) SULPHATE/NEB SOLN
96884992	FLUTICASONE PROPIONATE DISCS
96885990	IPRATROPIUM BROMIDE
96885992	FLUTICASONE PROPIONATE DISCS
96888992	SALBUTAMOL (ALBUTEROL)
96926992	SODIUM CROMOGLYCATE/SPACER
96935988	BECLOMETASONE
96935989	BECLOMETASONE
96935990	BECLOMETASONE
96938990	AMINOPHYLLINE
96940992	AMINOPHYLLINE
96988992	TERBUTALINE SULPHATE
96989992	TERBUTALINE SULPHATE RESPULES 5MG/2ML
97006988	BECLOMETASONE
97006989	BECLOMETASONE
97006990	BECLOMETASONE

97013992	CAFFEINE/EPHEDRINE
97085997	SALBUTAMOL
97085998	SALBUTAMOL
97088998	EPHEDRINE
97098989	SALBUTAMOL
97098990	SALBUTAMOL
97101989	PREDNISOLONE
97101990	PREDNISOLONE
97121997	SALBUTAMOL
97121998	SALBUTAMOL
97137992	CHOLINE THEOPHYLLINATE
97147998	PREDNISOLONE
97148997	PREDNISOLONE
97148998	PREDNISOLONE
97149997	PREDNISONE
97149998	PREDNISONE
97155997	PREDNISOLONE
97155998	PREDNISOLONE
97156997	PREDNISONE
97156998	PREDNISONE
97163997	AMINOPHYLLINE
97163998	AMINOPHYLLINE
97164997	AMINOPHYLLINE
97164998	AMINOPHYLLINE
97172996	NEDOCROMIL SODIUM
97172997	NEDOCROMIL SODIUM
97172998	NEDOCROMIL SODIUM
97177990	TERBUTALINE
97203992	CORTISONE ACETATE
97237992	PREDNISOLONE ACETATE
97238992	PREDNISOLONE ACETATE
97240992	PREDNISOLONE
97242998	TERBUTALINE
97243992	DEXAMETHASONE
97253996	THEOPHYLLINE
97253997	THEOPHYLLINE
97253998	THEOPHYLLINE
97255988	BECLOMETASONE
97255989	BECLOMETASONE
97255990	BECLOMETASONE
97334998	IPRATROPIUM BROMIDE
97354992	EPHEDRINE HCL/BUTETHAMATE CITRATE
97356992	EPHEDRINE 11MG/THEOPHYLLINE 120MG
97357992	EPHEDRINE/GUAIPHEN/PHENOBAR/THEOPHYLLINE
97358992	EPHEDRINE HCL/AMINOPHYLLINE E/C
97359992	EPHEDRINE
97391997	THEOPHYLLINE+ EPHEDRINE HCL
97391998	THEOPHYLLINE+ EPHEDRINE HCL
97418992	FENOTEROL HYDROBROMIDE
97419992	FENOTEROL HYDROBROMIDE COMPLETE UNIT
97436998	PREDNISOLONE
97463998	SALBUTAMOL
97484998	SALBUTAMOL
97485997	SALBUTAMOL
97485998	SALBUTAMOL
97492997	HYDROCORTISONE
97492998	HYDROCORTISONE
97502998	DEXAMETHASONE
97517997	BECLOMETASONE
97517998	BECLOMETASONE
97583992	HYDROCORTISONE
97585998	SALBUTAMOL
97586997	SALBUTAMOL
97586998	SALBUTAMOL
97672997	FLUTICASONE
97672998	FLUTICASONE
97680997	FLUTICASONE
97680998	FLUTICASONE
97698998	BECLOMETASONE
97726990	PREDNISOLONE
97740992	METHYLPREDNISOLONE
97758997	SALBUTAMOL
97758998	SALBUTAMOL
97778997	SALBUTAMOL
97778998	SALBUTAMOL
97779998	SODIUM CROMOGLICATE
97791990	AMINOPHYLLINE
97822990	IPRATROPIUM BROMIDE
97829998	METHYLPREDNISOLONE
97832998	METHYLPREDNISOLONE
97862998	SODIUM CROMOGLICATE
97872996	BECLOMETASONE
97872997	BECLOMETASONE
97872998	BECLOMETASONE
97929990	PREDNISOLONE
97933990	TERBUTALINE
97942992	PREDNISONE
97943992	PREDNISONE

97950998	SODIUM CROMOGLICATE
97967989	SALBUTAMOL
97967990	SALBUTAMOL
98046990	SALBUTAMOL
98057996	EPHEDRINE
98057997	EPHEDRINE
98057998	EPHEDRINE
98072990	DEXAMETHASONE
98100990	THEOPHYLLINE
98101996	AMINOPHYLLINE
98101997	AMINOPHYLLINE
98101998	AMINOPHYLLINE
98107990	PREDNISOLONE
98167988	SALBUTAMOL
98167989	SALBUTAMOL
98167990	SALBUTAMOL
98169992	THEOPHYLLINE/NOSCAPINE
98170992	THEOPHYLLINE 100MG/LYSINE 74MG
98171992	THEOPHYLLINE
98172992	THEOPHYLLINE
98208990	AMINOPHYLLINE
98219990	AMINOPHYLLINE
98223996	SODIUM CROMOGLICATE
98223997	SODIUM CROMOGLICATE
98223998	SODIUM CROMOGLICATE
98277998	IPRATROPIUM BROMIDE
98288998	BECLOMETASONE
98326997	TRIAMCINOLONE
98326998	TRIAMCINOLONE
98332996	BECLOMETASONE
98332997	BECLOMETASONE
98332998	BECLOMETASONE
98333990	AMINOPHYLLINE
98394998	BETAMETHASONE SODIUM PHOSPHATE
98438990	SALBUTAMOL
98439990	SALBUTAMOL
98440990	SALBUTAMOL
98441988	SALBUTAMOL
98441989	SALBUTAMOL
98441990	SALBUTAMOL
98442990	SALBUTAMOL
98455990	PREDNISOLONE
98456988	PREDNISOLONE
98456989	PREDNISOLONE
98456990	PREDNISOLONE
98514997	PREDNISOLONE
98514998	PREDNISOLONE
98561990	EPHEDRINE
98562997	PREDNISOLONE
98562998	PREDNISOLONE
98580998	SALBUTAMOL+BECLOMETASONE
98586998	SALBUTAMOL
98588998	BECLOMETASONE
98590996	BECLOMETASONE
98590997	BECLOMETASONE
98590998	BECLOMETASONE
98595997	BUDESONIDE
98595998	BUDESONIDE
98596997	BUDESONIDE
98596998	BUDESONIDE
98601998	TERBUTALINE+ GUAIFENESIN
98602998	TERBUTALINE
98615998	THEOPHYLLINE
98623998	THEOPHYLLINE
98644989	DEXAMETHASONE
98644990	DEXAMETHASONE
98659996	SALBUTAMOL
98659997	SALBUTAMOL
98659998	SALBUTAMOL
98718998	SODIUM CROMOGLICATE+ ISOPRENALINE
98724997	DEXAMETHASONE
98724998	DEXAMETHASONE
98804998	SALBUTAMOL
98805998	SALBUTAMOL
98806996	SALBUTAMOL
98806997	SALBUTAMOL
98806998	SALBUTAMOL
98808998	THEOPHYLLINE
98809998	THEOPHYLLINE
98810998	THEOPHYLLINE
98887996	BUDESONIDE
98887997	BUDESONIDE
98887998	BUDESONIDE
98934998	THEOPHYLLINE+ EPHEDRINE HCL
98975997	SALBUTAMOL
98975998	SALBUTAMOL
98976998	SALBUTAMOL
98977996	SALBUTAMOL

98977997	SALBUTAMOL
98977998	SALBUTAMOL
98978997	SALBUTAMOL
98978998	SALBUTAMOL
98979996	SALBUTAMOL
98979997	SALBUTAMOL
98979998	SALBUTAMOL
98981996	SALBUTAMOL
98981997	SALBUTAMOL
98981998	SALBUTAMOL
99003996	THEOPHYLLINE
99003997	THEOPHYLLINE
99003998	THEOPHYLLINE
99013992	SALBUTAMOL (ALBUTEROL)
99050997	THEOPHYLLINE
99050998	THEOPHYLLINE
99051998	AMINOPHYLLINE+DRIED AL HYDROX GEL
99060989	PREDNISONE
99060990	PREDNISONE
99061989	PREDNISONE
99061990	PREDNISONE
99062990	PREDNISONE
99098989	PREDNISONE
99098990	PREDNISONE
99099988	PREDNISOLONE
99099989	PREDNISOLONE
99099990	PREDNISOLONE
99100989	PREDNISOLONE
99100990	PREDNISOLONE
99134996	THEOPHYLLINE
99134997	THEOPHYLLINE
99134998	THEOPHYLLINE
99137998	PREDNISOLONESTEAGLATE
99163998	AMINOPHYLLINE
99214990	EPHEDRINE
99226998	PREDNISOLONE SODIUM PHOSPHATE
99228997	PREDNISOLONE
99228998	PREDNISOLONE
99254998	IPRATROPIUM BROMIDE+FENOTEROL HYDROBROM
99256998	IPRATROPIUM BROMIDE+FENOTEROL HYDROBROM
99326992	SODIUM CROMOGLYCATE
99336998	THEOPHYLLINE
99393988	SALBUTAMOL
99393989	SALBUTAMOL
99393990	SALBUTAMOL
99394988	SALBUTAMOL
99394989	SALBUTAMOL
99394990	SALBUTAMOL
99395988	SALBUTAMOL
99395989	SALBUTAMOL
99395990	SALBUTAMOL
99396988	SALBUTAMOL
99396989	SALBUTAMOL
99396990	SALBUTAMOL
99397988	SALBUTAMOL
99397989	SALBUTAMOL
99397990	SALBUTAMOL
99423988	PREDNISOLONE
99423989	PREDNISOLONE
99423990	PREDNISOLONE
99424989	PREDNISOLONE
99424990	PREDNISOLONE
99425988	PREDNISOLONE
99425989	PREDNISOLONE
99425990	PREDNISOLONE
99531998	SODIUM CROMOGLICATE
99550998	HYDROCORTISONE
99609988	EPHEDRINE
99609989	EPHEDRINE
99609990	EPHEDRINE
99624998	THEOPHYLLINE+PHENOBARB &GUAIFEN
99626998	THEOPHYLLINE+ EPHEDRINE SULPHATE
99718998	FENOTEROL+ IPRATROPIUM BR
99781998	PREDNISONE
99802998	CORTISONE ACETATE
99803997	CORTISONE ACETATE
99803998	CORTISONE ACETATE
99804998	CORTISONE ACETATE
99806998	HYDROCORTISONE
99817992	AMINOPHYLLINE
99818992	AMINOPHYLLINE
99827992	AMINOPHYLLINE/ALUMINIUM HYDROXIDE DRIED
99828992	AMINOPHYLLINE
99829992	AMINOPHYLLINE
99830992	AMINOPHYLLINE INTRAMUSCULAR
99831992	AMINOPHYLLINE PAEDIATRIC
99833996	CHOLINE THEOPHYLLINATE
99833997	CHOLINE THEOPHYLLINATE

99833998	CHOLINE THEOPHYLLINATE
99859998	EPHEDRINE
99873989	AMINOPHYLLINE
99873990	AMINOPHYLLINE
99876998	TERBUTALINE+ GUAIFENESIN
99877997	TERBUTALINE
99877998	TERBUTALINE
99878996	TERBUTALINE
99878997	TERBUTALINE
99878998	TERBUTALINE
99879997	TERBUTALINE
99879998	TERBUTALINE
99890998	BETAMETHASONE
99893996	FENOTEROL
99893997	FENOTEROL
99893998	FENOTEROL
99896992	HYDROCORTISONE SODIUM PHOSPHATE
99910998	BECLOMETASONE
99914997	BECLOMETASONE
99914998	BECLOMETASONE
99922990	AMINOPHYLLINE
99930998	IPRATROPIUM BROMIDE
99965997	BECLOMETASONE
99965998	BECLOMETASONE
99966998	ORCIPRENALINE
99967996	ORCIPRENALINE
99967997	ORCIPRENALINE
99967998	ORCIPRENALINE

10.8.10 Medical codes for mental illnesses combined

Medcode	Description
13Y3.00	Manic-depression association member
1464.00	H/O: schizophrenia
1465.00	H/O: depression
1466.00	H/O: anxiety state
146D.00	H/O: manic depressive disorder
1B13.00	Anxiousness
1B13.11	Anxiousness - symptom
1B17.00	Depressed
1B17.11	C/O - feeling depressed
1B17.12	C/O - feeling unhappy
1B1E.00	Hallucinations
1B1N.00	Poor self esteem
1B1U.00	Symptoms of depression
1B1U.11	Depressive symptoms
1B1V.00	C/O - panic attack
1BH..00	Delusions
1BH..11	Delusion
1BI..00	Blunted affect
1BO..00	Mood swings
1BP..00	Loss of interest
1BQ..00	Loss of capacity for enjoyment
1BT..00	Depressed mood
1BT..11	Low mood
1BU..00	Loss of hope for the future
1BY..00	Elevated mood
1Ba0.00	Obsessional thoughts
1P01.00	Psychomotor retardation
2254.00	O/E - apathetic
2257.00	O/E - depressed
2258.00	O/E - anxious
225C.00	O/E - elated
62T1.00	Puerperal depression
6G00.00	Postnatal depression counselling
8BK0.00	Depression management programme
8G94.00	Anxiety management training
9HA0.00	On depression register
E10..00	Schizophrenic disorders
E100.00	Simple schizophrenia
E100000	Unspecified schizophrenia
E100200	Chronic schizophrenic
E100400	Acute exacerbation of chronic schizophrenia
E100500	Schizophrenia in remission
E100z00	Simple schizophrenia NOS
E101.00	Hebephrenic schizophrenia
E101z00	Hebephrenic schizophrenia NOS
E102.00	Catatonic schizophrenia
E103.00	Paranoid schizophrenia
E103000	Unspecified paranoid schizophrenia
E103200	Chronic paranoid schizophrenia
E103300	Acute exacerbation of subchronic paranoid schizophrenia
E103400	Acute exacerbation of chronic paranoid schizophrenia
E103500	Paranoid schizophrenia in remission
E103z00	Paranoid schizophrenia NOS
E104.00	Acute schizophrenic episode
E106.00	Residual schizophrenia

E107.00	Schizo-affective schizophrenia
E107000	Unspecified schizo-affective schizophrenia
E107100	Subchronic schizo-affective schizophrenia
E107200	Chronic schizo-affective schizophrenia
E107300	Acute exacerbation subchronic schizo-affective schizophrenia
E107400	Acute exacerbation of chronic schizo-affective schizophrenia
E107z00	Schizo-affective schizophrenia NOS
E10y000	Atypical schizophrenia
E10yz00	Other schizophrenia NOS
E10z.00	Schizophrenia NOS
E11..12	Depressive psychoses
E110.00	Manic disorder, single episode
E110.11	Hypomanic psychoses
E110000	Single manic episode, unspecified
E110100	Single manic episode, mild
E110200	Single manic episode, moderate
E110300	Single manic episode, severe without mention of psychosis
E110400	Single manic episode, severe, with psychosis
E110z00	Manic disorder, single episode NOS
E111.00	Recurrent manic episodes
E111000	Recurrent manic episodes, unspecified
E111100	Recurrent manic episodes, mild
E111200	Recurrent manic episodes, moderate
E111300	Recurrent manic episodes, severe without mention psychosis
E111400	Recurrent manic episodes, severe, with psychosis
E111600	Recurrent manic episodes, in full remission
E111z00	Recurrent manic episode NOS
E112.00	Single major depressive episode
E112.11	Agitated depression
E112.12	Endogenous depression first episode
E112.13	Endogenous depression first episode
E112.14	Endogenous depression
E112000	Single major depressive episode, unspecified
E112100	Single major depressive episode, mild
E112200	Single major depressive episode, moderate
E112300	Single major depressive episode, severe, without psychosis
E112400	Single major depressive episode, severe, with psychosis
E112500	Single major depressive episode, partial or unspec remission
E112600	Single major depressive episode, in full remission
E112z00	Single major depressive episode NOS
E113.00	Recurrent major depressive episode
E113.11	Endogenous depression - recurrent
E113000	Recurrent major depressive episodes, unspecified
E113100	Recurrent major depressive episodes, mild
E113200	Recurrent major depressive episodes, moderate
E113300	Recurrent major depressive episodes, severe, no psychosis
E113400	Recurrent major depressive episodes, severe, with psychosis
E113500	Recurrent major depressive episodes,partial/unspec remission
E113600	Recurrent major depressive episodes, in full remission
E113700	Recurrent depression
E113z00	Recurrent major depressive episode NOS
E114.00	Bipolar affective disorder, currently manic
E114.11	Manic-depressive - now manic
E114000	Bipolar affective disorder, currently manic, unspecified
E114100	Bipolar affective disorder, currently manic, mild
E114200	Bipolar affective disorder, currently manic, moderate
E114300	Bipolar affect disord, currently manic, severe, no psychosis
E114400	Bipolar affect disord, currently manic,severe with psychosis
E115.00	Bipolar affective disorder, currently depressed
E115.11	Manic-depressive - now depressed
E115000	Bipolar affective disorder, currently depressed, unspecified
E115100	Bipolar affective disorder, currently depressed, mild
E115200	Bipolar affective disorder, currently depressed, moderate
E115300	Bipolar affect disord, now depressed, severe, no psychosis
E115500	Bipolar affect disord, now depressed, part/unspec remission
E116.00	Mixed bipolar affective disorder
E116000	Mixed bipolar affective disorder, unspecified
E116200	Mixed bipolar affective disorder, moderate
E116300	Mixed bipolar affective disorder, severe, without psychosis
E116400	Mixed bipolar affective disorder, severe, with psychosis
E116500	Mixed bipolar affective disorder, partial/unspec remission
E116600	Mixed bipolar affective disorder, in full remission
E116z00	Mixed bipolar affective disorder, NOS
E117.00	Unspecified bipolar affective disorder
E117000	Unspecified bipolar affective disorder, unspecified
E117100	Unspecified bipolar affective disorder, mild
E117200	Unspecified bipolar affective disorder, moderate
E117400	Unspecified bipolar affective disorder,severe with psychosis
E117500	Unspecified bipolar affect disord, partial/unspec remission
E117600	Unspecified bipolar affective disorder, in full remission
E117z00	Unspecified bipolar affective disorder, NOS
E118.00	Seasonal affective disorder

E11y.00	Other and unspecified manic-depressive psychoses
E11y000	Unspecified manic-depressive psychoses
E11y200	Atypical depressive disorder
E11yz00	Other and unspecified manic-depressive psychoses NOS
E11z.00	Other and unspecified affective psychoses
E11z000	Unspecified affective psychoses NOS
E11z100	Rebound mood swings
E11z200	Masked depression
E11zz00	Other affective psychosis NOS
E12..00	Paranoid states
E120.00	Simple paranoid state
E121.00	Chronic paranoid psychosis
E122.00	Paraphrenia
E123.11	Folie a deux
E12y.00	Other paranoid states
E12yz00	Other paranoid states NOS
E12z.00	Paranoid psychosis NOS
E13..00	Other nonorganic psychoses
E13..11	Reactive psychoses
E130.00	Reactive depressive psychosis
E130.11	Psychotic reactive depression
E131.00	Acute hysterical psychosis
E132.00	Reactive confusion
E133.00	Acute paranoid reaction
E134.00	Psychogenic paranoid psychosis
E135.00	Agitated depression
E13y.00	Other reactive psychoses
E13y000	Psychogenic stupor
E13y100	Brief reactive psychosis
E13yz00	Other reactive psychoses NOS
E13z.00	Nonorganic psychosis NOS
E13z.11	Psychotic episode NOS
E1y..00	Other specified non-organic psychoses
E200.00	Anxiety states
E200000	Anxiety state unspecified
E200100	Panic disorder
E200111	Panic attack
E200200	Generalised anxiety disorder
E200300	Anxiety with depression
E200400	Chronic anxiety
E200500	Recurrent anxiety
E200z00	Anxiety state NOS
E203.00	Obsessive-compulsive disorders
E203000	Compulsive neurosis

E203100	Obsessional neurosis
E203z00	Obsessive-compulsive disorder NOS
E204.00	Neurotic depression reactive type
E204.11	Postnatal depression
E211100	Hypomanic personality disorder
E211200	Depressive personality disorder
E211300	Cyclothymic personality disorder
E214.00	Compulsive personality disorders
E214.11	Anancastic personality
E275111	Compulsive eating disorder
E275711	Compulsive water drinking
E290.00	Brief depressive reaction
E290z00	Brief depressive reaction NOS
E291.00	Prolonged depressive reaction
E2B..00	Depressive disorder NEC
E2B0.00	Postviral depression
E2B1.00	Chronic depression
E2D0.00	Disturbance of anxiety and fearfulness childhood/adolescent
E2D0000	Childhood and adolescent overanxiousness disturbance
E2D0100	Childhood and adolescent fearfulness disturbance
E2D0z00	Disturbance anxiety and fearfulness childhood/adolescent NOS
Eu2..00	[X]Schizophrenia, schizotypal and delusional disorders
Eu20.00	[X]Schizophrenia
Eu20000	[X]Paranoid schizophrenia
Eu20100	[X]Hebephrenic schizophrenia
Eu20211	[X]Catatonic stupor
Eu20213	[X]Schizophrenic catatonia
Eu20214	[X]Schizophrenic flexibilatis cerea
Eu20400	[X]Post-schizophrenic depression
Eu20511	[X]Chronic undifferentiated schizophrenia
Eu20600	[X]Simple schizophrenia
Eu20y13	[X]Schizophrenifrm psychos NOS
Eu20z00	[X]Schizophrenia, unspecified
Eu21.00	[X]Schizotypal disorder
Eu21.12	[X]Borderline schizophrenia
Eu21.18	[X]Schizotypal personality disorder
Eu22.00	[X]Persistent delusional disorders
Eu22000	[X]Delusional disorder
Eu22011	[X]Paranoid psychosis
Eu22012	[X]Paranoid state
Eu22015	[X]Paranoia
Eu22y11	[X]Delusional dysmorphophobia
Eu23.00	[X]Acute and transient psychotic disorders
Eu23000	[X]Acute polymorphic psychot disord

	without symp of schizoph
Eu23012	[X]Cycloid psychosis
Eu23100	[X]Acute polymorphic psychot disord with symp of schizophren
Eu23112	[X]Cycloid psychosis with symptoms of schizophrenia
Eu23200	[X]Acute schizophrenia-like psychotic disorder
Eu23300	[X]Other acute predominantly delusional psychotic disorders
Eu23312	[X]Psychogenic paranoid psychosis
Eu23y00	[X]Other acute and transient psychotic disorders
Eu23z00	[X]Acute and transient psychotic disorder, unspecified
Eu23z11	[X]Brief reactive psychosis NOS
Eu23z12	[X]Reactive psychosis
Eu24.00	[X]Induced delusional disorder
Eu24.12	[X]Induced paranoid disorder
Eu24.13	[X]Induced psychotic disorder
Eu25.00	[X]Schizoaffective disorders
Eu25000	[X]Schizoaffective disorder, manic type
Eu25011	[X]Schizoaffective psychosis, manic type
Eu25012	[X]Schizophreniform psychosis, manic type
Eu25100	[X]Schizoaffective disorder, depressive type
Eu25111	[X]Schizoaffective psychosis, depressive type
Eu25112	[X]Schizophreniform psychosis, depressive type
Eu25200	[X]Schizoaffective disorder, mixed type
Eu25212	[X]Mixed schizophrenic and affective psychosis
Eu25z00	[X]Schizoaffective disorder, unspecified
Eu25z11	[X]Schizoaffective psychosis NOS
Eu2y.00	[X]Other nonorganic psychotic disorders
Eu2y.11	[X]Chronic hallucinatory psychosis
Eu2z.00	[X]Unspecified nonorganic psychosis
Eu2z.11	[X]Psychosis NOS
Eu30.00	[X]Manic episode
Eu30.11	[X]Bipolar disorder, single manic episode
Eu30000	[X]Hypomania
Eu30100	[X]Mania without psychotic symptoms
Eu30200	[X]Mania with psychotic symptoms
Eu30212	[X]Mania with mood-incongruent psychotic symptoms
Eu30y00	[X]Other manic episodes
Eu30z11	[X]Mania NOS
Eu31.00	[X]Bipolar affective disorder
Eu31.11	[X]Manic-depressive illness
Eu31.12	[X]Manic-depressive psychosis
Eu31.13	[X]Manic-depressive reaction
Eu31000	[X]Bipolar affective disorder, current episode hypomanic
Eu31100	[X]Bipolar affect disorder cur epi manic wout psychotic symp
Eu31200	[X]Bipolar affect disorder cur epi manic with psychotic symp
Eu31300	[X]Bipolar affect disorder cur epi mild or moderate depressn
Eu31400	[X]Bipol aff disord, curr epis sev depress, no psychot symp
Eu31500	[X]Bipolar affect dis cur epi severe depres with psyc symp
Eu31600	[X]Bipolar affective disorder, current episode mixed
Eu31700	[X]Bipolar affective disorder, currently in remission
Eu31y00	[X]Other bipolar affective disorders
Eu31z00	[X]Bipolar affective disorder, unspecified
Eu32.00	[X]Depressive episode
Eu32.11	[X]Single episode of depressive reaction
Eu32.12	[X]Single episode of psychogenic depression
Eu32.13	[X]Single episode of reactive depression
Eu32000	[X]Mild depressive episode
Eu32100	[X]Moderate depressive episode
Eu32200	[X]Severe depressive episode without psychotic symptoms
Eu32211	[X]Single episode agitated depressn w'out psychotic symptoms
Eu32212	[X]Single episode major depression w'out psychotic symptoms
Eu32300	[X]Severe depressive episode with psychotic symptoms
Eu32311	[X]Single episode of major depression and psychotic symptoms
Eu32312	[X]Single episode of psychogenic depressive psychosis
Eu32313	[X]Single episode of psychotic depression
Eu32314	[X]Single episode of reactive depressive psychosis
Eu32400	[X]Mild depression
Eu32y00	[X]Other depressive episodes
Eu32y11	[X]Atypical depression
Eu32z00	[X]Depressive episode, unspecified
Eu32z11	[X]Depression NOS
Eu32z12	[X]Depressive disorder NOS
Eu32z13	[X]Prolonged single episode of reactive depression
Eu32z14	[X] Reactive depression NOS
Eu33.00	[X]Recurrent depressive disorder
Eu33.11	[X]Recurrent episodes of depressive reaction
Eu33.12	[X]Recurrent episodes of psychogenic depression
Eu33.13	[X]Recurrent episodes of reactive depression
Eu33.14	[X]Seasonal depressive disorder
Eu33.15	[X]SAD - Seasonal affective disorder
Eu33000	[X]Recurrent depressive disorder, current episode mild
Eu33100	[X]Recurrent depressive disorder, current episode moderate
Eu33200	[X]Recurr depress disorder cur epi severe without psyc sympt
Eu33211	[X]Endogenous depression without psychotic symptoms
Eu33212	[X]Major depression, recurrent without psychotic symptoms

Eu33213	[X]Manic-depress psychosis,depressd,no psychotic symptoms
Eu33300	[X]Recurrent depress disorder cur epi severe with psyc symp
Eu33311	[X]Endogenous depression with psychotic symptoms
Eu33312	[X]Manic-depress psychosis,depressed type+psychotic symptoms
Eu33313	[X]Recurr severe episodes/major depression+psychotic symptom
Eu33314	[X]Recurr severe episodes/psychogenic depressive psychosis
Eu33315	[X]Recurrent severe episodes of psychotic depression
Eu33316	[X]Recurrent severe episodes/reactive depressive psychosis
Eu33400	[X]Recurrent depressive disorder, currently in remission
Eu33y00	[X]Other recurrent depressive disorders
Eu33z00	[X]Recurrent depressive disorder, unspecified
Eu33z11	[X]Monopolar depression NOS
Eu34000	[X]Cyclothymia
Eu34012	[X]Cycloid personality
Eu34013	[X]Cyclothymic personality
Eu34100	[X]Dysthymia
Eu34111	[X]Depressive neurosis
Eu34112	[X]Depressive personality disorder
Eu34113	[X]Neurotic depression
Eu34114	[X]Persistant anxiety depression
Eu3y011	[X]Mixed affective episode
Eu3y111	[X]Recurrent brief depressive episodes
Eu40012	[X]Panic disorder with agoraphobia
Eu41.00	[X]Other anxiety disorders
Eu41000	[X]Panic disorder [episodic paroxysmal anxiety]
Eu41011	[X]Panic attack
Eu41012	[X]Panic state
Eu41100	[X]Generalized anxiety disorder
Eu41111	[X]Anxiety neurosis
Eu41112	[X]Anxiety reaction
Eu41113	[X]Anxiety state
Eu41200	[X]Mixed anxiety and depressive disorder
Eu41211	[X]Mild anxiety depression
Eu41300	[X]Other mixed anxiety disorders
Eu41z00	[X]Anxiety disorder, unspecified
Eu41z11	[X]Anxiety NOS
Eu42.00	[X]Obsessive - compulsive disorder
Eu42.12	[X]Obsessive-compulsive neurosis
Eu42000	[X]Predominantly obsessional thoughts or ruminations
Eu42100	[X]Predominantly compulsive acts [obsessional rituals]
Eu42200	[X]Mixed obsessional thoughts and acts
Eu42z00	[X]Obsessive-compulsive disorder, unspecified
Eu51511	[X]Dream anxiety disorder

Eu53011	[X]Postnatal depression NOS
Eu53012	[X]Postpartum depression NOS
Eu53111	[X]Puerperal psychosis NOS
Eu60500	[X]Anankastic personality disorder
Eu60511	[X]Compulsive personality disorder
Eu60512	[X]Obsessional personality disorder
Eu60513	[X]Obsessive-compulsive personality disorder
Eu92000	[X]Depressive conduct disorder
R001.00	[D]Hallucinations
R001000	[D]Hallucinations, auditory
R001100	[D]Hallucinations, gustatory
R001200	[D]Hallucinations, olfactory
R001300	[D]Hallucinations, tactile
R001400	[D]Visual hallucinations
R001z00	[D]Hallucinations NOS
R007z13	[D]Postoperative depression
R00z600	[D]Unhappiness
Z4I7.00	Acknowledging anxiety
Z4I7200	Alleviating anxiety
Z4I7211	Reducing anxiety
Z4L1.00	Anxiety counselling
ZV11000	[V]Personal history of schizophrenia
ZV11100	[V]Personal history of affective disorder
ZV11111	[V]Personal history of manic-depressive psychosis
ZV11112	[V]Personal history of manic-depressive psychosis

10.8.11 Medical codes for epilepsy

Medcode	Description
R003100	[D]Convulsions, infantile
R003z00	[D]Convulsion NOS
F256000	Hypsarrhythmia
Q480.11	Fits in newborn
Q480.00	Convulsions in newborn
F258.00	Post-ictal state
1B64.00	Had a convulsion
R003.00	[D]Convulsions
282..11	O/E - a convulsion
2825.00	O/E - psychomotor fit
2824.11	O/E - Jacksonian fit
R003y00	[D]Other specified convulsion
6676.00	Last fit
282..00	O/E - fit/convulsion
282..12	O/E - a fit
R003200	[D]Fit
2822.00	O/E - grand mal fit
F252.00	Petit mal status
2824.12	O/E - focal fit
Ryu7100	[X]Other and unspecified convulsions
F253.00	Grand mal status
282Z.00	O/E - fit/convulsion NOS
1B63.11	Fit - had one, symptom
6675.00	Fit frequency
1B64.11	Convulsion - symptom
2824.00	O/E - focal (Jacksonian) fit
1B63.00	Had a fit
2823.00	O/E - petit mal fit
F25y500	Panayiotopoulos syndrome
667N.00	Epilepsy severity
667D.00	Epilepsy control poor
667Z.00	Epilepsy monitoring NOS
ZS82.00	Acquired epileptic aphasia
F250100	Pykno-epilepsy
F251.00	Generalised convulsive epilepsy
F250000	Petit mal (minor) epilepsy
667V.00	Many seizures a day
667G.00	Epilepsy restricts employment
F255600	Simple partial epileptic seizure
F255500	Unilateral epilepsy
667W.00	Emergency epilepsy treatment since last appointment
F132z12	Myoclonic seizure
667S.00	1 to 7 seizures a week
F250011	Epileptic absences
F25A.00	Juvenile myoclonic epilepsy
F250z00	Generalised nonconvulsive epilepsy NOS
F25y200	Locl-rlt(foc)(part)idiop epilep&epilptic syn seiz locl onset
6678.00	Epilepsy treatment changed
F25z.00	Epilepsy NOS
667R.00	2 to 4 seizures a month
Q480.12	Seizures in newborn
282..13	O/E - a seizure
667A.00	Epilepsy treatment stopped
F254000	Temporal lobe epilepsy
F250y00	Other specified generalised nonconvulsive epilepsy
F256.12	West syndrome
F255z00	Partial epilepsy without impairment of consciousness NOS
9Of4.00	Epilepsy monitoring telephone invite
F255200	Somatosensory epilepsy
F256.00	Infantile spasms
667K.00	Epilepsy limits activities
F250500	Lennox-Gastaut syndrome
1O30.00	Epilepsy confirmed
667P.00	No seizures on treatment
2126000	Epilepsy resolved
667C.00	Epilepsy control good
6672.00	Follow-up epilepsy assessment
667X.00	No epilepsy drug side effects
F251z00	Generalised convulsive epilepsy NOS
667J.00	Epilepsy impairs education
F256.11	Lightning spasms
6677.00	Epilepsy drug side effects
Fyu5000	[X]Other generalized epilepsy and epileptic syndromes
667L.00	Epilepsy does not limit activities
F253.11	Status epilepticus
2828.00	Absence seizure
8BIF.00	Epilepsy medication review
667Q.00	1 to 12 seizures a year
F255000	Jacksonian, focal or motor epilepsy
212J.00	Epilepsy resolved
F254100	Psychomotor epilepsy
1B1W.00	Transient epileptic amnesia
R003400	[D]Nocturnal seizure
F254500	Complex partial epileptic seizure

