PREGNANCY OUTCOMES FOR WOMEN EMPLOYED AS

HAIRDRESSERS, COSMETOLOGISTS AND LABORATORY WORKERS

Systematic Review of the Literature and Data-analysis of Finnish Medical

Birth Registry.

Dr Jacqueline Halliday-Bell

A thesis submitted to the University of Birmingham for the degree of

MEDICAL DOCTORATE

Institute of Occupational and Environmental Medicine

School of Health and Population Sciences

University of Birmingham

August 2015

UNIVERSITY OF BIRMINGHAM

University of Birmingham Research Archive

e-theses repository

ABSTRACT

The process of human reproduction is complex and exposures during pregnancy may have an impact on the outcomes. The use of chemicals during pregnancy is suspected to affect the unborn child. The precise mechanisms for most potentially harmful chemicals are not known but earlier research has looked at outcomes to identify adverse trends and gender ratios as a step towards identifying occupations most at risk.

Hairdressers, cosmetologists and laboratory workers are regularly exposed to occupational hazards including chemicals, poor ergonomics and psychological stress.

This study aimed to replicate previous research using improved methods to consolidate earlier findings.

A systematic review of the literature, using Embase, MEDLINE and CINAHL, yielded studies on all three categories of workers for the specific pregnancy outcomes of interest in this study. There were 8 papers that related to the hairdressers' pregnancy outcomes, 3 papers that related to cosmetologists and 6 papers that related to laboratory workers.

A portion of this thesis was based on original research. It examined pregnancy outcomes for women who gave birth to singletons in Finland between 1990 and 2010 and had been included on the Finish Medical Birth Registry (FMBR). This registry accounted for over 99% of the births in Finland and included a record of the mother's occupation from 1990 onwards. A wide range of data about the mother, the pregnancy and the infant is recorded on the register. This study collated findings for 3 subject and 3 control populations for the following parameters: increased male gender, low birth-

weight (LBW), high birth-weight HBW, pre-term delivery and post-term delivery, small for gestational age (SGA), large for gestational age LGA, stillbirth and early neonatal death (END).

FMBR data included 507,659 prima gravida women who delivered singleton with at least 22 weeks' gestation between 1990 and 2010. Among these there were 12,854 hairdressers, 1841 cosmetologists and 3587 laboratory workers. The control populations consisted of 40,405 teachers, 1968 musicians and 447,004 women from the general population.

Adjusted odds ratios (aOR) were calculated using binomial logistic regression analysis. Adjustments were made for maternal age, smoking habit, marital status and socioeconomic status.

When hairdressers were compared to the general public, there were three marginally statistically significant results for new-borns: SGA, (OR 1.01, 95% CI 1.00 - 1.02), LGA, (OR 1.02, 95% CI 1.00 - 1.03) and post-term delivery (OR 1.06, 95% CI 1.02 -1.11).

The papers from the systematic review and original work were combined under their occupational headings for the purpose of meta-analysis. This was performed using STATA and produced a series of pooled estimates for parameters where there were 2 or more studies of relevance. Both fixed effect and random effect models were used for the purpose of meta-analysis.

Marginal increased statistically significant results for pooled effect size (ES) from the meta-analysis were found for LBW among hairdressers (fixed effect) ES 1.083 (95% CI, 1.017-1.153) and SGA infants among hairdressers (fixed effect) ES 1.077 (95% CI, 1.006-1.153).

The reduction of pooled effect size for LGA infants among hairdressers reached marginal statistical significance, indicating a lowered risk of LGA infants (fixed and random effect) ES 0.81 (95% CI, 0.72-0.93) and ES 0.81 (95% CI 0.72-0.94) respectively.

The 3 papers on cosmetologists and 6 papers for laboratory workers were also combined with the original study. Pooled independent variable (IV) effect sizes of the meta-analyses did not demonstrate any statistically significant results for pregnancy outcomes.

The thesis concludes that hairdressers may be at a marginally increased risk of low birth weight and small size for gestational age. This may be due to occupational exposure. There is an indication that epidemiological research should include occupational exposure measurements or biological monitoring to help identify factors that may be contributing to the marginal increase in risk identified in this thesis.

No increased risk of the pregnancy outcome parameters was found for cosmetologists or laboratory workers but again further prospective epidemiological research that incorporates exposure monitoring could highlight relevant information to improve protection of workers and new-born.

DEDICATION

I dedicate this work to my family and particularly my late mother Sarah Ann Elizabeth Halliday who encouraged my persistence, my dear husband Duran Bell who offered wisdom and support and our three children Vanessa, James and Theodore who gave up family time to enable me to complete this work.

ACKNOWLEDGMENTS

TABLE OF CONTENTS

X

LIST OF FIGURES

LIST OF PHOTOGRAPHS

LIST OF TABLES

LIST OF ABBREVIATIONS

AD	aggregate data
(AOP)	adverse outcome pathway
aOR	adjusted odds ratio
CI	confidence interval
CERHR	Centre for the evaluation of risks to human reproduction
CINHAL	Cumulative Index to Nursing and Allied Health Literature
D+L	differences and lags of time
DARE	Database of Abstracts of Reviews of Effectiveness
d.f.	Degrees of freedom
DNA	Deoxyribonucleic acid
DNBC	Danish National Birth Cohort
EC	European Commission
ECM	cell-extracellular matrix
END	early neonatal death
ES	effect size
Et al	and others
ETS	Environmental tobacco smoke
g	grammes
GnRH	gonadotropin releasing hormone
FMBR	Finnish Medical Birth Registry
ETS	environmental tobacco smoke

HBW	High birth-weight
H^0	Null hypothesis
H^1	Alternative hypothesis
HSE	Health and Safety Executive
ICD	International Classification of Disease.
ISCO	International Standard Coding of Occupations
IUGR	intra-uterine growth retardation
I-V	Independent Variable
KELA	Social Insurance Institution of Finland
LBW	low birth-weight
LFD	large for dates
LGA	large for gestational age
MIEs	molecular initiating events
NERC	Natural Environment Research Council
P	p-value
PD	premature delivery
POF	Primary ovarian failure
PTD	pre-term delivery
ND	neonatal death
OECD	Organisation for Economic Co-operation and Development
OR	odds ratio
PEG-4	Polyethylene glycol
REVC	random effects variable component
RR	relative risk

SA	spontaneous abortion
SE	standard error of the mean
SES	Socioeconomic status
SFD	small-for-dates
SGA	small-for-gestational-age
STATA	Statistics and data software
Tvent OBLA	ventilatory threshold
TLV	threshold limit value
TWA	time weighted average
UK	United Kingdom
TEG	tri-ethylene glycerol
TTP	Time to pregnancy
TVOC	total volatile organic compounds
WHO	World Health Organisation
WRMDs	Work related musculoskeletal disorders
Vs.	versus
VDAs	Vascular Disruption Agents
VEGF	Vascular Endothelial Growth Factor

LIST OF DEFINITIONS

Acrosome reaction a structure at the end of a sperm cell that releases enzymes to digest the cell membrane of an egg, enabling the sperm to penetrate the egg.

Adjusted odds ratio (AOR) the estimated odds ratio after any confounding factors have been taken into account.

Ampulla the widened portion of the fallopian tube where fertilisation takes place.

Angiogenesis the formation of new blood vessels, e.g. in an embryo or as a result of a tumour.

The blastocyst is a structure formed in the early development of mammals.

Blastomere a cell of an animal embryo blastula formed by the division of a fertilised egg cell.

Blastula an embryo at an early stage of development, consisting of a hollow ball of cells.

Bulbourethral glands paired male glands which add a slippery clear secretion to lubricate the passage of semen in the urethral tract.

Cell is the basic structural, functional, and biological unit of all known living organisms.

Cellular differentiation is the process by which a less specialised cell becomes a more specialised cell type.

Cell division is the process by which a parent cell divides into two or more daughter cells.

Cervix the neck of the uterus that stretches during childbirth to allow passage of the foetus.

Conceptus denotes the embryo and its adnexa (appendages or adjunct parts) or associated membranes (i.e. the products of conception).

Confidence interval, a method of estimating the probability that the true population mean lies within a range around a sample mean.

D+L unary operators in STATA used to account for effect of lags and differences of time in a data series.

Early neonatal death (end) the death of new-born infant less than 7 days after birth.

EBSCO, an electronic journal and publication service available to both academic and corporate subscribers. It aggregates access to electronic documents from various publishers.

Egg cell is the female reproductive cell (gamete).

Embryo is a multicellular diploid eukaryote in its earliest stage of development, from the time of fertilisation until birth, hatching, or germination.

Endometrium is the inner mucous membrane of the uterus.

Epididymis is a long, coiled tube that rests on the back of each testicle. It transports and stores sperm cells that are produced in the testes.

Eukaryote is any organism whose cells contain a nucleus and other structures (organelles) enclosed within membranes.

Fallopian tube or oviduct in vertebrates is the passageway from the ovaries to the outside of the body.

Fertilisation is the fusion of gametes to initiate the development of a new individual organism.

Forest plot, a graphical display used to illustrate the relative strength of odds ratios or relative risk effects from a meta-analysis for a number of quantitative scientific studies that deal with a particular question.

Gamete is a cell that fuses with another cell during fertilisation in organisms that sexually reproduce.

Gastrulation is a phase early in the embryonic development of most animals, during which the single-layered blastula is reorganised into a trilaminar ("three-layered") structure known as the gastrula.

Genotype the genetic makeup of an organism.

Gestation, the time from fertilisation to birth.

Human embryogenesis is the process of cell division and cellular differentiation of the embryo that occurs during the early stages of development.

Implantation is the very early stage of pregnancy at which the fertilised ovum adheres to the wall of the uterus.

Intra-uterine growth retardation (IUGR) the failure of a foetus to attain its expected growth potential at any gestational stage.

Large for gestational age (LGA) a new-born whose length or weight is above the 95th percentile.

Late neonatal death, the death of a new-born infant between 7 and 28 days after birth of the new-born.

Low birth-weight (LBW) an infant weighing less than 2500g and very low birth-weight less than 1500g at birth.

Macrosomia a condition in which a baby is abnormally large before birth.

MAK Commission German Permanent Senate Commission for the investigation of health hazards of chemical compounds at work.

Morula an early stage in the development of an animal embryo, consisting of a solid ball of cells derived by cleavage of the fertilized egg zygote.

Mutagen is a physical or chemical agent that changes the dna, of an organism thereby increasing the frequency of mutations to a level above the natural background.

Neonatal death (nd) the death of new-born infant within the period 0-28 days after birth.

Neurulation refers to the folding process in vertebrate embryos, which includes the transformation of the neural plate into the neural tube.

Odds ratio (OR) a measure of effect size, describing the strength of association or non-independence between two binary data values.

Organisation for Economic Co-operation and Development (OECD) the organisation that provides a setting where governments compare policy experiences, seek answers to common problems, identify good practice and coordinate domestic and international policies.

Oocyte the egg cell released from the female ovary.

Organism is any contiguous living system.

Organogenesis is the process by which the ectoderm, endoderm and mesoderm develop into the internal organs of the organism.

Oviduct or fallopian tube in vertebrates is the passageway from the ovaries to the outside of the body.

P-value, the probability that an outcome as large as or larger than that observed would occur in a properly designed, executed, and analysed analytical study if in reality there was no difference between the groups, i.e., that the outcome was due entirely to chance variability of individuals or measurements alone.

Parity the number of live offspring a female has borne. It is contrasted with gravidity, which refers to the number of pregnancies, regardless of outcome.

Perinatal death includes stillbirths plus early neonatal deaths- the death of a new-born less than 7 days old.

Perinatal mortality includes stillbirths plus early neonatal deaths.

Power is the likelihood that a study will detect a true difference of a given magnitude between groups if it actually exists (i.e., a true positive).

Premature delivery (pd) / pre-term birth (ptb) / pre-term delivery (ptd) **the birth of an infant of less than 37 weeks gestational age.**

Pre-term labour, onset of labour before 37 completed weeks of gestation.

Prolonged or continuous standing upright posture for more than three hours.

Qualitative (subjective) data typically categorical, that are prone to observer variation and to low repeatability without strict, validated criteria (e.g., disease severity 0, 1+, 2+, 3+, ...).

Quantitative (objective) data typically measured with calibrated instrument, that are less prone to observer variation (age, weight, heart rate etc).

Small-for-dates (SFD) new-born whose weight and size at birth fall below the tenth percentile of appropriate for gestational age infants, whether delivered at term or earlier or later than term.

Sample a group of individuals that is a subset of a population and has been selected from the population in some fashion (random or haphazard).

Sample size (n) the number of individuals in a group under study. The larger the sample size, the greater the precision and thus power for a given study design to detect an effect of a given size.

Seminal vesicles sac-like pouches that attach to the vas deferens near the base of the bladder. The seminal vesicles produce a sugar-rich fluid (fructose) that provides sperm with a source of energy to help them move.

Small-for-gestational-age (SGA) infants who are defined as below the 10th percentile birth-weight for gestational age in the source population. This can also refer to the head circumference and abdominal circumference in relation to age during gestation or after birth.

Spontaneous abortion (SA) any pregnancy that is not viable (the foetus cannot survive) or in which the foetus is born before the 22nd week of pregnancy (icd-10 and who definition).

Standard Error (SE) of the mean estimation, the standard deviation of the sampling distribution associated with the estimation method.

STATA, statistics and data software used for data management, statistical analysis, graphics, simulations, regression analysis (linear and multiple) and custom programming.

Statistically significant, the conclusion that the results of a study are not likely to be due to chance alone because the p-value derived from the statistical analysis is smaller than the critical alpha value (usually 0.05).

Statistically insignificant, the conclusion that the results of a study are likely to be due to chance alone because the p-value derived from the statistical analysis is larger than the critical alpha value (usually 0.05).

Stillbirth is the death of an unborn foetus equal to or greater than 22 weeks gestation contained in the womb.

Teratogen, any environmental influence that has the capacity to adversely affect the normal development of the foetus.

Prostate a gland in the male reproductive system responsible for proofing semen.

Seminal vesicle either of a pair of glands that secrete the fluid component of semen into the ejaculatory duct in males.

Sperm the male reproductive cells.

Spermatozoon (plural - spermatozoa) motile sperm cell, or moving form of the haploid cell that is the male gamete.

Uterus or womb is a major female hormone-responsive reproductive sex organ of most mammals, including humans.

Vas deferens are paired thick-walled tubes in the male reproductive system that transport sperm cells from the epididymis, where they are stored prior to ejaculation.

Zona pellucida is a glycoprotein layer surrounding the plasma membrane of mammalian oocyte

Zygote is a fertilised biological cell.

World Health Organisation (WHO) the directing and coordinating authority for health within the united nations system.

Xenobiotics describe chemical compounds such as a drug or pesticide that is foreign to the body of a living organism.

LIST OF ORIGINAL PUBLICATIONS

Work as a hairdresser and cosmetologist and adverse pregnancy outcomes.

Halliday-Bell J.A., Gissler M. and Jaakkola J.J. Occupational Medicine (London). 2009 May, 59(1): 180-4.

The co-authors roles were as follows: Professor M. Gissler enabled the release of data for analysis. Professor JJ Jaakkola reviewed the draft paper and made comments that enabled redrafting to the standard required for publication.

Laboratory work and adverse pregnancy outcomes.

Halliday-Bell J.A., Quansah R., Gissler M. and Jaakkola J.J. Occupational Medicine (London). 2010 June, 60(4): 310-313.

The co-authors roles were as follows: Professor M. Gissler enabled the release of data for analysis. Professor JJ Jaakkola and Dr R Quansah reviewed the draft papers and made comments that enabled redrafting to the standard required for publication.

1 AIMS

The overall aims of this study were firstly to examine the international pre-existing research published in English, from 1990 onwards, for offspring of women employed in hairdressing, cosmetology and laboratory work to identify evidence of increased male gender and adverse pregnancy outcomes.

Secondarily, the original portion of this research aimed to interrogate the Finnish Medical Birth Registry (FMBR) and to use data from it to establish the risks of increased male gender and adverse pregnancy outcomes and their statistical significance.

The third aim was to combine the pre-existing research and original research by way of meta-analysis for effect sizes to be calculated for each outcome. This enabled further assessment of the risk of male gender and adverse pregnancy outcomes and their statistical significance.

2   HUMAN REPRODUCTIVE PROCESS

2.1   Introduction

This narrative literature review covered information extracted from research articles and book publications that described and discussed the state of the science for the reproductive process in humans. It also summarises information on agents identified as harmful to human reproduction to date. Where possible the narrative literature review also identified the mechanisms used by the agents to adversely affect human reproduction.

2.2   Method of narrative review

A qualitative, evidence based approach was used to provide an overview of human reproduction and adverse agents' mechanisms. This involved using the online literature search tools provided by University of Birmingham Library. These allow for 'simple' or 'advanced' searching. The advanced search option was selected primarily for each topic in the first chapter of this thesis. A preference for systematic reviews was indicated. This specification was selected in a hierarchical pattern for the 'Title', followed by the 'Subject' category, which would allow for key words and Medical Subject Headings (MeSH) to be highlighted. At the lowest level of the hierarchical approach used the selection was made for the 'Any' range. The Advanced search facility was also used to select papers written in English. No limit was made on the dates for searching.

If large numbers of results were found the search was refined by using more specific terms. If fewer papers were found, typically less than 50, they were individually reviewed by title and abstract. Those relevant to the review were accessed and read to find information relevant to the thesis. If no results were found the search terms were altered to be more wide ranging or truncated using the asterisk (*) for the same effect. If this still produced no results as search was made in Google Scholar and Google.

The hardcopy textbooks from the University of Birmingham Library and the authors own collection, also provided a series of relevant references to articles that could be accessed by author, date and title from the advanced search of the online facility.

Membership of the library allows ready access to most papers and where this did not lead to easy access the articles were sought in Highwire, Google Scholar and Google.

Textbooks held in the library and articles accessible online where used to gather detailed information on the topics and the studies of relevance. Each item was included in the review with a citation and listed in the table of references.

2.3 Results from the narrative review

Sexual reproduction is a complex process in humans through which genes are passed to a surviving generation. It is known to be affected by health, social, cultural and environmental factors. The outcomes of reproduction are wide ranging and varied in every case. The following sections will cover the male and female reproductive systems and the process of fertilisation that

progresses through various stages to the point of delivery of a new-born infant.

2.4   Male reproductive system

The human male reproductive system consists of two structures both of which are outside the abdominal cavity: the testes where sperm are produced, and the penis. Sperm production commences at puberty in males. Other tissues in the male reproductive system include the epididymis, a whitish mass of tightly coiled tubes that partially encase the testicles and serve for maturation and storage of sperm before they pass into the vas deferens, or sperm duct which is approximately 30 centimetres long and carries sperm to the ampullary gland and prostatic ducts and from there to the pelvic cavity (Heffner and Schust, 2010).

Three accessory glands provide fluids that lubricate the duct system and nourish the sperm cells. They are the seminal vesicles, the prostate gland, and the bulbourethral glands (Cowper glands). The seminal vesicles are sac-like structures attached to the vas deferens. They produce a fructose rich, yellow fluid that provides sperm cells' energy and aids their motility (Heffner and Schust 2010).

The prostate gland surrounds the ejaculatory ducts at the base of the male urethra, just below the bladder. It is responsible for proofing semen: a liquid made up of a mixture of sperm cells, prostatic fluid, seminal fluid, calcium and the enzyme prostatic pro-fibrinolysin. The third organ is the bulbourethral glands or Cowper's glands. These pea-sized structures are located on the sides of the urethra just below the prostate gland. They produce a clear,

slippery fluid that serves to lubricate the urethra for the passage of semen and neutralise acidity (Heffner and Schust, 2010).

Freshly ejaculated sperm is unable to fertilise effectively until the active sperm cell undergoes potentiation changes at the beginning of the process. Full capacitation occurs in the female's reproductive tract over a number of hours resulting in the sperm having increased motility and destabilised cell membranes. These changes facilitate the acrosome reaction, where a single sperm produces hyaluronidase and acrosin enzymes facilitating penetration of the oocyte's tough zona pellucida membrane. The active sperm then fuses with the membrane of the oocyte and fertilisation proceeds (Bedford, 2011).

2.5 Female reproductive system

The female reproduction system works closely with the hypothalamo-pituitary axis. Prolactin, follicle-stimulating hormone and luteinising hormone are three hormonal proteins produced by the anterior pituitary that are essential for reproduction in the human female. They maintain the ovarian cycle, control follicle recruitment and maturation. They are also responsible for the manufacture of steroids, ova maturation, ovulation and luteinisation.

The female reproductive system consists of ovaries, the fallopian tube, the uterus and the vagina. The ovaries are the female gonads. They are the source of oocytes and also synthesise and secrete oestrogens and progesterone and other major female sex hormones. The fallopian tube transport oocytes to and the sperm from the uterus. The uterus is a pear shaped muscular organ which communicates through the fallopian tubes to the pelvic cavity the lower portion the vagina communicates to the exterior (Heffner and Schust 2010).

For both the female and the male, the hypothalamus is located at the top of the brain stem. It is the intermediary organ between the nervous and endocrine systems the two most significant control systems in the body regulating pituitary gland and hormone production (Johnson, 2013).

After ovulation, the single active ovum is captured by one of the oviducts or fallopian tubes which lead from the ovaries to the uterus (Heffner and Schust, 2010).

2.6   The uterus

The uterus is the muscular, major female reproductive organ. It accepts and implants the fertilised ovum into its endometrium. Normal pregnancy usually takes between 38 and 42 weeks to complete. The uterus provides the fertilised ovum – known at this stage as an embryo (weeks 1 to 8 after fertilisation) with mechanical protection, nutritional support, and waste removal. This continues as it develops into a foetus (week 9 until delivery of the new-born). The muscular wall of the uterus is also important in pushing out the foetus at the time of birth (Bulletti et al., 1997; Larson, 2001).

2.7   Fertilisation

Fertilisation takes place when a spermatozoon has successfully entered the ovum. Then two sets of genetic material carried by the gametes, each carrying a haploid complement (or half) of the parental DNA, fuse together, resulting in the zygote, (a single diploid cell). This usually takes place in the ampulla of one of the fallopian tubes. The sperm can only achieve this after capacitation where the surface charge of the spermatozoa and this is

associated with change in the tail movement from an undulating to a whip like movement (Heffner and Schust, 2010).

Successful fertilisation is enabled by three processes which also act as controls to ensure species-specificity. The first is that of chemotaxis which directs the movement of the sperm towards the ovum. Secondly there is an adhesive compatibility between the sperm and the egg. Thirdly, once the sperm is adhered to the ovum, an acrosomal reaction takes place. This is the consequence of the cap on the front portion of the spermatozoon known as the acrosome releasing digestive enzymes to break down the zona pellucida, forming a cone shaped elevation, known as the cone of attraction and allowing its entry. The entry of the sperm causes calcium to be released this leads to a zona reaction where cortical granules release enzymes, digesting sperm receptor proteins and modifying the zona pellucida to form the perivitelline membrane, which blocks entry to other sperm cells (Jones, 2006). The zygote (days 0-5 after fertilisation) then moves toward the uterus, a journey that can take up to a week to complete. It is pushed along by movements of cilia on the inner lining of the tubes over a period of several hours.

2.8 Morula formation

Cell division by mitosis, begins approximately 24 to 36 hours after the male and female cells unite. This first division marks the beginning of the cleavage process which continues with the division of the first two cells to give four cells which then divide to give eight cells and so on. This is quite a slow process taking between 12 and 24 hours for each division

The dividing cells which are individually called blastomeres, are enclosed within the strong zona pellucida of the ovum. The zygote (which is large compared to any other cell) undergoes further cleavage, increasing the number of cells without any increase in the size of the initial zygote. Consequently the nuclear genetic material takes up a greater proportion of the space in the zygote than that of the cytoplasm. When eight blastomeres have formed they are undifferentiated and aggregated into a sphere known as a morula (Gray's Anatomy, accessed November 2014).

The cells of the morula are at first closely aggregated, binding firmly together in a process called compaction. Cleavage then continues as cellular differentiation progresses. This is distinguished by the formation of an outer or peripheral layer, the trophoblast, (which does not contribute to the formation of the embryo itself) and an inner cell mass (from which the embryo is developed).

2.9 Blastocyst formation

Between days 5 and 9, fluid collects between the trophoblast and the greater part of the inner cell-mass then the morula is converted into a vesicle, called the blastomeric vesicle (Gray's Anatomy, accessed November 2014). The inner cell mass remains in contact with the trophoblast at one pole; this is named the embryonic pole (Gray's Anatomy, accessed November 2014). The trophoblasts secrete fluid into the blastocoel; as it enlarges, the blastocyst 'hatches' through the zona pellucida, which itself then disintegrates (Brison, 2014).

2.10 Implantation of the conceptus

Around day 8 after fertilisation, the inner cell mass of the conceptus (the embryo plus its membranes) begins formation of the amnion and allantois. The foetal part of the placenta forms from the outer trophoblast layer. The exposed cells of the trophoblast allow the blastocyst to attach itself to the endometrium, where it will implants by day 12 (Forgács and Newman, 2005; Moore and Persaud, 2003).

2.11 Primary utero-placental formation

By day 10 the embryo is sited in the amniotic cavity. Thereafter the trophoblast develops two sub-layers known as the cytotrophoblast and the exocoelomic membrane or Heuser's membrane which surrounds the cytotrophoblast and the primitive yolk sac. A further layer, the syncytiotrophoblast grows and enters a lacunar phase, in which a number of vacuoles appear and are filled by blood over the following days (Forgács and Newman, 2005). This is the primary stage of uteroplacental circulation formation (Larson et al., 2001).

New cells derived from the yolk sac then form between trophoblast and exocelomic membrane and give rise to extra-embryonic mesoderm, which forms the chorionic cavity. By day 15 cells of the trophoblast penetrate maternal uterine tissue and form primary villi - rounded columns which move into the syncytiotrophoblast.

2.12 Placenta formation

The syncytiotrophoblast produces human chorionic gonadotropin (hCG) a hormone that stimulates the release of progesterone from the corpus luteum

that has been left after ovulation. Progesterone enriches the uterus with a thick lining of blood vessels and capillaries so that it can sustain the developing embryo. The villi begin to branch and establish blood vessels of the embryo. Other villi, called terminal or free villi, have the role of nutrient exchange. The embryo is joined to the trophoblastic shell by a narrow connecting stalk that develops into the umbilical cord to attach the placenta to the embryo (Larson et al., 2001). Arteries in the decidua are remodelled to increase the maternal blood flow into the intervillous spaces of the placenta, allowing gas exchange to take place as well as the transfer of nutrients to the embryo. Waste products from the embryo will diffuse across the placenta (Larson et al., 2001).

2.13 Embryo formation

At the same time (day 8 after fertilisation) that the syncytiotrophoblast progresses to penetrate the uterine wall, the inner cell mass (embryoblast) also develops. This is the source of embryonic stem cells, which are pluripotent and can develop into any one of the three germ layer cells (Bruce, 1999).

During the first 10 weeks of gestation as the embryo forms cells differentiate into the various bodily systems. This is the most critical time of development. By the end of the embryonic stage, the early external features of fingers, eyes, mouth and ears become visible.

2.14 Foetus

From 10 weeks gestation the new human is known as a foetus. At this stage it measures 30 mm in length and its heart beat and involuntary motions can be

detected by ultrasound (Tunón et al., 2000). Sex organs begin to appear during the third month of gestation. The foetus continues to grow in both weight and length.

Weight gain does not begin in a real sense until the second trimester. The weight at birth is dependent on the rate of growth and the gestation at the point of delivery. A SGA infant is one that is growth retarded.

Reduced foetal growth can be distinguished into asymmetrical and symmetrical growth retardation. In asymmetrical growth retardation the weight tends to be more affected than the skeletal structure i.e. it is primarily associated with a risk factor operating in late pregnancy. Symmetrical growth retardation on the other hand is more likely associated with a cause that operates over the entire period of gestation (Beattie and Whittle, 1993).

2.15 Inhibin, oestrogen and progesterone

The ovary is responsible for the production of oocytes. Inhibin a protein hormone is produced as a result of the effect of increase in luteinising hormone; it acts at on the anterior pituitary to decrease the release of follicle-stimulating hormone and allows the continued development of the dominant follicle destined to ovulate. Oestrogen production increases as a result of this process and stimulates both the luteinising hormone surge and secretory changes in vagina cervix and uterus and the vagina to enhance spermatozoa viability and transport. After ovulation, thecal and granulosa cells in the follicular cavity of the ovary, lead to the formation of corpus luteum that is responsible for secretion of progesterone that stimulates the uterus to provide an environment suitable for implantation of the fertilised embryo.

Morphological and biochemical changes occur as the primordial follicle progresses towards ovulation. This entire process highlights that there are a number of sites at each stage of follicular growth that exhibit unique patterns of gonadotropin sensitivity and steroid production; these in turn affect feedback pathways. Infertility can be induced by chemical agents that affect these particular stages of follicle development (Johnson, 2013).

2.16 Effects of xenobiotics

Xenobiotics are foreign chemicals or medications. They can be toxic to granulosa cells (Johnson, 2013). Oestradiol suppresses of progesterone production by granulosa cells; measurement of this hormone serves to verify granulosa cell responsiveness. Pesticide p, p'-DDTD and its isomer o, p' DDT cause suppression of progesterone production that is comparable with the effects of oestradiol. But other pesticides such as Malathion do not have the same effect.

Thecal cells provide precursors for steroids synthesised by the granulosa cells. Their recruitment may involve proliferation of the stromal cell layer and migration to regions around the follicle. Impairment of this process can affect thecal cell function. Androgens, metabolised to oestrogens by granulosa cells that generate from thecal cell layer, can be increased or decreased due to xenobiotics (Mattison, 2011).

During the period of between 2 and 6 days after fertilisation when the morula is travelling along the fallopian tube into the uterus it may be exposed to chemical compounds that penetrate into the uterine fluids. Absorption of xenobiotic compounds may lead to degenerative changes, alteration of the blastocystic protein profile and failure of implantation.

12

Overall the embryo is fairly resistant to teratogenic insults at this early stage as the cells have not yet begun the complex sequence of chemical differentiation (Server, 2011).

2.17 Effects of teratogens

The later stages of embryogenesis, differentiation, mobilisation and organisation of cells and tissues, can be affected by teratogens. The factors that determine susceptibility include the route and level of exposure, the pattern and timing of exposure and the foetal and maternal genotype (Johnson, 2013).

Most early aborted foetuses have chromosomal abnormalities but later foetal loss can occur due to the abnormalities caused by teratogens (Källén, 1988). The effects of teratogenesis can also be the cause of early neonatal death.

The developmental growth of the foetus that normally occurs between 54 days and birth is characterised by, histiogenesis and functional maturation. Foetal exposure to toxic levels during these stages can lead to nervous system abnormalities; the brain is still sensitive to injury and myelination is only partially complete. There remains a risk of functional defects and further disruption of pregnancy due to transplacental carcinogen exposure. This can lead to death of the foetus if toxic exposures occur (Lemasters, 1998).

2.18 Molecular initiating events and adverse outcome pathways

The mechanisms of teratogens' initial interaction with the developing human, identified as molecular initiating events (MIEs) may be through formation of covalent bonds to proteins or DNA by way of reactive chemistry or non-covalent interactions with receptors and enzymes. In these circumstances,

potency drives toxicity. MIEs represent a primary event anchoring the adverse outcome pathway (AOP) to produce a range of pathogenesis. In general, teratogenesis is initiated by chemical-biological interactions at a molecular level (Ankley et al, 2010) or at the site of action (Saxén, 1976).

2.19 Embryonic vascular disruption

Some occupational exposures, for example in laboratories, pharmacies and nursing tasks, when control systems have failed, lead to potentially harmful exposure to cytotoxic drugs. The newer drugs in this category include Vascular Disruption Agents (VDAs). They target angiogenesis through the Vascular Endothelial Growth Factor (VEGF) pathway, in contrast to the earlier VDAs that principally disrupt established tumour vasculature through a different set of molecular targets (Spear et al., 2011).

Vascular disruption agents (VDAs) can result in hypoxia and the formation of angioblasts which affect the endothelial cells' function in the embryo. They can also affect the chemokine pathway, cell-extracellular matrix interactions (ECM) and vessel remodelling via the macrophage and mural cells. These reactions affect placental function physiology, nutrient exchange and blood flow causing the embryo to suffer altered haemodynamics. This in turn leads to altered growth (Knudsen and Kleinstreuer, 2011).

2.20 Signalling networks

The embryo normally has a network of systems that govern structure and function of cells. Exposure to chemicals can lead to cell degradation. This can have more profound effects on the foetus (Johnson, 2013).

The sequences of steps controlling the flow of molecular regulatory information between cells (e.g., cell-cell communication) or within cells (cellular control), patterning (setting up future events), timing (clocks and oscillators), differentiation (cell diversification), morphogenesis (tissue organisation), cellular behaviours, growth (proliferation), cell death (apoptosis), cell differentiation (function), adhesion, cell shape (geometry), motility (cell migration), ECM (cell-extracellular matrix remodelling) and morphogenetic movements. These are all steps that are essential for normal embryonic development (Johnson, 2013).

Organs in the embryo also develop through folding, epiboly, convergent extension, branching morphogenesis, fusion, cell condensation, sorting, trans-differentiation, cavitation, involution and traction (Johnson, 2013).

The timing of various exposures can determine the level of damage to the reproductive process as the various agents will be most damaging are certain points in germ cell formation or in the maintenance of the fertilised ovum though gestation (Johnson 2013).

2.21 Dose effects on reproductive outcomes

The dose of the environmental agents in general, determines the reproductive outcome; this is clearly demonstrated in many animal and in-vitro studies (Brent, 2004). Multiple reproductive outcomes within specific dose ranges can lead to a suggestion of the dose response relationship. This is reflected in the increasing rates of particular outcomes with increasing dose observed in animal studies. Brent (2004) argues that interpretation of tests on animals could be improved if chemicals were administered to achieve pharmaco-kinetically equivalent serum levels in the animal and the human, rather than

the higher levels of animal dosing determined by mg per kg. He (Brent, 2004) adds that most human teratogens have been discovered by alert physicians or epidemiology studies, rather than through animal studies. The limb truncating effects of thalidomide is cited as one example.

In-vitro studies play an even less important role, although they are helpful in describing the cellular or tissue effects of the drugs or chemicals, they do not serve to determine the magnitude of in-vivo human risks (Brent, 2004).

The principal action of a human teratogen may target cells with a vulnerable genotype. This effect may be dependent on its presence at concentrations that overwhelm the natural protective mechanisms or occur at vulnerable stages of development. These factors contribute to the interplay of bioavailability of the teratogen. Varying degrees of exposure in different workers may result in varied manifestations. Consequently there may be little uniformity in the exposed population (Saxén, 1976; Ankley et al, 2010).

2.22 Propagation of events across scales

Disruptions at the molecular level can propagate to higher levels of biological organisation. This is dependent on intermediate key events. If these take place at sufficient frequency, they can produce adverse effects, which can alter development of the embryo (Green et al., 2007).

2.23 Effects of physical work on pregnancy

The unfavourable pregnancy outcomes associated with physical work in pregnancy include preterm delivery and low birth weight. These outcomes can be associated with significant complications for the new-born. Mozurkewich et al. (2000) undertook a systematic review and meta-analysis of the data that

highlights the public health risk of physical work as more women work while pregnant and extend the gestational stage at which work is ceased for maternity leave. The systematic review highlighted that the quality of research of many earlier studies lacked adjustment for confounders and may have been subject to recall bias.

Studies dating back to the late 1980s imply that other physical characteristics of employment such as standing and strenuous activity for any occupation may have unfavourable effects on pregnancy (Åhlborg et al., 1990; Bonzini et al., 2007; Bonzini et al., 2009; Clapp, 1996 and Fortier et al., 1995).

Among the studies included in the review by Mozurkewich et al. (2000) was a study by Mamelle et al. (1984). Task analysis allowed identification of the sources of occupational fatigue these are posture, work with industrial machines, physical workload, mental workload and the work environment. Each of these sources of fatigue was noted to constitute a risk factor for preterm delivery. Exposure to multiple sources of fatigue was associated with a greater risk of unfavourable pregnancy outcome.

Mamelle et al. (1984) concluded that retail sector workers, medical, social workers and service personnel had increased risk of preterm delivery (8.3% versus 3.8%) compared to office workers teachers, management, skilled workers or supervisors.

McDonald and McDonald (1988), Homer et al. (1990), Teitleman et al., (1990) included many thousands of pregnant women in their studies and confirm an association between physical workload and an increased risk of preterm delivery. There have been some contradictory results to this association but it is possible that these were due to protective measures being implemented

(Åhlborg et al., 1990). These measures can include early access to paid maternity leave and redeployment to less tiring work.

It is postulated that stress associated with physical work leads to the release of catecholamines, which Luke and Papiernik (1997) and separately Axmon et al. (2006) suggest increases of blood pressure and uterine contractility leading to decreased placental function and preterm delivery among other possible complications.

2.24 Other occupational exposures with known effects on pregnancy

Many chemicals have been investigated for their impact on fertility, pregnancy outcome and childhood illness. Findings suggesting an adverse impact have been noted for lead (Hu et al., 2006), mercury (Tasker et al., 2005), pesticides (Saadi and Abdollahi, 2012), petroleum-based chemicals (Zhou et al., 2014), and solvents (Schreiber, 1993).

No clear association has been found for polychlorinated bi-phenols (Nieminen et al., 2013; N Ribas-Fito et al., 2001) or non-ionising radiation (Calvente et al., 2010)

Radiation is in its ionising form is damaging to highly proliferative cells and can be harmful to the developing foetus or neonate (Woolf and Woolard, 1998; Ogilvy-Stuart, and Shalet 1993; Wakeford, 2012).

2.25 Control populations

2.25.1 Teachers

It is considered that some professions such as teaching present a different, less hazardous range of exposures. Some specialist areas of teaching may be considered stressful, for example when working in areas of significant

social deprivation. Similarly work with pupils who demonstrate challenging behaviour or learning difficulties may act as stressors. Ergonomically challenging postures with intermittent moving and handling and long periods of standing or paced work may also act as hazards associated with teaching and poses a health risk when pregnant (Ha et al., 2002; Hickey et al., 1995). A study of a population of 949 German teachers by Bauer et al. (2007) identified that teaching, particularly in secondary education, exposed a significant proportion of employees to negative or threatening school related events. The researchers evaluated the mental health strain caused by occupational burden and threatening school-associated events. They found that 42% of teachers reported verbal insults, 7% reported pupils had threatened deliberate damage to their personal belongings and 4.4% had been threatened with violence during the preceding 12 months. Alarmingly, 29.8% of the sample reported significant mental health problems most likely to be work related. Secondary modern schools caused more issues than grammar schools.

This finding had been supported by earlier research (Travers, 2001). Extensive exposure to stress can lead to burnout and premature retirement among teachers (Bellingrath et al., 2008).

For this original study, teachers were selected as a referent population to hairdressers, cosmetologists and laboratory workers. There are differences in posture at work and standing between these groups. In terms of psychosocial demands at work, the teacher population is more often exposed to verbal aggression. Teachers also have a holiday structure different to all three subject populations.

Compared to hairdressing, cosmetology and laboratory work, there is typically less exposure to chemicals for teachers. In Finland it is considered that primary school teachers have similar economic status to hairdressers and cosmetologists (World Press, 2002). As this study will rely on a Finnish database, it is considered that teachers serve as an appropriate referent or control population for the study group of hairdressers and cosmetologists.

Teachers were among the occupational groups studied by Herdt–Losavio et al. (2009). They looked at 45 birth defects for hypothesis generating purposes and found that women working as janitors had an increased likelihood of offspring having various defects compared to teachers.

2.25.2 Musicians

Comparable with hairdressers, cosmetologists and laboratory workers there is a large proportion of female workers who work as professional musicians. They tend to be relatively young in age and with childbearing capacity. In order to become professionals, new musicians would have had to undergo years of training or even degree qualifications.

The population of professional musicians tends to be exposed to very few chemicals directly related to their work. Most places where they practice and perform are within indoor facilities. In the developed world these environments are smoke free. Some outdoor work can be engaged upon and this poses the risk of ETS exposure.

Musicians do face a range of other health and safety issues at work (Harper, 2001). In some countries like the UK musicians are often freelance workers with a necessity to take responsibility for their own health and safety at work, while in countries such as Germany they are more often employed. In either

form of employment the hazards are common, with moving and handling and ergonomic issues over the long-term presenting as musculoskeletal symptoms (Greer and Panush, 1994; Hansen and Reed, 2006).

Noise is a recognised risk factor for pregnancy and musicians are by nature of their occupation exposed to noise (McIlvaine, 2012 and Nurminen et al., 1989). There may also be a requirement to work long or unsociable hours with little flexibility. In some scenarios this can interfere with the pregnant worker getting adequate rest (Guidance development Group, Royal College of Physicians 2009). The studies on pregnant musicians are very scarce in terms of assessment of the impact of work on pregnancy outcomes and neonatal problems (Worz-Bilfinger, 2012).

The working environment will vary and musicians are often peripatetic working in schools, various performance venues and customers' homes, which can be comparable with the work of hairdressers and cosmetologist who sometimes take their work in customers' homes and or work in residential establishments and care homes for the elderly. Kenny et al. (2004) recognised the impact of state and trait anxiety in a group of elite operatic chorus artists typical of performers who were employed full-time by a national opera company was further aggravated by occupational personal strain compared to a control population. This hazard would still be present for pregnant musicians. In situations where the individual is self-employed, they would be able to facilitate the use of strategies to help them cope by altering schedules and reducing their working commitments and exposure to stress.

2.26 Lifestyle factors

Lifestyle factors of smoking, alcohol and illicit drug use have been noted to have adverse impacts on pregnancy outcome.

2.26.1 Smoking in pregnancy

Maternal smoking and passive smoking during pregnancy has been shown to decrease the birth weight of offspring by between 150-400 g and can cause a 30% higher risk of prematurity (Rogers, 2009). It can also cause a wide range of behavioural, neurological, and physical abnormalities (Hackshaw et al., 2011; Center for Disease Control and Prevention, 2014).

Nicotine and carbon monoxide are the most likely causative agents as they are rapidly and preferentially transferred cross the placenta. Nicotine acts as a powerful vasoconstrictor and causes significant size reduction in the umbilical vessels of smoking mothers has been demonstrated. Carbon monoxide levels in cigarette smoke range from between 20,000 to 60,000 ppm. It has an affinity for haemoglobin 210 times that of oxygen and because of the lower arterial oxygen tension, the foetus is particularly at risk.

The scientific evidence available confirms that cigarette smoking (Brown, 1996; Floyd et al., 1993 and McCowan et al., 2009) or environmental tobacco smoke exposure (ETS) during pregnancy has an impact on pregnancy outcome (Leonardi-Bee et al., 2011 and Samet, 1991). Some authors have not confirmed the same effect of smoking on pregnancy outcome (Flaws et al., 2009).

Numerous studies have been undertaken in this area and the possible mechanisms for action of nicotine and tobacco may be on neurotransmitter function resulting in neurodevelopmental abnormalities and alteration to the

timing of neurotrophic activities during early development (Leonardi-Bee et al., 2011).

2.26.2 Alcohol in pregnancy

Alcohol is widely used in social settings and research has shown associations with growth retardation of the foetus and congenital anomalies (Flak et al., 2014). Smaller infant length and head circumference have been identified for over a decade to be related to maternal alcohol ingestion (Lemasters, 1998).

2.26.3 Illicit drugs in pregnancy

Illicit drug dependence among pregnant women is now more widely recognised and like other confounding factors it is likely to impact on pregnancy outcomes. A number studies have been undertaken to date. A literature search did not highlight any systematic reviews or meta-analyses for this topic.

Linn et al (1983) examined the association between marijuana and pregnancy outcome. They included 12 424 women and found low birth weight, and pre-term delivery, occurred more often among offspring of marijuana users. However when they adjusted for other confounders they found these trends were not statistically significant.

Soepatmi (1994) found less favourable outcomes for infants of drug-dependent mothers on heroin or heroin/methadone compared to infants of mothers who were not drug dependent or infants in the general population. The outcomes observed included gestational age, birth weight, physical growth and neurological development.

Abdel-Latif et al (2007) prospectively examined the outcome of infants of substance-using mothers (ISMs) in the neonatal intensive care unit (NICU)

setting compared to unexposed infants who served as controls. The state-wide study covering New South Wales and the Australian Capital Territory included 10 NICUs over a 3-years period (2001–2003). The study found a trend towards, prematurity and risk of neonatal morbidities but these results were without statistical significance.

Kuhn et al. (2000) measured prenatal cocaine use by expectant mothers. They ascertained cocaine use during pregnancy by maternal hair testing for a sample of 691 patients at one hospital in New York City hospital for the period 1990-1992. Their findings did confirm a statistically significant association between cocaine use and low birth weight. There was a dose-response relationship with birth weight: a 27g decrease (95% CI: -51.9, -1.04) with each log-unit increase in concentration. In this study birth weights were similar among infants of never users and infants of users who stopped using cocaine before delivery. Heavier use of cocaine, but not lighter use, was associated with intrauterine growth retardation, and this was only evident for mothers who used the drug in late pregnancy. Similar statistically significant results for cocaine use on pregnancy outcome were found by Strano-Rossi (1996) and Pichini et al. (2005). The study by Pichini et al. (2005) involved meconium analysis to confirm the trans-placental transfer of opiates, cocaine, ecstasy and arecoline. The last of these is the main areca nut alkaloid found in Betel nuts. Their approach and spread of data collection was novel compared to other studies and their findings interestingly showed higher tendency toward drug consumption in professional and partly skilled mothers. It also highlighted that consumption of opiates and cocaine during pregnancy was associated with active tobacco smoking, a higher number of cigarettes

smoked daily and cannabis use. This combination of drug exposure status and smoking behaviour correlated with significantly lower birth weight in new-borns.

Su et al (2012) quantified the heroin, methadone and amphetamine in hair samples of neonates born to three drug using mothers in Taiwan. The researchers found hyper tonicity and cerebral dysfunction was found in one of the infants but no comment was made on birth weight, gestation or size in this study.

Joya et al (2012) used hair sampling to confirm cocaine misusers showed lower birth weight, crown-heel length and cranial perimeter than new-borns from non-using mothers, but these differences did not reach significance. There was no withdrawal syndrome or malformation in any of the drug exposed new-born.

2.27 Maternal age

Maternal age is considered as a confounder for which adjustment should be made in the logistic regression analysis. This is based on a breadth of earlier research demonstrating this as an independent risk factor for adverse pregnancy outcomes of interest in this study.

Very young mothers who are less than 16 years old had confounding risk factors for poor birth outcomes, which when adjustments were made still revealed increased risk of pre-term delivery, LBW, SGA (SGA) babies and neonatal mortality (Cooper, Leland and Alexander, 1995).

Chibber (2004) noted that birth-weight and gestational age at delivery for infants delivered by older nulliparous women were significantly lower than those among younger nulliparous controls (P<0.01). Elbareg and Essadi

(2013) concluded that advanced maternal age has an adverse effect on pre-term and early pre-term deliveries, LBW, stillbirth and neonatal death. Jahromi and Husseini (2008) undertook a cohort study, that found the frequency of pre-term delivery, was significantly higher in the older group (average age of 41). In addition they concluded that although no statistically significant result was achieved, increased perinatal mortality was more common in the older mothers. Kenny et al. (2011) concluded in their study of deliveries in western England that mothers aged 35-39 and 40+ at delivery were at increased risk of having stillborn, pre-term and very pre-term babies. However there was no evidence to support an association between advanced maternal age and LBW or neonatal death in this study. They also identified that increased risk of macrosomia which could mask HBW or LGA in the older populations appeared to be due to associated gestational diabetes.

Yogev et al., (2010) explored pregnancy outcome in extreme advanced maternal age greater than 45 years and identified a statistically significant increased risk of a number of adverse outcomes including pre-term delivery (OR 2.41, 95% CI 1.2-3.6) for less than 37 weeks gestation and 31.8 (95% CI 18.0–56.41) for pre-term delivery at less than 34 weeks gestation.

Delbaere et al. (2007) undertook a retrospective cohort study and found that higher maternal age (>35 years) correlated with very pre-term birth (gestational age <32 weeks) [adjusted odds ratio (AOR) 1.51, 95% CI 1.04-2.19], LBW (birth-weight <2500 g) (AOR 1.69, 95% CI 1.47-1.94) and perinatal death (AOR 1.68, 95% CI 1.06-2.65).

This sample of studies is among those which explore the effect of advanced maternal age on pregnancy outcome. The overall conclusion indicates that

this is a relevant confounder for the parameters of interest in the current study.

2.28 Marital status

There are suggestions that marital status is unimportant in epidemiological studies provided the home is supportive. There is value in recognising that although a woman is married, she may be subject to psychological and physical challenges in her domestic situation, which could place her and the unborn child at risk.

Lurie et al. (2010) found for Israeli subjects that married and unmarried pregnant women had almost similar pregnancy outcomes when they were examined for the ratios of pre-term delivery, LBW and size for gestational age.

Shah et al. (2011) studied the pregnancy outcomes for married and unmarried (single and co-habitant) women. Their review found that odds ratios for LBW, pre-term birth and SGA infants were increased among unmarried and single mothers at statistically significant levels.

Some studies have not supported these findings for marital status fully (Hickey et al., 1995) perhaps due to methodological reasons such as the presence of strong confounders, it is evident that marital status is a relevant, confounder when analysing pregnancy outcomes, for prematurity, LBW and small size for gestational age. Marital status may be a proxy for socioeconomic status.

2.29 Socioeconomic status

Socioeconomic disparities and their impact on birth outcomes has been the subject of a recent systematic review by Kim and Saada (2013). They recognised that the impact of this factor can have significant health consequences beyond infancy, into childhood and adulthood. They paid specific attention to the strength and consistency of effects across socioeconomic measures, birth outcomes, and populations of United States of America (USA) and Western Europe (WE). The adverse birth or pregnancy outcomes examined were: preterm birth, low birth weight and SGA. The socioeconomic measures were: income, education, occupational class and area-based socioeconomic measures. Kim and Saada (2013) reviewed articles published between 1999 and 2007. They found that the large majority of papers confirmed a significant association between socioeconomic disadvantage and birth outcomes. The review identified considerable heterogeneity between the studies consequently meta-analytic measures were not appropriate.

Kramer et al. (2000) reviewed the evidence on socio-economic disparities and pregnancy outcome. They focused on disparities in intrauterine growth restriction (IUGR) and preterm birth. They acknowledged that cigarette smoking during pregnancy appears to be the most important mediating factor for IUGR. For preterm birth, socio-economic gradients in bacterial vaginosis and cigarette smoking appeared to explain some of the disparities; psychosocial factors were also suspected to contribute.

Parker et al. (1994) compared associations between five indicators of socioeconomic status (maternal education, paternal education, maternal

occupation, paternal occupation and family income) and three reproductive outcomes (LBW, SGA and preterm delivery). They used a representative sample of US births selected from the 1988 National Maternal and Infant Health Survey. They found that almost all socioeconomic indices were associated with LBW. Among the indicators they found that maternal and paternal education levels were the best overall predictors for LBW.

Morrison et al. (2005) undertook a prospective cohort of 8556 pregnant women attending a hospital in Brisbane. They considered the impact of socio-economic status using 3 indicators: family income, maternal education and paternal occupational status on pregnancy outcome. Pregnancy out-comes considered were preterm delivery, low birth weight, LBW for gestational age, and perinatal death. After adjustment the findings of this study suggested that observed differences in pregnancy outcome are attributable to the mother's personal characteristics (height/weight^2, parity) and her lifestyle.

2.30 Summary

Chemical and physical exposures at work and lifestyle factors have a range of adverse impacts on pregnancy outcome. Many of these topics have been researched using qualitative analyses but further quantitative studies and meta-analysis of these studies are likely to provide stronger evidence of adverse effects and a clear interpretation of the mechanisms at play.

Some occupations have minimal exposures compared to the hazards of hairdressing, cosmetology and laboratory work. This makes them suitable for control populations when logistic regression analysis is undertaken to identify the risk of subject populations.

Confounders contribute to adverse outcomes and adjustments should be made for those that have been quantified in the process of analysis of risk ratios for occupational reproductive hazards.

3   HAIRDRESSING AND COSMETOLOGY

The hairdressing and cosmetology industries are very prosperous (Smith 2013). The hair care market has a few big companies dominating the market. There is forecast for further growth for this market in the coming years (ReportLinker, 2013b).

The growth of the worldwide cosmetics and perfume industry was estimated to have generated an annual turnover of US$270 billion (£169 Billion) in 2012 the global facial care market that total revenues of US$51,743.5 million (£32,351 million) in 2012, there had been 4.3% growth between 2009 and 2012. The forecast for future performance in this market is positive (ReportLinker, 2013a).

These markets are growing in spite of the recognition that many of the products in use contain potentially harmful ingredients; particularly those that are produced containing parabens, petroleum or sodium lauryl sulphate. Common exposures are ammonia, hydrogen peroxide ethanol, propane butane and other volatile organic compounds (VOCs) but these concentrations even in the worst case scenarios as cited by Van der Wal et al. (1997) do not tend to exceed the threshold limit values (TLVs) of acceptable exposure in occupational settings. Fragrance and surfactants in widespread use are also recognised to have caused concern in terms of their safety (Löffler and Effendy, 1999 and Frosch et al., 1995).

3.1   Possible reproductive hazards

There are potentially 9000 chemicals in use by hairdressers, cosmetologists and laboratory workers (Labreche, 2003; Chapot et al, 2009). There is a high

level of suspicion that occupational exposure in these groups of workers is associated with adverse pregnancy outcomes. The narrative literature review did not identify any specific documented molecular initiating events (MIEs) or teratogenic mechanisms associated with occupational exposure in these worker populations.

The occupational groups, hairdressers, cosmetologists and laboratory workers will be considered in the sections below to identify workplace hazards most likely to contribute to adverse reproductive outcomes.

Hair products include shampoos, antidandruff agents, conditioners, placenta-containing products, hair dye, permanent waving agents, chemical straighteners, relaxers, glues, mousses, serum, hairsprays, hair waxes, tonics and pomades.

Some recent studies have measured exposure data, yet none have highlighted specific mechanisms or harmful dose levels. As highlighted above, the adverse impact of environmental factors on developing tissues will depend on the nature, dose and timing of exposure for the agent. Susceptibility may also depend on the genotype of the conceptus and the manner in which this interacts with environmental factors.

Hairdressers are regularly exposed to persulphates contained in hair bleaches. These are hydrophilic agents and are among the hazardous chemicals contained in hairdressing products in common usage (Lind et al., 2007). They are potentially teratogenic and could affect organ development and growth in the human foetus. Exposure timing and dose are data not available from existing research that can reliably indicate what levels would be determinant in causation of adverse pregnancy outcomes.

Nohynek et al. (2010) reviewed seven epidemiological studies that had been published on the potential adverse human reproductive effects of hair dyes. Six of the seven studies found no evidence of reproductive disorders for hairdressers or their offspring, whereas a single study reported a slight association (International Agency for the Research of Cancer, 1993). Overall, there is no epidemiological evidence of any occupational exposure in hairdressing that adversely affects human reproduction.

Exposure to chemicals found in hair care products has been recognised to lead to skin and respiratory ill health (Labreche et al., 2003; Leino et al., 1999; Axmon and Hagmar, 2005; van Muiswinkel et al., 1997). Exposure levels depended on the tasks undertaken, use of ventilation and use of personal protective equipment (Leino 1999).
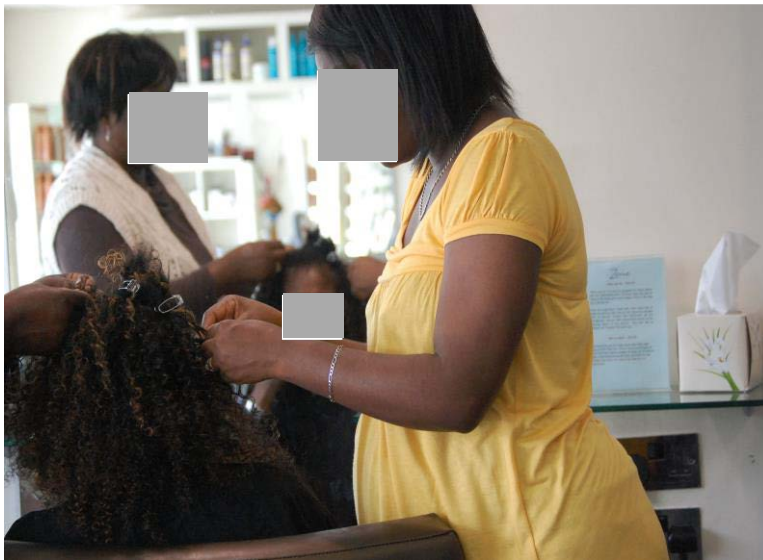
Photograph 3.1 Pregnant hairdresser and colleague standing for a period of 5 hours continuously to complete an
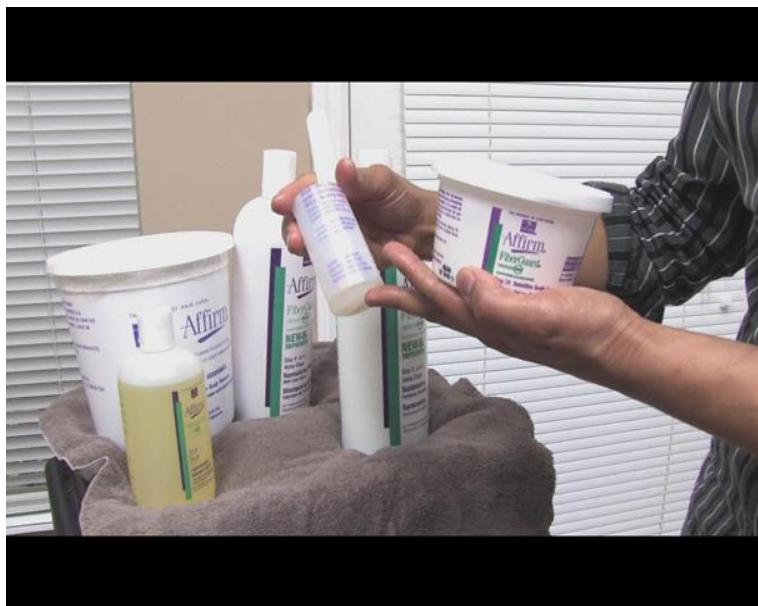
Photograph 3.2
Exposure to
chemicals
occurs when
containers are

3.2   Animal, bioassay and human data.

Hair and beauty products permitted for use in EU and the US must meet standards developed from human, in-vitro and animal studies (Merker, 1987 and European Commission, 2009). Some of the effects of a number of these agents are outlined below.

There are an estimated 9000 chemicals commonly used in hairdressing and cosmetics. Many of the chemicals that make up hair and beauty products have been tested on animals to quantify the dermatological, respiratory, neurological, mutagenic and reproductive effects. Solvents are still widely used in the industry and are known to cross the placenta. Some of these agents have been identified as genotoxic, embryotoxic and teratogenic in laboratory animals (Axmon et al., 2005).

Other studies have failed to highlight a definitive reproductive risk that is transferable to humans (Cosmetic Ingredient Review Expert Panel, 1994, 1997, 2001, 2003, 2005 and 2006).

The relevance of animal models to humans in the hairdressing and cosmetics industry may be questioned, as the species usually used for research are rabbit, rat and mouse. In these species the yolk sac placenta, which supplies nutrients to the foetus, is unlike the human placenta in terms of structure and function (Werkman, 1987; Brent, 2004).

Hair dye ingredients including O-phenylenediamine, 2, 4- diaminoanisole 2 – amino-4-nitrophenol, catechol and pyrogallol have been banned for use in the European Union due to their positive carcinogenicity bioassay indicators (Nohynek, 2004a).

A few of the more widely used chemicals in hairdressing and cosmetics will be covered in the following sections in more detail with reference to their health effects on animals and humans.

3.2.1 Benzyl alcohol

Benzyl alcohol is an aromatic alcohol used to fragrance cosmetics and as a preservative solvent and degreasing agent. It is used in hair products including dyes, conditioners, sprays and rinses. It is metabolised to benzoic acid in humans. The salt of benzoic acid, sodium benzoate is used a preservative in a range of cosmetics including hair dyes, conditioners, sprays, straighteners, rinses, shampoos and wave sets. Benzoic acid is used as a preservative. In the human body it reacts with glycine and forms hippuric acid, which is excreted in the urine.

Acceptable daily limits of human intake for all benzyl related chemicals have been established by the World Health Organisation (Cosmetic Ingredient Review, 2001). This is set at 5mg/kg. The U.S. Food and Drug Administration consider them safe for inclusion in food. In contrast, animal studies suggest

that these agents fluidise cell membranes affecting radical scavenging activity; they also compete with glycine and inhibit certain enzymes.

In studies on mice, administration of high doses of benzyl alcohol affects maternal weight and average litter weight. It has a genotoxic effect on mammalian cells. Benzoic acid and sodium benzoate were found to reduce feed intake and growth rates in mice. In addition, sodium benzoate resulted in an increased number of resorptions and malformations in hamsters. Short term, sub chronic and chronic oral toxic effects of these chemicals have been observed in humans, they cause child neurotoxicity (Cosmetic Ingredient Review 2001).