F25X.00	Status epilepticus, unspecified
F255012	Motor epilepsy
F254400	Epileptic automatism
F25y100	Gelastic epilepsy
9Of3.00	Epilepsy monitoring verbal invite
F251000	Grand mal (major) epilepsy
F132100	Progressive myoclonic epilepsy
6671.00	Initial epilepsy assessment
F251500	Tonic-clonic epilepsy
6679.00	Epilepsy treatment started
667H.00	Epilepsy prevents employment
F254.00	Partial epilepsy with impairment of consciousness
F251400	Epileptic seizures - tonic
F257.00	Kojevnikov's epilepsy
F255311	Partial epilepsy with autonomic symptoms
F251300	Epileptic seizures - myoclonic
R003z11	[D]Seizure NOS
F25y000	Cursive (running) epilepsy
F132200	Myoclonic encephalopathy
F256100	Salaam attacks
F251011	Tonic-clonic epilepsy
F251200	Epileptic seizures - clonic
1473.00	H/O: epilepsy
F25F.00	Photosensitive epilepsy
F255.00	Partial epilepsy without impairment of consciousness
F25y400	Benign Rolandic epilepsy
F25C.00	Drug-induced epilepsy
F25B.00	Alcohol-induced epilepsy
667M.00	Epilepsy management plan given
F259.11	Ohtahara syndrome
F259.00	Early infant epileptic encephalopathy wth suppression bursts
667..00	Epilepsy monitoring
F256z00	Infantile spasms NOS
F25..00	Epilepsy
F255100	Sensory induced epilepsy
SC20000	Traumatic epilepsy
667B.00	Nocturnal epilepsy
F25D.00	Menstrual epilepsy
F254z00	Partial epilepsy with impairment of consciousness NOS
6674.00	Epilepsy associated problems
667T.00	Daily seizures
F255400	Visual reflex epilepsy
F251600	Grand mal seizure
F255300	Visceral reflex epilepsy

667F.00	Seizure free >12 months
F250.00	Generalised nonconvulsive epilepsy
Fyu5200	[X]Other status epilepticus
F255011	Focal epilepsy
F251111	Otohara syndrome
F250300	Epileptic seizures - akinetic
F25y.00	Other forms of epilepsy
F25E.00	Stress-induced epilepsy
F25z.11	Fit (in known epileptic) NOS
Fyu5100	[X]Other epilepsy
F251y00	Other specified generalised convulsive epilepsy
8CE7.00	Epilepsy leaflet given
F254300	Limbic system epilepsy
F251100	Neonatal myoclonic epilepsy
F250400	Juvenile absence epilepsy
F254200	Psychosensory epilepsy
F255y00	Partial epilepsy without impairment of consciousness OS
F250200	Epileptic seizures - atonic
F25yz00	Other forms of epilepsy NOS
Fyu5900	[X]Status epilepticus, unspecified

10.8.12 Drug codes for epilepsy

Multilexe id	Genericname
99332998	BECLAMIDE tabs 500mg
96914998	BECLAMIDE tabs 500mg
93771990	LAMOTRIGINE disp tab 25mg
95532997	PHENYTOIN susp 30mg/5ml
92200990	TOPIRAMATE tabs 25mg
93016996	VALPROIC ACID ec soft gelatin ca 0mg
95186990	GABAPENTIN tabs 800mg
96339990	PARALDEHYDE inj
92332990	TOPIRAMATE tabs 50mg
92735998	CARBAMAZEPINE supp 125mg
92734997	CARBAMAZEPINE supp 250mg
93934990	LAMOTRIGINE disp tab 25mg
94409997	SODIUM VALPROATE ec tab 500mg
94834996	GABAPENTIN caps 400mg
94090990	LAMOTRIGINE tabs 200mg
83946998	OXCARBAZEPINE oral liq
87401998	PREGABALIN caps 25mg
95409992	PHENOBARBITONE 10 MG PUL
86843998	ZONISAMIDE caps 25mg
92131997	CARBAMAZEPINE mr tab 400mg
92969990	GABAPENTIN caps 100mg
97955992	PRIMIDONE/PHENYTOIN SODIUM TAB
91051997	TOPIRAMATE tabs 100mg
96479992	TEGRETOL liq 100 MG/5ML LIQ
94285992	PHENOBARBITONE 50 MG CAP
84667998	SODIUM VALPROATE mr cap 150mg
95216990	SODIUM VALPROATE + VALPROIC ACID r tab 500mg
94119990	LAMOTRIGINE tabs 50mg
95417992	PHENOBARBITONE 5 MG ELI
96446990	CARBAMAZEPINE mr tab 200mg
94520992	PHENOBARBITONE 75 MG SUP
96697990	CARBAMAZEPINE tabs 400mg
98315996	PHENYTOIN SODIUM caps 100mg
94116990	GABAPENTIN caps 300mg
94282992	PHENOBARBITONE 15 MG CAP
97884992	PHENOBARBITONE & PHENYTOIN 60 G CAP
92291990	TOPIRAMATE caps 50mg
96885998	CARBAMAZEPINE liq 100mg/5ml
94049990	LAMOTRIGINE tabs 25mg
94834997	GABAPENTIN caps 300mg
94835996	GABAPENTIN caps 400mg
99751990	CARBAMAZEPINE tabs 100mg
99752988	CARBAMAZEPINE tabs 400mg
92197990	TOPIRAMATE tabs 200mg
91625997	OXCARBAZEPINE tabs 300mg
94121990	GABAPENTIN caps 400mg
94092990	LAMOTRIGINE tabs 50mg
93806990	LAMOTRIGINE tabs 200mg
94606997	SODIUM VALPROATE ec tab 500mg
93939990	LAMOTRIGINE tabs 25mg
94568997	SODIUM VALPROATE sf liq 200mg/5ml
94010990	LAMOTRIGINE tabs 200mg
93808990	LAMOTRIGINE tabs 50mg
92700996	LAMOTRIGINE disp tab 100mg
95187990	GABAPENTIN tabs 600mg
94013990	LAMOTRIGINE tabs 25mg
94428992	CANTIL + PHENOBARB TAB
98049990	PHENOBARBITAL tabs 15mg
92388990	OXCARBAZEPINE tabs 300mg
99124989	PHENOBARBITAL tabs 30mg
94166990	GABAPENTIN caps 300mg
91596998	LAMOTRIGINE tabs 200mg
94165990	GABAPENTIN caps 400mg
92284990	TOPIRAMATE caps 25mg
92297990	TOPIRAMATE tabs 50mg
83511998	LACOSAMIDE tabs 150mg
94283992	PHENOBARBITONE 15 MG SUP
83518998	LACOSAMIDE soln for inf 200mg/20ml
92734998	CARBAMAZEPINE supp 125mg
92917997	SODIUM VALPROATE + VALPROIC ACID r tab 300mg
93769997	VIGABATRIN sf pwdr 500mg
94409996	SODIUM VALPROATE crushable tab 0mg
99459989	PHENOBARBITAL tabs 30mg
99176997	CLONAZEPAM tabs 2mg
96676990	SODIUM VALPROATE crushable tab 0mg
97203997	PHENOBARBITAL tabs 30mg
95444998	LAMOTRIGINE tabs 50mg
97140990	PHENYTOIN SODIUM tabs 50mg
94068998	VALPROIC ACID (AS SEMISODIUM ALT) ec tab 250mg
98049989	PHENOBARBITAL tabs 30mg
94093990	LAMOTRIGINE tabs 25mg
83707998	SODIUM VALPROATE MR granules 0mg
95553998	PHENOBARBITAL SODIUM inj 0mg/1ml
84095998	STIRIPENTOL sach 500mg

94105990	LAMOTRIGINE tabs 25mg
93493990	LAMOTRIGINE tabs 25mg
99454990	PHENYTOIN SODIUM tabs 50mg
95361992	OSPOLOT 50 MG TAB
92802996	SODIUM VALPROATE sf liq 200mg/5ml
83705998	SODIUM VALPROATE MR granules 0mg
93876990	LAMOTRIGINE disp tab 100mg
93769998	VIGABATRIN tabs 500mg
98111990	PHENOBARBITAL SODIUM inj 0mg/1ml
93460992	LAMICTAL NON-VALPROATE ADD-ON ART PACK TAB 25 mg
98658998	PHENYTOIN susp 30mg/5ml
94120990	LAMOTRIGINE tabs 25mg
82857998	SODIUM VALPROATE MR granules 00mg
83790998	SODIUM VALPROATE + VALPROIC ACID R granules 1000mg
95161990	GABAPENTIN caps 100mg
96916990	CARBAMAZEPINE tabs 100mg
96536990	CARBAMAZEPINE mr tab 200mg
92918997	SODIUM VALPROATE mr tab 300mg
92389990	OXCARBAZEPINE tabs 150mg
84097998	STIRIPENTOL caps 500mg
97514997	PHENYTOIN paed tab 50mg
98338988	CARBAMAZEPINE tabs 400mg
96128990	CARBAMAZEPINE mr tab 200mg
96159990	SODIUM VALPROATE sf liq 200mg/5ml
84668998	SODIUM VALPROATE MR granules 00mg
96195992	DIAZEPAM 10 MG INJ
95444996	LAMOTRIGINE tabs 25mg
92331990	TOPIRAMATE tabs 100mg
93882990	LAMOTRIGINE tabs 25mg
93769990	LAMOTRIGINE disp tab 5mg
96407998	DIAZEPAM rectal tubes 5mg
89210996	LEVETIRACETAM tabs 1000mg
93530998	CARBAMAZEPINE chewable tab 100mg
89408998	TIAGABINE tabs 5mg
88868997	TOPIRAMATE caps 25mg
93935990	LAMOTRIGINE disp tab 5mg
98385989	SODIUM VALPROATE ec tab 500mg
96536989	CARBAMAZEPINE mr tab 400mg
94087990	LAMOTRIGINE disp tab 100mg
86604998	CLONAZEPAM sf soln 0micrograms/5ml
93768992	PHENOBARBITONE 100 MG SPA
96648997	CLOBAZAM tabs 10mg
90776998	PHENYTOIN SODIUM caps 300mg
87400998	PREGABALIN caps 50mg

95852998	METHYLPHENOBARBITAL tabs 30mg
96978990	PHENYTOIN SODIUM tabs 100mg
95189990	GABAPENTIN caps 300mg
93404992	PHENOBARBITONE 10 MG TAB
96407997	DIAZEPAM rectal tubes 10mg
83896998	PHENYTOIN SODIUM oral liq
94047990	LAMOTRIGINE tabs 100mg
92701990	PHENYTOIN SODIUM inj 250mg/5ml
91050997	TOPIRAMATE tabs 100mg
99110990	PHENOBARBITAL tabs 100mg
99751989	CARBAMAZEPINE tabs 200mg
87193998	LEVETIRACETAM oral soln 100mg/ml
96767998	ETHOSUXIMIDE caps 250mg
93443990	SODIUM VALPROATE ec tab 500mg
93511990	LAMOTRIGINE disp tab 25mg
93530997	CARBAMAZEPINE chewable tab 200mg
97736997	PHENYTOIN SODIUM tabs 100mg
83708998	SODIUM VALPROATE MR granules mg
91839998	OXCARBAZEPINE sf oral susp 60mg/ml
87398998	PREGABALIN caps 100mg

10.9 DETAILED DESCRIPTION OF SURVEYS AND STUDIES CONDUCTED IN THE UK ON SMOKING DURING PREGNANCY

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
	Background: The first infant feeding survey took place in 1975 as a result of recommendation from the Committee on Medical Aspects of Food and Nutrition Policy (COMA) working party to establish basic information about infant feeding practices. Information on smoking during pregnancy was asked for the first time in 1985. All infant feeding surveys were postal surveys, with three stages of each survey. Stage 1: when babies were approx. 6-8 weeks Stage 2: when babies were approx. 4-5 months Stage 3: when babies were approx. 8-10 months [59,62,138,139,315,316]	**Background:** Health education authority commissioned these surveys of pregnant women to monitor the effectiveness of its smoking and pregnancy campaign targeted at women aged 15-24 years in the social grade C2DE. The 1992 survey was to provide the HEA with some baseline figures. All 9 tracks of HEA survey were conducted in England, based on quota sampling techniques, where door-step screening was used to sample pregnant women, who were home-interviewed after press advertising aimed at reducing smoking during pregnancy each year. [63,64]	Smoking behaviour in pregnancy is collected at a woman's first antenatal booking appointment which usually takes place within the first three months of pregnancy. These booking appointments take place either at hospital or in the community and are recorded on the Scottish Woman Held Maternity Record, with data being subsequently transcribed onto the Scottish Morbidity Record (SMR02). Estimates are based on financial year so each year ends on March 31st.	
1984				This study was performed between 1st October 1982 and 31 March 1984 on patients attending the antenatal clinics at the Stobhill General Hospital , Glasgow. Total sample obtained: 2,765. *Results* 34.5% of pregnant women smoked

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
				during pregnancy [317]
1985	**Sample:** Babies born between August to September 1985 in Great Britain, chosen through systematic random sampling of births in a sample of 100 registration sub-districts in England and Wales and birth registrations in Scotland. Social class V was oversampled. **Sample size, response rate at each stage** Stage 1: initial sample 8,154, response rate (90%), sample obtained 7,396 Stage 2: response rate (81%), sample obtained 5,969 Stage 3: response rate (83%) , sample obtained 4,946 **Results:** 39% of women smoked before pregnancy 30% of women smoked during pregnancy 24% gave up smoking during pregnancy[62]			
1986				Self-administered questionnaires given to 3882 pregnant women attending antenatal clinics at the Nottingham City Hospital and University Hospital Nottingham between July to August 1986 for six weeks. Response rate 90%, final study sample 3,483. *Results* 31% of women smoked in pregnancy. 36% never smoked, 26% stopped before getting pregnant, 7% stopped

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
				on hearing about pregnancy, 21% reduced their smoking consumption while 2% increased their smoking. 41% of women aged 14-20 smoked during pregnancy compared to 30% aged 21-30 and 22% aged 31 and over. [318]
1987				
1988				
1989				
1990	**Sample:** Babies born between August to October 1990, in the UK. Sampling methodology and frame same as the 1985 survey except for the inclusion of births from Northern Ireland chosen randomly from birth registrations. **Sample size, response rate at each stage** Stage 1: initial sample 11,105, response rate (88%), sample obtained 9,778 Stage 2: response rate (90%), sample obtained 8,793 Stage 3: response rate (81%) , sample obtained 7,083 **Results:** 28% of women smoked before pregnancy 30% of women smoked during pregnancy 27% of women gave up smoking during pregnancy [316]			

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
1992		**Track 1:** Baseline measures – January 1992. Sampled 625 pregnant women. **Results:** 40% of the women in the sample were smoking in the 12 months before pregnancy 27% were smoking during pregnancy 44% women had never smoked 36% in C2DE class smoked compared to 14% in ABC1. [64]		A systematic random sample of 3200 adults aged over 18 from each of the 19 districts within the North Western Region of UK was taken from the Family Health Services Authority registers. The total sample was 60,800 out of which 38,014 replied, in which 513 women were pregnant. *Results* 29% of pregnant women stated that they smoked and 8.4% smoked more than 15 cigarettes a day. Pregnant smokers were more likely to be under 25 years of age, tenants, and less likely to be engaged in any formal work or education. [319]
		Track 2: March 1992 after the launch of HEA campaign, sampled 606 women. **Results:** 39% of the women in the sample were smoking in the 12 months before pregnancy 26% were smoking during pregnancy 45% women had never smoked 34% in C2DE class smoked compared to 14% in ABC1. [64]		
1993		**Track 3:** March 1993. Sample size = 526 pregnant women.		

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
		Results: 37% of the women in the sample were smoking in the 12 months before pregnancy 27% were smoking during pregnancy 44% women had never smoked 36% in C2DE class smoked compared to 11% in ABC1. [64]		
1994		**Track 4:** March 1994. Sample size = 1,039 **Results:** 41% of the women in the sample were smoking in the 12 months before pregnancy 26% were smoking during pregnancy 43% women had never smoked 35% in C2DE class smoked compared to 14% in ABC1 [64]		
1995	**Sample:** Babies born between August to October 1995 in the UK chosen randomly from birth registers compiled by the General Register Offices in the UK. Social class V was oversampled. **Sample size, response rate at each stage** Initial sample 12,314, response rate (74%) sample obtained 9,130.	**Track 5:** March 1995. Sample size = 1,002 **Results:** 39% of the women in the sample were smoking in the 12 months before pregnancy 27% were smoking during	Total women:59,862 Current smokers : 29.0% Former smokers: 7.9% Never smokers: 58.1% Not known: 5.0% [320]	

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td>Results:
35% of women smoked before pregnancy
23% of women smoked during pregnancy
33% gave up smoking during pregnancy [315]

Smoking in pregnancy by social class
<table><tr><td>social class</td><td>Before pregnancy</td><td>During pregnancy</td><td>Gave up smoking</td></tr><tr><td>I</td><td>14%</td><td>7%</td><td>50%</td></tr><tr><td>II</td><td>22%</td><td>12%</td><td>44%</td></tr><tr><td>IIINM</td><td>27%</td><td>14%</td><td>47%</td></tr><tr><td>IIIM</td><td>35%</td><td>23%</td><td>33%</td></tr><tr><td>IV</td><td>40%</td><td>28%</td><td>31%</td></tr><tr><td>V</td><td>52%</td><td>37%</td><td>29%</td></tr></table></td><td>pregnancy
46% women had never smoked
41% in C2DE class smoked
compared to
11% in ABC1 [64]</td><td></td><td></td></tr>
<tr><td>1996</td><td></td><td>Track 6: March 1996. Sample size = 1,004

Results:
41% of the women in the sample were smoking in the 12 months before pregnancy
28% were smoking during pregnancy
46% women had never smoked
39% in C2DE class smoked compared to 15% in ABC1 [64]</td><td>Total women: 58,478
Current smokers: 28.8%
Former smokers: 7.9%
Never smokers: 58.2%
Not known: 5.1% [320]</td><td></td></tr>
<tr><td>1997</td><td></td><td>Track 7: March 1997. Sample size = 1,018</td><td>Total women:57,500
Current smokers: 29.4%</td><td></td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td>Results:
38% of the women in the sample were smoking in the 12 months before pregnancy
26% were smoking during pregnancy
47% women had never smoked
37% in C2DE class smoked compared to 13% in ABC1

[64]</td><td>Former smokers: 8.0%
Never smokers: 54.2%
Not known: 8.5% [320]</td><td></td></tr>
<tr><td>1998</td><td></td><td>Track 8: March 1998. Sample size = 1,019

Results:
38% of the women in the sample were smoking in the 12 months before pregnancy
22% were smoking during pregnancy
46% women had never smoked
32% in C2DE class smoked compared to 10% in ABC1 [64]</td><td>Total women: 57,560
Current smokers: 28.7%
Former smokers: 8.2%
Never smokers: 56.5%
Not known: 6.6% [320]

Smoking by SES
<table><tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>SIMD1</td><td>47.8%</td><td>8.1%</td><td>40.%</td><td>4.2%</td></tr><tr><td>SIMD2</td><td>34.3%</td><td>8.3%</td><td>51.3%</td><td>6.0%</td></tr><tr><td>SIMD3</td><td>24.5%</td><td>8.4%</td><td>58.5%</td><td>8.5%</td></tr><tr><td>SIMD4</td><td>17.1%</td><td>8.9%</td><td>66.7%</td><td>7.4%</td></tr><tr><td>SIMD5</td><td>9.8%</td><td>7.3%</td><td>74.9%</td><td>7.9%</td></tr><tr><td>NK</td><td>17.9%</td><td>6.0%</td><td>61.5%</td><td>14.7%</td></tr></table>
Smoking by age
<table><tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr></table></td><td></td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td><20</td><td>48.2%</td><td>10.2%</td><td>36.0%</td><td>5.6%</td></tr>
<tr><td>20-24</td><td>42.0%</td><td>9.6%</td><td>42.3%</td><td>6.0%</td></tr>
<tr><td>25-29</td><td>27.2%</td><td>8.3%</td><td>58.4%</td><td>6.0%</td></tr>
<tr><td>30-34</td><td>20.4%</td><td>7.1%</td><td>65.2%</td><td>7.3%</td></tr>
<tr><td>35.39</td><td>20.6%</td><td>7.1%</td><td>64.9%</td><td>7.5%</td></tr>
<tr><td>40+</td><td>21.2%</td><td>6.3%</td><td>63.2%</td><td>9.3%</td></tr>
</table>
</td><td></td></tr>
<tr><td>1999</td><td></td><td>Track 9: March 1999. Sample size = 999

Results:
45% of the women in the sample were smoking in the 12 months before pregnancy
30% were smoking during pregnancy
42% women had never smoked
43% in C2DE class smoked compared to 15% in ABC1 [64]</td><td>Total women:55,776
Current smokers: 27.6%
Former smokers: 8.2%
Never smokers: 57.0%
Not known: 7.1% [320]

Smoking by SES
<table>
<tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td>SIMD1</td><td>45.9%</td><td>8.6%</td><td>40.6%</td><td>4.9%</td></tr>
<tr><td>SIMD2</td><td>32.5%</td><td>9.0%</td><td>51.7%</td><td>6.7%</td></tr>
<tr><td>SIMD3</td><td>24.9%</td><td>8.2%</td><td>57.9%</td><td>9.0%</td></tr>
<tr><td>SIMD4</td><td>17.2%</td><td>7.8%</td><td>66.3%</td><td>8.6%</td></tr>
<tr><td>SIMD5</td><td>9.1%</td><td>7.3%</td><td>76.7%</td><td>7.0%</td></tr>
<tr><td>NK</td><td>18.5%</td><td>8.7%</td><td>54.4%</td><td>18.5%</td></tr>
</table>
Smoking by age
<table>
<tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td><20</td><td>45.5%</td><td>11.5%</td><td>36.0%</td><td>7.0%</td></tr>
<tr><td>20-24</td><td>39.9%</td><td>9.7%</td><td>43.6%</td><td>6.8%</td></tr>
<tr><td>25-29</td><td>26.7%</td><td>8.5%</td><td>57.9%</td><td>7.0%</td></tr>
<tr><td>30-34</td><td>19.8%</td><td>7.2%</td><td>66.0%</td><td>7.1%</td></tr>
</table>
</td><td></td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>35.39</td><td>20.2%</td><td>6.1%</td><td>66.0%</td><td>7.7%</td></tr>
<tr><td>40+</td><td>20.5%</td><td>6.2%</td><td>63.9%</td><td>9.4%</td></tr>
</table>
</td><td></td></tr>
<tr><td>2000</td><td>Sample: Babies born between August to October 2000 in the UK chosen randomly from birth registers compiled by the General Register Offices in the UK. In England and Wales a clustered sample within 100 registration districts was selected and Scotland and NI sample was chosen from all registration districts. Social class V was oversampled.

Sample size, response rate at each stage
Stage 1: initial sample 13,112, response rate (72%), sample obtained 9,492
Stage 2: response rate (87%), sample obtained 8,299
Stage 3: response rate (88%) , sample obtained 7,267

Results:
35% of women smoked before or during pregnancy
20% of women smoked throughout pregnancy
44% gave up smoking during or before pregnancy [138]

Smoking in pregnancy by social class
<table>
<tr><td>NS-SEC</td><td>Before/during pregnancy</td><td>Throughout pregnancy</td><td>Gave up smoking</td></tr>
<tr><td>Higher</td><td>22%</td><td>8%</td><td>63%</td></tr>
<tr><td>Intermediate</td><td>29%</td><td>13%</td><td>55%</td></tr>
<tr><td>Lower</td><td>46%</td><td>29%</td><td>38%</td></tr>
<tr><td>Never</td><td>50%</td><td>36%</td><td>29%</td></tr>
</table>
</td><td></td><td>Total women: 53,355
Current smokers: 26.6%
Former smokers: 8.2%
Never smokers: 57.3%
Not known: 7.9% [320]

Smoking by SES
<table>
<tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td>SIMD1</td><td>44.7%</td><td>8.5%</td><td>40.6%</td><td>6.1%</td></tr>
<tr><td>SIMD2</td><td>31.7%</td><td>8.8%</td><td>52.0%</td><td>7.4%</td></tr>
<tr><td>SIMD3</td><td>23.4%</td><td>8.4%</td><td>59.5%</td><td>8.7%</td></tr>
<tr><td>SIMD4</td><td>16.2%</td><td>8.0%</td><td>66.9%</td><td>8.8%</td></tr>
<tr><td>SIMD5</td><td>9.5%</td><td>7.1%</td><td>74.4%</td><td>9.0%</td></tr>
<tr><td>NK</td><td>16.1%</td><td>4.0%</td><td>60.3%</td><td>19.6%</td></tr>
</table>
Smoking by age
<table>
<tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td><20</td><td>44.5%</td><td>10.5%</td><td>37.0%</td><td>8.0%</td></tr>
<tr><td>20-24</td><td>38.8%</td><td>10.5%</td><td>43.5%</td><td>7.2%</td></tr>
<tr><td>25-29</td><td>25.8%</td><td>8.1%</td><td>58.4%</td><td>7.6%</td></tr>
<tr><td>30-34</td><td>19.0%</td><td>7.1%</td><td>66.1%</td><td>7.8%</td></tr>
<tr><td>35.39</td><td>19.0%</td><td>6.5%</td><td>65.3%</td><td>9.2%</td></tr>
<tr><td>40+</td><td>17.7%</td><td>6.6%</td><td>64.0%</td><td>11.7%</td></tr>
</table>
</td><td></td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td>
<table>
<tr><td>worked</td><td></td><td></td><td></td></tr>
<tr><td>unclassified</td><td>38%</td><td>22%</td><td>44%</td></tr>
</table>
Smoking in pregnancy by mother's age
<table>
<tr><td>age</td><td>Before/during pregnancy</td><td>Throughout pregnancy</td><td>Gave up smoking</td></tr>
<tr><td>< 20</td><td>65%</td><td>40%</td><td>38%</td></tr>
<tr><td>20-24</td><td>53%</td><td>30%</td><td>43%</td></tr>
<tr><td>25-29</td><td>36%</td><td>20%</td><td>45%</td></tr>
<tr><td>30-34</td><td>25%</td><td>13%</td><td>48%</td></tr>
<tr><td>35+</td><td>24%</td><td>13%</td><td>45%</td></tr>
</table>
</td><td></td><td></td><td></td></tr>
<tr><td>2001</td><td></td><td></td><td>Total women:51,791
Current smokers: 25.4%
Former smokers: 8.4%
Never smokers: 52.8%
Not known: 13.5% [320]

Smoking by SES
<table>
<tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td>SIMD1</td><td>43.5%</td><td>8.8%</td><td>38.9%</td><td>8.8%</td></tr>
<tr><td>SIMD2</td><td>30.6%</td><td>9.3%</td><td>48.1%</td><td>12.0%</td></tr>
<tr><td>SIMD3</td><td>21.8%</td><td>9.4%</td><td>54.8%</td><td>14.1%</td></tr>
<tr><td>SIMD4</td><td>15.0%</td><td>8.2%</td><td>61.9%</td><td>14.9%</td></tr>
<tr><td>SIMD5</td><td>8.0%</td><td>6.2%</td><td>66.3%</td><td>19.5%</td></tr>
<tr><td>NK</td><td>19.9%</td><td>4.5%</td><td>54.7%</td><td>20.9%</td></tr>
</table>
</td><td>Millenium cohort study – first survey

The Millennium Cohort Study is a large-scale survey of the new century's babies, and the families who are bringing them up, for the four countries of the United Kingdom. Its first sweep was carried out during 2001-2002 and contains information about 18819 babies in 18553 families, collected from parents when the babies were aged nine months. The sample design allowed for disproportionate representation of families living in areas of child poverty</td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>Smoking by age<table><tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td><20</td><td>42.4%</td><td>11.3%</td><td>34.7%</td><td>11.6%</td></tr><tr><td>20-24</td><td>38.3%</td><td>10.7%</td><td>39.5%</td><td>11.6%</td></tr><tr><td>25-29</td><td>24.8%</td><td>8.3%</td><td>54.4%</td><td>12.5%</td></tr><tr><td>30-34</td><td>18.2%</td><td>7.2%</td><td>60.2%</td><td>14.4%</td></tr><tr><td>35.39</td><td>16.9%</td><td>6.7%</td><td>60.6%</td><td>15.8%</td></tr><tr><td>40+</td><td>17.0%</td><td>7.3%</td><td>56.0%</td><td>19.7%</td></tr></table></td><td>in Northern Ireland, Scotland and Wales and in areas with high ethnic minority populations in England.

Results
35.3% of mothers reported smoking at some point during pregnancy while 28.4% mothers reported smoking at 9 month interview. Women who smoked during pregnancy were younger than non-smokers, and more likely to be single mothers [321]</td></tr>
<tr><td>2002</td><td></td><td></td><td>Total women:50,063
Current smokers: 25.5%
Former smokers: 8.6%
Never smokers: 55.2%
Not known: 10.7% [320]

Smoking by SES<table><tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>SIMD1</td><td>7.5%</td><td>8.8%</td><td>40.8%</td><td>7.5%</td></tr><tr><td>SIMD2</td><td>30.8%</td><td>9.7%</td><td>50.0%</td><td>9.5%</td></tr><tr><td>SIMD3</td><td>22.4%</td><td>9.2%</td><td>56.8%</td><td>11.5%</td></tr><tr><td>SIMD4</td><td>15.3%</td><td>8.6%</td><td>64.3%</td><td>11.8%</td></tr><tr><td>SIMD5</td><td>8.5%</td><td>6.6%</td><td>70.5%</td><td>14.4%</td></tr><tr><td>NK</td><td>21.8%</td><td>2.9%</td><td>59.2%</td><td>16.1%</td></tr></table>Smoking by age<table><tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr></table></td><td>Smoking status at time of delivery, England

Since 2002/03, PCTs have been submitting data on smoking at delivery on a quarterly basis. This provides more timely, frequent and local information on smoking among pregnant women than the Infant Feeding Survey and Health Survey for England.
Collection was initially done via the Strategic Executive Information System (STEIS) and then via the DH data collection tool called Unify. From 2008/09 quarter 2 this information has been collected using the IC's Omnibus system, a web based system set up to</td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td><20</td><td>44.2%</td><td>11.5%</td><td>34.5%</td><td>9.8%</td></tr>
<tr><td>20-24</td><td>37.5%</td><td>10.3%</td><td>42.6%</td><td>9.5%</td></tr>
<tr><td>25-29</td><td>24.6%</td><td>9.0%</td><td>56.4%</td><td>9.9%</td></tr>
<tr><td>30-34</td><td>18.6%</td><td>7.6%</td><td>62.9%</td><td>10.9%</td></tr>
<tr><td>35.39</td><td>17.3%</td><td>6.6%</td><td>63.2%</td><td>12.9%</td></tr>
<tr><td>40+</td><td>19.5%</td><td>6.4%</td><td>59.9%</td><td>14.1%</td></tr>
</table>
</td><td>collect performance and other central returns directly from the NHS.
Each Primary Care Trust (PCT) is required to submit actual figures for the quarter and the year-to-date and forecasts for the year as a whole for the following three items:
• The number of maternities;
• The number of mothers recorded as smoking at delivery; and
• The number of mothers recorded as not smoking at delivery.

Data for this year didn’t pass the data quality checks hence percentage not given [322]</td></tr>
<tr><td>2003</td><td></td><td></td><td>Total women:50,224
Current smokers: 25.3%
Former smokers: 9.0%
Never smokers: 57.5%
Not known: 8.1% [320]

Smoking by SES
<table>
<tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td>SIMD1</td><td>42.7%</td><td>8.9%</td><td>41.7%</td><td>6.7%</td></tr>
<tr><td>SIMD2</td><td>30.9%</td><td>10.3%</td><td>51.2%</td><td>7.6%</td></tr>
<tr><td>SIMD3</td><td>22.4%</td><td>9.5%</td><td>58.9%</td><td>9.2%</td></tr>
<tr><td>SIMD4</td><td>15.3%</td><td>9.2%</td><td>66.8%</td><td>8.8%</td></tr>
<tr><td>SIMD5</td><td>8.4%</td><td>7.3%</td><td>75.6%</td><td>8.7%</td></tr>
</table>
</td><td>Smoking status at time of delivery, England
Data for this year didn’t pass the data quality checks hence percentage not given [322]</td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>NK</td><td>14.6%</td><td>6.3%</td><td>58.7%</td><td>20.4%</td></tr>
</table>

Smoking by age
<table>
<tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td><20</td><td>44.6%</td><td>10.7%</td><td>36.8%</td><td>7.9%</td></tr>
<tr><td>20-24</td><td>37.0%</td><td>11.1%</td><td>44.4%</td><td>7.5%</td></tr>
<tr><td>25-29</td><td>25.2%</td><td>9.4%</td><td>58.1%</td><td>7.3%</td></tr>
<tr><td>30-34</td><td>17.8%</td><td>8.0%</td><td>65.6%</td><td>8.6%</td></tr>
<tr><td>35.39</td><td>17.1%</td><td>7.3%</td><td>66.3%</td><td>9.2%</td></tr>
<tr><td>40+</td><td>18.5%</td><td>6.4%</td><td>65.6%</td><td>9.5%</td></tr>
</table>
</td><td></td></tr>
<tr><td>2004</td><td></td><td></td><td>Total women: 51,894
Current smokers: 23.8%
Former smokers: 9.1%
Never smokers: 59.2%
Not known: 7.9% [320]

Smoking by SES
<table>
<tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td>SIMD1</td><td>40.0%</td><td>9.8%</td><td>42.0%</td><td>8.2%</td></tr>
<tr><td>SIMD2</td><td>29.1%</td><td>9.7%</td><td>53.4%</td><td>7.9%</td></tr>
<tr><td>SIMD3</td><td>20.7%</td><td>9.7%</td><td>60.0%</td><td>9.6%</td></tr>
<tr><td>SIMD4</td><td>14.9%</td><td>9.3%</td><td>67.8%</td><td>8.0%</td></tr>
<tr><td>SIMD5</td><td>8.0%</td><td>6.5%</td><td>79.6%</td><td>5.9%</td></tr>
<tr><td>NK</td><td>20.1%</td><td>4.9%</td><td>60.4%</td><td>14.6%</td></tr>
</table>

Smoking by age
<table>
<tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
</table>
</td><td>Smoking status at time of delivery, England

Data for this year didn’t pass the data quality checks hence percentage not given [322]</td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td><20</td><td>42.3%</td><td>11.1%</td><td>39.3%</td><td>7.4%</td></tr>
<tr><td>20-24</td><td>35.2%</td><td>10.3%</td><td>45.7%</td><td>8.7%</td></tr>
<tr><td>25-29</td><td>23.2%</td><td>10.1%</td><td>58.9%</td><td>7.8%</td></tr>
<tr><td>30-34</td><td>17.1%</td><td>8.3%</td><td>67.1%</td><td>7.5%</td></tr>
<tr><td>35.39</td><td>16.2%</td><td>7.1%</td><td>68.6%</td><td>8.1%</td></tr>
<tr><td>40+</td><td>17.4%</td><td>5.1%</td><td>68.0%</td><td>9.5%</td></tr>
</table>
</td><td></td></tr>
<tr><td>2005</td><td>Sample: A completely unclustered sample of 19,848 births selected from all births registered in the period August to October 2005. No oversampling of mothers from lower social class groups. Births with no partner oversampled.

Sample size, response rate at each stage
Stage 1: initial sample 19,848, response rate (62%), sample obtained 12,290
Stage 2: response rate (88%), sample obtained 10,814
Stage 3: response rate (87%) , sample obtained 9,416

Results:
33% of women smoked before or during pregnancy
17% of women smoked throughout pregnancy
48% gave up smoking during or before pregnancy [139]

Smoking in pregnancy by social class
<table>
<tr><td>NS-SEC</td><td>Before/during pregnancy</td><td>Throughout pregnancy</td><td>Gave up smoking</td></tr>
<tr><td>Manag/prof.</td><td>22%</td><td>8%</td><td>63%</td></tr>
<tr><td>Intermediate</td><td>29%</td><td>13%</td><td>55%</td></tr>
</table>
</td><td></td><td>Total women:52,646
Current smokers: 22.5%
Former smokers: 9.3%
Never smokers: 60.9%
Not known: 7.3% [320]

Smoking by SES
<table>
<tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td>SIMD1</td><td>38.5%</td><td>8.8%</td><td>44.1%</td><td>8.6%</td></tr>
<tr><td>SIMD2</td><td>27.1%</td><td>10.6%</td><td>55.5%</td><td>6.7%</td></tr>
<tr><td>SIMD3</td><td>19.8%</td><td>10.7%</td><td>61.9%</td><td>7.5%</td></tr>
<tr><td>SIMD4</td><td>13.6%</td><td>9.2%</td><td>69.6%</td><td>7.6%</td></tr>
<tr><td>SIMD5</td><td>7.1%</td><td>7.1%</td><td>80.4%</td><td>5.4%</td></tr>
<tr><td>NK</td><td>18.0%</td><td>7.9%</td><td>64.0%</td><td>10.1%</td></tr>
</table>
Smoking by age
<table>
<tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td><20</td><td>41.8%</td><td>10.3%</td><td>39.5%</td><td>8.3%</td></tr>
<tr><td>20-24</td><td>34.3%</td><td>10.9%</td><td>47.5%</td><td>7.2%</td></tr>
<tr><td>25-29</td><td>22.0%</td><td>10.6%</td><td>60.3%</td><td>7.2%</td></tr>
<tr><td>30-34</td><td>15.4%</td><td>8.2%</td><td>69.4%</td><td>7.0%</td></tr>
</table>
</td><td>Smoking status at time of delivery, England

Data for this year didn’t pass the data quality checks hence percentage not given [322]</td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td>
<table>
<tr><td>Rout./manual</td><td>46%</td><td>29%</td><td>38%</td></tr>
<tr><td>Never worked</td><td>50%</td><td>36%</td><td>29%</td></tr>
<tr><td>Unclassified</td><td>38%</td><td>22%</td><td>44%</td></tr>
</table>
Smoking in pregnancy by mother's age
<table>
<tr><td>age</td><td>Before/during pregnancy</td><td>Throughout pregnancy</td><td>Gave up smoking</td></tr>
<tr><td>< 20</td><td>65%</td><td>40%</td><td>38%</td></tr>
<tr><td>20-24</td><td>53%</td><td>30%</td><td>43%</td></tr>
<tr><td>25-29</td><td>36%</td><td>20%</td><td>45%</td></tr>
<tr><td>30-34</td><td>25%</td><td>13%</td><td>48%</td></tr>
<tr><td>35+</td><td>24%</td><td>13%</td><td>45%</td></tr>
</table>
</td><td></td><td>
<table>
<tr><td>35.39</td><td>14.9%</td><td>7.7%</td><td>70.0%</td><td>7.4%</td></tr>
<tr><td>40+</td><td>16.0%</td><td>6.1%</td><td>70.4%</td><td>7.6%</td></tr>
</table>
</td><td></td></tr>
<tr><td>2006</td><td></td><td></td><td>Total women:52,261
Current smokers: 21.7%
Former smokers: 8.5%
Never smokers: 60.4%
Not known: 9.4% [320]

Smoking by SES
<table>
<tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td>SIMD1</td><td>35.7%</td><td>8.2%</td><td>43.9%</td><td>12.2%</td></tr>
<tr><td>SIMD2</td><td>25.9%</td><td>10.1%</td><td>55.3%</td><td>8.7%</td></tr>
<tr><td>SIMD3</td><td>19.3%</td><td>9.6%</td><td>62.7%</td><td>8.5%</td></tr>
<tr><td>SIMD4</td><td>13.4%</td><td>8.1%</td><td>69.1%</td><td>9.4%</td></tr>
<tr><td>SIMD5</td><td>7.6%</td><td>6.5%</td><td>78.9%</td><td>6.9%</td></tr>
<tr><td>NK</td><td>15.1%</td><td>9.2%</td><td>61.6%</td><td>14.1%</td></tr>
</table>
Smoking by age</td><td>Smoking status at the time of delivery

15.1% maternities smoking out of total 601,262 maternities (95% CI 15.0-15.2%) 2006-07 [322]</td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td><20</td><td>39.8%</td><td>10.0%</td><td>40.2%</td><td>10.1%</td></tr>
<tr><td>20-24</td><td>32.2%</td><td>10.2%</td><td>47.8%</td><td>9.8%</td></tr>
<tr><td>25-29</td><td>21.3%</td><td>9.8%</td><td>59.5%</td><td>9.4%</td></tr>
<tr><td>30-34</td><td>14.9%</td><td>7.5%</td><td>68.7%</td><td>8.9%</td></tr>
<tr><td>35.39</td><td>14.8%</td><td>6.5%</td><td>69.2%</td><td>9.5%</td></tr>
<tr><td>40+</td><td>15.0%</td><td>5.2%</td><td>70.9%</td><td>8.9%</td></tr>
</table>
</td><td></td></tr>
<tr><td>2007</td><td></td><td></td><td>Total women:54,197
Current smokers: 20.8%
Former smokers: 9.4%
Never smokers: 57.8%
Not known: 12.0% [320]

Smoking by SES
<table>
<tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td>SIMD1</td><td>33.3%</td><td>8.3%</td><td>40.8%</td><td>17.7%</td></tr>
<tr><td>SIMD2</td><td>26.1%</td><td>11.1%</td><td>51.6%</td><td>11.2%</td></tr>
<tr><td>SIMD3</td><td>18.5%</td><td>10.6%</td><td>60.4%</td><td>10.5%</td></tr>
<tr><td>SIMD4</td><td>12.7%</td><td>9.3%</td><td>67.7%</td><td>10.3%</td></tr>
<tr><td>SIMD5</td><td>7.6%</td><td>7.6%</td><td>76.8%</td><td>8.0%</td></tr>
<tr><td>NK</td><td>13.7%</td><td>7.3%</td><td>62.0%</td><td>17.1%</td></tr>
</table>
Smoking by age
<table>
<tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr>
<tr><td><20</td><td>40.4%</td><td>9.9%</td><td>36.2%</td><td>13.4%</td></tr>
<tr><td>20-24</td><td>31.8%</td><td>10.8%</td><td>44.7%</td><td>12.8%</td></tr>
<tr><td>25-29</td><td>20.3%</td><td>10.1%</td><td>57.4%</td><td>12.2%</td></tr>
<tr><td>30-34</td><td>13.8%</td><td>8.9%</td><td>66.2%</td><td>11.1%</td></tr>
<tr><td>35.39</td><td>13.6%</td><td>7.4%</td><td>67.1%</td><td>11.9%</td></tr>
</table>
</td><td>Smoking status at time of delivery, England

14.4% (95% CI 14.4%-14.5%) maternities smoking out of total 634,035 maternities - 2007-08 [322]</td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>40+</td><td>13.6%</td><td>7.7%</td><td>67.6%</td><td>11.2%</td></tr>
</table>
</td><td></td></tr>
<tr><td>2008</td><td></td><td></td><td>
Total women: 56,927
Current smokers: 19.1%
Former smokers: 9.0%
Never smokers: 57.7%
Not known: 14.2% [320]

Smoking by SES
<table>
<tr><th>SES</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr>
<tr><td>SIMD1</td><td>30.1%</td><td>8.2%</td><td>41.1%</td><td>20.6%</td></tr>
<tr><td>SIMD2</td><td>24.2%</td><td>9.7%</td><td>52.8%</td><td>13.3%</td></tr>
<tr><td>SIMD3</td><td>16.9%</td><td>10.7%</td><td>60.2%</td><td>12.1%</td></tr>
<tr><td>SIMD4</td><td>11.8%</td><td>8.9%</td><td>67.5%</td><td>11.8%</td></tr>
<tr><td>SIMD5</td><td>6.5%</td><td>7.6%</td><td>75.7%</td><td>10.2%</td></tr>
<tr><td>NK</td><td>16.3%</td><td>6.4%</td><td>58.7%</td><td>18.6%</td></tr>
</table>
Smoking by age
<table>
<tr><th>Age</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr>
<tr><td><20</td><td>37.9%</td><td>10.7%</td><td>36.1%</td><td>15.4%</td></tr>
<tr><td>20-24</td><td>29.2%</td><td>10.5%</td><td>45.5%</td><td>14.7%</td></tr>
<tr><td>25-29</td><td>18.7%</td><td>9.7%</td><td>57.2%</td><td>14.4%</td></tr>
<tr><td>30-34</td><td>12.4%</td><td>8.1%</td><td>65.7%</td><td>13.9%</td></tr>
<tr><td>35.39</td><td>12.2%</td><td>7.4%</td><td>66.8%</td><td>13.6%</td></tr>
<tr><td>40+</td><td>13.4%</td><td>6.1%</td><td>67.9%</td><td>12.6%</td></tr>
</table>
</td><td>Smoking status at time of delivery, England
14.4% (95% CI 14.3%-14.5%) maternities smoking out of a total 640,681 maternities – 2008-09 [322]</td></tr>
<tr><td>2009</td><td></td><td></td><td>Total women: 57,338
Current smokers: 18.1%
Former smokers: 8.8%</td><td>Smoking status at time of delivery, England</td></tr>
</table>

<table>
<tr><th>Year</th><th>Infant Feeding Survey</th><th>HEA/HDA survey*</th><th>Scottish Morbidity Record Data</th><th>Other studies</th></tr>
<tr><td></td><td></td><td></td><td>Never smokers: 58.9%
Not known: 14.3% [323]

Smoking by SES
<table><tr><th>SES</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr><tr><td>SIMD1</td><td>29.4%</td><td>7.6%</td><td>44.2%</td><td>18.8%</td></tr><tr><td>SIMD2</td><td>22.1%</td><td>9.8%</td><td>54.8%</td><td>13.3%</td></tr><tr><td>SIMD3</td><td>15.9%</td><td>9.8%</td><td>62.4%</td><td>11.9%</td></tr><tr><td>SIMD4</td><td>10.9%</td><td>9.5%</td><td>67.6%</td><td>12.0%</td></tr><tr><td>SIMD5</td><td>5.8%</td><td>7.4%</td><td>73.6%</td><td>13.2%</td></tr><tr><td>NK</td><td>8.9%</td><td>7.0%</td><td>51.4%</td><td>32.7%</td></tr></table>
Smoking by age
<table><tr><th>Age</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr><tr><td><20</td><td>36.8%</td><td>11.2%</td><td>38.1%</td><td>13.9%</td></tr><tr><td>20-24</td><td>27.8%</td><td>10.7%</td><td>47.0%</td><td>14.4%</td></tr><tr><td>25-29</td><td>17.2%</td><td>9.4%</td><td>59.4%</td><td>13.9%</td></tr><tr><td>30-34</td><td>11.7%</td><td>7.6%</td><td>66.3%</td><td>14.4%</td></tr><tr><td>35.39</td><td>11.1%</td><td>6.8%</td><td>67.6%</td><td>14.5%</td></tr><tr><td>40+</td><td>13.4%</td><td>6.2%</td><td>65.8%</td><td>14.7%</td></tr></table></td><td>14.1% (14.0%-14.2%) maternities smoking out of a total 647,505 maternities – 2009-10 [322]</td></tr>
<tr><td>2010</td><td>Sample: A sample of 22,400 births selected from all births registered in the period August to November 2010. All births in Wales and Northern Ireland were sampled and over-sampling of deprived mothers was done in England and Scotland.

Sample size, response rate at each stage
Stage 1: initial sample 22,400, response rate (52%), further 7,788 questionnaires sent</td><td></td><td>Total women: 57,398
Current smokers: 18.8%
Former smokers: 10%
Never smokers: 60.6%
Not known: 10.7% [203]

Smoking by SES
<table><tr><th>SES</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr><tr><td>SIMD1</td><td>30.6%</td><td>8.9%</td><td>50.7%</td><td>9.9%</td></tr></table></td><td>Smoking status at time of delivery, England [322]

13.5% (95% CI 13.4%-13.6%) maternities smoking out of a total 659,763 maternities – 2010-11</td></tr>
</table>

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies

Results:

26% of women smoked before or during pregnancy

12% of women smoked throughout pregnancy

54% gave up smoking during or before pregnancy [59]

Smoking in pregnancy by social class

NS-SEC	Before/during pregnancy	Throughout pregnancy	Gave up smoking
Manag/prof.	14%	4%	72%
Intermediate	26%	10%	61%
Rout./manual	40%	20%	50%
Never worked	30%	21%	29%
Unclassified	29%	14%	53%

Smoking in pregnancy by mother's age

age	Before/during pregnancy	Throughout pregnancy	Gave up smoking
< 20	57%	35%	38%
20-24	44%	22%	50%
25-29	26%	11%	58%
30-34	17%	7%	62%
35+	15%	9%	58%

SIMD2	22.0%	10.6%	56.8%	10.6%
SIMD3	16.9%	11.0%	62.2%	9.9%
SIMD4	11.3%	10.1%	69.3%	9.2%
SIMD5	6.1%	9.6%	70.3%	14.0%
NK	12.1%	6.9%	53.4%	27.6%

Smoking by age

Age	Current	Former	Never	NK
<20	38.2%	12.0%	40.0%	9.8%
20-24	29.7%	10.8%	50.0%	9.5%
25-29	17.9%	10.0%	61.8%	10.3%
30-34	12.2%	9.6%	67.0%	11.2%
35.39	11.5%	9.0%	67.5%	12.0%
40+	12.8%	8.6%	67.8%	10.8%

10.10 MEDICAL READ CODES FOR CONGENITAL ANOMALIES

Med codes	Description
14H..00	H/O: congenital anomaly
14H1.00	H/O: cardiac anomaly
14H1.11	H/O: heart anomaly
14H2.00	H/O: cleft palate
14H3.00	H/O: cleft lip
14H4.00	H/O: urinary anomaly
14H5.00	H/O: cong. dislocation - hip
14HZ.00	H/O: congenital anomaly NOS
66g..00	Congenital heart condition monitoring
7010111	Insertion of Halber valve for spina bifida
7031000	Repair of meningoencephalocele
7043.00	Repair of spina bifida
7043000	Freeing of spinal tether
7043100	Closure of spinal myelomeningocele
7043200	Closure of spinal meningocele
7043y00	Other specified repair of spina bifida
7043z00	Repair of spina bifida NOS
7406200	Correction of congenital atresia of choana
7409.00	Correction of cleft lip nasal deformity
7409000	Primary correction of cleft lip nasal deformity
7409011	Primary correction of alar cartilage
7409012	McComb primary correction of cleft nose
7409013	Pigott alar leap-frog correction
7409100	Secondary correction of cleft lip nasal deformity
7409111	Secondary correction of alar slump
7409112	Kernahan correction of alar slump
7409113	Skoog correction of alar slump
7409114	Dibbell correction of alar slump
7409200	Correction of cleft lip nasal tip deformity
7409211	Alar base advancement
7409212	Kilner inroll
7409300	Columella lengthening procedure unspecified
7409400	Unilateral columella lengthening operation
7409411	Tajima unilateral columella lengthening operation
7409500	Rhinoplasty for cleft lip nasal deformity
7409600	Septorhinoplasty for cleft lip nasal deformity
7409700	Septoplasty for cleft lip nasal deformity
7409800	Correction of nostril stenosis
7409z00	Correction of nasal deformity NOS
7502.00	Correction of deformity of lip
7502.11	Repair of cleft lip operations
7502000	Primary closure of cleft lip, unspecified
7502011	Lemesurier cleft lip repair
7502012	Millard cleft lip correction
7502013	Randall cleft lip repair
7502014	Tenison cleft lip repair
7502100	Revision of primary closure of cleft lip
7502200	Adjustment to vermilion border of lip NEC
7502300	Unilateral lip adhesion
7502400	Bilateral lip adhesion
7502500	Repair of unilateral cleft lip using straight line technique
7502511	Kilner repair unilateral cleft lip
7502600	Repair unilat cleft lip - rotation advancement flp technique
7502611	Millard repair unilateral cleft lip
7502700	Repair of unilateral cleft lip with triangular flap
7502711	Randall repair unilateral cleft lip
7502712	Skoog repair unilateral cleft lip
7502713	Tennyson repair unilateral cleft lip
7502800	Repair unilateral cleft lip with quadrilateral flap
7502811	Repair unilateral cleft lip with quadrilateral flap
7502900	Repair of unilateral cleft lip unspecified
7502A00	Repair bilateral cleft lip - rotation advancement flap tech
7502A11	Rep bilat cleft lip Millard
7502B00	Repair of bilateral cleft lip with quadrilateral flap
7502B11	Barsky repair bilateral cleft lip
7502C00	Repair of bilateral cleft lip using straight line technique
7502C11	Manchester bilateral cleft lip repair
7502C12	Veau type III bilateral cleft lip repair
7502D00	Repair of bilateral cleft lip unspecified
7502E00	Synchronous bilateral cleft lip repair
7502F00	Asynchronous bilateral cleft lip repair
7502y00	Other specified correction of deformity of lip
7502z00	Correction of deformity of lip NOS
7525.00	Correction of deformity of palate
7525.11	Repair of deformity of palate
7525.12	Repair of cleft palate
7525000	Primary repair of cleft palate, unspecified
7525011	Kilner repair of cleft palate
7525012	Langenbeck repair of cleft palate
7525013	Wardill repair of cleft palate
7525100	Revision of repair of cleft palate
7525200	Repair cleft hard palate post based axial transposition flap
7525211	Repair cleft hard palate post based axial transposition flap

7525212	Wardill repair cleft palate
7525213	Veau flap repair cleft palate
7525300	Repair of cleft hard palate with bipedicled flaps
7525311	Langenbeck repair cleft palate
7525400	Repair of cleft soft palate with Z-plasty
7525411	Furlow repair cleft palate
7525500	Repair of anterior cleft palate with local flap
7525600	Repair of anterior cleft palate with vomerine flap
7525700	Repair of cleft soft palate with intra-velar veloplasty
7525711	Rep anterior cleft palate local flap
7525712	Plastic repair palate mucosal graft
7525800	Repair cleft soft palate with other musculature correction
7525y00	Other specified correction of deformity of palate
7525z00	Correction of deformity of palate NOS
7606000	Closure of tracheooesophageal fistula
7606011	Excision of tracheooesophageal fistula
7606200	Correction of congenital atresia of oesophagus
761B100	Repair of congenital atresia of pylorus
7902.00	Correction of tetralogy of Fallot
7902000	Correct Fallot tetralogy- valved right ventr outflow conduit
7902100	Correct Fallot tetralogy- right ventric outflow conduit NEC
7902200	Correct Fallot tetralogy- right ventricular outflow patch
7902300	Revision of correction of tetralogy of Fallot
7902y00	Other specified correction of tetralogy of Fallot
7902z00	Correction of tetralogy of Fallot NOS
7903.00	Atrial inversion ops for transposition of great vessels
7903.11	Mustard interatrial tr venous return
7903.12	Senning correction for transposition of great vessels
7903000	Atrium reconstruction atrial patch for transpos great vessel
7903100	Atrium reconstruction atrial wall for transpos great vessels
7903y00	Atrial inversion op for transposition of great vessels OS
7903z00	Atrial inversion op for transposition of great vessels NOS
7904.00	Other correction of transposition of great vessels
7904000	Repositioning of transposed great vessels
7904y00	Other correction of transposition of great vessels OS
7904z00	Other correction of transposition of great vessels NOS
7905.00	Correction of total anomalous pulmonary venous connection
7905000	Correct total anomal pulm venous connect to supracard vessel
7905100	Correct total anomal pulm venous connect to coronary sinus
7905200	Correct total anomal pulm venous connect to infradiaph vess
7905y00	Correction of total anomalous pulmonary venous connection OS
7905z00	Correction total anomalous pulmonary venous connection NOS
7906.00	Closure of defect of atrioventricular septum
7906000	Close defect atrioventric septum using dual prosthetic patch
7906100	Close defect atrioventric septum using prosthetic patch NEC
7906200	Closure defect atrioventricular septum using tissue graft
7906300	Closure of persistent ostium primum
7906400	Primary closure of defect of atrioventricular septum NEC
7906500	Revision of closure of defect of atrioventricular septum
7906y00	Other specified closure of defect of atrioventricular septum
7906z00	Closure of defect of atrioventricular septum NOS
7907.00	Closure of defect of interatrial septum
7907000	Closure defect of interatrial septum using prosthetic patch
7907100	Closure defect of interatrial septum using pericardial patch
7907200	Closure defect of interatrial septum using tissue graft NEC
7907300	Primary closure of defect of interatrial septum NEC
7907400	Revision of closure of defect of interatrial septum
7907y00	Other specified closure of defect of interatrial septum
7907z00	Closure of defect of interatrial septum NOS
7908.00	Closure of defect of interventricular septum
7908000	Close defect interventricular septum using prosthetic patch
7908100	Close defect interventricular septum using pericardial patch
7908200	Close defect interventricular septum using tissue graft NEC
7908300	Primary closure of defect of interventricular septum NEC
7908400	Revision of closure of defect of interventricular septum
7908y00	Other specified closure of defect of interventricular septum
7908z00	Closure of defect of interventricular septum NOS
7909.00	Closure of defect of unspecified septum of heart
7909000	Closure of defect of heart septum using prosthetic patch NEC
7909100	Closure defect of heart septum using pericardial patch NEC
7909200	Closure of defect of septum of heart using tissue graft NEC
7909300	Primary closure of defect of septum of heart NEC
7909400	Revision of closure of septum of heart NEC
7909y00	Other specified closure of defect unspecified heart septum
7909z00	Closure of defect of unspecified septum of heart NOS
7A00.00	Open operations for combined abnormality of great vessels
7A00000	Correction of persistent truncus arteriosus
7A00100	Application of band to persistent truncus arteriosus
7A00200	Repair of hemitruncus arteriosus
7A00300	Closure of aortopulmonary window
7A00y00	Open operation for combined abnormality of great vessels OS

7A00z00	Open operation for combined abnormality of great vessels NOS
7A01.00	Open correction of patent ductus arteriosus
7A01.11	Open correction of patent ductus arteriosus (PDA)
7A01000	Division of patent ductus arteriosus
7A01100	Ligation of patent ductus arteriosus
7A01200	Closure of patent ductus arteriosus NEC
7A01300	Revision of correction of patent ductus arteriosus
7A01y00	Other specified open correction of patent ductus arteriosus
7A01z00	Open correction of patent ductus arteriosus NOS
7A02.00	Transluminal operations on abnormality of great vessel
7A02000	Percut transluminal prosth occlusion patent ductus arterios
7A02011	Percut translum prosth occlus patent ductus arteriosus (PDA)
7A02y00	Transluminal operation on abnormality of great vessel OS
7A02z00	Transluminal operation on abnormality of great vessel NOS
7B41000	Other hypospadias repair
7B41011	Byars hypospadias repair
7B41012	Cecil reconstruction of urethra
7B41013	Denis - Browne hypospadias repair
7B41014	Ombredanne hypospadias repair
7B41015	Van der Meulen hypospadias repair
7B41016	Young hypospadias repair
7B41017	First stage hypospadias repair
7B41018	Second stage hypospadias repair
7B41100	Epispadias repair
7B41111	Browne-Denis epispadias repair
7B41112	Denis-Browne epispadias repair
7B41113	Young-Dees epispadias repair
7B41700	MAGPI hypospadias repair
7B41800	Duckett hypospadias repair
7C04200	Excision of cyst of male hydatid of Morgagni
7C09700	Excision of appendix of testis
7C09711	Excision of male hydatid of Morgagni
7F1A300	Drainage of hydrocephalus of fetus to facilitate delivery
7H01000	Correction of pectus deformity of chest wall
7H01011	Correction of pectus carinatum
7H01012	Correction of pectus excavatum
7H0D300	Repair of congenital diaphragmatic hernia
7L0D.00	Correction of congenital deformity of shoulder or upper arm
7L0E.00	Correction of congenital deformity of forearm
7L0F.00	Correction of congenital deformity of hand
7L0F000	Reduction of gigantism of hand
7L0F100	Correction of mirror hand
7L0F200	Correction of syndactyly of fingers using skin graft
7L0F300	Correction of syndactyly of fingers using skin expander
7L0F400	Amputation of duplicate thumb
7L0F500	Amputation of supernumerary finger NEC
7L0F600	Stabilisation of hypoplastic thumb
7L0F700	Repositioning of thumb for cleft hand
7L0F800	Correction of cleft hand
7L0F900	Release of thumb-in-palm deformity
7L0FA00	Realignment of congenital ulnar drift
7L0FB00	Correction of camtodactyly
7L0FC00	Correction of clinodactyly with osteotomy and bone graft
7L0FD00	Correction of clinodactyly with closing wedge osteotomy
7L0FE00	Correction of clinodactyly with reversed wedge osteotomy
7L0FF00	Correction of radial polydactyly
7L0FG00	Excision of radial digit & skeletal repair for polydactyly
7L0FH00	Excision of ulnar digit and skeletal repair for polydactyly
7L0FJ00	Correction of macrodactyly
7L0Fy00	Other specified correction of congenital deformity of hand
7L0Fz00	Correction of congenital deformity of hand NOS
7L0G.00	Correction of congenital deformity of hip
7L0G000	Open reduction of congenital dislocation of hip
7L0G011	Ferguson open reduction of congenital deformity of hip
7L0G012	Ludloff open reduction of congenital deformity of hip
7L0G100	Primary osteotomy pelvis correction congenital deformity hip
7L0G111	Albee osteotomy of pelvis
7L0G112	Bosworth osteotomy of pelvis
7L0G113	Chiari osteotomy of pelvis
7L0G114	Dial osteotomy of pelvis
7L0G115	Gill osteotomy of pelvis
7L0G116	Pemberton osteotomy of ilium
7L0G117	Salter osteotomy of pelvis
7L0G118	Shelf procedure for stabilisation of hip joint
7L0G119	Steez osteotomy of pelvis
7L0G11A	Sutherland osteotomy of pelvis
7L0G200	Secndry arthroplasty hip for correctn congenital deformity
7L0G211	Colonna arthroplasty of hip
7L0G300	Intraartic soft tiss proced correct congenital deformity hip
7L0G400	Extraarticular proced correction congenital deformity of hip
7L0G500	Osteotomy of ilium correction of congenital deformity of hip
7L0G600	Femoral osteotomy for correction congenital deformity of hip
7L0G700	Pelvic osteotomy for congenital deformity of hip
7L0G800	Salter osteotomy for congenital deformity of hip