3.2.2 Propylene glycol

Propylene glycol (PG) has widespread public use in antifreeze, paints foods drugs and cosmetics there is evidence PG is toxic to reproduction and development. This is based on in-vitro human studies and animal studies. PG is present in shampoos, hair conditioners, straighteners, permanent waves rinses, shampoos, hair bleaches and a wide range of cosmetics, blushers, nail creams, polishers, manicure preparations, lipstick, leg/ body paints, skin cleansers and shaving preparations etc. (Centre for the Evaluation of Risks to Human Reproduction 2004).

Propylene glycol (PG) is generally presented in a 1-10% product formulation concentration. In high doses, PG can lead to lactic acidosis. The lactic acid is efficiently converted to glucose through detoxification. Human studies suggest that the placenta has only a limited ability to metabolise PG. The enzymes used to metabolise it, alcohol dehydrogenase and aldehyde dehydrogenase are present in relatively low concentrations in the placenta. They begin

appearing in a developing foetus at around 20-36 weeks. Consequently after early foetal exposure the half-life is prolonged and PG can accumulate in the tissues.

Reproductive toxicity data for PG exposure in humans is not widely available, but for animals there was no apparent effect on fertility and reproduction in adult or second-generation CD1 mice (Centre for the evaluation of risks to human reproduction, 2005).

3.2.3 Tri-ethylene glycol and polyethylene glycol

Tri-ethylene glycol (TEG) and polyethylene glycol (PEG-4) are both used in non-colouring hair care tints, make-up, nail care and cleansing creams. They act as fragrancing and decreasing agents in low concentrations in the range of 0.0001-0.03% for TEG for PEG-4 in doses of 0.08-1%.

The metabolites of TEG are excreted in urine and faeces and it can be lethal in animal studies but do not cause significant embryotoxicity or teratogenicity in rats and mice and no mutagenicity or genotoxicity in Chinese hamster.

PEG-4 is a humectant and solvent used in cosmetics. It has a lethal effect in high does for rats but PEG-4 and its derivatives are not mutagenic or genotoxic and hence both are considered safe in cosmetic practices (Final report on the Safety of assessment of Tri-ethylene Glycol and PEG-4 2006).

3.2.4 Di-butyl adipate ester

Di-butyl adipate ester of butyl alcohol (DBA) and adipic acid are plasticisers in skin conditioning agents and also used as a solvent. Typically the concentration is 5% in nail polish and 8% in suntan gels creams and liquids. In-vitro studies report that DBA was not genotoxic in mammals. The expert panel concluded there was no reproductive toxicity and it was considered safe in current practices (Cosmetics Ingredients Review Panel, 2006).

3.2.5 M-Phenylenediamine and M phenylenediamine

M-Phenylenediamine and M-phenylenediamine sulphate are used in hair colourants and cosmetics up to a 3% concentration. Clinical data showed some evidence of skin sensitisation, toxic effects in the animal foetuses but no teratogenesis. There was some evidence of mutagenesis but no evidence of carcinogenesis. Anderson (1997) concluded that it was safe to use these chemicals in products used on humans in doses up to 10% composition.

3.2.6 Parabens

Parabens is used as a cosmetic preservative and is also present in food and pharmaceutical products. It has been used in antifungal treatments. Rodent studies suggest that it is practically non-toxic. It is rapidly absorbed, metabolised and excreted. It leads to sensitisation on broken skin. It does not appear to be carcinogenic. It has oestrogenic properties and may therefore have an effect on sperm production in male rats and similarly in humans by affecting testosterone levels in male offspring (Soni et al., 2005).

3.2.7 Silicates

Numerous silicates are used in cosmetics as abrasive, opacifying, viscosity increasing anti caking emulsion stabiliser and suspending agents. They include aluminium, calcium magnesium and zirconium silicates.

In terms of reproductive impact of silicates, those reported upon did not affect nidation and were not teratogenic for rabbits. However kaolin caused mild maternal anaemia in female rats receiving 20% kaolin diet. The products were not genotoxic using the Ames test (Cosmetic ingredient review Panel, 2003).

3.2.8 Polyacrylamide and monoacrylamide

Polyacrylamide and monoacrylamide are used in well over 110 cosmetic formulations in concentrations between 0.05% and 2.8%. Acrylamide has a simple structure and tends to be distributed evenly throughout the body of rats when ingested. When tested on rats in higher doses of 30ppm it had no reported female reproductive toxicity but may impair fertility in male rats when put into drinking water (Cosmetic Ingredient Review Expert Panel Amended Final Report, 2005).

3.2.9 Propylene glycol and polypropylene glycols

Propylene glycol and polypropylene glycols when tested on mice had embryotoxic effects at the highest doses orally and via intra-peritoneal injection. This effect may be mediated by direct alteration of the cell membrane (Cosmetic Ingredient Review Expert Panel 1994).

3.2.10 t-Butyl Alcohol

t-Butyl Alcohol is used as a solvent or an alcohol denaturant and as a perfume carrier. Concentrations in cosmetic products range from 0.00001% to

0.3%. Fertility problems in rats increased with dose. Foetal weights were decreased at concentrations of 0.5% to 1%. There was also increased resorptions per litter, decrease in the number of foetuses per litter, reduced maternal weight gain, reduced weight at of the offspring at birth, at the stage of weaning and also perinatal and post natal mortality. It was felt to be safe in the concentrations used in cosmetic products (Amended final report of the safety Assessment, 2005).

3.2.11 Cetrimonium chloride

Cetrimonium chloride and bromide are quaternary ammonium salts used in various cosmetics up to 10% concentration. When cetrimonium bromide was administered to rats orally- foetal survival was reduced, resorption rate was increased but there was no effect on litter size viability or litter weight, (Cosmetic Ingredient Review Panel, 2005).

In a study involving the intra-peritoneal administration of cetrimonium bromide to rabbits, there was a higher death rate in foetuses exposed to higher doses and increased cleft palate and skeletal defects at low and high doses. By comparison there were no reproductive abnormalities noted when dermal application of chlorides were made at varying doses (Cosmetic Ingredient Review Expert Panel final report, 1997).

3.3 Cosmetologists - possible reproductive hazards

Thousands of chemicals are present in cosmetic products such as nail varnish, lipstick, mascara, eyeliners, eye shadows, blushers, foundation, face powders, concealers, moisturisers, sunscreens etc. There are also beauty therapy treatments such as anti-agers, anti-wrinkle creams, hair removers, depilatory waxes, fake tanning agents, skin lightening agents, exfoliates, toners, cleansers a range of treatments and oils, solvents lacquers and polishes used in manicures and pedicures.

Cosmetic and personal care products are widely used in developed countries. Many of these products are complex mixtures of many chemical types, including some which are suspected to be toxic in pregnancy. The phototoxic effects that are attributable to cosmetic ingredients such as methyl paraben was shown by in-vitro testing to significantly increase nitric oxide production and lipid peroxidation when cells were exposed to ultraviolet B light (Handa et al., 2006).

The photo-mutagenic sunscreen, padimate-O (octyl dimethyl PABA) used in cosmetics, generates free radicals that cause DNA strand breaks in animal cells cultivated in-vitro, when illuminated with simulated sunlight. This agent has been shown increase sunlight-related cancers (McHugh et al., 1997; Knowland et al., 1993). There is no evidence that it crosses the placenta to cause damage to the developing foetus.

Another ingredient of sunscreens, titanium dioxide, absorbs 70% of incident UV radiation. In aqueous solutions, this reaction leads to the generation of free radicals and these in turn damage human cells both in-vitro and in vivo (Dunford et al., 1997). Again there is no evidence that this crosses the placenta to cause damage to the developing foetus.

Two popular skin-conditioning compounds, azulene and guaiazulene, are mutagenic when mixed with UV and visible light (Wang et al., 2003). This suggests the potential risk of damage to the foetus but no research studies to date confirm this.

Studies of hazards to cosmetologists are few in number, but those undertaken suggest that they work with a wide range of products skin and nail treatments including solvents, varnishes, debriding and exfoliating agents. They are also exposed to awkward postures and psychological stress (Harris-Roberts, 2008; Gallicchio et al. 2011).

Nail salon workers are exposed to a number of organic solvents including and methylene glycol, toluene, formaldehyde, formalin, ethyl acetate, n-butyl acetate, methacrylic acid, methyl methacrylate and ethyl methacrylate. Some of these agents, at high levels may affect the nervous system of the fœtus (Boyer et al., 2013) but none of the agents studied to date have been found to adversely affect birth weight, size for gestation, prematurity, gender or neonatal survival.

Some cohort and case control studies have been used to observe the impact of cosmetology on of a variety of outcomes taking into account potential confounders and wherever possible gathering detailed exposure information about work environment and frequency of certain occupational tasks and the number of hours worked per week (John et al. 1994, Flaws et al. 2009, Gallicchio et al., 2011).

Photograph 3.3
Cosmetologists adopt
awkward postures for long
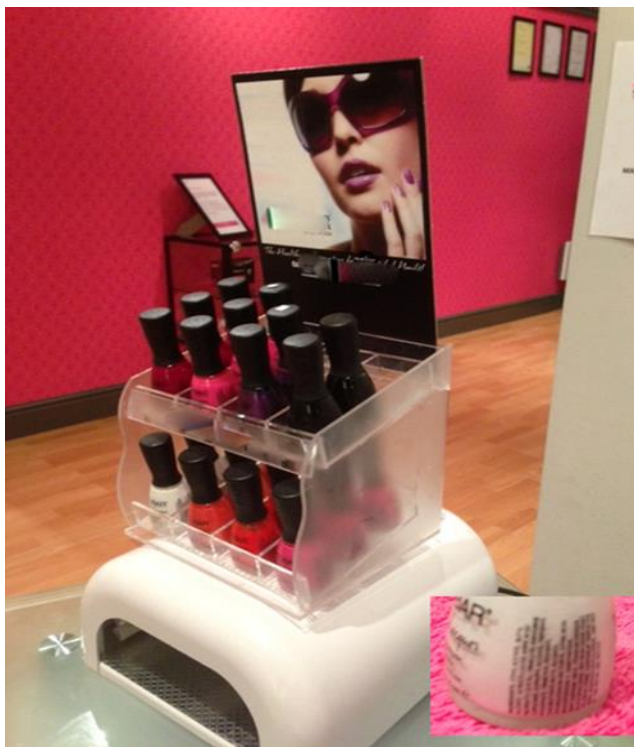
Photograph 3.4 Cosmetology
products contain numerous
chemicals

3.4 Exposure assessments

To ascertain the levels of exposure in Canadian hair salons Labreche et al.

(2003) undertook a study where hairdressing and beauty salons were monitored

for 20 hygiene measures that highlighted the toxic potency of the work environment. These included average temperature, humidity, carbon dioxide concentration, number of clients and range of services offered was also measured.

Labreche et al. (2003) found there was variance among the salons for the concentration of chemicals in air. The researchers concluded that solvent levels were related to ambient carbon dioxide levels and possibly affected by humidity and meteorological factors relevant to the work environment. They found that working in salons was associated with up to 30 times the occupational exposure limit for some organic chemicals. Other studies have suggested similar levels of hazardous exposure for hairdressers (Leino et al., 1999 and Van Muiswinkel et al., 1997 and Tsigonia et al., 2010).

Kersemaekers et al. (1997) recognised that there was scope for the chemicals in use to be potentiated synergistically by each other and thereafter may form additional unspecified biochemical compounds. These combinations may have an indirect association with adverse pregnancy outcome but the evidence on this is lacking.

The complex array of chemicals used in salons and the benefit of making proxy measurements for exposures in the workplace was recognised by Kersemaekers et al. (1998a). This study classified workers' exposures into high or low using a questionnaire that required the participant to record tasks completed and the presence of any ventilation device. Ethanol levels were measured and recorded on visits to the salons. The researchers established that the levels of indicators were predictive for the observed levels of ethanol exposure.

Although a link between work exposure and pregnancy outcome is suspected and mild effects have been noted in animals with high chemical exposure, the

conclusion must be drawn that the impact of workplace chemical exposure is likely to vary between species. Furthermore the mechanism of action of chemicals is not always clear. With various agents interacting there may synergistic or multiplicative effects on what would otherwise appear to be a low level of exposure in terms of the individual chemicals involved.

3.5 Ergonomics in hairdressers

Mussi and Gouveia (2008) undertook a cross-sectional epidemiological study of 220 hairdressers from beauty parlours in São Paulo (Brazil). Each hairdresser completed a self-administered questionnaire, which included information on socio-demographic characteristics, working conditions and health-related musculoskeletal system complaints. Ergonomic analyses were also performed in six parlours. The prevalence of work-related musculoskeletal disorders (WRMDs) was 71%. The risk of WRMDs was increased where psychosocial factors and poor ergonomics causing discomfort or work fatigue were of concern. Psychosocial factors such as lack of acknowledgement of work and uncomfortable posture at work was associated with increased OR for WRMDs of 3.54 (95% CI, 1.51-8.30) compared to controls. Workers reporting that they did not feel comfortable in the body/neck/shoulders while working had an increased odds ratio for WRMDs (OR 2.78, 95% CI 1.40-5.54). Those who had more than 15 years of professional activity in this field of work also had an increased risk of WRMDs (OR = 3.04; 95% CI 1.17-7.91).

Wahlström et al. (2008) examined upper arm postures in Finnish hairdressers. They found the right arm in most cases the dominant arm, to be used in an elevated position more often than the left and although there was considerable variability between hairdressers the overall exposure was more found to be

strenuous during customer-handling tasks than during auxiliary non-customer facing tasks.

Bradshaw et al. (2011) undertook a study of 147 hairdressers, most of whom were female (86%) and compared them to 67 female non-hairdressers. They were administered an interviewer-led questionnaire which included training and reports of respiratory, skin, musculoskeletal and non-specific symptoms. The analysis allowed adjustment for age, smoking and years worked. The hairdresser cohort reported more musculoskeletal problems affecting the shoulder (OR 11.6, 95% CI 2.4–55.4), wrist and hand (2.8, 1.1–7.6), upper back pain (3.8, 1.0–14.9), lower back pain (4.9, 1.5–15.9) and leg/foot pain (31.0, 3.8–267.4). Most had undergone training but this did not lead to consistent awareness of relevant workplace health risks.

Tsigonia et al. (2009) also examined the musculoskeletal disorders in cosmetologists and found increases in upper limb and back symptoms that were work related.

3.6 Summary

The variable outcomes in animals exposed to high doses of the cosmetic ingredients outlined above suggest the products above may have teratogenic effects on humans if high doses or long-term exposures occur.

The individual concentrations of harmful chemicals in the products handled by hairdressers and cosmetologists have been thought to be low enough to negate any reproductive risk in humans (Soni et al., 2005). The difference in function of the yolk sac present in rats and mice compared to the placenta in humans means that the direct transfer of conclusions from animal studies may not be valid (Werkman, 1987).

Environmental monitoring will has an important role in comparing exposures of workers in these occupations. Proxy measurements may be an effective way of collecting this data from large numbers of workers.

Physical and psychological factors in the work environments of hairdressers and cosmetologists do appear to have an impact on general health.

4 LABORATORY WORK

Laboratory work is the most wide-ranging of the subject occupations in this study. The occupations in this field expose workers to hazardous biological, chemical and physical agents (Health and safety Executive, online accessed December 2014, Natural Environment Research Council, online accessed December 2014). Workers in each setting are exposed to a diverse range of hazards determined by the nature of the research, pathological analysis, manufacturing or refining etc. being undertaken. This work will often be done to exacting standards. In the course of laboratory work hazardous agents may be inhaled, absorbed through the skin or ingested.

Like nail salon workers laboratory workers are also exposed to a wide range of solvents. Typically, higher standards of control measures are used in laboratories than are seen in nail salons. A number of studies have undertaken studies for the effects of laboratory agents on animals or humans. Barlow and Sullivan (1982) looked at animal studies and found that chemicals typically found in laboratory settings were teratogenic to male and females guinea pigs and rats but less so to other species. They concluded that for animals, maternal exposure to toxic doses of chemicals resulted in teratogenic and embryo lethal effects, which may be independent of maternal toxicity. A few individual chemicals and agents with potential impact on reproduction are discussed below.

4.1 Glutaraldehyde

The general health effects of laboratory workers' exposure to glutaraldehyde has been examined (Smith and Wang 2006; Duong et al 2011). No significant increased risk was found for laboratory workers compared to controls.

Photograph 4.1 Laboratory workers are exposed to solvents, other chemicals, microbiological and radiation hazards. The work can be adjusted during pregnancy to reduce risk.

4.2 Formaldehyde

Reproductive and developmental toxic effects of solvents may have several potential modes of action. In the case of formaldehyde, reproductive and developmental outcomes have been suggested by animal studies. The mechanism may include endocrine disruption, genotoxic effects on gametes, and oxidative stress or damage (Ozen et al., 2005, Sarsilmaz et al., 2007). The evidence for causality is weak. In addition, it is not clear that inhaled formaldehyde or its metabolites can cross the placenta, blood–testis barrier or blood–brain barrier.

The United States National Research Council (NRC) noted that a small number of epidemiological studies (Collins et al., 2001; John at al., 1994; Taskinen et al., 1999 and Im et al., 2006) suggest an association between occupational exposure to formaldehyde and adverse reproductive outcomes in women. There was no clear association of harmful effect.

Inhalation bioassays do not show genotoxicity and clear evidence of systemic mutagenicity in animals; although reactivity and mutagenicity was demonstrated in isolated mammalian cells (Im et al., 2006; Speit, 2006 and Speit et al 2009). The evidence that inhaled formaldehyde may be directly genotoxic to humans is inconsistent and contradictory (Costa et al., 2008; Orsiere et al, 2006).

4.3 Exposure assessments

A large number of solvents, which have been shown in animal studies to be mutagenic (Axelsson et al., 1984) genotoxic, embryotoxic and teratogenic (Axmon et al. 2005; Barlow and Sullivan, 1982) are found in laboratory settings. Chapot et al. (2009) identified the frequent use of 163 agents in molecular biology laboratories based on a self-administered questionnaire. Of the agents listed, ethanol was used by the largest proportion of staff (70%) followed by ethidium bromide (55%). Among the products used were known or suspected carcinogens (International Agency for Research on Cancer Group categorisation, 1 and 2A, respectively (accessed on line, December 2014).

Several population studies have extensively examined laboratory workers' exposure and found neuromotor (Herpin et al., 2008), olfactory (Zibrowski and Robertson, 2006), urinary mutagenicity (Varella et al, 2008) and chromosomal aberrations/sister chromatid exchange (Funes-Cravioto et al., 1977). There can also be exposure to oncogenic viruses (Chapot et al., 2009).

A few teams of researchers have examined the relative risks of adverse outcomes of pregnancy in laboratory workers. One review by Leffingwell et al. (1983) did not find a higher rate of adverse pregnancy outcomes in laboratory workers. However, a review by Dement and Cromer (1992) examined epidemiological studies of pregnancy outcome for laboratory workers and identified that 8 out of 10 studies formed an association between this field of employment and increased risks of miscarriages, perinatal death and congenital anomalies.

4.4 Radio isotopes

Zhu et al., 2006 considered radio labelling and radio immunoassay work in laboratories to pose a reproductive risk by increasing pre-term deliveries among regular workers. Frequent exposure appeared to increase the risk here.

Ericson et al. (1984) found that infants born to laboratory workers in Sweden had a higher rate of neonatal death and congenital anomalies but no specific aspect of laboratory work was identified as the cause.

4.5 Summary

Laboratory work exposes workers to a wide range of harmful agents. Solvent exposure is a particular concern. Stringent control measures should be in place to manage exposure risk in laboratories. In spite of this there is an indication that reproductive outcomes can be affected.

Although not widely reported in papers examining workplace exposure and reproductive outcome, it is possible that laboratory workers are exposed to the psychological stress of working unsociable hours, working to deadlines to

complete of specific process dependant tasks, long periods of standing and ergonomic challenges.

5 RATIONALE FOR ORIGINAL RESEARCH

5.1 Introduction

This thesis examines specific pregnancy outcomes of male gender, LBW, HBW, pre-term delivery, post-term delivery, SGA, LGA and END. The hypothesis is that these outcomes could be due to environmental insults that occur in the developmental stages of gestation.

The scientific approach to establish the links between exposures to chemicals, physical factors and psychological stress in hairdressing, cosmetology or laboratory work, requires research methodology that identifies biologically meaningful groupings of outcomes to provide insight into less well understood mechanisms. The original work aims to strengthen the findings of previous studies on workers in these occupations.

There have been no findings of adverse outcomes for the individual chemicals currently used in hairdressing, cosmetology and laboratory work but the combinations of chemicals regularly used, perhaps contributed by physical, biological and psychological exposures during pregnancy present a more complex challenge. Therefore there is added value from a study which adds epidemiologic data and could spur further detailed population based research.

Research in reproductive health, public health policy and employment related health and safety regulation has highlighted a need for issues relating to maternal occupational health to be reviewed regularly in order to incorporate

emerging knowledge. This approach should serve to promote and maintain awareness and maximise the protection offered to pregnant workers.

The service industries are more commonly the sources of employment in modern western society. There is a corresponding reduction of work in the heavier industries of the past.

Hairdressers, cosmetologists and laboratory workers are three occupations in the service industries, which employ large proportions of female workers with childbearing capacity (The European Industrial Relations Observatory, 2005; Silicone Valley Blogger, 2007). They are therefore considered to be a suitable series of populations for the focus of this thesis.

5.2 Gaps in knowledge

The effects of exposure during pregnancy constitute a critical gap in the scientific knowledge. This study is reliant on data from a birth registry. This included data on confounders and details for infant birth-weight, size at birth and neonatal death, where available from the database. The preferred study design would have included measurements of exposure i.e. 'years in role', 'hours worked per week' and some indication of the level of exposure to chemicals while at work.

There are many chemicals whose profile on reproductive health have not been tested or established. There is a possible synergistic effect of chemicals often used in combination that would also be worthy of exploration.

More fundamentally, the results from previous studies show varying results some suggesting the study occupations are hazardous to human reproductive health and other suggesting they are safe. A large epidemiological study will highlight if any general risk on reproduction applies to the study populations.

The subject occupations have been loosely defined and more detailed categorisation would strengthen the analyses by providing proxy indicators of exposure relevant to the specialist areas of hairdressing, cosmetology or laboratory work where this data is available. This would go some way to identifying the work conditions and exposures for subgroups under the main occupational headings.

Epidemiological data, when analysed effectively has the potential to identify effects of work exposures in certain careers and professions on pregnancy outcomes. This can in due course have a bearing on public health policy.

5.3 Link between previous research and current thesis

Earlier research has highlighted a number of factors that affect pregnancy outcome and act as potential confounders when they are present. These include smoking (Brown, 1996; Floyd et al., 1993; Leonardi-Bee et al., 2011 and Samet 1991), maternal age (Hansen, 1986; Chibber, 2004; Frey (2007), Jahromi and Husseini, 2008; Yogev et al., 2010, Alshami et al., 2011; Kenny et al., 2011 and Elbareg and Essadi, 2013), marital status, socioeconomic status (Morrison et al., 1989; Jonas et al., 1992 and Jorgensen et al., 2008).

The tasks undertaken in all of these areas of employment potentially expose workers to chemicals (Kersemaekers, 1995; Labreche et al. 2003; Nohynek et al., 2004b), physical exertion (Fenster et al., 1995; Eskenazi et al., 1994; Wolfe and Mottola, 1993 and Homer et al., 1990), extended periods of standing (Ronda et al., 2010; Ha et al., 2002), adoption of awkward postures (Bonzini et al., 2009 and Eskenazi, 1994) and psychological stress (Cassidy, 2009; Clapp, 1996; Schenker et al., 1995; Hickey et al., 1995; Fortier, 1995 and Fenster, 1995).

For pregnant workers there may be significant exposure to hazards at various stages of reproduction from the preconception phase, throughout pregnancy and during breast-feeding. Previous studies have established that these exposures can have an impact on pregnancy outcome (Ronda et al., 2009; Snijder 2012). Bodies such as the State of California Environmental Protection Agency have listed a vast number of chemicals with toxic effects on the reproductive system (OEHHA, Revised chemical list website accessed November 2013).

5.4 Selection of control populations

Professions such as teaching have exposure to fewer hazards at work. Some aspects of teaching may be considered stressful (Travers, 2001; Bauer et al., 2007 and Bellingrath et al., 2008). At times, there may be ergonomic challenges including moving and handling and visual display unit work.

DiPietro (2012) undertook a review of papers examining prenatal exposure to stress and child outcomes. The studies were difficult to interpret. There was difference in methodology and uncertainties in the inference of causality among the studies. The review study aimed to take into account maternal psychological factors and genetic factors. Some studies included in the review made adjustments for maternal psychological attributes and personality. Others took account of maternal stress but overall, the existing research was unsatisfactory due to the lack of measurement of stress and cortisol levels.

DiPietro (2012) discussed the methodological issues and focused on foetal neurobehaviour as an alternative method for discerning potential mechanisms for maternal psychological functioning and the impact this has on the developing foetal nervous system. These findings could have some relevance for the subject populations of this study.

Stress is common to all occupational groups in this study and for the control populations of teachers and musicians. Typically, there is less exposure to chemicals for teachers.

In terms of socioeconomic status of teachers this is not always high. In some countries and particularly Finland where this study is centred, it is considered that teachers have similar economic status to hairdressers and cosmetologists. It seems that primary school teachers have relatively low pay compared to their secondary school and college counterparts (World Press Organisation, 2002).

Musicians are a group of workers who are exposed to a range of range of hazards that may overlap with the study populations and the other control population of teachers (Greer and Panush, 1994; Harper, 2001; McIlvaine et al., 2012 and Worz-Bilfinger, 2012).

They were therefore selected as a second appropriate control population for the study groups in this research.

5.5 Salon and laboratory exposure

Levels of exposure to solvents and other readily monitored chemicals used in Finnish hairdressing salons have been studied in the past. In a number of studies the focus has been on various skin and respiratory effects (Leino et al., 1997, Leino et al., 1998 and Leino et al., 1999).

Leino et al. (1999), assessed the working conditions in 20 randomly sampled hairdressing salons hairdressing salons in the Helsinki, Finland metropolitan area. Data was collected during winter 1994-1995. The study included measurement of physical and chemical working conditions and a self-

administered questionnaire to collect information on health of the workers. The concentration of volatile organic compounds was 84-465 μ/m^3 and the peaks rose to 25-45 μ/m^3 during busier times. The highest concentration of ammonia detected was 3.5 μ/m^3. The highest concentrations of thioglycolates was 1.8 μ/m^3 and 4.7 μ/m^3 for persulphates, but some peaks of persulphates reached 30 μ/m^3. On average, the chemical exposures in the hairdressing salons were satisfactory compared with the Finnish standards for indoor climate but high peak concentrations of chemicals during dyeing, bleaching, permanenting, and aerosol spraying had the potential to cause significant health problems.

Workers reported awkward work postures and repetitive movements caused discomfort and in a few cases work-related disease. The study concluded that local exhaust ventilation with an air exchange rate up to 5 to 7 times per hour was recommended at the mixing stations for hairdressing chemicals and in locations where they are applied to the hair (Leino et al, 1999).

Mounier-Geyssant et al. (2006) examined exposure of 300 French hairdressing apprentices to airborne hazardous substances. 28 of these undertook personal monitoring. The researchers found that personal exposure values for hydrogen peroxide and ammonia were greater than workplace ambient air concentrations. The relatively higher workplace concentrations of persulpates was consistent with the practice where senior hairdressers more often undertake bleaching. All exposure values were lower than the current TLV TWA values. This study also showed that most areas of the salons where chemical substances used for dyeing, permanenting or bleaching are manipulated had no ventilation system and not even a door or a window opening to the outside. They felt the exposure data could be viewed as indicative of typical values currently found across large

and small facilities. Both studies suggest that hairdressing is associated with exposure to chemicals above the occupational exposure levels.

5.6 Finnish Medical Birth Registry

It is difficult to access large quantities of good quality population health data for epidemiological studies to identify risk factors for disease in the United Kingdom (Ward et al., 2004). The nature of confounders in reproductive outcomes would also indicate that data collated on UK registers pertaining to birth outcomes would be insufficient for the purpose of this study.

The total population in Finland is 5.4 million and it has gradually increased over the last decade. The estimated total number of births per annum is 58,000. The culture is comparable with the United Kingdom population where the estimated total births per annum for England and Wales is 718,500 (Office for National Statistics UK, 2012). In both countries a large proportion of the women who become pregnant continue working in their various occupations. There is support for women in terms of finance and health during pregnancy in Finland whatever their employment status (Appendix 11). In the UK financial support in pregnancy would depend on the employment status of the female worker.

The Finnish Medical Birth Register was established in 1987. Revisions of the Register have taken place in 1990, 1996 and 2004 to improve its reliability. It includes data on live births and on stillbirths of foetuses with a birth weight of at least 500 g or with a gestational age of at least 22 weeks, as well as data on the mothers in the pre-partum and post-partum stages of delivery. It is populated with data form three main sources: maternity hospitals (maternity wards and neonatal

58

wards), data from the Population Register Centre and Statistics Finland, Population Statistics provide information on causes of death

For the last 10 years, since 1 November 2004, FMBR also incorporates a data on preterm infants for those with a birth weight of less than 1501 g or with a gestational age at birth of less than 32+0 weeks. The data are collected until the infant's age corresponds to 42 weeks' gestation.

The data on the Register includes the mother's personal data (personal identity code, surname and forenames, profession, municipality of residence, nationality, marital status, cohabitation and smoking). It also incorporates data on her previous pregnancies and deliveries and the outcomes of monitoring throughout the reference gestation. The FMBR includes details concerning the delivery of the infant as recorded by the maternity hospitals. This includes diagnoses relating to pregnancy and delivery.

Hospitals are responsible for reporting all stillborn and live born babies on a FMBR data sheet, which is to be filled in not later than seven days after birth. A ward clerk or midwife usually completes most of the details, and a doctor records any diagnostic data. In 1987, most hospitals transferred their data on a monthly basis to the National Board of Health (NBH) on the original data sheets. At the NBH the data were computerised and then sent to the State Computing Centre (SCC) on disks. Twenty hospitals sent their data every six months on magnetic tapes directly to the SCC. After a routine data validation procedure to locate extreme or otherwise implausible values, internal inconsistencies and missing data for the more important variables, an error listing of the annual data was sent to all hospitals. The hospitals were expected to return the corrected data to NBH

within a few months. The data content of the FMBR and the list of structured questions are presented in Appendix 12.7.

Supplementary data is sourced from the Population Information System database held by the Population Register Centre and Statistics Finland and Population Statistics particularly, when referencing causes of death for neonates.

The FMBR is controlled by the National Institute for Health and Welfare (THL) in Helsinki. The grounds for maintaining the register are Statutory, in order to comply with Finnish law- specifically the following:

- Act on National Personal Data Registers kept under the Health Care System (556/1989)

- Decree on National Personal Data Registers kept under the Health Care System (774/1989: Sections 1 and 3)

- Act on the National Research and Development Centre for Welfare and Health (1073/1992: Section 2)

- Act on the National Institute for Health and Welfare (THL) (668/2008)

THL is authorised to disclose data in the Medical Birth Register to researchers for scientific research purposes after consulting the Data Protection Ombudsman (Gissler and Hemminki, 1994). The data subjects included on the register have no right of access to and no right to rectify the data entered into the register, because it is a statutory statistical and research register and the personal data are not used in decision-making or reviewing the care offered to data subjects.

Gissler and Hemminki (1994) are among a number of authors who have used the Finnish Medical Birth Register (FMBR) to examine pregnancy outcome in was studied using the 1987 Finnish Medical Birth Registry.

Gissler et al (1997) found Nordic maternity birth registers were reliable sources of data used in various studies and in combination with data from other sources for studying maternal biological and obstetric outcome, interventions in pregnancy and at the time of delivery and short term data on the new-born. The key data linkage element is the unique person number, assigned to each resident, regardless of whether they are citizens or non-citizens living in each of the Nordic countries permanently. The existence of a unique code for each person has considerably increased the value of MBR data for research purposes.

Teperi (1993) undertook work to comprehensively assess the validity of the data in the Finnish Medical Birth Registry (FMBR) in 1987. His work involved the combined use of several controls and internal analysis of the data. The design of the study relied on FMBR data being individually linked to the medical record samples (n=775) and to all perinatal death certificates in that year. The data were also compared with annual hospital statistics. To ensure the birth weight and gestational age of infants recorded on the register were accurate, the distributions of these parameters were examined for all stillborn and live born infants. This work concluded that with regard to most variables, the data quality was 'good' or 'satisfactory' with there being agreement between the database and medical records being consistent in 95% or more registrants. A further conclusion was that for the majority of variables, the amount of missing data was less than 1%.

This research highlighted an exception for births by caesarean section and other medical procedures where the Registry contained only between 30 and 72% of the cases, with wide variation being evident between the hospitals included in the study.

A further study (Gissler and Shelley, 2002) explored the quality of the data on FMBR. It highlighted that information on reproductive history corresponded with the earlier entries on the register in 98.5% of cases and the amount of missing data was less than 1%. But the same study (Gissler and Shelley 2002) identified that the overall data quality decreased over time and with increasing parity. Further conclusions from this study identified that question formats may change the quality of register data significantly and check-boxes seemed to improve quality compared to open-ended questions.

In this original work the data for over 1.2 million (1,229,181) births contained on the register for the period between October 1990 and December 2012 was used to sample the subjects of interest.

The original description of occupation was identified from the text format encoded used for the database (Finnish Classification of Occupations based on International Standard Coding of Occupations [Accessed 20 November 2013]).

The prima gravida women in the population were selected from the main sample based upon the previous pregnancy criteria being equal to 0.

6 METHOD OF SYSTEMATIC LITERATURE REVIEW

6.1 Introduction

This chapter reviews relevant literature on pregnancy outcomes for hairdressers, cosmetologists, and laboratory workers. It includes a summary of the results for the study populations. The data from these studies is used for a meta-analysis and where possible, forest plotting. The chapter also discusses the outcome of animal studies. There is particular reference to types of research methodologies employed for other studies and the conclusions drawn. This facilitated an understanding of relevant concepts used to establish an analytical framework for the current study.

The literature review is structure around the three occupations being studied, the various pregnancy outcomes being studies and the methodology used in each of the studies.

The period of January 1990 to December 2012 was selected. In 1990 the FMBR began collecting occupation of pregnant women and this therefore correlates with the time period during which methodology in research improved to include larger populations of workers employed during pregnancy in various cohort studies. There was improved methodology is assessing the pregnancy outcomes from this point going forward which mean the quality of papers used for the systematic review and used to compare with the original research included modern techniques. In addition in this time period better measures were being made, in some of the studies, of occupational exposure to agents in the work setting for hairdressers, cosmetologists and laboratory workers.

The main project is an original cohort study examining the epidemiological evidence for various pregnancy outcomes among Finnish women. The results of the systematic review were used to perform a series of meta-analyses, highlighting the areas where improved research is needed.

There was also a search of exposures in UK and Finnish work places of interest in this study to explore the hygiene measurements that may give an indication of the exposures relevant to the three subject populations.

6.2 Review questions and inclusion criteria

6.2.1 Objective 1:

When compared with a control population, what is the effect (presented as a crude odds ratio, adjusted odds ratio or relative risk) of working as a hairdresser on pregnancy outcome with specific reference to pre-term delivery, post-term delivery, SGA, LGA, stillbirth, END and male to female gender ratio?

6.2.2 Objective 2:

When compared with a control population, what is the effect (presented as a crude odds ratio, adjusted odds ratio or relative risk) of working as a cosmetologist on pregnancy outcome with specific reference to pre-term delivery, post-term delivery, SGA, LGA, stillbirth, END and male to female gender ratio?

6.2.3 Objective 3:

When compared with a control population, what is the effect (presented as a crude odds ratio, adjusted odds ratio or relative risk) of working as laboratory worker on pregnancy outcome with specific reference to pre-term delivery, post-term delivery, SGA, LGA, stillbirth, END and male to female gender ratio?

6.3 Systematic review databases

A review of databases holding systematic reviews was undertaken to identify reviews covering the topic of interest. This consisted of Cochrane, Database of Abstracts of Reviews of Effectiveness (DARE), Prospero and the systematicreviewsjournal website.

6.4 Sources of original articles and work

Articles, reports, research work, original articles covering this topic published between 1 January 1990 and 31 December 2012 were identified from EBSCO host, Embase, MEDLINE and CINAHL databases (Appendices 13 and 14). This period was selected as it matched the data collection period for FMBR and there was evidence that after 1990 the quality of research undertaken in this filed had become more refined and more often incorporating population studies.

6.5 Publication type/status

It was recognised that papers, particularly those that show no significant results or show results which differ from the mainstream findings, are not always published in peer-reviewed journals and that on occasions relevant studies are published as reports, book chapters, conference abstracts or theses. It is suspected that in some cases, where studies had not met the publishing criteria or were undertaken for non-degree qualifications as dissertations, papers and research in the area of pregnancy outcomes amongst different occupations of interest in this systematic review remain unpublished.

In order to reduce publication bias, leading authors were approached via an emailed letter to request grey or unpublished work of relevance (see Appendix 4). If after 2 weeks, there had been no response to the initial letter, a further copy of

the same letter was sent. Any additional work presented was incorporated in the systematic review. It is recognised that unpublished studies were more difficult to access.

Further relevant publications were sought from the citations in articles and publications found via the systematic review.

6.6 Data base search

The EBSCO host site was accessed via the University of Birmingham 'Mylibrary', 'Advanced search' and 'find databases' portals. *CINAHL plus* (EBSCO host) was selected and the specific databases of *CINAHL plus* and *MEDLINE* were selected from the selection of 25 databases for the search.

CINAHL Plus provides indexing for 4,500 journals from the fields of nursing and allied health, with indexing back to 1937. *CINAHL Plus* also contains searchable cited references for more than 1,340 journals. Full text material includes nearly 80 journals plus legal cases, clinical innovations, critical paths, drug records, research instruments and clinical trials.

MEDLINE provides authoritative medical information on medicine, nursing, dentistry, veterinary medicine, the health care system, pre-clinical sciences, and much more. Created by the National Library of Medicine, *MEDLINE* uses MeSH (Medical Subject Headings) indexing with tree, tree hierarchy, subheadings and explosion capabilities to search citations from over 5,400 current biomedical journals.

The process of selecting research papers was refined by selecting dates January 1990 to December 2012, selecting papers printed in English and studies involving humans.

The search process involved initial identification of papers that covered the broader topics of pregnancy outcome and then more specific outcomes of interest for this study i.e. low birth weight small for gestation age and preterm birth. Where pregnancy outcomes had more than one descriptor, each of these were used in order to capture as much of the existing literature as possible.

The outcomes were then combined with each of the subject occupations of interest in this study: hairdressers, cosmetologists and laboratory workers.

The search process and all of the papers were saved in a folder on EBSCO host for later retrieval. The process of searching and the list of the numbers of papers identified at each stage is included in Appendices 13.12 and 13.13.section 5.2.7.

6.7 Study selection

There was an initial screening of titles and abstracts against the inclusion criteria to identify potentially relevant papers in line with the criteria above. The relevant papers were obtained in full.

All of the full papers were shared with the supervisor for his review to ensure that there was consistency in the agreement that appropriate papers had been selected for inclusion.

The search for articles in systematic review databases: Cochrane, Database of Abstracts of Reviews of Effectiveness (DARE), Prospero and the systematic reviews journal website did not yield any papers that covered hairdressers, cosmetology or laboratory workers during the period of study (1 January 1990 and 31 December 2012).

Grey or unpublished literature was requested from ten previous researchers who were selected on the basis of them being the lead author for one or more papers

in this field and the availability of an e-mail address on at least one of their publications.

The period 1 January 1990 to 31 December 2012 was selected as this was the year that the Finnish Medical Birth Register began collecting data on entrants' occupation in 1990. Data were retrieved from FMBR up until December 2010.Citations from publications where relevant were retrieved and included in the systematic review of the literature.

6.8 Populations

The populations included in the review were female hairdressers, cosmetologists, or laboratory workers, who were pregnant with singletons, who at the time the data was collected undertook employment during their pregnancy on part or full time basis.

Some epidemiological studies identified in the systematic review contained mixed populations that included populations of hairdressers, cosmetologists or laboratory workers grouped with other occupations that did not allow these workers pregnancy outcomes to be identified in a way that would allow presentation of clear risk ratios or odds ratios. Alternatively some researchers had presented the study populations separately but the cell sizes were small and odds ratios/risk ratios had not been calculated. The studies with incomplete data could not be incorporated into the systematic review and meta-analysis. Where the populations under observation were clearly identified and studied including large numbers with clear identification of their careers from questionnaires or database entries, these studies were included for tabulation and meta-analysis.

The control populations for studies included in the review varied from realtor to members of the public. The varied control populations used in the various studies

were not consistent and the reports comment on the reasons for selecting the various controls. This variation is a source for bias and confounding in the process of meta-analysis.

6.9 Outcomes

The outcomes of relevance were related to pregnancies of the subjects within the studies. The key words refer to the occupational designations as well as to the different reproductive outcomes. This included some Medical Subject Headings (MeSH). The terms were pre-term birth (less than 37 completed weeks of gestation), stillbirth (an infant born with no signs of life at or after 28 weeks' gestation.), END (death of live born infant occurring less than 7 completed days from the time of birth), LBW (< 2500g), HBW (>4500 g), SGA, (those whose size is below the 10th percentile of normal for the infant's sex and gestational age) and LGA (whose size is above the 90th percentile for the infant's sex and gestational age). The following search terms were used for occupations: hairdresser/s, hair stylist/s, hairdressing occupation, hairdressing profession, professional hairdressing or professional hair care, cosmetologist, beautician, beauty therapist, laboratory worker, laboratory technician, laboratory scientist. These were sought in combination with pregnancy outcome terms: reproductive disorders, reproduction outcomes, pregnancy outcomes, pre-term birth, premature delivery, perinatal death, LBW, HBW, SGA, LGA, stillbirth, END and male to female gender ratio, male sex, male or boy.

6.10 Study design

For some areas of research many types of study design may apply due to the scope for randomisation, use of controls and blinding. All of these factors improve

reliability of the review through the reduction of bias. The types of study that were included in this review are mainly observational studies where there has been variable exposure amongst the subjects that is not allocated by the investigator and that is in fact historically pre-determined by their occupation, the types of tasks they engage in and the hours spent undertaking the task. The studies explored the usually relied on effects of the general exposure in the work undertaken and prevalence of certain pregnancy outcomes.

Predominantly the studies were cohort studies wherein defined groups of hairdressers, cosmetologists and laboratory workers and their infants are observed typically prior to, and at the time they gave birth. Comparisons of the ratios of pregnancy outcomes among the different occupations were made. Some prospective cohort studies were available which followed women in occupational groups of interest up to 7 days after delivery before the pregnancy outcomes were collated and analysed. Randomised controlled studies did not exist for these populations. The construction of experimental studies where the participants are allocated to intervention and control groups was not feasible.

6.11 Defining inclusion criteria

The inclusion criteria are as follows:

- Participants should be employed in the categories of employment listed above i.e. hairdresser, cosmetologist and laboratory worker; the controls can be of any other occupational groups or the general public. Ideally the control populations would be teachers and musicians but these studies are not easily found.

- Studies should include a record of pregnancy outcomes for the workers included in line with definitions of outcome identical to those used in the author's study.

- The studies included were published between January 1990 and December 2012. This matched the years of the analysis of the original research described later in this thesis.

- For studies of laboratory workers, the inclusion criteria allowed all fields of laboratory workers to be included.

- Interpretation and comparison of the different pregnancy outcomes was feasible for studies undertaken in developed countries, which recorded pregnancy outcomes in line with those defined by the World Health Organisation (1977). In these studies, pregnant women and new mothers are typically asked about confounders such as smoking, maternal age, marital status, socioeconomic status, parity and birth order of the foetus. The studies generally include adjustment for some or all of these confounders. The typical measures of risk for pregnancy outcomes are crude odds ratios, adjusted odds ratios and relative risk.

6.12 Methodological quality

The studies considered for inclusion were those that were conducted using defined populations, specific criteria for the parameters of study and reliable and consistent recording of the pregnancy outcomes for workers employed as hairdressers, cosmetologists or laboratory workers. Generally researchers chose to undertake observational cohort studies, but some case-control studies were identified through the review.

6.13 Language

This review included studies written in English. It is recognised that some studies including the subjects of interest in this research have been undertaken in non-English speaking countries and the resulting papers are often not published in English.

6.14 Data extraction

Each of the studies contained information regarding the pregnancy outcomes for populations of hairdressers, cosmetologists or laboratory workers. The information extracted included the crude odds ratios, adjusted odds ratios and in some cases relative risks for the pregnancy outcomes described above. There was scope to contact the authors of primary studies to access missing or additional data for completeness where necessary.

6.15 Quality assessment

The methods of study appraisal looked at specific criteria. These required

- a high proportion of inclusion of subjects for the populations assessed (above 50%)

- administration of a questionnaire or some other form of registration to establish the expected date of delivery

- recording of specific data on smoking habit, marital status, occupation

- recording of at least one of the pregnancy outcome parameters under observation.

The selected papers were shared with the main supervisor. There were no disagreements on quality but the process allowed the opportunity for discussion in detail of the relevant papers.

6.16 Data synthesis

The strategies for data synthesis were to extract crude odds ratios, adjusted odds ratios and relative risks for the pregnancy outcomes listed above. Where researchers had adopted a similar methodology to that incorporated by the author presenting the thesis then these papers were selected for a meta-analysis. Heterogeneity was explored by looking at the definition of the occupations hairdresser, cosmetologist and laboratory worker, for which odds ratios, adjusted odds ratios and relative risks had been calculated across the range of pregnancy outcomes listed above.

The narrative synthesis was outlined in tabular form, by outcome summarised and including the year of publication, the authors' details, the type of study, the population size and the main findings by way of the odds ratios, adjusted odds ratios, relative risks and the corresponding 95% confidence intervals.

6.17 Approval of the draft protocol

The protocol was discussed with a systematic review expert Dr David Moore. He was asked to 'sign off' the protocol as suitable for gathering the information required as part of the review.

6.18 Amendments

Where necessary, amendments to the draft were made in line with the recommendations of the systematic review expert and supervisor. No notable amendments were needed so a review of the key questions was not necessary.

6.19 Summary of results from systematic review

A series of papers and publications relevant to hairdressers (8), cosmetologists (3) and laboratory workers' (6) pregnancy outcomes were identified. These will be outlined in alter chapters.

With respect to Grey literature requests, the majority of researchers, nine in total responded to the request for grey and unpublished literature.

In all, nine cases where responses were received from the researchers. Each responded to confirm that they did not have any unpublished literature of relevance to this study.

7 METHOD OF DATA EXTRACTION AND BINARY LOGISTIC REGRESSION

7.1 Ethical clearance and application for access to FMBR

After application, ethical clearance was gained from the University of Birmingham (UK) Science, Technology, Engineering and Mathematics Ethical Review Committee on 24 November 2011 (Appendix 3). This facilitated application to the Finnish National Institute for Health and Welfare (THL - STAKES) for access to the Finnish Medical Birth Register (Appendices 6, 7, 8, 9 and 10).

The data for the subject and control cohorts were made available to the researcher in the form of an Excel spread sheet. The data were exported into SPSS. The data filter was applied to select those with gravidity of 0 for prima gravida.

7.2 Value of FMBR to access pregnancy outcome data

As highlighted in some detail above the Finnish Medical Birth Registry has collected nationwide information on all deliveries of new-borns with gestation of 22 or more weeks in Finnish hospitals since January 1, 1987 using a standard proforma (see Appendix 7). It records 99.9% of deliveries in Finland. This excludes spontaneous and induced abortions. The level of reporting and selection bias is therefore negligible (Appendix 8). Each expectant mother is registered during the first trimester and once the infant is delivered, the birth outcomes including birth-weight, length and head circumference are all measured and recorded.

The outcome information was based on standardised measurements on birth-weight and gestational age. Most pregnant women undergo an ultrasound

examination between 16 and 22 gestational weeks that is used to estimate the gestational age. Categorisation as SGA was based on nationwide age, gender and sex specific estimates (Appendix 5). Information on potential confounders, such as maternal age, parity, and maternal smoking during pregnancy and marital status are routinely collected as part of the process of joining the FMBR by midwives or ward clerks who have undergone training on data collection (Appendix 7). It was possible to adjust for the confounders in binomial logistic regression analysis.

7.3 Categorisation of covariates

The covariates for which adjustments were made in this study were maternal age group, smoking status, marital status and socio-economic status. This was comparable with other research previously undertaken and took into account confounders most likely to impact on the outcomes that were being examined in this research.

The subjects and controls were categorised according to age group. The age range was 12 to 54. Maternal age group was stratified into 5 year bands:

- group (1) < 19 years or less.

- group (2) age 20 to 24,

- group (3) age 25 to 29,

- group (4) age 30 to 34,

- group (5) age 35 to 39,

- group (6) age 40 to 44,

- group (7) age 45 to 49 years and

- group (8) age 50 and above.

Smoking status was categorised according to the duration of smoking in pregnancy:

- group (1) were non-smokers

- group (2) were smokers who ceased during the first trimester

- group (3) were smokers who continued beyond the first trimester

Socioeconomic status fell into 4 bands:

- upper white collar were classed as group (1)

- lower white-collar workers were classed as group (2)

- blue-collar workers were classed as group (3)

- housewives were classed as group (4)

- others including students were classed as group (5).

Marital status fell into 3 groups:

- married- group (1)

- Cohabiting or living with a partner -group (2)

- Single, divorced, widowed or separated - group (3).

The various cohorts of subjects and controls were selected and the data were further analysed using SPSS to calculate the odds ratio and adjusted odds ratio for various parameters.

7.4 Power calculation

To estimate the real effect size for the parameters under consideration in the study populations- the meta-analysis detailed above was undertaken for each parameter. This produced few statistically significant results.

In order to show true statistical effect size when planning this research, some consideration was made for the calculation of power for the original research. For the meta-analysis the power of the studies was indirectly evident from the confidence intervals of the final pooled risk estimates. Typically predictive power calculations are made before clinical trials to measure the population size at the point of recruitment. There was no scope to control population size in this work where the meta-analysis summarised the available relevant literature for the topics under consideration.

The population sizes in the original work, an epidemiological study of a medical database were significantly greater than those seen in the studies that contributed to the meta-analysis. .

7.5 Outcomes analysed

For the purpose of binomial logistic regression the subjects and controls were individually categorised as a case or non-case for each of the parameters under observation. This applied when the data were presented as discrete entities for example male or female new-borns and when data were presented as a continuum for example gestational week of delivery.

The health outcomes examined were:

- foetal sexual differentiation (male = 1, female = 0)

- LBW (less than2500g = 1, greater than 2500g = 0)

- HBW (greater than 4000g = 1, less than 4001g=0)

- IUGR in accordance with Finnish population-based growth curves in the lowest 10 percentile for gestational age as summarised in Appendix 5 (small size for gestational age = 1, average size or large size for gestational age = 0)

- excessive growth in accordance with Finnish population-based growth curves in the highest 90 percentile for gestational age as summarised in Appendix 5 (large size for gestational age = 1, average or small size for gestational age = 0)

- duration of pregnancy, pre-term (delivered at 37 weeks or less gestation = 1, delivery after 37 weeks gestation = 0)

- post-term delivery (delivery after 42 weeks or after = 1, delivery before 42 weeks = 0)

- perinatal death was defined using the Finnish version of the World Health Organisation definition as "death occurring during late pregnancy at 22 completed weeks (154 days gestation) or more, or a birth-weight of 500g or more, up to seven completed days of life" and

- stillbirth (still born child = 1, live birth = 0), END (death of neonate within 7 days of birth =1, alive beyond 7 days after birth = 0).

7.6 Binomial logistic regression analysis

Binomial logistic regression analysis enabled consideration of the various outcomes for a parameter and its association with a specific main variable of

occupation in this study. This analysis also allowed consideration of the impact of four confounders on the identification of a case. These were included as covariates in the analysis.

For each of the parameters reviewed, binomial logistic regression was used with the cases for the parameter under observation being coded as "1" and a non-case as "0". The resulting odds ratio enabled measurement of effect size where the prevalence of cases in the subject population was compared with the prevalence of cases in the control or referent population. An odds ratio of 1 indicated that the odds or the likelihood of a case outcome for a specific parameter is equally likely for both groups in the comparison. The greater the variance from 1 the more likely it is that the population under observation has a greater or lesser likelihood of presenting individual cases for the pregnancy outcomes considered.

To activate the analysis for each parameter within SPSS the selection of the parameter concerned was denoted as the dependent variable while explanatory or potential confounding variables were added to the covariates selection enabling adjustment of the odds ratio in accordance with these variables. The variables for which adjustment was made were: maternal age group, smoking status, socioeconomic status and marital status.

The odds ratio is denoted as exponent of B in the analysis within SPSS.

Among the options section of logistic regression the confidence interval for the exponent of B of 95% was selected. Once this had been selected the analyses were allowed to run and this produced outputs in tabular form, which included the relationship between the response variable and the explanatory variables.

The exponent of B in the outcome table represented the odds ratio for covariates and 95% confidence interval for the odds ratios were also presented. The output also produced the adjusted odds ratios and 95% confidence intervals for the dependent variables where the covariates had been included in the analysis.

8 METHOD FOR META-ANALYSIS

The systematic review identified a number of studies, which have explored the same parameters in various populations of pregnant women and were published between 1990 and 2012.

The selection of studies was undertaken based on the provision of odds ratios, adjusted odds ratios or relative risks with 95% confidence intervals for the various parameters.

The Aggregate Data (AD) model was the analysis type selected, as individual participant data were not available for the other studies.

8.1 Random and fixed effects modelling

Both fixed and random effect models were used as part of the meta-analysis undertaken using STATA statistical software to measure effect size. The fixed effect treats the observed quantities e.g. measures of LBW in cosmetologists as being due to variables that are not random or are known causes. The random effects model treats the observed quantities as if they are due to random or unknown causes.

The model applies an inverse variance weighting and then enables un-weighting of this inverse variance (IV) weighting through the use of a random effects variance component (REVC), which is derived from the underlying studies' effect size variability.

8.2 Effect of confounders

A weakness of the meta-analysis process is that confounders and sources of bias are not consistently accounted for or controlled for. Consequently stronger and weaker studies will be combined and the true effect may still not be evident

in spite of the increased power that the meta-analysis provides (Greenland and O' Rourke, 2008).

A further challenge is that some agents may only affect the embryo or foetus in certain windows of the gestational period. For some hazards, long term and high dose exposures may also be relevant in the extent of the impact on pregnancy outcome.

8.3 Use of STATA

The odds ratios, adjusted odds ratios and relative risks were tabulated for each of the outcomes under observation. These tables were used to perform a series of meta-analyses using statistical software STATA, combining the results of the various studies to identify the I-V pooled for fixed effect models and D+L pooled effect size for random effect models. The meta-analysis results were presented as forest plots which gave a visual representation of the meta-analysis results. The 'DO ' instructions for the STATA meta-analyses is listed in the Appendix18).

The meta-analysis approach enabled combination of the results of several distinct studies in order to estimate the true effect size for the various parameters through the increased power of a larger study population.

For each meta-analysis the effect size was measured in the form of a weighted average with confidence intervals. Weighting is generally related to the sample sizes of the individual studies with larger studies carrying more weight. The weight for each study is expressed as a percentage of the total weighting for the combined body of selected research that answers a specific question

9   RESULTS

9.1   Introduction

The results section will cover data from all three aspects of this thesis, the papers retrieved from the systematic review will be summarised as a collection. Following this each of the parameters studied for each subject cohort, this will be followed by the meta-analysis results in the form of a table and forest plot for each subjects group compared to each control group. Then the complete set of binary logistic regression analysis results will be presented for each of the parameters in turn for the FMBR data.

The order of the parameters will be: gender ratio, low birth weight, high birth weight, SGA, LGA, pre-term delivery, post-term delivery, still birth and END.

Where the systematic review has not produced any papers by other authors, the results from the original work from this thesis will be presented alone with an accompanying summary of the findings.

9.2   Results for hairdressers

Other researchers have established that hairdressers come into contact with various chemicals found in hair care products for washing, dyeing, bleaching, styling, conditioning, perming etc. Exposure to these agents has been recognised to lead to skin and respiratory ill health and effects of LBW, SGA and PTD have been suggested in previous research (Labreche et al. 2003, Leino et al. 1999, van Muiswinkel et al. 1997 and Flaws et al. 2009).

Exposure risk has depended on the tasks undertaken, use of ventilation, use of personal protective equipment, and redeployment of the worker to alternative duties (Leino 1999).

Along with chemical risks, other workplace factors have the potential to impact on reproduction. Psychosocial and ergonomic factors appear to have an impact on the wellbeing of a pregnant worker (Cassidy 2009, Hickey et al. 1995, Ronda et al. 2009, Wahlstrom et al. 2010).

Kersemaekers et al. (1997) undertook an epidemiological study of 9,000 hairdressers and compared them to 9,000 clothing sales clerks to determine whether exposure to chemicals used in hair products impacted on risk of reproductive disorders. They concluded that there was evidence of an increased risk of LBW infants in the earlier of two time periods (1986-1988 compared to 1991-1993). They also suggested that the risk had declined with time due to improvement to the system of work. A systematic review highlighted that other studies of hairdressers have shown inconsistent results, which may be due to methodological weaknesses and small sample size (Peters et al., (2010).

In combination with exposure to chemical agents, work as a hairdresser consists of extended periods of standing, repeated bending, awkward postures (McDonald, 1998; van Muiswinkel, 2000) and work-related stress (Hjollund 1999). These factors can be hazardous for reproduction.

The effects of maternal parity have not been discussed in detail here but are referred to elsewhere among the research literature on confounders. Essentially, confounders are important if their strength of association with the factor of primary interest is high and if the prevalence of the particular confounder among the subject or referent populations is high. It is noted for the characteristics of the study population that more of the teachers were married (85%) compared to hairdressers (57 %), cosmetologists (62%) and laboratory workers (66%). Some of each group were cohabiting and a few were noted as single (hairdressers and cosmetologists, 11.0 %, laboratory workers 8% and teachers 4%)

Comparable with hairdressers' research, literature has highlighted not only the potential for chemicals to cause general health effects but also a possible impact on pregnancy outcome (Gallicchio, 2011; Herdt-Losavio et al., 2008; Herdt-Losavio et al., 2009; Herdt-Losavio et al., 2011; John et al., 1994 and Peretz et al., 2009).

Some cohort and case control studies have been used to observe the impact of cosmetology on of a variety of outcomes taking into account potential confounders and wherever possible gathering detailed exposure information about work environment and frequency of certain occupational tasks and the number of hours worked per week (John et al. 1994, Flaws et al. 2009, Gallicchio et al. 2011).

Table 9.1 shows the outcome of the systematic literature review for pregnancy outcomes in hairdressers. It includes a brief author and reference citation, the country where the study was undertaken and years over which data was collected for the study. The size of the study is demonstrated by the number of hairdressers and controls. The criteria, which make the study eligible for inclusion and the parameters of relevance are listed in the table

Table 9.1 The Risks of pregnancy outcomes for hairdressers

Reference, country and years of study	Number of hairdressers and controls	Criteria for eligibility and comments	Parameters of relevance
Axmon et Rylander (2008) Sweden 1970- 2000	6223 infants of hairdressers 8388 infants controls.	6223 born to 3137 hairdressers and 8388 infants born to 3952 hairdressers' sisters. Population-based study of women who had graduated from 29 Swedish vocational hairdressing schools between 1970 and 2000 compared with their sisters	SGA, LGA Low -birth-weight
Goulet et al. (1991) Canada 1982–1984	103 hairdressers 127 others	Study of stillbirths among women with at least one stillbirth >28 weeks gestation	Stillbirth rate compared to controls
Li et al. (2010) Sweden 1990–2004	266 hairdressers 43 956 other occupations	Cross-sectional cohort study, Swedish Medical Birth Register, women 20 years old and above who were in employment	Pre-term birth (< 37 weeks) and Very pre-term delivery (<32 weeks) LBW
Kersemaekers et al. (1997) Netherlands 1986-1988 1991–1993	3358 hairdressers 2796 sales clerks	Hairdressers who worked at least 10 hours per week as a hairdresser during the first 2 months of pregnancy. Crude relative risk was calculated, binomial model for distinguishing data and the random effect model using the distribution of educational level The data were collected for two time periods: January 1986 to October 1988 and January 1991 October 1993	

Ronda et al. (2010) Spain January –June 2006	94 hairdressers 138 controls	Hairdressers from 248 salons in Alicante, Spain who worked during their pregnancy (shop assistant and office workers)	LBW, pre-term delivery
Rylander et al. (2002) Sweden 1973- 1994	7202 hairdressers 7353 referents	Referents matched for calendar year of births to hairdressers Swedish Medical Birth Register link to cohorts which contains information about lifestyle factors such as smoking in early pregnancy but no information about spouses	HBW, pre-term delivery SGA Stillbirths and END
Rylander and Källén (2005) Sweden 1983–2001	14,492 deliveries hairdressers 775,840 deliveries for referents	Swedish Medical Birth Register. Occupation as a hairdresser part-time or full-time compared to workers of different occupations	
Zhu et al. (2006a) Denmark 1997–2003	550 hairdressers and 3216 shops assistants as reference	Occupation around 17 weeks gestation is recorded, series of 3 further interviews until the child is 19 months old	Gender ratio, pre-term delivery, SGA
Halliday-Bell (2014)	12854 hairdressers and 447004 women from general public	Occupation and inclusion on Finnish Medical Birth Register 1990-2010	Gender ratio, low birth weight, high birth weight, pre-term delivery, post-term delivery, SGA, LGA, still birth and early neonatal death.

Table 9.2 highlights the results for systematic review of the literature. Figures 9.1 and 9.2 summarise the meta-analysis for two papers citing gender ratios. The review identified only three other studies, which explored the ratio of male to female gender ratio of new-borns amongst hairdressers. Of the two Swedish studies (Rylander et al., 2002 and Rylander and Källén, 2005) cited the ratios as percentages. The quoted longstanding male to female gender ratio in Sweden is reported as 1.06 (Rylander and Källén, 2005).The more recent of the two Swedish studies concluded that there was a small but statistically significant increased percentage of 51.1% (95% CI 50.2–52.0) of male offspring among hairdressers compared to controls.

The remaining study in this section (Zhu et al., 2006) did not support any significant variation in ratio of new-borns' gender.

The Swedish studies citing percentages could not be included in the meta-analysis.

The meta-analysis of effect sizes (relative risks) for the study by Zhu (2006) and this original study (Halliday-Bell) is shown table 9.3 (fixed effects) and a corresponding analysis using a random effects model is shown in table 9.4. Forest plots for both analyses are shown in figures 9.1 and 9.2. There was no statistically significant difference for hairdressers.

Table 9.2. The percentage or ratio of male to female gender ratio outcomes among hairdressers

Reference, country and years of study	Adjusted sex ratio-male/female (95% Confidence intervals)	Adjustment covariates	Comments
Rylander et al. (2002) Sweden 1973- 1994	51.7% (50.6–52.9)	Smoking habit more than 10 cigarettes a day, maternal weight and maternal age, maternal height	Certified hairdressers who were asked to complete a questionnaire on exposure
Rylander and Källén (2005) Sweden 1983–2001	51.1% (50.2–52.0)	Year of birth, parity, maternal country of birth and smoking	Result was similar to the referents 51.5%
Zhu et al. (2006a) Denmark 1997–2003	1.0 (0.9–1.2)	Spontaneous abortion, pre-pregnancy body mass index, smoking and alcohol consumption, parity, only the first pregnancy was counted	No statistically significant difference was found. This result was for singletons only. Results were almost the same without adjustment four confounders.
Halliday-Bell (2014) Finland 1990-2010	1.02 (0.99-1.06)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.3 Meta-analysis results for percentage or ratio of male to female gender ratio outcomes among hairdressers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Zhu (2006)	1.00	0.866	1.155	5.34
Halliday-Bell (2014)	1.02	0.986	1.055	94.66
I-V pooled Effect Size	1.019	0.986	1.053	100.00

Heterogeneity chi-squared = 0.07(d.f. = 1) p = 0.793

I-squared (variation in ES attributable to heterogeneity) = 0.0%

Test of ES=1 : z= 1.11 p = 0.269
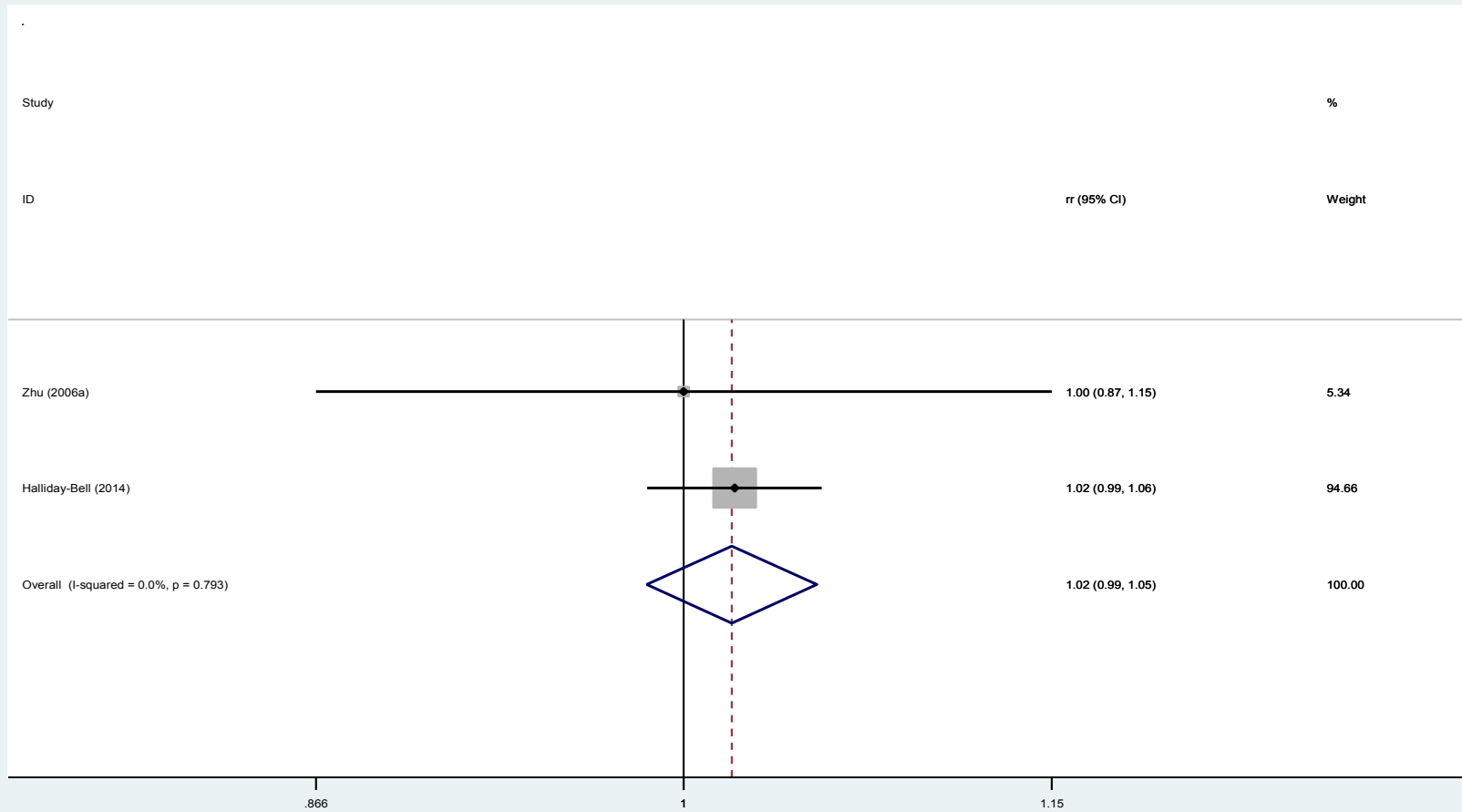
Figure 9.1 Forest plot for male to female ratio among hairdressers (fixed effect model)

Table 9.4 Meta-analysis results for percentage or ratio of male to female gender ratio outcomes among hairdressers (random effect model).

Study	Effect Size	[95% Conf. Interval]		% Weight
Zhu (2006)	1.00	0.866	1.155	5.34
Halliday-Bell (2014)	1.02	0.986	1.055	94.66
I-V pooled Effect Size	1.019	0.986	1.053	100.00

Heterogeneity chi-squared = 0.07(d.f. = 1) p = 0.793

I-squared (variation in ES attributable to heterogeneity) = 0.0%

Estimate of between-study variance Tau-squared = 0.000

Figure 9.2 Forest plot for male to female ratio among hairdressers (random effect model)

The tables 9.5, 9.6 and 9.7 and figures 9.3 and 9.4 are the risk ratio tables, meta-analyses and forest plots for LBW infants among hairdressers. Studies providing data on LBW outcomes among hairdressers are summarised in table 9.5. A meta-analysis of effect sizes (relative risks) for these studies is shown table 9.6 (fixed effects) and a corresponding analysis using a random effects model is shown in table 9.7. Forest plots for both analyses are shown in figures 9.3 and 9.4.

The I-V pooled Effect Size for LBW was 1.10 (95% CI, 1.01 - 1.20). This was a small statistically significant result suggesting that hairdressers have an increased risk of LBW infants.

It was of note that a close to 40% of the weighting for this meta-analysis was from the study by Rylander et al. (2005) which utilised the Swedish Medical Birth Register for the period 1973 to 1994. The database held data for a total of 775,840 deliveries for referents who were workers of different occupations. This incorporated 14,492 women who are employed as hairdressers, part-time or full-time. After selection for maternal age the response rate of 65% yielded a cohort of 3706 hairdressers who gave birth to 6960 infants. They were compared with 3462 referents in varying occupations who had 6629 deliveries.

This original study (Halliday-Bell, 2014) also accounted for close to 40% of the weighting in the meta-analysis.

Table 9.5. The risk of LBW outcomes among hairdressers

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Axmon et al. (2009a) Sweden 1970- 1995	0.72 (0.50–1.03)	Gender, maternal age and parity	The infants of hairdressers had birth weights over a narrower range than their sisters.
Kersemaekers et al. (1997) Netherlands 1986-1988 1991-1993	1.5 (0.7–3.1) 1.2 (0.8–1.9)	Educational level and gravidity	
Ronda et al. (2010) Spain January – June 2006	1.2 (0.3–2.0)	Maternal age, nulliparous women only	Control group shop assistants and office workers interviewed and used a questionnaire
Rylander et al. (2002) Sweden 1973- 1994	1.2 (1.0–1.5)	Smoking habit more than 10 cigarettes a day, maternal weight, maternal age maternal height	Hairdressers and their sisters were compared. No increased risk of HBW was found.
Rylander and Källén (2005) Sweden 1983–2001	1.10 (0 .99–1.21)	Year of birth, parity, maternal country of birth and smoking	
Zhu (2006)	0.830 (0.567-1.214)	Spontaneous abortion, pre-pregnancy body mass index, smoking and alcohol consumption	
Halliday-Bell (2014)	1.08 (0.98-1.19)	Pprima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.6 Meta-analysis results for the risk of LBW outcomes among hairdressers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Axmon (2008)	0.72	0.502	1.033	3.01
Kersemaekers (1997)	1.5	0.713	3.157	0.71
Kersemaekers (1997)	1.2	0.779	1.849	2.11
Ronda (2010)	1.2	0.465	3.098	0.44
Rylander (2002)	1.2	0.98	1.47	9.56
Rylander (2005)	1.1	0.995	1.216	39.76
Zhu (2006)	0.830	0.567	1.214	2.71
Halliday-Bell (2014)	1.08	0.98	1.19	41.70
I-V pooled Effect Size	1.083	1.017	1.153	100.00

Heterogeneity chi-squared = 8.86 (d.f. = 7) p = 0.263
 I-squared (variation in ES attributable to heterogeneity) = 21.6%
Test of ES=1 : z= 2.5 p = 0.012
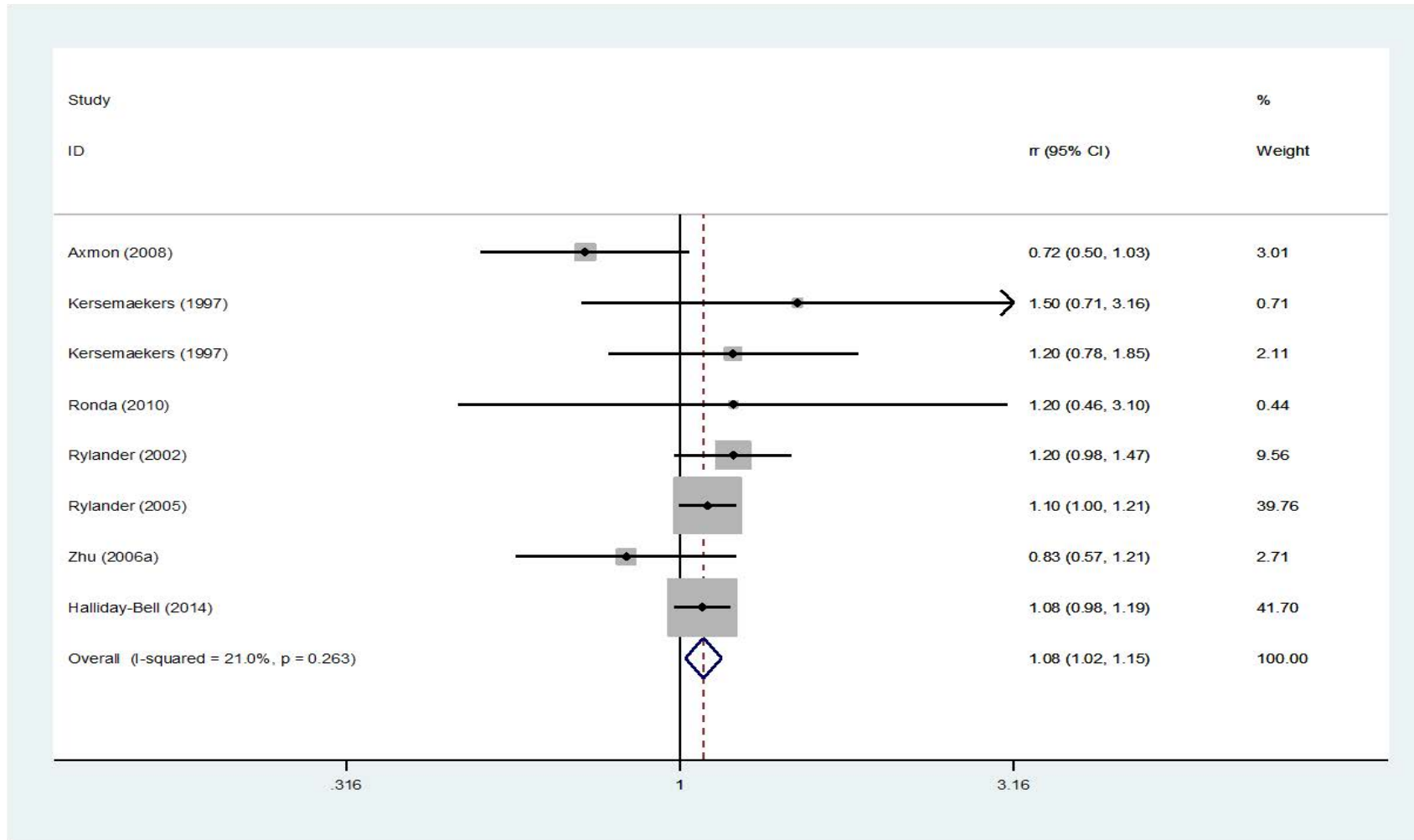
Figure 9.3 Forest plot for LBW among hairdressers (fixed effect model)

Table 9.7 Meta-analysis results for the risk of LBW outcomes among hairdressers (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Axmon (2009a)	0.72	0.50	1.03	5.16
Kersemaekers (1997)	1.50	0.71	3.16	1.29
Kersemaekers (1997)	1.20	0.78	1.85	3.70
Ronda (2010)	1.20	0.47	3.10	0.80
Rylander (2002)	1.20	0.98	1.47	13.99
Rylander (2005)	1.10	1.00	1.22	34.80
Zhu (2006)	0.830	0.567	1.214	4.69
Halliday-Bell (2014)	1.08	0.98	1.19	35.58
D+L pooled Effect Size	1.016	0.880	1.173	100.00

Heterogeneity chi-squared = 8.86 (d.f. = 7) p = 0.263

I-squared (variation in ES attributable to heterogeneity) = 42.6%

Estimate of between-study variance Tau-squared = 0.0029

Test of ES=1 : z=   1.69 p = 0.091

Study ID		rr (95% CI)	% Weight
Axmon (2008)		0.72 (0.50, 1.03)	5.16
Kersemaekers (1997)		1.50 (0.71, 3.16)	1.29
Kersemaekers (1997)		1.20 (0.78, 1.85)	3.70
Ronda (2010)		1.20 (0.46, 3.10)	0.80
Rylander (2002)		1.20 (0.98, 1.47)	13.99
Rylander (2005)		1.10 (1.00, 1.21)	34.80
Zhu (2006a)		0.83 (0.57, 1.21)	4.69
Halliday-Bell (2014)		1.08 (0.98, 1.19)	35.58
Overall (I-squared = 21.0%, p = 0.263)		1.08 (0.99, 1.17)	100.00

NOTE: Weights are from random effects analysis

.316   1   3.16

Figure 9.4 Forest plot for LBW among hairdressers (random effect model)

Tables 9.8, 9.9 and 9.10 and figures 9.5 and 9.6 below show the risk ratios tables, meta-analysis and forest plots for SGA infant rates among hairdressers compared to controls. There were two Swedish studies (Rylander et al., 2002) and (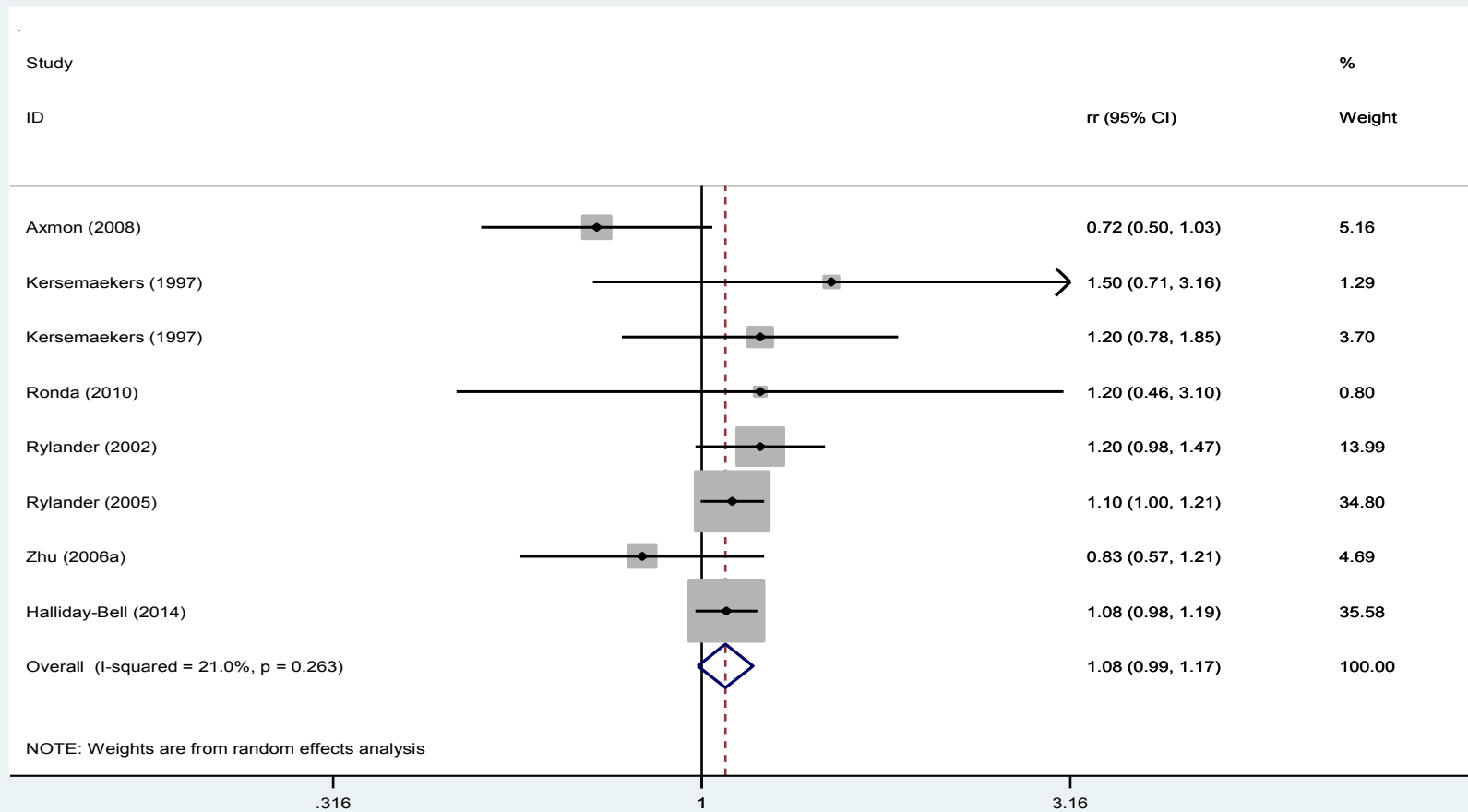Rylander and Källén, 2005) which demonstrated statistically significant effect size (ES) with aOR results for SGA (1.4, 95% CI 1.1–1.7 and 1.2, 95% CI 1.06–1.36 respectively) among hairdressers, certified in Sweden. The referent cohorts for both studies were women from the general population. Exposure data were collected via questionnaires that identified types of work undertaken and whether the participant was working full time or part time. The studies suggested that frequency of permanent waving and spraying were associated with increased risk of having a SGA infant.

It was of note that Rylander et al. (2005) accounted to close to 60% of the weighting for this meta-analysis. As noted above this was a large epidemiological study.

The I squared result (variation in Effect Size attributable to heterogeneity) was 77.0% and the I-V pooled effect size for the fixed effect model was 1.077 (95% CI, 1.006-1.153). This was marginally statistically significant. The pooled effect for the random effects model incorporated a value that includes 1.00 and was therefore not statistically significant.

Table 9.8 The risk of SGA outcomes among hairdressers

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Axmon and Rylander (2008) Sweden 1970- 1995	0.73 (0.46-1.17)	Gender, maternal age and parity	A particular strength of this study was the use of sisters as the control cohort.
Rylander et al. (2002) Sweden 1973- 1994	1.4 (1.13-1.74)	Smoking habit more than 10 cigarettes a day, maternal weight and maternal age, maternal height	
Rylander and Källén (2005) Sweden 1983–2001	1.2 (1.06–1.36)	Year of birth, parity, maternal country of birth and smoking	An increased risk of SGA amongst hairdressers who worked in early pregnancy compared other deliveries in the same time period. Gestation length may not be accurate this was therefore based on 2nd trimester ultrasound measurements
Zhu et al. (2006a) Denmark 1997–2003	1.0 (0.7–1.37)	Spontaneous abortion, pre-pregnancy body mass index, smoking and alcohol consumption	
Halliday-Bell (2014)	0.95 (0.86-1.06)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.9 Meta-analysis results for the risk of small -for -gestational -age outcomes among hairdressers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Axmon (2008)	0.73	0.46	1.16	2.20
Rylander (2002)	1.40	1.13	1.74	10.10
Rylander (2005)	1.19	1.07	1.33	39.78
Zhu (2006a)	1.00	0.73	1.36	4.86
Halliday-Bell (2014)	0.95	0.86	1.06	43.05
I-V pooled Effect Size	1.077	1.006	1.153	100.00

Heterogeneity chi-squared =   17.37 (d.f. = 4) p = 0.002

I-squared (variation in ES attributable to heterogeneity) = 77.0%

Test of ES=1 : z=   2.12 p = 0.034

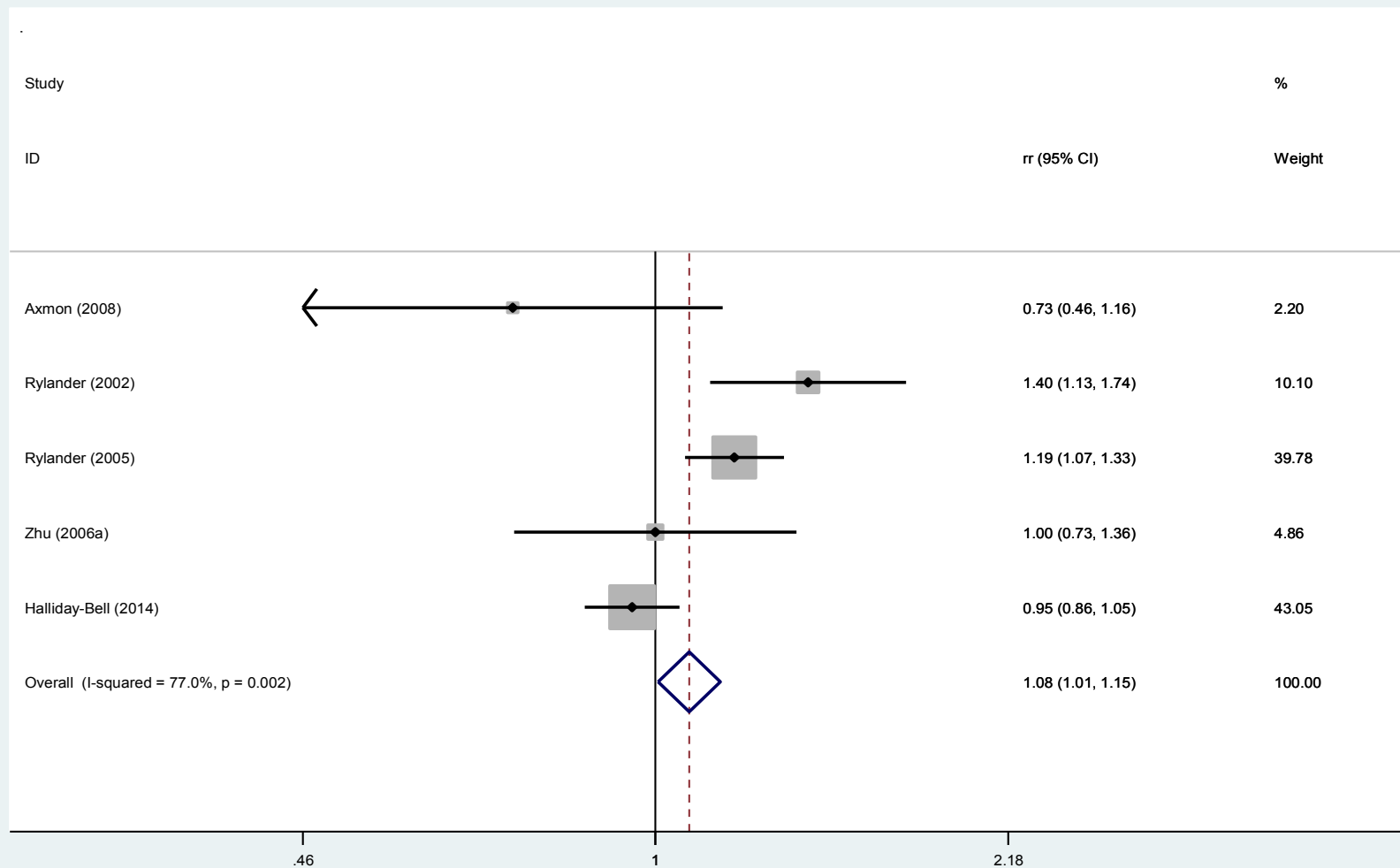| Study		
ID	rr (95% CI)	Weight
Axmon (2008)	0.73 (0.46, 1.16)	2.20
Rylander (2002)	1.40 (1.13, 1.74)	10.10
Rylander (2005)	1.19 (1.07, 1.33)	39.78
Zhu (2006a)	1.00 (0.73, 1.36)	4.86
Halliday-Bell (2014)	0.95 (0.86, 1.05)	43.05
Overall (I-squared = 77.0%, p = 0.002)	1.08 (1.01, 1.15)	100.00

Figure 9.5: Forest plot for SGA (fixed effect model)

105

Table 9.10 Meta-analysis results for the risk of small -for -gestational -age outcomes among hairdressers (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Axmon (2008)	0.73	0.46	1.16	9.55
Rylander (2002)	1.40	1.13	1.74	20.62
Rylander (2005)	1.19	1.07	1.33	27.15
Zhu (2006a)	1.00	0.73	1.36	15.30
Halliday-Bell (2014)	0.950	0.86	1.06	27.38
D+L pooled Effect Size	1.075	0.905	1.278	100.00

Heterogeneity chi-squared = 17.37 (d.f. = 4) p = 0.002

I-squared (variation in ES attributable to heterogeneity) = 77.0%

Estimate of between-study variance Tau-squared = 0.0255

Test of ES=1 : z= 0.82 p = 0.410

Study ID	rr (95% CI)	% Weight
Axmon (2008)	0.73 (0.46, 1.16)	9.55
Rylander (2002)	1.40 (1.13, 1.74)	20.62
Rylander (2005)	1.19 (1.07, 1.33)	27.15
Zhu (2006a)	1.00 (0.73, 1.36)	15.30
Halliday-Bell (2014)	0.95 (0.86, 1.05)	27.38
Overall (I-squared = 77.0%, p = 0.002)	1.08 (0.90, 1.28)	100.00

NOTE: Weights are from random effects analysis
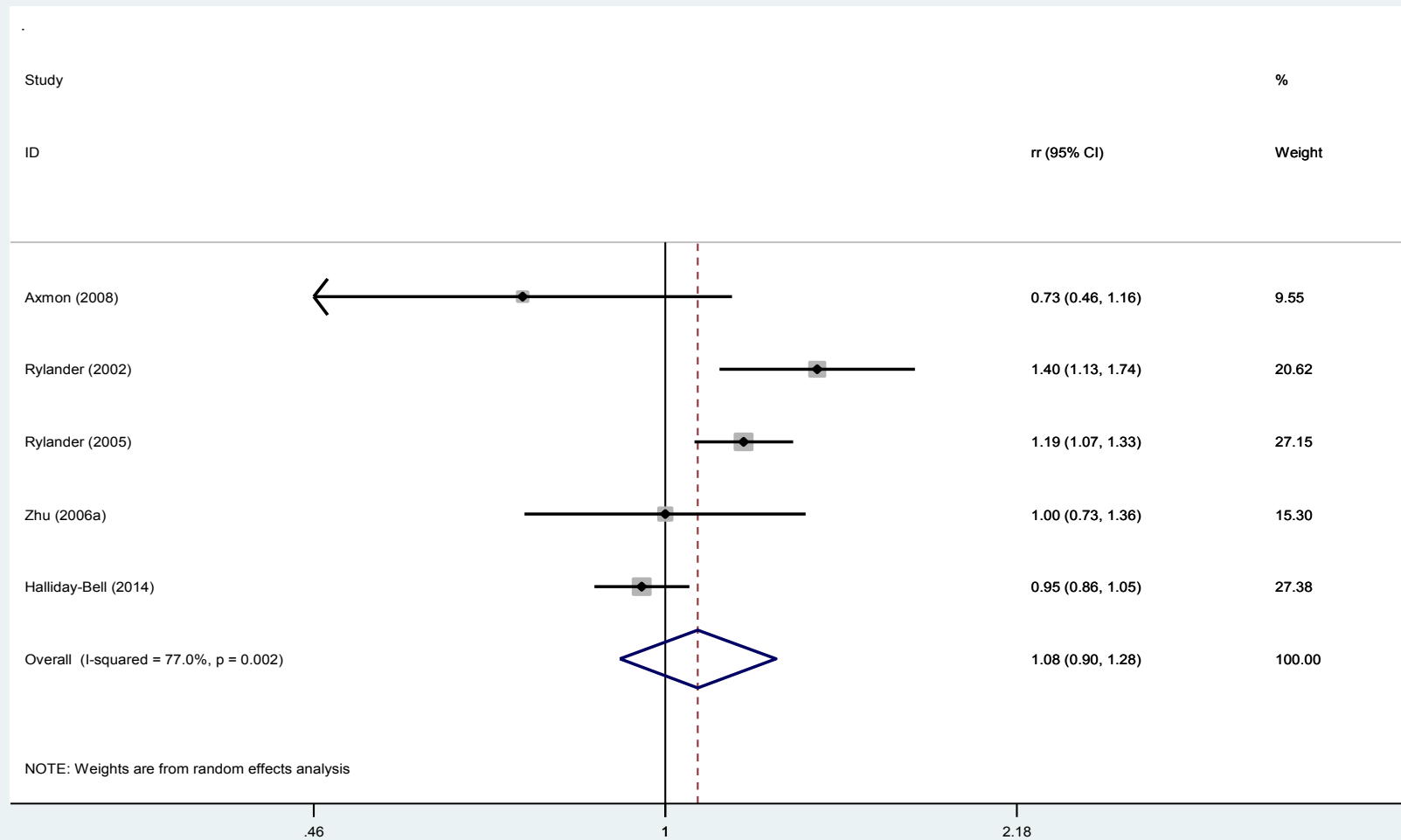
.46   1   2.18

Figure 9.6. Forest plot for SGA among hairdressers (random effects model)

Tables 9.11, 9.12 and 9.13 and figures 9.7 and 9.8 present the summary, meta-analysis and forest plots for this (Halliday-Bell, 2014) and two other studies, which included the measurement of large -for-gestational-age (LGA) infants in hairdressers. Axmon and Rylander (2009a) did not produce statistically significant positive results when pregnancy outcomes for 6223 infants born to 3137 hairdressers were compared to 8388 infants born to 3952 of their sisters. This study aimed to investigate birth-weight and foetal growth in women who had trained as hairdressers compared to their sisters. Their method enabled adjustment for genetics and childhood exposures.

Axmon and Rylander (2009a) included adjusted odds ratios for various subgroups that were determined by work status. The finding of most relevance was the aOR for LGA, which measured 0.64 (95% CI 0.44 to 0.93), which applied to women who confirmed that they had worked as hairdressers during their most recent pregnancy. This suggested that they had a statistically significant lowered risk or likelihood of being LGA. No obvious mechanism was put forward that could account for this but there is a suggestion of SGA being relevant in hairdressers that has been summarised above.

The study by Zhu (2006a) that referred to the Danish National Birth Cohort (DNBC) equally did not produce statistically significant results when this team undertook a study that included measurement of LGA infant among 550 hairdressers compared to 3216 shop assistants. The study took into account the characteristics of the work undertaken by the subjects and controls.

Infants become large for their gestational age infant (LGA) due to high prenatal growth rate. This outcome is usually diagnosed post-delivery, but is occasionally picked up prenatally by ultrasound.

One of the contributing medical factors for LGA is maternal gestational diabetes or pre-existing type 2 diabetes. This condition causes high plasma glucose and insulin levels in the expectant mother. These raised levels stimulate excessive foetal growth. In other cases LGA infants develop due to congenital anomalies of the circulation such as transposition of great vessels and foetal hydrops conditions.

Certain complications are recognised to be associated with LGA infants when these occur during the neo-natal period. These include birth trauma, cardiovascular and respiratory problems, anaemia and haemorrhagic disorders as well as nervous system and musculoskeletal problems and infections (Ng et al., 2010).

The results for the pooled I-V effect size as part of the meta-analysis in this study was an OR of 0.82 (95% CI, 0.72-0.93). Both the fixed and random effect models yielded similar results. This was in agreement with the study by Axmon and Rylander (2008).

Table 9.11. The risk of LGA outcomes among hairdressers

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Axmon et al. (2008) Sweden 1970- 1995	0.64 (0.44–0.93)	Gender, maternal age and parity	
Zhu et al. (2010) Denmark 1997–2003	0.77 (0.54–1.09)	Maternal smoking, maternal age, pre-pregnancy maternal body mass index	Only the first pregnancy was counted. No statistically significant difference was found
Halliday-Bell (2014)	0.86 (0.74-1.0)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.12 Meta-analysis results of the risk of LGA outcomes among hairdressers (fixed effects Mode**)**

Study	Effect Size	[95% Conf. Interval]		% Weight
Axmon (2008)	0.64	0.44	0.93	12.03
Zhu (2006a)	0.77	0.54	1.09	13.66
Halliday-Bell (2014)	0.86	0.74	1.00	74.31
I-V pooled Effect Size	0.81	0.72	0.93	100.00

Heterogeneity chi-squared =   4.62 (d.f. = 2) p = 0.099

I-squared (variation in ES attributable to heterogeneity) = 56.7%
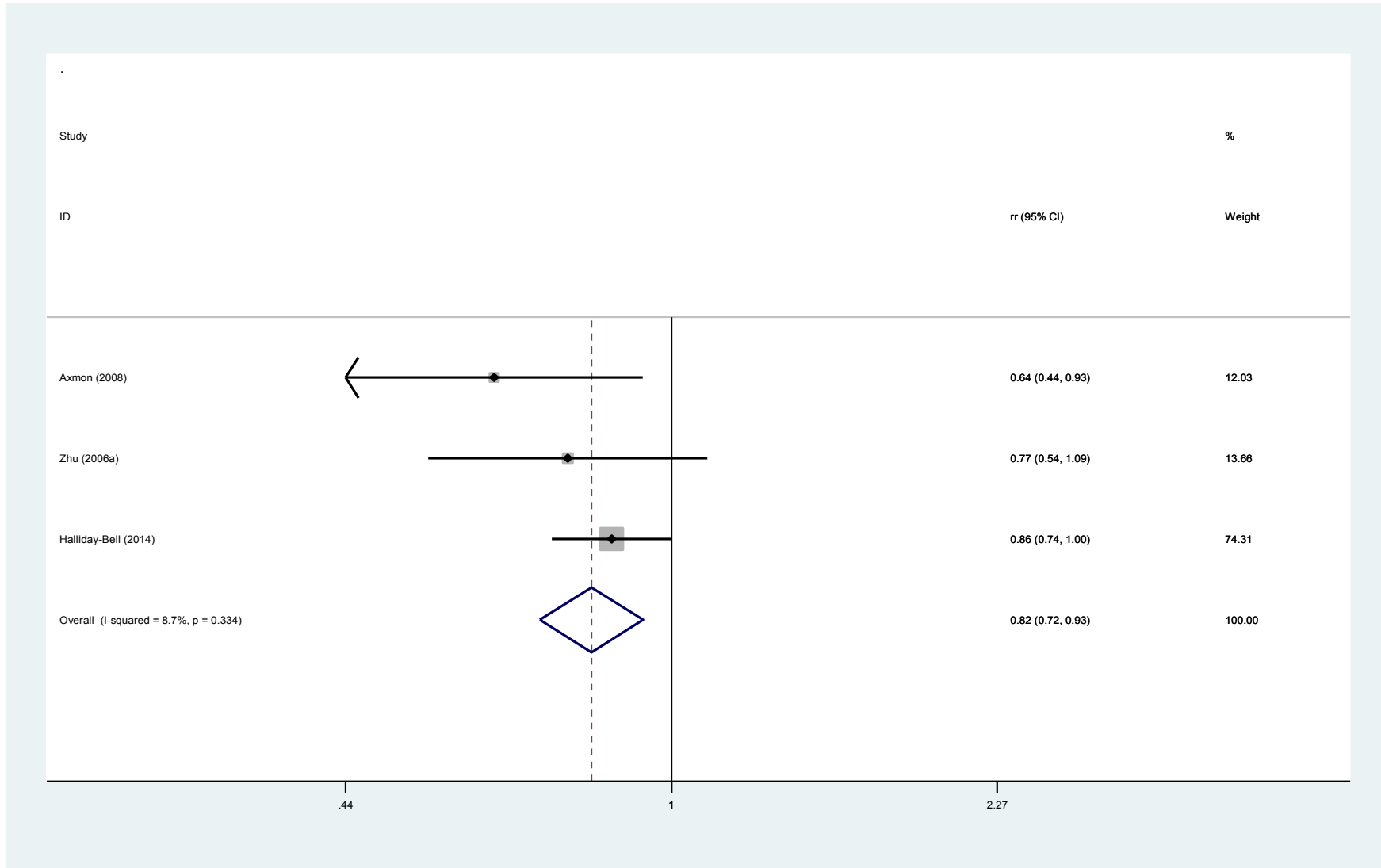
Test of ES=1 : z=   1.94 p = 0.053

Figure 9.7 . Forest Plot of the risk of LGA outcomes among hairdressers (fixed effect model)

Table 9.13 Meta-analysis results of the risk of LGA outcomes among hairdressers
(random Effects Model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Axmon (2008)	0.64	0.44	0.93	14.31
Zhu (2006a)	0.77	0.54	1.09	16.14
Halliday-Bell	0.86	0.74	1.00	69.55
D+L pooled Effect Size	0.81	0.70	0.94	100.00

Heterogeneity chi-squared = 2.19 (d.f. = 2) p = 0.334
I-squared (variation in ES attributable to heterogeneity) = 8.7%

Estimate of between-study variance Tau-squared = 0.002
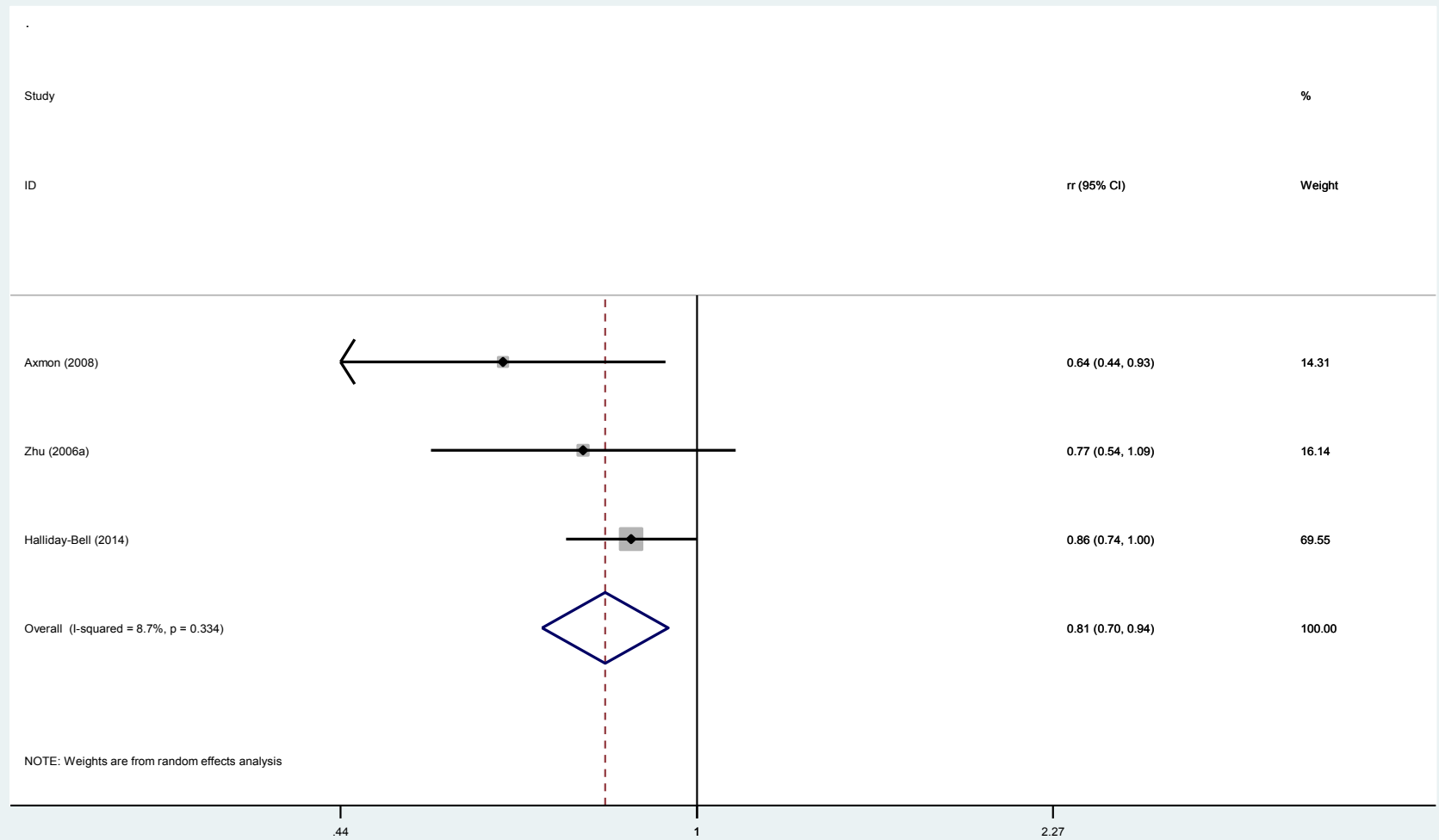
Test of ES=1 : z= 2.84 p = 0.004

Study		
ID	rr (95% CI)	% Weight
Axmon (2008)	0.64 (0.44, 0.93)	14.31
Zhu (2006a)	0.77 (0.54, 1.09)	16.14
Halliday-Bell (2014)	0.86 (0.74, 1.00)	69.55
Overall (I-squared = 8.7%, p = 0.334)	0.81 (0.70, 0.94)	100.00

NOTE: Weights are from random effects analysis

.44　　　　　　1　　　　　　2.27

Figure 9.8 Forest plot of the risk of LGA outcomes among hairdressers (random effect model).

Tables 9.14, 9.15 and 9.16 and figures 9.9 and 9.10 below show the risk factors

tables, meta-analysis and forest plots for pre-term delivery for infants delivered by

hairdressers compared to controls. Kersemaekers et al. (1997) looked at hairdressers

and controls in the Netherlands during two time periods (1986-1988 and 1991-1993).

They did not find any significant difference in the adjusted odds rations for either time

period (aOR 0.5, 95% CI 0.1–2.3 and aOR 1.0, 95% CI, 0.8–1.3).

Studies by other researchers: Li et al. (2010), Ronda et al. (2010), Rylander et al. (

2002), Rylander and Källén (2005) and Zhu et al. (2010) were all undertaken over

single time periods. They made adjustments for several various confounders in each

case.

None of the individual studies nor the meta-analysis of all of the studies demonstrated

statistically significant results.

Table 9.14. The risk of pre-term delivery outcomes among hairdressers

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Kersemaekers et al. (1997) Netherlands		Educational level and gravidity	No increased risk amongst hairdressers
1986-1988	0.5 (0.1–2.3)		
1991-1993	1.0 (0.8–1.3)		
Li et al. (2010) Sweden 1990–2004	0.96 (0.83-1.11)		
Ronda et al. (2010) Spain January –June 2006	1.0 (0.4–2.7)	Cross-sectional study, adjusted for age of mother only nulliparous women were included	Exposure proxy measured by questionnaire
Rylander et al. (2002) Sweden 1973- 1994	1.1 (0.9–1.3)	Maternal weight, maternal age and maternal height	Hairdressers did not have more pre-term infants than the reference population
Rylander and Källén (2005) Sweden 1983–2001	1.05 (0.96–1.14)	Year of birth, parity, maternal country of birth and smoking	No evidence of increase of pre-term deliveries. Swedish
Zhu et al. (2006a) Denmark 1997–2003	1.0 (0.7 – 1.5)	Spontaneous abortion, Pre-pregnancy body mass index, smoking and alcohol consumption.	No statistically significant difference was found
Halliday-Bell (2014)	1.00 (0.93-1.09)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.15 Meta-analysis results for the risk of pre-term delivery outcomes among hairdressers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Kersemaekers (1997)	0.50	0.11	2.35	0.11
Kersemaekers (1997)	1.00	0.76	1.32	3.26
Li (2010)	0.96	0.83	1.11	12.08
Ronda (2010)	1.08	0.40	2.91	0.24
Rylander et al.(2002)	1.10	0.92	1.32	7.83
Rylander and Källén	1.05	0.96	1.14	34.58
Zhu (2006a)	1.00	0.65	1.51	1.38
Halliday-Bell (2014)	1.00	0.92	1.08	40.52
I-V pooled Effect Size	1.019	0.969	1.072	100.00

Heterogeneity chi-squared = 2.86 (d.f. = 7)p=0.898

I-squared (variation in ES attributable to heterogeneity) = 0.0%

Test of ES=1 : z= 0.72 p = 0.469

Study		
ID	rr (95% CI)	% Weight
Kersemaekers (1997)	0.50 (0.11, 2.35)	0.11
Kersemaekers (1997)	1.00 (0.76, 1.32)	3.26
Li (2010)	0.96 (0.83, 1.11)	12.08
Ronda (2010)	1.00 (0.36, 2.80)	0.24
Rylander (2002)	1.10 (0.92, 1.32)	7.83
Rylander (2005)	1.05 (0.96, 1.14)	34.58
Zhu (2006a)	1.00 (0.65, 1.54)	1.38
Halliday-Bell (2014)	1.00 (0.92, 1.08)	40.52
Overall (I-squared = 0.0%, p = 0.898)	1.02 (0.97, 1.07)	100.00

.107   1   9.38
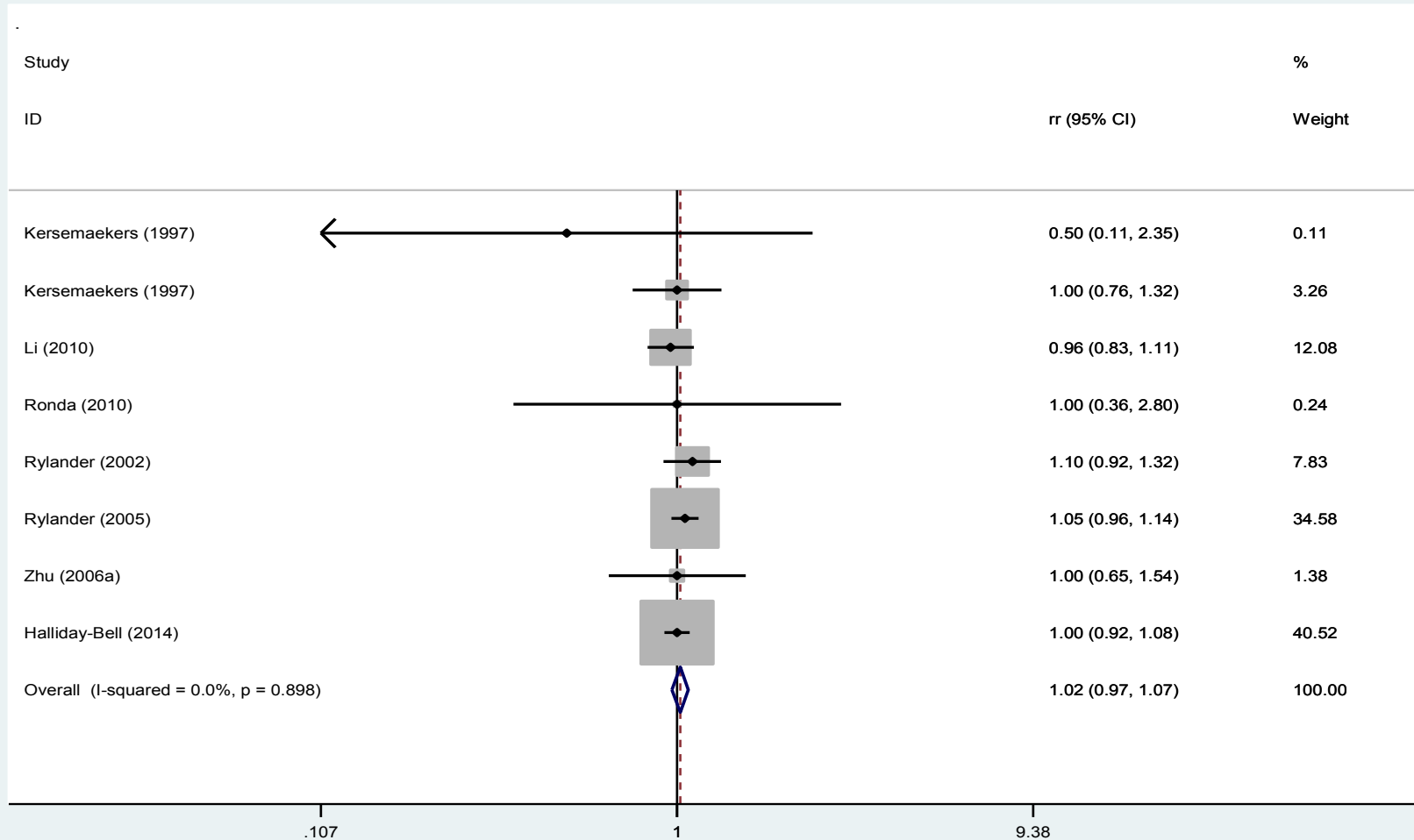
Figure 9.9 Forest plot for pre-term delivery among hairdressers (fixed effects model)

Table 9.16 Meta-analysis results for the risk of pre-term delivery outcomes among hairdressers (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Kersemaekers (1997)	0.50	0.11	2.35	0.11
Kersemaekers (1997)	1.00	0.76	1.32	3.26
Li (2010)	0.96	0.83	1.11	12.08
Ronda (2010)	1.08	0.40	2.91	0.24
Rylander et al.(2002	1.10	0.92	1.32	7.83
Rylander and Källén	1.05	0.96	1.14	34.58
Zhu (2006a)	1.00	0.66	1.51	1.38
Halliday-Bell (2014)	1.00	0.93	1.09	40.52
D+L pooled Effect Size	1.019	0.969	1.072	100.00

Heterogeneity chi-squared =   2.86 (d.f. = 7) p = 0.898

I-squared (variation in ES attributable to heterogeneity) =   0.0%

Estimate of between-study variance Tau-squared = 0.0000

Test of ES=1 : z=   1.05 p = 0.295

Study ID		rr (95% CI)	% Weight
Kersemaekers (1997)		0.50 (0.11, 2.35)	0.11
Kersemaekers (1997)		1.00 (0.76, 1.32)	3.26
Li (2010)		0.96 (0.83, 1.11)	12.08
Ronda (2010)		1.00 (0.36, 2.80)	0.24
Rylander (2002)		1.10 (0.92, 1.32)	7.83
Rylander (2005)		1.05 (0.96, 1.14)	34.58
Zhu (2006a)		1.00 (0.65, 1.54)	1.38
Halliday-Bell (2014)		1.00 (0.92, 1.08)	40.52
Overall (I-squared = 0.0%, p = 0.898)		1.02 (0.97, 1.07)	100.00

NOTE: Weights are from random effects analysis

.107   1   9.38
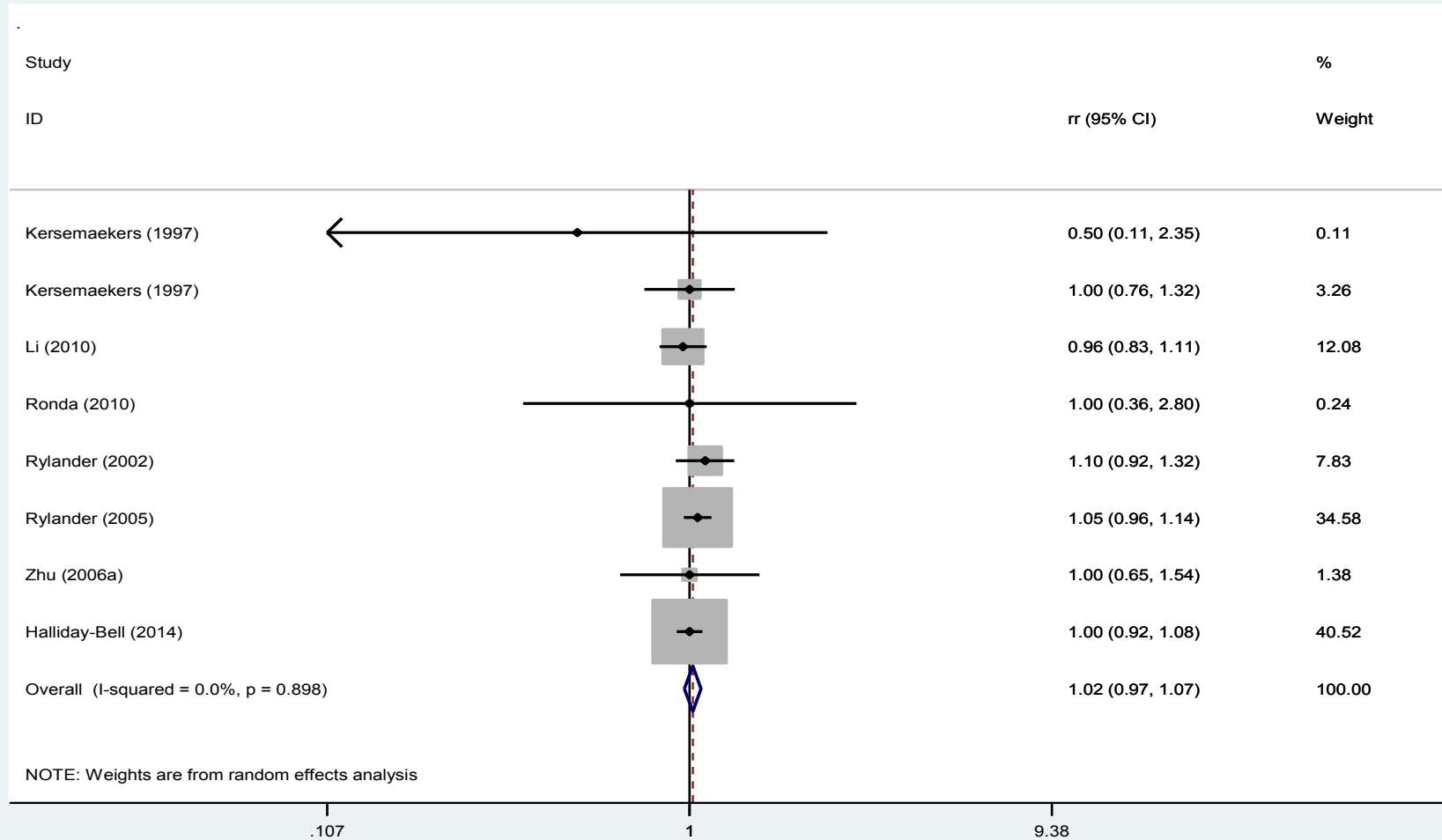
Figure 9.10 Forest plot for pre-term delivery among hairdressers (random effects model)

Table 9.17 highlights the meta-analysis, which included stillbirths and ENDs among hairdressers. Goulet and Theriault (1991) undertook their study on hairdressers in Canada. Matching was made with women in various areas of industry - health, personal services and manufacturing for mother's age, gravidity and socioeconomic status. Furthermore, the conditional logistic regression analyses controlled for maternal education, race, cigarette smoking and alcohol use. Stillbirths (N=227) were matched with live births (N=227). The adjusted risk ratio for this study was 0.1(0.0–0.3)

Rylander et al. (2002) also examined the risk of stillbirth among various adverse pregnancy outcomes. The aOR was 1.1 (95% CI, 0.6–1.0).).

Meta-analysis of the data from these two studies in conjunction with the original data from the current study (Halliday-Bell, 2014) was not calculated in STATA. Forest plots could also not be made. The risk ratio from the study by Goulet and Theriault (1991) of a Canadian cohort of women produced results that varied too widely from the other two studies.

Table 9.17 The risk of stillbirth outcomes among hairdressers

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Goulet and Theriault (1991) Canada 1982–1984	0.1(0.0–0.3)	None	Chemical exposure frequency and intensity were estimated by questionnaire
Rylander et al. (2002) Sweden 1973-1994	1.1 (0.6–1.0)	Smoking habit more than 10 cigarettes a day, maternal weight, maternal age, maternal height.	
Halliday-Bell (2014)	1.11 (0.80-1.54)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.18 demonstrates the results and findings for END among hairdressers compared to controls. Only one other study has specifically looked at this parameter. This study by Rylander et al. (2002) Sweden revealed an Adjusted odds ratio of 1.7 (95% CI, 0.9–2.3). This was a non-significant result.

Tables 9.19 and 9.20 and figures 9.11 and 9.12 below show the risk factors tables, meta-analysis and forest plots for END for infants delivered by hairdressers compared to controls.

The meta-analysis combining the Rylander et al, (2002) data and the original findings (Halliday-Bell, 2014) was possible as the heterogeneity was 0.0%. The results of the meta-analysis produced no evidence an increased risk of END among hairdressers.