7L0G900	Pemberton osteotomy for congenital deformity of hip
7L0GA00	Chiari osteotomy for congenital deformity of hip
7L0GB00	Colonna osteotomy for congenital deformity of hip
7L0GC00	Shelf procedure for correction congenital deformity of hip
7L0Gy00	Other specified correction of congenital deformity of hip
7L0Gz00	Correction of congenital deformity of hip NOS
7L0Gz11	Adams correction of congenital dislocation of hip
7L0H.00	Correction of congenital deformity of leg
7L0H000	Open reduction of congenital dislocation of knee
7L0H100	Correction of pseudarthrosis of tibia
7L0H111	Boyd bone graft pseudarthrosis of tibia
7L0H112	McFarland bone graft pseudoarthrosis of tibia
7L0H200	Excision of anlage of fibula
7L0H300	Excision of anlage of tibia
7L0H400	Centralisation tarsus correction congenital deformity of leg
7L0H500	Reversal rotation plasty ankle correct congenital deform leg
7L0H511	Van Nes rotationplasty for congenital deformity
7L0H600	Coventry tibial osteotomy
7L0H700	Gruca tibial bifurcation procedure
7L0H800	Open reduction congenital dislocation of patella
7L0H900	Tibiofibular synostosis for congenital deformity
7L0Hy00	Other specified correction of congenital deformity of leg
7L0Hz00	Correction of congenital deformity of leg NOS
7L0J.00	Primary correction of congenital deformity of foot
7L0J.11	Primary correction of club foot
7L0J.12	Primary correction of talipes
7L0J000	Release pantalar joints correction congenital deformity foot
7L0J011	Turco soft tissue release for club foot
7L0J100	Post release foot joints for correction congenital deformity
7L0J200	Medial release foot joints- correction congenital deformity
7L0J211	Dillwyn operation for club foot
7L0J212	Evans operation for club foot
7L0J213	Medial release of joints of foot for correction of club foot
7L0J214	Perkins operation for club foot
7L0J300	Anterior release foot joints correction congenital deformity
7L0J400	Posteromedial release of clubfoot
7L0J500	Combined posteromedial + posterolateral release of clubfoot
7L0J600	Lateral release for congenital deformity of foot
7L0J700	Correction of congenital vertical talus
7L0J800	Complete subtalar release of clubfoot
7L0Jy00	Primary correction of congenital deformity of foot OS
7L0Jz00	Primary correction of congenital deformity of foot NOS
7L0K.00	Other correction of congenital deformity of foot
7L0K.11	Other operations for club foot
7L0K.12	Other correction of talipes
7L0K000	Osteotomy of body of os calcis
7L0K011	Baker osteotomy of body of os calcis
7L0K012	Dwyer osteotomy of body of os calcis
7L0K100	Wedge tarsectomy for correction congenital deformity of foot
7L0K111	Elmslie wedge tarsectomy
7L0K200	Reduction of gigantism of foot
7L0K300	Separation of tarsal coalition
7L0K400	Triple arthrodesis for correction of congenital deformity
7L0K500	Dilwyn Evans proc for correction of congenital deformity
7L0K600	Metatarsal osteotomy for correction of congenital deformity
7L0K700	Closure of cleft foot
7L0Ky00	Other correction of congenital deformity of foot OS
7L0Kz00	Other correction of congenital deformity of foot NOS
7L0L.00	Correction of minor congenital deformity of foot
7L0L000	Release of Streeter(constriction) band
7L0L100	Release of syndactyly of toes
7L0L200	Amputation of supernumerary toe
7L0L300	Correction of curly fifth toe
7L0L311	Lapidus transplantation of tendon of fifth toe
7L0L400	Correction of congenital crossed toes
7L0L500	Reduction of macrodactyly of toe
7L0Ly00	Correction of minor congenital deformity of foot OS
7L0Lz00	Correction of minor congenital deformity of foot NOS
7L0N.00	Correction of complex craniofacial deformity
7L0N000	Cranio-orbital remodelling for plagiocephaly
7L0N100	Cranio-orbital remodelling for trigonocephaly
7L0N200	Cranio-orbital remodelling, unspecified
7L0N400	Frontal advancement - fixed
7L0N500	Correction of oblique facial cleft
7L0Nz00	Correction of complex craniofacial deformity NOS
9RD0.00	Transfer of care from paediatric congenital heart service
A560200	Rubella deafness
AD00.00	Toxoplasma meningoencephalitis
F030700	Encephalitis due to cytomegalovirus
F030711	Cytomegaloviral encephalitis
F033400	Encephalitis due to toxoplasmosis
F033411	Toxoplasmosis encephalitis
F113000	Normal pressure hydrocephalus

F113011	Low pressure hydrocephalus
F115.00	Hydrocephalus
F11x300	Cerebral degeneration due to congenital hydrocephalus
F23y511	Congenital suprabulbar paresis
F427J00	Leber's congenital amaurosis
F480011	Congenital amblyopia
F486300	Congenital night blindness NOS
F4Gy011	Encephalocoele of orbit
F4K5100	Congenital nystagmus
F591800	Congenital prelingual deafness
L236.00	Hydrocephalic disproportion
L236000	Hydrocephalic disproportion unspecified
L236200	Hydrocephalic disproportion with antenatal problem
L236z00	Hydrocephalic disproportion NOS
L253.11	Fetus with suspected rubella damage via mother
L254.12	Suspect fetal damage from maternal toxoplasmosis
P0...00	Anencephalus and similar anomalies
P00..00	Anencephalus
P00..11	Congenital absence of brain
P000.00	Acrania
P001.00	Amyelencephalus
P002.00	Hemicephaly
P002.11	Hemianencephaly
P00y.00	Other specified anencephalus
P00z.00	Anencephalus NOS
P01..00	Craniorachischisis
P02..00	Iniencephaly
P020.00	Iniencephaly - closed
P021.00	Open iniencephaly
P02z.00	Iniencephaly NOS
P0z..00	Anencephalus and similar anomalies NOS
P1...00	Spina bifida
P10..00	Spina bifida with hydrocephalus
P10..11	Arnold - Chiari syndrome
P100.00	Unspecified spina bifida with hydrocephalus
P100000	Spina bifida with hydrocephalus, unspecified
P100100	Cervical spina bifida with hydrocephalus
P100200	Thoracic spina bifida with hydrocephalus
P100300	Lumbar spina bifida with hydrocephalus
P100z00	Spina bifida with hydrocephalus NOS
P101.00	Arnold - Chiari syndrome
P101.11	Closed spina bifida with Arnold-Chiari malformation
P101000	Chiari malformation type I
P101100	Chiari malformation type II
P101200	Chiari malformation type III
P101300	Chiari malformation type IV
P102.00	Spina bifida with hydrocephalus - open
P102.11	Fissured spine with hydrocephalus
P102.12	Hydromyelocele with hydrocephalus
P102.13	Myelocele with hydrocephalus
P102.14	Rachischisis with hydrocephalus
P102000	Unspecified spina bifida with hydrocephalus - open
P102100	Cervical spina bifida with hydrocephalus - open
P102200	Thoracic spina bifida with hydrocephalus - open
P102300	Lumbar spina bifida with hydrocephalus - open
P102400	Sacral spina bifida with hydrocephalus - open
P102z00	Spina bifida with hydrocephalus - open NOS
P103.00	Spina bifida with hydrocephalus - closed
P103000	Unspecified spina bifida with hydrocephalus - closed
P103100	Cervical spina bifida with hydrocephalus - closed
P103200	Thoracic spina bifida with hydrocephalus - closed
P103300	Lumbar spina bifida with hydrocephalus - closed
P103400	Sacral spina bifida with hydrocephalus - closed
P103z00	Spina bifida with hydrocephalus - closed NOS
P103z11	Thoracolumbar spina bifida with hydrocephalus - closed
P104.00	Spina bifida with hydrocephalus of late onset
P105.00	Spina bifida with stenosis of aqueduct of Sylvius
P10y.00	Other specified spina bifida with hydrocephalus
P10y000	Dandy - Walker syndrome with spina bifida
P10yz00	Other spina bifida with hydrocephalus NOS
P10z.00	Spina bifida with hydrocephalus NOS
P11..00	Spina bifida without mention of hydrocephalus
P110.00	Spina bifida without mention of hydrocephalus, unspecified
P110.11	Split notochord syndrome
P110000	Spina bifida without hydrocephalus, site unspecified
P110100	Cervical spina bifida without mention of hydrocephalus
P110200	Thoracic spina bifida without mention of hydrocephalus
P110300	Lumbar spina bifida without mention of hydrocephalus
P110z00	Unspecified spina bifida without hydrocephalus NOS
P111.00	Spinal hydromeningocele
P111000	Spinal hydromeningocele, unspecified
P111100	Cervical spinal hydromeningocele
P111200	Thoracic spinal hydromeningocele
P111z00	Spinal hydromeningocele NOS
P112.00	Hydromyelocele

P112000	Hydromyelocele of unspecified site
P112100	Cervical hydromyelocele
P112200	Thoracic hydromyelocele
P112300	Lumbar hydromyelocele
P112z00	Hydromyelocele NOS
P113.00	Spinal meningocele
P113000	Spinal meningocele of unspecified site
P113100	Cervical spinal meningocele
P113200	Thoracic spinal meningocele
P113300	Lumbar spinal meningocele
P113z00	Spinal meningocele NOS
P114.00	Meningomyelocele
P114000	Meningomyelocele of unspecified site
P114100	Cervical meningomyelocele
P114200	Thoracic meningomyelocele
P114300	Lumbar meningomyelocele
P114z00	Meningomyelocele NOS
P115.00	Myelocele
P115000	Myelocele of unspecified site
P115100	Cervical myelocele
P115200	Thoracic myelocele
P115300	Lumbar myelocele
P115z00	Myelocele NOS
P116.00	Myelocystocele
P116000	Myelocystocele of unspecified site
P116100	Cervical myelocystocele
P116200	Thoracic myelocystocele
P116300	Lumbar myelocystocele
P116z00	Myelocystocele NOS
P117.00	Spina bifida without hydrocephalus - open
P117.11	Fissured spine
P117.12	Rachischisis
P117000	Unspecified spina bifida without hydrocephalus - open
P117100	Cervical spina bifida without hydrocephalus - open
P117200	Thoracic spina bifida without hydrocephalus - open
P117300	Lumbar spina bifida without hydrocephalus - open
P117400	Sacral spina bifida without hydrocephalus - open
P117z00	Spina bifida without hydrocephalus - open NOS
P118.00	Spina bifida without hydrocephalus - closed
P118000	Unspecified spina bifida without hydrocephalus - closed
P118100	Cervical spina bifida without hydrocephalus - closed
P118200	Thoracic spina bifida without hydrocephalus - closed
P118300	Lumbar spina bifida without hydrocephalus - closed
P118400	Sacral spina bifida without hydrocephalus - closed
P118z00	Spina bifida without hydrocephalus - closed NOS
P118z11	Thoracolumbar spina bifida without hydrocephalus - closed
P11y.00	Other specified spina bifida without hydrocephalus
P11y.11	Syringomyelocele
P11z.00	Spina bifida without mention of hydrocephalus NOS
P11z.11	Rachischisis
P11z.12	Syringomyelocele
P11z.13	Billroth's disease
P11z.14	Congenital hernia of dura mater
P1z..00	Spina bifida NOS
P2...00	Other nervous system congenital anomalies
P20..00	Encephalocele
P20..11	Hydroencephalocele
P20..12	Cephalocele
P20..13	Congenital cerebral hernia
P20..14	Congenital endaural hernia
P20..15	Sinus pericranii
P20..16	Congenitalcerebral hernia
P200.00	Encephalocystocele
P201.00	Encephalomyelocele
P202.00	Hydromeningocele - cranial
P203.00	Meningocele - cerebral
P203.11	Meningocele - cranial
P204.00	Meningoencephalocele
P205.00	Frontal encephalocele
P206.00	Nasofrontal encephalocele
P20z.00	Encephalocele NOS
P20z000	Occipital encephalocele
P20z100	Encephalocele of other specified site
P20z111	Absence of roof of orbit
P21..00	Microcephalus
P210.00	Hydromicrocephaly
P211.00	Micrencephaly
P21z.00	Microcephalus NOS
P22..00	Reduction deformities of brain
P220.00	Agenesis of brain, part unspecified
P221.00	Aplasia of brain, part unspecified
P222.00	Hypoplasia of brain, part unspecified
P223.00	Agyria
P223.11	Lissencephaly
P224.00	Arhinencephaly
P225.00	Holoprosencephaly
P226.00	Microgyria

P226.11	Hypoplasia of brain gyri
P226000	Congenital bilateral perisylvian syndrome
P227.00	Anomalies of cerebrum
P227000	Agenesis of cerebrum
P227100	Congenital hypoplasia of cerebrum
P227z00	Anomaly of cerebrum NOS
P228.00	Anomalies of corpus callosum
P228000	Congenital absence of corpus callosum
P228011	Agenesis of corpus callosum
P228100	Hypoplasia of corpus callosum
P228200	Aplasia of corpus callosum
P228300	Aicardi syndrome
P228z00	Anomaly of corpus callosum NOS
P229.00	Anomalies of hypothalamus
P22A.00	Anomalies of cerebellum
P22A000	Congenital absence of cerebellum
P22A011	Agenesis of cerebellum
P22A100	Hypoplasia of cerebellum
P22A200	Aplasia of cerebellum
P22Az00	Anomaly of cerebellum NOS
P22y.00	Other specified reduction deformities of brain
P22y000	Cebocephaly
P22y100	Familial aplasia of the vermis
P22y111	Joubert syndrome
P22y200	Gillespie syndrome
P22y300	Partial absence of septum pellucidum
P22yz00	Other reduction deformity of brain NOS
P22z.00	Reduction deformities of brain NOS
P22z.11	Cerebellar hypoplasia
P22z.12	Agenesis of part of brain NEC
P22z.13	Hypoplasia of part of brain NEC
P22z.14	Aplasia of part of brain NEC
P23..00	Congenital hydrocephalus
P230.00	Aqueduct of Sylvius anomaly
P230.11	Hydrocephauls with anomaly of aqueduct of Sylvius
P230.12	Stenosis of aqueduct of Sylvius
P230000	Aqueduct of Sylvius obstruction
P230011	Aqueduct of Sylvius septum NEC
P230100	Aqueduct of Sylvius stenosis
P230200	Atresia of aqueduct of Sylvius NEC
P230z00	Aqueduct of Sylvius anomaly NOS
P231.00	Foramen of Magendie atresia
P232.00	Foramen of Luschka atresia
P233.00	Atresia of foramina of Magendie and Luschka

P233.11	Dandy - Walker syndrome
P233.12	Hydrocephalus with atresia of foramina of Magendie+Luschka
P234.00	Hydranencephaly
P23y.00	Other specified congenital hydrocephalus
P23z.00	Congenital hydrocephalus NOS
P24..00	Other specified brain anomalies
P240.00	Congenital cerebral cyst
P240.11	Congenital intracerebral cyst
P240000	Single congenital cerebral cyst
P240100	Multiple congenital cerebral cysts
P240200	Schizencephaly
P240z00	Congenital cerebral cyst NOS
P241.00	Macroencephaly
P241.11	Megalencephaly
P241.12	Enlarged brain
P241.13	Macrocephaly
P242.00	Macrogyria
P243.00	Porencephaly
P244.00	Ulegyria
P245.00	Congenital adhesions of cerebral meninges
P246.00	Septo-optic dysplasia
P247.00	Dysplasia of cerebral cortex
P248.00	Congenital dilated lateral ventricles of brain
P249.00	Megalencephaly
P24A.00	Hemimegalencephaly
P24x.00	Multiple brain anomalies
P24z.00	Other specified brain anomalies NOS
P25..00	Other specified spinal cord anomalies
P250.00	Diastematomyelia
P251.00	Hydromyelia
P251.11	Hydrorachis
P252.00	Congenital tethering of spinal cord
P25y.00	Other specified anomalies of spinal cord
P25y.11	Neuroenteric cyst
P25y000	Amyelia
P25y100	Atelomyelia
P25y111	Myelatelia
P25y112	Myelodysplasia of spinal cord
P25y200	Congenital anomaly of spinal meninges
P25y300	Defective development of the cauda equina
P25y400	Spinal cord hypoplasia
P25yz00	Other specified spinal cord anomalies NOS
P25z.00	Spinal cord anomalies NOS
P2x..00	Other specified nervous system anomalies

P2x0.00	Agenesis of nerve, unspecified
P2x1.00	Brachial plexus displacement
P2x2.00	Familial dysautonomia
P2x3.00	Jaw-winking syndrome
P2x4.00	Marcus - Gunn syndrome
P2x5.00	Riley - Day syndrome
P2x6.00	Chiari malformation type I
P2x7.00	Congenital facial nerve palsy
P2x8.00	Structural central nervous system abnormality
P2xz.00	Other specified nervous system anomalies NOS
P2xz000	Agenesis of nerve NEC
P2xz100	Congenital optic atrophy
P2y..00	Unspec nervous system anomaly of brain/cord/nervous system
P2y0.00	Congenital brain anomaly
P2y1.00	Congenital spinal cord anomaly
P2yz.00	Unspecified nervous system anomaly NOS
P2z..00	Nervous system anomalies NOS
P3...00	Congenital eye anomalies
P30..00	Anophthalmos
P300.00	Clinical anophthalmos, unspecified
P300100	Agenesis of eye
P300200	Congenital absence of eye
P300z00	Anophthalmos NOS
P301.00	Congenital cystic eyeball
P302.00	Cryptophthalmos syndrome
P303.00	Congenital absence of eyes
P30z.00	Anophthalmos NOS
P31..00	Microphthalmos
P310.00	Microphthalmos, unspecified
P310000	Dysplasia of eye
P310100	Hypoplasia of eye
P310200	Rudimentary eye
P310z00	Unspecified microphthalmos NOS
P311.00	Simple microphthalmos
P312.00	Microphthalmos with other eye anomaly
P313.00	Lenz microphthalmia syndrome
P31z.00	Microphthalmos NOS
P32..00	Buphthalmos
P320.00	Buphthalmos, unspecified
P320000	Congenital glaucoma
P320011	Newborn glaucoma
P320100	Hydrophthalmos
P320z00	Unspecified buphthalmos NOS
P321.00	Simple buphthalmos
P321.11	Enlarged eye NOS
P322.00	Buphthalmos with other eye anomaly
P322000	Congenital keratoglobus
P322100	Congenital megalocornea
P322111	Enlarged cornea
P322112	Congenital macrocornea
P322z00	Buphthalmos with other eye anomaly NOS
P32z.00	Buphthalmos NOS
P33..00	Congenital cataract and lens anomalies
P33..11	Congenital lens anomaly
P330.00	Congenital cataract, unspecified
P331.00	Capsular and subcapsular cataract
P331000	Capsular cataract
P331100	Subcapsular cataract
P331z00	Capsular or subcapsular cataract NOS
P332.00	Cortical and zonular cataract
P332000	Cortical cataract - congenital
P332100	Zonular cataract
P332z00	Cortical or zonular cataract NOS
P333.00	Nuclear cataract - congenital
P334.00	Total and subtotal congenital cataract
P334000	Total congenital cataract
P334100	Subtotal congenital cataract
P334z00	Total or subtotal congenital cataract NOS
P335.00	Congenital aphakia
P335.11	Congenital absence of lens
P335.12	Agenesis of lens
P336.00	Anomalies of lens shape
P336000	Microphakia
P336100	Spherophakia
P336111	Spherical lens
P336200	Coloboma of lens
P336z00	Anomalies of lens shape NOS
P337.00	Congenital ectopic lens
P337.11	Congenital displaced lens
P337.12	Congenital dislocation of lens
P33y.00	Other specified congenital cataract or lens anomaly
P33y000	Blue dot cataract
P33y100	Congenital membranous cataract
P33yz00	Other congenital cataract or lens anomaly NOS
P33z.00	Congenital cataract or lens anomaly NOS
P34..00	Anterior chamber anomalies
P340.00	Corneal size and shape anomalies
P340000	Microcornea

P340100	Congenital keratoconus
P340200	Cornea plana
P340z00	Corneal size or shape anomalies NOS
P341.00	Congenital corneal opacities
P341.11	Arcus juvenilis
P341000	Congenital corneal opacity with visual deficit
P341100	Congenital corneal opacity without visual deficit
P341z00	Congenital corneal opacities NOS
P342.00	Specified anterior chamber anomalies
P342000	Axenfield's anomaly
P342100	Peter's anomaly
P342200	Rieger's anomaly
P342z00	Specified anterior chamber anomalies NOS
P343.00	Aniridia
P343.11	Congenital absence of iris
P343.12	Agenesis of iris
P344.00	Other iris and ciliary body anomalies
P344.11	Goniodysgenesis
P344000	Congenital anisocoria
P344100	Atresia of pupil
P344200	Coloboma of iris
P344300	Corectopia
P344311	Ectopic pupil
P344400	Polycoria
P344500	Hypoplasia of iris
P344600	Aplasia of iris
P344z00	Other iris or ciliary body anomalies NOS
P345.00	Specified anomalies of sclera
P345000	Blue sclera
P345z00	Specified anomaly of sclera NOS
P346.00	Multiple anterior segment anomalies
P34y.00	Other specified anterior segment anomalies
P34z.00	Anterior segment anomalies NOS
P35..00	Posterior chamber congenital anomalies
P350.00	Vitreous anomalies
P350000	Congenital vitreous opacity
P350z00	Vitreous anomalies NOS
P351.00	Fundus coloboma
P352.00	Congenital chorioretinal degeneration
P353.00	Congenital folds and cysts of the posterior segment
P353000	Congenital folds of the posterior segment
P353100	Congenital cysts of the posterior segment
P353z00	Congenital folds or cysts of the posterior segment NOS
P354.00	Congenital macular changes
P355.00	Other congenital retinal changes
P355000	Coloboma of retina
P355100	Congenital retinal fold
P355200	Congenital hypertrophy of retinal pigment epithelium
P355z00	Other congenital retinal changes NOS
P356.00	Specified optic disc anomalies
P356.11	Optic disc congenital anomalies
P356000	Congenital optic disc coloboma
P356z00	Specified optic disc anomaly NOS
P357.00	Posterior chamber vascular anomalies
P357000	Congenital retinal aneurysm
P357100	Congenital arteriovenous malformation of retina
P357200	Congenital stricture of retinal artery
P357z00	Posterior chamber vascular anomalies NOS
P358.00	Specified anomalies of choroid
P358000	Coloboma of choroid
P358z00	Specified anomaly of choroid NOS
P35y.00	Other specified congenital anomalies of posterior chamber
P35z.00	Congenital anomalies of posterior chamber NOS
P36..00	Congenital anomalies of eyelid, lacrimal system and orbit
P360.00	Congenital ptosis
P360.11	Blepharoptosis
P361.00	Congenital eyelid deformity
P361000	Ablepharon -absent eyelids
P361100	Accessory eyelid
P361200	Congenital entropion
P361300	Congenital ectropion
P361400	Congenital blepharophimosis
P361500	Coloboma of eyelids
P361z00	Congenital eyelid deformity NOS
P362.00	Other specified congenital eyelid anomalies
P362000	Agenesis of cilia
P362100	Agenesis of eyelid
P362200	Fused eyelids
P362300	Hypoplasia of eyelid
P362z00	Other specified congenital eyelid anomalies NOS
P363.00	Congenital lacrimal gland anomalies
P364.00	Congenital lacrimal passage anomalies
P364.11	Congenital blocked tear duct
P364000	Agenesis of lacrimal apparatus
P364011	Congenital absence of lacrimal apparatus
P364100	Agenesis of punctum lacrimale
P364111	Congenital absence of punctum lacrimale

P364200	Accessory lacrimal canal
P364300	Stenosis or stricture of lacrimal duct
P364400	Congenital blocked tear duct
P364y00	Other specified congenital anomaly of lacrimal passages
P364z00	Congenital anomaly of lacrimal passages NOS
P365.00	Congenital orbit anomalies
P36z.00	Other/unspecified anomalies of eyelid/lacrimal system/orbit
P36z000	Accessory eye muscles
P36z100	Hypoplasia of eye muscle
P36zz00	Eyelid, lacrimal system and orbit congenital anomalies NOS
P37..00	Macrophthalmos
P3y..00	Other specified eye anomalies
P3y0.00	Ocular albinism
P3yz.00	Other eye anomalies NOS
P3z..00	Congenital eye anomalies NOS
P4...00	Ear, face and neck congenital anomalies
P40..00	Ear anomalies with hearing impairment
P400.00	Ear anomalies with hearing impaired, unspecified
P401.00	Congenital absence of external ear
P401000	Congenital absence of external ear, unspecified
P401011	Absence of ear NOS
P401100	Absence of external auditory canal
P401200	Ear auricle and external auditory canal absent
P401211	Congenital absence ear auricle
P401300	Congenital absence of auricle
P401z00	Absence of external ear NOS
P402.00	Other external ear anomaly with hearing impairment
P402000	Atresia of external auditory canal
P402100	Stenosis of external auditory canal
P402111	Congenital stricture of external auditory canal
P402112	Congenital stricture of osseous meatus
P402z00	Other external ear anomaly with hearing impairment NOS
P403.00	Middle ear anomaly, excluding ossicles
P403000	Ear osseous meatus atresia
P403100	Ear osseous meatus stricture
P403z00	Middle ear anomaly NEC NOS
P404.00	Anomaly of ossicles
P404000	Congenital fusion of ear ossicles
P404z00	Anomaly of ossicles NOS
P405.00	Inner ear anomalies
P405000	Congenital anomaly of the membranous labyrinth
P405100	Congenital anomaly of the organ of Corti
P405z00	Inner ear anomalies NOS

P40z.00	Other and unspecified ear anomaly with hearing impaired
P40z.11	Deafness due to congenital anomaly NEC
P40z000	Congenital absence of ear NOS
P40zz00	Ear anomaly with hearing impaired NOS
P41..00	Accessory ear auricle
P41..11	Polyotia
P410.00	Supernumerary ear
P411.00	Accessory tragus
P412.00	Supernumerary ear lobule
P413.00	Preauricular appendage, tag or lobule
P413.11	Preauricular appendage
P413.12	Preauricular tag
P413.13	Preauricular lobule
P414.00	Other ear appendage or tag
P414.11	Other ear appendage
P414.12	Other ear tag
P41z.00	Accessory ear auricle NOS
P42..00	Other specified ear anomalies
P420.00	Congenital ear lobe absence
P421.00	Macrotia - abnormally big ears
P421.11	Congenital big ears
P422.00	Microtia - abnormally small ears
P422.11	Congenital small ears
P423.00	Eustachian tube anomalies
P423000	Congenital absence of eustachian tube
P423100	Congenital stenosis of eustachian tube
P423z00	Eustachian tube anomalies NOS
P42z.00	Other specified ear anomalies NOS
P42z000	Congenital Bat ear
P42z100	Darwin's tubercle
P42z200	Congenital pointed ear
P42z300	Congenital prominent auricle
P42z400	Congenital ridge ear
P42z500	Other mis-shapen ear
P42z511	Aztec ear
P42z512	Cat ear
P42z513	Vulcan ear
P42z600	Misplaced ears
P42z611	Low-set ears
P42zz00	Other ear anomalies NOS
P43..00	Congenital ear anomaly NOS
P44..00	Branchial cleft, cyst or fistula; preauricular sinus
P440.00	Branchial cleft sinus and fistula
P440.11	Branchial cleft

P440.12	Branchial cleft sinus
P440000	Branchial cleft vestige, unspecified
P440100	Branchial cleft external sinus
P440200	Branchial cleft internal sinus
P440300	Branchial cleft fistula
P440z00	Branchial cleft vestige NOS
P441.00	Branchial cleft cyst
P442.00	Cervical auricle
P443.00	Preauricular sinus and fistula
P443000	Preauricular sinus
P443100	Preauricular fistula
P443z00	Preauricular sinus or fistula NOS
P444.00	Preauricular cyst
P44y.00	Other branchial cleft anomalies
P44z.00	Branchial cleft,cyst,or fistula preauricular anomaly OS/NOS
P44z000	Fistula of congenital auricle
P44z100	Cervicoaural fistula
P44zz00	Branchial cleft, cyst or fistula preauricular anomaly NOS
P45..00	Congenital webbing of neck
P450.00	Congenital neck webbing, unspecified
P451.00	Pterygium colli
P45z.00	Congenital webbing of neck NOS
P4y..00	Other specified face and neck anomalies
P4y0.00	Macrocheilia
P4y0.11	Lip hypertrophy
P4y1.00	Microcheilia
P4y2.00	Macrostomia
P4y2.11	Congenital hypertrophy of lip
P4y3.00	Microstomia
P4y4.00	Congenital absence of chin
P4y5.00	Mid-facial hypoplasia
P4yz.00	Other specified face and neck anomalies NOS
P4z..00	Congenital face or neck anomaly NOS
P4z0.00	Congenital anomaly of neck NOS
P4z1.00	Congenital anomaly of face NOS
P5...00	Bulbus cordis and cardiac septal closure anomalies
P5...11	Cardiac septal defects
P5...12	Congenital heart disease, septal and bulbar anomalies
P5...13	Heart septal defects
P50..00	Common aorto-pulmonary trunk
P50..11	Aortic septal defect
P50..12	Common truncus
P50..13	Persistent truncus arteriosus
P500.00	Absent septum between aorta and pulmonary artery
P500.11	Persistent truncus arteriosus
P500.12	Truncus arteriosus
P501.00	Aortic septal defect
P501.11	Aortopulmonary window
P501.12	Aorticopulmonary septal defect
P502.00	Persistent truncus arteriosus
P502.11	Truncus arteriosus
P50z.00	Common aorto-pulmonary trunk NOS
P51..00	Transposition of great vessels
P510.00	Total great vessel transposition
P511.00	Double outlet right ventricle
P511000	Double outlet right ventricle, unspecified
P511100	Dextratransposition of aorta
P511200	Incomplete great vessel transposition
P511300	Taussig-Bing syndrome
P511z00	Double outlet right ventricle NOS
P512.00	Corrected great vessel transposition
P51y.00	Other specified transposition of great vessels
P51y.11	Transposition of aorta
P51z.00	Great vessel transposition NOS
P51z.11	Transposition of arterial trunk NEC
P52..00	Tetralogy of Fallot
P520.00	Tetralogy of Fallot, unspecified
P520.11	Ventricular septal defect in Fallot's tetralogy
P520.12	Dextraposition of aorta in Fallot's tetralogy
P521.00	Pentalogy of Fallot
P52z.00	Tetralogy of Fallot NOS
P53..00	Common ventricle
P54..00	Ventricular septal defect
P540.00	Ventricular septal defect, unspecified
P541.00	Interventricular septal defect
P542.00	Left ventricle to right atrial communication
P543.00	Eisenmenger's complex
P544.00	Gerbode's defect
P545.00	Roger's disease
P54y.00	Other specified ventricular septal defect
P54z.00	Ventricular septal defect NOS
P55..00	Ostium secundum atrial septal defect
P550.00	Atrial septal defect NOS
P550.11	Auricular septal defect NOS
P550.12	Interatrial septal defect NEC
P550.13	Interauricular septal defect
P551.00	Patent foramen ovale
P552.00	Persistent ostium secundum