Table 9.18. The risk of END outcomes among hairdressers

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Rylander et al. (2002) Sweden 1973-1994	1.1 (0.63–1.91)	More than 10 cigarettes a day, maternal weight and maternal age maternal height	Exposure data were estimated by questionnaire
Halliday-Bell (2014)	1.11 (0.80-1.54)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.19 Meta-analysis results for the risk of neonatal death delivery outcomes among hairdressers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Rylander et al.(2002	1.10	0.64	1.91	26.22
Halliday-Bell (2014)	1.11	0.80	1.54	73.78
I-V pooled Effect Size	1.107	0.836	1.467	100.00

Heterogeneity chi-squared =   0.00 (d.f. = 1)p=0.978

I-squared (variation in ES attributable to heterogeneity) =   0.0%

Test of ES=1 : z=   0.71 p = 0.477
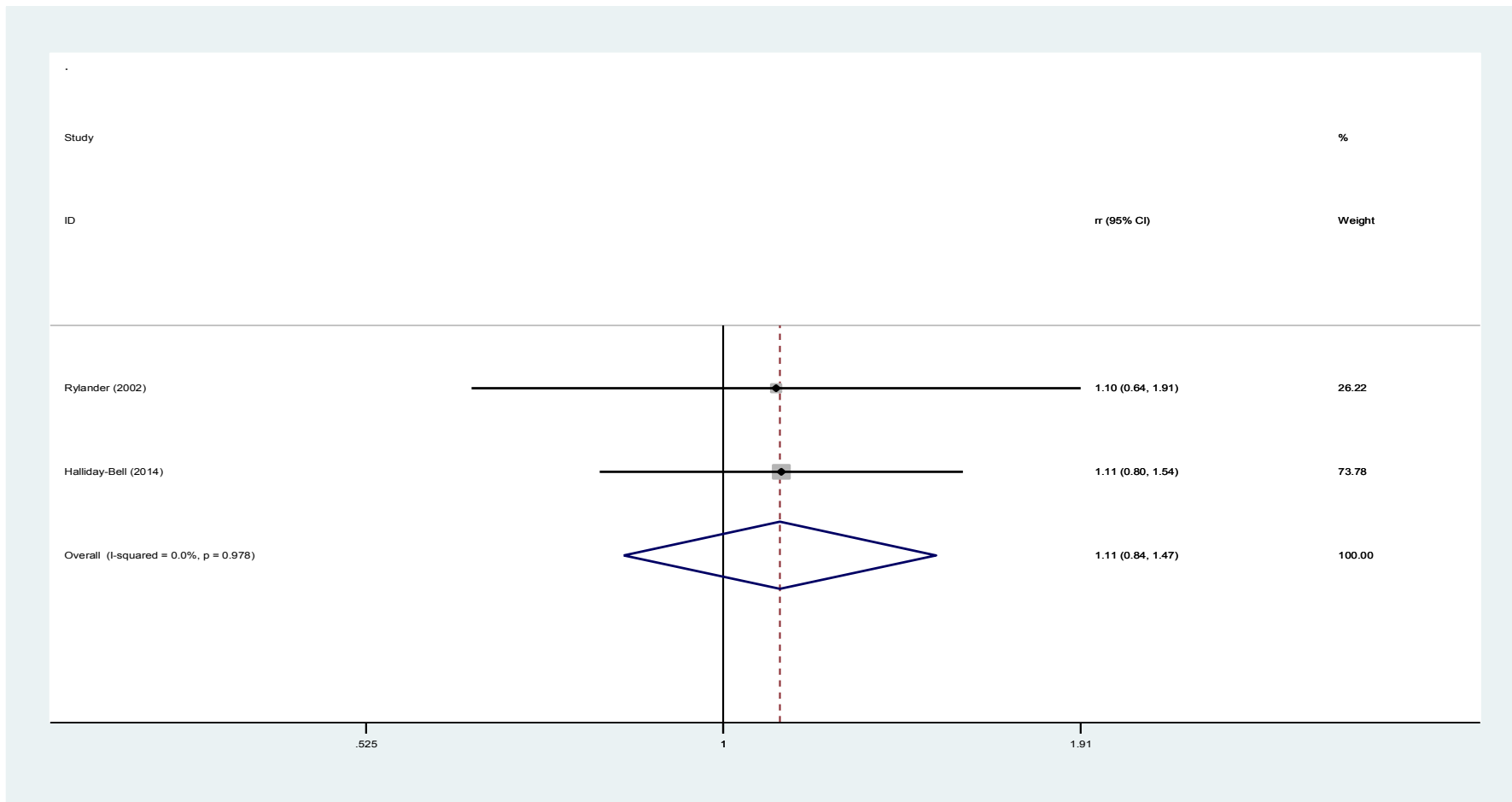
Figure 9.11 Forest plot for END among hairdressers (fixed effects model)

Table 9.20 Meta-analysis results for the risk of END among hairdressers (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Rylander et al.(2002	1.10	0.64	1.91	26.22
Halliday-Bell (2014)	1.11	0.80	1.54	73.78
I-V pooled Effect Size	1.107	0.836	1.467	100.00

Heterogeneity chi-squared =   0.00 (d.f. = 1) p=0.978

I-squared (variation in ES attributable to heterogeneity) =   0.0%

Estimate of between-study variation Tau-squared = 0.00
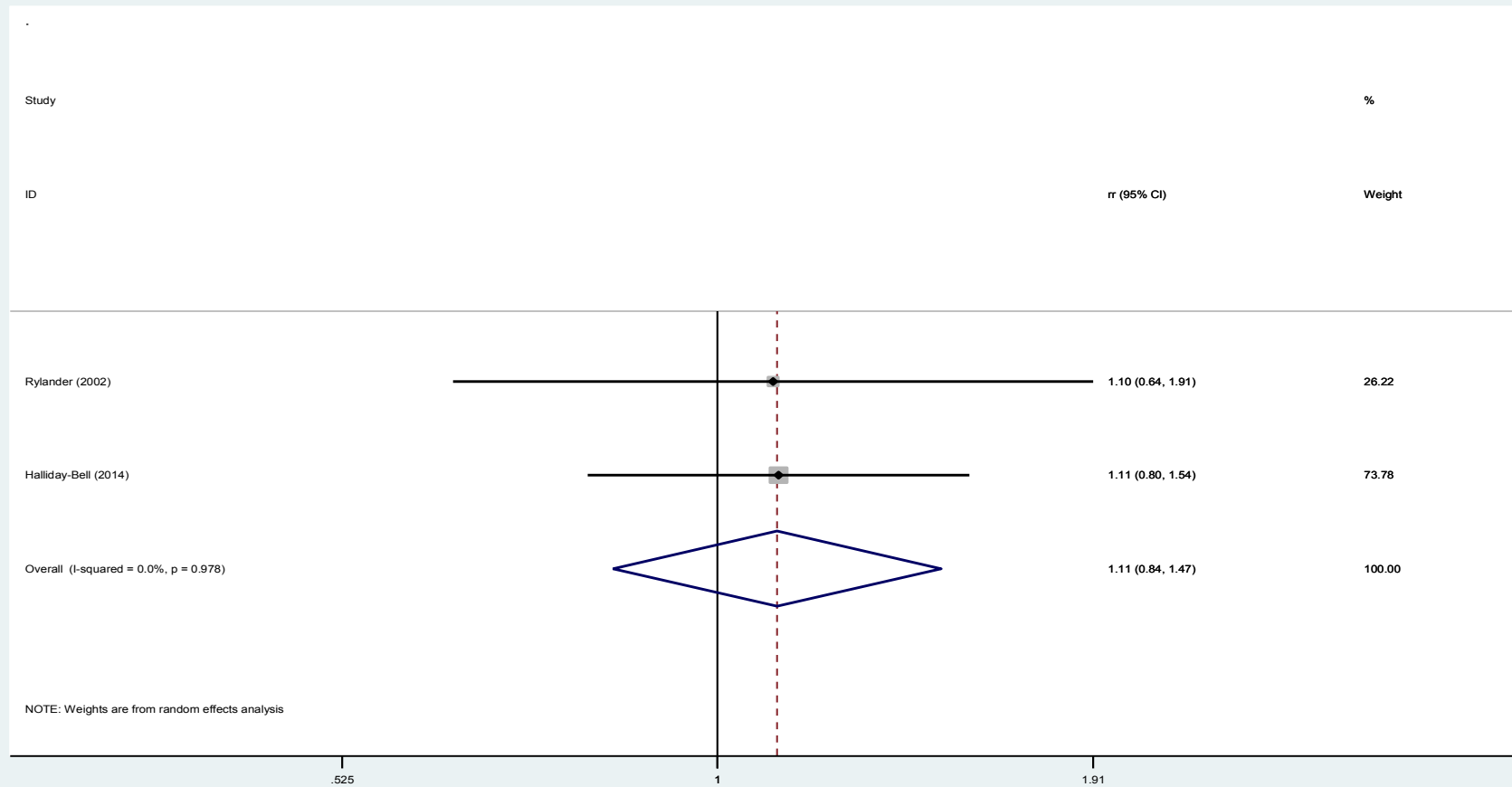
Figure 9.12 Meta-analysis results for the risk of END among hairdressers (random effect model)

9.3 Results for cosmetologists

Table 9.21 summarises various studies, which have previously been undertaken to explore the effects cosmetology on pregnancy outcome. There appeared to be one study, (Herdt-Losavio et al. 2008) which included several tens of thousands of individuals and other smaller studies, which included up to 750 individuals.

The study by Herdt-Losavio et al. (2011) was a nested study that aimed to identify exposure levels to cosmetic products based on types and frequency of tasks undertaken. Flaws et al. (2009) tested the hypothesis that cosmetologists are at increased risk of adverse pregnancy outcomes than controls compared with women of the same age who are not cosmetologists. The participants were recruited through mass mailing of questionnaires. The result showed no statistically significant associations between occupation and the pregnancy outcomes.

Herdt-Losavio et al. (2008) studied female licensed cosmetologists for risk of LBW, SGA, and pre-term delivery compared to two different comparison groups in New York State. They found a positive association for LBW compared to realtors.

A further study by this lead author (Herdt-Losavio et al., 2011) compared cosmetologists with children born between 1997 and 2003 weighing <2,500 g, compared to controls who were cosmetologists with full-term children who weighed >2,500 grams. They examined how the various workplace tasks compared between the cases and controls but found no difference to explain the LBW occurrences. Working in non-purpose built and solely dedicated

premises was associated with having a LBW child which may suggested a higher level of exposure to airborne products or ergonomic challenges.

The studies made adjustments for various confounders. All three except the current study (Halliday-Bell, 2014) used subjects from the US population.

Table 9.21 Population studies on pregnancy outcomes among cosmetologists

Reference, country and years of study	Number of exposed and non-exposed	Criteria for eligibility and comments	Parameters of relevance
Flaws et al. (2009) United States 2005-2008	350 Cosmetologists, 397 Other occupations	Controls: matched for similar educational levels, socioeconomic status, stress and workplace environments but not exposed to chemicals, 5 or fewer singleton pregnancies, and not missing data for any pregnancy.	Premature delivery LBW stillbirth
Herdt-Losavio et al. (2008) United States 1997-2003	73,607 Cosmetologists: 15,003 births 32,357 Realtors: 4246 births General population: 12,171 Births	Cohort study of cosmetologists living in New York State compared with realtor and general public referents matched to cosmetologists for singleton new-borns' names and address.	LBW Pre-term delivery SGA
Herdt-Losavio et al. (2011) United States 1997-2003	125 cases, 158 controls	Nested case control study. Cases and controls working at least 3 months before and during pregnancy with index child, exposures gauged by hours worked, types of applications, frequency of tasks. Various adjusted odds ratios calculated according to tasks undertaken.	LBW Pre-term delivery SGA
Halliday-Bell (2014) Finland 1990--2010	1841 Cosmetologists, 447004 women of the general population	All prima gravida subjects, on Finish Medical Birth Register	

Tables 9.22, 9.23 and 9.24 and Figures 9.13 and 9.14 demonstrate the risk of LBW outcomes among cosmetologists, the meta-analysis and the forest plots for both fixed effects model and random effect model.

Herdt-Losavio et al. (2008) produced a statistically significant adjusted odds ratio when cosmetologists were compared with realtors. (aOR 1.38, 95% CI 1.09-1.74). This was not sustained when the cosmetologists were compared with the general public (aOR 0.97, 95% CI 0.85-1.10).

The meta-analysis results were not statistically significant for the fixed or random models when cosmetologists were compared with controls as shown below.

Table 9.22 The risk of LBW outcomes among cosmetologists

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Flaws et al. (2009) United States 2005-2008	0.61 (0.29-1.27)	Maternal age, race, education level, cigarette smoking, alcohol	No increased risk for cosmetologists, smoking and alcohol use data during pregnancy were collected, data were self-reported, no exposure data, similar findings to Zhu et al. 2006
Herdt-Losavio et al. (2008) United States 1997-2003	Cosmetologist: vs. Realtors 1.38 (1.09-1.74) vs. General public 0.97 (0.85-1.10)	Race, ethnicity, education, income, prenatal care, tobacco, alcohol, drug use, medical risk factors, parity, pre-pregnancy weight, and height, and employment during pregnancy	Matched cases and referents, no exposure data, no maternal age available stronger effects/associations noted in non-whites for birth-weight when compared to realtor; this may be due to different products in use
Herdt-Losavio et al. (2011) United States 1997-2003	1.43 (0.82-2.49)	Year of birth, maternal age, race, ethnicity, government assistance smoking, alcohol and standing at work. Various adjusted odds ratios according to tasks undertaken	Cases and controls working at least 3 months before and during pregnancy with index child, exposures gauged by hours worked types of applications, frequency of tasks
Halliday-Bell (2014) Finland 1990-2010	1.08 (0.98-1.19)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

133

Table 9.23 Meta-analysis results for the risk of LBW outcomes among cosmetologists (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Flaws (2009)	0.61	0.29	1.28	0.20
Herdt-Losavio (2008)	1.38	1.09	1.74	1.98
Herdt-Losavio (2008)	0.97	0.85	1.10	6.51
Herdt-Losavio (2011)	1.43	0.82	2.49	0.35
Halliday-Bell (2014)	1.08	0.98	1.19	90.96
I-V pooled effect size	1.01	0.98	1.05	100.00

Heterogeneity chi squared =   10.47 (d.f. = 4) p = 0.033

 I squared (variation in ES attributable to heterogeneity) = 61.8%
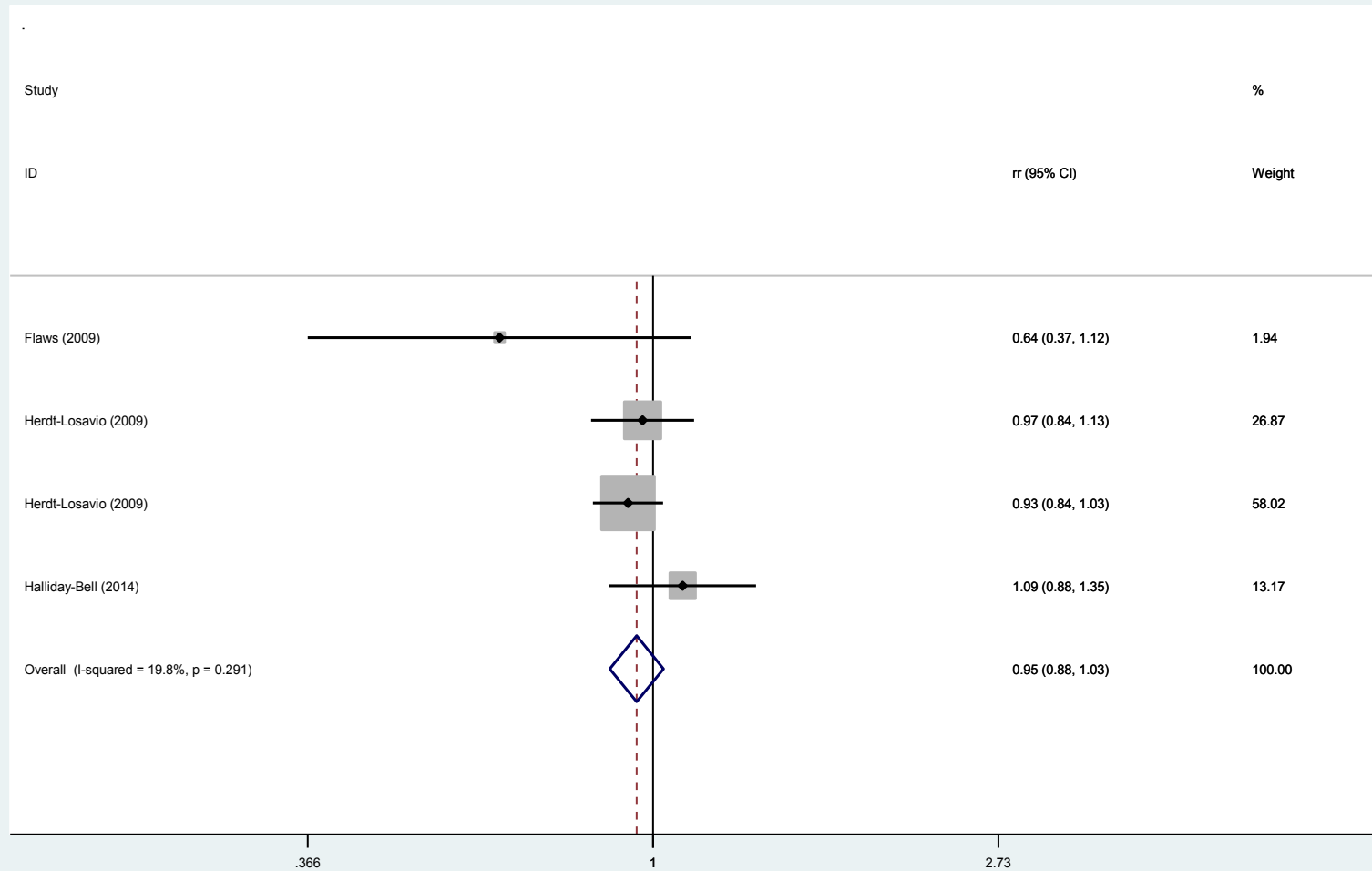
Test of ES=1 : z=   0.82 p = 0.414

Study		
ID	rr (95% CI)	% Weight
Flaws (2009)	0.61 (0.29, 1.28)	0.20
Herdt-Losavio (2008)	1.38 (1.09, 1.74)	1.98
Herdt-Losavio (2008)	0.97 (0.85, 1.10)	6.51
Herdt-Losavio (2010)	1.43 (0.82, 2.49)	0.35
Halliday-Bell (2014)	1.01 (0.98, 1.05)	90.96
Overall (I-squared = 61.8%, p = 0.033)	1.01 (0.98, 1.05)	100.00

.291   1   3.43
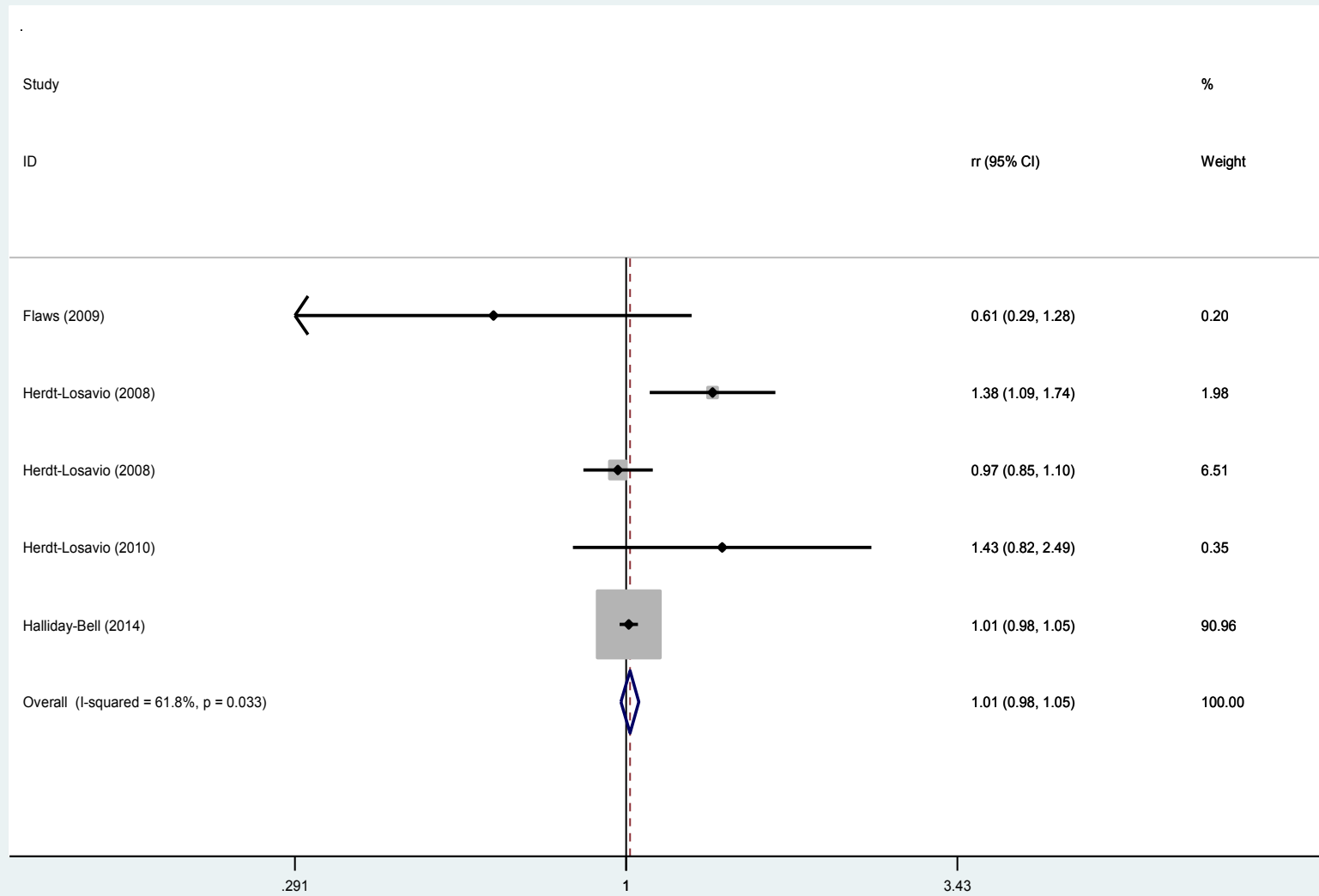
Figure 9.13 Forest Plot for the risk of LBW outcomes among cosmetologists (fixed effect model)

Table 9.24 Meta-analysis results for the risk of LBW outcomes among cosmetologists (random effect model)

Study	Effect Size		[95% Conf. Interval]	% Weight
Flaws (2009)	0.61	0.29	1.27	3.07
Herdt-Losavio (2008)	1.38	1.09	1.74	18.72
Herdt-Losavio (2008)	0.97	0.85	1.10	30.95
Herdt-Losavio (2011)	1.43	0.82	2.49	5.15
Halliday-Bell (2014)	1.08	0.98	1.19	42.10
D+L pooled effect size	1.06	0.93	1.21	100.00

Heterogeneity chi squared = 10.47 (d.f. = 4) p = 0.033

I squared (variation in ES attributable to heterogeneity) = 61.8%

Estimate of between study variance = 0.0108

Test of ES=1 : z= 0.85 p = 0.395

Study		
ID	rr (95% CI)	Weight
Flaws (2009)	0.61 (0.29, 1.28)	3.07
Herdt-Losavio (2008)	1.38 (1.09, 1.74)	18.72
Herdt-Losavio (2008)	0.97 (0.85, 1.10)	30.95
Herdt-Losavio (2010)	1.43 (0.82, 2.49)	5.15
Halliday-Bell (2014)	1.01 (0.98, 1.05)	42.10
Overall (I-squared = 61.8%, p = 0.033)	1.06 (0.93, 1.21)	100.00

NOTE: Weights are from random effects analysis

.291   1   3.43
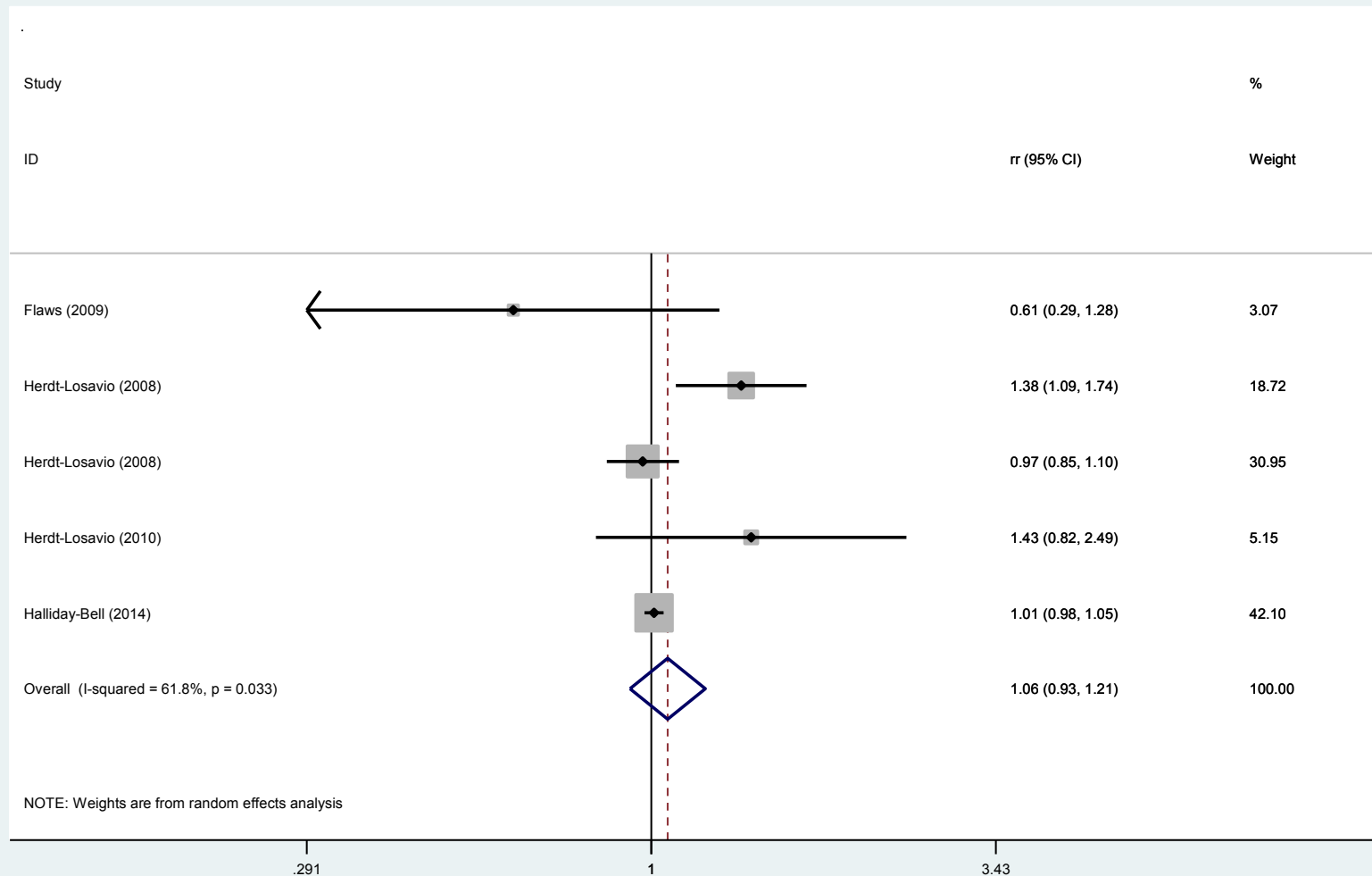
Figure 9.14 Forest Plot for the risk of LBW outcomes among cosmetologists (random effect model)

Tables 9.25, 9.26 and 9.27 and figures 9.15 and 9.16 summarise the results of the systematic review, meta-analysis and forest plots for the risk of pre-term delivery (PTD) amongst cosmetologists. None of the 4 studies revealed significant results in terms of the increased risk of PTD in cosmetologists, even though their roles often involve adopting awkward postures for relatively long periods of time. The pooled effect size was also not statistically significant.

Table 9.25.The risk of pre-term delivery among cosmetologists

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Flaws et al. (2009) Illinois United States 2005-2008	0.64 (0.37-1.13)	Maternal age, race, education level, cigarette smoking, alcohol	
Herdt-Losavio et al. (2008) New York United States 1997-2003	Cosmetologist: vs. Realtors: 0.97(0.83-1.12) vs. General public: 0.93(0.84-1.03)	Race, ethnicity, education, income, prenatal care, tobacco, alcohol, drug use, medical risk factors, parity, pre-pregnancy weight, and height, and employment during pregnancy	Matched cases and referents women aged 18-64, stronger effects/associations noted in non-white cosmetologists for birth-weight when compared to realtors this may be due to different products in use. No exposure data, no adjustment for maternal age.
Halliday-Bell (2014)	1.00 (0.93-1.09)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.26 Meta-analysis results for the risk of pre-term delivery among cosmetologists (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Flaws (2009)	0.64	0.37	1.12	1.94
Herdt-Losavio (2008)	0.97	0.84	1.13	26.87
Herdt-Losavio (2008)	0.93	0.84	1.03	58.02
Halliday-Bell (2014)	1.00	0.93	1.09	13.17
I-V pooled effect Size	0.95	0.882	1.03	100.00

Heterogeneity chi-squared = 3.74 (d.f. = 3) p = 0.29

I-squared (variation in effect size attributable to heterogeneity) = 19.8%

Test of effect size=1: z= 1.2 p = 0.230

Study		
ID	rr (95% CI)	Weight
Flaws (2009)	0.64 (0.37, 1.12)	1.94
Herdt-Losavio (2009)	0.97 (0.84, 1.13)	26.87
Herdt-Losavio (2009)	0.93 (0.84, 1.03)	58.02
Halliday-Bell (2014)	1.09 (0.88, 1.35)	13.17
Overall (I-squared = 19.8%, p = 0.291)	0.95 (0.88, 1.03)	100.00

.366   1   2.73

Figure 9.15 Forest Plot for the risk of pre-term delivery among cosmetologists (fixed effect model)

Table 9.27 Meta-analysis results for the risk of pre-term delivery among cosmetologists (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Flaws (2009)	0.64	0.37	1.12	2.85
Herdt-Losavio (2008)	0.97	0.84	1.13	30.10
Herdt-Losavio (2008)	0.93	0.84	1.03	50.05
Halliday-Bell (2014)	1.00	0.93	1.09	17.00
D+L pooled effect Size	0.97	0.90	1.05	100.00

Heterogeneity chi-squared = 3.74 (d.f. = 3) p = 0.29

I-squared (variation in effect size attributable to heterogeneity) = 19.8%

Estimate of between-study variance Tau-squared = 0.002

Test of effect size=1: z= 0.89 p = 0.371
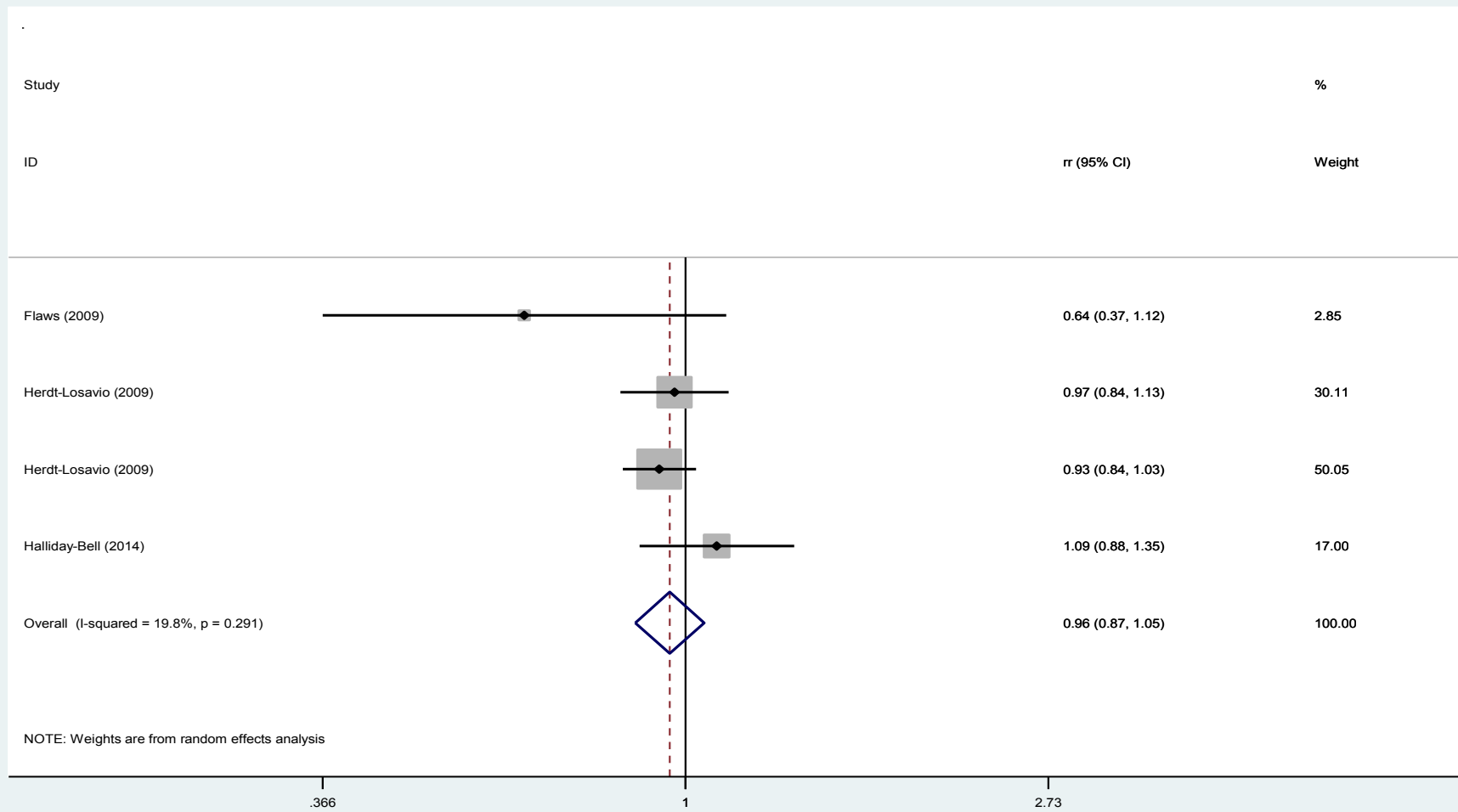
Figure 9.16. Forest Plot for the risk of pre-term delivery among cosmetologists (random effect model)

Tables 9.28, 9.29 and 9.30 and figures 9.17 and 9.18 summarise the results of the systematic review, meta-analysis and forest plots for the risk of SGA amongst cosmetologists. Only one other study was found to investigate this parameter. The study by Flaws et al. (2009) did not produce any statistically significant results for this parameter when cosmetologists were compared with controls (aOR 0.53, 95% CI 0.20801.348).

A meta-analysis combining the results of the Flaws (2009) study with this study (Halliday-Bell, 2014) did not produce any statistically significant findings for the fixed or random effect models.

Table 9.28 The risk of SGA among cosmetologists

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Herdt-Losavio et al. 2008 United States 1997-2003	Cosmetologists: vs. Realtors 1.10 (0.93-1.30) vs. General public 1.10 (0.99-1.22)	Race, ethnicity, education, income, prenatal care, tobacco, alcohol, drug use, medical risk factors, parity, pre-pregnancy weight, and height and employment during pregnancy.	Matched cases and referents, no exposure data, no maternal age available stronger effects/associations noted in non-white for birth-weight when compared to realtor this may be due to different products in use.
Halliday-Bell (2014)	0.98 (0.89-1.09)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	

Table 9.29 Meta-analysis results for the risk of SGA among cosmetologists (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Flaws (2009)	0.53	0.21	1.34	20.33
Halliday-Bell (2014)	0.98	0.89	1.09	79.67
I-V pooled effect Size	0.973	0.88	1.08	100.00

Heterogeneity chi-squared =   3.74 (d.f. = 3) p = 0.29

I-squared (variation in effect size attributable to heterogeneity) =   19.8%

Test of effect size=1: z= 1.2 p = 0.230

Study		
ID	rr (95% CI)	Weight
Flaws(2009)	0.53 (0.21, 1.35)	1.19
Halliday-Bell (2014)	0.98 (0.88, 1.09)	98.81
Overall (I-squared = 39.2%, p = 0.200)	0.97 (0.88, 1.08)	100.00

.208   1   4.8
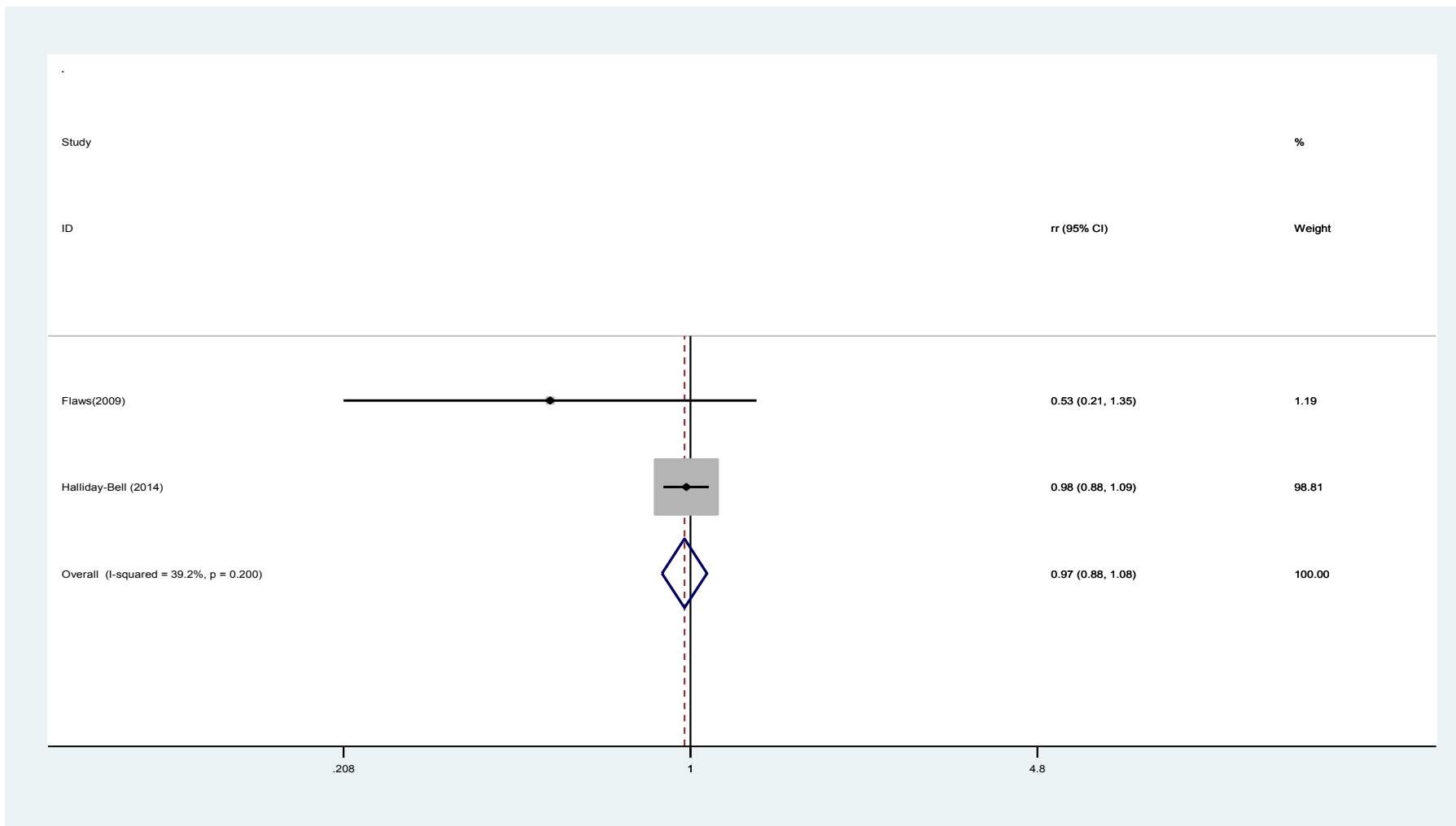
Figure 9.17 Forest Plot for the risk of SGA among cosmetologists (fixed effect model)

Table 9.30 Meta-analysis results for the risk of SGA among cosmetologists (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Flaws (2009)	0.53	0.21	1.34	20.33
Halliday-Bell (2014)	0.98	0.89	1.09	79.67
D+L pooled effect Size	0.87	0.533	1.41	100.00

Heterogeneity chi-squared = 1.65 (d.f. = 1) p = 0.20

I-squared (variation in effect size attributable to heterogeneity) = 39.2%

Estimate of between-study variance Tau-squared = 0.0741

Test of effect size=1: z= 0.59 p = 0.557
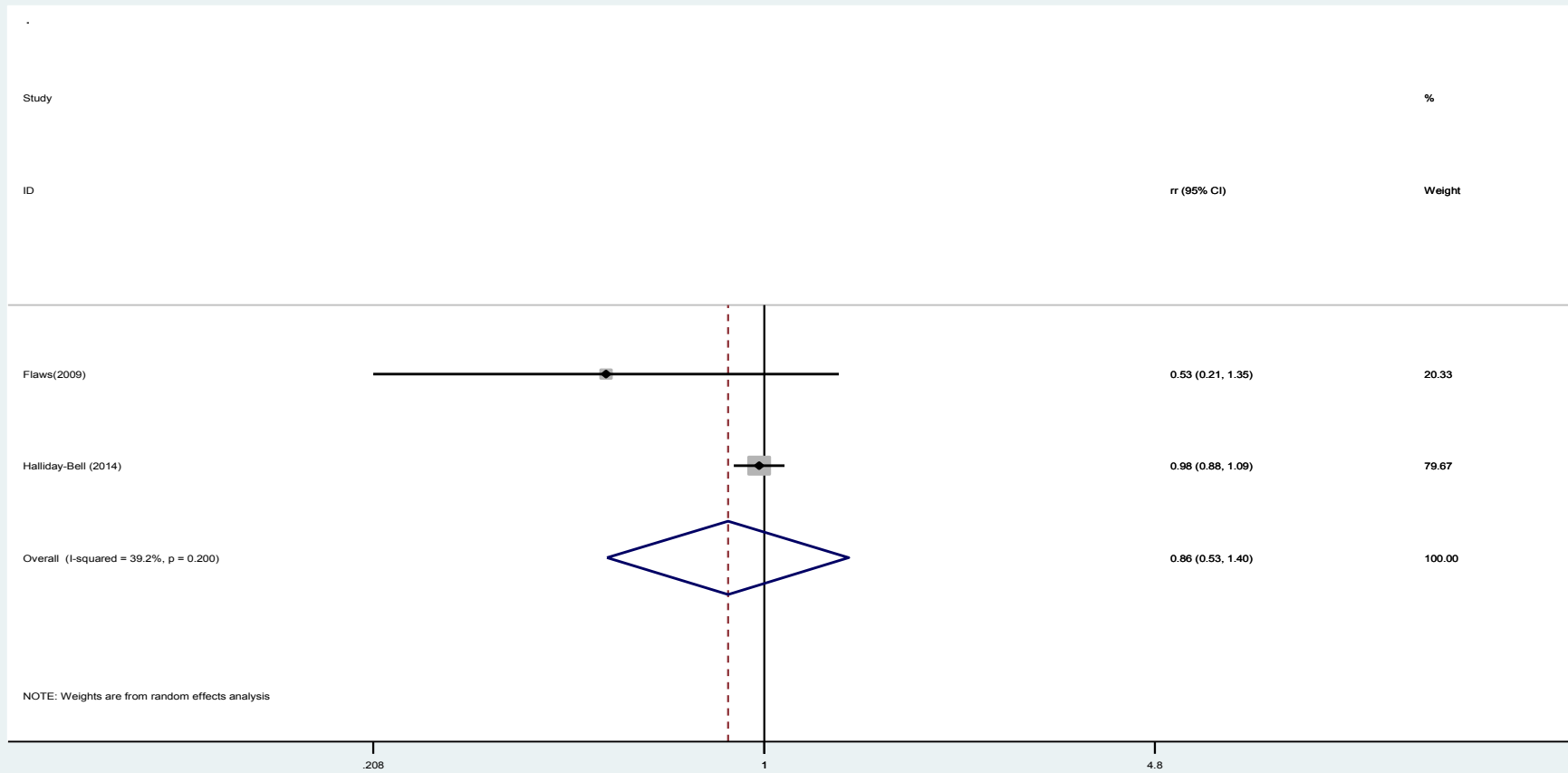
Figure 9.18 Forest Plot for the risk of SGA among cosmetologists (random effect model)

Table 9.31 summarises the results of the systematic review for the risk of stillbirth among cosmetologists.

One other study by Flaws et al. (2009) is presented with the results of this original study (Halliday-Bell 2014). This did not show significant increase in the adjusted odds ratio for the stillbirths among cosmetologists.

The data available did not allow a meta-analysis to be undertaken for the risk of stillbirth among cosmetologists.

Table 9.31 The risk of stillbirth among cosmetologists

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Flaws et al. (2009) United States 2005-2008	0.53 (0.17-1.1)	Maternal age, race, education level, cigarette smoking, alcohol	No increased risk for cosmetologist, data were self-reported no exposure data.
Halliday-Bell (2014) Finland 1990-2010	0.98 (0.88-1.08)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	General public controls were used for this analysis

Table 9.32 outlines the risk of END amongst cosmetologists. Only one other study was found to investigate this parameter. The study by Herdt-Losavio et al. (2008) did not produce any statistically significant results for this parameter when cosmetologists were compared with the realtors and the general public in two separate analyses (OR 1.10, 95% CI 0.93–1.30; 1.10, 95% CI 0.99–1.22).

The data did not allow for a meta-analysis to be undertaken for the risk of END among cosmetologists.

Table 9.32 The risk of early neonatal death amongst cosmetologists

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Herdt-Losavio et al. (2008) United States 2005-2008	Cosmetologists: vs Realtors 1.10 (95% CI 0.93–1.30); vs General public 1.10 (95% CI 0.99–1.22).	Maternal age, race, education level, cigarette smoking, alcohol	No increased risk for cosmetologist, data were self-reported no exposure data.
Halliday-Bell (2014) Finland 1990-2010	0.54 (0.29-1.01)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	General public controls were used for this analysis

9.4   Results for laboratory workers

Table 9.33 is a summary of the findings from 6 studies, which explored the pregnancy outcomes for laboratory workers. Of these, one study was smaller than others (Vergieva, 1998).

Taskinen et al. (1994) undertook a retrospective cohort study in Finland. Subjects were assigned occupational hygiene estimation for solvents (toluene, xylene or formalin) with exposure based on description of work tasks. The study looked at low birth weight for 500 women and found a decrease citing that the mother's employment in a laboratory was associated with lower birth weight of the child. Decrease of 133g (CI -246 to -20g). The findings were not cited as odds rations or risk ratios an d the data could not be included in the meta-analysis

Vergieva (1998) explored reproductive outcomes for women working as laboratory assistants and chemists in analytical and control laboratories in the petrochemical industry. The population was divided into a high exposure group and a low exposure group. Each participant completed a questionnaire and was interviewed on reproductive outcome. The researchers formed an impression on work exposure through short term dosimetry of what were deemed fairly homogenous working conditions. The researchers included 70 women in their study and considered pregnancies prior to starting work in the premises as those not exposed and for pregnancies that had occurred during employment as exposed. They found no difference in measured birth weight for exposed and non- exposed pregnancies. The cell sizes for this study were

small. The results were not cited as risk ratios or odds ratios and could not be included in the analysis.

Vergieva et al. (1998) undertook a study that included the administration of a questionnaire about the participants' experience of reproductive problems, working environment, work tasks and a visit to the workplace by the researchers where air monitoring was undertaken to determine whether there was relatively high or low exposure to hydrocarbons at work. They concluded that although there was no statistically significant increase in stillbirths or LBW infants, maternal exposure to aromatic hydrocarbons may represent a hazard to the developing foetus. Fertile women working in petrochemical laboratories should be informed of the risks of pregnancy and potentially require transfer to areas of work do not include exposure to benzene and other aromatic hydrocarbons.

Wennborg et al. (2000) examined reproduction outcomes of female laboratory personnel in Sweden from compared with in non-laboratory personnel. The individual woman constituted the primary sampling unit, with her pregnancies defined as the unit of analysis. They found no increase in LGA infants.

Wennborg et al. (2002) examined risk of high and LBW, and pre-term births and post-term births for laboratory workers compared to controls. A questionnaire investigation was used but no environmental hygiene measurements were made. The researchers concluded that exposure to laboratory work with solvents was associated with an increased risk of pre-term births and work with bacteria was associated with post-term births.

Wennborg et al. (2000) and Wennborg et al. (2002) explored a range of outcomes: pre-term delivery, LGA, SGA, and infant birth-weight and pre-term deliveries for workers based in biomedical laboratories. Exposures to biologicals, chemical and physical agents were assessed via questionnaire. Odds ratios were adjusted for confounders of mother's age, unsuccessful pregnancies ending in death of the foetus or neonate, smoking and gestational age. Adjusted odds ratios were presented for low and high birth weight, pre-term births, post-term births, SGA and LGA.

Zhu (2006) prospectively explored pre-term deliveries through a telephone questionnaire administered to 1025 laboratory workers compared to 8037 controls employed as teachers. These workers were based in hospitals, universities, medical industries and food industries. The questionnaire included items on laboratory work undertaken during pregnancy to allow calculation of an exposure index. The parameters of interest were preterm birth, low birth weight and gender of the new-born.

Table 9.33 Risk tables for laboratory workers

Reference, country and years of study	Number of cases and controls	Criteria for eligibility	Parameters of relevance
Frey (2007) Germany 1997-2002	444 lab technicians 603 office admin	Expected date of delivery between January 1997 and August 2003.	Stillbirth and pre-term delivery
Taskinen et al. (1994) Finland 1970-1987	500 laboratory workers All of general population	Retrospective case- referent study. Women from the payroll of state employed laboratory personnel, Finnish state- employed laboratory personnel, Finnish union of laboratory assistants and Register of Employees Occupationally Exposed to Carcinogens.	Birth-weight
Vergieva et al. (1998) Bulgaria 1996-1997	43 women in the lower exposure group, 27 in the higher exposure group	Women working as laboratory assistants and chemists in analytical and control laboratories in the petrochemical industry - questionnaire and interview on reproductive outcome.	Stillbirth, LBW
Wennborg et al.(2000) Sweden 1990-1994	419 laboratory workers 278 non laboratory	Cohort study of female laboratory workers exposed to organic solvents including chloroform.	Pre-term delivery, LGA, SGA
Wennborg et al.(2002) Sweden 1970-1989	2676 laboratory employees 1147 controls	Cohort study of university biomedical researcher in contact with solvents or bacteria. Controls were personnel from the Faculty of the Social Sciences and Natural Sciences. The period of employment was for at least one year.	Reproductive outcomes: birth-weight, pre-term deliveries,
Zhu et al. (2006) Denmark 1997-2003	1025 laboratory technicians 8037 teachers.	Pregnant laboratory technicians; who worked in laboratories of hospitals, universities, medical industry, food industry or public services	Pre-term birth
Halliday-Bell (2014) Finland 1990-2010	3587 laboratory workers 44 7007 General population	Prima gravida women on Finish Medical Birth Register	General public controls were used for this analysis

Tables 9.34, 9.35 and 9.36 and figures 9.19 and 9.20 present the meta-analysis and forest plots for ratio of male gender in laboratory workers. There were no statistically significant findings for pregnancy outcomes.

Table 9.34 Ratio of male gender among laboratory workers.

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Zhu (2006b)	1.00 (0.9-1.1)	Maternal age, previous adverse outcome of death, smoking	Study only took account of first birth in exposed employment
Halliday-Bell 2014	0.94 (0.84-1.06)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	General public controls were used for this analysis

Table 9.35 Meta-analysis results for the ratio of male gender among laboratory workers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		%Weight
Zhu (2006b)	1.00	0.9	1.1	57.33
Halliday-Bell (2014)	0.94	0.84	1.06	42.67
I-V pooled effect Size	0.974	0.90	1.05	100.00

Heterogeneity chi-squared =   0.62 (d.f. = 1) p = 0.43

I-squared (variation in effect size attributable to heterogeneity) = 0.0%
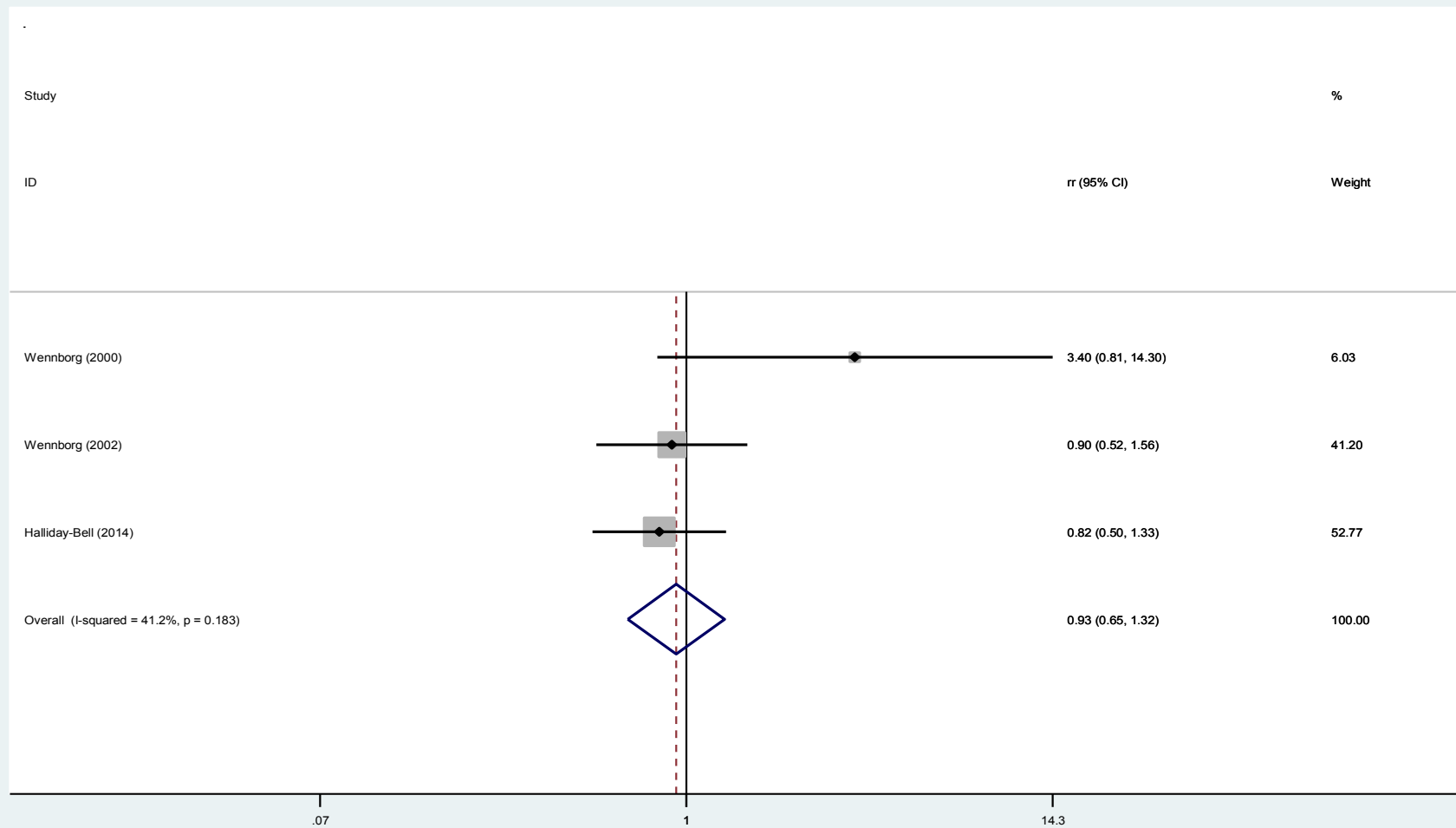
Test of effect size=1: z= 0.68 p = 0.50

Study			
ID		rr (95% CI)	Weight
Zhu (2006b)		1.00 (0.90, 1.11)	57.33
Halliday-Bell (2014)		0.94 (0.84, 1.06)	42.67
Overall (I-squared = 0.0%, p = 0.430)		0.97 (0.90, 1.05)	100.00

.837   1   1.2
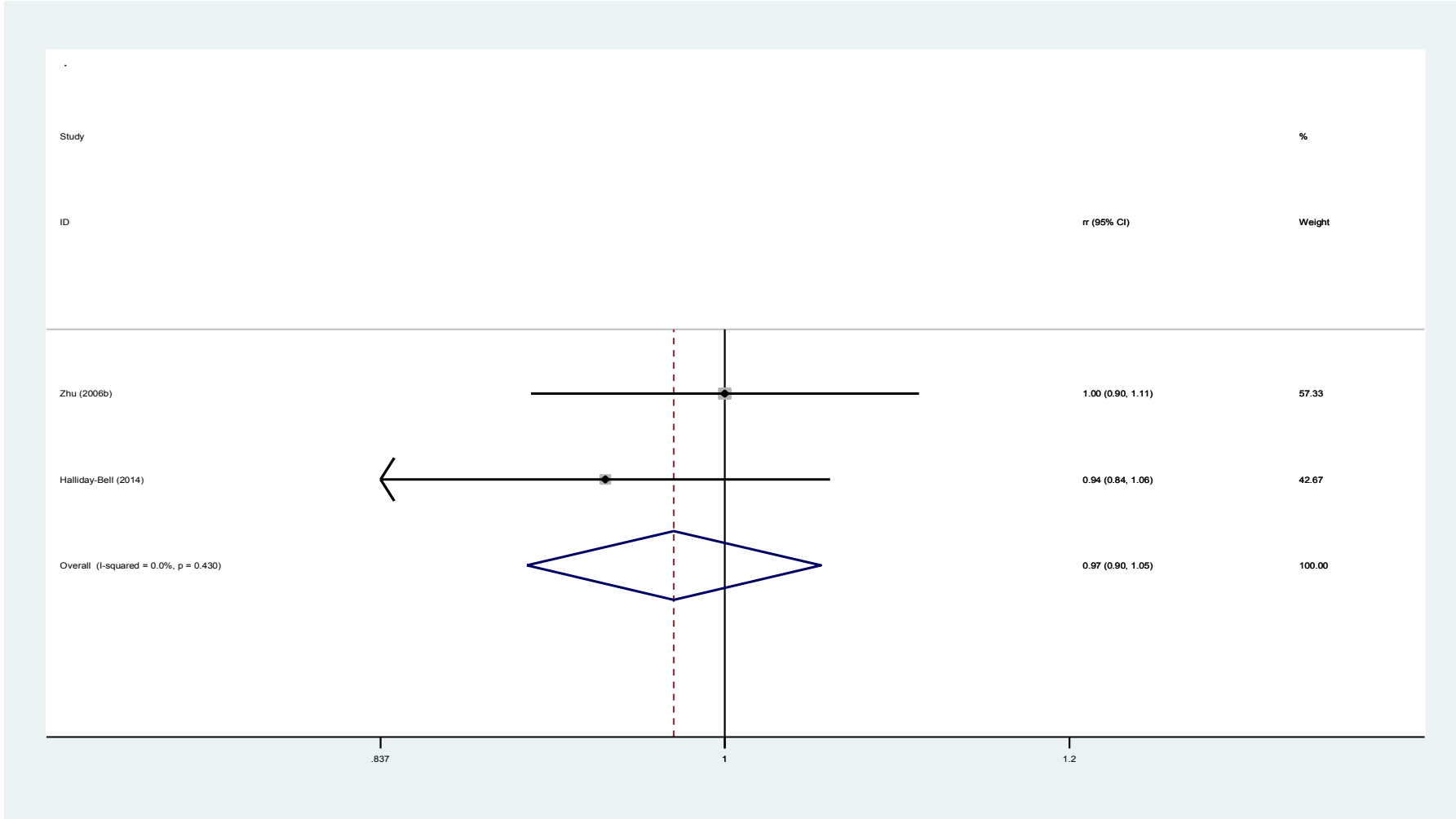
Figure 9.19 Forest Plot for the ratio of male gender among laboratory workers (fixed effect model)

Table 9.36 Meta-analysis results for the ratio of male gender among laboratory workers (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Zhu (2006b)	1.00	0.91	1.10	57.33
Halliday-Bell (2014)	0.94	0.84	1.05	42.67
I-V pooled effect Size	0.974	0.90	1.05	100.0

Heterogeneity chi-squared = 0.62 (D.F. = 1) p = 0.43

I-squared (variation in effect size attributable to heterogeneity) = 0.0%

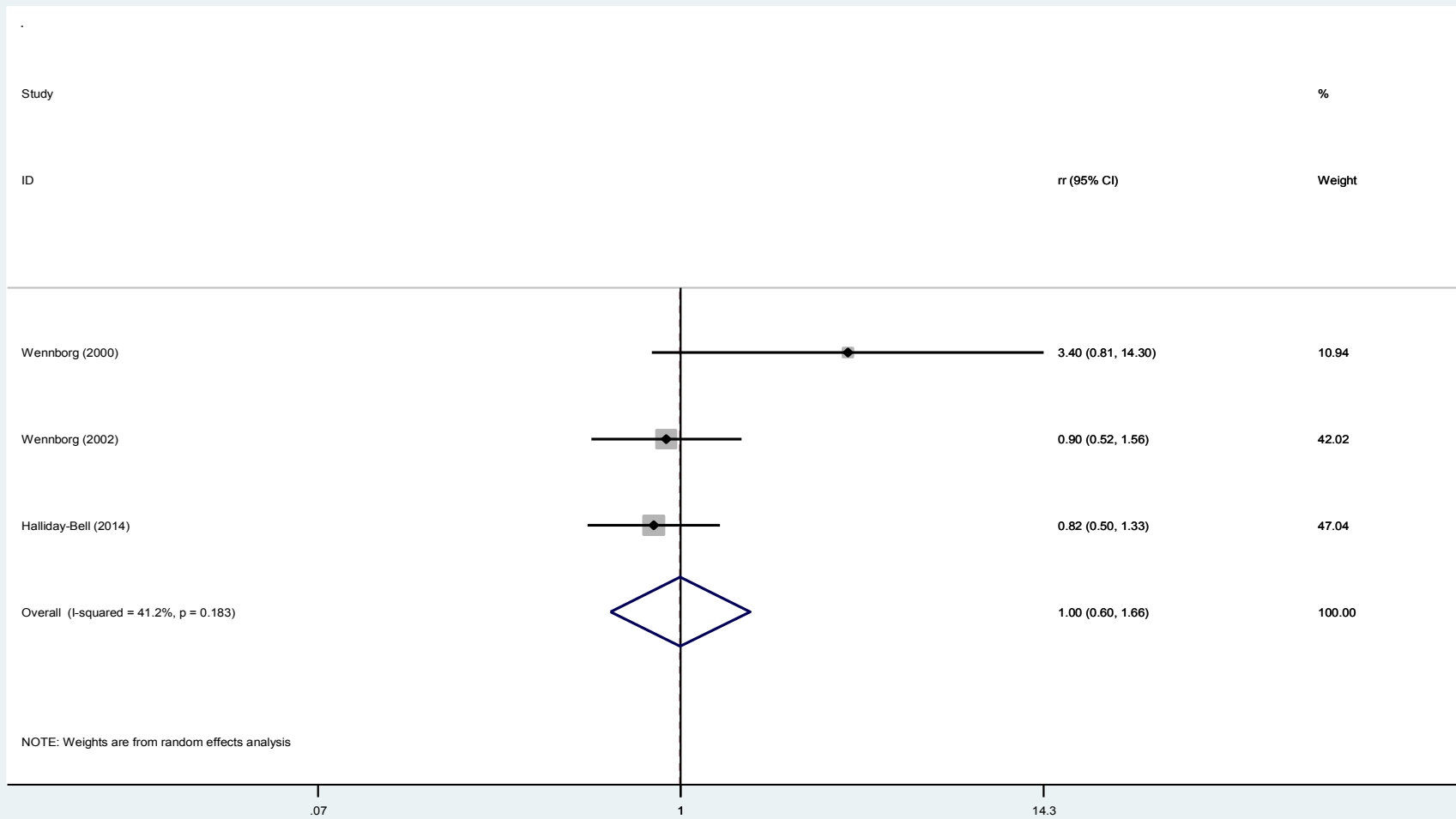Estimate of between study variance Tau-squared = 0.0

Test of effect size=1: z= 0.68 p = 0.50
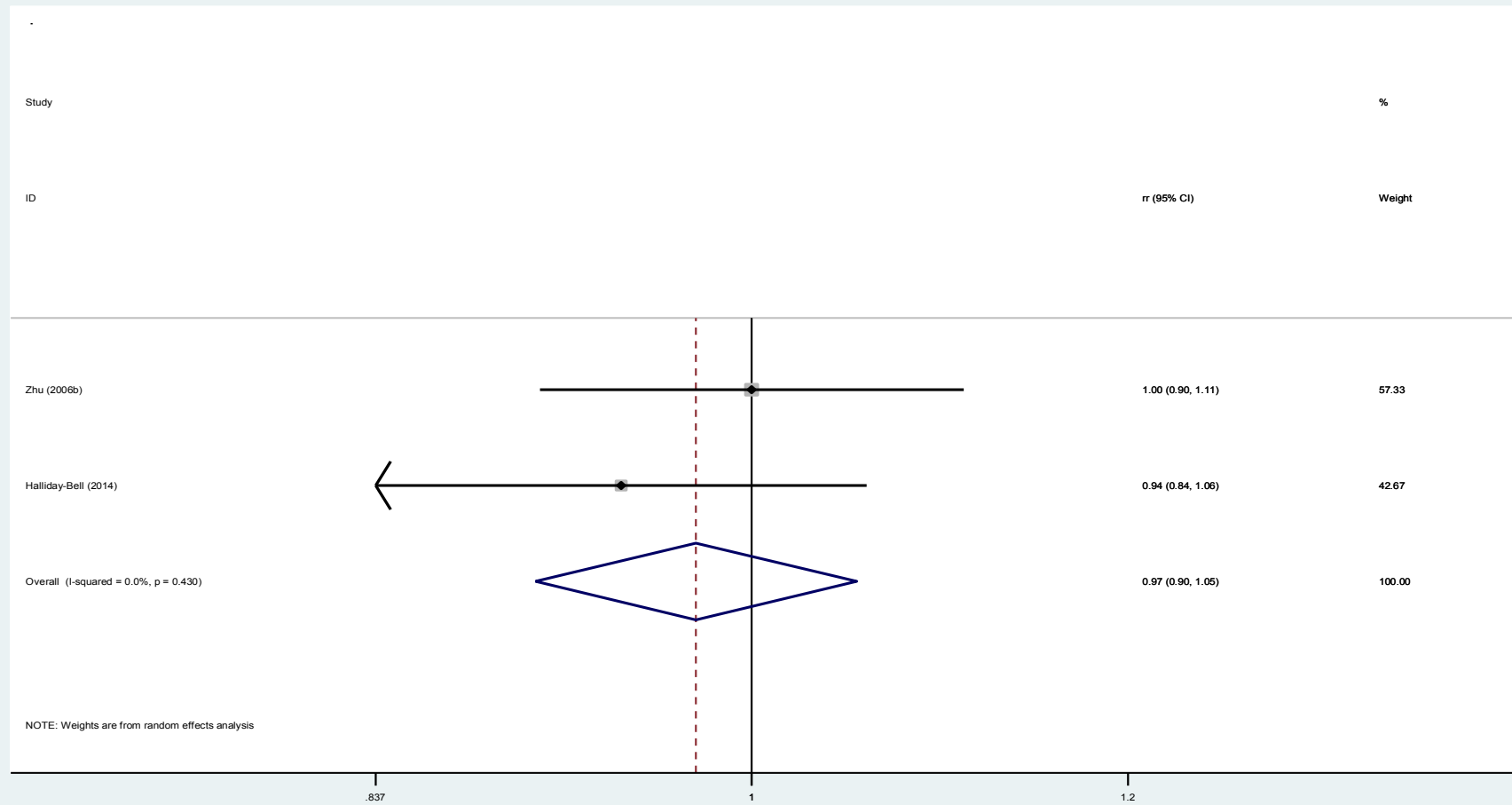
Figure 9.20 Forest Plot for the ratio of male gender among laboratory workers (random effect model)

Tables 9.37 present the odds ratios, meta-analyses and forest plots for findings from research papers that explored the risk of LBW among laboratory workers.