P552.11	Patent ostium secundum
P553.00	Lutembacher's syndrome
P55y.00	Other specified ostium secundum atrial septal defect
P55y.11	Other specified atrial septal defect
P55z.00	Ostium secundum atrial septal defect NOS
P56..00	Endocardial cushion defects
P560.00	Endocardial cushion defects, unspecified
P561.00	Ostium primum defect
P561.11	Persistent ostium primum
P561.12	Ostium primum type interauricular septal defect
P56y.00	Other specified endocardial cushion defects
P56z.00	Endocardial cushion defects NOS
P56z000	Common atrium
P56z011	Cor triloculare biventriculare
P56z100	Common atrioventricular canal
P56z200	Common atrioventricular-type ventricular septal defect
P56zz00	Endocardial cushion defects NOS
P57..00	Cor biloculare
P58..00	Double outlet left ventricle
P59..00	Isomerism of atrial appendages
P5X..00	Congenital malforms of cardiac chambers+connections unsp
P5y..00	Other heart bulb and septal closure defect
P5z..00	Heart bulb or septal closure defects NOS
P6...00	Other congenital heart anomalies
P60..00	Pulmonary valve anomalies
P600.00	Pulmonary valve anomaly, unspecified
P601.00	Congenital atresia of the pulmonary valve
P601000	Hypoplasia of pulmonary valve
P601z00	Congenital atresia of pulmonary valve NOS
P602.00	Congenital pulmonary stenosis
P602000	Congenital fusion of pulmonic cusps
P602100	Congenital fusion of pulmonary valve segment
P602z00	Congenital pulmonary stenosis NOS
P603.00	Right hypoplastic heart syndrome
P603.11	Pseudotruncus arteriosus
P60z.00	Other pulmonary valve anomalies
P60z000	Congenital insufficiency of the pulmonary valve
P60z100	Fallot's trilogy
P60z200	Supernumerary pulmonary valve cusps
P60zz00	Other pulmonary valve anomaly NOS
P61..00	Congenital tricuspid atresia and stenosis
P610.00	Congenital tricuspid atresia
P611.00	Congenital tricuspid stenosis
P61z.00	Congenital tricuspid atresia or stenosis NOS
P62..00	Ebstein's anomaly
P63..00	Congenital aortic valve stenosis
P64..00	Congenital aortic valve insufficiency
P640.00	Congenital aortic valve insufficiency, unspecified
P641.00	Bicuspid aortic valve
P64z.00	Congenital aortic valve insufficiency NOS
P65..00	Congenital mitral stenosis
P65..11	Duroziez's disease
P650.00	Congenital mitral stenosis, unspecified
P651.00	Fused commissure of the mitral valve
P652.00	Parachute deformity of the mitral valve
P653.00	Supernumerary cusps of the mitral valve
P65z.00	Congenital mitral stenosis NOS
P66..00	Congenital mitral insufficiency
P67..00	Hypoplastic left heart syndrome
P68..00	Congenital heart disease
P6W..00	Congenital malformation of aortic and mitral valves unsp
P6X..00	Congenital malformation of tricuspid valve, unspecified
P6y..00	Other specified heart anomalies
P6y0.00	Subaortic stenosis
P6y1.00	Cor triatriatum
P6y2.00	Pulmonary infundibular stenosis
P6y3.00	Obstructive heart anomaly NEC
P6y3000	Uhl's disease
P6y3z00	Obstructive heart anomaly NEC NOS
P6y4.00	Coronary artery anomaly
P6y4000	Congenital absence of coronary artery
P6y4100	Single coronary artery
P6y4200	Coronary artery from aorta
P6y4300	Coronary artery from pulmonary trunk
P6y4400	Anomalous coronary artery communication
P6y4411	Congenital coronary arterio-venous fistula
P6y4500	Congenital coronary aneurysm
P6y4600	Congenital stricture of coronary artery
P6y4z00	Coronary artery anomaly NOS
P6y5.00	Congenital heart block
P6y5000	Congenital heart block, unspecified
P6y5100	Congenital complete atrio-ventricular heart block
P6y5200	Congenital incomplete atrio-ventricular heart block
P6y5z00	Congenital heart block NOS
P6y6.00	Heart and cardiac apex malposition
P6y6.11	Ectopic heart
P6y6000	Dextrocardia

P6y6100	Levocardia
P6y6111	Laevocardia
P6y6200	Mesocardia
P6y6300	Ectopia cordis
P6y6400	Abdominal heart
P6y6z00	Heart or cardiac apex malposition NOS
P6y7.00	Myocardial bridge of coronary artery
P6y8.00	Congenital dextroposition of heart
P6yy.00	Other specified heart anomalies
P6yy.11	Hypoplastic aortic orifice or valve
P6yy.12	Hypoplasia of heart NOS
P6yy.13	Congenital insufficiency of heart valve NEC
P6yy000	Atresia of cardiac vein
P6yy100	Hypoplasia of cardiac vein
P6yy200	Congenital cardiomegaly
P6yy300	Congenital left ventricular diverticulum
P6yy400	Congenital pericardial defect
P6yy411	Congenital absence of pericardium
P6yy500	Congenital anomaly of myocardium
P6yy600	Congenital aneurysm of heart
P6yy700	Atresia of heart valve NEC
P6yy800	Cor triloculare
P6yy900	Congenital epicardial cyst
P6yyA00	Hemicardia
P6yyB00	Supernumerary heart valve cusps NEC
P6yyC00	Fusion of mitral valve cusps
P6yyD00	Fusion of heart valve cusps NEC
P6yyD11	Fusion of tricuspid valve cusps NEC
P6yyz00	Other specified heart anomalies NOS
P6z..00	Congenital heart anomaly NOS
P6z..11	Chiari's malformation
P6z0.00	Unspecified anomaly of heart valve
P6z1.00	Anomalous bands of heart
P6z1000	Anomalous atrial bands
P6z1100	Anomalous ventricular bands
P6z1z00	Anomalous bands of heart NOS
P6z2.00	Acyanotic congenital heart disease NOS
P6z3.00	Cyanotic congenital heart disease NOS
P6z3.11	Blue baby
P6zz.00	Congenital heart anomaly NOS
P7...00	Other congenital circulatory system anomalies
P70..00	Patent ductus arteriosus
P70..11	Botalli's patent ductus
P71..00	Coarctation of aorta

P710.00	Hypoplasia of aortic arch, unspecified
P711.00	Preductal coarctation of aorta
P711.11	Preductal hypoplasia of aorta
P711.12	Preductal interruption of aorta
P711.13	Preductal aortic stenosis
P712.00	Postductal coarctation of aorta
P712.11	Postductal hypoplasia of aorta
P712.12	Postductal interruption of aorta
P712.13	Postductal aortic stenosis
P713.00	Interruption of aortic arch
P713.11	Stenosis of aortic arch
P71z.00	Coarctation of aorta NOS
P72..00	Other anomalies of aorta
P72..11	Anomalies of the aorta excluding coarction
P720.00	Anomaly of aorta, unspecified
P721.00	Aortic arch anomalies
P721000	Anomalous origin of the aortic arch
P721100	Dextraposition of aorta
P721111	Overriding aorta
P721200	Double aortic arch
P721211	Vascular ring
P721300	Kommerell's diverticulum
P721400	Persistent aortic arch convolutions
P721500	Persistent right aortic arch
P721600	Vascular ring, aorta
P721700	Overriding aorta
P721z00	Aortic arch anomalies NOS
P722.00	Atresia and stenosis of aorta
P722000	Congenital absence of aorta
P722100	Aplasia of aorta
P722200	Hypoplasia of aorta
P722211	Tubular hypoplasia of aorta
P722300	Stricture of aorta
P722400	Supra-valvular aortic stenosis
P722411	Congenital stenosis of ascending aorta
P722500	Atresia of aorta
P722z00	Atresia or stenosis of aorta NOS
P72z.00	Other anomalies of aorta NOS
P72z000	Aneurysm of sinus of Valsalva
P72z100	Congenital aneurysm of aorta
P72z111	Congenital dilatation of aorta
P72zz00	Other anomaly of aorta NOS
P73..00	Pulmonary artery anomalies
P730.00	Pulmonary artery anomaly, unspecified

P731.00	Pulmonary artery agenesis
P731.11	Congenital absence of pulmonary artery
P732.00	Pulmonary artery atresia
P733.00	Coarctation of the pulmonary artery
P734.00	Hypoplasia of the pulmonary artery
P735.00	Stenosis of pulmonary artery
P735.11	Congenital stricture of pulmonary artery
P736.00	Pulmonary arterio-venous aneurysm
P736.11	Pulmonary arterio-venous fistula
P736.12	Pulmonary arterio-venous malformation
P737.00	Pulmonary artery aneurysm
P737.11	Dilatation of pulmonary artery
P738.00	Atresia of pulmonary artery with septal defect
P73y.00	Other specified anomaly of pulmonary artery
P73z.00	Pulmonary artery anomaly NOS
P74..00	Anomalies of great veins
P740.00	Anomaly of great veins, unspecified
P740000	Anomaly of the pulmonary veins, unspecified
P740100	Anomaly of the vena cava, unspecified
P740z00	Unspecified anomaly of the great veins, NOS
P741.00	Total anomalous pulmonary venous return - TAPVR
P741000	Subdiaphragmatic total anomalous pulmonary venous return
P741100	Supradiaphragmatic total anomalous pulmonary venous return
P741z00	Total anomalous pulmonary venous return NOS
P742.00	Partial anomalous pulmonary venous return
P742.11	Anomalous termination of right pulmonary vein
P743.00	Anomalous portal vein termination
P744.00	Portal vein - hepatic artery fistula
P74z.00	Other great vein anomalies
P74z.11	Persistent left posterior cardinal vein
P74z000	Absence of inferior vena cava
P74z100	Absence of superior vena cava
P74z200	Stenosis of inferior vena cava
P74z300	Stenosis of superior vena cava
P74z400	Persistent left posterior cardinal vein
P74z500	Persistent left superior vena cava
P74z600	Scimitar syndrome
P74z700	Transposition of pulmonary veins
P74z800	Atresia of pulmonary vein
P74zz00	Other great vein anomaly NOS
P75..00	Absence or hypoplasia of the umbilical artery
P750.00	Congenital absence of umbilical artery, unspecified
P751.00	Umbilical artery hypoplasia, unspecified

P752.00	Single umbilical artery
P753.00	Two umbilical vessels
P75z.00	Absence or hypoplasia of the umbilical artery NOS
P76..00	Other peripheral vascular system anomalies
P76..11	Other congenital anomalies of peripheral arteries
P76..12	Other congenital anomalies of peripheral veins
P760.00	Absence of artery NEC
P761.00	Anomaly of artery NEC
P762.00	Atresia of artery NEC
P763.00	Absence of vein NEC
P764.00	Anomaly of vein NEC
P765.00	Atresia of vein NEC
P766.00	Peripheral arterio-venous aneurysm
P766.11	Peripheral arterio-venous malformation
P767.00	Congenital peripheral aneurysm
P767.11	Cirsoid aneurysm
P768.00	Congenital phlebectasia
P769.00	Congenital arterial stricture
P769000	Renal artery stenosis
P76A.00	Congenital varix
P76B.00	Multiple renal arteries
P76B.11	Accessory renal artery
P76C.00	Anomalies of renal artery NEC
P76C000	Aberrant main renal artery
P76Cz00	Anomaly of renal artery NEC NOS
P76D.00	Arteriovenous malformation
P76E.00	Aber retro-oesophag subclavian artery causing dysphag lusori
P76y.00	Congenital anomaly of peripheral vascular system OS
P76y000	Hypoplasia of spinal vessel
P76y100	Four vessels in umbilical cord
P76yz00	Other congenital anomaly of peripheral vascular system NOS
P76z.00	Peripheral vascular system anomaly NOS
P77..00	Arteriovenous malformation of precerebral vessels
P7W..00	Congenital malformation of circulatory system, unspecif
P7X..00	Congenital malformation of great arteries, unspecified
P7y..00	Other specified circulatory system anomalies
P7y0.00	Cerebrovascular system anomalies
P7y0000	Congenital anomaly of cerebral vessel, unspecified
P7y0100	Congenital cerebral arteriovenous aneurysm
P7y0111	Congenital arteriovenous fistula of brain
P7y0112	Congenital cerebral arteriovenous malformation
P7y0200	Congenital brain aneurysm NEC
P7y0300	Congenital stricture of cerebral artery

P7y0400	Vein of Galen malformation
P7y0y00	Other specified cerebrovascular anomaly
P7y0z00	Cerebrovascular system anomaly NOS
P7yz.00	Other cardiovascular system anomaly NOS
P7yz000	Congenital aneurysm NEC
P7yz100	Congenital chylothorax
P7yzz00	Other cardiovascular system anomaly NOS
P7z..00	Circulatory system anomaly NOS
P7z..11	Fetal circulation
P8...00	Respiratory system congenital anomalies
P80..00	Choanal atresia
P800.00	Choanal atresia, unspecified
P801.00	Atresia of the anterior nares
P802.00	Atresia of the posterior nares
P803.00	Congenital stenosis of the anterior nares
P804.00	Congenital stenosis of the posterior nares
P80z.00	Choanal atresia NOS
P81..00	Other anomalies of nose
P810.00	Congenital nose deformity, unspecified
P811.00	Absent nose
P811.11	Agenesis of nose
P811000	Agenesis of nose
P811100	Underdevelopment of nose
P811z00	Absent nose NOS
P812.00	Accessory nose
P813.00	Congenital cleft nose
P814.00	Deformity of nasal sinus wall
P815.00	Congenital notching of tip of nose
P816.00	Congenital perforation of the nasal sinus wall
P817.00	Perforated nasal septum
P818.00	Congenital fissure of nose
P819.00	Congenital hypoplastic nose
P81z.00	Other anomalies of nose NOS
P81z.11	Single nostril
P82..00	Congenital web of larynx
P820.00	Congenital web of larynx, unspecified
P821.00	Congenital glottic web of larynx
P822.00	Congenital subglottic web of larynx
P82z.00	Congenital web of larynx NOS
P83..00	Other anomalies of larynx, trachea and bronchus
P830.00	Agenesis of larynx, trachea and bronchus
P830000	Agenesis of bronchus
P830100	Agenesis of larynx
P830111	Congenital absence of larynx
P830200	Agenesis of trachea
P830211	Congenital absence of trachea
P830z00	Agenesis of larynx, trachea or bronchus NOS
P831.00	Anomaly of laryngeal and tracheal cartilage
P831000	Anomaly of cricoid cartilage
P831100	Anomaly of epiglottis
P831200	Anomaly of thyroid cartilage
P831300	Anomaly of tracheal cartilage
P831400	Tracheomalacia
P831500	Laryngeal hypoplasia
P831600	Laryngomalacia
P831z00	Anomaly of laryngeal or tracheal cartilage NOS
P832.00	Atresia of larynx and trachea
P832000	Atresia of epiglottis
P832100	Atresia of glottis
P832200	Atresia of larynx
P832300	Atresia of trachea
P832z00	Atresia of larynx or trachea NOS
P833.00	Congenital stenosis of larynx, trachea and bronchus
P833000	Congenital stenosis of larynx
P833100	Congenital stenosis of trachea
P833200	Congenital stenosis of bronchus
P833300	Congenital subglottic stenosis
P833400	Congenital supraglottic stenosis
P833z00	Congenital stenosis of larynx or trachea NOS
P83y.00	Other anomaly of larynx, trachea and bronchus
P83y000	Congenital cleft thyroid cartilage
P83y100	Congenital dilatation of trachea
P83y200	Congenital tracheocele
P83y300	Congenital laryngocele
P83y400	Congenital diverticulum of bronchus
P83y500	Congenital diverticulum of trachea
P83y600	Congenital fissure of epiglottis
P83y700	Congenital cleft of posterior cricoid cartilage
P83y800	Rudimentary tracheal bronchus
P83y900	Congenital laryngeal stridor
P83yA00	Congenital fissure of larynx
P83yB00	Congenital bronchomalacia
P83yX00	Congenital malformation of larynx, unspecified
P83yw00	Other anomaly of larynx
P83yx00	Other anomaly of trachea
P83yy00	Other anomaly of bronchus
P83yz00	Other anomaly of larynx, trachea or bronchus NOS

P83z.00	Other anomalies of larynx, trachea or bronchus NOS
P84..00	Congenital cystic lung
P840.00	Congenital cystic lung disease, unspecified
P841.00	Congenital polycystic lung
P841.11	Multiple lung cysts
P841.12	Multiple congenital bronchogenic cysts
P842.00	Congenital honeycomb lung
P843.00	Single lung cyst
P843.11	Lung cyst
P843.12	Congenital bronchogenic cyst
P844.00	Congenital cystic adenomatoid malformation of the lung
P84y.00	Other specified congenital cystic lung
P84z.00	Congenital cystic lung NOS
P85..00	Lung agenesis, hypoplasia and dysplasia
P850.00	Aplasia of lung
P851.00	Hypoplasia of lung
P852.00	Sequestration of lung
P853.00	Agenesis of lung
P853.11	Congenital absence of lung
P853000	Congenital absence of lung fissures
P853100	Congenital absence of lobe of lung
P853z00	Agenesis of lung NOS
P85y.00	Other specified lung agenesis, hypoplasia or dysplasia
P85y000	Fusion of lobes of lung
P85yz00	Other lung agenesis, hypoplasia or dysplasia NOS
P85z.00	Lung agenesis, hypoplasia or dysplasia NOS
P86..00	Other lung anomalies
P860.00	Anomaly of lung, unspecified
P861.00	Congenital bronchiectasis
P86y.00	Other lung anomaly
P86y000	Accessory lung
P86y100	Azygos lobe of lung
P86y200	Accessory lobe of lung
P86y300	Ectopic tissues in lung
P86y311	Ectopic bone and cartilage in lung
P86yz00	Other lung anomaly NOS
P86z.00	Lung anomaly NOS
P8y..00	Other specified respiratory system anomalies
P8y0.00	Abnormal pericardio-pleural communication
P8y1.00	Anomaly, pleural folds
P8y2.00	Atresia of nasopharynx
P8y3.00	Congenital cyst of mediastinum
P8y4.00	Congenital pulmonary lymphangiectasis
P8yz.00	Other specified respiratory system anomaly NOS
P8z..00	Respiratory system anomaly NOS
P9...00	Cleft palate and lip
P90..00	Cleft palate
P900.00	Cleft palate, unspecified
P900.11	Palatoschisis
P901.00	Unilateral complete cleft palate
P901.11	Cleft hard palate, unilateral
P902.00	Unilateral incomplete cleft palate
P902.11	Cleft uvula
P902.12	Cleft soft palate, unilateral
P903.00	Bilateral complete cleft palate
P903.11	Cleft hard palate, bilateral
P904.00	Bilateral incomplete cleft palate
P904.11	Cleft soft palate, bilateral
P905.00	Central complete cleft palate
P905.11	Cleft hard palate, central
P906.00	Central incomplete cleft palate
P906.11	Cleft soft palate, central
P907.00	Complete cleft palate NOS
P907.11	Cleft hard palate NOS
P908.00	Incomplete cleft palate NOS
P908.11	Cleft soft palate NOS
P909.00	Cleft uvula
P90A.00	Cleft soft palate, bilateral
P90B.00	Cleft hard palate, bilateral
P90C.00	Cleft hard palate, unilateral
P90z.00	Cleft palate NOS
P91..00	Cleft lip (harelip)
P91..11	Cheiloschisis
P91..12	Congenital fissure of lip
P910.00	Cleft lip, unspecified
P911.00	Unilateral complete cleft lip
P912.00	Unilateral incomplete cleft lip
P913.00	Bilateral complete cleft lip
P914.00	Bilateral incomplete cleft lip
P915.00	Central cleft lip
P91z.00	Cleft lip NOS
P92..00	Cleft palate with cleft lip
P92..11	Cheilopalatoschisis
P920.00	Cleft palate with cleft lip, unspecified
P921.00	Unilateral complete cleft palate with cleft lip
P922.00	Unilateral incomplete cleft palate with cleft lip
P923.00	Bilateral complete cleft palate with cleft lip

P924.00	Bilateral incomplete cleft palate with cleft lip
P925.00	Central complete cleft palate with cleft lip
P926.00	Central incomplete cleft palate with cleft lip
P927.00	Cleft hard palate with cleft soft palate, bilateral
P928.00	Cleft hard palate with cleft soft palate, unilateral
P92A.00	Cleft hard palate with cleft lip, bilateral
P92B.00	Cleft hard palate with cleft lip, unilateral
P92z.00	Cleft palate with cleft lip NOS
P9z..00	Cleft palate or cleft lip NOS
PA...00	Other congenital upper alimentary tract anomalies
PA0..00	Tongue tie - ankyloglossia
PA0..11	Ankyloglossia
PA0..12	Tongue tie
PA1..00	Other tongue anomalies
PA10.00	Anomaly of tongue, unspecified
PA11.00	Aglossia
PA11.11	Congenital absence of tongue
PA12.00	Congenital adhesions of tongue
PA13.00	Fissure of tongue
PA13.11	Bifid tongue
PA13.12	Double tongue
PA14.00	Macroglossia
PA14.11	Congenital tongue hypertrophy
PA15.00	Microglossia
PA15.11	Hypoplasia of tongue
PA15.12	Short tongue
PA16.00	Dislocation of tongue
PA16.11	Displacement of tongue
PA17.00	Cleft tongue
PA17.11	Whiteman's syndrome
PA18.00	Congenital plicated tongue
PA1z.00	Other tongue anomalies NOS
PA2..00	Other specified mouth and pharynx anomalies
PA20.00	Congenital absence of salivary gland
PA21.00	Accessory salivary gland
PA22.00	Atresia, salivary duct
PA23.00	Congenital salivary gland fistula
PA24.00	Congenital fistula of lip
PA24.11	Congenital pits of lip
PA25.00	Other mouth anomalies
PA25.11	Fordyce's disease of mouth
PA25000	Congenital absence of uvula
PA25100	High arched palate
PA25y00	Other congenital anomaly of palate
PA25y11	Flat palate
PA25z00	Other mouth anomalies NOS
PA26.00	Diverticulum of pharynx
PA26.11	Pharyngeal pouch
PA27.00	Other pharynx anomalies
PA27000	Imperforate pharynx
PA27100	Congenital pharyngeal polyp
PA27z00	Other pharynx anomalies NOS
PA28.00	Ranula, congenital
PA29.00	Other anomalies of salivary glands or ducts
PA29.11	Displacement of Wharton's duct
PA2A.00	Other anomalies of lip
PA2A000	Congenital ectropion of lip
PA2Az00	Other anomaly of lip NOS
PA2z.00	Other mouth and pharynx anomalies NOS
PA3..00	Oesophageal atresia, stenosis and fistula
PA3..11	Congenital oesophageal ring
PA30.00	Atresia of oesophagus
PA31.00	Congenital oesophageal stricture
PA31.11	Congenital oesophageal stenosis
PA32.00	Congenital oesophageal fistula
PA32000	Oesophagobronchial fistula
PA32100	Oesophagotracheal fistula
PA32111	Congenital tracheo-oesophageal fistula
PA32z00	Congenital oesophageal fistula NOS
PA33.00	Imperforate oesophagus
PA34.00	Webbed oesophagus
PA35.00	Congenital absence of oesophagus
PA36.00	Cong.absence of oesophagus with tracheo-oesophageal fistula
PA37.00	Atresia of oesophagus with tracheo-oesophageal fistula
PA3y.00	Other specified oesophageal atresia, stenosis or fistula
PA3z.00	Oesophageal atresia, stenosis or fistula NOS
PA4..00	Other specified oesophageal anomalies
PA40.00	Congenital dilatation of oesophagus
PA41.00	Congenital displacement of oesophagus
PA42.00	Congenital diverticulum of oesophagus
PA43.00	Congenital duplication of oesophagus
PA44.00	Giant oesophagus
PA45.00	Congenital oesophageal pouch
PA4z.00	Other specified oesophageal anomaly NOS
PA5..00	Congenital hypertrophic pyloric stenosis
PA50.00	Congenital pyloric hypertrophy
PA51.00	Congenital pyloric spasm
PA51.11	Congenital pylorospasm

PA52.00	Congenital pyloric stenosis
PA52.11	Congenital pyloric stricture
PA5y.00	Other specified congenital pyloric obstruction
PA5z.00	Congenital pyloric obstruction NOS
PA6..00	Congenital hiatus hernia
PA7..00	Other specified stomach anomalies
PA70.00	Congenital cardiospasm
PA70.11	Congenital achalasia of cardia
PA71.00	Congenital hourglass stomach
PA72.00	Congenital stomach displacement
PA73.00	Congenital stomach diverticulum
PA74.00	Duplication of stomach
PA75.00	Megalogastria
PA76.00	Microgastria
PA77.00	Transposition of stomach
PA78.00	Ectopic gastric mucosa
PA7z.00	Other specified stomach anomaly NOS
PA7z.11	Congenital displacement of gastric mucosa
PAy..00	Other specified upper alimentary tract anomaly
PAz..00	Upper alimentary tract anomalies NOS
PAz0.00	Unspecified anomalies of mouth and pharynx
PAz1.00	Unspecified anomalies of oesophagus
PAz2.00	Unspecified anomalies of stomach
PAzz.00	Anomalies of upper alimentary tract NOS
PAzz.11	Malformation of throat
PB...00	Other congenital digestive system anomaly
PB0..00	Meckel's diverticulum
PB0..11	Persistent omphalomesenteric duct
PB0..12	Persistent vitelline duct
PB00.00	Meckel's diverticulum, unspecified
PB01.00	Displaced Meckel's diverticulum
PB02.00	Hypertrophic Meckel's diverticulum
PB03.00	Persistent omphalomesenteric duct
PB03.11	Persistent vitelline duct
PB0z.00	Meckel's diverticulum NOS
PB1..00	Small intestine atresia and stenosis
PB10.00	Atresia of small intestine
PB10000	Atresia of small intestine, unspecified
PB10100	Atresia of duodenum
PB10200	Atresia of ileum
PB10300	Atresia of jejunum
PB10z00	Small intestine atresia NOS
PB11.00	Congenital absence of small intestine
PB11000	Congenital absence of duodenum
PB11100	Congenital absence of jejunum
PB11200	Congenital absence of ileum
PB12.00	Congenital obstruction of small intestine
PB13.00	Congenital stenosis of small intestine
PB13000	Congenital stenosis of duodenum
PB13100	Congenital stenosis of jejunum
PB13200	Congenital stenosis of ileum
PB13z00	Congenital stenosis of small intestine NOS
PB13z11	Congenital stricture of small intestine
PB14.00	Imperforate jejunum
PB15.00	Imperforate small intestine NEC
PB1z.00	Small intestine atresia or stenosis NOS
PB2..00	Atresia and stenosis of large intestine/rectum/anal canal
PB2..11	Atresia large intestine
PB2..12	Stenosis large intestine
PB20.00	Congenital absence of large intestine
PB20000	Congenital absence of anus
PB20100	Congenital absence of appendix
PB20200	Congenital absence of rectum
PB20211	Agenesis of rectum
PB20300	Congenital absence of anus with fistula
PB20400	Congenital absence of rectum with fistula
PB20411	Agenesis of rectum with fistula
PB20z00	Congenital absence of large intestine NOS
PB21.00	Atresia of large intestine
PB21000	Atresia of anus
PB21100	Atresia of colon
PB21200	Atresia of rectum
PB21300	Atresia of appendix
PB21400	Atresia of anus with fistula
PB21500	Atresia of rectum with fistula
PB21z00	Atresia of large intestine NOS
PB22.00	Congenital obstruction of large intestine
PB22.11	Congenital stenosis of large intestine
PB22.12	Congenital stenosis of appendix
PB23.00	Congenital occlusion of anus
PB23.11	Anal septum
PB23000	Congenital occlusion of anus with fistula
PB23z00	Congenital occlusion of anus NOS
PB24.00	Congenital stricture of anus
PB24.11	Congenital anal stricture
PB24000	Congenital stricture of anus with fistula
PB24011	Congenital stenosis of anus with fistula
PB24100	Congenital stricture of anus without mention of fistula

PB24111	Congenital stenosis of anus without mention of fistula
PB24z00	Congenital stricture of anus NOS
PB25.00	Congenital stricture of rectum
PB25.11	Congenital rectal stricture
PB25000	Congenital stricture of rectum with fistula
PB25011	Congenital stenosis of rectum with fistula
PB25100	Congenital stricture of rectum without mention of fistula
PB25111	Congenital stenosis of rectum without mention of fistula
PB25z00	Congenital stricture of rectum NOS
PB26.00	Imperforate anus
PB26000	Imperforate anus with fistula
PB26z00	Imperforate anus NOS
PB27.00	Imperforate rectum
PB27000	Imperforate rectum with fistula
PB27z00	Imperforate rectum NOS
PB28.00	Imperforate large intestine
PB2z.00	Atresia and stenosis of large intestine/rectum/anus NOS
PB3..00	Hirschsprung's disease and allied congenital conditions
PB3..11	Aganglionosis
PB3..12	Congenital dilatation colon
PB30.00	Hirschsprung's disease
PB30000	Long segment Hirschsprung's disease
PB30100	Short segment Hirschsprung's disease
PB30z00	Hirschsprung's disease NOS
PB31.00	Idiopathic congenital megacolon
PB31.11	Congenital giant colon NEC
PB32.00	Macrocolon
PB33.00	Total intestinal aganglionosis
PB33.11	Aganglionic macrocolon
PB33.12	Congenital aganglionic megacolon
PB3z.00	Hirschsprung's disease and allied congenital conditions NOS
PB4..00	Intestinal fixation anomalies
PB40.00	Congenital intestinal adhesions
PB40000	Congenital omental adhesions
PB40011	Congenital omental bands
PB40100	Jackson's membrane
PB40200	Congenital peritoneal adhesions
PB40211	Congenital peritoneal bands
PB40z00	Congenital intestinal adhesions NOS
PB41.00	Malrotation of colon and caecum
PB41000	Malrotation of colon
PB41100	Malrotation of caecum
PB41z00	Malrotation of colon or caecum NOS
PB42.00	Universal mesentery
PB43.00	Other anomalies of mesentery
PB4y.00	Other specified intestinal fixation anomaly
PB4z.00	Intestinal fixation anomaly NOS
PB4z.11	Malfixation of gut NEC
PB4z.12	Malrotation of gut
PB4z.13	Malrotation of intestine
PB5..00	Other anomalies of intestine
PB50.00	Congenital diverticulum of colon
PB51.00	Dolichocolon
PB52.00	Duplication of intestine
PB52000	Duplication of intestine, unspecified
PB52100	Duplication of anus
PB52200	Duplication of appendix
PB52300	Duplication of caecum
PB52z00	Duplication of intestine NOS
PB52z11	Congenital redundant rectal mucosa
PB52z12	Congenital redundant colon
PB53.00	Transposition of intestine
PB53000	Transposition of intestine, unspecified
PB53100	Transposition of appendix
PB53200	Transposition of caecum
PB53300	Transposition of colon
PB53z00	Transposition of intestine NOS
PB54.00	Ectopic anus
PB55.00	Megaloappendix
PB56.00	Megaloduodenum
PB57.00	Microcolon
PB58.00	Persistent cloaca
PB58.11	Anal fusion
PB58.12	Anal and urogenital canal fusion
PB59.00	Congenital anal fistula
PB5A.00	Enterogenous cyst
PB5B.00	Dysplasia of colon
PB5X.00	Congenital malformation of intestine, unspecified
PB5z.00	Other intestine anomalies NOS
PB5z.11	Congenital volvulus
PB5z.12	Short bowel syndrome
PB5z000	Congenital faecal fistula
PB6..00	Liver and biliary system anomalies
PB6..11	Bile duct anomalies
PB6..12	Biliary anomalies
PB6..13	Gallbladder anomalies
PB6..14	Liver anomalies
PB60.00	Liver and biliary system anomalies, unspecified

PB60000	Liver anomaly, unspecified
PB60100	Gallbladder anomaly, unspecified
PB60200	Bile duct anomaly, unspecified
PB60z00	Unspecified liver and biliary system anomaly NOS
PB61.00	Biliary atresia
PB61.11	Bile duct atresia
PB61000	Congenital absence of bile duct
PB61011	Agenesis of bile duct
PB61100	Congenital hypoplasia of bile duct
PB61200	Congenital obstruction of bile duct
PB61300	Congenital stricture of bile duct
PB61311	Congenital stricture of common bile duct
PB61400	Atresia of bile duct
PB61411	Intrahepatic atresia of bile duct
PB61412	Extrahepatic atresia of bile duct
PB61500	Congenital absence of hepatic ducts
PB61511	Agenesis of hepatic ducts
PB61600	Atresia of hepatic ducts
PB61z00	Biliary atresia NOS
PB62.00	Congenital cystic liver disease
PB62.11	Congenital hepatic cyst
PB62000	Congenital polycystic liver disease
PB62100	Fibrocystic liver disease
PB62z00	Congenital cystic liver disease NOS
PB63.00	Congenital absence of liver and gallbladder
PB63000	Congenital absence of gallbladder
PB63011	Agenesis of gallbladder
PB63100	Congenital absence of liver lobe
PB63111	Congenital agenesis of liver lobe
PB63200	Congenital small left lobe of liver
PB63300	Riedel's lobe liver
PB63400	Congenital absence of liver,total
PB63411	Congenital agenesis liver,total
PB63500	Alagille syndrome
PB63z00	Absence of liver or gallbladder NOS
PB64.00	Liver and biliary duplication
PB64000	Duplication of biliary duct
PB64100	Duplication of cystic duct
PB64200	Duplication of gallbladder
PB64300	Duplication of liver
PB64311	Accessory liver
PB64400	Accessory hepatic ducts
PB64z00	Liver or biliary duplication NOS
PB6y.00	Other liver and biliary anomalies