Two studies are displayed. The first (Taskinen, 1994) presents OR results with 95% confidence intervals, the second (Vergieva, 1998) presents ratios of the number of LBW cases between subject and the controls in a cross-sectional study.

Taskinen examined birth-weights of the children delivered by laboratory workers in a retrospective cohort study. The analysis of birth-weights involved 500 women who were referents rather than cases as the main focus of the study was on spontaneous abortions in this employment group.

Employment in the laboratory was associated with a reduced birth-weight of an average of 133g (95% CI -246–-20) this was statistically significant. The researchers also report that exposure for at least two days a week to xylene was associated with an increased birth-weight while exposure to ethyl acetate and metal compounds was associated with a decreased birth-weight, but none of these findings were statistically significant.

Vergieva et al. (1998) explored the effects of laboratory work via a study using retrospective information from workers in a petrochemical plant where exposure to aromatic hydrocarbons was evident. Chemical exposure was measured by short-term individual dosimetry that was undertaken by air sampling. The exposure data was applied to the retrospective information regarding pregnancy outcomes as the participants confirmed that the working environment had not changed over the relevant time period. The study only included those employed in the analytical and control laboratories. The results suggested that women who have higher levels of chemical exposure were at increased risk of LBW babies

compared to those who experienced lower levels of exposure (LBW cases 3/43 compared to 1/27). There was no publication of odds ratio or statistical significance calculations in the report for this study.

There was insufficient data to undertake meta-analysis or prepare forest plots for this parameter among laboratory workers.

Table 9.37 Risk of LBW among laboratory workers.

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Taskinen (1994) Finland 1970-1987	Minus 133 g; (95% CI – 246 to – 20 g)	Smoking, alcohol consumption and employment status	Exposure to xylene (max 2 days weekly) associated significantly with increased birth-weight– Odds ratios (not supplied).Boys weighed significantly more than girls +204 g, (95% CI +106 to +302 g)
Vergieva et al. (1998) Bulgaria 1996	**LBW** **=< 2500 g** Groups 1&2 (High level): Before Employment 1/43 During Employment 2/43 Groups 3 &4 (Low level): Before Employment 0/27, During Employment 1.3/27 **2501-3000g** Groups 1&2(High level): Before Employment 3/43 During Employment 5/43 Groups 3&4(Low level):Before Employment 2/27 During Employment 7/27	Maternal age	Cross- sectional study High and low level exposure categories. No association proved between for low level exposure, compared to the general population.
Wennborg et al. 2002 Sweden 1970-89	1.5 (95% CI 0.7,3.10)	Maternal age, previous adverse outcome of death, smoking	Only took account of first birth in exposed employment
Halliday-Bell 2014 Finland 1990-2010	1.01 (0.98-1.05)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	General public controls were used for this analysis

Table 9.38 is a summary of the findings from studies that examined LGA infants among laboratory workers. The same author conducted both parts of the study. Neither study revealed a statistically significant result. The meta-analysis revealed an I-V pooled effect size of 1.07 (95% CI 0.65 -1.32. The I squared (variation in ES attributable to heterogeneity) was 65.1%. The D+L pooled effect size was 0.996 (95% CI, 0.598-1.660).

Table 9.38 Results for the risk of LGA among laboratory workers

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Wennborg (2000)	3.4 (0.8-14.2) radio isotope work	Mother's age, smoking, spontaneous abortion, alcohol , stress and father's laboratory work	Not all data were provided in the paper. The adjustments were applied differently for the various parameters.
Wennborg (2002)	1.1 (0.3-4.0) solvent work	Mother's age, smoking death of foetus and father's laboratory work	Same study as above, different cohort
Halliday-Bell (2014)	1.03 (0,98-1.09)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	General public controls were used for this analysis

Table 9.39 Meta-analysis results for the risk of LGA among laboratory workers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Wennborg (2000)	3.4	0.81	14.30	6.03
Wennborg (2002)	0.9	0.52	1.56	41.20
Halliday-Bell (2014)	0.82	0.505	1.33	52.77
I-V pooled effect Size	0.928	0.652	1.321	100.00

Heterogeneity chi-squared =   3.40 (d.f. = 2) p = 0.183

I-squared (variation in effect size attributable to heterogeneity) =   41.2%

Test of effect size=1: z= 0.41 p = 0.679

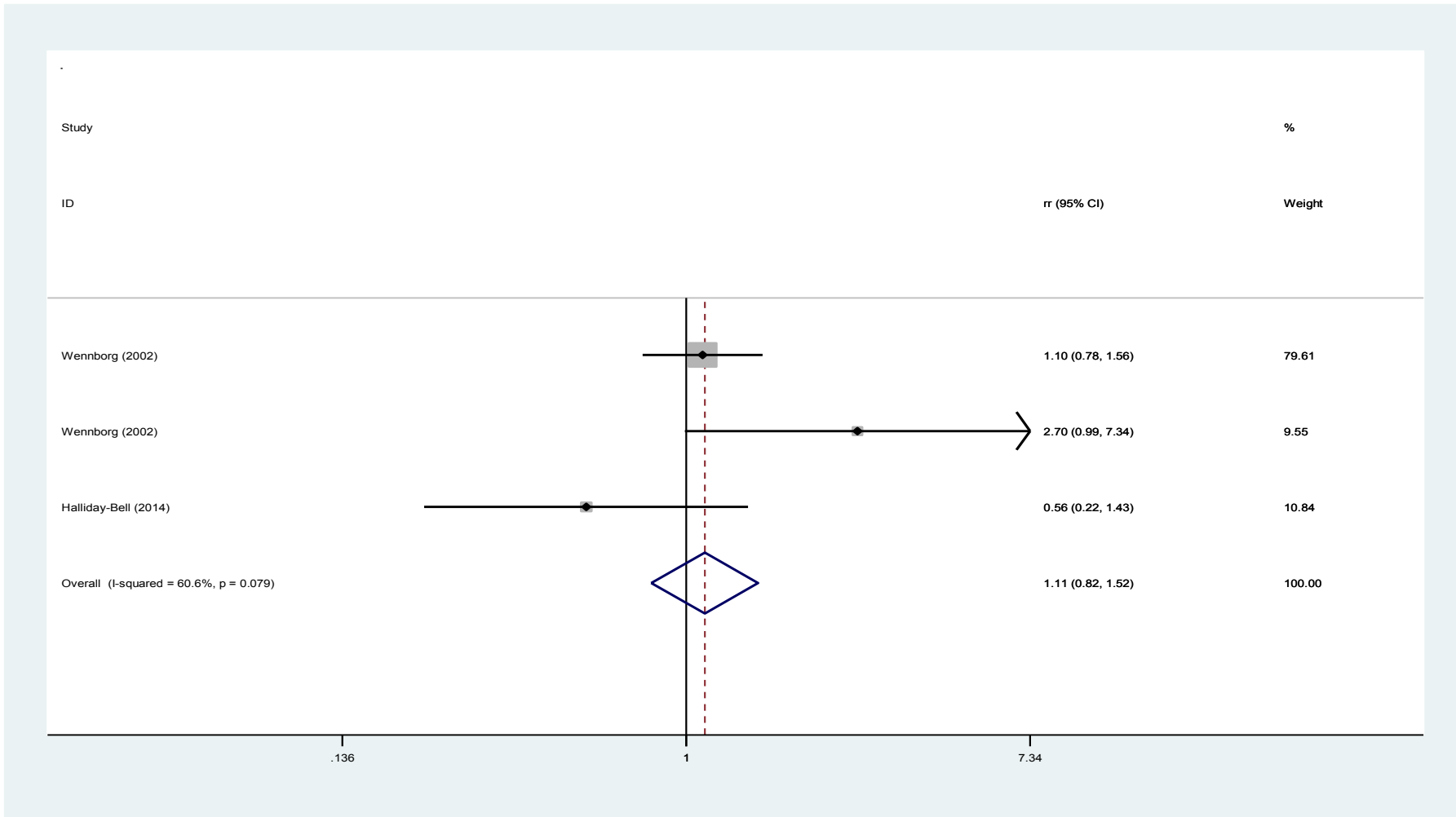| Study		
ID	rr (95% CI)	Weight
Wennborg (2000)	3.40 (0.81, 14.30)	6.03
Wennborg (2002)	0.90 (0.52, 1.56)	41.20
Halliday-Bell (2014)	0.82 (0.50, 1.33)	52.77
Overall (I-squared = 41.2%, p = 0.183)	0.93 (0.65, 1.32)	100.00

.07   1   14.3

Figure 9.21 forest plot for the risk of LGA among laboratory workers (fixed effect model)

Table 9.40 Meta-analysis results for the risk of LGA among laboratory workers (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Wennborg (2000)	3.40	0.81	14.30	10.94
Wennborg (2002)	0.90	0.52	1.56	42.02
Halliday-Bell (2014)	0.82	0.51	1.33	47.04
D+L pooled effect Size	0.996	0.598	1.660	100.00

Heterogeneity chi squared =   3.40 (d.f. = 2) p = 0.183

I squared (variation in ES attributable to heterogeneity) =41.2%

Estimate of between study variance Tau-squared = 0.083

Test of ES=1 : z=   0.01 p = 0.998

Study		
ID	rr (95% CI)	Weight
Wennborg (2000)	3.40 (0.81, 14.30)	10.94
Wennborg (2002)	0.90 (0.52, 1.56)	42.02
Halliday-Bell (2014)	0.82 (0.50, 1.33)	47.04
Overall (I-squared = 41.2%, p = 0.183)	1.00 (0.60, 1.66)	100.00

NOTE: Weights are from random effects analysis

.07   1   14.3

Figure 9.22 Forest Plot for the risk of LGA among laboratory workers (random effect model)

172

Tables 9.41, 9.42 and 9.43 and forest plots 9.23 and 9.24 present the risk ratios, meta-analyses and forest plots of pre-term delivery among laboratory workers. Four studies have covered this parameter. Two of the four studies (Wennborg, 2002 and Frey, et al. 2007) suggest that there were significant results for this parameter.

Wennborg et al. (2002) found an odds ratio for pre-term deliveries amongst laboratory workers. OR 2.5 (CI 1.0 to 6.4). More specifically, exposure to laboratory work with solvents was associated with an increased risk of pre-term deliveries, OR 3.4 (95% CI, 1.0-11.9).

The study by Frey (2007) revealed an adjusted relative risk that ranged between 0.6 (95% CI, 0.4-1.1) and 1.6 (95% CI, 0.5–2.0) for a range of chemicals that pregnant workers reported they had had contact with in their laboratories.

A statistically significant result for pre-term delivery (RR 2.5, 95% CI 1.0–6.4) was found in this study (Frey 2007) with increased maternal age and alcohol intake of one or more drinks per day. This result was therefore not directly related to occupational exposure but other non-occupational confounders.

The meta-analysis did not reveal any significant results for either the fixed or random models.

Table 9.41 The risk of pre-term delivery among laboratory workers

Author, Country, Year	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates (if any)	Comments
Frey et al. (2007) Germany 1997-2002	2.5 (1.0 to 6.4)		Maternal alcohol intake and maternal age for pre-term delivery increased the risk
Wennborg et al. (2000) Sweden 1990-1994	1.2, (0.5–2.7)	Mother's age smoking and father's laboratory work	Not all data were provided in the paper. The adjustments were applied differently for the various parameters.
Wennborg et al. (2002) Sweden 1970-1989	aOR 3.4 (95% confidence interval 1.0 - 11.9)	Maternal age, previous pregnancies not resulting in a live birth, smoking and gestational age	Exposure to laboratory work with solvents was associated with an increased risk of pre-term deliveries.
Zhu et al. (2006b) Denmark 1997-2003	Crude OR 2.2, (95% CI 0.8 to 6.2) for radioimmunoassay and OR = 1.9, (95% CI 0.8 to 4.6) for radio-labelling	None	Laboratory technicians working with radioimmunoassay and radiolabelling have an increase of pre-term delivery. The OR of pre-term delivery doubled for women working with these tasks every day or several times a week.
Halliday-Bell (2014) Finland 1990-2010	aOR 1.0 (95% OR,0.78-1.29)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	General public controls were used for this analysis

Table 9.42 . Meta-analysis results for the risk of pre-term delivery among laboratory workers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Frey (2007)	0.80	0.50	1.29	17.04
Wennborg (2000)	1.20	0.52	2.79	5.51
Wennborg (2002)	1.30	0.63	2.71	7.24
Zhu (2006b)	2.20	0.79	6.12	3.67
Zhu (2006b)	1.90	0.79	4.56	5.06
Halliday-Bell (2014)	1.00	0.778	1.29	61.48
I-V pooled effect Size	1.05	0.87	1.28	100.00

Heterogeneity chi squared =   5.55 (d.f. = 5) p = 0.352

I squared (variation in ES attributable to heterogeneity) = 9.9%

Test of ES=1 : z=   0.52 p = 0.602
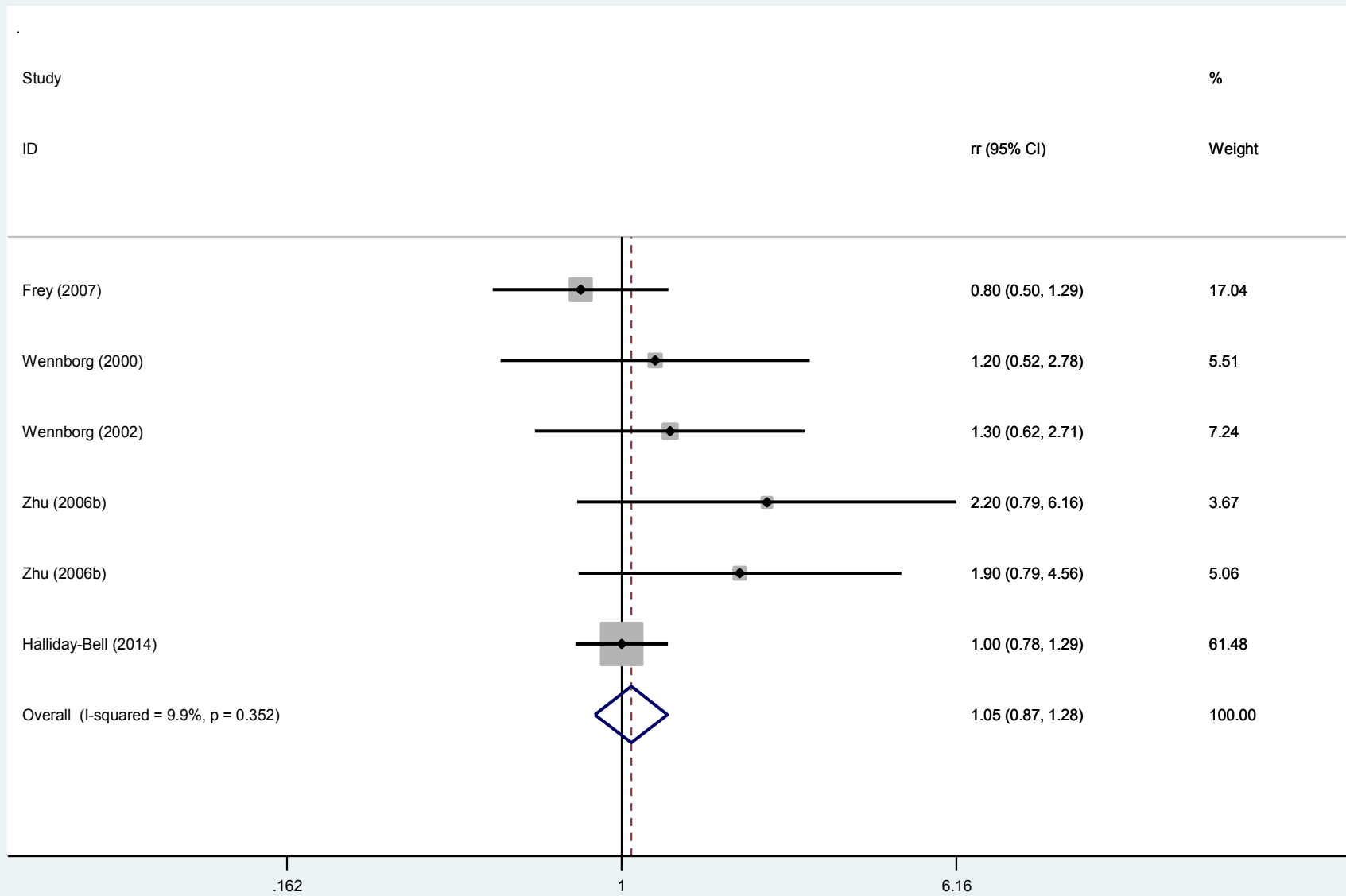
Figure 9.23 Forest Plot for the risk of pre-term delivery among laboratory workers (fixed effect model)

Table 9.43 . Meta-analysis results for the risk of pre-term delivery among laboratory workers (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Frey (2007)	0.80	0.50	1.29	36.47
Wennborg (2000)	1.20	0.52	2.79	16.24
Wennborg (2002)	1.30	0.63	2.71	20.29
Zhu (2006b)	2.20	0.79	6.20	11.71
Zhu (2006b)	1.90	0.79	4.56	15.30
D+L pooled effect Size	1.21	0.83	1.77	100.00

Heterogeneity chi squared =   5.14 (d.f. = 4) p = 0.273
I squared (variation in ES attributable to heterogeneity) = 22.2%

Estimate of between study variance = 0.0415

Test of ES=1 : z=   1.00 p = 0.317
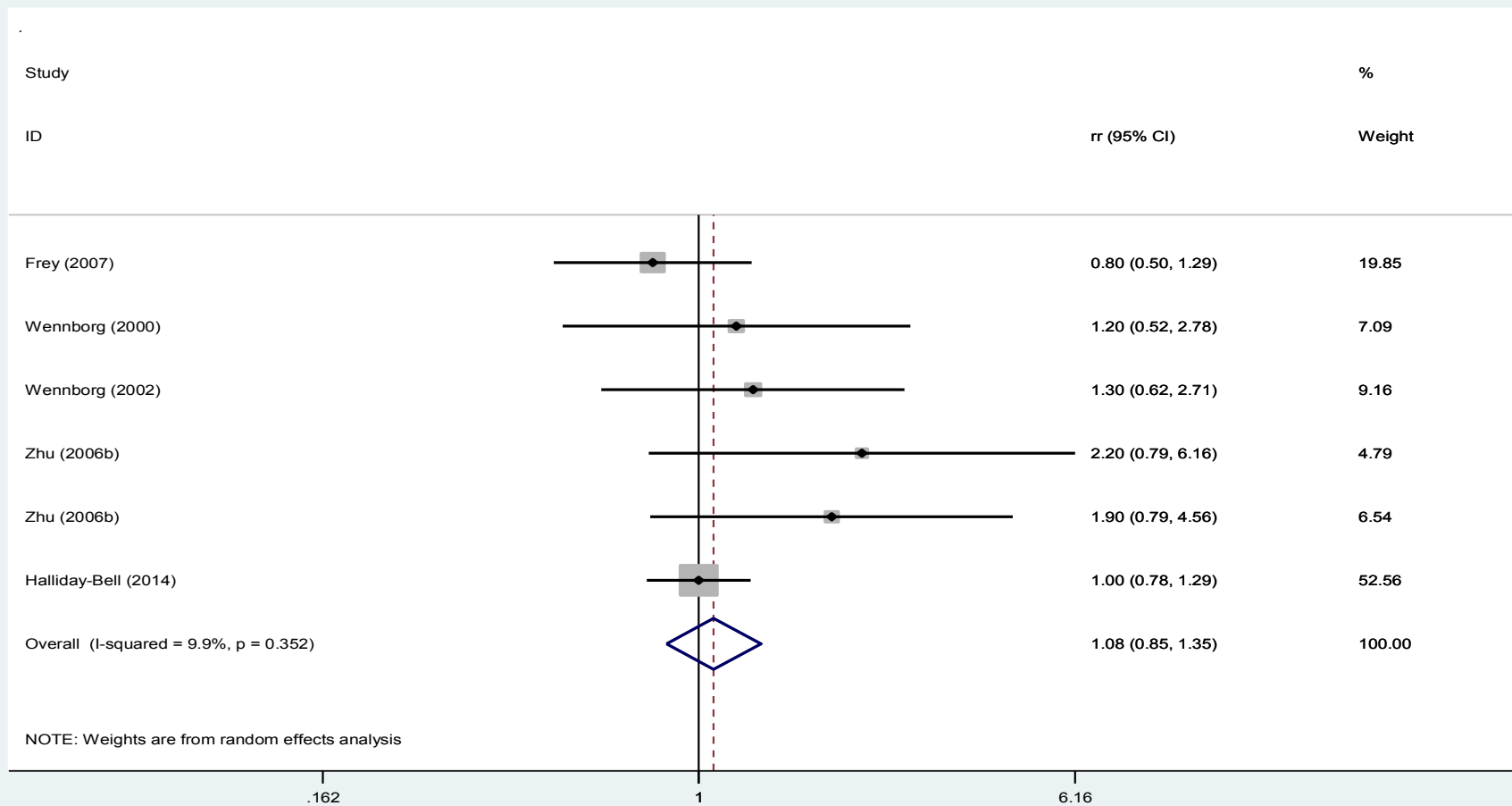
Figure 9.24 Forest Plot for the risk of pre-term delivery among laboratory workers (random effect model)

Tables 9.44, 9.45 and 9.46 and figures 9.25 and 9.26 present the results and meta-analysis for the risk post-term delivery among laboratory workers. One study (Wennborg et al., 2002) presented data on this topic and found an association with work with bacteria and post-term births (OR 2.7, 95% CI, 1.0-7.4). This was not statistically significant. The association with laboratory work in general did not have a statistically significant result for post-term delivery (OR 1.1, 95% CI 0.8-1.6).

The study observed gestation duration for various cohorts of laboratory workers. There were no other studies from the meta-analysis that recorded post-term births.

The meta-analysis did not yield any statistically significant findings.

Table 9.44 The risk post-term delivery among laboratory workers

Reference, country and years of study	Adjusted odds ratio/ crude odds ratio/ relative risk (95% Confidence intervals)	Adjustment covariates	Comments
Wennborg et al. (2002) Sweden 1970-1989	Work with bacteria: 2.7 (1.0-7.4)	Maternal age, previous pregnancies not resulting in a live birth, smoking and gestational age	Work with bacteria can interact on post-term births
Wennborg et al. (2002) Sweden 1970-1989	All lab workers: 1.1 (0.8-1.6)	Maternal age, previous pregnancies not resulting in a live birth, smoking and gestational age	In general, work in laboratories was not associated with an increased risk of post-term delivery
Halliday-Bell (2014) Finland 1990-2010	1 (0.78-1.29)	All prima gravida subjects, maternal age, marital status, socioeconomic status and smoking habit	General public controls were used for this analysis

Table 9.45 Meta-analysis results for the risk of post-term delivery among laboratory workers (fixed effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Wennborg (2002)	1.10	0.78	1.56	79.61
Wennborg (2002)	2.70	0.99	7.35	9.55
Halliday-Bell (2014)	0.56	0.219	1.43	10.84
I-V pooled effect Size	1.114	0.818	1.518	100.00

Heterogeneity chi squared = 5.07 (d.f. = 2) p = 0.079

I squared (variation in ES attributable to heterogeneity) = 60.6%

Test of ES=1 : z= 0.68 p = 0.494

Study		
ID	rr (95% CI)	Weight
Wennborg (2002)	1.10 (0.78, 1.56)	79.61
Wennborg (2002)	2.70 (0.99, 7.34)	9.55
Halliday-Bell (2014)	0.56 (0.22, 1.43)	10.84
Overall (I-squared = 60.6%, p = 0.079)	1.11 (0.82, 1.52)	100.00

.136   1   7.34

Figure 9.25 forest plot for the risk of post-term delivery among laboratory workers (fixed effect model)

Table 9.46 Meta-analysis results for the risk of post-term delivery among laboratory workers (random effect model)

Study	Effect Size	[95% Conf. Interval]		% Weight
Wennborg (2002)	1.10	0.78	1.56	47.98
Wennborg (2002)	2.70	0.99	7.35	25.15
Halliday-Bell (2014)	0.5	0.219	1.438	26.87
D+L pooled effect Size	1.15	0.58	2.28	100.00

Heterogeneity chi squared =   5.07 (d.f. = 2) p = 0.079

I squared (variation in ES attributable to heterogeneity) = 60.6%

Test of ES=1 : z=   0.40 p = 0.688
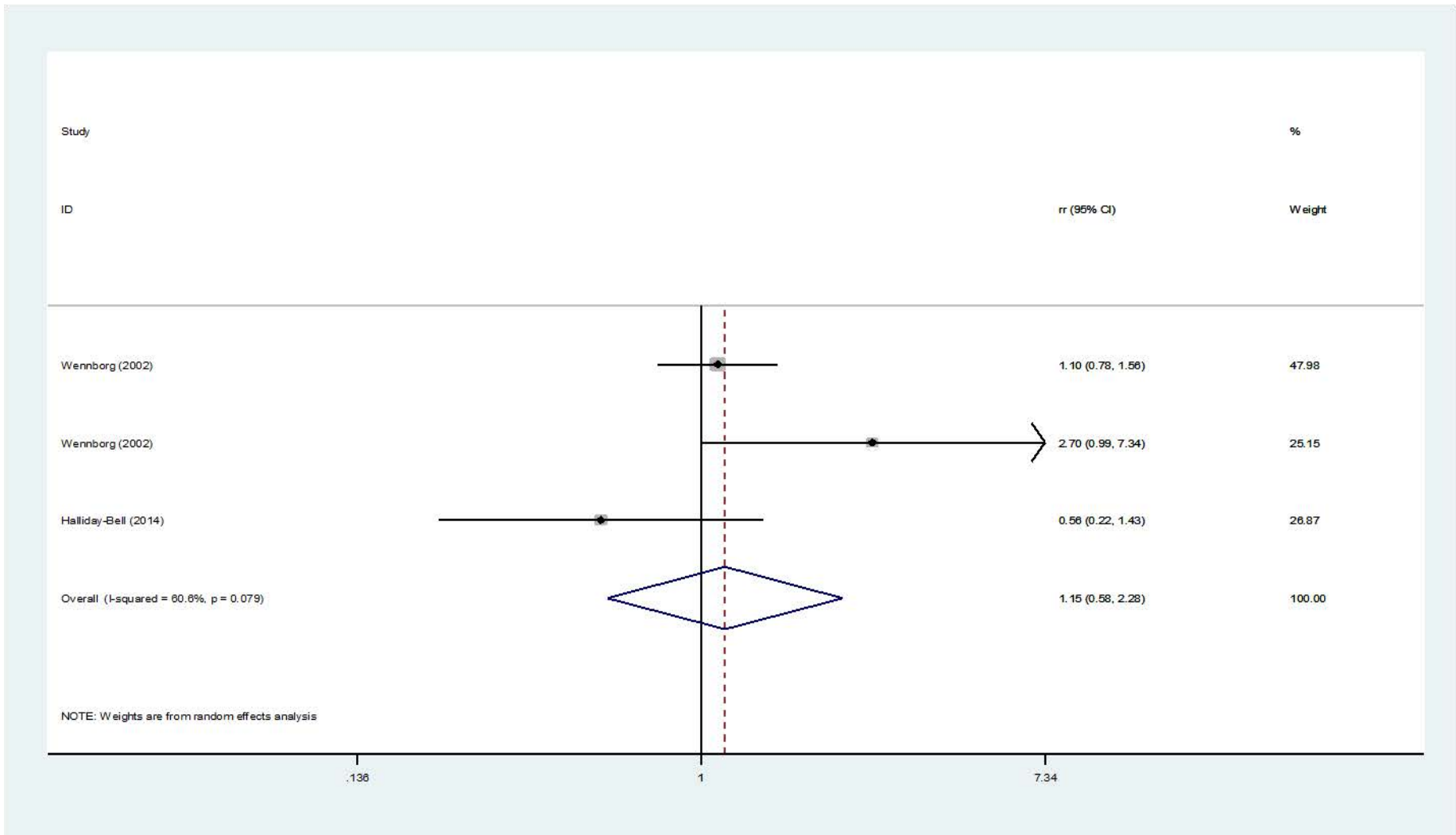
Figure 9.26 forest plot for the risk of post-term delivery among laboratory workers (random effect model)

9.5   Data from FMBR

The subject and control populations of infants born of prima gravida hairdressers, cosmetologists, laboratory workers, teachers, musicians and the 'others' made up of the general population from the FMBR 1990- 2010, were identified from the FMBR data for analysis.

Hairdressers were distinguishable in the FMBR by the ISCO code 5141. They numbered 12854. This code is also used to identify barbers and related professions. Cosmetologists were listed under code 5142. They numbered 1841.

Female laboratory workers in categories medical and pathology laboratory technicians were recorded with ISCO code 3212. They numbered 3587.

Teachers and musicians were considered a suitable reference group for assessing the effects of prenatal exposures at work.

In terms of control populations the teachers' who numbered 40405 were identified through a series of codes:

- 023 (teaching professionals)

- 0231 (university and higher education teachers)

- 0232 (vocational education teachers)

- 0233 (secondary education teachers)

- 0234 (primary school and early childhood teachers) and

- 0235 (other teaching professionals).

Musicians were coded 2652. They numbered 1968. 'Others' were the third control group. This consisted prima gravida women of the general public whose codes were not included in the above categories. They totalled 447004. This included

unemployed women, students, homemakers and those engaged in other employment.

Table 8.47 shows the characteristics of the number of singleton prima gravida births among the different occupations in the groups under observation (hairdressers, cosmetologists and laboratory workers) and the number for the control populations (teachers, musicians and others). The characteristics include sex or gender of the infants, marital status of the mother, the smoking status of the mother, maternal age and socioeconomic status. For each of the figures presented, the percentage is calculated highlighting the proportion that each occupation contributed to the total number for each of the categories within the characteristics shown.

The key criteria refer to the occupational designations as well as to the different reproductive outcomes, pre-term birth (less than 37 completed weeks of gestation), stillbirth (an infant born with no signs of life at or after 28 weeks' gestation), END (death of live born infant occurring less than 7 completed days from the time of birth), LBW (LBW < 2500g), HBW (HBW >4000g), SGA infants are those whose size is below the 10th percentile for the infant's sex and gestational age, LGA infants whose size is above the 90th percentile for gender and gestational age.

Other researchers have established that hairdressers come into contact with various chemicals found in hair care products for washing, dyeing, bleaching, styling, conditioning, perming etc. Exposure to these agents has been recognised to lead to skin and respiratory ill health and effects of LBW, SGA and PTD have been suggested in previous research (Labreche et al. 2003, Leino et al. 1999, van Muiswinkel et al. 1997 and Flaws et al. 2009). Exposure risk has depended

on the tasks undertaken, use of ventilation, use of personal protective equipment, and redeployment of the worker to alternative duties (Leino 1999).

Along with chemical risks, other workplace factors have the potential to impact on reproduction. Psychosocial and ergonomic factors appear to have an impact on the wellbeing of a pregnant worker (Cassidy 2009, Hickey et al. 1995, Ronda et al. 2009, Wahlstrom et al. 2010).

Kersemaekers et al. (1997) undertook an epidemiological study of 9,000 hairdressers and compared them to 9,000 clothing sales clerks to determine whether exposure to chemicals used in hair products impacted on risk of reproductive disorders. They concluded that there was evidence of a heightened risk of LBW infants in the earlier of two time periods (1986-1988 compared to 1991-1993). They also suggested that the risk had declined with time due to improvement to the system of work. A systematic review highlighted that other studies of hairdressers have shown inconsistent results, which may be due to methodological weaknesses and small sample size (Peters et al., (2010).

In combination with exposure to chemical agents, work as a hairdresser consists of extended periods of standing, repeated bending, awkward postures (McDonald, 1998; van Muiswinkel, 2000) and work-related stress (Hjollund 1999). These factors can be hazardous for reproduction.

The effects of maternal parity have not been discussed in detail here but are referred to elsewhere among the research literature on confounders. Essentially, confounders are important if their strength of association with the factor of primary interest is high and if the prevalence of the particular confounder among the subject or referent populations is high. It is noted for the characteristics of the study population that more of the teachers were married (85%) compared to

hairdressers (57 %), cosmetologists (62%) and laboratory workers (66%). Some of each group were cohabiting and a few were noted as single (hairdressers and cosmetologists, 11.0 %, laboratory workers 8% and teachers 4%)

Comparable with hairdressers' research, literature has highlighted not only the potential for chemicals to cause general health effects but also a possible impact on pregnancy outcome (Gallicchio, 2011; Herdt-Losavio et al., 2008; Herdt-Losavio et al., 2009; Herdt-Losavio et al., 2011; John et al., 1994 and Peretz et al., 2009).

Some cohort and case control studies have been used to observe the impact of cosmetology on of a variety of outcomes taking into account potential confounders and wherever possible gathering detailed exposure information about work environment and frequency of certain occupational tasks and the number of hours worked per week (John et al. 1994, Flaws et al. 2009, Gallicchio et al. 2011).

Table 9.47 shows the characteristics of the number of singleton prima gravida births among the different occupations in the groups under observation (hairdressers, cosmetologists and laboratory workers) and the number for the control populations (teachers, musicians and others). The characteristics include sex or gender of the infants, marital status of the mother, the smoking status of the mother, maternal age and gender. For each of the figures presented, the percentage is calculated highlighting the proportion that each occupation contributed to the total number for each of the categories within the characteristics shown.

The key criteria refer to the occupational designations as well as to the different reproductive outcomes, pre-term birth (less than 37 completed weeks of

gestation), stillbirth (an infant born with no signs of life at or after 28 weeks' gestation), END (death of live born infant occurring less than 7 completed days from the time of birth), LBW (LBW < 2500g), HBW (HBW >4000g), SGA infants are those whose size is below the 10th percentile for the infant's sex and gestational age, LGA infants whose size is above the 90th percentile for sex and gestational age).

Table 9.47 Characteristics of the study population of infants born of prima gravida hairdressers, cosmetologists, laboratory workers, teachers, musicians and the 'others' made up of the general population from the FMBR 1990- 2010.

Occupation	Hairdressers n (%)	Cosmetologists n (%)	Laboratory workers n (%)	Teachers n (%)	Musicians n (%)	Others inc. missing n (%)	Total n (%)
Infants born	12854 (2.5)	1841 (0.4)	3587 (0.7)	40405 (8)	1968 (0.4)	447004(88.1)	507659 (100.0)
Sex							
Boy	6652(51.8)	1640 (50.1)	1840 (51.3)	20610 (51.0)_	1042 (52.9)	228753 (51.2)	259819 (51.2)
Girl	6202(48.2)	919 (49.9)	1747 (48.7)	19795 (49.0)	926 (47.1)	218241 (48.8)	247830 (48.8)
Marital status							
Married	5316 (1.1)	846 (0.2)	2006 (0.4)	25242 (5.0)	1292 (0.3)	217597(43.0)	252299 (49.9)
Cohabiting	5722 (1.1)	699 (0.1)	1180 (0.2)	11348 (2)	494 (0.1)	164852 (32.6)	184295 (36.5)
Single, divorced widowed	1784 (0.4)	292(0.1)	390 (0.1)	3675 (0.7)	177(0.0)	62677 (12.4)	68995 (13.6)
Total	12822 (2.5)	1837 (0.4)	3576 (0.7)	40265 (8.0)	1963	445126 (88.0)	505589 (100.0)
Smoking							
No	9774 (2.0)	1517 (0.3)	3091 (0.6)	35753 (7.2)	1816(0.4)	357473 (71.9)	409424 (82.4)
Stopped after 1st trimester	710 (0.1)	73(0.0)	94(0.0)	783(0.2)	33(0.0)	16972 (3.4)	18665 (3.8)
Yes, beyond 1st trimester	2118 (0.4)	206(0.1)	348(0.1)	3163(0.6)	79(0.0)	63076 (12.7)	68990 (13.9)
Total	12602 (2.5)	1796 (0.4)	3533 (0.7)	39699 (8.0)	1928(0.4%)	437521(88.0)	497079 (100.0)
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Maternal age group							
<20	376 (0.1)	31 (0.0)	27 (0.0)	627 (0.1)	2 (0.0)	29161 (5.7)	30224 (6.0)
21-25	4844 (1.0)	573 (0.1)	547 (0.1)	4964 (1.0)	137 (0.0)	120944 (23.8)	13200 (26.0)
26-30	4908 (1.0)	766 (0.2)	1645 (0.3)	17886 (3.5)	892 (0.2)	167110 (32.9)	193207(38.1)
31-35	2066 (0.4)	345 (0.1)	1014 (0.2)	12214 (2.4)	611 (0.1)	93894 (18.5)	110144 (21.7)
36-40	564 (0.1)	111 (0.0)	303 (0.1)	3903 (0.8)	269 (0.1)	30001(5.9)	35151 (6.9)
41-45	94 (0.0)	14 (0.0)	50 (0.0)	781 (0.2)	55 (0.0)	5675 (1.1)	6669 (1.3)
46-50	2 (0.0)	1 (0.0)	1 (0.0)	30 (0.0)	2 (0.0)	214 (0.0)	250 (0.0)
>51	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (0.0)	5 (0.0)
Total	12854 (2.5)	1841 (0.4)	3587 (0.7)	40405 (8.0)	1968 (0.4)	447004 (88.1)	507659(100)

Table 9.47 continued

Occupation	Hairdressers n (%)	Cosmetologists n (%)	Laboratory workers n (%)	Teachers n (%)	Musicians n (%)	Others inc. missing n (%)	Total n (%)
Socioeconomic status							
3	0 (0)	0	387 (10.8)	26181 (64.8)	600 (30.6)	42634 (9.5)	74613 (14.7)
4	14(0.11)	1 (0.5)	3033 (84.5)	5956 (14.7)	1362(69.1)	206952 (46.)	218456 (43)
5	12836 (1.0)	1839 (99)	161 (4.5)	8249 (20.5)	0	71356 (16.0)	89254 (17.6)
Not known		1 (0.5)	6 (0.2)	0	6 (0.3)	40685 (9.1)	275386 (54.2)
Other	4 (0.3)			19 (0.05)		85377 (19.1)	84862(16.7)
Total	12854	1841	3587	40405	1968	447004	507659
	100%	100%	100%	100%	100%	100%	100%

Table 9.48 demonstrates the results of the binary logistic regression analysis of pregnancy outcomes for hairdressers when compared to control population of teachers. Adjustments were made for maternal age, maternal smoking, socioeconomic status and marital status.

Among the various parameters, none of the crude odds ratios were statistically significant. Review of the adjusted odds ratios was undertaken. The adjusted odds ratios indicate that most of the parameters did not show a statistically significant difference compared to the control population of teachers except the male to female gender ratio parameter which demonstrated an adjusted odds ratio 0.92 (95% CI 0.87, 0.98). This suggests that there were fewer deliveries of male infants among hairdressers than among teachers.

Table 9.48 Pregnancy outcomes for hairdressers (12854) vs. teachers as control population (n= 40405)

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	0.99 (0.98 to 1.00)	0.92(0.87 to 0.98)
LBW (<2500g)	1.00 (0.97 to 1.04)	0.99 (0.89 to 1.11)
HBW (>4200g)	1.03 (0.98 to 1.08)	0.98 (0.83 to 1.16)
SGA [a]	1.01 (0.97 to 1.05)	0.96 (0.85 to 1.10)
LGA	1.02 (0.97 to 1.08)	0.96 (0.80 to 1.14)
Pre-term (<37 weeks)	1.00 (0.97 to 1.04)	0.99 (0.90 to 1.09)
Post-term delivery (>42 weeks)	1.09 (0.96 to 1.20)	0.68 (0.45 to 1.02)
Stillbirth	1.00 (0.89 to 1.13)	1.03 (0.70 to 1.51)
Early neo-natal death (7 days)[d]	1.20 (0.98 to 1.47)	0.67 (0.34 to 1.35)

[a] **SGA**: Weight is below the 10th percentile at gestational age
[b] **LGA**: Weight is above the 90th percentile at gestational age
[c] **Stillbirth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth-weight of 500g or more.
[d] **END**: All neonates born live that subsequently die within first 7 days

Table 9.49 outlines the binary logistic regression analysis crude odds ratios and adjusted odds ratios for pregnancy outcomes among cosmetologists compared to the control group of teachers. The adjusted odds ratio for the risk of post-term delivery greater than 42 weeks was a significant result 2.13 (95% CI 1.04 to 4.35). None of the other crude or adjusted odds ratios demonstrated significant results for pregnancy outcomes among cosmetologists compared to teachers.

Table 9.49. Pregnancy outcomes for Cosmetologists (1640) vs. Teachers as control population (n= 40405)

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	1.02 (0.97 to 1.07)	0.99 (0.94 to 1.04)
LBW (<2500g)	1.01 (0.89 to 1.13)	1.13 (0.99 to 1.29)
HBW (>4200g)	1.09 (0.91 to 1.32)	1.14 (0.93 to 1.40)
SGA[a]	1.00 (0.87 to 1.15)	1.12 (0.96 to 1.31)
LGA[b]	0.99 (0.82 to 1.19)	1.14 (0.93 to 1.40)
Pre-term (<37 weeks)	1.02 (0.92 to 1.13)	1.11 (0.99 to 1.25)
Post-term delivery (>42 weeks)	1.12 (0.72 to 1.75)	2.13 (1.04 to 4.35)
Stillbirth	0.87 (0.61 to 1.24)	1.05 (0.69 to 1.60)
Early neo-natal death (7 days)	0.86 (0.52 to 1.43)	1.09 (0.62 to 1.89)

[a] **SGA**: Weight is below the 10th percentile at gestational age
[b] **LGA**: Weight is above the 90th percentile at gestational age
[c] **Stillbirth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth-weight of 500g or more.
[d] **END**: All neonates born live that subsequently die within first 7 days

Table 9.50 outlines the binomial logistic regression crude odds ratios and adjusted odds ratios for pregnancy outcomes among laboratory workers compared to the control group of teachers. None of the crude or adjusted odds ratios demonstrated significant increases in the pregnancy outcomes among laboratory workers compared to teachers.

Table 9.50 . Pregnancy outcome Laboratory workers (n=3586) vs. Teachers as control population (n= 40405)

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	0.99 (0.92 to 1.06)	0.98 (0.91 to 1.06)
LBW (<2500g)	0.96 (0.81 to 1.14)	0.93 (0.76 to 1.12)
HBW (>4200g)	1.30 (0.98 to 1.73)	1.23 (0.90 to 1.69)
SGA[a]	1.01 (0.82 to 1.23)	0.99 (0.79 to 1.25)
Large-for-gestational -age[b]	1.19 (0.99 to 1.60)	1.17 (0.84 to 1.63)
Pre-term (<37 weeks)	0.96 (0.83 to 1.11)	0.99 (0.84 to 1.17)
Post-term delivery (>42 weeks)	1.23 (0.65 to 2.33)	1.06 (0.52 to 2.16)
Stillbirth [c]	1.18 (0.62 to 2.25)	1.02 (0.50 to 2.09)
Early neo-natal death (<7 days) [d]	0.64 (0.32 to 1.29)	0.48 (0.21 to 1.07)

[a] **SGA**: Weight is below the 10th percentile at gestational age
[b] **LGA**: Weight is above the 90th percentile at gestational age
[c] **Stillbirth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth-weight of 500g or more.
[d] **END**: All neonates born live that subsequently die within first 7 days

Table 9.51 outlines the crude odds ratios and adjusted odds ratios for pregnancy outcomes among hairdressers compared to the control group of musicians. None of the crude or adjusted odds ratios demonstrated significant increases in the pregnancy outcomes among teachers compared to musicians.

Table 9.51. Pregnancy outcomes for Hairdressers (12854) vs. Musicians as control population (n= 1921)

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	1.01 (0.90 to 1.04)	0.95 (0.86 to 1.05)
LBW (<2500g)	0.97 (0.91 to 1.03)	1.31 (0.98 to 1.75)
HBW (>4200g)	1.00 (0.91 to 1.09)	2.12 (0.73 to 6.16)
SGA[a]	0.99 (0.91 to 1.05)	1.35 (0.03 to 1.95)
LGA[b]	1.01 (0.91 to 1.11)	1.09 (0.39 to 3.02)
Pre-term (37 weeks)	1.00 (0.95 to 1.05)	1.06 (0.83 to 1.36)
Post-term delivery (>42 weeks)	1.15 (0.95 to 1.38)	0.56 (0.24 to 1.28)
Stillbirth [c]	0.89 (0.69 to 1.15)	1.42 (0.48 to 4.22)
END (<7 days) [d]	1.22 (0.92 to 1.61)	0.73 (0.20 to 2.60)

[a] **SGA**: Weight is below the 10th percentile at gestational age

[b] **LGA**: Weight is above the 90th percentile at gestational age

[c] **Stillbirth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth-weight of 500g or more.

[d] **END**: All neonates born live that subsequently die within first 7 days

Table 9.52 outlines the binary logistic regression crude odds ratios and adjusted odds ratios for pregnancy outcomes among cosmetologists compared to the control group of musicians. The crude odds ratio for male to female gender ratio was almost statistically significant 1.04 (95% CI 1.00 to 1.08).

None of the other crude or adjusted odds ratios demonstrated significant increase or variation in the ratio of pregnancy outcomes among cosmetologists.

Table 9.52 Pregnancy outcomes for Cosmetologists (n=1841) vs. Musicians as control population (n= 1921)

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	1.04 (1.00 to 1.08)	1.03 (0.98 to 1.08)
LBW (<2500g)	0.95 (0.85 to 1.06)	0.91 (0.80 to 1.03)
HBW	1.03 (0.88 to 1.22)	0.79 (0.55 to 1.15)
SGA[a]	0.96 (0.84 to 1.09)	0.90 (0.77 to 1.06)
LGA[b]	0.98 (0.83 to 1.16)	0.95 (0.65 to 1.38)
Pre-term (<37 weeks)	1.00 (0.91 to 1.10)	1.02 (0.91 to 1.14)
Post-term (>42 weeks)	1.19 (0.83 to 1.72)	1.50 (0.87 to 2.56)
Stillbirth [c]	0.78 (0.52 to 1.16)	0.84 (0.54 to 1.31)
END (<7 days) [d]	0.98 (0.62 to 1.55)	0.83 (0.50 to 1.36)

[a] **SGA**: Weight is below the 10th percentile at gestational age
[b] **LGA**: Weight is above the 90th percentile at gestational age

[c] **Stillbirth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth-weight of 500g or more.

[d] **END**: All neonates born live that subsequently die within first 7 days

Table 9.53 outlines the crude odds ratios and adjusted odds ratios for pregnancy outcomes among laboratory workers compared to the control group of musicians. None of the other crude or adjusted odds ratios demonstrated significant increase or variation in the ratio of pregnancy outcomes among laboratory workers compared to musicians.

Table 9.53 Pregnancy outcomes for Laboratory workers (n=3586) vs. Musicians as control population (n= 1921)

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	1.03 (0.98 to 1.09)	1.06 (0.95 to 1.19)
Low birth weight (<2500g)	0.90 (0.78 to 1.04)	0.81 (0.60 to 1.10)
High birth weight (4200g)	1.09 (0.88 to 1.36)	1.25 (0.79 to 1.98)
SGA[a]	0.94 (0.79 to 1.12)	0.92 (0.64 to 1.32)
LGA[b]	1.07 (0.85 to 1.35)	1.24 (0.77 to 2.01)
Preterm (<37 weeks)	0.97 (0.86 to 1.10)	1.00 (0.77 to 1.29)
Post-term delivery (>42 weeks)	1.28 (0.82 to 2.01)	1.84 (0.71 to 4.76)
Still birth c	0.84 (0.48 to 1.53)	0.97 (0.29 to 3.27)

a. **SGA**: Weight is below the 10th percentile at gestational age
b. **LGA**: Weight is above the 90th percentile at gestational age
c. **Still birth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth-weight of 500g or more.
d. **END**: All neonates born live that subsequently die within first 7 days

Table 9.54 outlines the binary logistic regression crude odds ratios and adjusted odds ratios for pregnancy outcomes among hairdressers compared to the control group of the general population.

The crude odds ratio for SGA reached marginal statistical significance 1.01 (95% CI 1.00 to 1.02). The crude odds ratio for LGA infants almost reached statistical significance 1.02 (95% CI 1.00 to 1.03).

The crude odds ratio for post-term delivery (greater than 42 weeks) reached marginal statistical significance 1.06 (95% CI 1.02 to 1.11).

The crude odds ratio for END almost reached statistical significance 1.07 (95% CI 1.00 to 1.15).

None of the other crude or adjusted odds ratios demonstrated statistically significant increase or variation for pregnancy outcomes among cosmetologist is workers compared to the general population.

Table 9.54 Pregnancy outcomes for Hairdressers (12854) vs. General population as control population (n= 447)

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	1.00 (0.99 to 1.01)*	1.02 (0.99 to1.06)
Low birth weight (<2500g)	1.00 (0.99 to 1.02)	1.08 (0.98 to1.19)
High birth weight (4200g)	1.01 (0.99 to 1.02)	0.93 (0.81 to 1.06)
SGA[a]	1.01 (1.00 to 1.02)	0.95 (0.86 to 1.06)
LGA[b]	1.02 (1.00 to 1.03)	0.86 (0.74 to1.00)
Preterm (<37 weeks)	1.00 (0.99 to 1.01)	1.00 (0.93 to 1.09)
Post-term delivery (>42 weeks)	1.06 (1.02 to 1.11)	0.73 (0.51 to 1.03)
Still birth [c]	1.01 (0.98 to 1.05)	1.11 (0.80 to 1.54)
END (<7 days)	1.07 (1.00 to 1.15)	0.54 (0.29 to 1.01)

* to 3 decimal places

[a] **SGA**: Weight is below the 10th percentile at gestational age

[b] **LGA**: Weight is above the 90th percentile at gestational age

[c] **Still birth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth weight of 500g or more.

[d] **END**: All neonates born live that subsequently die within first 7 days

Table 9.55 presents binary logistic regression crude odds ratios and adjusted odds ratios for pregnancy outcomes for Cosmetologists (n=1841) vs. General population as control population (n= 447004). There were no statistically significant findings among these calculations.

Table 9.55. Pregnancy outcomes for Cosmetologists (n=1841) vs. General population as control population (n= 447004).

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	1.01 (0.99 to 1.02)	1.04 (0.95 to 1.45)
LBW (<2500g)	1.00 (0.97 to 1.04)	1.01 (0.98 to 1.05)
HBW (4200g)	1.02 (0.97 to 1.08)	1.04 (0.99 to 1.10)
SGA[a]	1.01 (0.99 to 1.05)	1.12 (0.84 to 1.49)
LGA[b]	1.01 (0.96 to 1.06)	1.03 (0.98 to 1.09)
Pre-term (<37 weeks)	1.00 (0.98 to 1.03)	1.09 (0.88 to 1.35)
Post-term delivery (>42 weeks)	1.07 (0.94 to 1.21)	1.18 (0.97 to1.45)
Stillbirth [c]	0.97 (0.88 to 1.08)	0.98 (0.88 to1.09)
Early neo-natal death (<7 days)	0.96 (0.84 to 1.11)	0.82 (0.30 to 2.22)

* to 3 decimal places

a. **SGA**: Weight is below the 10th percentile at gestational age

b. **LGA**: Weight is above the 90th percentile at gestational age

c. **Still birth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth weight of 500g or more.

d. **END**: All neonates born live that subsequently die within first 7 days

Table 9.56 outlines the crude odds ratios and adjusted odds ratios for pregnancy outcomes among laboratory workers compared to the control group of the general population.

None of the crude or adjusted odds ratios demonstrated significant increase or variation in the ratio of pregnancy outcomes among laboratory workers compared to general population.

Table 9.56 Pregnancy outcomes for Laboratory workers (n=3587) vs. General population as control population (n= 447004)

Pregnancy outcome	Crude OR (95% CI)	Adjusted OR (95% CI)
Male	1.00 (0.99 to 1.01)	0.94 (0.84 to 1.06)
LBW (<2500g)	1.00 (0.97 to 1.02)	1.23 (0.91 to 1.67)
HBW (4200g)	1.04 (0.99 to 1.09)	0.80 (0.50 to 1.27)
SGA[a]	1.01 (0.97 to 1.04)	1.08 (0.75 to 1.55)
LGA[b]	1.04 (0.99 to 1.09)	0.82 (0.50 to 1.32)
Pre-term (<37 weeks)	0.99 (0.97 to 1.02)	1.00 (0.78 to 1.29)
Post-term delivery (>42 weeks)	1.07 (0.97 to 1.19)	0.56 (0.22 to 1.44)
Stillbirth [c]	1.04 (0.94 to 1.16)	1.01 (0.30 to 3.43)
Early neo-natal death (<7 days)	0.93 (0.84 to 1.04)	1.28 (0.38 to 4.38)

* to 3 decimal places

[a] **SGA**: Weight is below the 10th percentile at gestational age

[b] **LGA**: Weight is above the 90th percentile at gestational age

[c] **Still birth**: Dead at the time of delivery at 22 or more weeks' or born dead with gestation or a birth weight of 500g or more.

[d] **END**: All neonates born live that subsequently die within first 7 days

10 DISCUSSION

The study found some marginally statistically signifcant results for adverse pregnancy outcomes in the subject populations compared to the control populations of. Teachers, musicians and others, a group mainly consisting of the general population. The null hypothesis that there is no difference did not apply in a small number of exmaples. There is a suspicion that occupational factors may contribute to the findings but no strong direct conclusions can be drawn.

Although the complex mechanism of human reproduction has been summarised earlier in this work, Burdorf et al. (2006) have highlighted the challenges of attributing chemical exposure to adverse pregnancy outcomes. This study concurs the overall findings from other research as demonstrated by the meta-analysis, that chemicals or agents currently applicable to the subject populations may interact on foetal development and contribute adverse outcomes or an increased incidence of male gender. Burdorf et al. (2006) and many other researchers listed above have further emphasised the range of non-occupational and lifestyle factors that are associated with adverse pregnancy outcomes.

10.1 Main findings

The sections below will cover the main positive findings from the systematic review, the binary logistic regression analyses from the original work and the meta-analysis for the various studies combined. Non-significant findings were numerous and will not be discussed in this section, except if there is a specific point of interest.

10.2 Hairdressers findings

On joining the industry hairdressers undertake a course of training that equips them from the theoretic and practical standpoints. They develop interpersonal skills to autonomously cope with stress through problem solving, communication and behaviour (Appendix 14). They must also learn about the risks to health and safety at work. It is evident that the teaching and level of understanding in this area are not always optimal (Bradshaw et al., 2011). More detailed understanding of the risks from epidemiological studies may eventually increase awareness and understanding of reproductive risks.

This original study found that in comparison to the control cohort of prima gravida teachers (n=40,405) sourced from the same birth register, prima gravida hairdressers (n=12,854) experienced a few marginally statistically significant increased crude and adjusted odds ratios for the parameters measured. These marginally significant findings were also evident when hairdressers were examined in the meta-analysis using data from pre-existing epidemiological research.

10.3 Male to female gender ratio

The binary logistic regression analysis for male to female gender ratio was marginal significant for a reduction of the adjusted odds ratio in favour of female gender offspring (aOR 0.92, 95% CI, 0.87 to 0.98). This was not evident when the results from Zhu et al. (2006) were combined with this original data. None of the other pre-existing research had measured risk ratios for this parameter.

10.4 Low birth weight

The meta-analysis results for the risk of LBW outcomes among hairdressers (fixed effect model) gave an I-V pooled Effect Size of 1.083 (95% CI, 1.017-1.153). The random effects model did not give a comparable result (D+L pooled Effect Size 1.016, 95% CI 0.880-1.173) and none of the individual studies including the original data yielded a statistically significant result when adjusted odds ratios were calculated.