PB6y000	Congenital choledochal cyst
PB6y100	Congenital hepatomegaly
PB6y200	Congenital floating gallbladder
PB6y300	Congenital floating liver
PB6y400	Intrahepatic gallbladder
PB6y500	Hypoplasia of gallbladder
PB6y600	Atrophy of left lobe of liver
PB6y700	Congenital dilation of bile duct
PB6y800	Congenital diverticulum of bile duct
PB6y900	Liver hyperplasia
PB6yw00	Other congenital anomaly of liver
PB6yw11	Liver hamartoma
PB6yw12	Abnormal liver lobulation
PB6yw13	Trilobular liver
PB6yx00	Other congenital anomaly of gallbladder
PB6yy00	Other congenital anomaly of hepatic or bile ducts
PB6yy11	Congenital kink of cystic duct
PB6yz00	Other liver or biliary system anomalies NOS
PB6z.00	Liver or biliary system anomalies NOS
PB7..00	Anomalies of pancreas
PB70.00	Congenital absence of pancreas
PB71.00	Agenesis of pancreas
PB72.00	Hypoplasia of pancreas
PB73.00	Accessory pancreas
PB74.00	Annular pancreas
PB75.00	Ectopic pancreas
PB76.00	Pancreatic heterotopia
PB77.00	Pancreatic cyst, congenital
PB7y.00	Other specified anomalies of pancreas
PB7z.00	Anomalies of pancreas NOS
PBy..00	Other specified digestive system anomalies
PBy0.00	Congenital absence of digestive system NOS
PBy0000	Complete absence of alimentary tract NOS
PBy0100	Partial absence of alimentary tract NOS
PBy0z00	Absence of digestive system NOS
PBy1.00	Duplication of digestive system NOS
PBy2.00	Congenital malposition of digestive system NOS
PBy2.11	Ectopic digestive organs NOS
PByz.00	Other specified digestive system anomalies NOS
PBz..00	Digestive system anomalies NOS
PC...00	Congenital genital organ anomalies
PC0..00	Anomalies of ovaries
PC00.00	Congenital absence of ovary
PC00.11	Agenesis of ovary

PC01.00	Accessory ovary
PC02.00	Ectopic ovary
PC03.00	Streak ovary
PC04.00	Developmental ovarian cyst
PC05.00	Congenital torsion of ovary
PC0y.00	Other specified congenital anomalies of ovaries
PC0y.11	Congenital ovarian dysplasia
PC0z.00	Congenital anomalies of ovaries NOS
PC1..00	Fallopian tube and broad ligament anomalies
PC10.00	Fallopian tube and broad ligament anomalies, unspecified
PC11.00	Embryonic cyst of fallopian tube and broad ligament
PC11.11	Cyst of mesenteric remnant
PC11000	Epoophoron cyst
PC11100	Fimbrial cyst
PC11200	Gartner's duct cyst
PC11211	Persistent Gartner's duct
PC11300	Parovarian cyst
PC11z00	Embryonic cyst of fallopian tube or broad ligament NOS
PC1y.00	Other fallopian tube and broad ligament anomalies
PC1y000	Congenital absence of fallopian tube
PC1y011	Congenital absence of oviduct
PC1y100	Accessory fallopian tube
PC1y200	Atresia of fallopian tube
PC1y300	Absent broad ligament
PC1y400	Accessory broad ligament
PC1y500	Atresia of broad ligament
PC1yz00	Other fallopian tube or broad ligament anomalies NOS
PC1z.00	Fallopian tube or broad ligament anomalies NOS
PC2..00	Doubling of uterus
PC20.00	Doubling of uterus, unspecified
PC21.00	Didelphic uterus
PC22.00	Doubling of uterus, including cervix and vagina
PC2z.00	Doubling of uterus NOS
PC3..00	Other anomalies of uterus
PC30.00	Congenital absence of uterus
PC31.00	Agenesis of uterus
PC32.00	Aplasia of uterus
PC33.00	Bicornuate uterus
PC34.00	Uterus unicornis
PC35.00	Displaced uterus
PC35.11	Congenital prolapse of uterus
PC36.00	Fistulae involving uterus with digestive or urinary tract
PC36000	Uterointestinal fistula, congenital
PC36100	Uterovesical fistula, congenital
PC36z00	Fistula involving uterus with digestive or urinary tract NOS
PC3y.00	Other specified anomalies of uterus
PC3z.00	Anomalies of uterus NOS
PC4..00	Cervical, vaginal and external female genital anomalies
PC40.00	Cervical/vaginal/external female genital anomalies, unspec
PC41.00	Embryonic cyst of cervix/vagina/external female genitalia
PC41000	Congenital cyst of canal of Nuck
PC41011	Patent canal of Nuck
PC41100	Embryonal cyst of vagina
PC41200	Congenital cyst of vulva
PC41300	Embryonic cyst of cervix
PC41z00	Embryonic cyst cervix/vagina/external female genitalia NOS
PC42.00	Imperforate hymen
PC43.00	Rectovaginal fistula, congenital
PC4y.00	Other cervical, vaginal and external female genital anomaly
PC4y000	Congenital absence of cervix
PC4y100	Agenesis of cervix
PC4y200	Congenital absence of clitoris
PC4y300	Agenesis of clitoris
PC4y400	Congenital absence of vagina
PC4y411	Rudimentary vagina
PC4y500	Agenesis of vagina
PC4y600	Congenital absence of vulva
PC4y611	Congenital absence of labium major
PC4y612	Congenital absence of labium minor
PC4y700	Agenesis of vulva
PC4y800	Congenital stenosis of cervical canal
PC4y900	Congenital stenosis of vagina
PC4y911	Congenital stricture of vagina
PC4yA00	Atresia of cervix
PC4yB00	Atresia of vagina
PC4yB11	Imperforate vagina
PC4yC00	Congenital vaginal cyst NEC
PC4yD00	Fusion of vulva
PC4yD11	Fusion of labia
PC4yE00	Congenital labial adhesions
PC4yv00	Other congenital anomaly of cervix
PC4yw00	Other congenital anomaly of vagina
PC4yw11	Vaginal septum
PC4yx00	Other congenital anomaly of vulva
PC4yy00	Other congenital anomaly of clitoris
PC4yy11	Hooded clitoris
PC4yy12	Hypertrophy of clitoris

PC4yz00	Other cervical/vaginal/external female genital anomaly NOS
PC4z.00	Cervical, vaginal and external female genital anomaly NOS
PC5..00	Undescended testicle
PC50.00	Cryptorchidism
PC50000	Cryptorchidism, unilateral
PC50100	Cryptorchidism, bilateral
PC50z00	Cryptorchidism NOS
PC51.00	Ectopic testis
PC5z.00	Undescended testicle NOS
PC5z.11	Retractile testis
PC5z.12	Maldescent of testicle
PC5z000	Undescended testis, unilateral
PC5z011	Maldescent of testis, unilateral
PC5z100	Undescended testis, bilateral
PC5z111	Maldescent of testis, bilateral
PC6..00	Hypospadias and epispadias
PC60.00	Hypospadias
PC60.11	Anaspadias
PC60000	Hypospadias, penile
PC60100	Hypospadias, penoscrotal
PC60200	Hypospadias, perineal
PC60300	Hypospadias, balanic
PC60311	Hypospadias, glanular
PC60312	Hypospadias, glandular
PC61.00	Epispadias
PC61.11	Anaspadias
PC62.00	Congenital chordee
PC6z.00	Hypospadias or epispadias NOS
PC7..00	Indeterminate sex and pseudohermaphroditism
PC7..11	Gynandrism
PC70.00	True hermaphroditism
PC70.11	Ovotestis
PC71.00	Male pseudohermaphroditism
PC72.00	Female pseudohermaphroditism
PC73.00	Pure gonadal dysgenesis
PC7z.00	Indeterminate sex or pseudohermaphroditism NOS
PC7z000	Indeterminate sex NOS
PC7z011	Intersex NEC
PC7z100	Pseudohermaphrodite NOS
PC7z111	False hermaphrodite
PC8..00	Congenital anomaly of male genital system
PC80.00	Other specified congenital anomaly of male genital system
PCy..00	Other specified genital organ anomaly
PCy0.00	Absence of genital organ NEC
PCy0000	Congenital absence of penis
PCy0100	Congenital absence of prostate
PCy0200	Congenital absence of spermatic cord
PCy0300	Congenital absence of vas deferens
PCy0311	Congenital absence of seminal tract
PCy0z00	Genital organ absence NEC NOS
PCy1.00	Congenital aplasia of genital organ NEC
PCy1000	Congenital aplasia of prostate
PCy1100	Congenital aplasia of round ligament
PCy1200	Congenital aplasia of testicle
PCy1300	Congenital aplasia of scrotum
PCy1400	Aplasia of penis
PCy1z00	Congenital aplasia of genital organ NEC NOS
PCy2.00	Hypoplasia of genital organ NEC
PCy2000	Hypoplasia of penis
PCy2100	Hypoplasia of testis
PCy2200	Hypoplasia of scrotum
PCy2z00	Hypoplasia of genital organ NEC NOS
PCy3.00	Atresia of genital organ NEC
PCy3000	Atresia of ejaculatory duct
PCy3100	Atresia of vas deferens
PCy3z00	Atresia of genital organ NEC NOS
PCy4.00	Anorchism
PCy4.11	Congenital absence of both testes
PCy4.12	Testicular agenesis, bilateral
PCy5.00	Monorchism
PCy5.11	Congenital absence of testis, unilateral
PCy5.12	Testicular agenesis, unilateral
PCy6.00	Polyorchism
PCy7.00	Congenital lateral curvature of penis
PCy8.00	Fusion of testes
PCy9.00	Paraspadias
PCyA.00	Cysts of embryonic remnants NEC
PCyA000	Hydatid cyst of Morgagni
PCyA100	Wolffian duct cyst
PCyA200	Hydatid cyst of Morgagni - male
PCyA300	Hydatid cyst of Morgagni - female
PCyA400	Wolffian duct cyst - male
PCyA500	Wolffian duct cyst - female
PCyA600	Cyst of embryonic remnant - male
PCyA700	Cyst of embryonic remnant - female
PCyAz00	Cyst of embryonic remnant NEC NOS
PCyB.00	Doubling of vagina
PCyw.00	Other congenital anomaly of testis or scrotum

PCyx.00	Other congenital anomaly of vas deferens or prostate
PCyy.00	Other congenital anomaly of penis
PCyy000	Hooded penis
PCyy100	Webbed penis
PCyyz00	Other congenital anomaly of penis NOS
PCyz.00	Other specified genital organ anomaly NOS
PCz..00	Genital organ anomaly NOS
PD...00	Urinary system congenital anomalies
PD0..00	Renal agenesis and dysgenesis
PD00.00	Renal agenesis, unspecified
PD00000	Bilateral renal agenesis
PD00100	Unilateral renal agenesis
PD00z00	Renal agenesis, unspecified NOS
PD01.00	Congenital renal atrophy
PD02.00	Congenital absence of kidney
PD02000	Bilateral congenital absence of kidneys
PD02100	Unilateral congenital absence of kidney
PD02z00	Congenital absence of kidney NOS
PD03.00	Hypoplasia of kidney
PD03000	Bilateral renal hypoplasia
PD03011	Potter's syndrome
PD03100	Unilateral renal hypoplasia
PD04.00	Dysplasia of kidney
PD04000	Bilateral renal dysplasia
PD04011	Bilateral renal dysgenesis
PD04100	Unilateral renal dysplasia
PD04111	Unilateral renal dysgenesis
PD04z00	Dysplasia of kidney NOS
PD0z.00	Renal agenesis or dysgenesis NOS
PD1..00	Congenital cystic kidney disease
PD1..11	Congenital cystic renal disease
PD1..12	Fibrocystic kidney
PD1..13	Polycystic kidney
PD1..14	Sponge kidney
PD10.00	Congenital renal cyst, single
PD11.00	Polycystic kidney disease
PD11000	Polycystic kidneys, infantile type
PD11100	Polycystic kidneys, adult type
PD11z00	Polycystic kidney disease NOS
PD11z11	Cystic kidney disease NEC
PD12.00	Medullary cystic disease
PD12000	Medullary cystic disease, juvenile type
PD12011	Nephronophthisis
PD12100	Medullary cystic disease, adult type
PD12111	Medullary sponge kidney
PD12y00	Medullary cystic disease OS
PD12z00	Medullary cystic disease NOS
PD13.00	Multicystic renal dysplasia
PD13.11	Multicystic kidney
PD1y.00	Other specified congenital cystic kidney disease
PD1y000	Fibrocystic kidney disease
PD1y011	Fibrocystic renal degeneration
PD1yz00	Other congenital cystic kidney disease NOS
PD1z.00	Congenital cystic kidney disease NOS
PD2..00	Renal pelvis and ureter obstructive defects
PD20.00	Atresia of ureter
PD21.00	Occlusion of ureter
PD21.11	Congenital ureteric valves
PD22.00	Congenital stricture of ureter
PD22.11	Congenital stenosis of ureter
PD22000	Congenital stricture of ureter, unspecified
PD22100	Congenital stricture of ureteropelvic junction
PD22200	Congenital stricture of ureterovesical orifice
PD22z00	Congenital stricture of ureter NOS
PD23.00	Congenital hydronephrosis
PD23.11	Congenital dilated renal pelvis
PD24.00	Congenital dilatation of ureter
PD25.00	Hydroureter - congenital
PD26.00	Megaloureter - congenital
PD27.00	Ureterocele - congenital
PD28.00	Impervious ureter
PD2y.00	Other specified obstructive defect of renal pelvis or ureter
PD2z.00	Obstructive defect of renal pelvis or ureter NOS
PD3..00	Other specified renal anomaly
PD30.00	Accessory kidney
PD30.11	Duplication of kidney
PD30.12	Renal duplication NEC
PD30.13	Supernumerary kidney
PD31.00	Congenital calculus of kidney
PD32.00	Congenital displaced kidney
PD33.00	Discoid kidney
PD34.00	Double kidney with double pelvis
PD34.11	Duplex kidneys
PD34.12	Pyelon duplex
PD35.00	Ectopic kidney
PD35.11	Pelvic kidney
PD36.00	Fusion of kidneys
PD37.00	Giant kidney

PD38.00	Horseshoe kidney
PD39.00	Hyperplasia of kidney
PD3A.00	Lobulation of kidney
PD3A.11	Ren arcuatus
PD3A.12	Ren unguliformis
PD3B.00	Malrotation of kidney
PD3C.00	Triple kidney with triple pelvis
PD3C.11	Trifid kidney
PD3C.12	Pyelon triplex
PD3D.00	Enlarged kidney
PD3z.00	Other specified renal anomaly NOS
PD4..00	Other specified ureter anomalies
PD40.00	Absent ureter
PD41.00	Accessory ureter
PD42.00	Deviation of ureter
PD43.00	Displaced ureteric orifice
PD44.00	Double ureter
PD44.11	Duplication of ureter
PD45.00	Ectopic ureter
PD45.11	Congenital displacement of opening of ureter
PD45.12	Ectopic insertion of ureter
PD46.00	Anomalous ureter implantation
PD47.00	Congenital vesico-uretero-renal reflux
PD4z.00	Other specified ureter anomaly NOS
PD5..00	Exstrophy of urinary bladder
PD5..11	Ectopia vesicae
PD5..12	Ectopic bladder
PD50.00	Ectopic bladder
PD50.11	Ectopia vesicae
PD5z.00	Exstrophy of urinary bladder NOS
PD6..00	Urethra and bladder neck atresia and stenosis
PD60.00	Congenital bladder neck obstruction
PD60000	Atresia of bladder neck
PD60100	Stenosis of bladder neck
PD60z00	Congenital bladder neck obstruction NOS
PD61.00	Congenital obstruction of urethra
PD61000	Atresia of anterior urethra
PD61100	Stenosis of anterior urethra
PD61z00	Congenital obstruction of urethra NOS
PD62.00	Congenital urethral valvular stricture
PD62.11	Congenital posterior urethral valves
PD62.12	Congenital urethral posterior valvular stricture
PD63.00	Congenital urinary meatus stricture
PD63.11	Congenital urinary meatus obstruction
PD63.12	Congenital pinhole urinary meatus
PD63000	Atresia of urinary meatus
PD63100	Stenosis of urinary meatus
PD63z00	Congenital urinary meatus stricture NOS
PD64.00	Congenital vesicourethral orifice stricture
PD65.00	Imperforate urinary meatus
PD66.00	Impervious urethra
PD67.00	Congenital posterior urethral valves
PD6y.00	Other specified urethra or bladder neck atresia or stenosis
PD6z.00	Urethra or bladder neck atresia or stenosis NOS
PD7..00	Anomalies of urachus
PD70.00	Cyst of urachus
PD71.00	Fistula of urachus
PD72.00	Patent urachus
PD72.11	Persistent urachus
PD73.00	Persistent umbilical sinus
PD7y.00	Other specified anomalies of urachus
PD7z.00	Anomalies of urachus NOS
PDy..00	Other specified bladder and urethral anomalies
PDy0.00	Congenital absence of bladder
PDy1.00	Congenital absence of urethra
PDy2.00	Accessory bladder
PDy3.00	Accessory urethra
PDy4.00	Congenital bladder diverticulum
PDy5.00	Congenital bladder hernia
PDy6.00	Congenital urethrorectal fistula
PDy7.00	Congenital prolapse of bladder mucosa
PDy8.00	Congenital prolapse of urethra
PDy9.00	Double urethra
PDyA.00	Double urinary meatus
PDyB.00	Congenital hourglass bladder
PDyz.00	Other bladder or urethral anomaly NOS
PDyz000	Epispadias, female
PDyz100	Hypospadias, female
PDz..00	Urinary system anomalies NOS
PDz0.00	Unspecified anomaly of kidney
PDz1.00	Unspecified anomaly of ureter
PDz2.00	Unspecified anomaly of bladder
PDz3.00	Unspecified anomaly of urethra
PE...00	Certain congenital musculoskeletal deformities
PE...11	Congenital musculoskeletal deformities
PE0..00	Skull, face and jaw congenital deformities
PE0..11	Face congenital deformities
PE0..12	Jaw congenital deformities

PE0..13	Skull congenital deformities
PE00.00	Asymmetry of face
PE00000	Hemifacial microsomia
PE00100	Asymmetrical crying face syndrome
PE01.00	Compression facies
PE02.00	Potter's facies
PE03.00	Depressions in skull
PE04.00	Dolichocephaly
PE05.00	Plagiocephaly
PE05.11	Asymmetric head
PE06.00	Congenital nasal septum deviation
PE07.00	Congenital bent or squashed nose
PE0z.00	Skull, face or jaw congenital deformities NOS
PE1..00	Congenital sternomastoid torticollis
PE1..11	Congenital wry neck
PE1..12	Sternomastoid tumour
PE2..00	Congenital spine deformity
PE20.00	Congenital spine deformity, unspecified
PE21.00	Congenital postural lordosis
PE22.00	Congenital postural scoliosis
PE23.00	Congenital scoliosis due to congenital bony malformation
PE2z.00	Congenital spine deformity NOS
PE2z.11	Congenital postural curvature of spine NOS
PE3..00	Congenital dislocation and subluxation of the hip
PE30.00	Congenital dislocation of hip
PE30000	Unilateral congenital dislocation of hip
PE30100	Bilateral congenital dislocation of hip
PE30z00	Congenital dislocation of hip NOS
PE31.00	Congenital subluxation of hip
PE31000	Unilateral congenital subluxation of hip
PE31011	Unstable hip
PE31012	Preluxation of hip
PE31013	Predislocation status of hip at birth
PE31014	Congenital instability of hip joint
PE31100	Bilateral congenital subluxation of hip
PE31z00	Congenital subluxation of hip NOS
PE32.00	Congenital dislocation one hip with subluxation other hip
PE33.00	Congenital clicking hip
PE33.11	Clicky hips - congenital
PE34.00	Dysplastic hip
PE34000	Unilateral dysplastic hip
PE34100	Bilateral dysplastic hip
PE35.00	Unstable hip
PE35000	Unilateral unstable hip
PE35100	Bilateral unstable hip
PE3z.00	Congenital dislocation of hip NOS
PE4..00	Genu recurvatum and long leg bone bowing
PE4..11	Congenital leg bone bowing
PE40.00	Congenital genu recurvatum
PE41.00	Congenital dislocation of knee
PE41000	Congenital dislocation of knee grade I
PE41100	Congenital dislocation of knee grade II
PE41200	Congenital dislocation of knee grade III
PE41300	Congenital dislocation of patella
PE42.00	Congenital bowing of femur
PE43.00	Congenital bowing of tibia and fibula
PE43000	Congenital bowing of tibia
PE43100	Congenital bowing of fibula
PE44.00	Congenital bowing of long leg bone, unspecified
PE44.11	Bow legs NOS
PE4z.00	Genu recurvatum and long leg bone bowing NOS
PE5..00	Varus deformities of feet
PE50.00	Congenital talipes varus
PE50.11	Pes varus
PE50.12	Congenital clubfoot - varus
PE51.00	Congenital talipes equinovarus
PE52.00	Metatarsus primus varus
PE53.00	Congenital metatarsus varus
PE54.00	Congenital metatarsus adductus
PE5x.00	Complex varus foot deformities
PE5y.00	Other specified varus feet deformity
PE5y000	Congenital talipes calcaneovarus
PE5yz00	Other specified varus foot deformity NOS
PE5z.00	Varus foot deformity NOS
PE6..00	Valgus deformities of feet
PE60.00	Congenital talipes valgus
PE60.11	Congenital clubfoot - valgus
PE61.00	Congenital pes planus
PE61.11	Congenital flat foot
PE61.13	Rigid flat foot
PE61.14	Spastic flat foot
PE61000	Congenital vertical talus
PE62.00	Congenital talipes calcaneovalgus
PE6y.00	Other valgus foot deformities
PE6y000	Congenital talipes equinovalgus
PE6y100	Congenital planovalgus
PE6yz00	Other valgus foot deformity NOS
PE6z.00	Valgus foot deformity NOS

PE6z.11	Congenital metatarsus valgus
PE7..00	Other deformities of feet
PE70.00	Talipes, unspecified
PE70.11	Clubfoot NOS
PE71.00	Talipes cavus
PE71.11	Congenital claw toe
PE71.12	Pes cavus
PE72.00	Congenital pes cavus
PE73.00	Congenital claw foot
PE74.00	Short Achilles tendon, congenital
PE7y.00	Other specified foot deformity
PE7y000	Asymmetric talipes
PE7y100	Congenital talipes calcaneus
PE7y200	Congenital talipes equinus
PE7y300	Congenital positional talipes
PE7yz00	Other specified foot deformity NOS
PE7z.00	Feet deformities NOS
PE8..00	Other specified nonteratogenic anomalies
PE80.00	Pectus excavatum, congenital
PE80.11	Congenital funnel chest
PE81.00	Pectus carinatum, congenital
PE81.11	Congenital pigeon chest
PE8y.00	Other nonteratogenic anomalies OS
PE8y000	Congenital club hand
PE8y011	Congenital club fingers
PE8y100	Congenital chest wall deformity NEC
PE8y111	Congenital thoracic wall deformity NEC
PE8y200	Congenital dislocation of elbow
PE8y300	Congenital flexion contractures of leg
PE8y400	Congenital spade-like hand
PE8y500	Guerin - Stern syndrome
PE8y600	Congenital flexion contracture of hip
PE8y700	Congenital abduction contracture of hip
PE8y800	Congenital flexion contracture of knee
PE8y900	Congenital short quadriceps
PE8yA00	Congenital dislocation of radial head
PE8yB00	Discoid meniscus - congenital
PE8yz00	Other nonteratogenic anomaly NOS
PE8yz11	Specified intrauterine postural deformity NEC
PE8yz12	Multiple congenital articular rigidities
PE8z.00	Nonteratogenic anomalies NOS
PE9..00	Other musc skeletal deformity
PE9..11	Other congenital musculoskeletal deformity
PEz..00	Congenital musculoskeletal deformity NOS

PF...00	Other congenital limb anomalies
PF0..00	Polydactyly - supernumerary digits
PF00.00	Supernumerary digits, unspecified
PF01.00	Accessory fingers
PF01000	Radial polydactyly Wassel 1
PF01100	Radial polydactyly Wassel 2
PF01200	Radial polydactyly Wassel 3
PF01300	Radial polydactyly Wassel 4
PF01400	Radial polydactyly Wassel 5
PF01500	Radial polydactyly Wassel 6
PF01600	Radial polydactyly Wassel 7
PF01700	Central polydactyly
PF01800	Ulnar polydactyly
PF02.00	Accessory toes
PF02000	Accesory hallux
PF02100	Accessory little toe
PF02200	Other accessory toe
PF03.00	Accessory thumbs
PF0z.00	Polydactyly NOS
PF1..00	Syndactyly - webbing of digits
PF10.00	Syndactyly of multiple digits, unspecified
PF11.00	Syndactyly of fingers without bone fusion
PF11.11	Webbed fingers
PF11000	Simple syndactyly - 1st web
PF11100	Simple syndactyly - 2nd to 4th web
PF12.00	Syndactyly of fingers with bone fusion
PF12.11	Fused fingers
PF12.12	Osseous syndactyly of fingers
PF12000	Osseous syndactyly - 1st web
PF12100	Osseous syndactyly - 2nd to 4th web
PF13.00	Syndactyly of toes without bone fusion
PF13.11	Webbed toes
PF13000	Simple syndactyly of toes 1st web space
PF13100	Simple syndactyly lesser toes
PF14.00	Syndactyly of toes with bone fusion
PF14.11	Fused toes
PF14.12	Conjoined toes
PF14.13	Syndactyly of toes with bone fusion
PF14000	Osseous syndactyly of toes 1st web space
PF14100	Osseous syndactyly lesser toes
PF15.00	Polysyndactyly
PF1z.00	Syndactyly NOS
PF1z.11	Polysyndactyly
PF1z.12	Symphalangism

PF2..00	Reduction deformity of upper limb
PF2..11	Arm reduction deformity
PF20.00	Congenital shortening of arm, unspecified
PF20.11	Brachymelia of arm
PF20100	Ectromelia of upper limb NOS
PF20200	Hemimelia of upper limb NOS
PF20z00	Unspecified congenital shortening of arm NOS
PF21.00	Transverse deficiency of arm
PF21.11	Congenital absence part of arm
PF21000	Transverse deficiency of arm, unspecified
PF21100	Transverse deficiency of arm, phalangeal level, all fingers
PF21200	Transverse deficiency of arm, forearm level
PF21300	Transverse deficiency of arm, shoulder level(amelia)
PF21400	Congenital amputation of upper limb
PF21500	Transverse deficiency of arm, elbow level(hemimelia)
PF21600	Transverse deficiency of arm, wrist level(hemimelia)
PF21611	Acheiria
PF21612	Rudimentary hand
PF21613	Congenital absence of hand
PF21700	Transverse deficiency of arm, upper arm level-short
PF21800	Transverse deficiency of arm, upper arm level-long
PF21z00	Transverse deficiency of arm NOS
PF21z11	Agenesis of hand
PF22.00	Longitudinal deficiency of arm NEC
PF22000	Phocomelia of upper limb NOS
PF22100	Rudimentary arm
PF22z00	Longitudinal deficiency of arm NEC NOS
PF23.00	Congenital absence upper arm and forearm with hand present
PF23.11	Complete phocomelia of upper limb
PF24.00	Congenital absence of upper arm only
PF24.11	Proximal phocomelia of upper limb
PF25.00	Congenital absence of forearm only
PF25.11	Distal phocomelia of upper limb
PF26.00	Agenesis of radial ray
PF26.11	Congenital absence of radius
PF26000	Hypoplasia of radius
PF26100	Partial radial absence
PF26200	Total radial absence
PF26300	Absent thumb
PF26400	Hypoplastic thumb-Blauth 1
PF26500	Hypoplastic thumb-Blauth 2
PF26600	Hypoplastic thumb-Blauth 3
PF26700	Hypoplastic thumb-Blauth 4
PF26800	Hypoplastic thumb-Blauth 5
PF27.00	Agenesis of ulna
PF27000	Partial defect of ulna
PF27100	Total absence of ulna
PF27200	Ulnar and humeroulnar synostosis
PF28.00	Agenesis of carpals and metacarpals
PF28.11	Transverse arrest of carpals and metacarpals
PF28000	Transverse arrest carpal level
PF28100	Transverse arrest metacarpal 1st ray
PF28200	Transverse arrest metacarpal other
PF29.00	Congenital absence of finger
PF29.11	Ectrodactyly of finger
PF29.12	Transverse arrest of phalanges
PF29000	Transverse arrest phalangeal level 1st ray
PF29100	Transverse arrest phalangeal level 2nd ray
PF29200	Transverse arrest phalangeal level 3rd ray
PF29300	Transverse arrest phalangeal level 4th ray
PF29400	Transverse arrest phalangeal level 5th ray
PF29z00	Congenital absence finger NOS
PF2y.00	Other specified reduction deformities of upper limb
PF2z.00	Reduction deformity of upper limb NOS
PF2z.11	Hypoplasia of upper limb
PF3..00	Reduction deformity of lower limb
PF3..11	Leg reduction deformity
PF30.00	Congenital shortening of leg, unspecified
PF30.11	Brachymelia of leg
PF30000	Ectromelia of lower limb NOS
PF30100	Hemimelia of lower limb NOS
PF30z00	Unspecified congenital leg shortening NOS
PF31.00	Transverse deficiency of leg
PF31000	Transverse deficiency lower limb - unspecified
PF31100	Transverse deficiency lower limb - ankle level
PF31111	Apodia
PF31112	Hemimelia - ankle level
PF31200	Congenital absence of leg and foot
PF31300	Transverse deficiency lower limb - hip level
PF31311	Amelia - lower limb
PF31400	Transverse deficiency lower limb - metatarsal level
PF31500	Transverse deficiency lower limb - knee level
PF31511	Hemimelia - knee level
PF31600	Transverse deficiency lower limb - through femur
PF31700	Transverse deficiency lower limb - through tibia/fibula
PF31800	Absent pelvis and lower limb

PF31z00	Transverse deficiency of leg NOS
PF32.00	Longitudinal reduction deformity of lower limb NEC
PF32.11	Phocomelia of lower limb NOS
PF33.00	Congenital absence of thigh and lower leg with foot present
PF33.11	Complete phocomelia of lower limb
PF34.00	Congenital absence of thigh only
PF34.11	Proximal phocomelia of lower limb
PF34000	Proximal femoral focal deficiency
PF34100	Congenital short femur
PF35.00	Congenital absence of lower leg only
PF35.11	Distal phocomelia of lower limb
PF36.00	Agenesis of tibia
PF36000	Congenital tibial deficiency type I
PF36100	Congenital tibial deficiency type II
PF36200	Congenital tibial deficiency type III
PF37.00	Agenesis of fibula
PF37000	Congenital fibular deficiency type I
PF37100	Congenital fibular deficiency type II
PF37200	Congenital fibular deficiency type III
PF38.00	Agenesis of tarsals and metatarsals
PF38000	Agenesis of talus
PF38100	Agenesis of calcaneum
PF38200	Agenesis of other tarsal bone
PF38300	Agenesis of multiple tarsal bones
PF38400	Agenesis of 1st metatarsal
PF38500	Agenesis of 5th metatarsal
PF38600	Agenesis of other metatarsal
PF38700	Agenesis of 4th and 5th metatarsals
PF38800	Agenesis of other multiple metatarsal
PF39.00	Congenital absence of toe
PF39000	Congenital absence of great toe
PF39100	Congenital absence of 5th toe
PF39200	Congenital absence of other lesser toe
PF39300	Congenital absence of 4th and 5th toes
PF39400	Congenital absence of other multiple toes
PF3A.00	Split foot
PF3y.00	Other specified reduction deformities of lower limb
PF3z.00	Reduction deformity of lower limb NOS
PF3z.11	Hypoplasia of lower limb
PF4..00	Reduction deformity of unspecified limb
PF40.00	Congenital absence of limb NOS
PF41.00	Amelia of unspecified limb
PF42.00	Ectromelia of unspecified limb
PF43.00	Hemimelia of unspecified limb

PF44.00	Phocomelia of unspecified limb
PF45.00	Congenital amputation of unspecified limb
PF46.00	Longitudinal reduction deformity of unspecified limb
PF47.00	Congenital absence of digits NOS
PF47.11	Adactyly
PF4y.00	Other specified reduction deformities of unspecified limb
PF4y000	Brachymelia NOS
PF4yz00	Other reduction deformity of unspecified limb NOS
PF4z.00	Reduction deformity of unspecified limb NOS
PF4z.11	Brachydactyly NOS
PF4z.12	Withered limb
PF4z.13	Hypoplasia of limb NOS
PF5..00	Other upper limb and shoulder anomaly
PF50.00	Upper limb anomaly, unspecified
PF51.00	Congenital deformity of clavicle
PF51.11	Clavicle agenesis
PF52.00	Congenital elevation of scapula
PF52.11	Sprengel's deformity
PF52000	Undescended shoulder
PF53.00	Radio-ulnar synostosis
PF53000	Proximal radioulnar synostosis
PF53100	Radioulnar synostosis and dislocation of radial head
PF53200	Distal radioulnar synostosis
PF54.00	Madelung's deformity
PF55.00	Acrocephalosyndactyly
PF55.11	Apert's syndrome
PF55.12	Acrocephalopolysyndactyly
PF55000	Acrocephalosyndactyly (Apert)
PF55100	Acrocephalosyndactyly (Pfeiffer)
PF55200	Acrocephalopolysyndactyly
PF55300	Saethre-Chotzen syndrome
PF56.00	Accessory carpal bones
PF57.00	Macrodactylia (fingers)
PF57000	Macrodactyly - simple
PF57100	Macrodactyly - fatty nerve tumor
PF58.00	Congenital cleft hand
PF58.11	Lobster-claw hand
PF58000	Cleft hand - first cleft
PF58100	Cleft hand - central
PF58200	Cleft hand with syndactyly
PF58300	Cleft hand with polydactyly
PF59.00	Other failure of differentiation of soft tissue of arm
PF59000	Windblown hand
PF59100	Aberrant forearm flexor muscle

PF59200	Aberrant forearm extensor muscle
PF59300	Aberrant intrinsic muscles
PF59400	Poland's syndrome
PF59500	Thumb in palm deformity
PF59600	Congenital trigger thumb
PF5A.00	Other failure of differentiation, skeletal tissues of arm
PF5A000	Lunate-triquetrum synostosis
PF5A100	Capitate-hamate synostosis
PF5A200	Scaphoid-lunate synostosis
PF5A300	Other carpal synostosis
PF5A400	PIP joint symphalangism
PF5A500	DIP joint symphalangism
PF5Az00	Other failure of differentiation skeletal tissues of arm NOS
PF5B.00	Other duplication of limb
PF5B000	Duplication of whole limb
PF5B100	Duplication of humerus
PF5B200	Duplication of radius
PF5B300	Duplication of ulnar ray
PF5B400	Duplication ulnar ray - mirror hand
PF5B500	Duplication of whole hand
PF5Bz00	Duplication of limb NOS
PF5C.00	Other overgrowth of upper limb
PF5C000	Overgrowth of whole upper limb
PF5C100	Overgrowth of partial upper limb
PF5Cz00	Other overgrowth of limb NOS
PF5D.00	Other undergrowth of limb
PF5D000	Undergrowth of whole limb
PF5D100	Undergrowth of whole hand
PF5D200	Brachymetacarpia
PF5Dz00	Other undergrowth of limb NOS
PF5E.00	Constriction ring syndrome of upper limb
PF5E000	Constriction ring
PF5E100	Constriction ring with lymphoedema
PF5E200	Acrosyndactyly
PF5E300	Intra-uterine amputation
PF5E400	Constriction ring with acrosyndactyly and amputation
PF5F.00	Congenital absence of both forearm and hand
PF5G.00	Congenital complete absence of upper limb(s)
PF5r.00	Other congenital anomalies of fingers
PF5r000	Triphalangeal thumb
PF5r100	Brachydactyly of fingers, unspecified
PF5r200	Camptodactyly
PF5r300	Clinodactyly
PF5r400	Flexion deformity of fingers
PF5r500	Brachydactyly-all 3 phalanges
PF5r600	Brachydactyly-missing phalanx
PF5r700	Symbrachydactyly
PF5r800	Camptodactyly-little finger
PF5r900	Camptodactyly-other or multiple
PF5rA00	Clinodactyly with delta phalanx
PF5rB00	Clinodactyly, no delta phalanx
PF5rC00	Brachymesophalangia
PF5rD00	Congenital malformation of thumb
PF5rz00	Other anomaly of fingers NOS
PF5s.00	Other congenital anomalies of hand
PF5t.00	Other congenital anomalies of wrist
PF5u.00	Other congenital anomalies of forearm
PF5u000	Radio-ulnar dysostosis
PF5uz00	Other congenital anomaly forearm NOS
PF5v.00	Congenital anomalies of elbow and upper arm
PF5v.11	Cubitus NOS
PF5w.00	Other congenital anomalies of shoulder
PF5w.11	Congenital deformity of scapula NEC
PF5x.00	Other congenital anomalies of whole arm
PF5y.00	Other upper limb and shoulder anomaly OS
PF5y000	Cleidocranial dysostosis
PF5y011	Cleidocranial dysplasia
PF5y100	Congenital cubitus valgus
PF5y200	Congenital cubitus varus
PF5y300	Congenital humeral varus
PF5y400	Humeroradial synostosis
PF5y500	Humeroulnar synostosis
PF5y600	Total elbow synostosis
PF5yz00	Other upper limb and shoulder anomaly NOS
PF5z.00	Upper limb or shoulder anomaly NOS
PF6..00	Other lower limb and pelvic girdle anomalies
PF60.00	Lower limb anomaly, unspecified
PF61.00	Congenital coxa valga
PF62.00	Congenital coxa vara
PF63.00	Other congenital hip joint deformity
PF63000	Congenital anteversion of femoral neck
PF63100	Congenital hip dysplasia
PF63111	Developmental dysplasia of the hip
PF63200	Congenital acetabular dysplasia
PF63X00	Congenital deformity of hip, unspecified
PF63z00	Other congenital hip joint deformity NOS
PF64.00	Congenital knee joint deformity
PF64000	Congenital absence of patella

PF64100	Congenital genu valgum - knock-knee
PF64200	Congenital genu varum - bowleg
PF64300	Rudimentary patella
PF64400	Congenital dislocation of patella
PF64500	Bipartite patella
PF64z00	Congenital knee joint deformity NOS
PF65.00	Macrodactylia of toes
PF65000	Macrodactyly of toes - simple
PF65100	Macrodactyly of toes - fatty nerve tumor
PF66.00	Other congenital anomalies of toe
PF66000	Congenital hallux valgus
PF66100	Congenital hallux varus
PF66200	Congenital hammer toe
PF66300	Brachydactyly of toes
PF66400	Congenital crossed toes
PF66411	Congenital overlapping toes
PF66500	Congenital curly toes
PF66600	Brachyphalangia of little toe
PF66700	Brachyphalangia of other toes
PF66800	Perodactylia of great toe
PF66900	Perodactylia of lesser toe
PF66A00	Perodactylia of multiple toes
PF66B00	Triphalangeal great toe
PF66z00	Other toe anomalies NOS
PF67.00	Congenital anomalies of foot NEC
PF67000	Astragaloscaphoid synostosis
PF67100	Calcaneonavicular bar
PF67200	Coalition of calcaneous
PF67300	Talonavicular synostosis
PF67400	Tarsal coalitions
PF67500	Lobster claw foot
PF67600	Rocker bottom foot
PF67700	Accessory tarsal bones
PF67800	Talocalcaneal bar
PF67900	Naviculocuneiform bar
PF67A00	Complex tarsal coalition
PF67z00	Anomalies of foot NEC NOS
PF68.00	Failure of soft tissue differentiation of lower limb
PF68000	Aberrant muscle of lower limb
PF69.00	Failure of differentiation of skeletal tissues of lower limb
PF69000	Congenital synostosis of lower limb bones
PF6A.00	Duplication of lower limb bone
PF6B.00	Congenital overgrowth of lower limb
PF6B000	Congenital overgrowth of proximal lower limb
PF6B100	Congenital overgrowth of distal lower limb
PF6B200	Congenital overgrowth of foot
PF6B300	Congen overgrowth of whole lower limb
PF6C.00	Congenital undergrowth of lower limb
PF6C000	Congenital undergrowth of proximal part of limb
PF6C100	Congenital undergrowth of distal part of limb
PF6C200	Congenital undergrowth of foot
PF6C300	Brachymetapodia of 1st metatarsal
PF6C400	Brachymetapodia of 4th metatarsal
PF6C500	Brachymetapodia of other metatarsal
PF6C600	Congen undergrowth of whole lower limb
PF6D.00	Constriction ring syndrome of lower limb
PF6D000	Constriction ring of lower limb
PF6D100	Constriction ring of lower limb with lymphoedema
PF6D200	Intrauterine amputation of lower limb
PF6D300	Constriction ring syndrome of lower limb with amputation
PF6E.00	Congenital absence of thigh and lower leg with foot present
PF6v.00	Other congenital anomalies of lower leg
PF6w.00	Other congenital anomalies of upper leg
PF6x.00	Other congenital anomalies of pelvis
PF6x000	Congenital absence of pubis NEC
PF6xz00	Other congenital anomalies of pelvis NOS
PF6y.00	Other lower limb anomalies
PF6y000	Congenital angulation of tibia
PF6y100	Congenital deformity of ankle joint
PF6y200	Congenital deformity of sacroiliac joint
PF6y300	Congenital fusion of sacroiliac joint
PF6y400	Congenital varus ankle
PF6y500	Congenital valgus ankle
PF6y600	Congenital pseudarthrosis of tibia
PF6y700	Congenital ball-and-socket ankle
PF6yz00	Other lower limb and pelvic girdle anomaly NOS
PFy..00	Other specified anomalies of unspecified limb
PFy0.00	Arthrogryposis multiplex congenita
PFy1.00	Larsen's syndrome
PFy2.00	Arthrogryposis, unspecified
PFy3.00	Distal arthrogryposis syndrome
PFy4.00	Other arthrogryposis syndromes
PFyz.00	Other anomaly of unspecified limb NOS
PFz..00	Congenital anomaly of unspecified limb NOS
PG...00	Other congenital musculoskeletal anomalies
PG0..00	Skull and face bone anomalies
PG0..11	Face bone anomalies

PG0..12	Skull and face bone anomalies
PG00.00	Congenital absence of skull bones
PG01.00	Acrocephaly
PG02.00	Congenital forehead deformity
PG03.00	Craniosynostosis
PG03.11	Scaphocephaly
PG03000	Muenke syndrome
PG04.00	Craniofacial dysostosis
PG04.11	Crouzon's disease
PG04.12	Trigorhinophalangeal dysplasia
PG05.00	Hypertelorism
PG06.00	Imperfect fusion of skull
PG07.00	Oxycephaly
PG08.00	Platybasia
PG09.00	Premature cranial suture closure
PG0A.00	Tower skull
PG0B.00	Trigonocephaly
PG0C.00	Pierre - Robin syndrome
PG0D.00	Mandibulofacial dysostosis
PG0D.11	Franceschetti syndrome
PG0D.12	Treacher - Collins syndrome
PG0E.00	Oculomandibular dysostosis
PG0E.11	Hallerman - Streif syndrome
PG0E.12	Oculomandibulofacial syndrome
PG0F.00	Goldenhar's syndrome
PG0G.00	Localised skull defects
PG0G.11	Craniolacunia
PG0G.12	Lacunar skull
PG0G.13	Parietal foramina
PG0H.00	Macrocephaly
PG0J.00	Pierre Robin association
PG0y.00	Other specified skull or face bone anomaly
PG0y.11	Defect of skull ossification
PG0y.12	Cranial dysostosis NEC
PG0y000	Brachycephaly
PG0yz00	Other anomaly of skull or face bone NOS
PG0z.00	Skull or face bone anomaly NOS
PG0z.11	Dysmorphic features
PG1..00	Anomalies of spine
PG10.00	Anomaly of spine, unspecified
PG11.00	Congenital lumbosacral spondylolysis
PG12.00	Congenital spondylolisthesis
PG13.00	Congenital absence of vertebra
PG13000	Congenital absence of cervical vertebra
PG13100	Congenital absence of thoracic vertebra
PG13200	Congenital absence of lumbar vertebra
PG13300	Congenital absence of sacrum
PG13311	Sacral agenesis
PG13z00	Congenital absence of vertebra NOS
PG14.00	Hemivertebra
PG14000	Cervical hemivertebra
PG14100	Thoracic hemivertebra
PG14200	Lumbar hemivertebra
PG14300	Cervical hemivertebra- balanced
PG14400	Cervical hemivertebra - unbalanced
PG14500	Thoracic hemivertebra- balanced
PG14600	Thoracic hemivertebra - unbalanced
PG14700	Lumbar hemivertebra - balanced
PG14800	Lumbar hemivertebra - unbalanced
PG14z00	Hemivertebra NOS
PG15.00	Congenital fusion of spine
PG15.11	Congenital lumbosacral fusion
PG15000	Congenital complete fusion of spine
PG15100	Congenital partial fusion of spine - balanced
PG15200	Congenital partial fusion of spine - unbalanced
PG15300	Congenital partial fusion spine with hemivertebra, balanced
PG15400	Congenit partial fusion spine with hemivertebra, unbalanced
PG16.00	Klippel-Feil syndrome
PG16000	Wilderwanck's syndrome
PG16z00	Klippel - Feil syndrome NOS
PG17.00	Spina bifida occulta
PG18.00	Congenital kyphosis
PG18.11	Congenital kyphoscoliosis
PG1u.00	Congenital anomalies of cervical vertebrae NEC
PG1u000	Supernumerary cervical vertebra
PG1uz00	Congenital anomaly of cervical vertebrae NEC NOS
PG1v.00	Congenital anomalies of thoracic vertebrae NEC
PG1v000	Supernumerary thoracic vertebra
PG1vz00	Congenital anomaly of thoracic vertebrae NEC NOS
PG1w.00	Congenital anomalies of lumbar vertebrae NEC
PG1w000	Supernumerary lumbar vertebra
PG1wz00	Congenital anomaly of lumbar vertebra NEC NOS
PG1x.00	Congenital sacrococcygeal anomalies NEC
PG1x000	Congenital absence of coccyx
PG1x100	Congenital absence of sacrum
PG1xz00	Congenital sacrococcygeal anomaly NOS
PG1y.00	Other anomaly of spine

PG1y.11	Congenital deformity of lumbosacral joint
PG1y.12	Congenital deformity of lumbosacral region
PG1y000	Platyspondylia
PG1y100	Supernumerary vertebra
PG1y200	Congenital absence of spine NEC
PG1y300	Defect of vertebral segmentation
PG1y400	Hypoplasia of spine
PG1yz00	Other anomaly of spine NOS
PG1z.00	Anomalies of spine NOS
PG2..00	Cervical rib
PG3..00	Other rib and sternum anomalies
PG30.00	Congenital absence of rib
PG31.00	Congenital absence of sternum
PG32.00	Congenital fissure of sternum
PG33.00	Congenital fusion of ribs
PG34.00	Sternum bifidum
PG35.00	Mis-shapen ribs
PG36.00	Extra ribs
PG36.11	Supernumerary ribs
PG37.00	Mis-shapen sternum
PG3x.00	Other congenital anomalies of ribs
PG3y.00	Other congenital anomalies of sternum
PG3z.00	Other rib or sternum anomaly NOS
PG3z.11	Anomalies of thoracic cage unspecified
PG4..00	Chondrodysplasia
PG40.00	Chondrodysplasia, unspecified
PG41.00	Achondroplasia
PG41.11	Dwarfism
PG41.12	Achondrogenesis
PG41.13	Achondroplastic dwarf
PG41000	Hypochondroplasia
PG42.00	Multiple enchondromata
PG42.11	Enchondromatosis
PG42.12	Ollier's disease
PG42.13	Chondrodysplasia
PG42.14	Chondrodystophy NEC
PG42.15	Hypochondroplasia
PG42.16	Osteopathia striata
PG42.17	Pseudochondroplasia
PG42.18	Dyschondroplasia
PG42000	Multiple enchondromata with haemangioma
PG42011	Kast's syndrome
PG42012	Maffuci's syndrome
PG42013	Chondrodysplasia with haemangioma

PG42100	Myotonic chondrodysplasia
PG42111	Catel-Schwartz-Jampel syndrome
PG42z00	Dyschondroplasia NOS
PG43.00	Asphyxiating thoracic dysplasia
PG43.11	Jeune's syndrome
PG44.00	Other specified dwarfing syndromes
PG44000	Diastrophic dwarfism
PG44011	Diastrophic dysplasia
PG44100	Metatropic dwarfism
PG44111	Metatropic dysplasia
PG44200	Thanatophoric dwarfism
PG44211	Thanatophoric dysplasia
PG44300	Mesomelic dysplasia
PG44400	Acromesomolic dysplasia
PG44500	Kniest dysplasia
PG44600	Pseudoachondroplasia
PG44z00	Other dwarfing syndromes NOS
PG45.00	Metaphyseal dysostosis
PG45.11	Jansen's metaphyseal dysostosis
PG45.12	Schmid's metaphyseal dysostosis
PG45.13	Craniometaphyseal dysostosis
PG45.14	Frontometaphyseal dysostosis
PG45.15	Metaphyseal dysplasia
PG46.00	Spondyloepiphyseal dysplasia
PG46.11	Pseudoachondroplasia
PG46000	Spondyloepiphyseal dysplasia congenita
PG46100	Spondyloepiphyseal dysplasia tarda
PG47.00	Congenital exostosis
PG47.11	Multiple congenital exostosis
PG48.00	Diaphyseal aclasis
PG49.00	Dysplasia epiphysealis hemimelica
PG4A.00	Metachondromatosis
PG4B.00	Lethal retarded ossification syndromes
PG4B000	Achondrogenesis
PG4B100	Hypochondrogenesis
PG4B200	Fibrochondrogenesis
PG4B300	Short-rib/polydactyly syndrome
PG4B400	Camptomelia dysplasia
PG4By00	Other lethal retarded ossification syndromes
PG4C.00	Chondrodysplasia punctata
PG4D.00	Metaphyseal chondrodysplasia
PG4E.00	Spondylometaphyseal dysplasia
PG4F.00	Lei-Weill dyschondrosteosis
PG4y.00	Chondrodysplasia OS

PG4z.00	Chondrodysplasia NOS
PG5..00	Osteodysplasia
PG5..11	Osteodystrophy
PG50.00	Osteodysplasia, unspecified
PG51.00	Osteogenesis imperfecta
PG51.11	Vrolik's disease
PG51.12	Eddowe's syndrome
PG51.13	Adair-Dighton syndrome
PG51.14	Lobstein's syndrome
PG51.15	Van der Hoeve's syndrome
PG51.16	Brittle bone disease
PG51000	Fragilitas ossium
PG51100	Osteopsathyrosis
PG51200	Osteogenesis imperfecta - unclassifiable
PG51300	Osteogenesis imperfecta type I
PG51400	Osteogenesis imperfecta type II
PG51500	Osteogenesis imperfecta type III
PG51600	Osteogenesis imperfecta type IV
PG51z00	Osteogenesis imperfecta NOS
PG52.00	Osteopetrosis
PG52.11	Albers - Schonberg syndrome
PG52.12	Marble bones
PG52000	Osteopetrosis - unclassified
PG52100	Osteopetrosis - congenita type
PG52200	Osteopetrosis - tarda type
PG53.00	Osteopoikilosis
PG53.11	Buschke-Ollendorff syndrome
PG54.00	Polyostotic fibrous dysplasia
PG55.00	Chondroectodermal dysplasia
PG55.11	Ellis - Van Creveld syndrome
PG56.00	Multiple epiphyseal dysplasia
PG56000	Chondrodysplasia calcificans congenita
PG56011	Chondrodysplasia calcificans congenita
PG56012	Conradi - Hunermann syndrome
PG56z00	Multiple epiphyseal dysplasia NOS
PG57.00	Infantile cortical hyperostosis
PG57.11	Caffey's syndrome
PG58.00	Progressive diaphyseal dysplasia
PG58.11	Engelmann's syndrome
PG58.12	Camurati-Engelmann disease
PG59.00	Pyknodysostosis
PG59.11	Pycnodysostosis
PG5A.00	Diaphyseal dysplasia
PG5B.00	Multiple synostosis syndrome

PG5C.00	Craniometaphyseal dysplasia
PG5D.00	Craniodiaphyseal dysplasia
PG5E.00	Frontometaphyseal dysplasia
PG5y.00	Other specified osteodysplasia
PG5y.11	Dyschondrosteosis
PG5y.12	Furst-Ostrum syndrome
PG5y000	Albright-Sternberg syndrome
PG5y011	Albright-McCune-Sternberg syndrome
PG5y012	Albright's polyostotic dysplasia
PG5yz00	Other osteodysplasia NOS
PG5z.00	Osteodysplasia NOS
PG5z.11	Osteochondrodysplasia
PG6..00	Anomalies of diaphragm
PG60.00	Congenital absence of diaphragm
PG61.00	Congenital diaphragmatic hernia
PG61.11	Congenital defect of diaphragmatic NEC
PG62.00	Congenital foramen Morgagni hernia
PG63.00	Eventration of diaphragm
PG6y.00	Other specified anomalies of diaphragm
PG6z.00	Diaphragm anomalies NOS
PG7..00	Abdominal wall anomalies
PG70.00	Exomphalos
PG71.00	Gastroschisis
PG72.00	Prune belly syndrome
PG7y.00	Other specified anomaly of abdominal wall
PG7z.00	Abdominal wall anomaly NOS
PG8..00	Congenital inguinal hernia
PGW..00	Osteochondrodyspl with defct growth tub bone spine unspec
PGX..00	Congenital malformation of bony thorax, unspecified
PGy..00	Other specified muscle, tendon and fascia anomaly
PGy0.00	Congenital absence of muscle and tendon
PGy0000	Absent tendon
PGy0100	Poland's syndrome
PGy0200	Other absent muscle
PGy0211	Muscle agenesis
PGy0212	Orbinsky syndrome
PGy0z00	Absent muscle or tendon NOS
PGy1.00	Accessory muscle
PGy2.00	Ehlers-Danlos syndrome
PGy2000	Ehlers-Danlos syndrome type I
PGy2100	Ehlers-Danlos syndrome type II
PGy2200	Ehlers-Danlos syndrome type III
PGy2300	Ehlers-Danlos syndrome type IV
PGy2400	Ehlers-Danlos syndrome type V

PGy2500	Ehlers-Danlos syndrome type VI
PGy2600	Ehlers-Danlos syndrome type VII
PGy2700	Ehlers-Danlos syndrome type VIII
PGy3.00	Nail-patella syndrome
PGy3.11	Osteo-onychodysostosis
PGy3.12	Onycho-osteodysplasia
PGy4.00	Fibrodysplasia ossificans congenita
PGyy.00	Other specified other anomalies of muscle, tendon and fascia
PGyy.11	Ayala's disease
PGyy000	Amyotrophica congenita
PGyy100	Congenital shortening of tendon
PGyy200	Hypoplasia of muscle
PGyy300	Popliteal web syndrome
PGyy400	Aplasia of muscle
PGyyz00	Other anomaly of tendon, fascia or muscle NOS
PGyz.00	Other muscle, tendon or fascia anomalies NOS
PGz..00	Congenital musculoskeletal anomalies NOS
PGz..11	Congenital deformity of musculoskeletal system NEC
PGz0.00	Unspecified anomaly of muscle
PGz1.00	Unspecified anomaly of tendon
PGz2.00	Unspecified anomaly of bones
PGz3.00	Unspecified anomaly of cartilage
PGz4.00	Unspecified anomaly of connective tissue
PH...00	Congenital integument anomalies
PH...11	Congenital skin anomalies
PH0..00	Hereditary oedema of legs
PH00.00	Congenital lymphoedema
PH01.00	Hereditary trophoedema
PH02.00	Milroy's disease
PH02.11	Meige's disease
PH03.00	Congenital elephantiasis
PH0z.00	Hereditary oedema of legs NOS
PH1..00	Ichthyosis congenita
PH10.00	Congenital ichthyosis, unspecified
PH11.00	Harlequin fetus
PH12.00	Ichthyosiform erythroderma
PH12.11	Sjogren - Larsson syndrome
PH13.00	Collodion baby
PH14.00	Ichthyosis vulgaris
PH15.00	X-linked ichthyosis
PH1y.00	Other specified ichthyosis congenita
PH1y000	Nethertons syndrome"
PH1z.00	Ichthyosis congenita NOS
PH1z.11	Congenital ichthyosiform erythroderma
PH1z.12	Alligator skin
PH2..00	Dermatoglyphic anomalies
PH20.00	Abnormal palmar creases
PH2z.00	Dermatoglyphic anomalies NOS
PH3..00	Other specified skin anomalies
PH30.00	Congenital ectodermal dysplasia
PH31.00	Vascular hamartomas
PH31.11	Vascular naevus
PH31.12	Naevus flammeus
PH31000	Birth mark, unspecified
PH31100	Port wine stain
PH31200	Strawberry naevus
PH31300	Angiomatosis
PH31z00	Vascular hamartoma NOS
PH32.00	Congenital pigmentary skin anomalies
PH32000	Congenital poikiloderma
PH32100	Urticaria pigmentosa
PH32111	Mast cell disease
PH32112	Mastocytosis
PH32113	Nettleship's syndrome
PH32200	Xeroderma pigmentosum
PH32211	Kaposi's xeroderma pigmentosum
PH32300	Incontinentia pigmenti
PH32311	Bloch - Sulzberger syndrome
PH32z00	Congenital pigmentary skin anomaly NOS
PH33.00	Specified syndromes NEC involving skin anomalies
PH33000	Brugsch's syndrome
PH33011	Acropachyderma
PH33100	Hailey-Hailey disease
PH33111	Benign familial chronic pemphigus
PH33200	Mibelli's disease
PH33300	Rothmund-Thomson syndrome
PH33311	Atrophic heredofamilial dermatosis
PH33312	Thomson's disease
PH33400	Focal dermal hypoplasia
PH33500	Pseudoxanthoma elasticum
PH33511	Darier's disease - pseudoxanthoma elasticum
PH33600	Siemen's syndrome
PH33z00	Specified syndromes involving skin anomalies NEC NOS
PH34.00	Other specified birthmark
PH34.11	Naevus NEC
PH34000	Naevus sebaceous
PH35.00	Mongolian blue spot
PH3y.00	Other congenital skin anomalies

PH3y.11	Keratosis palmaris
PH3y000	Congenital accessory skin tags
PH3y100	Congenital scar
PH3y200	Epidermolysis bullosa
PH3y211	Goldscheider's disease
PH3y212	Koebner's disease
PH3y213	Bullous eruption of hand
PH3y300	Congenital keratoderma
PH3y400	Congenital keratosis follicularis
PH3y411	Darier's disease - keratosis follicularis
PH3y500	Acanthosis nigricans, congenital
PH3y600	Keratosis palmaris et plantaris
PH3y611	Tylosis palmaris et plantaris
PH3y700	Epidermolysis bullosa simplex
PH3y800	Epidermolysis bullosa letalis
PH3y900	Epidermolysis bullosa dystrophica
PH3yA00	Bloom syndrome
PH3yz00	Other congenital skin anomaly NOS
PH3yz11	Lichen spinulosus
PH3z.00	Integument anomalies NOS
PH4..00	Specified hair anomalies
PH40.00	Congenital alopecia
PH40.11	Congenital atrichosis
PH40000	Congenital alopecia, unspecified
PH40100	Congenital localised alopecia
PH40200	Congenital generalised alopecia
PH40211	Atrichosis
PH40z00	Congenital alopecia NOS
PH41.00	Congenital monilethrix
PH41.11	Beaded hair
PH42.00	Congenital hypertrichosis
PH43.00	Persistent lanugo
PH43.11	Hypertrichosis lanuginosa
PH44.00	Twisted hair
PH44.11	Pili torti
PH45.00	Taenzer's hair
PH4z.00	Specified hair anomalies NOS
PH5..00	Specified anomalies of nails
PH50.00	Anonychia
PH50.11	Congenital absence of nails
PH51.00	Congenital clubnail
PH52.00	Congenital koilonychia
PH53.00	Congenital leukonychia
PH54.00	Congenital onychauxis

PH54.11	Enlarged nails
PH55.00	Congenital pachyonychia
PH55.11	Hypertrophic nails
PH5z.00	Specified nail anomalies NOS
PH6..00	Specified anomalies of breast
PH60.00	Absent breast
PH61.00	Absent nipple
PH62.00	Accessory breast
PH63.00	Accessory nipple
PH64.00	Supernumerary breast
PH65.00	Supernumerary nipple
PH66.00	Hypoplasia of breast
PH67.00	Small nipple
PH67.11	Hypoplasia of nipple
PH68.00	Ectopic breast tissue
PH6X.00	Congenital malformation of breast, unspecified
PH6z.00	Specified breast anomalies NOS
PH7..00	Cutis marmorata telangiectasia congenita
PHy..00	Other specified integument anomaly
PHz..00	Integument anomalies NOS
PHz..11	Congenital ectodermal defect
PHz0.00	Unspecified congenital anomalies of skin
PHz0.11	Congenital dermal defect
PHz1.00	Unspecified congenital anomalies of hair
PHz2.00	Unspecified congenital anomalies of nail
PHz2.11	Congenital deformity of nail
PJ...00	Chromosomal anomalies
PJ0..00	Down's syndrome - trisomy 21
PJ0..11	Mongolism
PJ0..12	Trisomy 21
PJ0..13	Trisomy 22
PJ00.00	Trisomy 21, meiotic nondisjunction
PJ01.00	Trisomy 21, mosaicism
PJ01.11	Trisomy 21, mitotic nondisjunction
PJ02.00	Trisomy 21, translocation
PJ02.11	Partial trisomy 21 in Down's syndrome
PJ0z.00	Down's syndrome NOS
PJ0z.11	Trisomy 21 NOS
PJ1..00	Patau's syndrome - trisomy 13
PJ10.00	Trisomy 13, meiotic nondisjunction
PJ11.00	Trisomy 13, mosaicism
PJ11.11	Trisomy 13, mitotic nondisjunction
PJ12.00	Trisomy 13, translocation
PJ12.11	Partial trisomy 13 in Patau's syndrome

PJ1z.00	Patau's syndrome NOS
PJ1z.11	Trisomy 13 NOS
PJ2..00	Edward's syndrome - trisomy 18
PJ20.00	Trisomy 18, meiotic nondisjunction
PJ21.00	Trisomy 18, mosaicism
PJ21.11	Trisomy 18, mitotic nondisjunction
PJ22.00	Trisomy 18, translocation
PJ22.11	Partial trisomy 18 in Edward's syndrome
PJ2z.00	Edward's syndrome NOS
PJ2z.11	TRISOMY 18 NOS
PJ3..00	Monosomies and deletions from the autosomes
PJ30.00	Antimongolism syndrome
PJ30.11	Deletion of long arm of chromosome 21
PJ31.00	Cri-du-chat syndrome
PJ31.11	Deletion of short arm of chromosome 5
PJ32.00	Deletion of short arm of chromosome 4
PJ32.11	Wolff - Hirschorn syndrome
PJ33.00	Other deletions of part of a chromosome
PJ33000	Deletion of long arm of chromosome 13
PJ33100	Deletion of long arm of chromosome 18
PJ33111	18p- syndrome
PJ33200	Deletion of short arm of chromosome 18
PJ33211	18q- syndrome
PJ33300	Smith-Magenis syndrome
PJ33400	Jacobsen syndrome
PJ33z00	Other deletion of part of a chromosome NOS
PJ34.00	Deletions seen only at prometaphase
PJ35.00	Deletions with other complex rearrangements
PJ36.00	Whole chromosome monosomy, meiotic nondisjunction
PJ37.00	Whole chromosome monosomy, mosaicism
PJ37.11	Whole chromosome monosomy, mitotic nondisjunction
PJ37.12	Autosomal deletion - mosaicism
PJ37000	Monosomy 21, mosaicism
PJ37z00	Whole chromosome monosomy, mosaicism NOS
PJ38.00	Chromosome replaced with ring or dicentric
PJ38.11	Chromosome replaced with dicentric
PJ38.12	Chromosome replaced with ring
PJ3y.00	Other deletions from the autosomes
PJ3y000	Shprintzen syndrome
PJ3y011	Velocardiofacial syndrome
PJ3z.00	Monosomies and deletions from the autosomes NOS
PJ4..00	Balanced autosomal translocation
PJ5..00	Other condition due to autosomal anomaly