10.5 Small for gestational age

In the original study, when prima gravida hairdressers (n=12,854) were compared to the prima gravida women of the general population (n=447,004) as the control cohort population, there were no statistically significant results. There were two Swedish studies (Rylander et al., 2002) and (Rylander and Källén, 2005) which demonstrated statistically significant aOR results for SGA (1.4, 95% CI 1.1–1.7 and 1.2, 95% CI 1.06–1.36 respectively) among hairdressers, certified in Sweden. The control cohorts for both studies were

women from the general population. In this study exposure data were collected via questionnaires that identified types of work undertaken and whether the participant was working full time or part time. The studies suggested that frequency of permanent waving and spraying were associated with increased risk of having a SGA infant.

In the meta-analysis, the I-V pooled effect size (fixed effect model) was 1.077 (95% CI, 1.006-1.153). This again was marginally statistically significant. The pooled effect for the random effects model incorporated a value that includes 1.00 and was therefore not statistically significant

10.6 Large for gestational age

The systematic review revealed one paper (Axmon and Rylander 2008) which yielded a negative statistically significant result for aOR of LGA new-borns (aOR 0.64, 95% CI 0.44–0.93). This finding suggested hairdressers were less likely to have LGA new-borns which may fit with the marginally statistically significant finding of increased SGA new-borns described above.

The meta-analysis and forest plots for this (Halliday-Bell, 2014) and two other studies also produced a negative statistically significant result for the fixed effect model (I-V pooled Effect Size 0.81, 95% CI 0.72-0.93). The random effect model yielded a similar result (D+L pooled Effect Size 0.81, 95% CI 0.70-0.94).

The study of hairdressers by Axmon and Rylander (2008) examined birth-weight and foetal growth in women who had trained as hairdressers. They

analysed 6223 infants born to 3137 hairdressers and compared them to 8388 infants born to 3952 of their sisters. Their method enabled adjustment for genetics and childhood exposures. No obvious mechanism was put forward that could account for the finding of lowered risk of LGA.

The study by Zhu (2006a) that referred to the Danish National Birth Cohort (DNBC) did not produce statistically significant results when this team undertook a study that included measurement of LGA infant among 550 hairdressers compared to 3216 shop assistants. The study took into account the characteristics of the work undertaken by the subjects and controls.

Infants become large for their gestational age infant (LGA) due to high prenatal growth rate. This outcome is usually diagnosed post-delivery, but is occasionally picked up prenatally by ultrasound.

One of the contributing medical factors for LGA is maternal gestational diabetes or pre-existing type 2 diabetes. This condition causes high plasma glucose and insulin levels in the expectant mother. These raised levels stimulate excessive foetal growth. In other cases LGA infants develop due to congenital anomalies of the circulation such as transposition of great vessels and foetal hydrops conditions.

Certain complications are recognised to be associated with LGA infants when these occur during the neo-natal period. These include birth trauma, cardiovascular and respiratory problems, anaemia and haemorrhagic disorders as well as nervous system and musculoskeletal problems and infections (Ng et al., 2010).

10.7 Pre-term delivery

The original study did not yield a statistically significant result for hairdressers on this parameter.

The systematic review revealed 6 papers that had published results for this parameter among workers in this occupation. It appears to be the most popular parameter to be measured in this field of study.

Kersemaekers et al. (1997) looked at hairdressers and controls in the Netherlands during two time periods (1986-1988 and 1991-1993). They did not find any significant difference in the adjusted odds rations for either time period (aOR 0.5, 95% CI 0.1–2.3 and aOR 1.0, 95% CI, 0.8–1.3).

Studies by other researchers: Li et al. (2010), Ronda et al. (2010), Rylander et al. (2002), Rylander and Källén (2005) and Zhu et al. (2010) were all undertaken over single time periods. They made adjustments for several various confounders in each case.

None of the individual studies nor the meta-analysis of all of the studies demonstrated a statistically significant result for this parameter.

10.8 Post-term delivery

The original study yielded a marginally statistically significant crude odds ratio for post-term deliveries when hairdressers were compared to the general population (1.06, 95% CI 1.02-1.11). The adjusted odds ratio was not statistically significant (0.73 (0.51-1.03). No one of the other studies of pregnancy outcome in hairdressers examined post-term deliveries.

10.9 Cosmetologists findings

Cosmetologists in Finland undergo training to become knowledgeable in their practice and to be aware of the health and safety risks of their work. Information pertaining to cosmetology training in Finland was not readily available but information for training in this role in the UK gives an indication of the person specification and training outline (Appendices 11 and 15).

The original study involved the analysis of FMBR data to measure the effect of occupational health hazards on reproduction. The picture among prima gravida cosmetologists (n=1841) compared to prima gravida teachers (n= 40405) revealed an adjusted crude odds ratio for post-term delivery of infants beyond 42 weeks gestation that was statistically significant 2.13 (95% CI 1.04-4.35). This suggests that their infants were delivered late. But this was not evident when they were compared to the general population.

None of the other parameters demonstrated statistically significant crude or adjusted odds ratios for this parameter.

When prima gravida cosmetologists (n=1841) were compared with the prima gravida general population control cohort (n=447,004) there were no statistically significant results for any of the parameters studied.

10.10 Low birth weight

The systematic review yielded one paper (Herdt-Losavio et al, 2008) which reported a marginal statistically significant result for low birth weight in new-borns of cosmetologists compared to controls (aOR1.38, 95% CI 1.09-1.74). The meta-analysis revealed this paper to have relatively low weight in terms

of percentage (1.98). The results seen in this paper was not replicated in the meta-analysis in neither the fixed or random effect models.

10.11 Laboratory workers findings of original study

The training to become a laboratory worker in Finland requires higher training in a range of relevant skills including the awareness of health and safety hazards in the workplace (Appendices 11 and 16). Although careers information for individuals planning to work in Finnish laboratories was not available, some information from the UK Careers Service offers some understanding of the person specifications and training involved in developing this career.

Prima gravida laboratory workers (n=3587) did not demonstrate any increased risk when measured by crude and adjusted odds ratios for the parameters included in the study against any of the control cohort populations used.

When prima gravida laboratory workers (n=35867) were compared with prima gravida musicians (n=1968) as the control cohort population, there were no statistically significant crude or adjusted odds ratio results for the parameters studied.

When prima gravida laboratory (n=3587) workers were compared with the prima gravida general population control cohort (n=447,004) there were no statistically significant results.

The meta-analysis results for the various studies of laboratory workers did not produce any statistically significant results or even marginally statistically

significant results suggesting that laboratory workers were not at greater risk of the pregnancy outcomes of interest in this study.

10.12 Importance of animal studies

The conclusion from many animals studies is that, some animal exposure to toxic doses of certain chemicals can result in teratogenic and embryo lethal effects; even in the absence of human maternal toxicity.

Brent (2004) highlighted the complexities of using animal studies to determine effects on human reproduction. The Cosmetic Ingredient Review Panels are all similar in structure and detail high-dose administration of cosmetic ingredients to animals, few of which appear to have had a significant effect on health effects for parameters including reproductive outcome.

The ethical issues presented by human research for these agents means that there is a high degree of reliance on the outcome of animal studies in determining the appropriate dose of exposure humans who regularly use or work with such chemicals. This factor makes it all the more important that future studies measure exposure data in some detail to enable the apportionment of possible causation of various chemicals used in hairdressing, cosmetology and laboratory work to the identification, in terms of their individual and synergistic impact on human reproduction.

10.13 Limitations of the study

This study of the adverse impact of occupation on pregnancy outcome among hairdressers, cosmetologists and laboratory workers compared to the control

cohorts of teachers, musicians and the general public was limited by factors that are incurred in the collection of data from individuals on the register, or analysis of the causal factors or due to the influence of bias or confounding. Years in current employment was not recorded on the Register. On that basis it was not possible to determine the length of possible exposure in the occupations amongst the study populations The Register was not primarily focused on occupational health impact but on a wide range of maternity factors.

Any study aiming to consider the impact of an occupational exposure would require large numbers of subjects, hygiene measurements or proxy measurements to identify levels of exposure.

10.14 Causal factors

This study aimed to examine the link between three occupational groups and pregnancy outcomes. There are numerous factors that have been identified as having a causal link on adverse pregnancy outcome. The high level of participation and homogeneity of the skills of observers is likely to be important in achieving consistency of data recording in this study. The causal factors in the work environments of the subjects and controls under consideration were not assessed in detail. The FMBR does not specifically record the individual specific hazards in individual workplaces and it does not give scope for proxy measure of workplace exposure the exposure of the pregnant workers to such hazards on a day-by-day basis or over time. Although a small number of statistically significant differences were observed

between subject and control groups it was not possible to correlate the exposure to possible causative agents.

10.15 Bias

The Finnish Medical Birth Registry records 99.9% of deliveries in Finland (Appendices 6, 7 and 8). This includes spontaneous and induced abortions. Confounding variables

Previous studies exploring the effect of occupational hazards on pregnancy outcome have adjusted for as many as 10 confounders. These include physical and genetic factors such as maternal or paternal height, maternal weight and weight gain through the gestational period, maternal age, parity, medical history, race, obstetric history and interval between pregnancies.

Environmental confounders that have been accounted for in other studies include: nutritional status, infections, low income, poor education, socioeconomic status, marital status, use of alcohol, tobacco exposure, medicinal or illicit drugs, altitude and domestic stressors. To incorporate a large number of confounding factors effectively, the methodology would require the accurate and consistent recording of each variable to ensure that the adjustment is valid and reliable.

Actual or proxy measurements of some confounding factors are included in the questionnaire administered to new entrants to the FMBR (Appendix 7). In this study, only four confounders were taken into account. These were maternal age, socioeconomic status, marital status and maternal smoking

during pregnancy. In addition the effect of parity was removed by selecting only prima gravida women for analysis.

The lack of hygiene data meant there was no scope to demonstrate risk between the different subject populations and it was therefore relevant to consider statistical power, exposure levels and imprecision of the definition of the occupational groups and the choice of outcome variables s and how these were measured between different observers.

This study may have been improved if confounders such as 'years in education', which has a link to socioeconomic status and professional training, could be accessed from the Finnish Medical Birth Register (FMBR) were used. The years in education were not recorded as a matter of routine. Ideally, quantitative exposure data could have been collected, or at least systematically estimated, for exposure to various hazards. Duration of the reported occupational exposure, both prior to conception and during the gestational period, could also have been recorded and factored into the analysis. It would have also been useful to record occupational history, through which previous exposure to potential and long latency reproductive hazards could be considered.

The effects of alcohol and illicit drugs are now more widely recognised. Access to exposure information on this range of substances and application of statistical adjustments will be important in improving the evidence of work related effects in future studies.

10.16 Chance

Although some of the results were marginally statistically significant, in general the strength of the findings was not sizeable and on this basis they could be due to chance. However the size of the participant populations included in this original piece of work that were collected over a number of years reduces the likelihood of the range of results for the crude and adjusted odds ratios being due to chance.

10.17 Control populations

Selection of control populations is a challenge that should be approached with good scientific reasoning. Various studies have selected various control populations. The ideal position would be to match the subject cohorts with cohorts who have similar risks for the potential confounding variables. These, as highlighted above can be numerous when examining pregnancy outcome. The primary challenge is to identify the probable causative occupational exposures, which in this field with little understanding of the mechanisms and animal data that may be invalid have proved difficult in past research and in this original work.

10.18 Validity of the results

The results of this study, albiet limited in terms of presenting statisitically significant findings, are considered to be valid as a large database with consistently recorded data was used. The meta-analysis supported this

theory as there were no striking differences across the research work reviewed.

The methods applied to measuring the effect of work on the prima gravida women who made up the three subject populations and the three control populations was consistent. The variables used were relevant to the adverse outcomes of interest in this study. Adjustment was made for a good range of confounders compared with pre-existing research. Further review of validity of the data follows in the sub-sections below:

Although there is the potential to increase validity of data, this study did not access other sources of information on pregnancy outcomes for the study and control populations, which would have allowed linkage or cross-referencing for the study population. The Finnish Medical Birth Registry (FMBR) has virtually all deliveries recorded in a detailed and consistent fashion. This minimised the impact of bias and maintained validity in terms of the study being repeatable and reliable.

There was adjustment for four confounders in this study, plus the limitation to prima gravida women. Three of these; the more significant for the populations under review will be discussed further below.

The maternal age group was stratified as part of this study on receipt of the original data. There was a skewed curve of distribution for age-group towards the younger ages in each cohort. The mode for hairdressers and

cosmetologists and laboratory workers was 26-30 years for all of the cohorts in the study.

Some reviewers of this research may query selection of teachers as controls. While in some countries teachers are highly qualified and well-paid individuals in other countries including Finland, this may not generally, be the case (World Press 2002, accessed August 2013).

It could be suggested that it is more likely that teachers as controls had more extensive education than the subject groups of hairdresser, cosmetologist and laboratory worker. A sizeable amount of data indicates that socioeconomic status and educational attainment of the mother are factors that impact on pregnancy outcome (Scholl et al., 1992; Hickey et al., 1995 and Jorgensen et al., 2008). On that basis, selection of teachers as controls could cause a bias. All of the professions within this study require post school training, typically undertaken over the course of 3 years (Appendix 11). Although laboratory workers could range from 'professor' or 'senior scientist to 'technician', it is likely that the majority would be skewed toward the role of technician side. This would therefore be an equivalent socioeconomic status to the other study groups. Teachers shared at least two occupational hazards with the subject populations in that it was common to undertake long periods of standing and be exposed to stress. There is no perfect control group for the occupational groups studied. Previous research has outlined the rationale for use of teachers as controls further (Zhu et al., 2006; Quansah et al., 2010 and Quansah et al., 2011).

10.19 OECD data

Finland is a member of The Organisation for Economic Co-operation and Development (OECD website accessed August 2013) a Paris-based international economic organisation of 31 countries. Most OECD members are high-income economies with a high Human Development Index (HDI) and are regarded as developed countries.

OECD data from 1994 highlighted the relatively low level of pay for teachers in Finland. Experienced primary teachers' actual pay was less than predicted when looking at rates of pay across oecd. This was relevant in countries that were poorer, had lower student to pupil ratios or shorter teaching hours per week than others elsewhere in europe. Some of these factors appear to apply in finland. It is thought that low income levels are typical for all public servant posts in finland. The pay for lower secondary school teaching is moderately higher in most oecd countries than that for primary school teaching. Finnish teachers work an average 874 hours per year. This is in the upper average group (746-912) for their profession across the oecd.

This study was designed to select subjects and controls who in general terms had similar socioeconomic status. That has enabled more realistic comparison between groups. Low socioeconomic status is known to be a confounder for pregnancy outcome.

10.20 Smoking

The scientific research evidence published by a wide range of authors confirms that cigarette smoking or indirect exposure to environmental tobacco smoke during pregnancy has an impact on pregnancy outcome (Åhlborg and Bodin, 1991; Brown, 1996 Floyd, et al., 1993; Hanke et al., 2004; Leonardi-Bee et al., 2011; McCowan et al., 2009; Lewis et al., 1998; Lindbohm et al., 2002 and Rebagliato, 1995). Some of the studies published suggest possible mechanisms of cigarette smoke action on the foetus. One epidemiological study that included consideration of the effects of smoking used data from the Finnish Medical Birth Register (Quansah et al. 2011).

10.21 Effect of dose- smoking

There appears to be a lower risk to the infant if the mother ceases smoking early in pregnancy rather than continuing this habit throughout gestation (McCowan et al. 2009). The FMBR includes data collection of the timing and extent of cigarette smoking but no measure of the exposure to ETS in domestic or work environments for non-smokers. While adjustments were made in the analysis for smoking or non-smoking status as confounders to pregnancy outcome, it was not feasible to undertake more sophisticated analysis of the dose response effect that smoking may have caused in terms of confounding when subjects and controls were compared. Furthermore there was limited scope to identify the exact patterns of smoking habit and how this differed amongst the 3 subject occupational groups and 3 control groups of pregnant women. It would have been of interest to consider the

226

overall percentage of smokers in each group and the average daily tobacco consumption, the percentage of non-smokers who were exposed to environmental tobacco smoke (ETS) with some indication of the doses of exposure.

10.22 Registration form- data collection

The questions on smoking habit that were incorporated in the registration form used by FMBR enabled the deployment of data for this study. It gathered what appears to be reliable data and facilitated identification of those who did not smoke, those who stopped smoking during the first trimester of the gestation period and those who continued smoking after the first trimester of the gestation period. There was no indication of the number of cigarettes smoked nor any measure of the exposure to ETS in domestic or work environments. While adjustments were made in the analysis for smoking or non-smoking status as confounders to pregnancy outcome, it was not feasible to undertake more sophisticated analysis of the dose response effect that smoking may have caused among the subject and controls. Furthermore there limited scope to identify the patterns of smoking habit amongst the four occupational groups of pregnant workers. There could also have been some interesting findings for timing of cessation of smoking amongst the expectant mothers studied as trends indicating the benefits of early cessation could have become evident through such an analysis. Newer methodology enables testing of cotinine in hair or urine due to ETS or smoking and this gives a more accurate level of exposure that can be correlated to adverse pregnancy

outcomes of intrauterine growth retardation and pre-term delivery (Jaakkola and Zahlsen, 2001).

10.23 Unknown factors

The unknown factors in this study could be wide ranging. The study populations were all based in Finland and there may have been specific genetic or hereditary factors that produced the outcomes noted (Ahmed and Jaakkola, 2007; Gissler et al., 2003).

Potentially, the combination of chemicals in the work environment may produce unidentifiable synergistic effects (Kersemaekers et al., 1995).

Non-specific environmental factors such as diet, nutrition, air quality, self-limiting illness and infection could not be accounted for. Similarly, significant underlying illness or the use of pharmaceutical products may affect outcomes. There is likely to be a number of unknown factors that have the potential to impact on pregnancy outcomes for female workers. They may explain the inconsistent findings among the research undertaken to date. The specific identity and size of effect of such unknown factors should become more consolidated as research progresses and techniques deployed allow consideration of them.

10.24 Synthesis with previous knowledge for occupational groups

10.24.1   Hairdressers

The results of the original study were in synthesis with the findings of the other 8 studies included in the meta-analysis. The occupation of the subjects

and controls, range of adjustments for confounders and overall findings as odd and adjusted odds ratios were similar.

There was one finding of a rarely examined parameter. The present study found a statistically significant reduction in the percentage of boys among new-borns of hairdressers compared with those of teachers (aOR 0.92, 95%CI 0.87-0.98).This was contrary to the background ratio of male to female births in Finland where the ratio is reported to be 1.04 marginally in favour of an increased prevalence of male births.

Zhu et al. (2006) found no difference in sex ratio between new-borns of hairdressers and shop assistants. Other studies that had included this observation, similarly did not report statistically significant findings for gender ratio.

The present study did not show a substantially increased risk of LBW, pre-term or post-term deliveries nor in terms of the ratio of stillbirths and the ENDs among new-borns of hairdressers compared to the control group of teachers. This was comparable with Axmon et al. (2008), Kersemaekers (1997) and Ronda et al. (2010) but at variance with other studies which including Rylander et al. (2002) and Rylander and Källén (2005) where the effect estimate for LBW among hairdressers compared to controls was statistically significant (aOR 0. 92, 95% CI 0.87 - 0.98).

This study did not find an increase in SGA among new-borns of hairdressers relative to teachers. However the crude odds ratio for SGA infants was 1.01 (95% CI 1.00, - 1.02). This is following the trend of the Swedish studies (Rylander et al. 2002, Rylander and Källén 2005). This result was moderately

at variance with a large Danish study (Zhu 2006b) and a smaller Swedish study (Axmon et al. 2008) that found no statistically significant increase in the risk of SGA.

One study of hairdressers that are included in the systematic review calculated the OR and aOR for LGA infants. Axmon et al. (2008) published an odds ratio of 0.64 (95% CI, 0.44 - 0.92). This research suggests a low likelihood of LGA infants.

Rylander et al. (2005) undertook a reproductive outcomes study among hairdressers. They used the Swedish Medical Birth Registry data for births between 1983 and 2001. The study concluded that full time hairdressers had an increased prevalence of intra-uterine growth retardation (IUGR) with infants being small-for-dates (SFDs) at birth.

Axmon and Rylander (2009a) investigated pregnancy outcomes for female hairdressers compared to their sisters with respect to their infants' birth-weight and foetal growth (measured as SGA or LGA respectively). There were 6,223 infants born to 3,137 hairdressers and 8,388 infants born to 3,952 hairdressers' sisters in the study. Hairdressers demonstrated neither increased rate of SGA (OR 0.80; 95% confidence interval 0.49 to 1.31) or LGA (0.77; 0.54 to 1.09) in this study. But they had infants with a significantly lower mean birth-weight (3387 g vs. 3419 g; p = 0.033).

The literature search identified four previous epidemiological studies that have compared the risk of adverse pregnancy outcomes among hairdressers with other workers as reference groups. Kersemaekers et al. (1997) conducted a cohort study of 9000 Dutch hairdressers and 9000 clothing sales clerks and

their new-borns. Rylander et al. (2002) identified 3706 women with 6960 new-borns from a list of certified hairdressers and a reference group of 3462 women and 6629 new-borns from the Swedish population registry Rylander and Källén (2005) identified all hairdressers from the Swedish Medical Birth Registry and their 12,061 infants born between 1983 and 2001. In this study all other infants born in the same period served as a reference group. Zhu et al. (2006) identified 550 hairdressers and 3216 shop assistants used as the reference group, from the Danish National Birth Cohort Study. Only one study was identified that compared the risk of adverse pregnancy outcomes among cosmetologists with other workers (McDonald and McDonald 1988).

Many of the studies included in the systematic review of the literature on pregnancy outcome amongst hairdressers included assessment of the risk of pre-term delivery or pre-term births. None of the studies produced a statistically significant result in either direction. The meta-analysis confirms this summary. This original piece of work similarly did not produce a statistically significant result when hairdressers were compared with teachers (aOR 0.99, 95% CI 0.90-1.09), musicians (aOR 1.06, 95% CI 0.83-1.36) or the general public (aOR 1.00, 95% CI 0.93 - 1.09).

For ENDs the crude odds ratio was 1.07 (95% CI, 1.00, 1.15) this was close to significance.

The present study results did not show a significantly increased risk of perinatal death among new-borns of hairdressers compared to teachers. This was at variance with Rylander et al. (2002), which found an elevated risk for

END among new-borns of hairdressers compared with controls from the general population, but the risk of stillbirth was not elevated.

Further, when hairdressers were compared to the general population as the control group there was one statistically significant result. The aOR for post-term deliveries beyond 42 weeks was 1.06 (95% CI 1.02-1.11). This parameter is infrequently measured. There were no other studies that had measured this outcome for hairdressers to enable a comparison.

The crude OR for hairdressers compared to the general population for SGA infants was 1.01 (95% CI 1.00-1.02), the crude odds ratio for LGA infants was 1.02 (95% CI, 1.00-1.03) and for ENDs the crude odds ratio was 1.07 (95% CI, 1.00-1.15).

10.24.2 Cosmetologists

This study compared cosmetologists (n=1640) with teachers (n=20,610) musicians (n=1042) and the general public (n=228,753). Few statistically significant results were identified.

When compared with teachers the adjusted odds ratio for post-term delivery of infants beyond 42 weeks gestation was marginally statistically significant 2.13 (95% CI 1.04-4.35).

Few epidemiological studies have been undertaken on the risk of pregnancy outcomes among cosmetologists. The OR for post-term delivery was not measured in other reports examined in the systematic review. It was not possible to compare this finding among other studies.

When cosmetologists were compared with musicians as the control population there was a crude odds ratio result close to statistical significance for increased proportion of male new-borns (1.04, 95% CI 1.0-1.08). Other authors whose work was identified through the systematic review of the literature had not measured the sex ratio of infants born to cosmetologists. Consequently was not possible to compare this result from the original study that was close to statistical significance with previous reports.

The adjusted odds ratio of pre-term deliveries amongst cosmetologists in this original study was not statistically different to the teacher control population, the musicians control population or the general population. This result was in accordance with two studies of cosmetologists by Herdt-Losavio et al. (2008) and Flaws et al. (2009).

The results of this original study also showed that the cosmetologists were not at increased risk for other outcomes under consideration.

Herdt-Losavio et al. (2008) undertook a retrospective study of birth records to ascertain the risk of LBW, SGA and pre-term delivery infants among 15,003 mothers who were employed as licensed cosmetologists. They were compared with two different control cohorts: 4,246 licensed realtors and women among the general public (n=12,171). Matching was made for the child's year of birth, mother's ethnicity and mother's education. In this example, there was a positive association between LBW for cosmetologists compared to realtors (aOR 1.38, 95% CI, 1.09-1.70). No significant link was found for SGA or pre-term births with either comparison group. There were no statistically significant results for any of the parameters studied and published by other authors as identified through the systematic review.

Flaws et al. (2009) measured the risk of adverse outcomes of pregnancy for 350 cosmetologists compared with 397 age matched controls via postal questionnaire. There were no statistically significant associations between occupation and the pregnancy outcomes after adjustment for 5 confounders that were age, race, education, and smoking and alcohol use.

The various results from previous studies have varied widely with no consistent pattern evident from these studies or this original piece of work on the reproductive risks to cosmetologists. The range of different types of tasks undertaken at work in the study cohort had not been discerned, this might have been useful for grouping the cosmetologists according to likely exposure.

10.24.3 Laboratory workers

A review by Dement and Cromer (1992) examined epidemiology studies of pregnancy outcome for laboratory workers and identified that 8 out of 10 studies formed an association between this field of work and miscarriages, perinatal death and congenital anomalies.

Zhu et al. (2006) undertook a prospective study that explored pregnancy outcome in women undertaking laboratory work. The source was the Danish National Birth cohort from 1997-2003. The 1,025 Laboratory workers were compared to 8037 female teachers. Hazard ratios were calculated and found not to be different to teachers for late foetal loss, congenital anomalies, pre-term births or SGA babies, but laboratory technicians working with radio-immuno assays (RI) or radiolabelling (RL) had a doubled odds ratio for pre-term birth. The OR was 2.2 for RI, (95% CI, 0.8-6.2) and OR for RL was 1.9 (95% CI, 0.8-4.6).

Wennborg et al. (2000) undertook a questionnaire based study. They included 1,052 laboratory-based staff. No increase OR was found for laboratory workers in general compared to non-laboratory based staff for spontaneous abortions. There was also an indication that laboratory workers had LGA infants (OR 1.9, 95% CI, 0.7-5.2). However, an OR for spontaneous abortions of 2.3 (95% CI, 0.9-5.9) indicated that this adverse outcome was associated with working involving chloroform exposure. Wennborg et al. (2002) looked at 249 laboratory workers in Sweden and compared their pregnancy outcomes with 613 non-laboratory workers also based at the university. Laboratory work

involving exposure to solvents was associated with increased risk of pre-term births, (OR 3.4, 95% CI, 1.0–11.9) work with bacteria appeared to be linked to increased post-term birth rate (OR 2.7, 95% CI 1.0-7.4).

Axelsson and Rylander (1984) performed a questionnaire-based study of women involved with laboratory work at a petrochemical plant. They found no indication of increased number of miscarriages for the period 1968 and 1979 (relative risk (RR) 1.31, 95% CI, 0.89-1.91). Their later studies of the relationship between solvent exposure and miscarriage did not highlight significant difference between subjects and referents for the risk of miscarriage. It is possible that the environmental controls improved and harmful substances were substituted for less harmful agents over the two periods.

Hansson (1980) focussed on the pharmaceutical industries in Sweden. This showed a slight increase in miscarriage and perinatal mortality rates between women working in laboratories using chemicals and those who worked in other laboratories (abnormal births Chi squared= 6.6 at 1 d.f., p=0.01). Further observation of the exposed population revealed a significant increase in the ratios of perinatal death in the group exposed to chemicals (Chi Square not published).

Leffingwell (1983) studied laboratory workers employed within the pharmaceutical industry. There were 191 subjects compared to 318 referents. Each was surveyed by telephone interview. The study did not highlight any

increase in miscarriages or alteration of birth-weight among the babies of laboratory workers.

In this original study laboratory workers when compared to teachers did not demonstrate any increased risk when crude and adjusted odds ratios were analysed for the parameters included in the study.

When laboratory workers were compared with musicians as the control population there were no statistically significant crude or adjusted odds ratio results for the parameters studied.

When laboratory workers were compared with the general population as controls there were no statistically significant results. Three crude odds ratios were close to significance when laboratory workers were compared to the general public. There was an increased risk of HBW OR 1.04 (95% CI, 0.99, 1.09) a suggestion of increased risk of SGA, OR 1.01 (95% CI 0.97-1.04) and indication of LGA, OR 1.04 (95 % CI 0.99-1.09). It is difficult to discuss synthesis with other studies as the cohort of laboratory workers in this study were not identified according to their area of specialty; it was not possible to group them in relation to the likely hazards and exposures. Had this been possible, some evidence of adverse reproductive outcomes might have been evident from this cohort.

10.25 Summary of findings

It is evident that various studies undertaken to explore the outcomes of pregnancy for hairdressers, cosmetologists and laboratory workers were undertaken using different methods for data collection, did not all measure or estimate exposure and did not all control for the same confounders in the analyses.

The FMBR, although successful in collating maternity and birth outcome data for virtually all Finnish pregnancies, did not collate data that would facilitate estimation of exposure or the number of weeks undertaking usual work during the gestational period amongst the study population. The study relied on data from a birth register and did not have scope to include data that would help to elucidate the possible mechanism of action and effect of some of the agents in use in these workplaces as the workers mothers' full employment history and reproductive history was not included and father's occupation was not analysed in our study.

This study did present some statistically significant outcomes and was therefore in in agreement with some of the previous studies that had examined these parameters.

10.26 Implications for policy

The European Directive (Pregnant Workers Directive 92/85/EC) cited above has an overall objective to protect the health and safety of women in the workplace when they are pregnant or after they have recently given birth and are breastfeeding.

The findings of this research project highlight a wider range of parameters that can be used to measure pregnancy outcomes and discuss the importance of adjusting for confounders and undertaking some form of exposure assessment for occupational hazards. No additional implications for policy can be drawn from this work.

The interpretation of any link between occupation and exposure to physical, chemical biological or psychosocial factors at work and reproductive health outcomes has not been consistently demonstrated for most occupational hazards.

Nonetheless where the biological, chemical, physical and psychosocial hazards that cannot be eliminated for pregnant women and in some cases all employees of childbearing age should lead employers to inform and train to minimise the potential risks.

11 CONCLUSIONS

The results of this study did not provide further evidence that work as a hairdresser, cosmetologist or laboratory worker during pregnancy may affect some aspects of foetal development. Some of the results were suggestive that foetal development is affected. From crude odds ratios the new-borns of hairdressers may be at a marginally higher risk for END, large-for-gestational age, post-term delivery, pre-term delivery and being small-for-gestational age compared with the general public cohort. The new-borns of cosmetologists are at higher risk of post-term delivery when compared to teachers and an excess ratio of male infants from the crude odds ratio comparing them to musicians. Laboratory workers had no statistically significant crude or adjusted odds ratio results but had a close to significance increase in crude odds ratios for HBW, large-for-gestational age and excess ratio of male infants when compared to the control population.

12 LIST OF REFERENCES

Abdel-Latif. M., Bajuk, B., Lui, K., Oei, J., and the NSW on ACT Neonatal Intensive Care Units' Study (NICUS) Group Issue (2007). Short-term outcomes of infants of substance-using mothers admitted to neonatal intensive care units in New South Wales and the Australian Capital Territory. **Journal of Paediatrics and Child Health** 43, (3), pp 127–133.

Åhlborg, G. and Bodin, L. (1991) Tobacco smoke exposure and pregnancy outcome among working women: A prospective study at prenatal care centers in Obero County Sweden. **American Journal of Epidemiology,** 133 (4): 338-347.

Åhlborg, G., Bodin, L. and Hosted, C. (1990). Heavy lifting during pregnancy - a hazard to the foetus? A prospective study. **International Journal of Epidemiology,** 19 (1): 90-97.

Ahmed, P. and Jaakkola, J.K. (2007) Maternal Occupational and adverse pregnancy outcomes: Finnish population-based study. **Occupational Medicine,** 57 (6): 417-423.

Alshami, H. A., Adasen, A. R. and Khalfan, M. (2011) Pregnancy outcome in late maternal age in a high-income developing country. **Archives of gynecology and obstetrics,** 284 (5): 1113-1116.

Anderson, F. (1997) Final Report on the Safety Assessment of m-Phenylenediamine and m-Phenylaminediamine Sulphate. **International Journal of Toxicology,** 16, 59-115.

Ankley, G., Bennett, R., Erickson, R., Hoff, D., Hornung, M., Johnson, R., Mount, D., Nichols, J., Russom, C., Schmieder, P.K, Serrano, J., Tietge, J. and Villeneuve, D. (2010) Adverse Outcome Pathways: A Conceptual Framework to Support Ecotoxicology Research and Risk Assessment. **Environmental Toxicology and Chemistry.** 29 pp 730-741.

Axelsson, G., Lütz, C., Rylander, R. (1984) Exposure to solvents and outcome of pregnancy in university laboratory employees. **British Journal of Industrial Medicine,** 41: 305-312.

Axmon A, Hagmar L. (2005) Time to pregnancy and pregnancy outcome. **Fertility and Sterility**, 84(4):966-74.

Axmon, A., Rylander L., Lillienberg L., Albin M. and Hagmar L. 2006 Fertility among female hairdressers. **Scandinavian Journal of Work Environment & Health,** 32(1):51-60.

Axmon, A. and Rylander, L. 2009a. Birth-weight and foetal growth in infants born to female hairdressers and their sisters. **Occupational and Environmental Medicine,** 66:198-204.

Axmon, A. and Rylander, L. 2009b No interaction between smoking and working as a hairdresser with respect to reproductive health. **Journal of Occupational and Environmental Medicine,** 51: 300-306.

Axmon, A., Rylander, L. and Lillienberg, L. et al. (2006) Fertility among female hairdressers. **Scandinavian Journal of Work Environment & Health,** 32: 51-60.

Barlow S. M. and Sullivan F. M. (1982) Reproductive hazards of industrial chemicals. An evaluation of animal and human data. **Molecular Nutrition and Food Research,** 28: 591-776.

Bauer, J., Unterbrink, T. and Hack, A. et al. (2007) Working conditions, adverse events and mental health problems in a sample of 949 German teachers. **International Archive Occupational and Environmental Health**, 80: 442-449.

Bedford J. (2011) Site of the mammalian sperm physiological acrosome reaction**. Proceedings of the National Academy of Sciences of the United States of America 1***08*, 4703-4704.

Beattie, B. and Whittle M. (1993) The aetiology of intrauterine growth retardation. **Current obstetrics and gynaecology** 3 (4) pp 184 – 189.

Bellingrath, S., Weigl, T. and Kudielka, B.M. (2008). Cortisol dysregulation in school teachers in relation to burnout, vital exhaustion, and effort-reward-imbalance. **Biological Psychology.** 78: 104-113.

Béranger, R., Hoffmann, P., Christin-Maitre, S. and Bonneterre, V. (2012). Occupational exposures to chemicals as a possible aetiology in premature ovarian failure: A critical analysis of the literature. **Reproductive Toxicology**, 33 (3) pp 269-279.

Blackmore-Prince, C., Harlow, S.D. and Gargiullo, P. et al. (1999). Chemical hair treatments and adverse pregnancy outcome among Black women in central North Carolina. **American Journal of Epidemiology,** 149: 712-716.

Bodin, L., Axelsson, G. and Åhlborg, G., Jr. (1999). The association of shift work and nitrous oxide exposure in pregnancy with birth-weight and gestational age. **Epidemiology**, 10: 429-436.

Bonzini, M., Coggan, D. and Palmer, K.T. (2007) Risk of prematurity, LBW and pre-eclampsia in relation to working hours and physical activities: a systematic review. **Occupational and Environmental Medicine,** 228-243.

Bonzini, M., Coggon, D. and Godfrey, K. et al. (2009) Occupational physical activities, working hours and outcome of pregnancy: findings from the Southampton Women's Survey. **Occupational and Environmental Medicine,** 66: 685-690.

Boyer, I. J., Heldreth, B., Bergfeld, W. F, Belsito, D. V., Hill, R. A.; Klaassen, C. D., Liebler, D. C., Marks, J. G., Shank, R. C., Slaga, T. J., Snyder, P. W., Andersen, F. A. (2013). Amended safety assessment of formaldehyde and methylene glycol as used in cosmetics. **International Journal of Toxicology,** 32 (6 suppl), pp.5S-32S

Bradshaw, L., Harris-Roberts, J. and Bowen, J. et al. (2011) Self-reported work-related symptoms in hairdressers. **Occupational Medicine,** 61(5): 328-334.

Brent, R.L. (2004) Utilization of animal studies to determine the effects and human risks of environmental toxicants (drugs, chemicals, and physical agents). **Pediatrics,** 113 (4) pp 984-995.

Brison, D., Sturmey, R., Leese, H. (2014). Metabolic heterogeneity during pre-implantation development: the missing link? **Human Reproduction Update** 20 (5) pp 632–640

Brown, D.C. (1996) Smoking cessation in pregnancy. **Canadian Family Physician,** 42: 102-105.

Bulletti, C., Deziegler, D., Rossi, S., Polli, V., Massoneau, M., Rossi, E., Albonetti, A., Negrini, V., Flamigni, C. (1997) Abnormal uterine contractility in non-pregnant women. **Uterus: Endometrium and Myometrium,** 828, pp.223-229

Burdorf, A., Figa-Talamanca, I. and Jensen, T.K. et al. (2006) Effects of occupational exposure on the reproductive system: core evidence and practical implications. **Occupational Medicine,** 56: 516-520.

Byford J.R., Shaw L.E. and Drew M.G., D. et al. Oestrogenic activity of parabens in MCF7 human breast cancer cells. **Steroid Biochemical Molecular Biology,** 80: 49–60.

Calvente, I., Fernandez, M.F., Olea, J., Calvente, N., Fernandez, M., Villalba, M., Olea, M. and Nuñez, M. (2010). Exposure to electromagnetic fields (non-ionizing radiation) and its relationship with childhood leukemia: A systematic review. **Science of the Total Environment**, 408(16) pp 3062-3069.

Carlson, B. (1999): Formation of germ layers and initial derivatives". **Human Embryology & Developmental Biology**. Chapter 4 pp. 62–68. Mosby, Inc. Missouri.

Cassidy, J. (2009). The Effect of Decibel Level of Music Stimuli and Gender on Head Circumference and Physiological Responses of Premature Infants in the NICU. **Journal of Music Therapy.** 46: 180-190.

Centers for Disease Control and Prevention (2014) Tobacco Use and Pregnancy [pdf] **Centers for Disease Control and Prevention** available at

<http://www.cdc.gov/reproductivehealth/tobaccousepregnancy/> [Accessed 20 December 2014].

Chapot, B.; Secretan, B. and Robert, A. et al. (2009) Exposure to Hazardous Substances in a Standard Molecular Biology Laboratory Environment: Evaluation of Exposures in IARC Laboratories. **Annals of Occupational Hygiene,** 53(5); 485-490

Chibber, R. (2004) Problems of older maternal age and pregnancy outcome. **Bahrain Medical Bulletin,** 26: 105-109.

Chua-Gocheco, A., Bozzo, P. and Einarson, A. (2008) Safety of hair products during pregnancy. Personal use and occupational exposure. **Canadian Family Physician,** 54: 1386-1388.

Forgács, G. and Newman, S. (2005) Cleavage and blastula formation. **Biological physics of the developing embryo**. Cambridge University Press. p. 27

Clapp, J.F. (1996) Pregnancy outcome: physical activities inside versus outside the workplace. **Seminars in Perinatology,** 20: 70-76.

Collective agreement with erga omnes applicability. Available from:

http://www.eurofound.europa.eu/emire/FINLAND/ANCHOR-YLEISSITOVATY-Ouml-EHTOSOPIMUSALLM-Auml-NTBINDANDEKOLLEKTIVAVTAL-FI.htm [Accessed 24 November 2013]

Collins, J., Esmen, N. and Hall, T. (2001) A review and meta-analysis of formaldehyde exposure and pancreatic cancer. **American Journal Industrial Medicine.** 39(3) pp 336-345.

Cooper L.G., Leland N.L. and Alexander G. (1995) Effect of maternal age on birth outcomes among young adolescents. **Bio demography and Social Biology,** 42: Issue 1-2.

Cosmetics Ingredients Review Panel (2001) Final report on the safety assessment of benzyl alcohol, Benzoic acid and Sodium Benzoate. **International Journal of Toxicology**, 20: 23-50.

Cosmetics Ingredients Review Panel (2003) Final report on the safety assessment of Aluminium silicate, Calcium silicate, magnesium aluminium silicate, magnesium Trisilicate, sodium magnesium silicate, zirconium silicate, atapulgite, bentonite, Fullers Earth, hectorite, Kaolin, Lithium Magnesium silicate, lithium, magnesium, sodium silicate, montmorilonite, pyrophyllite and zeolite. **International Journal of Toxicology**, 22: 37- 102.

Cosmetics Ingredients Review Panel (1994) **Final report on the safety assessment of Propylene Glycol and Polypropylene Glycols.** Journal American College of Toxicology, 13: 437- 491.

Cosmetics Ingredients Review Panel (1997) Final report on the safety assessment of Cetrimonium chloride. Cetrimonium bromide and Steatrimonium chloride. **International Journal of Toxicology**, 16: 195-220.

Cosmetics Ingredients Review Panel (2006) **Amended final report on the safety assessment of di-butyl adipate as used in cosmetics**. International Journal of Toxicology, 25: 129-134.

Cosmetics Ingredients Review Panel (2005) Amended final report of the safety assessment of t-Butyl Alcohol as Used in Cosmetics. **International Journal of Toxicology**, 24: 1-20.

Costa S, Coelho P, Costa C, et al. (2008). Genotoxic damage in pathology anatomy laboratory workers exposed to formaldehyde. **Toxicology**. 252(1-3) pp 40-48.

Delbaere, I., Verstraelen, H., Goetgeluk, S., Martens, G., De Backer, G., Temmerman, M., 2007. Pregnancy outcome in primiparae of advanced maternal age. **European Journal of Obstetrics Gynecology and Reproductive Biology** 135 pp 41-46.

DiPietro, J A. (2012) Maternal Stress in Pregnancy: Considerations for Fetal Development. **Journal of Adolescent Health,** 51(2) S3-S8

Dunford, R. Salinaro, A. Cai, L. (1997) Chemical oxidation and DNA damage catalysed by inorganic sunscreen ingredients, **Federation of European Biochemical Societies (FEBS) Letters.** 418 (1–1) pp 87–90.

Duong, A., Steinmaus, C., McHale, C., Vaughan, C., Zhang, L. (2011). Reproductive and developmental toxicity of formaldehyde: A systematic review: **Mutation Research-Reviews in Mutation Research**, 728(3), pp.118-138.

Elbareg, A. and Essadi, F. (2013) **Advanced maternal age and pregnancy outcome, Conference**: 11th World Congress of Perinatal Medicine 2013 Conference Publication: 41 (various paging). Russian Federation, Moscow.

Ericson, A., Källén, B., 1989. Pregnancy Outcome in Women Working as Dentists, Dental Assistants or Dental-Technicians. **International Archives of Occupational and Environmental Health** 61, pp 329-333.

European Commission E.E. (1992) Council Directive 92/85/EEC of 19 October 1992 on the introduction of measures to encourage improvements in

the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding. Tenth individual Directive within the meaning of Article 16 (1) of Directive 89/391/EEC.

European Commission (2009) **European Parliament and of the Council Regulation (EC) No**.**1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products Text with EEA relevance**. Available from:

http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:01:EN:HTML [Accessed 21 November 2013]

Feng, T. (1993) Substance abuse in pregnancy. **Current Opinion in Obstetrics & Gynecology** 5, 16-23.

Finnish National Board of Education (2009a) **Vocational Qualification in Hairdressing**. Available from:

http://www.oph.fi/english/curricula_and_qualifications/vocational_upper_secondary_education [Accessed August 2013]

Finnish National Board of Education. (2009b) **Vocational qualification for cosmetologists or beauty workers.** Available from:

http://www.oph.fi/english/curricula_and_qualifications/vocational_upper_secondary_education [Accessed August 2013]

Finnish National Board of Education. (2009c) **Vocational Qualification in Laboratory Technology.** Available from:

http://www.oph.fi/english/curricula_and_qualifications/vocational_upper_secondary_education [Accessed 28 August 2013].

Flak, A., Su, S., Bertrand, J., Denny, C., Kesmodel, U. and Cogswell, M. (2014). The Association of Mild, Moderate, and Binge Prenatal Alcohol Exposure and Child Neuropsychological Outcomes: A Meta-Analysis **Alcoholism: Clinical and Experimental Research.** 38(1) pp 214-226.

Flaws, J., Gallicchio, L., Miller, S. and Greene, T. et al. (2009) Cosmetologists and Reproductive Outcomes. **Obstetrics and Gynecology,** 113: 1018-1026.

Florack, E.I.M., Pellegrino, A.E.M.C. and Zielhuis, G.A. et al. (1995) Influence of Occupational Physical-Activity on Pregnancy Duration and Birth-Weight. **Scandinavian Journal of Work Environment & Health,** 21: 199-207.

Floyd, R.L., Rimer, B.K. and Giovino, G.A. et al. (1993) A review of smoking in pregnancy: effects on pregnancy outcomes and cessation efforts. **Annual Review of Public Health 14,** 379-411.

Fortier, I., Marcoux, S. and Brisson, J. (1995) Maternal work during pregnancy and the risks of delivering a SGA or pre-term infant. **Scandinavian Journal of Work Environment and Health,** 2: 412-418.

Frey, G.M., Ott M.G. and Messerer, P. M. et al. (2007) Pregnancy protection program in a large chemical company: infant outcomes. **Occupational and Environmental Medicine. 2007 May,** 49(5):519-25.

Fried, P.A. (1993). Prenatal exposure to tobacco and marijuana: effects during pregnancy, infancy, and early childhood. **Clinical Obstetrics & Gynecology,** 36: 319-337.

Funes-Cravioto, F., Kolmodin-Hedman, B., Lindsten, J., Nordenskjöld, M., Zapata-Gayon, C., Lambert, B., Norberg, E., Olin, R. and Swensson, Å. (1977) Chromosome aberrations and sister-chromatid exchange in workers in

chemical laboratories and a rotoprinting factory and in children of women laboratory workers. **The Lancet**, 310(8033) pp.322-325

Gallicchio, L., Miller, S. Greene, T., Zacur, H. and Flaws, J. (2009) Premature ovarian failure among hairdressers. **Human Reproduction**. 24 pp 2636–41.

Gallicchio, L., Miller, S.R. and Greene, T. et al. (2011) Somatic symptoms among cosmetologists compared to women in other occupations. **Journal Women's Health (Larchmt),** 20: pp 605-615.

Gissler, M. and Hemminki, E. (1994). Amount of antenatal care and infant outcome**. European Journal of Obstetrics and Gynecology**, 56(1), pp.9-14.

Gissler, M., Louhiala, P. and Hemminki, E. (1997) Nordic Medical Birth Registers in epidemiological research **European Journal of Epidemiology** 13: 169-175

Gissler, M. and Shelley, J. (2002). Quality of data on subsequent events in a routine Medical Birth Register. **Med Inform Internet Med.** Mar;27(1):33-8.

Gissler, M., Merilainen, J. and Vuori, E. et al. (2003) Register based monitoring shows decreasing socioeconomic differences in Finnish perinatal health. **Journal of Epidemiology and Community Health**, 57: 433-439.

Goulet, L. and Theriault, G. (1991) Stillbirth and chemical exposure of pregnant workers. **Scandinavian Journal Work Environmental Health,** 17: 25-31.

Gray's Anatomy. Fertilization of the Ovum. [Online] Available from http://theodora.com/anatomy/fertilization_of_the_ovum.html [Accessed December 2014].

Green, M., Singh, A., Zhang, Y., Nemeth, K., Sulik, K. and Knudsen, T. (2007) Reprogramming of genetic networks during initiation of the Fetal Alcohol Syndrome. **Developmental Dynamics,** 236 pp 613-631.

Greenland S. and O' Rourke K. (2008) Meta-Analysis. Page 652 in **Modern Epidemiology**, 3rd ed. Ed. Rothman KJ, Greenland S, Lash T. Lippincott Williams and Wilkins;

Greer, J.M. and Panush, R.S. (1994) Musculo skeletal problems of performing artists. **Clinical Rheumatology,** 8: 103-135.

Guidance Development Group. (2009) **Physical and shift work in pregnancy:** Occupational aspects of management; a national guideline. Royal College of Physicians, London.

Ha, E., Choi, S. and Park, H. et al. (2002) Does standing at work during pregnancy result in reduced infant birth-weight? **Journal of Occupational and Environmental Medicine,** 44: 815-821.

Hackshaw, A., Rodeck, C. and Boniface, S. (2011). Maternal smoking in pregnancy and birth defects: a systematic review based on 173 687 malformed cases and 11.7 million controls. **Human reproduction update** 17 (5) pp 589–604.

Halliday-Bell, J.A., Gissler, M. and Jaakkola, J.J.K. (2009) Work as a hairdresser and cosmetologist and adverse pregnancy outcomes. **Occupational Medicine (London),** 59: 180-184.

Halliday-Bell, J.A., Quansah, R. and Gissler, M. et al. (2010) Laboratory work and adverse pregnancy outcomes. **Occupational Medicine**. 60 pp 310-313.

Handa, O., Kokura, S., Adachi, S., Takagi, T., Naito, Y., Tanigawa, T., Yoshida, N. and Yoshikawa, T. (2006) Methylparaben potentiates UV-induced damage of skin keratinocytes. **Toxicology.** 227 (1–2) pp 62–72.

Hanke, W., Sobala, W. and Kalinka, J. (2004) Environmental tobacco smoke exposure among pregnant women: impact on foetal biometry at 20-24 weeks of gestation and new-born child's birth-weight. **International Archives of Occupational and Environmental Health.** 77: 47-52.

Hansen, P.A. and Reed, K. (2006) Common Musculoskeletal Problems in the Performing Artist. Physical Medicine & **Rehabilitation Clinics of North America,** 17 pp 789-801.

Hansson, E., Jansa, S. and Wande, H. et al. (1980) **Pregnancy Outcome for women working in laboratories in some of the pharmaceutical industries** in Sweden. Scandinavian Journal Work Environmental Health 6(2) pp 131-4.

Harper, B. (2001) Health and safety in the classical music industry in the UK and Germany. **Cultural Trends,** 11 pp 43-91.

Health and safety in nail bars

Harris-Roberts, J., Bowen, J., Sumner, J., McDowell, G., Stocks-Greaves, M., Bradshaw, L., Francis, M., Birtles, M., Adisesh, A., Fishwick., D and Barber, C. (2008) **Health and safety in nail bars** Health and Safety Executive: London

Health and Safety Executive (2002) **Control of lead at work: Approved code of practice and guidance** 3rd edition Health and Safety Executive: London.

Health and Safety Executive (2003a) **A guide for new and expectant mothers who work.** HSE, London.

Health and Safety Executive (2003b). **New and expectant mothers at work - a guide for health professionals.** HSE, London.

Health and Safety Executive (2005) **Biological agents: Managing the risks in laboratories and healthcare premises.** HSE, London.

Health and Safety Executive (2009). **The Chemicals (Hazard Information and Packaging for Supply) Regulations.** HSE, London.

Health and Safety Executive (2012). **What is work related contact dermatitis?** HSE, London.

Health and Safety Executive **Laboratories** [Available online]

http://www.hse.gov.uk/biosafety/laboratories.htm (Accessed December, 2014).

Health and Safety Executive **Blood-borne viruses in the workplace Guidance for employers and employees** [Available online]

 http://www.hse.gov.uk/pubns/indg342.htm (Accessed December, 2014).

Heffner, L., Schust, D. (2010). **The reproductive system at a glance** 3rd ed. Chichester; Hoboken: Wiley-Blackwell.

Herdt-Losavio, M., Lin, S. and Druschel, C. et al. (2008). The risk of having a LBW or pre-term infant among cosmetologists in New York State. **Maternal and Child Health Journal,** 13 pp 90-97.

Herdt-Losavio, M., Lin, S. and Druschel, C. et al. (2009) The Risk of Congenital Malformations and Other Neonatal and Maternal Health Outcomes

among Licensed Cosmetologists. **American Journal of Perinatology,** 26 pp 625-631.

Herdt-Losavio, M.L., Lin, S. and Druschel, C.M. et al. (2011) A nested case-control study of low birth weight among cosmetologists. **International Archives of Occupational and Environmental Health,** 84 pp 601-608.

Herpin, G., Gauchard, G., Vouriot, A., Hannhart, B., Barot, A., Mur, J., Zmirou-Navier, D. and Perrin, P. (2008). Impaired neuromotor functions in hospital laboratory workers exposed to low levels of organic solvents. **Neurotoxicity Research,** 13(3-4) pp185-196

Hickey, C., Cliver, S. and Mulvihill, F. et al. (1995). Employment-related stress and pre-term delivery: a contextual examination. **Public Health Report,** 110 pp 410-418.

Hjollund, N.H., Jensen, T.K. and Bonde, J.P. et al. (2000) Spontaneous abortion and physical strain around implantation: a follow-up study of first-pregnancy planners. **Epidemiology,** 11 pp 18-23.

Homer, C. J., Beresford, S. A. and James, S. A. et al. 1990 Work-related physical exertion and risk of pre-term, LBW delivery. 4 (2) pp161-74.

Hu, H., Téllez-Rojo, M., Bellinger, D. and Smith, D. (2006) Fetal lead exposure at each stage of pregnancy as a predictor of infant mental development. **Environmental Health Perspectives**, 114(11) pp 1730-5.

Im H., Oh E., Mun J., et al. (2006). Evaluation of toxicological monitoring markers using proteomic analysis in rats exposed to formaldehyde. **Journal of Proteome Research**, 5(6) pp 1354-1366.

Index mundi Finland Sex Ratio [Online]

http://www.indexmundi.com/finland/sex_ratio.html (Accessed 20 November 2013).

International Agency for the Research of Cancer, World Health Organisation (1993). **Occupational exposure of hairdressers and barbers and personal use of hair colorants. Some hair dyes, cosmetic colorants, industrial dyestuffs and aromatic amines.** IARC Monographs on the Evaluation of Carcinogenic Risk to Humans. 57. World Health Organisation: Geneva, Switzerland.

International Agency for the Research of Cancer, World Health Organisation **Agents Classified by the IARC Monographs**, [Online] Volumes 1–111 http://monographs.iarc.fr/ENG/Classification/ Accessed December 2014)

International Labour Organisation. **International Coding of Occupations.** [Online] http://www.ilo.org/public/english/bureau/stat/isco/index.htm (Accessed 10 November 2013).

Jaakkola, J., Jaakkola, N. and Zahlsen, K. (2001). Fetal growth and length of gestation in relation to prenatal exposure to environmental tobacco smoke assessed by hair nicotine concentration. **Environmental Health Perspectives,** 109 pp 557-561.

Jahromi, B.N. and Husseini, Z. (2008) Pregnancy outcome at maternal age 40 and older. **Taiwanese Journal of Obstetrics and Gynecology,** 47 pp 318-321.

Joffe, M., Bisanti, L. and Apostoli, P. et al. (1999) Time to pregnancy and occupational lead exposure. Asclepios. **Scandinavian Journal of Work, Environment & Health 25 Supplement,** 1 pp 64-65

John, E., Savitz, D. and Shy, C.M. (1994) Spontaneous abortions among cosmetologists. **Epidemiology,** 5 pp 147-155.

Johnson, M. (2013) **Essential Reproduction**. Wiley-Blackwell Chichester West Sussex.

Jonas, O., Roder, D. and Chan, A. (1992). The association of low socio-economic status in metropolitan Adelaide with maternal demographic and obstetric characteristics and pregnancy outcome. **European Journal of Epidemiology**, **8**: 708-714.

Jones, R. and Lopez, K. (2006) Fertilization: The Cortical Reaction. **Human Reproductive Biology**, page 238, 3rd Edition, London: Elsevier

Jorgensen, T., Mortensen, L.H. and Andersen, A.M. (2008) Social inequality in foetal and perinatal mortality in the Nordic countries. **Scandinavian journal of public health,** 36 pp 635-649.

Joya, X, Gomez-Culebras, M., Callejon, A., Friguls, B., Puig, C., Ortigosa, S., Morini, L., Garcia-Algar, O. and Vall, O. (2012). Cocaine use during pregnancy assessed by hair analysis in a Canary Islands cohort **BMC Pregnancy and childbirth** 9 Article12.

Källén, B. 1988. **Epidemiology of Human Reproduction**. Boca Raton: CRC Press

Kavlock RJ and Daston GP (Eds.) (1997) Drug Toxicity in Embryonic Development I. Advances in understanding mechanisms of birth defects: morphogenesis and processes at risk. Springer-Verlag (New York), 610 pp.

Keith, L.G., MacGregor, S. and Friedell, S. et al. (1989) Substance abuse in pregnant women: recent experience at the Perinatal Center for Chemical

Dependence of Northwestern Memorial Hospital. **Obstetrics and gynecology,** 73 pp 715-720.

KELA, Maternity grant and maternity package. [Online] Available From:

http://www.kela.fi/web/en/pregnancy_maternity-grant [Accessed September 2013].

Kenny, D.T., Davis, P. and Oates, J. (2004). Music performance anxiety and occupational stress amongst opera chorus artists and their relationship with state and trait anxiety and perfectionism. **Journal of Anxiety Disorders,** 18 pp 757-777.

Kenny, L.C., Lavender, T. and Mills, T. et al. (2011) Advanced maternal age and adverse pregnancy outcome, Reproductive Sciences. **Conference: 58th Annual Scientific Meeting of the Society for Gynecologic Investigation**, SGI 2011 Miami Beach, FL United States. pp. 267A-268A.

Kersemaekers, W.M., Roeleveld, N. and Zielhuis, G.A. (1995) Reproductive Disorders Due to Chemical-Exposure among Hairdressers. **Scandinavian Journal of Work Environment & Health,** 21: 325-334.

Kersemaekers, W.M., Roeleveld, N. and Zielhuis, G.A. (1995) Reproductive disorders due to chemical exposure among hairdressers. **Scandinavian Journal Work Environment and Health,** 21: 325-334.

Kersemaekers, W.M., Roeleveld, N. and Zielhuis, G.A. (1997) Reproductive disorders among hairdressers. **Epidemiology,** 8: 396-401.

Kersemaekers, W.M., Verheijen, N. and Kromhout, H. et al. (1998) Assessment of exposure to solvents among hairdressers: reliability of a

classification scheme and questionnaire. **Occupational and Environmental Medicine,** 55: 37-42.

Khan K.S., Ter Riet G., Glanville J., Sowden A.J., Kleijnen J. (2009). The NHS Centre for Reviews and Dissemination (CRD). [Online] **Undertaking Systematic Reviews of Research on Effectiveness. CRD's Guidance for Carrying Out or Commissioning Reviews**. 2nd Ed. New York: NHS Centre for Reviews and Dissemination, University of York, 2000. [CRD Report No. 4]. Available from: http://www.york.ac.uk/_inst/cdr/report4.htm [Accessed April 2014].

Kim, D. and Saada, A. (2013). The social determinants of infant mortality and birth outcomes in Western developed nations: a cross-country systematic review. **International journal of environmental research and public health**. 10(6) pp.2296-335.

Kuhn, L, Kline, J, Ng, S, Levin, B. and Susser, M. (2000). Cocaine use during pregnancy and intrauterine growth retardation: new insights based on maternal hair tests. **American journal of epidemiology**, 152 (2) pp112-9.

Kleinstreuer N, Dix D, Rountree M, Baker N, Sipes N, et al. (2013) A Computational Model Predicting Disruption of Blood Vessel Development. PLoS Comput Biol 9(4): e1002996. doi:10.1371/journal.pcbi.1002996.

Knowland, J., McKenzie, E., McHugh, P. and Cridland, N. (1993) Sunlight-induced mutagenicity of a common sunscreen ingredient. **Federation of European Biochemical Societies (FEBS) Letters.** 324 (3) 309–313.

Knudsen TB and Kavlock RJ (2008) Comparative bioinformatics and computational toxicology. Developmental Toxicology 3rd edition. (B Abbott and D Hansen, editors) New York: Taylor and Francis, Chapter 2, pp 3-360.

Knudsen, T. and Kleinstreuer N. (2011) Disruption of embryonic vascular development in predictive toxicology. **Birth Defects Research***: Part C* 93 pp 312-323.

Kramer, M. Séguin, L., Lydon J. and Goulet, L. (2000). Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? **Paediatric and Perinatal Epidemiology** 14(3) pp 194–210.

Labreche, F.K., Forest, J. and Trottier, M. (2003) Characterization of chemical exposure in hairdressing salons. **Applied Occupational and Environmental Hygiene,** 18 pp 1014-1021

Larsen, W., Sherman, L., Potter, S., Scott, W. (2001) Bilaminar embryonic disc development and establishment of the uteroplacental circulation. **Human Embryology.** Chapter 2: New York: Churchill Livingstone

Lemasters, G. (1998). **Maternal occupational exposures and adverse pregnancy outcomes embryonic and foetal loss.** In Encyclopaedia of Occupational Health International Labour Organisation: Geneva, Switzerland.