PJ50.00	Whole chromosome trisomy syndromes
PJ50000	Trisomy 6
PJ50100	Trisomy 7
PJ50200	Trisomy 8
PJ50300	Trisomy 9
PJ50400	Trisomy 10
PJ50500	Trisomy 11
PJ50600	Trisomy 12
PJ50700	Other trisomy C syndromes
PJ50800	Trisomy 22
PJ50w00	Whole chromosome trisomy, meitotic nondisjunction
PJ50x00	Whole chromosome trisomy, mosaicism
PJ50x11	Whole chromosome trisomy, mitotic nondisjunction
PJ50y00	Other specified whole chromosome trisomy syndrome
PJ50z00	Whole chromosome trisomy syndrome NOS
PJ51.00	Partial trisomy syndromes
PJ51000	Major partial trisomy
PJ51100	Minor partial trisomy
PJ51z00	Partial trisomy syndrome NOS
PJ52.00	Trisomies of autosomes NEC
PJ52000	Duplications seen only at prometaphase
PJ52100	Duplications with other complex rearrangements
PJ52200	Extra marker chromosomes
PJ52300	Triploidy
PJ52400	Polyploidy
PJ52z00	Trisomy of autosomes NEC NOS
PJ53.00	Balanced rearrangements and structural markers NEC
PJ53.11	Balanced translocations
PJ53000	Chromosome inversion in normal individual
PJ53100	Balanced autosomal rearrangement in abnormal individual
PJ53200	Balanced sex/autosomal rearrangement in abnormal individual
PJ53300	Individual with marker heterochromatin
PJ53400	Individual with autosomal fragile site
PJ53500	Shwachman-Diamond syndrome
PJ53z00	Balanced rearrangement or structural marker NEC NOS
PJ5y.00	Other specified conditions due to autosomal anomalies
PJ5z.00	Unspecified conditions due to autosomal anomalies
PJ5z.11	Aneuploidy NEC
PJ6..00	Gonadal dysgenesis
PJ60.00	Mixed gonadal dysgenesis
PJ62.00	Ovarian dysgenesis
PJ63.00	Turner's syndrome
PJ63000	Turner's phenotype, karyotype normal

PJ63100	Turner's phenotype, karyotype 45X
PJ63200	Turner's phenotype, karyotype 46X iso (Xq)
PJ63300	Turner's,karyotype 46X + abnorm. sex chromosome,not iso(Xq)
PJ63400	Turner's phenotype, mosaicism 45X/46XX or 45X/46XY
PJ63500	Turner's,mosaic, 45X/other cell line with abn.sex chromosome
PJ63600	Turner's phenotype, other variant karyotypes
PJ63611	Turner's phenotype, ring chromosome karyotype
PJ63612	Turner's phenotype, partial X deletion karyotype
PJ63z00	Turner's syndrome NOS
PJ63z11	Bonnevie-Ullrich syndrome NOS
PJ63z12	Ovarian dwarfism NEC
PJ64.00	Other gonadal dysgenesis phenotype
PJ64000	XY, female phenotype
PJ64z00	Other gonadal dysgenesis phenotype NOS
PJ6z.00	Gonadal dysgenesis NOS
PJ7..00	Klinefelter's syndrome
PJ70.00	Klinefelter's phenotype, karyotype 47XXY
PJ71.00	Klinefelter's syndrome,male with more than two X chromosomes
PJ71.11	Klinefelter's syndrome, XXXY
PJ71.12	Klinefelter's syndrome, XXXXY
PJ72.00	Klinefelter's syndrome, male with 46XX karyotype
PJ73.00	Klinefelter's syndrome, XXYY
PJ74.00	Klinefelter's syndrome, XY/XXY mosaic
PJ7z.00	Klinefelter's syndrome NOS
PJ8..00	Balanced translocation and insertion in normal individual
PJ9..00	Mowat-Wilson syndrome
PJX..00	Sex chromosome abnormality, male phenotype, unspecified
PJy..00	Other sex chromosome anomaly
PJy0.00	Additional sex chromosome
PJy1.00	Sex chromosome mosaicism
PJy1000	Mosaic XO/XY
PJy1100	Mosaic XO/XX
PJy1200	Mosaic XY/XXY
PJy1300	Mosaic including XXXXY
PJy1z00	Sex chromosome mosaicism NOS
PJy2.00	XXX syndrome
PJy2.11	Triple X female
PJy2.12	Karyotype 47, XXX
PJy3.00	XXY syndrome
PJy4.00	Female with more than three X chromosomes
PJy5.00	Mosaicism, lines with various numbers of X chromosomes
PJy6.00	Male with structurally abnormal sex chromosome
PJyy.00	Other specified sex chromosome anomaly

PJyy.11	Absence of sex chromosome
PJyy000	Chimera 46XX/46XY
PJyy011	Chimera 46XX/46XY, true hermaphrodite
PJyy100	46XX true hermaphrodite
PJyy200	Fragile X chromosome
PJyy300	Karyotype 47,XYY
PJyy400	Fragile X syndrome
PJyyz00	Other sex chromosome abnormality NOS
PJyz.00	Sex chromosome anomaly NOS
PJz..00	Chromosomal anomalies NOS
PJz0.00	Mosaicism NOS
PJz1.00	Additional chromosome NOS
PJz2.00	Deletion of chromosome NOS
PJz3.00	Duplication of chromosome
PJzz.00	Conditions due to anomaly of unspecified chromosome NOS
PK...00	Other and unspecified congenital anomalies
PK0..00	Anomalies of spleen
PK00.00	Aberrant spleen
PK01.00	Absent spleen
PK01.11	Asplenia
PK02.00	Accessory spleen
PK03.00	Congenital splenomegaly
PK03.11	Hyperplasia of spleen
PK04.00	Ectopic spleen
PK05.00	Congenital lobulation of spleen
PK06.00	Hypoplasia of spleen
PK07.00	Mis-shapen spleen
PK0y.00	Other specified anomalies of spleen
PK0z.00	Anomalies of spleen NOS
PK1..00	Anomalies of adrenal gland
PK10.00	Aberrant adrenal gland
PK11.00	Absent adrenal gland
PK12.00	Accessory adrenal gland
PK13.00	Hypoplasia of adrenal gland
PK14.00	Ectopic adrenal gland
PK15.00	Aplasia of adrenal gland
PK1y.00	Other specified anomalies of adrenal gland
PK1y000	Congenital cyst of adrenal gland
PK1yz00	Other congenital anomaly of adrenal gland NOS
PK1z.00	Anomalies of adrenal gland NOS
PK2..00	Other endocrine gland anomalies
PK20.00	Absent parathyroid gland
PK21.00	Accessory thyroid gland
PK22.00	Persistent thyroglossal duct

PK22.11	Persistent thyrolingual duct
PK23.00	Thyroglossal duct cyst
PK24.00	Anomalies of pituitary gland
PK24000	Aberrant pituitary gland
PK24100	Congenital absence of pituitary gland
PK24200	Accessory pituitary gland
PK24z00	Anomaly of pituitary gland NOS
PK25.00	Anomalies of thyroid gland NEC
PK25000	Aberrant thyroid gland
PK25011	Retrosternal thyroid gland
PK25100	Congenital absence of thyroid gland
PK25z00	Anomaly of thyroid gland NEC NOS
PK26.00	Anomalies of thyroglossal duct NEC
PK27.00	Anomalies of parathyroid gland NEC
PK27000	Aberrant parathyroid gland
PK27100	Accessory parathyroid gland
PK27z00	Anomaly of parathyroid gland NEC NOS
PK28.00	Anomalies of thymus
PK28000	Aberrant thymus gland
PK28100	Congenital absence of thymus
PK28200	Accessory thymus gland
PK28z00	Anomaly of thymus gland NOS
PK2y.00	Other specified endocrine gland anomaly
PK2z.00	Endocrine gland anomaly NOS
PK3..00	Situs inversus
PK30.00	Situs inversus, unspecified
PK30.11	Transposition of viscera unspecified
PK31.00	Situs inversus abdominalis
PK31.11	Transposition of abdominal viscera
PK32.00	Situs inversus thoracis
PK32.11	Transposition of thoracic viscera
PK33.00	Complete situs inversus with dextrocardia
PK34.00	Situs inversus with levocardia
PK35.00	Kartagener's syndrome
PK3z.00	Situs inversus NOS
PK4..00	Conjoined twins
PK40.00	Craniopagus
PK40.11	Head-joined twins
PK40000	Craniopagus frontalis
PK40100	Craniopagus occipitalis
PK40200	Craniopagus parietalis
PK40300	Craniopagus parasiticus
PK40z00	Craniopagus NOS
PK41.00	Dicephalus

PK41.11	Conjoined twins with two heads
PK42.00	Pygopagus
PK42.11	Buttock-joined twins
PK43.00	Thoracopagus
PK43.11	Thorax-joined twins
PK44.00	Xiphopagus
PK44.11	Xiphoid- and pelvis-joined twins
PK45.00	Diaxial (double) monster
PK4y.00	Other specified conjoined twins
PK4z.00	Conjoined twins NOS
PK5..00	Tuberous sclerosis
PK5..11	Bourneville's disease
PK5..12	Epiloia
PK6..00	Other hamartoses NEC
PK60.00	Peutz - Jegher's syndrome
PK61.00	Sturge-Weber syndrome
PK61.11	Kalischer's disease
PK61.12	Encephalocutaneous angiomatosis
PK62.00	Von Hippel-Lindau syndrome
PK62.11	Lindau's disease
PK63.00	Gardner's syndrome
PK64.00	Proteus syndrome
PK6y.00	Other specified hamartoses NEC
PK6z.00	Hamartoses NOS
PK7..00	Multiple congenital anomalies NOS
PK70.00	Monster NOS
PK7z.00	Multiple congenital anomalies NOS
PK8..00	Congenital malformation syndromes due to known exogen causes
PK80.00	Fetal alcohol syndrome
PK81.00	Fetal hydantoin syndrome
PK82.00	Dysmorphism due to warfarin
PK83.00	Fetus and newborn affected by maternal use of alcohol
PK84.00	Fetal valproate syndrome
PKy..00	Other specified anomalies
PKy0.00	Multiple system congenital anomalies NEC
PKy0.11	Prader-Willi Syndrome
PKy0.12	Prader-Willi syndrome
PKy0.13	Noonan's syndrome
PKy0000	Bannayan-Riley-Ruvalcaba syndrome
PKy0100	Currarino triad
PKy0200	Adams-Oliver syndrome
PKy0300	Weaver syndrome
PKy1.00	Laurence-Moon-Biedl syndrome
PKy1.11	Biedl-Bardet syndrome

PKy2.00	Marfan's syndrome
PKy3.00	Single monster, specified type
PKy4.00	William syndrome
PKy5.00	Congen malformation syndromes affecting facial appearance
PKy5000	Oral - facial - digital syndrome
PKy5011	Papillon-Leage-Psaume syndrome
PKy5100	Mohr's syndrome
PKy5200	Cyclops
PKy5300	Whistling face syndrome
PKy5311	Freeman Sheldon syndrome
PKy5400	Waardenburg's syndrome
PKy5500	Gorlin-Chaudhry-Moss syndrome
PKy5600	Marchesani syndrome
PKy5611	Weill-Marchesani syndrome
PKy5612	Spherophakia-brachymorphia syndrome
PKy5700	Otopalatodigital syndrome
PKy5800	Usher's syndrome
PKy5900	Oculo-palato-digital syndrome
PKy5A00	Trichorhinophalangeal syndrome
PKy5B00	Costello syndrome
PKy5C00	Treacher Collins syndrome
PKy5D00	Kabuki make-up syndrome
PKy5E00	Branchio-otorenal dysplasia
PKy5F00	Coffin-Lowry syndrome
PKy5G00	Carey Fineman Ziter syndrome
PKy5H00	Simpson-Golabi-Behmel syndrome
PKy5z00	Congenital malform syndrome affecting facial appearance NOS
PKy6.00	Congenital malformation syndromes with short stature
PKy6000	Amsterdam dwarf
PKy6011	Cornelia de Lange syndrome
PKy6012	Bruck-de Lange syndrome
PKy6013	Degenerative amsterodamensis typus
PKy6100	Cockayne syndrome
PKy6200	Russell - Silver syndrome
PKy6300	Smith - Lemli - Opitz syndrome
PKy6400	Seckel syndrome
PKy6500	Aarskog syndrome
PKy6600	Dubowitz syndrome
PKy6700	Robinow syndrome
PKy6800	Floating-Harbor syndrome
PKy6z00	Congenital malformation syndrome with short stature NOS
PKy7.00	Congenital malformation syndromes involving limbs
PKy7000	Carpenter's syndrome
PKy7100	Holt - Oram syndrome
PKy7200	Klippel - Trenaunay - Weber syndrome
PKy7300	Rubenstein - Tayi syndrome
PKy7400	Sirenomelia
PKy7411	Sympus
PKy7412	Mermaid sirenomelia
PKy7500	Arachnodactyly
PKy7600	Aglossia - adactyly syndrome
PKy7611	Hanhart syndrome
PKy7700	Caudal dysplasia sequence
PKy7800	Multiple pterygium syndrome
PKy7900	Popliteal pterygium syndrome
PKy7A00	Congenital contractural arachnodactyly
PKy7A11	Beals syndrome
PKy7B00	Stickler syndrome
PKy7z00	Congenital malformation syndrome involving limbs NOS
PKy8.00	Congenital malformation syndromes with other skeletal change
PKy8000	Noonan's syndrome
PKy8z00	Congenital malformation syndrome+other skeletal changes NOS
PKy9.00	Congenital malformation syndromes with metabolic disturbance
PKy9000	Alport's syndrome
PKy9100	Beckwith's syndrome
PKy9111	Wiedemann - Beckwith syndrome
PKy9200	Menke's syndrome
PKy9211	Kinky hair syndrome
PKy9212	Congenital kinking hair
PKy9300	Prader - Willi syndrome
PKy9400	Zellweger's syndrome
PKy9500	Biemond's syndrome
PKy9600	VATER association
PKy9z00	Congenital malformation syndrome + metabolic disturbance NOS
PKyA.00	Cloacal exstrophy
PKyB.00	CHARGE association
PKyC.00	Pena-Shokeir syndrome type I
PKyD.00	Nicolaides-Baraitser syndrome
PKyE.00	Barber-Say syndrome
PKyF.00	Alstrom syndrome
PKyG.00	Men ret congen heart dis blepharophim blepharop hypopl teeth
PKyG.11	Ohdo blepharophimosis syndrome
PKyH.00	Moulded baby syndrome
PKyJ.00	Lujan-Fryns syndrome
PKyK.00	Loeys-Dietz syndrome
PKyz.00	Other specified anomalies NOS
PKyz.11	Cockayne's syndrome
PKyz.12	Local gigantism NEC

PKyz000	Ullrich - Feichtiger syndrome, chimaera
PKyz100	Acardia
PKyz200	Acephalobrachius
PKyz300	Acephalogaster
PKyz400	Acephalothorax
PKyz500	Happy puppet syndrome
PKyz511	Angelman syndrome
PKyz600	Congenital hemihypertrophy
PKyz700	Angelman's syndrome
PKyz711	Angelman syndrome
PKyz800	DOOR - Deafness, triphalangeal thumbs, onychodystrophy
PKz..00	Other anomalies NOS
PKz0.00	Anomalies of umbilicus
PKz1.00	Embropathia NEC
PKzz.00	Congenital anomaly NOS
Pyu0.00	[X]Congenital malformations of the nervous system
Pyu0000	[X]Encephalocele of other sites
Pyu0100	[X]Other congenital hydrocephalus
Pyu0200	[X]Other reduction deformities of brain
Pyu0300	[X]Other specified congenital malformations of brain
Pyu0400	[X]Unspecified spina bifida with hydrocephalus
Pyu0500	[X]Other congenital cauda equina malformations
Pyu0600	[X]Other specified congenital malformations of spinal cord
Pyu0700	[X]Other specif congenital malformations of nervous system
Pyu1.00	[X]Congenital malformations of eye, ear, face and neck
Pyu1000	[X]Other congenital malformations of eyelid
Pyu1100	[X]Other congenital malformations of lacrimal apparatus
Pyu1200	[X]Other anophthalmos
Pyu1300	[X]Other congenital lens malformations
Pyu1400	[X]Other congenital malformations of iris
Pyu1500	[X]Other congenital corneal malformations
Pyu1600	[X]Other congenital malforms of anterior segment of eye
Pyu1700	[X]Other cong malformations of posterior segment of eye
Pyu1800	[X]Other specified congenital malformations of eye
Pyu1900	[X]Other congenital malformations of middle ear
Pyu1A00	[X]Congenital malformation of inner ear
Pyu1B00	[X]Malformation of ear with impairment of hearing, unspec
Pyu1C00	[X]Other misshapen ear
Pyu1D00	[X]Other specified congenital malformations of ear
Pyu1E00	[X]Other branchial cleft malformations
Pyu1F00	[X]Other specified congenital malformations of face & neck
Pyu2.00	[X]Congenital malformations of the circulatory system
Pyu2000	[X]Other cong malformatn of cardiac chambers & connections
Pyu2100	[X]Other congenital malformations of cardiac septa
Pyu2200	[X]Other congenital malformations of pulmonary valve
Pyu2300	[X]Other congenital malformations of tricuspid valve
Pyu2400	[X]Other congenital malformations of aortic & mitral valves
Pyu2500	[X]Other specified congenital malformations of the heart
Pyu2600	[X]Other congenital malformations of aorta
Pyu2700	[X]Other congenital malformations of pulmonary artery
Pyu2800	[X]Other congenital malformations of great arteries
Pyu2900	[X]Other congenital malformations of great veins
Pyu2A00	[X]Other congenital malformations of renal artery
Pyu2B00	[X]Oth specified cong malform of peripheral vascular system
Pyu2C00	[X]Other malformations of precerebral vessels
Pyu2D00	[X]Other malformations of cerebral vessels
Pyu2E00	[X]Other specified cong malformations of circulatory system
Pyu2F00	[X]Congenital malforms of cardiac chambers+connections unsp
Pyu2G00	[X]Congenital malformation of tricuspid valve, unspecified
Pyu2H00	[X]Congenital malformation of aortic and mitral valves unsp
Pyu2J00	[X]Congenital malformation of great arteries, unspecified
Pyu2K00	[X]Congenital malformation of circulatory system, unspecif
Pyu3.00	[X]Congenital malformations of the respiratory system
Pyu3000	[X]Other congenital malformations of nose
Pyu3100	[X]Other congenital malformations of larynx
Pyu3200	[X]Other congenital malformations of trachea
Pyu3300	[X]Other congenital malformations of bronchus
Pyu3400	[X]Other congenital malformations of lung
Pyu3500	[X]Other specified congen malformation respiratory system
Pyu3600	[X]Congenital malformation of larynx, unspecified
Pyu4.00	[X]Cleft lip and cleft palate
Pyu4000	[X]Cleft palate, unspecified, bilateral
Pyu4100	[X]Unspecified cleft palate with cleft lip, bilateral
Pyu5.00	[X]Other congenital malformations of the digestive system
Pyu5000	[X]Other congenital malformations of tongue
Pyu5100	[X]Congenital malformations of palate, NEC
Pyu5200	[X]Other congenital malformations of mouth
Pyu5300	[X]Other congenital malformations of pharynx
Pyu5400	[X]Other congenital malformations of oesophagus
Pyu5500	[X]Other specified congenital malformations of stomach
Pyu5600	[X]Other specif congen malformations upper alimentary tract
Pyu5700	[X]Cong absence/atresia/stenos oth spec parts small intest

Pyu5800	[X]Cong absence/atresia/stenos of other parts large intest
Pyu5900	[X]Cong abs, atresia & stenosis of large intest, part unsp
Pyu5A00	[X]Other congenital functional disorders of colon
Pyu5B00	[X]Other specified congenital malformations of intestine
Pyu5C00	[X]Other congenital malformations of gallbladder
Pyu5D00	[X]Other congenital malformations of bile ducts
Pyu5E00	[X]Other congenital malformations of liver
Pyu5F00	[X]Other congen malformation of pancreas & pancreatic duct
Pyu5G00	[X]Other specified congen malformation of digestive system
Pyu5H00	[X]Congenital malformation of intestine, unspecified
Pyu6.00	[X]Congenital malformations of genital organs
Pyu6000	[X]Other congenital malformations of ovary
Pyu6100	[X]Other congen malform of fallopian tube & broad ligament
Pyu6200	[X]Other doubling of uterus
Pyu6300	[X]Other congenital malformations of uterus and cervix
Pyu6400	[X]Other congenital malformations of vagina
Pyu6500	[X]Other congenital malformations of vulva
Pyu6600	[X]Other specified congenital malform of female genitalia
Pyu6700	[X]Other specified hypospadias
Pyu6800	[X]Other congenital malformations of testis and scrotum
Pyu6900	[X]Oth cong malform vas def/epidid/semin vesicles/prostate
Pyu6A00	[X]Other congenital malformations of penis
Pyu6B00	[X]Other specified congenit malform of male genital organs
Pyu7.00	[X]Congenital malformations of the urinary system
Pyu7000	[X]Other cystic kidney diseases
Pyu7100	[X]Other obstructive defects of renal pelvis and ureter
Pyu7200	[X]Other congenital malformations of ureter
Pyu7300	[X]Other specified congenital malformations of kidney
Pyu7400	[X]Other atresia and stenosis of urethra and bladder neck
Pyu7500	[X]Other congenital malformations of bladder and urethra
Pyu7600	[X]Other specified congenital malform of urinary system
Pyu8.00	[X]Congenital malformations+deformations musculoskeletal sys
Pyu8000	[X]Other congenital deformities of hip
Pyu8100	[X]Other congenital varus deformities of feet
Pyu8200	[X]Other congenital valgus deformities of feet
Pyu8300	[X]Other congenital deformities of feet
Pyu8400	[X]Other congenital deformities of skull, face and jaw
Pyu8500	[X]Other congenital deformities of chest
Pyu8600	[X]Other specified congenital musculoskeletal deformities
Pyu8700	[X]Other reduction defects of upper limb(s)
Pyu8800	[X]Other reduction defects of lower limb(s)
Pyu8900	[X]Other reduction defects of unspecified limb(s)
Pyu8A00	[X]Other congen malform upper limb(s), incl shoulder girdle
Pyu8B00	[X]Other congen malform lower limb(s), includ pelvic girdle
Pyu8C00	[X]Other specified congenital malformations of limb(s)
Pyu8D00	[X]Other specified congenit malformation skull & face bones
Pyu8E00	[X]Other congen malform of spine, not assoc with scoliosis
Pyu8F00	[X]Other congenital malformations of ribs
Pyu8G00	[X]Other congenital malformations of bony thorax
Pyu8H00	[X]Oth osteochondrodyspl with def growth tub bones & spine
Pyu8J00	[X]Other specified osteochondrodysplasias
Pyu8K00	[X]Other congenital malformations of diaphragm
Pyu8L00	[X]Other congenital malformations of abdominal wall
Pyu8M00	[X]Other congenital malforms of the musculoskeletal system
Pyu8N00	[X]Congenital deformity of hip, unspecified
Pyu8P00	[X]Congenital malformation of bony thorax, unspecified
Pyu8Q00	[X]Osteochondrodyspl with defct growth tub bone spine unspec
Pyu9.00	[X]Other congenital malformations
Pyu9000	[X]Other congenital ichthyosis
Pyu9100	[X]Other epidermolysis bullosa
Pyu9200	[X]Other specified congenital malformations of skin
Pyu9300	[X]Other congenital malformations of breast
Pyu9400	[X]Other congenital malformations of hair
Pyu9500	[X]Other congenital malformations of nails
Pyu9600	[X]Other specified congenital malformations of integument
Pyu9700	[X]Other phakomatoses, not elsewhere classified
Pyu9800	[X]Other cong malformat syndr due to known exogenous causes
Pyu9900	[X]Other congen malform syndromes with other skelet changes
Pyu9A00	[X]Other specified congenital malformation syndromes, NEC
Pyu9B00	[X]Other specified congenital malformations
Pyu9C00	[X]Congenital malformation of breast, unspecified
Pyu9D00	[X]Primary ciliary dyskinesia
PyuA.00	[X]Chromosomal abnormalities, not elswhere classified
PyuA000	[X]Oth specif trisomies & partial trisomies of autosomes
PyuA100	[X]Other deletions of part of a chromosome
PyuA200	[X]Other deletions from the autosomes
PyuA300	[X]Other balanced rearrangements and structural markers
PyuA400	[X]Balanced rearrangement & structural marker, unspecified
PyuA500	[X]Other variants of Turner's syndrome
PyuA600	[X]Other specif sex chromosome abnormalit, female phenotype

PyuA700	[X]Other male with 46,XX karyotype
PyuA800	[X]Other specif sex chromosome abnormalit, male phenotype
PyuA900	[X]Other specified chromosome abnormalities
PyuAA00	[X]Sex chromosome abnormality, male phenotype, unspecified
PyuAB00	[X]Pallister-Killian syndrome
PyuAC00	[X]Townes-Brocks syndrome
Pz...00	Congenital anomaly NOS
Q400.00	Congenital rubella
Q400.11	Extended rubella syndrome
Q48y500	Megalencephaly
ZV13600	[V]Personal history of congenital malformations

10.11 DETAILED DESCRIPTION OF MATERNAL NRT USE AND CORRESPONDING ANOMALIES IN EACH MOTHER-CHILD PAIR

	NRT FORM	TIME	TOT PRSC. WEEKS	CONGENITAL ANOMALY
1	inhalation cartridge 10mg	month 2	1 day	congenital dislocation of hip
2	sublingual tablet 2mg	month 2	2 days	congenital dilated renal pelvis enlarged kidney
3	nicotine patch 21mg	month 1	4 weeks	Unilateral congenital dislocation of hip
	nicotine patch 21mg	month 2	2 weeks	
4	nicotine patch 5mg	month 3	2 weeks	thyroglossal duct cyst
5	nicotine patch 5mg	month 1	2 weeks	patent ductus arteriosis
6	nicotine patch 21mg	month 1	2 weeks	polycystic kidneys, infantile type
	nicotine patch 21mg	at sp	2 weeks	
	nicotine patch 7mg	month 2	4 weeks	
	nicotine patch 14mg	month 1	4 weeks	
7	nicotine patch 15mg	month 2	8 weeks	ankyloglossia
8	nicotine patch 15mg	month 1	1 week	ventricular septal defect
	nicotine patch 21mg	month 2	1 week	
	nicotine patch 15mg	month 1	1 week	
	nicotine patch 21mg	month 1	1 week	
	nicotine patch 21mg	month 2	1 week	
	nicotine patch 7mg	month 2	2 weeks	
	nicotine patch 10mg	month 2	1 week	
	nicotine patch 15mg	month 2	1 week	
	nicotine patch 7mg	month 2	2 weeks	
9	nicotine chewing gum 2mg	month 3	1 week	patent ductus arteriosis
10	inhalation cartridge 10mg	month 3	1 week	atrial septal defect NOS
11	nicotine patch 21mg	14 days before	6 weeks	talipes, unspecified
	nicotine patch 14mg	month 3	2 weeks	congenital absence of toe
12	nicotine patch 14mg	first week preg		ventricular septal defect
	nicotine patch 7mg	month 1		
	nicotine patch 14mg	21 days before		

	NRT FORM	TIME	TOT PRSC. WEEKS	CONGENITAL ANOMALY
13	nicotine patch 21mg	month 1	2 weeks	hypospadias
	nicotine patch 21mg	month 1	2 weeks	
	nicotine chewing gum 2mg	month 2	1 week	
	nicotine patch 21mg	month 2	2 weeks	
	nicotine patch 21mg	month 1	1 week	
14	nicotine ptch 14mg	month 2	2 weeks	undescended testicle
				hirschprung's disease
15	inhalation cartridge 10mg	month 1	1 day	congenital dilated renal pelvis
16	nicotine patch 15mg	month 3	2 weeks	other lung anomaly NOS
17	nicotine patch 10mg	month 1	2 weeks	congenital bowing of long leg bone, unspecified
				hypospadias
18	nicotine lozenges 2mg	month 3	2 days	patent ductus arteriosis
19	nicotine patch 21mg	month 3	2 weeks	dandy-Walker syndrome
	nicotine patch 14mg	month 3	2 weeks	coloboma of retina
	inhalation cartridge 10mg	month 2	4 days	cleft palate and lip
				other musculoskeletal deformity
				coloboma of iris
20	nicotine patch 15mg	month 3	2 weeks	hirschprung's disease
21	nicotine patch 10mg	month 1	2 weeks	other lung anomalies
22	nicotine patch 15mg	first week preg	1 week	balanced translocations
	nicotine patch 15mg	month 1	1 week	
	nicotine patch 15mg	month 1	4 weeks	
23	nicotine patch 21mg	25 days before	3 weeks	congenital dislocation and subluxation of the hip
	nicotine patch 14mg	month 1	2 weeks	
24	nicotine patch 15mg	month 3	1 week	fragile X chromosome
25	nicotine patch 15mg	month 2	4 weeks	congenital cystic adenomatoid malformation of the lung
				bow legs NOS
26	nicotine patch 21mg	month 3	1 week	multicystic kidney
27	nicotine patch 15mg	at sp	2 weeks	hypospadias, glandular
28	nicotine patch 10mg	month 3	2 weeks	supernumerary finger NEC

	NRT FORM	TIME	TOT PRSC. WEEKS	CONGENITAL ANOMALY
	nicotine patch 10mg	month 3	2 weeks	
29	nicotine lozenges 2mg	month 3	4 days	stenosis of pulmonary atrety pulmonary artery anomalies
30	nicotine patch 10mg	month 3	2 weeks	Poland's syndrome
31	nicotine patch 7mg	month 2	1 week	ventricular septal defect hypospadias
32	nicotine patch 21mg	month 3	4 weeks	patent ductus arteriosis
33	inhalation cartridge 10mg	month 3	1 day	craniosynostosis undescended testis, bilateral plagiocephaly
34	nicotine patch 21mg nicotine patch 21mg	month 2 month 3	2 weeks 2 weeks	pulmonary infundibular stenosis
35	nicotine chewing gum 2mg nicotine chewing gum 2mg	month 1 month 3	2 days 2 days	undescended testes congenital dislocation and subluxation of the hip
36	nicotine lozenges 2mg	month 3	2 days	congenital hypertrophic pyloric stenosis ventricular septal defect
37	nicotine patch 14mg	month 2	2 weeks	congenital posterior urethral valves
38	nicotine nasal spray 10mg/ml nicotine patch 21mg	at sp month 1	1 day 4 weeks	choanal atresia hypoplasia of upper limb aplasia of muscle congenial club hand
39	nicotine sublingual tab 2mg	month 1	1 week	congenital dislocation and subluxation of the hip primary ciliary dyskinesia
	nicotine patch 10mg		2 weeks	
40	nicotine patch 21mg nicotine patch 21mg nicotine patch 14mg	month 2 month 3 month 3	2 weeks 2 weeks 2 weeks	Lissencephaly
41	nicotine patch 21mg	28 days before	2 weeks	undescended testes, unilateral congenital posterior urethral valves

	NRT FORM	TIME	TOT PRSC. WEEKS	CONGENITAL ANOMALY
42	nicotine lozenges 2mg	month 3	5 days	congenital bronchomalacia
	nicotine chewing gum 2mg	month 3	6 days	laryngeomalacia
43	nicotine patch 21mg	month 1	3 weeks	congenital cleft nose
				cleft lip
44	nicotine patch 5mg	month 3	2 weeks	plagiocephaly
	nicotine patch 5mg	month 3	4 weeks	craniosynostosis
45	inhalation cartridge 10mg	month 3	4 days	congenital laryngeal stridor
	inhalation cartridge 10mg	month 3	1 day	
46	nicotine patch 15mg	month 3	1 week	hypospadias
	nicotine patch 10mg	month 3	1 week	
47	nicotine patch 7mg	month 3	2 weeks	congenital laryngeal stridor
	nicotine patch 21mg	month 3	2 weeks	
48	nicotine patch 7mg	month 1	2 weeks	patent ductus arteriosis
	nicotine patch 14mg	month 1	2 weeks	patent foramen ovale
	nicotine patch 21mg	month 2	2 weeks	
49	nicotine patch 10mg	month 2	2 weeks	hypospadias
	nicotine patch 5mg	month 3	2 weeks	
50	nicotine patch 21mg	month 3	2 weeks	undescended testes, bilateral
				congenital talipes varus
				Down's syndrome
51	nicotine patch 15mg	month 2	2 weeks	ankyloglossia
52	nicotine patch 15mg	month 2	2 weeks	microcephalus
53	inhalation cartridge 10mg	month 1	4 days	hypospadias
	inhalation cartridge 10mg	month 2	1 day	
	nicotine patch 15mg	month 2	2 weeks	
54	nicotine patch 14mg	month 1	4 weeks	patent ductus arteriosis

	NRT FORM	TIME	TOT PRSC. WEEKS	CONGENITAL ANOMALY
55	nicotine chewing gum 2mg	month 2	3 days	ventricular septal defect
56	nicotine patch 21mg	month 3	1 week	multicystic kidney
57	nicotine patch 21mg	month 2	2 weeks	ventricular septal defect patent ductus arteriosis
58	nicotine patch 10mg	month 1	2 weeks	other lung anomalies

* Prescription days not recorded in more than 95% of the prescriptions, therefore the duration of prescription was recalculated by approximating the average daily dose according to the British National Formulary and then dividing the total dose prescribed by the average daily dose.