Leino, T., Kahkonen, E. and Saarinen, L. et al. (1999) Working conditions and health in hairdressing salons. **Applied Occupational and Environmental Hygiene,** 14 pp 26-33.

Leonardi-Bee, J., Britton, J. and Venn, A. (2011) Second-hand Smoke and Adverse Foetal Outcomes in Non-smoking Pregnant Women: A Meta-analysis. **Pediatrics,** 127 pp 734 -741.

Li, X., Sundquist, J. and Kane, K. et al. (2010) Parental occupation and pre-term births: A nationwide epidemiological study in Sweden. **Paediatric and Perinatal Epidemiology,** 24: 555-563.

Lind, M., Albin, M., Brisman, J., Diab, K., Lillienberg, L., Mikoczy, Z., Jörn Nielsen, J., Rylander, L., Torén, K. and Meding, B. (2007) Incidence of hand eczema in female Swedish hairdressers, **Occupational and Environmental Medicine.** 64 (3) pp 191–195.

Lindbohm, M., Sallmen, M. and Taskinen, H. (2002) Effects of exposure to environmental tobacco smoke on reproductive health. **Scandinavian Journal of Work, Environment and Health**, 28 (Supplement 2) pp 84-96.

Linn, S., Schoenraum, S., Monson, R., Rosner, R., Stubblefield, P., Ryan, K. (1983). The Association of Marijuana Use with Outcome of Pregnancy. **American Journal of Public Health**, 73 (10) pp 1161-1165

Luke, B. and Papiernik, E. (1997). The effects of lifestyle on prematurity. **In Preterm labor.** pp 127–52. Eds. Elder M., Lamont R. and Romero R. New York: Churchill Livingstone

Lurie, S., Zalmanovitch, A. and Golan, A. et al. (2010). The effect of marital status on pregnancy outcome in Israel: A retrospective case-control study. **Journal of Obstetrics and Gynaecology Research,** 36 pp 1161-1164.

Mamelle, N., Laumon, B. and Lazar, P. (1984) Prematurity and occupational activity during pregnancy. **American Journal of Epidemiology.** 119 pp 309–22.

Mattison, D. (2011) in **Reproductive System**, in Encyclopedia of Occupational Health and Safety Chapter 9. Editor Lemasters, G and Editor-in-Chief Jeanne Mager Stellman. International Labor Organization, Geneva.

McAnarney E. (1987) Young Maternal Age and adverse neonatal outcome. **American Journal of Diseases of Children**, 141 pp 1053-59.

McCowan M.E.L., Dekker, G.A. and Chan, E. et al. (2009) Spontaneous preterm birth and SGA infants in women who stop smoking early in pregnancy: prospective cohort study. **BMJ338b1081** ONLINE FIRST 2009. Available from: http://www.bmj.com/content/338/bmj.b1081.pdf%2Bhtml [Accessed August 2013]

McDonald, A., McDonald, J. and Armstrong, B. et al. (1988) Prematurity and work in pregnancy. **British Journal of Industrial Medicine,** 45 pp 56-62.

McIlvaine, D., Stewart, M. and Anderson, R. (2012) Noise exposure levels for musicians during rehearsal and performance times. **Medical problems of performing artists,** 27 (1) p 31.

McHugh, P. and Knowland, J. (1997) Characterization of DNA damage inflicted by free radicals from a mutagenic sunscreen ingredient and its location using an in-vitro genetic reversion assay. **Photochemistry and Photobiology.** **66** (2) 276–281.

Misra D. and Ananth C. (2002) Infant mortality among singletons and twins in the US during two decades: effect of maternal age. **Pediatrics,** 110(6) pp 1163–8.

Moore, K., Torchia, M. and Persaud, V.N. (2003). **Formation of the bilaminar embryonic disc: second week.** The Developing Human, Clinically Oriented Embryology. Elsevier: India

Mounier-Geyssant, E., Oury, V. and Mouchot, L. et al. (2006) Exposure **of hairdressing apprentices to airborne hazardous substances** [online]. Environmental Health: A Global Access Science Source, 5, 23. Available from: <http://www.ehjournal.net/content/5/1/23> (Accessed August 2013).

Morrison, J., Najman, J. M. and Williams, G. M. Keeping, J. and Andersen M. (2005) Socio-economic status and pregnancy outcome. An Australian study. **British Journal of Obstetrics and Gynecology,** 96 (3) 298-307.

Mozurkewich, E., Luke, B., Avni, M. and Wolf, F. (2000) Working conditions and adverse pregnancy outcome: a meta-analysis. **Obstetrics and Gynecology** 95(4) pp 623–635.

Mussi, G. and Gouveia, N. (2008). Prevalence of work-related musculoskeletal disorders in Brazilian hairdressers. **Occupational Medicine State of the Art Reviews,** 58 pp 367-369.

Naeye, R. and Peters E. (1982). Working during pregnancy**. Pediatrics**, 69 pp 724-727.

National Research Council (2000) **Scientific frontiers in developmental toxicology and risk assessment.** The National Academies Press, Washington DC.

National Research Council (2007) Toxicity Testing in the 21st Century: A Vision and a Strategy. The National Academies Press, Washington DC.

Natural Environment Research Council (2014) **Guidance on exposure control approaches for laboratory uses of hazardous chemicals Version 1.7** [Online]

http://www.nerc.ac.uk/about/policy/safety/procedures/guidance_exposure_control_approaches.pdf [Accessed, December 2014]

Ng, S-K., Olog, A., Spinks, A., Cameron, C., Searle, J. and McClure, R. (2010) Risk factors and obstetric complications of LGA births with adjustments for community effects: results from a new cohort study. **BMC Public Health,** 10(1), pp.460

Nieminen, P., Lehtiniemi, H., Huusko, A., Vähäkangas, K. and Rautio, A. (2013) Polychlorinated biphenyls (PCBs) in relation to secondary sex ratio – A systematic review of published studies. **Chemosphere** 91(2), pp 131–138.

Nohynek, G., Fautz, R., Benech-Kieffer, F. and Toutain, H. (2004a) Toxicity and human health risk of hair dyes. **Food and Chemical Toxicology,** 42 (4), pp 517-543.

Nohynek, G., Skare, J. and Meuling, W. et al. (2004b) Urinary acetylated metabolites and N-acetyltransferase-2 genotype in human subjects treated with a para-phenylenediamine-containing oxidative hair dye. **Food and Chemical Toxicology,** 42(11) pp 1885-1891.

Nohynek, G., Antignac, E., Re, T. and Toutain, H. (2010). Safety assessment of personal care products/cosmetics and their ingredients. **Toxicology and Applied Pharmacology** 243 pp 239–259.

NTP-CERHR. (2006) Expert panel report on the reproductive and developmental toxicity of propylene glycol triethylene glycol and polyethylene

glycol (PEG-4). Final report on the Safety of assessment of triethylene Glycol and PEG-4. **International Journal of Toxicology**, 25: 121-138.

Nurminen, T. and Kurppa, K. (1989) Occupational noise exposure and course of pregnancy. **Scandinavian Journal of Work, Environment & Health,** 15: 117-124.

European Foundation for the Improvement of Living and Working Conditions. (2005) **Minimum wages in Europe**. [Online] Available from:

http://www.eurofound.europa.eu/pubdocs/2007/83/en/1/ef0783en.pdf

[Accessed November 2013]

Office of Environmental Health State of California Environmental Protection Agency**,** Hazard Assessment Safe Drinking Water and Toxic Enforcement Act 1986 .**Chemicals Known to The State to Cause Cancer or Reproductive Toxicity.** [Online] Available from:

Http://oehha.ca.gov/prop65/prop65_list/files/p65single110813.pdf   [Accessed November 2013].

Office National Statistics. (2012). **Gestation-specific infant mortality in England and Wales**, Statistics Bulletin 2010. [Online] Available from

http://www.ons.gov.uk/ons/dcp171778_282579.pdf [Accessed 24 November 2013].

Ogilvy-Stuart, A., & Shalet, S. (1993). Effect of radiation on the human reproductive system. **Environmental Health Perspectives,** 101(Suppl 2), pp 109-116.

Orsiere T, Sari-Minodier I, Iarmarcovai G, Botta A. (2006). Genotoxic risk assessment of pathology and anatomy laboratory workers exposed to

formaldehyde by use of personal air sampling and analysis of DNA damage in peripheral lymphocytes. **Mutation Research**, 605(1-2) pp 30-41.

Ozen OA, Akpolat N, Songur A, et al. (2005). Effect of formaldehyde inhalation on Hsp70 in seminiferous tubules of rat testes: an immuno-histochemical study. **Toxicology and Industrial Health**. 21(10) pp 249-254.

Parker, J., Schoendorf, K. and Kiely J. (1994). Associations between measures of socioeconomic status and LBW, SGA, and premature delivery in the United States. **Annals of Epidemiology**. 4 (4) pp 271–278.

Peretz, J., Gallicchio, L. and Miller, S. et al. (2009). Infertility among cosmetologists. **Reproductive Toxicology,** 28 pp 359-364.

Peters, C., Harling, M. and Dulon, M. et al. (2010). Fertility disorders and pregnancy complications in hairdressers - a systematic review. **Journal of Occupational Medicine and Toxicology,** 5 pp 24-30.

Pichini, S., Puig, C., Zuccaro, P., Marchei, E., Pellegrini, M., Murillo, J., Vall, O., Pacifici, Roberta and García-algar, O. (2005). Assessment of exposure to opiates and cocaine during pregnancy in a Mediterranean city: preliminary results of the "Meconium Project". **Forensic science international,** 153(1), pp 59-65.

Pond, S. (2005) **Attributes You Need To Be a Successful Hairdresser**. [Online] Available from:

http://www.cobellavideos.com/articles/sarra/01print.htm [Accessed November 2013]. See Appendix 13.

Quansah, R. (2011). **Occupational determinants of adverse pregnancy outcomes**: work in healthcare and exposure to welding fumes and metal dust. Ph.D. thesis: University of Birmingham.

Rebagliato, M., Bolumar, F. and Florey C du, V. et al. (1995). Assessment of exposure to environmental tobacco smoke in non-smoking pregnant women in different environments of daily living. **American journal of epidemiology,** 142 pp 525-530.

ReportLinker. (2013a) **Global Hair Care Market 2012-2016**. [Online] Available from: http://www.reportlinker.com/p01171785/Global-Hair-Care-Market.html [Accessed November 2013]

Reportlinker. (2013b) **Global Facial Care**, MarketLine Industry Guides. [Online] Available from:

http://www.reportlinker.com/p01352221-summary/Global-Facial-Care-MarketLine-Industry-Guides.html [Accessed 24 November 2013].

Ribas-Fito, N., Sala, M., Kogevinas, M., and Sunyer, J. (2001) Polychlorinated biphenyls (PCBs) and neurological development in children: a systematic review. **Journal of Epidemiology and Community Health.** 55(8) pp 537–546.

Rogers J. (2009) Tobacco and pregnancy. **Reproductive Toxicology** 28 (2) pp152–160

Ronda, E., Hjollund, B. and Moen, B. (2009). Airborne exposure to chemical substances in hairdresser salons. **Environmental Monitoring and Assessment,** 153 pp 83-93.

Ronda, E., Moen, B.E. and Garcia, A.M. et al. (2010). Pregnancy outcomes in female hairdressers. **International Archives of Occupational and Environmental Health,** 83 pp 945-951.

Rylander, L., Axmon, A. and Toren, K. et al. (2002). Reproductive outcome among female hairdressers. **Occupational and Environmental Medicine,** 59: pp 517-522.

Rylander, L. and Källén, B. (2005). Reproductive outcomes among hairdressers. **Scandinavian Journal of Work Environment and Health,** 31 pp 212-217.Saadi, H. and Abdollahi, M. (2012). The Importance of Pesticides Effects on Human Reproduction in Farmers. **International journal of pharmacology**, 8(6) pp 467-469.

Samet JM. (1991). New effects of active and passive smoking on reproduction? **American Journal of Epidemiology**, 133 (4) pp 348–350.

Saxén L. (1976). Mechanisms of teratogenesis. **Journal of Embryology and Experimental Morphology,** 36 pp 1-12.

Sarsilmaz M., Kaplan S., Songur A., et al. (2007). Effects of postnatal formaldehyde exposure on pyramidal cell number, volume of cell layer in hippocampus and hemisphere in the rat: a stereological study. **Brain Research**. 1145 pp157-167.

Schaumburg, I. and Olsen, J. (1991). Birth-weight and gestational age among children of Danish pharmacy assistants. **Journal of Epidemiology and Community Health,** 45(1) pp 49–51.

Scholl, T.O., Hediger, M.L. and Huang, J. (1992). Young maternal age and parity influences on pregnancy outcome. **Annals of Epidemiology,** 2 pp 565-575.

Sever, L. (2011). **Reproductive System**, in Encyclopedia of Occupational Health and Safety Chapter 9. Editor Lemasters, G and Editor-in-Chief Jeanne Mager Stellman. International Labor Organization, Geneva.

Shah, P.S., Zao, J. and Ali, S. Knowledge Synthesis Group of Determinants of pre-term, LBW babies. Maternal marital status and birth outcomes: a systematic review and meta-analyses. **Maternal & Child Health Journal,** 15 pp 1097-1109.

Silicon Valley Blogger. (2007) Traditional jobs for men and women and the gender divide, **The Digerati life**. [Online] Available from:

http://www.thedigeratilife.com/blog/index.php/2007/05/29/traditional-jobs-for-men-and-women-the-gender-divide (Accessed November 2013).

Smith, D.; Wang, R-S. (2006). Glutaraldehyde exposure and its occupational impact in the health care environment. **Environmental Health and Preventive Medicine,** 11(1) pp 3-10

Smith, G. (2013). Global Cosmetics Manufacturing Industry Market Research Report Now Available from **IBIS World**, prweb. [Online] Available from:

http://www.ibisworld.com/industry/global/global-cosmetics-manufacturing.html [Accessed September 2013].

Snijder, C. A., de Velde, E. and Roeleveld, N. (2012). Occupational exposure to chemical substances and time to pregnancy: a systematic review. **Human Reproduction Update,** 18 (3) pp 284-300

Soni, M.G., Carabin, I.G. and Burdock, G.A. (2005). Safety assessment of esters of p-hydroxybenzoic acid (parabens). **Food and chemical toxicology**: an international journal published for the British Industrial Biological Research Association. 43 pp 985-1015.

Soepatmi, S (1994). Developmental outcomes of children of mothers dependent on heroin or heroin/methadone during pregnancy. **Acta Pædiatrica**.83, pp 36-39.

Spear, M., LoRusso, P., Mita, A., and Mita M. (2011) Vascular disrupting agents (VDA) in oncology: advancing towards new therapeutic paradigms in the clinic. **Current Drug Targets.** 12 (14) pp 2009-15.

Speit G. (2006). The implausibility of systemic genotoxic effects measured by the comet assay in rats exposed to formaldehyde. **Journal Proteome Research**. 5 (10) pp 2523-2524.

Speit, G., Zeller, J., Schmid, O., Elhajouji, A., Ma-Hock, L. and Neuss, S. (2009). Inhalation of formaldehyde does not induce systemic genotoxic effects in rats. **Mutation Research**. 677(1-2) pp 76-85.

Stillerman, K., Mattison D., Giudice, L. and Woodruff T. (2008). Environmental exposures and adverse pregnancy outcomes: A review of the science. **Reproductive Sciences,** 15 pp 631-650.

Stern, A. and Smith, A. (2003). An assessment of the cord blood: maternal blood methyl mercury ratio: implications for risk assessment. **Environmental Health Perspectives,**.111 pp 1465-1470.

Strano-Rossi, S., Chiarotti, M., Fiori, A., Auriti, C., Seganti, G. and Strano-Rossi, S. (1996). Cocaine abuse in pregnancy: Its evaluation through hair analysis of pathological new-borns. **Life Sciences**, 59(22) pp 1909-1915.

Su, P-H.; Ng, Y-Y., Chen, J-Y., Su, P-H., Chen, J-Y., Chang, Y-Z., Chen, S-C. and Yang, C. (2012). Perinatal effects of combined use of heroin, methadone, and amphetamine during pregnancy and quantitative measurement of metabolites in hair. **Pediatrics and Neonatology,** 53(2) pp.112-117.

Takser, L., Mergler, D., Baldwin, M. and de Grosbois, S. (2005). Thyroid Hormones in Pregnancy in Relation to Environmental Exposure to Organochlorine Compounds and Mercury. **Environmental Health Perspectives,** 113(8) pp1039-45.

Taskinen, H., Kyyrönen, P., Hemminki, K., Hoikkala, M., Lajunen, K., Lindbohm, M-L. (1994). Laboratory work and pregnancy outcome. **Journal of Occupational Medicine**, 36 pp 311-319.

Taskinen HK, Kyyronen P, Sallmen M., Virtanen, S., Liukkonen, T., Huida, O., Lindbohm, M-L. and Anttila, A. (1999). Reduced fertility among female wood workers exposed to formaldehyde. **American Journal of Industrial Medicine.** 36(1) pp 206-212.

Teperi, J. (1993). Multi Method Approach to the Assessment of Data Quality in the Finnish Medical Birth Registry. **Journal of Epidemiology and Community Health** 47(3), pp 242-247.

Travers, C. (2001). Stress in teaching: Past, present and future. In Dunham, JE (Ed) **Stress in the Workplace: Past, Present and Future**, pp.164-190 Whurr Publishers: London.

Teperi, J. (1993). Multi method approach to the assessment of data quality in the Finnish Medical Birth Registry. **Journal of Epidemiology and Community Health**, 47(3) pp 242-7.

Tunón, K., Eik-Nes, H., Grøttum, P., Von Düring, V. and Kahn, J. (2000). Gestational age in pregnancies conceived after in-vitro fertilization: a comparison between age assessed from oocyte retrieval, crown-rump length and biparietal diameter. **Ultrasound Obstetrics and Gynecology** 15 (1) pp 41–6.

Tsigonia, A., Tanagra, D. and Linos, A. et al. (2009) Musculoskeletal disorders among cosmetologists. **International Journal of Environmental Research and Public Health,** 6(12) pp 2967-79

Tsigonia, A., Lagoudi, A. and Chandrinou, S. et al. (2010). Indoor Air in Beauty Salons and Occupational Health Exposure of Cosmetologists to Chemical Substances. **International Journal; Environmental Research and Public Health,** 7(1) pp 314–324

United Kingdom Government 1998, Data Protection Act. [Online] Available from: http://www.legislation.gov.uk/ukpga/1998/29/contents [Accessed November 2013].

Van der Wal, J. , Hoogeveen, A. and Moons, A. et al. (1997) Investigation on the exposure of hairdressers to chemical agents. **Environment International**, 23(4) pp 433–439.

Van Muiswinkel, W.J., Kromhout, H. and Onos, T. et al. (1997). Monitoring and modelling of exposure to ethanol in hairdressing salons. **The Annals of Occupational Hygiene,** 41 pp 235-247.

Varella, S, Rampazo, R. and Varanda, E. (2008) Urinary mutagenicity in chemical laboratory workers exposed to solvents. **Journal of Occupational Health**, 50 (5) pp 415-422.

Vergieva, T., Panev, T. and Popov. et al. (1998). Aromatic hydrocarbons as reproductive hazards for women in a control laboratory of petrochemical plant. **International Archives of Occupational and Environmental Health,** 71 pp S70-S74.

Wahlstrom, J., Mathiassen, S.E., Liv, P., Hedlund, P., Ahlgren, C., Forsman, M., 2010. Upper arm postures and movements in female hairdressers across four full working days. **Annals of Occupational Hygiene,** 54 pp 584-594.

Wakeford, R. (2013). The risk of childhood leukaemia following exposure to ionising radiation—a review. **Journal of Radiological Protection**, 33(1) pp1-25.

Wang L., Yan, L., Fu P.P., et al. (2003). Photomutagenicity of cosmetic ingredient chemicals azulene and guaiazulene. **Mutation Research** 530 (1–2) pp 19–26.

Ward, H., Cousens, N. and Smith-Bathgate, B. et al. (2004). Obstacles to conducting epidemiological research in the UK general population. **British Medical Journal,** 329 (7460) pp 277–279.

Wennborg, H., Bodin, L. and Vainio, H. G. A. (2000). Pregnancy outcome of personnel in Swedish biomedical research laboratories, **Journal Occupational Environmental Medicine,** 42 (4) pp 438-446.

Wennborg, H., Bonde, J.P. and Stenbeck, M. et al. (2002). Adverse reproduction outcomes among employees working in biomedical research

laboratories. **Scandinavian Journal of Work, Environment & Health,** 28 pp 5-11.

Wikipedia, Nov 2012. Value of worldwide beauty. [Online] Available from: http://en.wikipedia.org/wiki/Beauty_products#Ingredients_2   value   of worldwide beauty [Accessed 24 November 2013].

Wolfe, L. and Mottola, M. (1993). Aerobic exercise in pregnancy: an update. **Canadian Journal of Applied Physiology,** 18 pp 119-147.

Woolf M. and Woolard, P. (1998). **Occupational and Environmental Exposures to the New-born.** In Stellman, J. (Ed) Encyclopedia of Occupational Safety and Health. 1 pp 9.1-9.30 International Labor Organisation: Geneva.

World Press.org. (2002). **Finland's Teacher Trap - Low Pay, Low Prestige, World Press Review**. [Online] Available from http://worldpress.org/Europe/654.cfm [Accessed November 2013].

Worz-Bilfinger, D. (2012) Special performing problems of female musicians: Three case studies. **Work,** 41 pp 33-36.

Yogev, Y., Melamed, N. and Bardin, R.et al. (2010). Pregnancy outcome at extremely advanced maternal age. **American journal of obstetrics and gynecology,** 203 pp 551-557.

Zhou, Y., Zhang, S., Li, Z., Zhu, J., Bi, Y., Bai, Y. and Wang, H. (2014). Maternal Benzene Exposure during Pregnancy and Risk of Childhood Acute Lymphoblastic Leukemia: A Meta-Analysis of Epidemiologic Studies PLoS One [Online], 9(10),

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0110466

[accessed 14 Dec 2014].

Zhu, J.L., Hjollund, N.H. and Andersen, A-M. et al. (2004a). Shift work, job stress and late foetal loss: The National Birth Cohort in Denmark. **Journal of Occupational and Environmental Medicine 46,** pp 1144-1149.

Zhu, J.L., Hjollund and N.H., Olsen J. (2004b). Shift work, duration of pregnancy and birth-weight The National Birth Cohort in Denmark. **American**

Zhu, J., Vestergaard, M. and Hjollund, N. et al. (2006a). Pregnancy outcomes among female hairdressers who participated in the Danish National Birth Cohort. **Scandinavian Journal of Work Environment and Health,** 32 pp 61-66.

Zhu, J., Knudsen, L. Andersen, A-M., Hjollund, N. and Olsen, J. (2006b). Laboratory work and pregnancy outcomes: a study within the National Birth Cohort in Denmark. **Occupational and Environmental Medicine**. 63, pp 53-58.

Zibrowski, E., Robertson, J. (2006). Olfactory sensitivity in medical laboratory workers occupationally exposed to organic solvent mixtures **Occupational Medicine** 56(1) pp.51-54.

13 APPENDICES

13.1 Appendix: Original paper: Work as a hairdresser and cosmetologist and adverse pregnancy outcomes.

Halliday-Bell JA, Gissler M, Jaakkola JJ.

Occupational Medicine (London). 2009 May; 59:180-4.
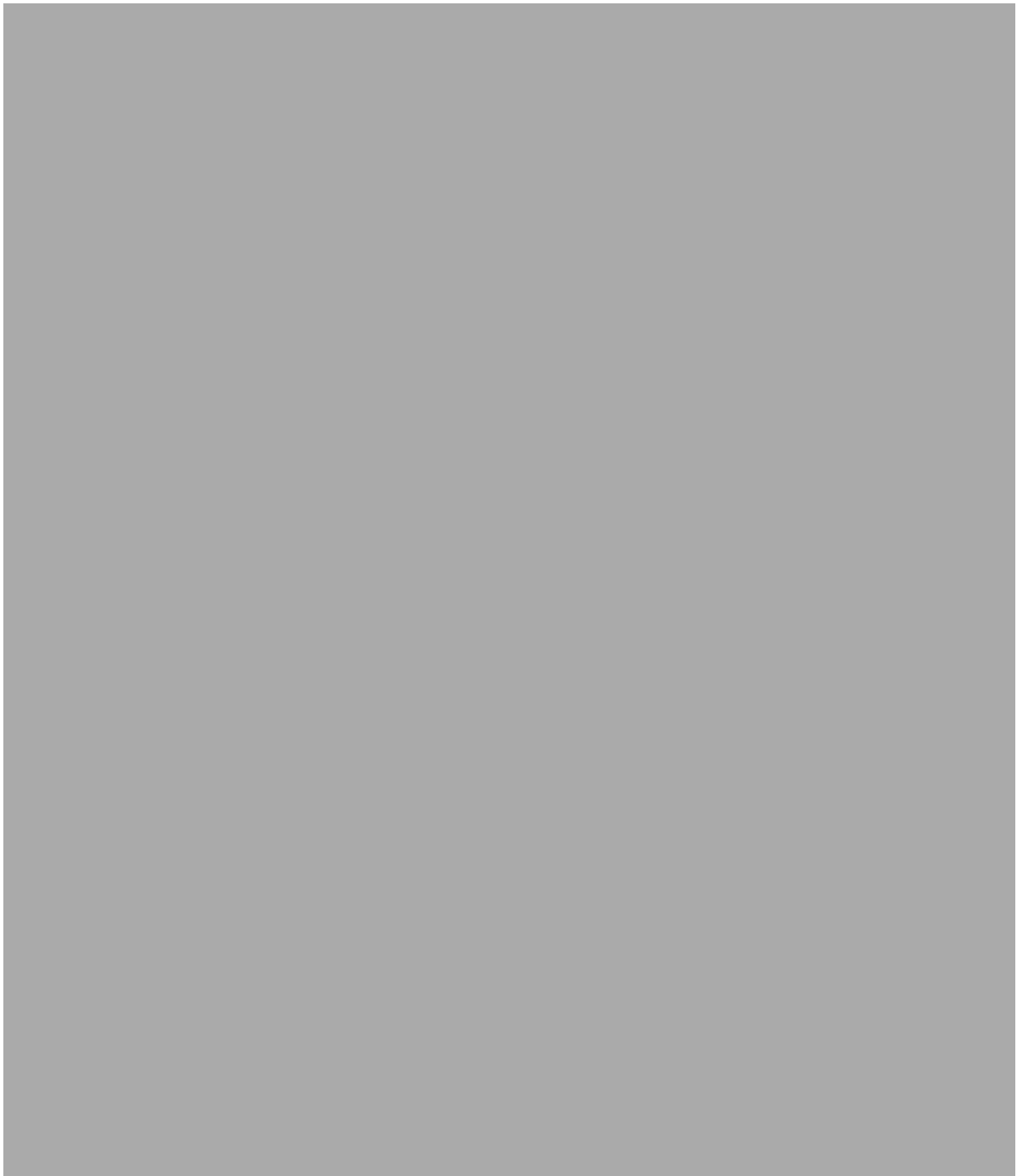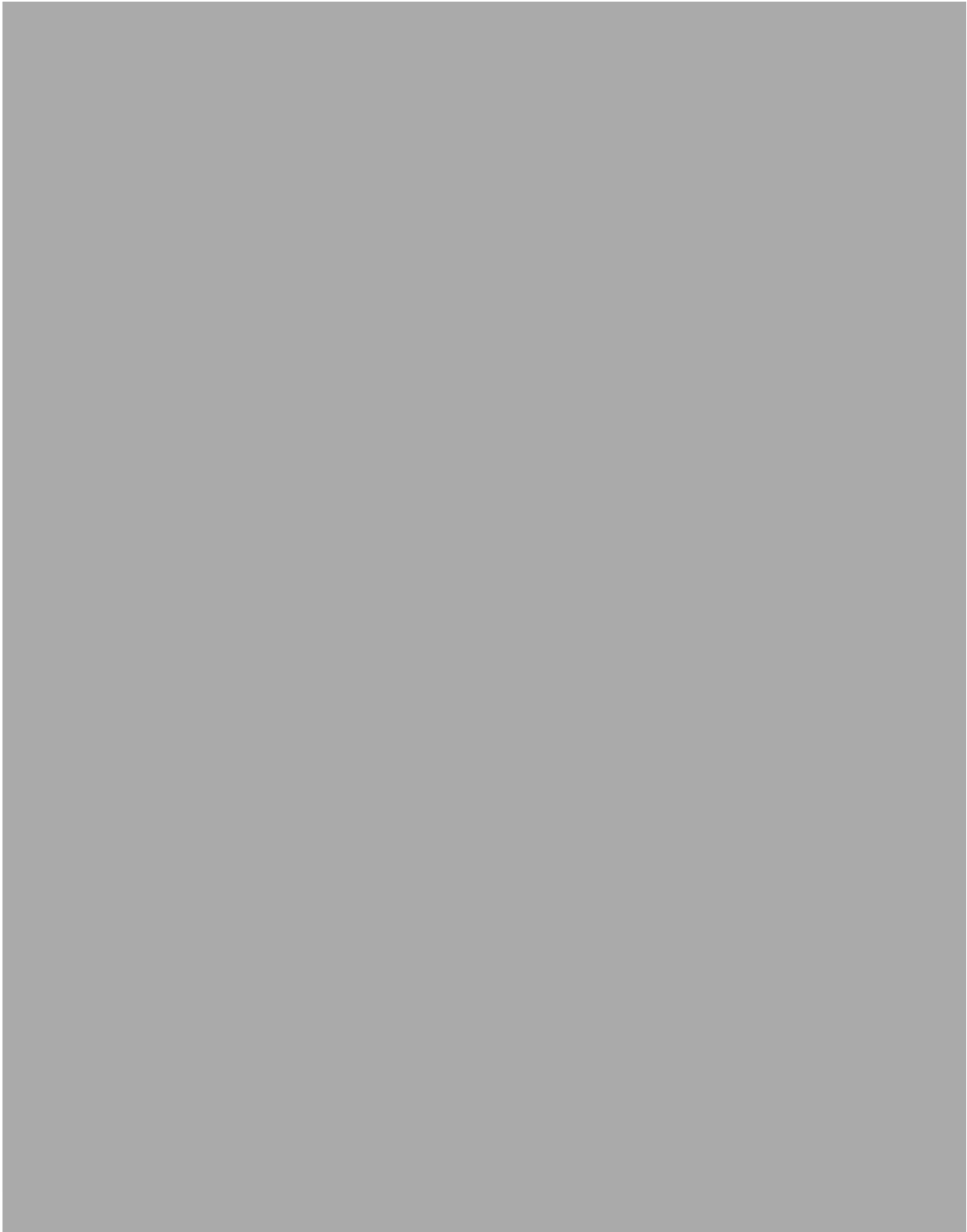
13.2 Appendix: Original paper

Laboratory work and adverse pregnancy outcomes. Halliday-Bell J.A., Quansah R., Gissler, M. and Jaakkola J.J. Occupational Medicine (London). 2010 June, 60, (4):310-313.
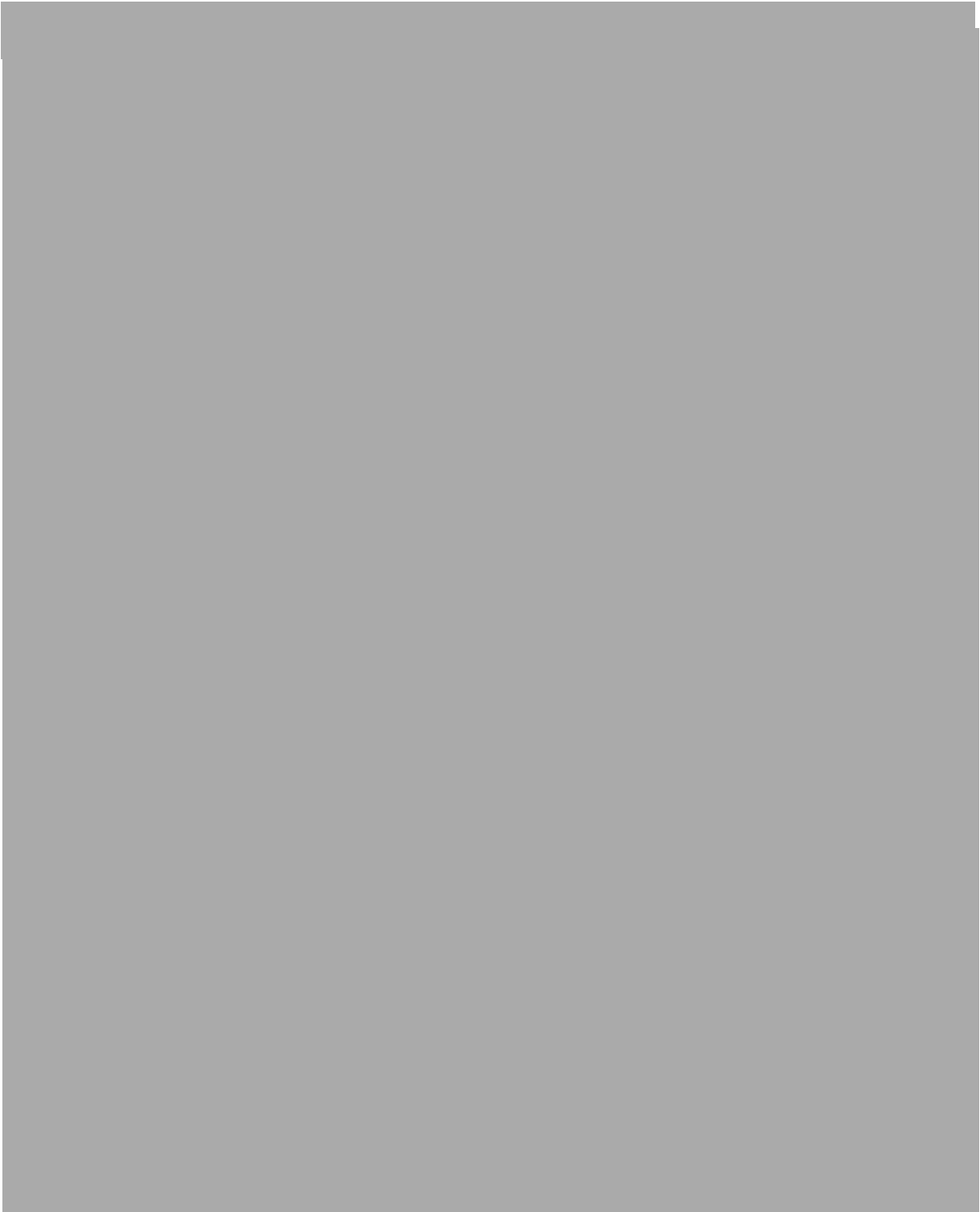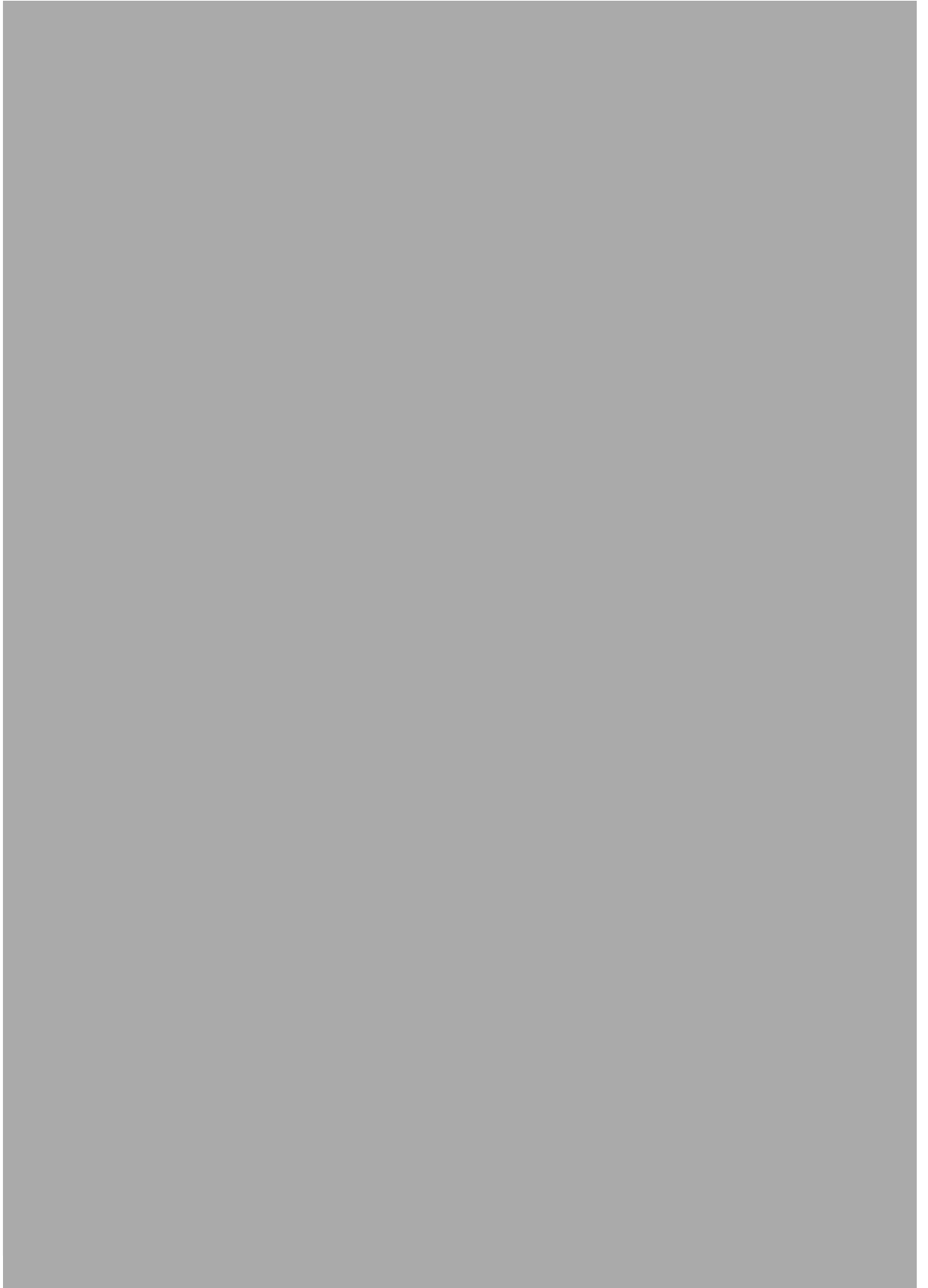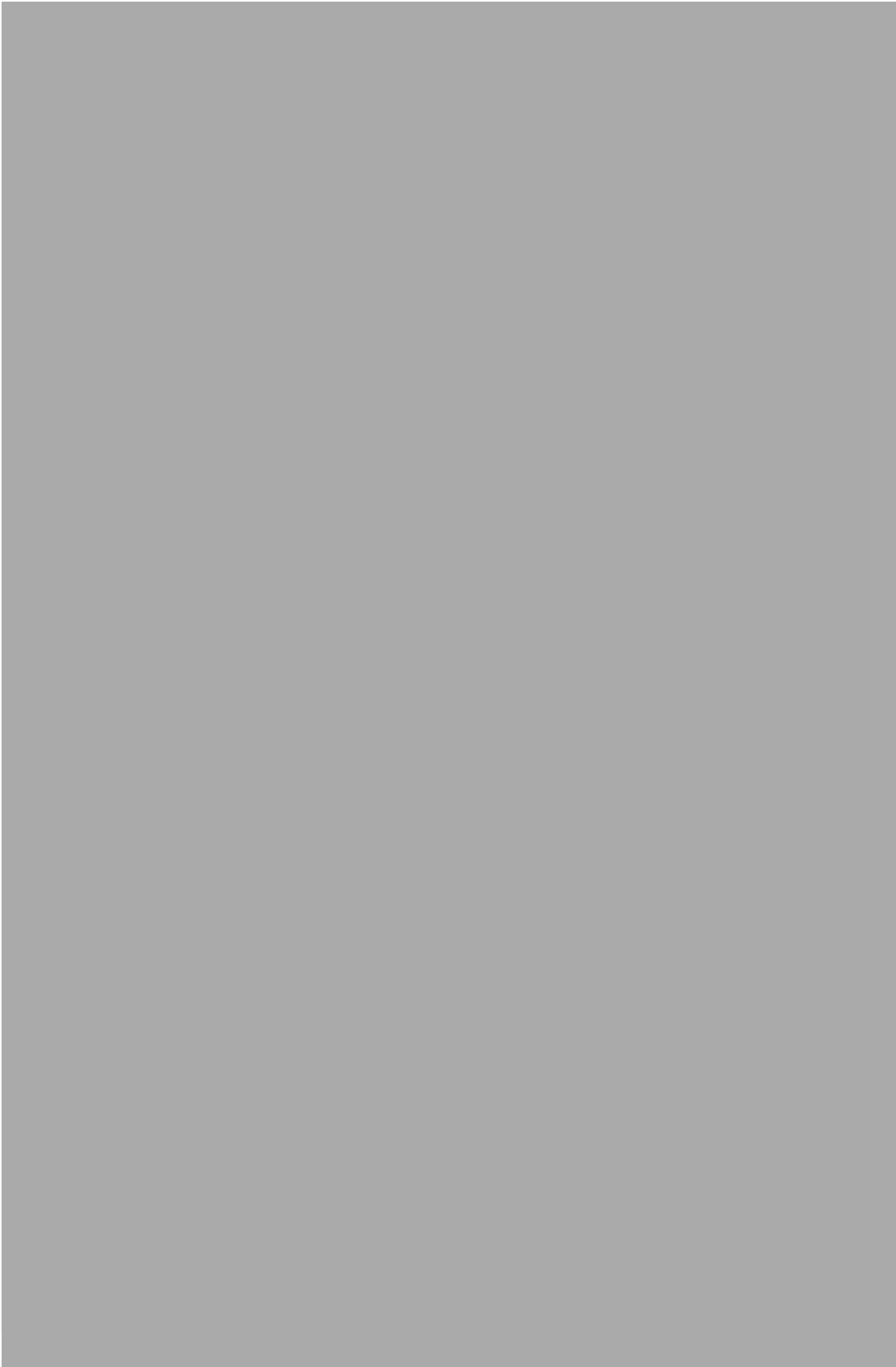
13.3 Appendix: Ethics Committee Approval Confirmation
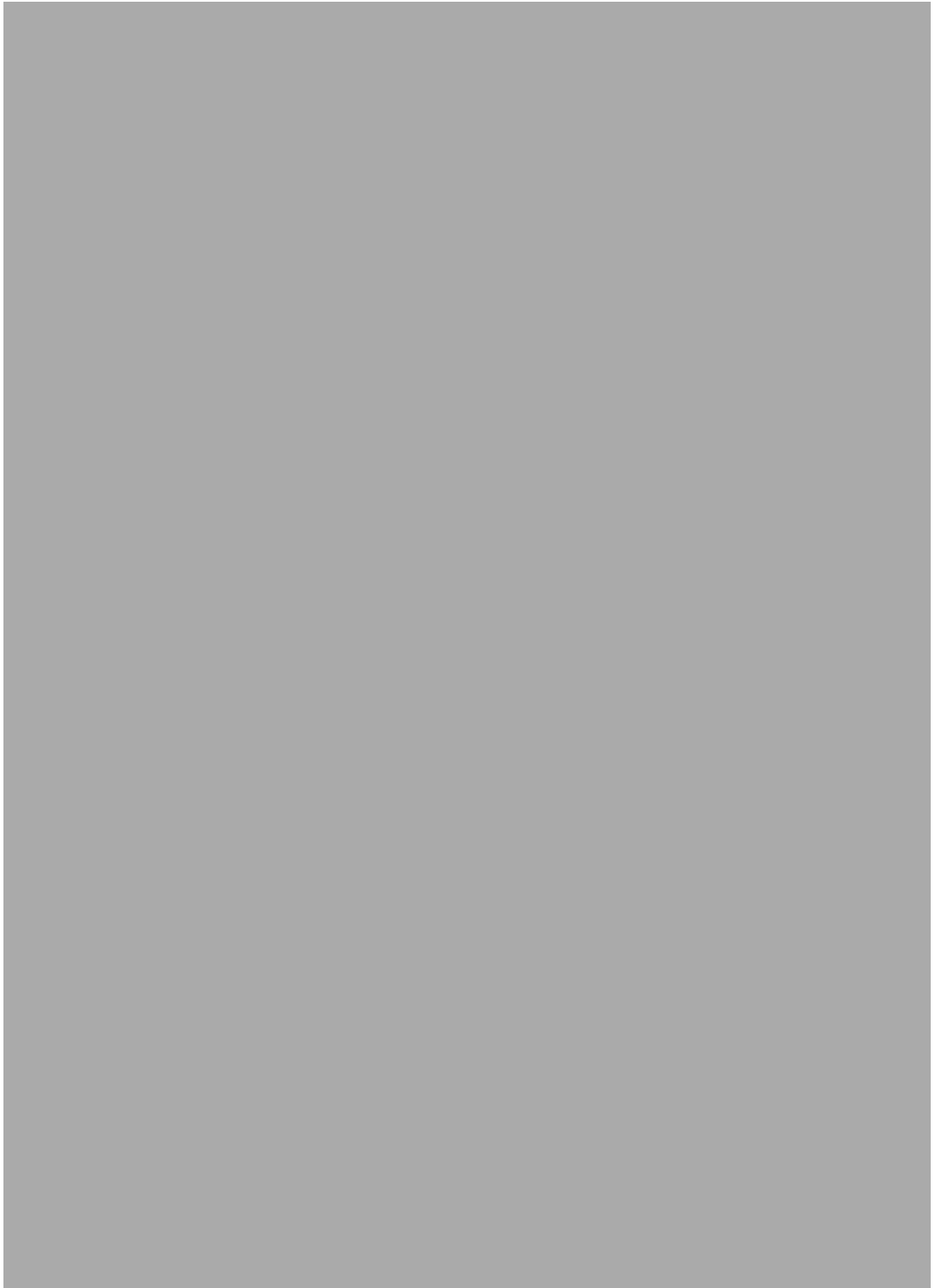
13.4 Appendix: Letter to researchers

Friday, March 15, 2013

Dear Fellow researcher,

Re: Pregnancy outcomes in hairdressers, cosmetologist and laboratory workers

I am a medical doctorate postgraduate student at the University of Birmingham in England. I am in the process of undertaking a systematic review of the evidence on possible pregnancy outcomes amongst hairdressers, cosmetologist and laboratory workers. This work will contribute to my thesis on the same topic where I will undertake an epidemiological cohort study of a large population of women who have given birth over a period of time between 1990 and 2010. It is necessary for me to complete a systematic review of existing evidence. I plan to utilise Embase CINAHL and MEDLINE and examine Cochrane CORE, DARE, Prospero, Central trials, HTA and the *systematicreviewsjournal* websites at minimum.

I am aware of your involvement in this area of research. It would therefore be helpful if you would be kind enough to share with me any unpublished work or grey literature that may exist to your knowledge. This will enable me to undertake a full systematic review to the satisfaction of my assessors. I'm keen to complete the systematic review by the end of May 2013. This would include time taken to access the relevant reports and prepare tables summarising the nature of the studies and the outcomes found. I may also need to undertake a meta-analysis of any works that are similar in composition to my own.

Please would you be kind enough to take the time to identify any documents and forward them to me, as you feel appropriate. Any confidence that you require to be kept in relation to this material will be observed. Should you have any queries please do not hesitate to contact me.

Yours sincerely

Dr Jacqueline Halliday-Bell MB ChB FFOM

Postgraduate researcher in Occupational Medicine.

Institute of Occupational and Environmental Medicine,

University of Birmingham

Edgbaston, Birmingham B15 4TT

United Kingdom

Telephone number: ⬛⬛⬛⬛⬛⬛-mail address:

13.5 Appendix: Finnish antenatal growth charts
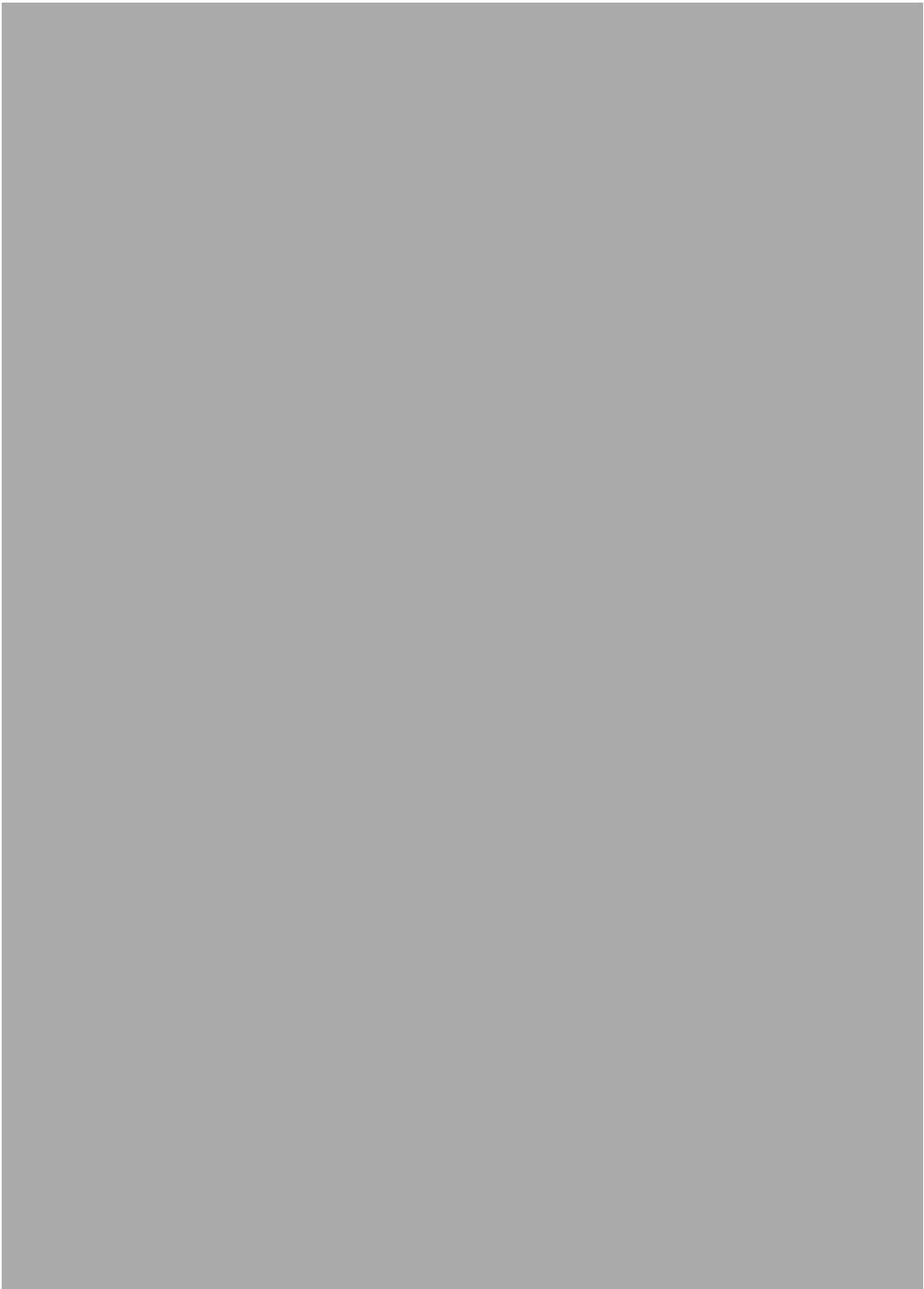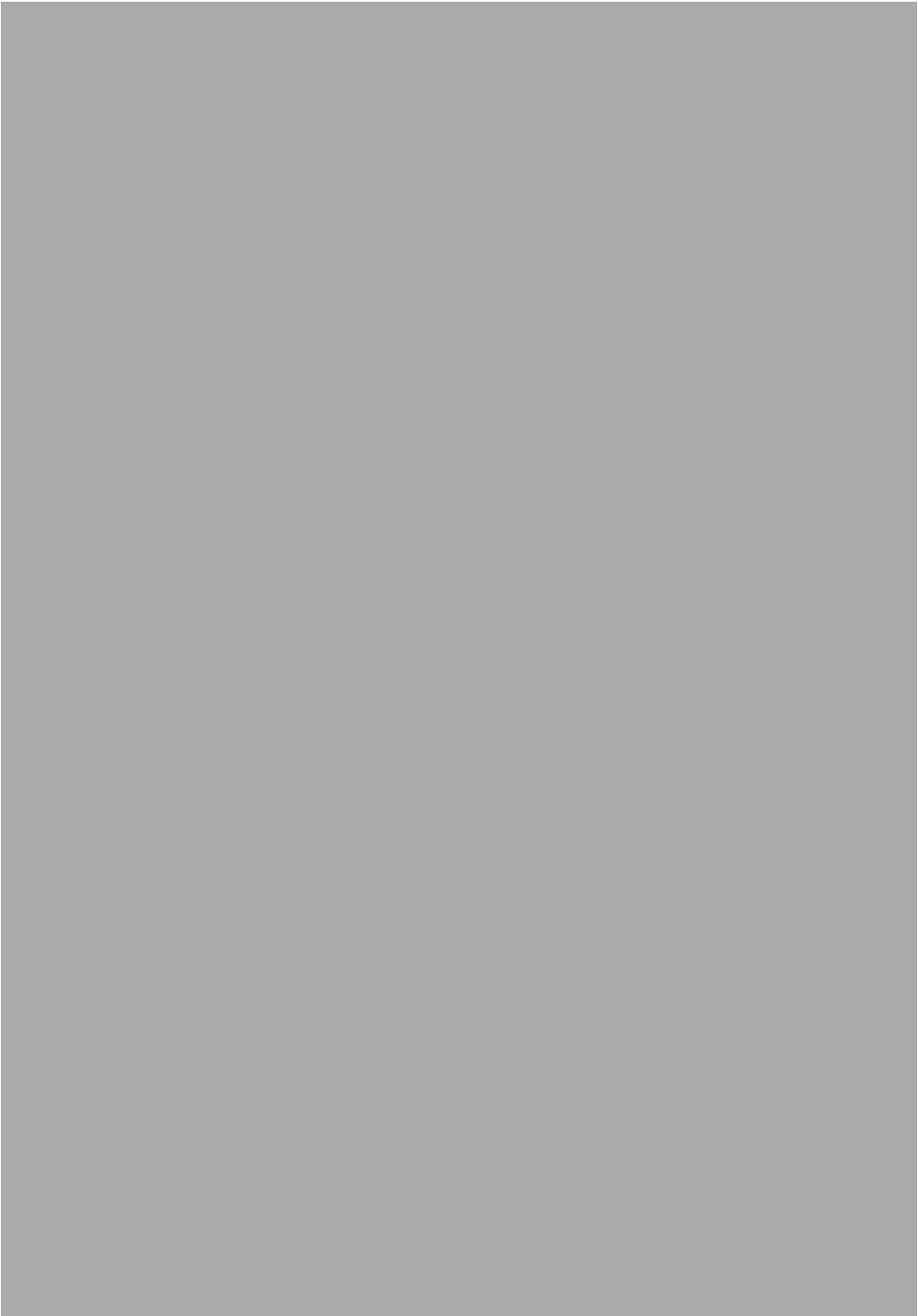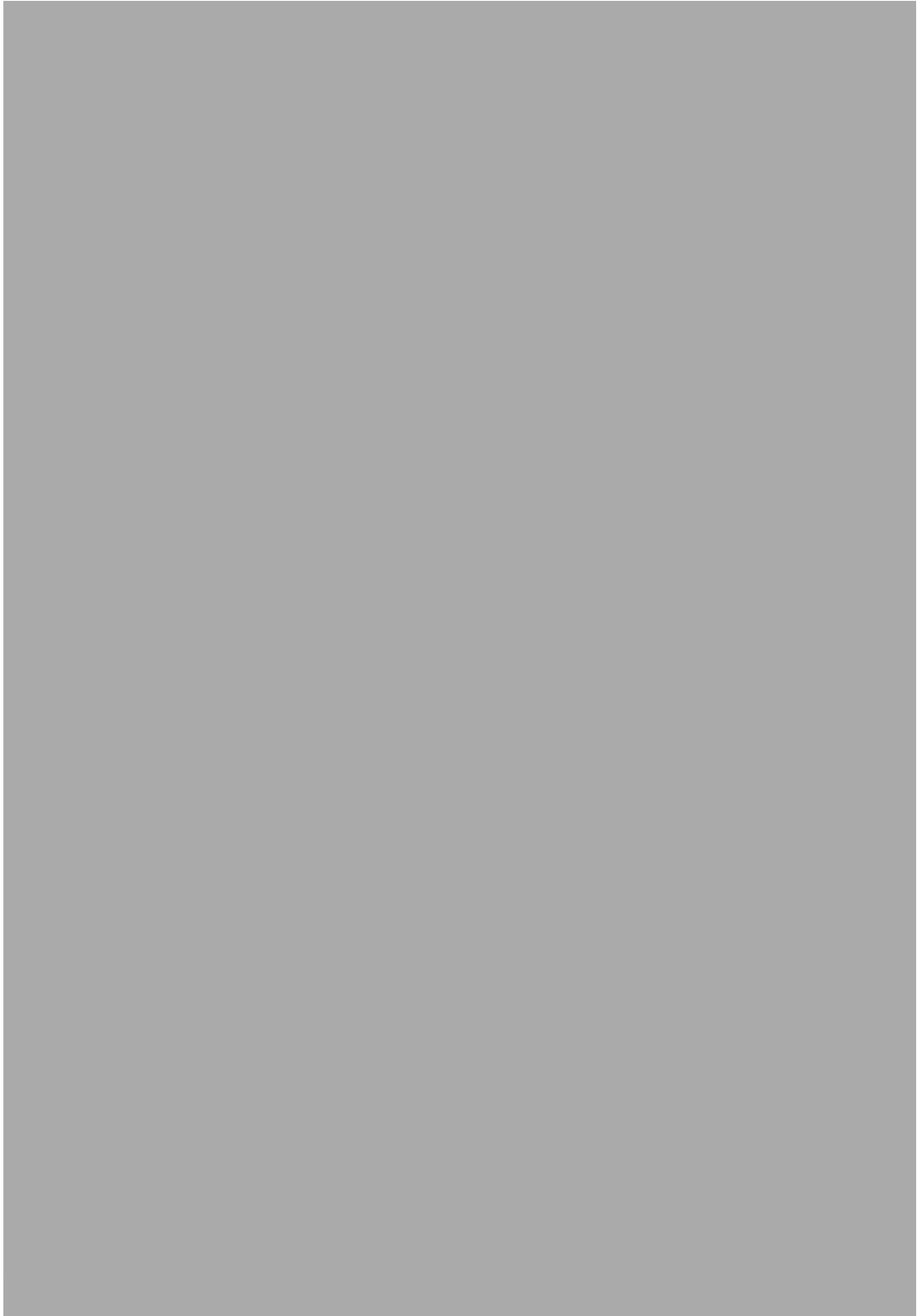
13.6 Appendix: National Institute for Health and Welfare (THL)

296
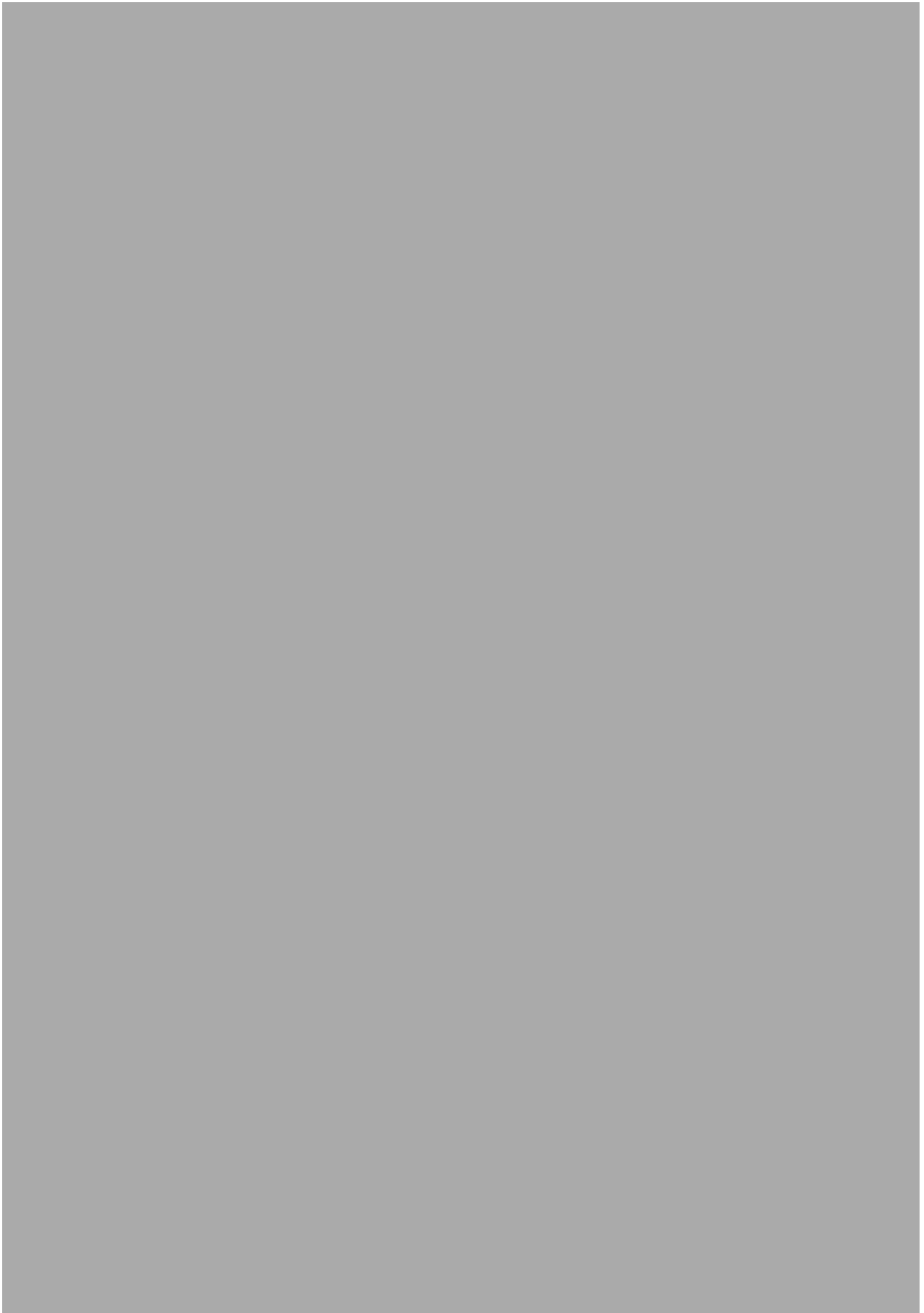
13.7 Appendix: Finnish Medical Birth Register (1996 onwards) - Registration Form

Completion of the form

The following information is to be supplied to Stakes (National Research and Development Centre for Welfare and Health) in respect of each infant born:

Personal particulars

1.   Mother's personal identity number

If the mother's personal identity number is not known, enter her date of birth in the first six columns. Leave the control characters (four) of the personal identity number blank rather than use an invented number, which may pass the verification.

2.   Mother's family name and first names

The mother's own family name need not be given.

3.   Maternity hospital

Code number and name. Use Stakes' five-digit code number currently in force as the hospital code number (Health care authorities and institutions). Concerning delivery at home, indicate the name of the hospital responsible for issuing the notice of birth. Apart from that, fill in the details of the delivery at home under item 8 (alternatives 3 and 4).

4.   Date of birth, identity number and time of birth of infant

Supply the date (day, month and year), the individual control characters of the identity number and the time of birth. Fill in the individual number of the personal identity number, if it is known.

5.   Sex of infant

6.   Number of foetuses

Always put a tick, even in the case of a single foetus.

7.   Letter indicating order in case of in multiple birth

Put a tick against the letter indicating the order in the case of multiple birth only.

Infant's place of birth

8.   Place of birth

Indicate here whether the infant was born at a hospital, on the way there or outside the hospital.

Mother

9.   Mother's municipality of residence

The municipality where the mother lives at the time of the birth of the infant. Use the three-digit municipality numbers of the Population Register Centre.

10.   Citizenship

11.   Marital status of mother

Always fill in, even when information on cohabitation is not available.

12.   Information on cohabitation

Always fill in, whether the marital status is known or not.

297

13.   Mother's occupation

Fill in the occupation as is in capital letters. Use the actual occupation, not an academic or other qualification. Avoid using abbreviations.

Previous pregnancies and deliveries

14.   Previous pregnancies

Indicate the total number of previous pregnancies and miscarriages, abortions and ectopic pregnancies.

15.   Previous deliveries

Fill in here the number of pregnancies preceding this one. The latter item also includes multiple births, when at least one infant was stillborn.

Present pregnancy and its monitoring

16.   Check-ups during pregnancy

Fill in here the total number of visits to the maternity clinic, out-patient obstetrics clinic and private physician. Regular routine measuring, e.g. for the KTG value, shall be included in the number of visits. Enter visits to the maternity out-patient department of a hospital separately.

17.   Date of the first visit to maternity clinic

The date of the first visit to the maternity out-patient department refers to the first date entered in the pregnancy card. Do not include visits for the purpose of planning the pregnancy.

18.   Mother's smoking habits during pregnancy

- Did not smoke
- Stopped smoking during the first third of the gestation period
- Continued smoking after the first third of the gestation period
- Unknown

19.   First day of the last periods.

- Enter the date (day, month, year)

20.   Best estimate of the duration of gestation

- The best estimate of the duration of gestation refers to that estimate of the duration of gestation, as entered the delivery journal, considered most reliable at the time of the delivery.

21.   Risk factors associated with gestation

1   Previous caesarean section

2   Insulin-treated diabetes

3   Cerclage

4   Chorionic villus biopsy

5   Amniocentesis before the 25th week of gestation

6   Ultrasonography before the 21st week of gestation

7   In-vitro   fertilization

Planting a fertilized egg cell (a pre-embryo or embryo), an egg cell or an egg cell and spermatozoa in the woman (e.g. IVF, ZIFT and GIFT pregnancies, frozen embryo transplants and micro-manipulations)

8   Pregnancy following other assisted fertilisation, such as artificial insemination or drug-induced ovulation

Hospital care

22.   Hospital care during gestation.

Enter any hospitalisation during this pregnancy only. Exclude the cases in which the mother has been admitted to hospital to await the natural or induced delivery.

1   Due to haemorrhage

2   Due to hypertension

3   Due to the threat of premature delivery

4   Other causes

Delivery

23.   Gestation and delivery diagnoses.

1   Placenta previa; only if diagnosed during delivery

2   Ablatio placentae (premature detachment of placenta)

3   Eclampsia

4   Asphyxia; diagnosed either from the pulse curve or the capillary blood.

5   Breech presentation, if diagnosed during gestation

6   Other abnormal presentation, e.g. face or frontal presentation or transverse or longitudinal lie

24.   Type of delivery.

1   Vaginal delivery

2   Assisted breech presentation or breech extraction

3   Forceps delivery

4   Vacuum extraction delivery

5   Elective caesarean section; this refers to an elective section planned prior to the onset of the delivery

6   Other caesarean section

25.   Alleviation of labour pains during delivery

1   Epidural anaesthesia; does not refer only to anaesthesia administered during caesarean section.

2   Paracervical block anaesthesia

3   Pudendal block

4   Nitrous oxide

5   Other anaesthesia or medication

26.   Other procedures during delivery.

01   Induced labour

02   Amniotomy

03   Oxytocin

04   Prostaglandin; also the stimulation of the orifice of uterus with prostaglandin

05   Episiotomy

06   Manual extraction of the placenta

07   Curettage

08   Electronic monitoring of the foetus

09   Determining the pH value of the foetal blood; it means determining the acid-alkaline balance from a capillary blood sample taken from the part of the foetus presenting itself, as well as chordocentesis.

10   Mother was transferred from another hospital; refers only to transfers during delivery.

The infant

27.   The infant born live/stillborn.

1   Live birth

2   Stillborn, died before delivery began

3   Stillborn, died during the delivery

4   Stillborn, time of death unknown; it is unknown whether the infant died before or during the delivery

28.   Weight at birth

The infant's weight during the first hour following its birth.

29.   Length at birth

The length if the infant measured from the crown to the heel, rounded off to the nearest full figure (e.g. 51.4 cm = 51 cm and 51.5 cm = 52 cm).

30.   Apgar score

Enter the Apgar score at one minute. The Apgar score is to be determined according to the definition issued by the National Board of Health (given in Standing Order 1252/31.12.1961 repealed since then).

31.   pH value of the umbilical artery blood

If available, enter the value with three digits omitting the decimal point (e.g. pH 7.29 = 729).

32.   Cord serum TSH

Enter the TSH value of the cord serum with three digits. If the screening has been performed but the result is not available, enter '0'. If the screening has not been performed, enter '-99.'

Fill in the following information when the infant is seven days old, or earlier if it is discharged from hospital or dies before that day:

33.   Diagnoses of the infant

If the infant was transferred to another ward or hospital or was temporarily cared for there before it was seven days old, the maternity ward shall obtain the information covering that period.

Enter the diagnoses of the infant using the ICD-10 codes. Space is provided for five diagnoses. If the total number of diagnoses exceeds five, enter the five that are the most significant for the infant's health. Always enter any possible symptom-cause pairs together.

34.   Procedures concerning the infant

If the infant was transferred to another ward or hospital or was temporarily cared for there before it was seven days old, the maternity ward shall obtain the information covering that period.

1   Care in an observation ward.

2   Care in an intensive care ward

3   Care in another hospital.

4   Respirator care.

5   Revival (intubation); only revival using intubation.

6   Exchange transfusion

7   Phototherapy

8   Antibiotic therapy

35.   Date of mother's admission to hospital

Enter the day the mother was admitted to hospital for the actual delivery.

36.   Date mother was discharged from hospital

Enter the date of the mother's discharge from hospital, if she went home or to another institution within seven days following the delivery.

37.   The infant at seven days

If the infant was transferred to another ward or hospital, or was temporarily cared for there before it was seven days old, the maternity ward shall obtain the information covering that period. In the event that the infant was receiving treatment elsewhere, but returned to the maternity ward before its seventh day, enter such details under section 34 (items 1 to 3). Enter the name of the hospital under item 4, if the infant was receiving treatment at another hospital. Enter the date and time in respect of live births only. For stillborn infants this item should be left blank.

5. Supplying the information

The information covered by the notice form is to be supplied to Stakes in respect of every live birth or stillborn infant in the form specified in the instructions supplied.

Define live births or stillborn infants using the current classification of diseases (ICD-10/Systematic section, Stakes: Instructions and classifications 1995: 3, pages 21 to 24). The notice of birth is issued by the hospital, health centre or other health care institution with patient beds. In the case of delivery elsewhere, the person issuing the birth certificate shall complete the notice form.

Fill in the following information **when the infant is seven days old**, or earlier in the case of earlier discharge from hospital or death.

In the case of delivery at a hospital, the maternity ward concerned shall fill in the notice form.

If the infant was transferred to another ward or hospital or was temporarily cared for there before it was seven days old, the maternity ward that delivered the infant shall obtain the information covering that period (preceding the seventh day of age of the infant, i.e. not older than 6 days, 23 hours, 59 minutes and 59 seconds).

13.8 Appendix: Relevance of statistical information

305
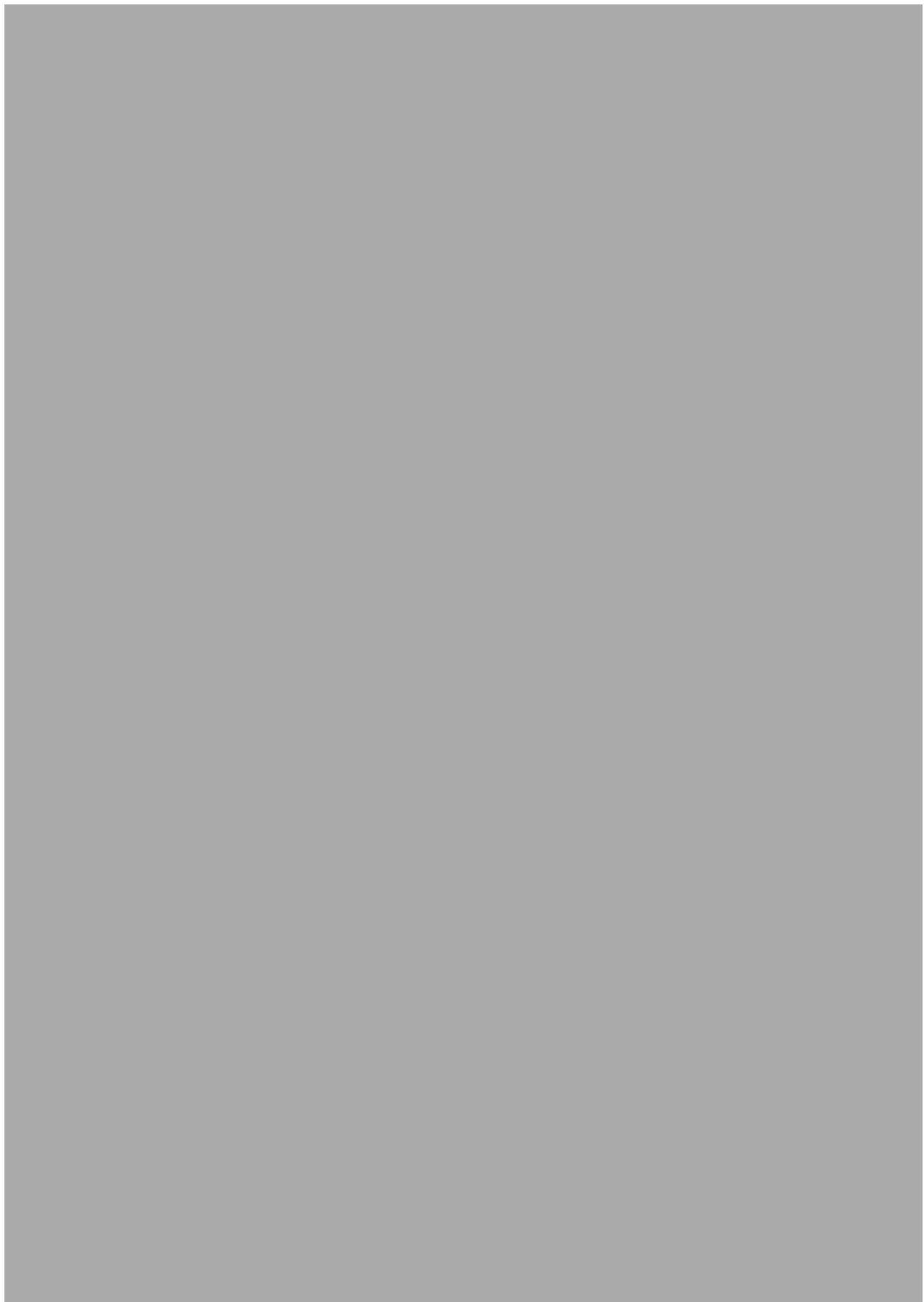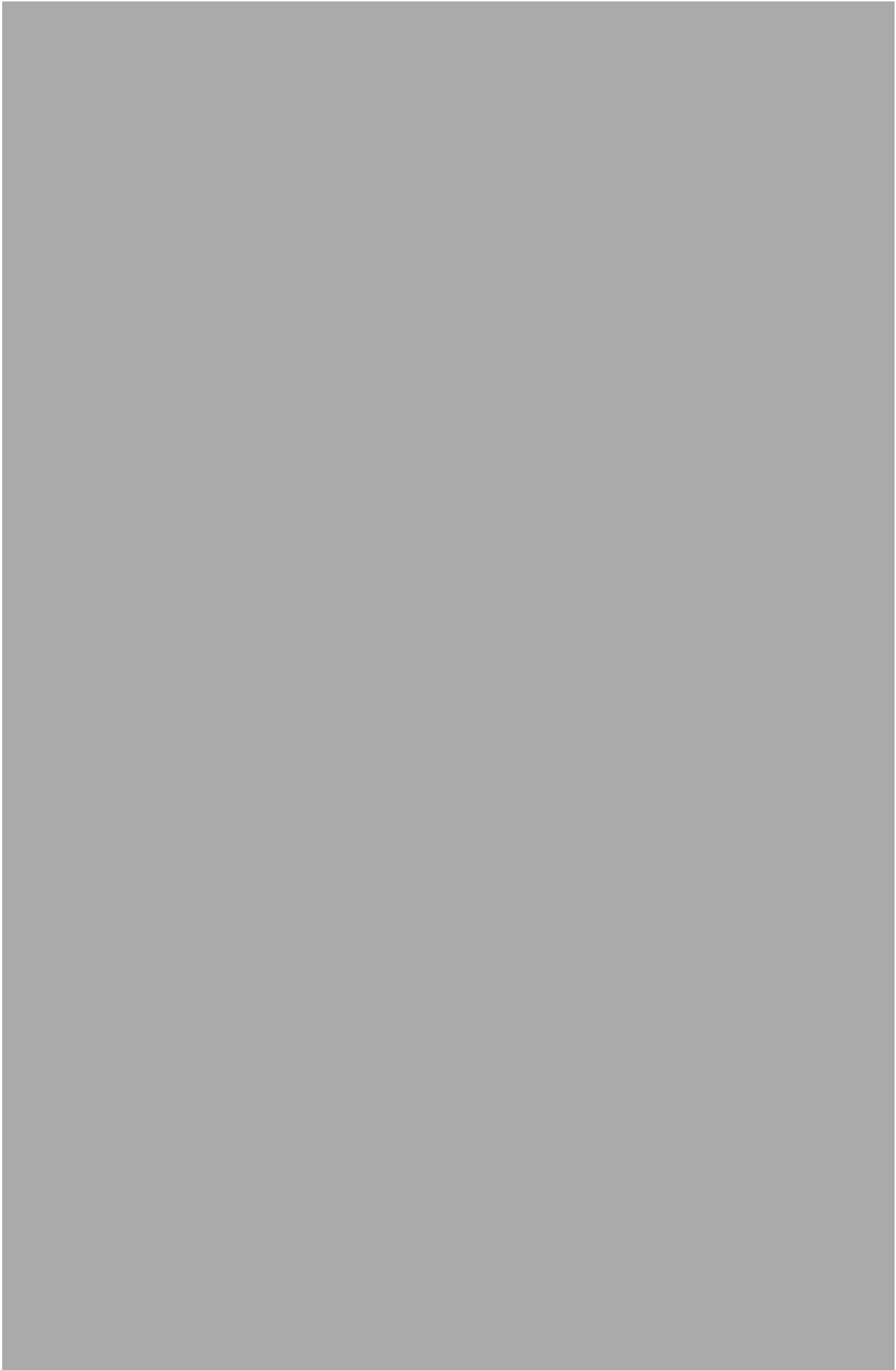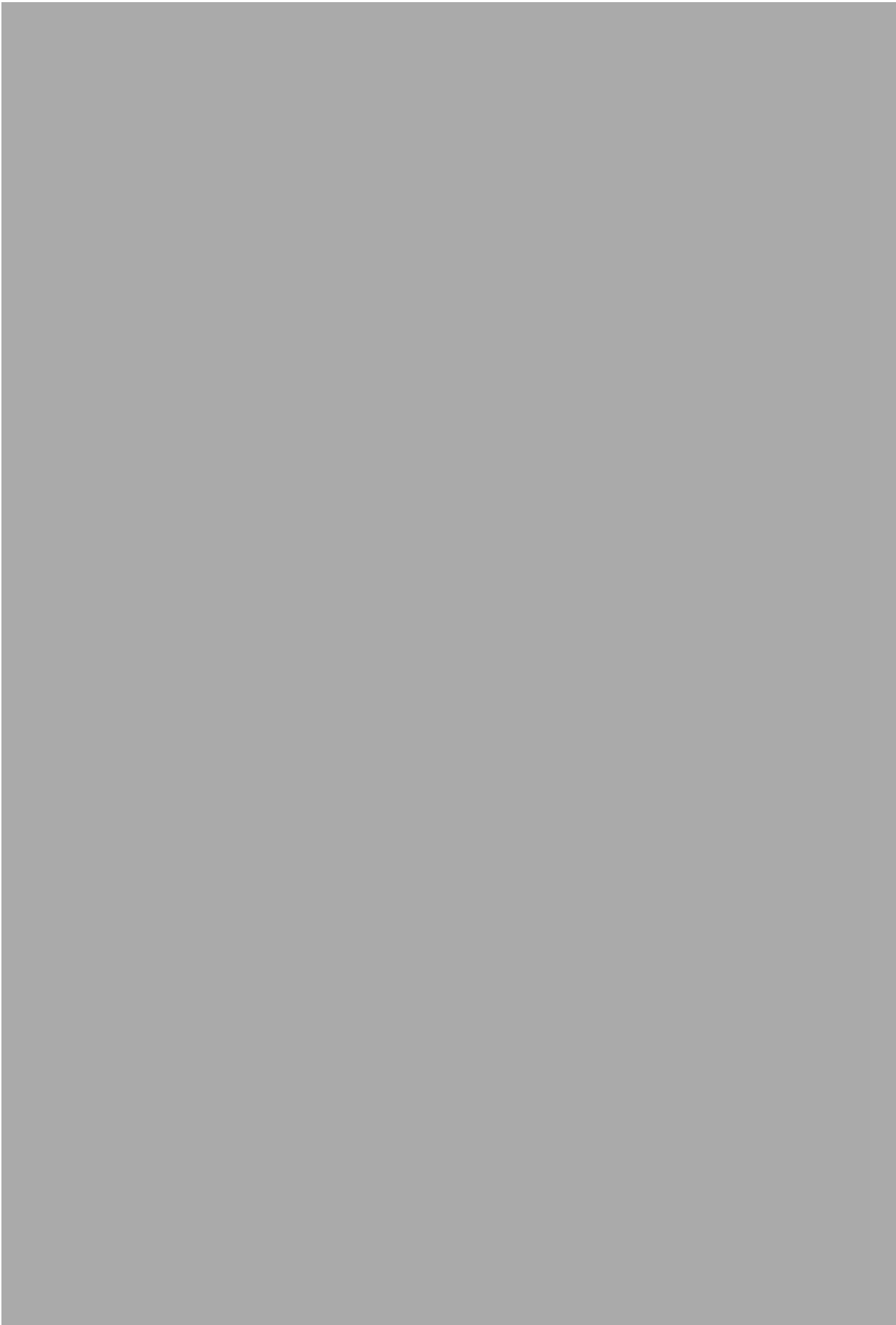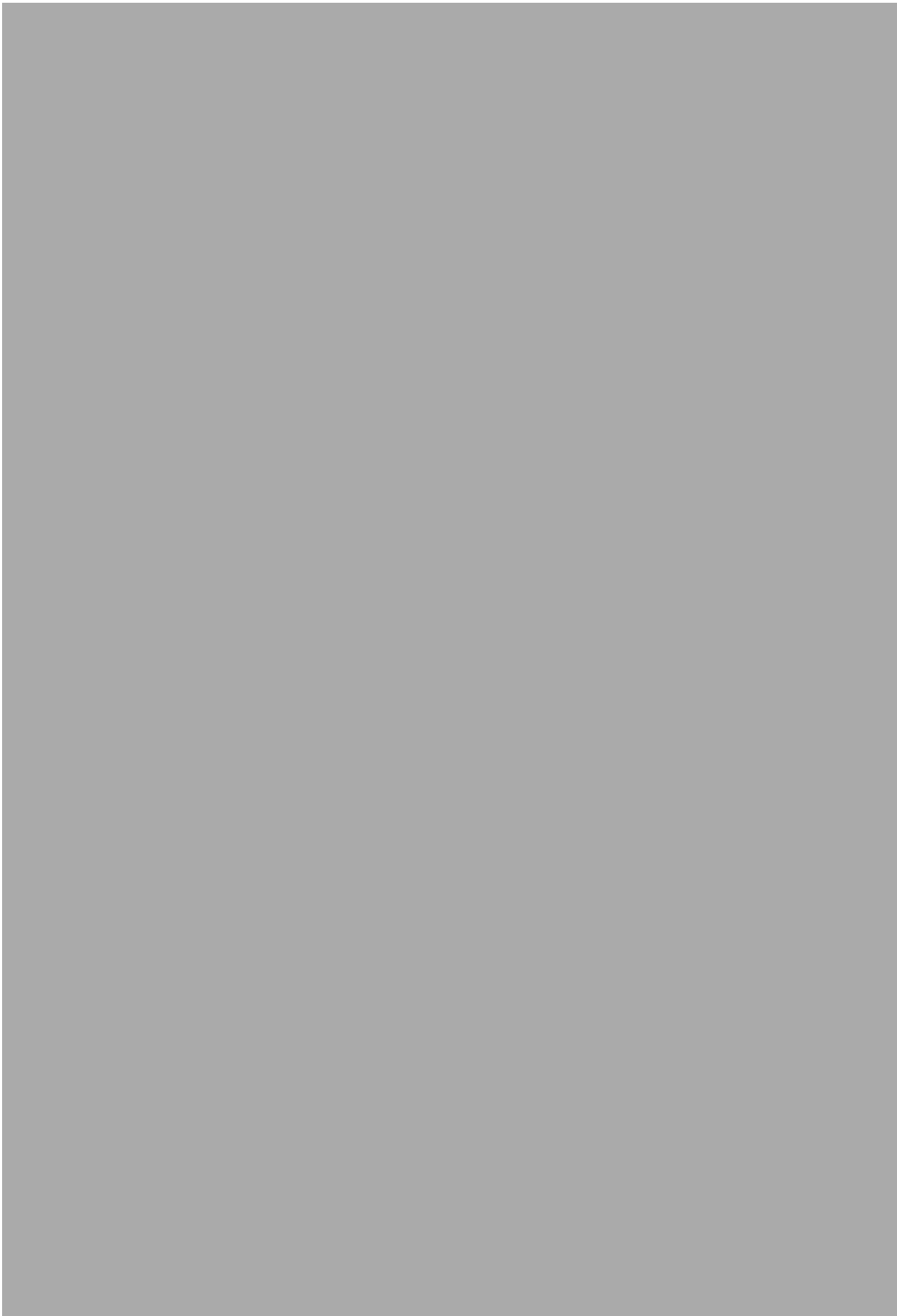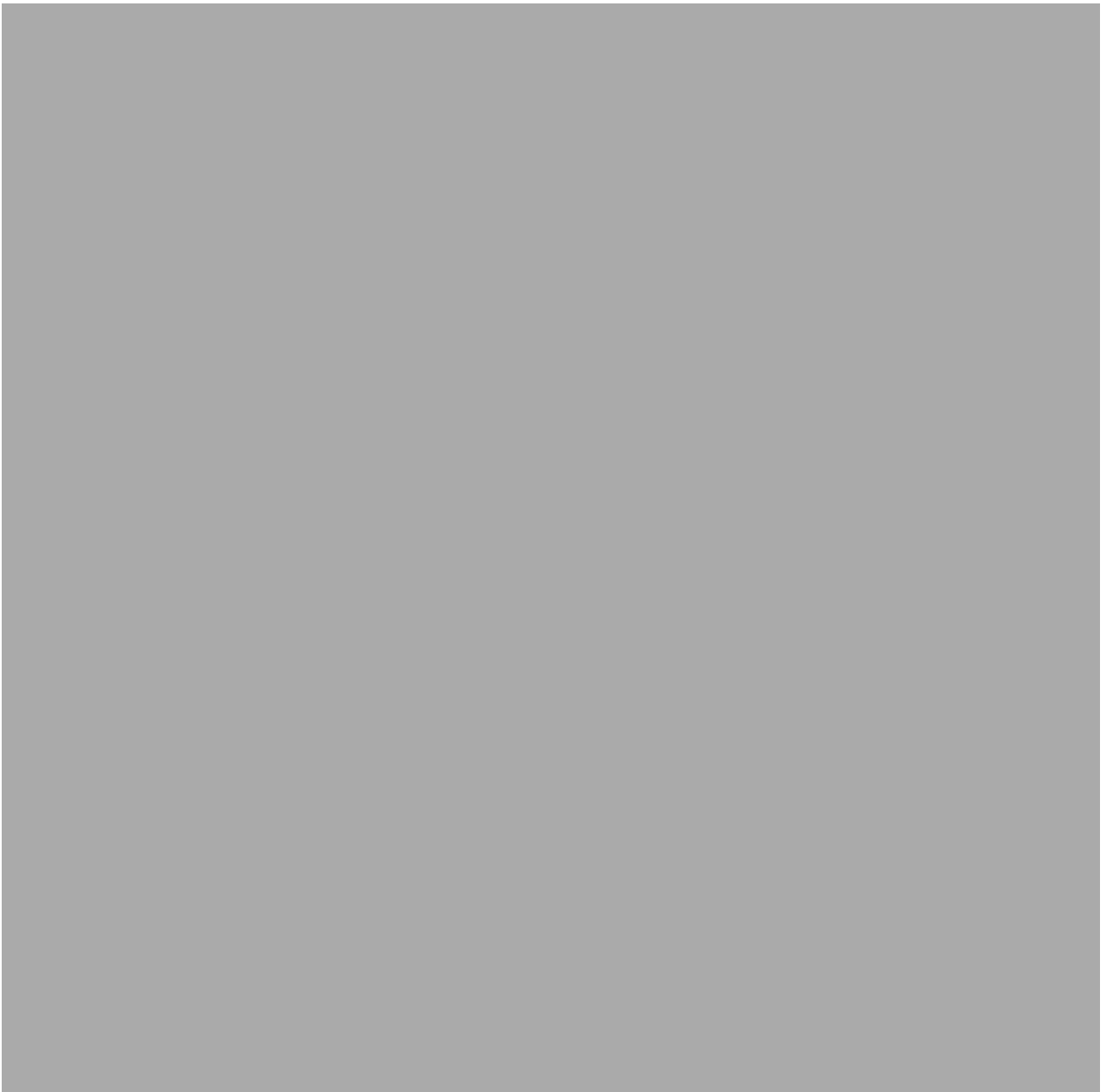
13.9 Appendix: Application to THL (STAKES) for access to data from FMBR

Personal Data Act (523/1999) Section 10

Date of drafting: 29th January 2011_____

NB.!
The form has been modified for the purposes of scientific research and is therefore more informative than an ordinary data file description. Guidelines for filling in the form are attached. If necessary, use a separate attachment for answering. The controller must make the data file description generally available.

1a. **Research Data file controller** (person / organisation carrying out research) - an organisation / a private researcher for the use of whom the data file is set up and who is entitled to determine the use of the file (in case of joint research projects, all parties and their responsibilities and duties must be explained also from the viewpoint of personal data processing)	Name and contact information (address, telephone...) • Dr J Halliday-Bell • c/o Institute of Occupational and Environmental Medicine • University of Birmingham B15 4TT
1b. Person responsible for research or corresponding group	Dr J Halliday-Bell

1c. **Persons involved in the research** **-** all researchers or other persons who have a right to access the file during research	Prof M Gissler Dr J Halliday-Bell
2. Person responsible for and/or contact person on research data file issues	Name and contact information (address, telephone...) Dr J Halliday-Bell c/o institute of Occupational and Environmental Medicine Birmingham University B15 4TT Telephone number

3. **Object of research / purpose of research**
  - the name of the research data file / research has to specify the purpose of the data file created during the research
	X one-off research project,
	    title: Pregnancy outcome among hairdressers, cosmetologists and laboratory workers.
	☐ follow-up research,
	    title: ---------
	-- 	
	                             --------- 	
	-- 	
	duration: ongoing for 3 years

13.10 Appendix: Data file guidelines for filling in the description of the research data file

311
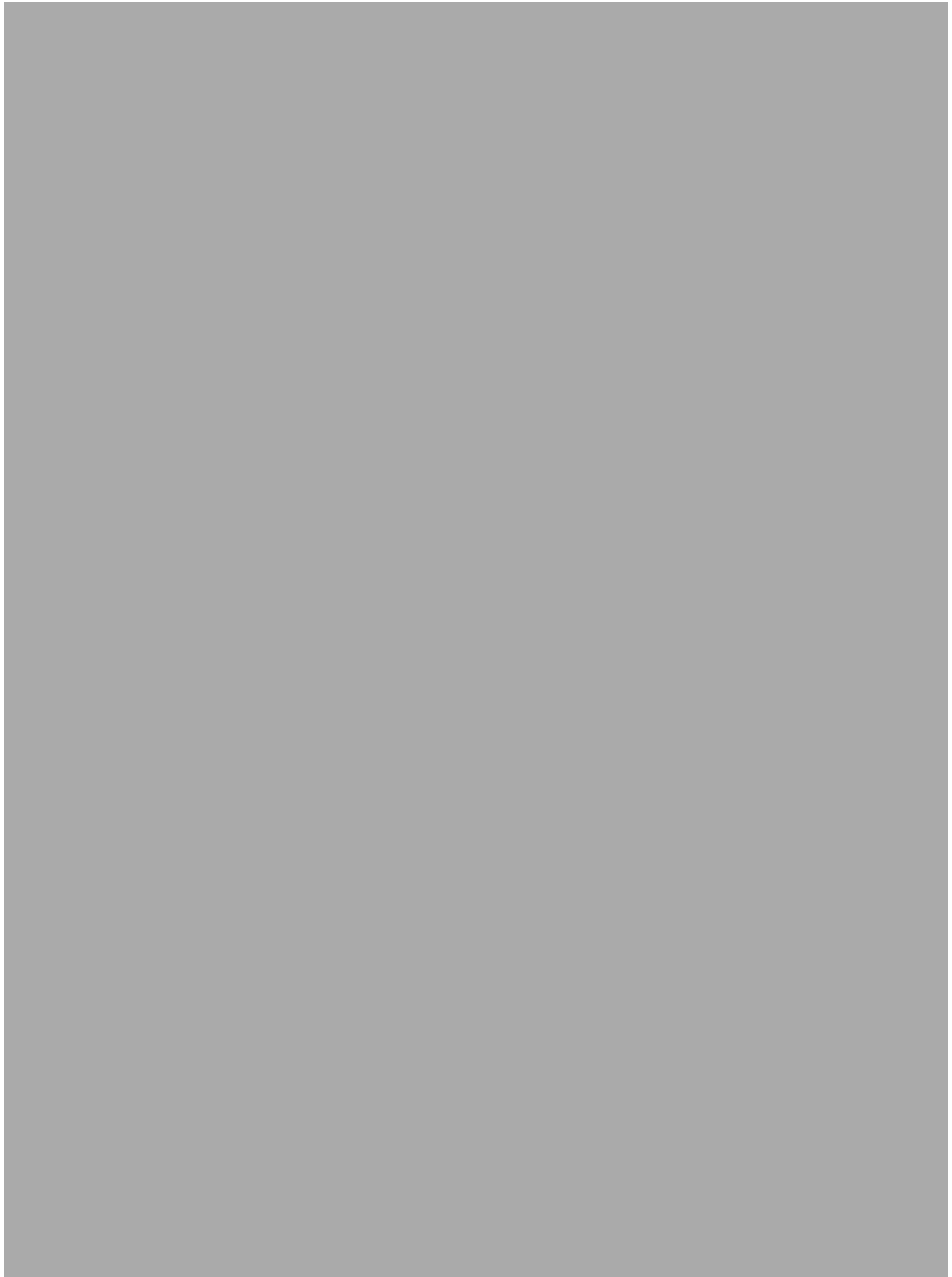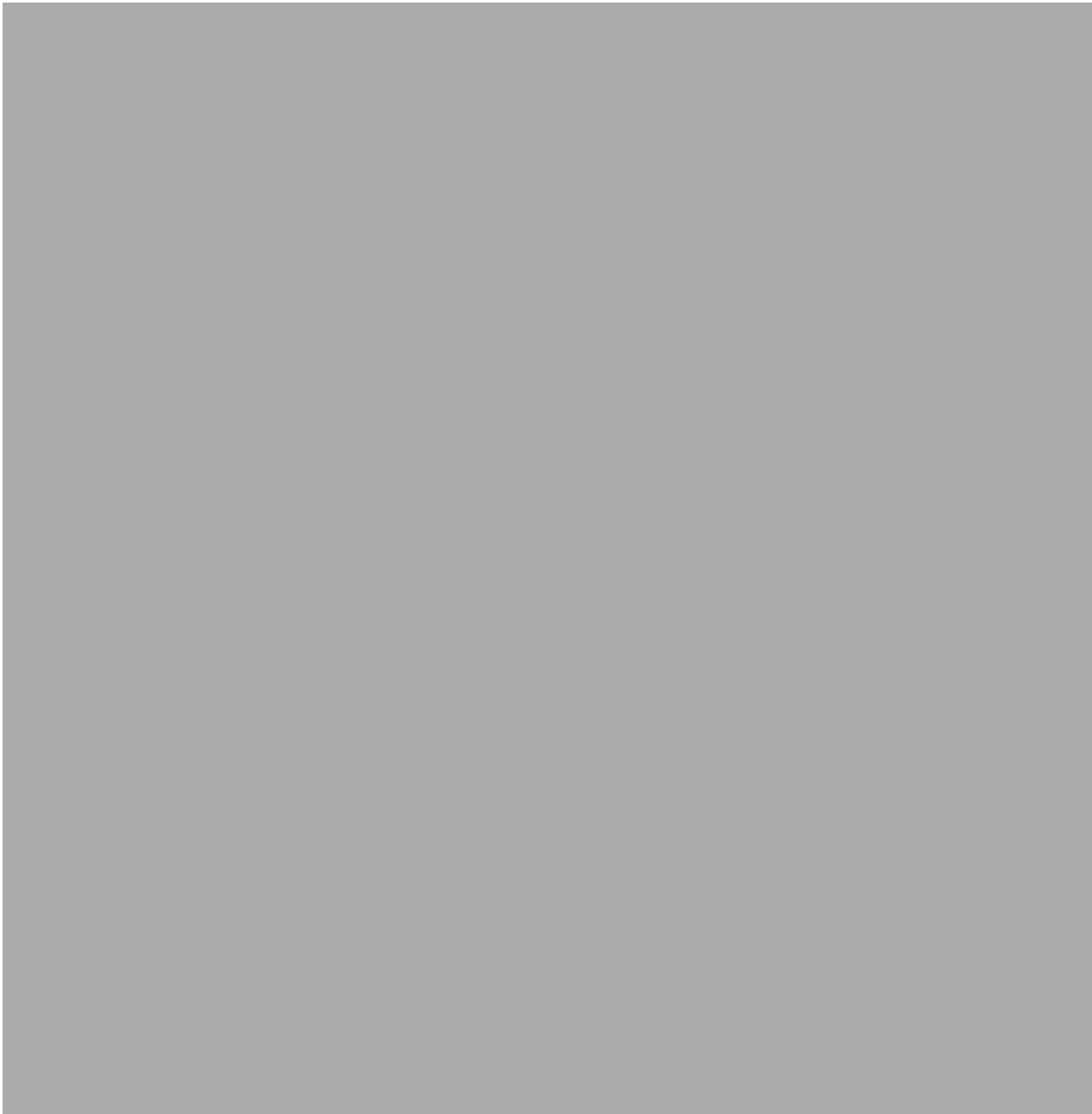
13.11 Appendix: Hairdressing and beautician/cosmetology work in Finland

13.12   Appendix: Results of literature search CINAHLplus, MEDLINE   and EBSCO Host

#	Query	Limiters/Expanders	Last Run Via	Results
S72	S18 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S71	S16 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S70	S15 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	3
S69	S14 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S68	S13 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S67	S12 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	7
S66	S11 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	5
S65	S10 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	6
S64	S9 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2

S63	S8 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S62	S7 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S61	S6 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S60	S5 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S59	S4 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	1
S58	S3 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S57	S2 AND S56	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	7
S56	TX cosmetologist* OR TX beautician OR beauty therapist	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	160
S55	S18 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S54	S17 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S53	S16 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2

315

S52	S15 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	1
S51	S14 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S50	S13 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S49	S12 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	3
S48	S11 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S47	S10 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	1
S46	S9 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S45	S8 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S44	S7 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S43	S6 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	1
S42	S5 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	1

S41	S4 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S40	S3 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S39	S2 AND S38	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S38	AB laboratory scientist OR AB laboratory worker OR laboratory technicians	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	1,448
S37	S2 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	11
S36	S3 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S35	S4 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	1
S34	S5 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	3
S33	S6 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S32	S7 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S31	S8 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2

317

S30	S9 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S29	S9 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S28	S10 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	5
S27	S11 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	9
S26	S12 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	12
S25	S13 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S24	S14 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	4
S23	S15 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	5
S22	S16 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2
S21	S17 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0
S20	S18 AND S19	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	0

S19	SU hairdress* OR AB hairdress*	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	670
S18	gender of infant	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	611
S17	gender ratio of newborns	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	3
S16	END OR neonatal death	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	5,223
S15	stillbirth	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	7,714
S14	large for gestational age	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2,026
S13	small for gestation age	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	402
S12	small for gestational age or birth weight	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	94,226
S11	small for gestational age	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	11,189
S10	low birth weight	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	40,769
S9	post-term gestational age	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	42

S8	post-term delivery	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	69
S7	post-term pregnancy	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	286
S6	premature babies	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	2,125
S5	premature birth	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	11,760
S4	premature infant	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	70,110
S3	pre term delivery	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	391
S2	pregnancy outcomes	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	25,588
S1	TX pregnancy outcome OR TX male to female gender OR gender ratio OR post-term delivery	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus; MEDLINE	51,037

Appendix: Results from Ovid SP

Search History (109 searches) (close)

# ▲	Searches	Results	Search Type	Actions
1	Pregnancy outcome.mp. or pregnancy/ or perinatal mortality/ or pregnancy outcome/ or birth weight/ or stillbirth/	627832	Advanced	Display More ≫
2	limit 1 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	253372	Advanced	Display More ≫
3	sex ratio/ or gender/ or male to female gender ratio.mp.	181164	Advanced	Display More ≫
4	limit 3 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	127153	Advanced	Display More ≫
5	pregnancy outcome/ or prolonged pregnancy/ or pregnancy/ or post-term delivery.mp. or gestational age/	628714	Advanced	Display More ≫
6	limit 5 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	253193	Advanced	Display More ≫
7	premature labor/ or low birth weight/ or pre term delivery.mp. or prematurity/	116718	Advanced	Display More ≫
8	limit 7 to (human and English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	60234	Advanced	Display More ≫

9	premature infant.mp. or prematurity/	80366	Advanced	Display More »
10	limit 9 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	44463	Advanced	Display More »
11	premature birth.mp. or prematurity/	81842	Advanced	Display More »
12	limit 11 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	45506	Advanced	Display More »
13	premature bab*.mp.	6363	Advanced	Display More »
14	limit 13 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	4300	Advanced	Display More »
15	prolonged pregnancy/ or gestational age/	92115	Advanced	Display More »
16	limit 15 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	57458	Advanced	Display More »
17	prolonged pregnancy/ or gestational age/	92115	Advanced	Display More »
18	limit 17 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	57458	Advanced	Display More »

322

19	gestational age/ or prolonged pregnancy/ or post-term gestational.mp. or prematurity/ or low birth weight/	165669	Advanced	Display More »
20	limit 19 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	96445	Advanced	Display More »
21	low birth weight.mp. or low birth weight/	72755	Advanced	Display More »
22	limit 21 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	53056	Advanced	Display More »
23	small for gestational age.mp. or small for date infant/	23350	Advanced	Display More »
24	limit 23 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	17134	Advanced	Display More »
25	small for date infant/ or large for gestational age/ or pregnancy/ or large for gestational.mp.	568131	Advanced	Display More »
26	limit 25 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	210752	Advanced	Display More »
27	stillbirth.mp. or stillbirth/	24124	Advanced	Display More »
28	limit 27 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	17519	Advanced	Display More »

29	newborn death/ or infant mortality/ or newborn mortality/ or early neonatal.mp.	41730	Advanced
30	limit 29 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	23833	Advanced
31	hairdresser.mp. or exp hairdresser/	2124	Advanced
32	limit 31 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	1509	Advanced
33	2 and 32	30	Advanced
34	4 and 32	24	Advanced
35	6 and 32	23	Advanced
36	8 and 32	8	Advanced
37	10 and 32	5	Advanced
38	12 and 32	6	Advanced

			39	14 and 32	0	Advanced	Delete Save
			40	16 and 32	2	Advanced	Display More »
			41	18 and 32	2	Advanced	Display More »
			42	20 and 32	8	Advanced	Display More »
			43	22 and 32	17	Advanced	Display More »
			44	24 and 32	17	Advanced	Display More »
			45	26 and 32	23	Advanced	Display More »
			46	28 and 32	8	Advanced	Display More »
			47	30 and 32	1	Advanced	Display More »
			48	laboratory personnel/ or laboratory scientist.mp. or scientist/	29102	Advanced	Display More »

49	limit 48 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	18627	Advanced	Display More »
50	worker/ or laboratory personnel/ or occupational exposure/	79126	Advanced	Display More »
51	limit 50 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	53134	Advanced	Display More »
52	laboratory personnel/ or occupational disease/	57988	Advanced	Display More »
53	limit 52 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	18089	Advanced	Display More »
54	49 or 51 or 53	80091	Advanced	Display More »
55	2 and 54	1416	Advanced	Display More »
56	4 and 54	1540	Advanced	Display More »
57	6 and 54	1343	Advanced	Display More »
58	8 and 54	243	Advanced	Display More »

☐ ☐ ☐ ☐	59	10 and 54		112	Advanced		Display More »
☐ ☐ ☐ ☐	60	12 and 54		114	Advanced		Display More »
☐ ☐ ☐ ☐	61	14 and 54		4	Advanced		Display More »
☐ ☐ ☐ ☐	62	16 and 54		100	Advanced		Display More »
☐ ☐ ☐ ☐	63	18 and 54		100	Advanced		Display More »
☐ ☐ ☐ ☐	64	20 and 54		271	Advanced		Display More »
☐ ☐ ☐ ☐	65	22 and 54		145	Advanced		Display More »
☐ ☐ ☐ ☐	66	24 and 54		53	Advanced		Display More »
☐ ☐ ☐ ☐	67	26 and 54		1262	Advanced		Display More »
☐ ☐ ☐ ☐	68	28 and 54		68	Advanced		Display More »

69	30 and 54	50	Advanced	Display More »
70	cosmetologist*.mp.	349	Advanced	Display More »
71	limit 70 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	289	Advanced	Display More »
72	beautician.mp.	296	Advanced	Display More »
73	limit 72 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	213	Advanced	Display More »
74	beauty therapist.mp.	34	Advanced	Display More »
75	limit 74 to (English language and yr="1990 - 2012") [Limit not valid in Books@Ovid,Journals@Ovid; records were retained]	28	Advanced	Display More »
76	71 or 73 or 75	513	Advanced	Display More »
77	2 and 76	9	Advanced	Display More »
78	4 and 76	1	Advanced	Display More »

☐ ☐ ☐ ☐	79	6 and 76	3	Advanced	Display More »
☐ ☐ ☐ ☐	80	8 and 76	4	Advanced	Display More »
☐ ☐ ☐ ☐	81	10 and 76	1	Advanced	Display More »
☐ ☐ ☐ ☐	82	12 and 76	3	Advanced	Display More »
☐ ☐ ☐ ☐	83	14 and 76	0	Advanced	Delete Save
☐ ☐ ☐ ☐	84	16 and 76	0	Advanced	Delete Save
☐ ☐ ☐ ☐	85	18 and 76	0	Advanced	Delete Save
☐ ☐ ☐ ☐	86	20 and 76	3	Advanced	Display More »
☐ ☐ ☐ ☐	87	22 and 76	14	Advanced	Display More »
☐ ☐ ☐ ☐	88	24 and 76	9	Advanced	Display More »

☐ ☐ ☐ ☐	89	26 and 76	2	Advanced	Display More »
☐ ☐ ☐ ☐	90	28 and 76	5	Advanced	Display More »
☐ ☐ ☐ ☐	91	30 and 76	1	Advanced	Display More »
☐ ☐ ☐ ☐	92	from 33 keep 1, 4-5, 7, 9, 13, 17...	9	Advanced	Display More »
☐ ☐ ☐ ☐	93	from 34 keep 19	1	Advanced	Display More »
☐ ☐ ☐ ☐	94	from 35 keep 4, 7, 16-17	4	Advanced	Display More »
☐ ☐ ☐ ☐	95	from 36 keep 1	1	Advanced	Display More »
☐ ☐ ☐ ☐	96	from 44 keep 3	1	Advanced	Display More »
☐ ☐ ☐ ☐	97	from 45 keep 9, 18	2	Advanced	Display More »
☐ ☐ ☐ ☐	98	from 55 keep 6, 30, 69, 92, 156, 164...	33	Advanced	Display More »

330

99	from 55 keep 702, 715, 731, 746, 750, 851...	35	Advanced	Display More »
100	from 58 keep 64, 78, 99, 118, 123, 136...	10	Advanced	Display More »
101	from 59 keep 65, 88	2	Advanced	Display More »
102	from 62 keep 78	1	Advanced	Display More »
103	from 64 keep 57, 76, 143, 191, 203, 218...	7	Advanced	Display More »
104	from 66 keep 28, 42, 50	3	Advanced	Display More »
105	from 67 keep 601, 727, 933, 1101, 1105	5	Advanced	Display More »
106	from 65 keep 93, 108, 113	3	Advanced	Display More »

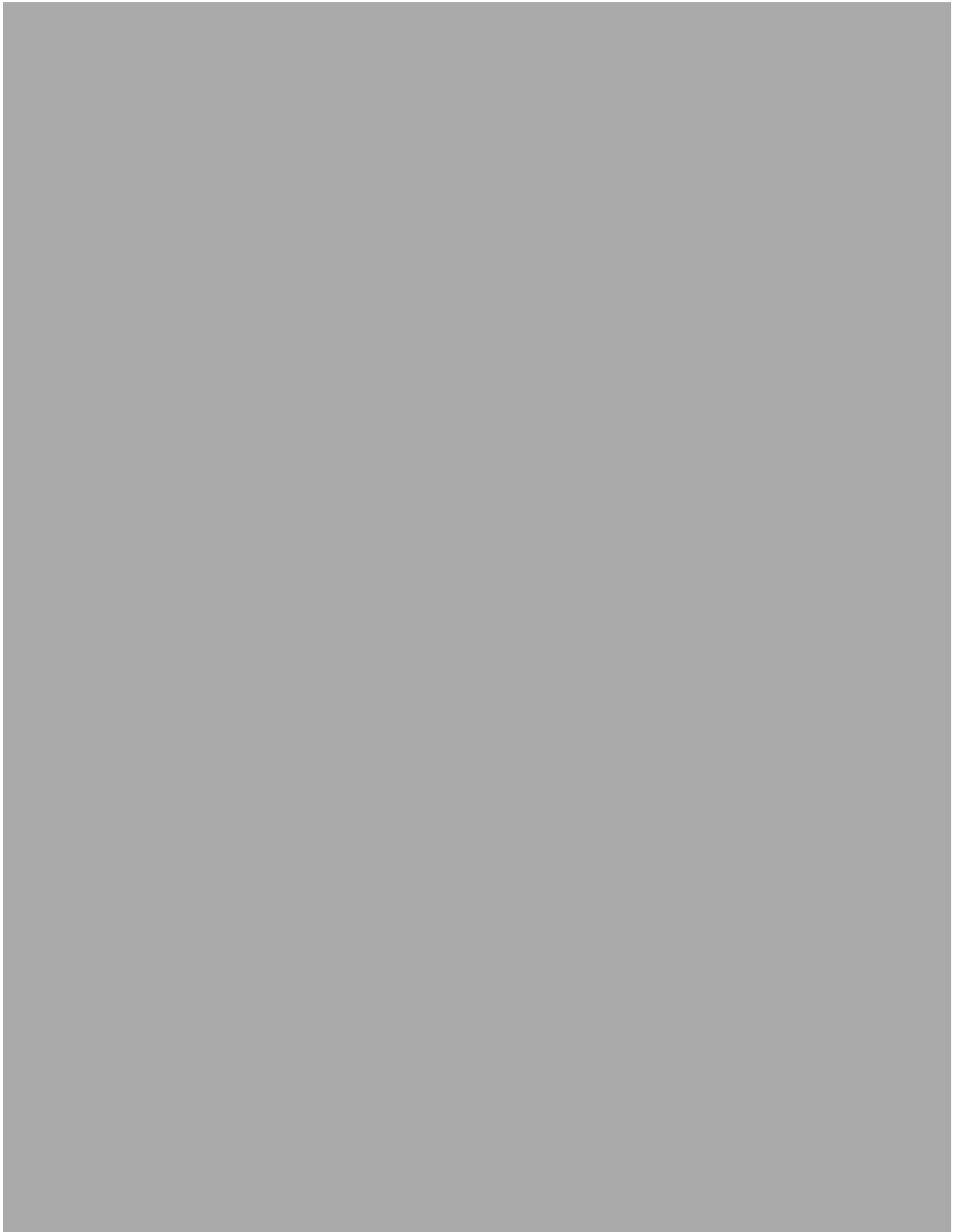13.14   Appendix: What kind of person becomes a hairdresser
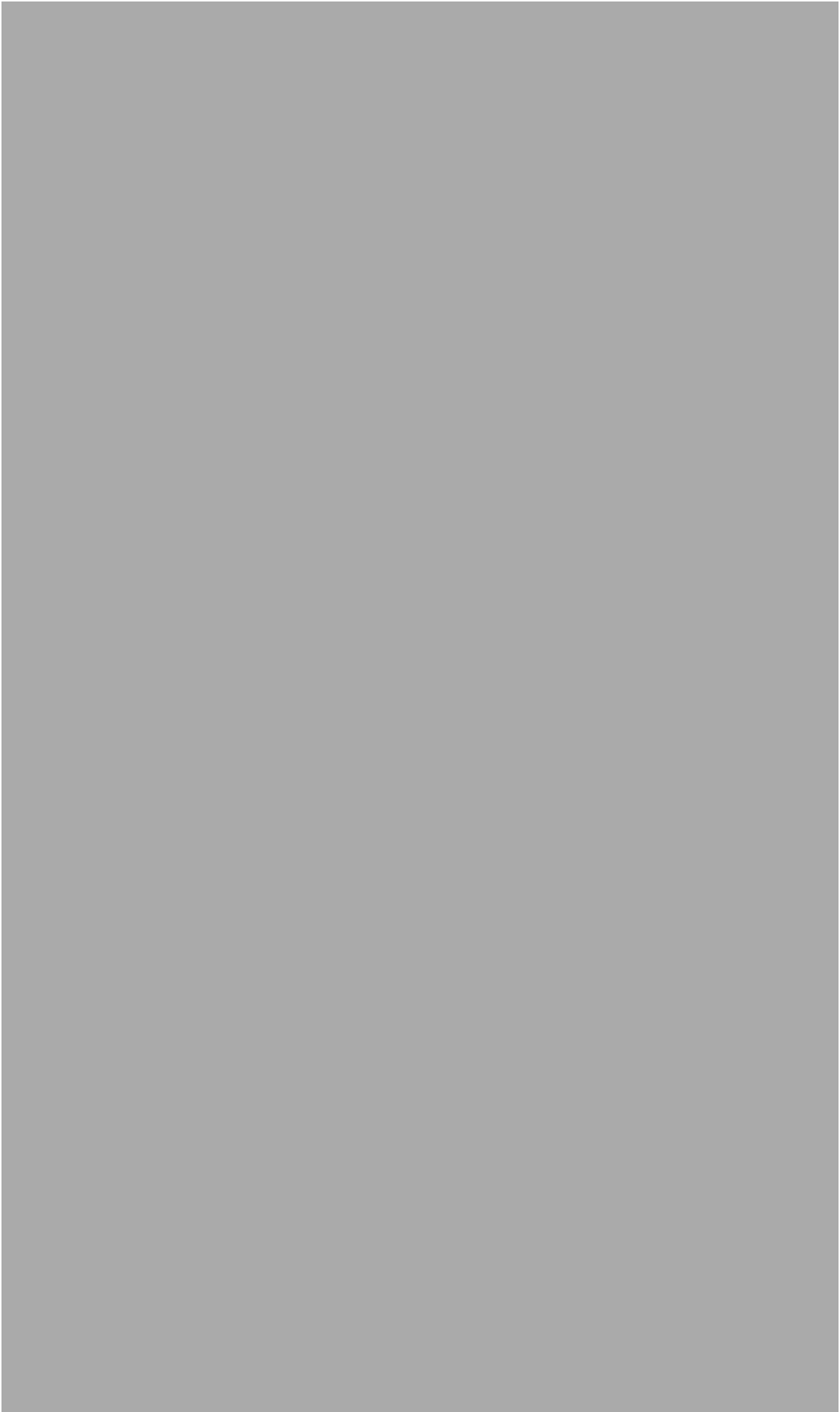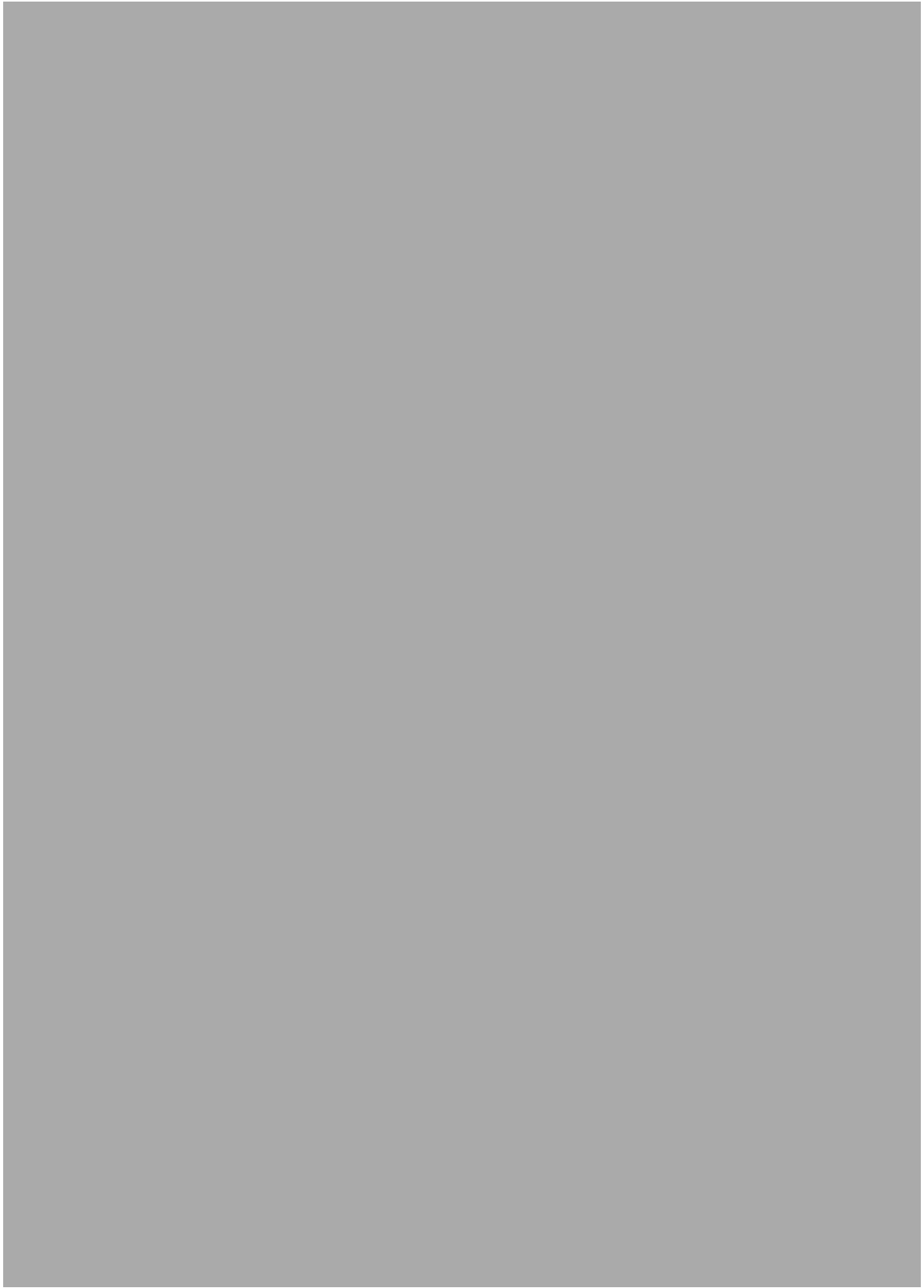
13.15 Appendix: What kind of person becomes a cosmetologist?

(wisegeek.com 2013)

13.16 Appendix: What kind of person becomes a laboratory technician in the UK

13.17 Appendix . Statistics Finland includes data from Censuses.

13.18 Appendix Do file for STATA analysis.

```
                                    jhb1.do
generate lnrr =ln(rr)
generate selnrr=(ln(ucl)-ln(lcl))/3.92

metan lnrr selnrr if table==3, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g3f)
metan lnrr selnrr if table==3, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g3r)


metan lnrr selnrr if table==5, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g5f)
metan lnrr selnrr if table==5, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g5r)

metan lnrr selnrr if table==6, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g6f)
metan lnrr selnrr if table==6, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g6r)


metan lnrr selnrr if table==8, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g8f)
metan lnrr selnrr if table==8, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g8r)


metan lnrr selnrr if table==9, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g9f)
metan lnrr selnrr if table==9, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g9r)


metan lnrr selnrr if table==13, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g13f)
metan lnrr selnrr if table==13, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g13r)

metan lnrr selnrr if table==14, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g14f)
metan lnrr selnrr if table==14, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g14r)

metan lnrr selnrr if table==17, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g17f)
metan lnrr selnrr if table==17, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g17r)

metan lnrr selnrr if table==18, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g18f)
metan lnrr selnrr if table==18, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g18r)

metan lnrr selnrr if table==19, eform label (namevar=name) effect (rr)
saving(j:\epidem\jhb\g19f)
metan lnrr selnrr if table==19, eform label (namevar=name) effect (rr)
random saving(j:\epidem\jhb\g19r)
```

Page 1