HORMONAL CONTRACEPTIVE USE IN CANADA: LEVELS, TRENDS, AND DETERMINANTS AMONG REPRODUCTIVE-AGED WOMEN IN BRITISH COLUMBIA

By

Katharine Suzanne Maginley
B.A., The University of British Columbia, 2009

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES
(Population and Public Health)

THE UNIVERSITY OF BRITISH COLUMBIA
(Vancouver)

April 2017

ABSTRACT

Background: Despite widespread use of contraception worldwide, Canadian research on hormonal contraceptive trends is limited. This thesis aims to address this knowledge gap through an investigation of the levels, trends, and determinants of: (1) hormonal contraceptive use in British Columbia (BC) (Study 1), and (2) the use of cyproterone acetate and ethinyl estradiol (CPA-EE), an acne drug that is also known to be prescribed as an oral contraceptive (OC) despite safety concerns (Study 2).

Methods: This thesis consists of two retrospective analyses of de-identified administrative datasets containing health care, pharmaceutical, and sociodemographic information for residents of BC between 2006–2013, inclusive. Study 1 examined incident and prevalent hormonal contraceptive use in a cohort of reproductive-aged women (15–49 years). Study 2 measured incident off-label use of CPA-EE in women aged 15–34. In both studies, logistic regression was used to model relationships between contraceptive use and sociodemographic factors.

Results: Study 1 revealed (1) stable prevalence, but declining incidence of overall hormonal contraceptive use, (2) declining rates of OC use, (3) increased rates of hormonal intrauterine device (IUD) use, and (4) decreased odds of hormonal contraceptive use among Chinese and South Asian women. Despite a decline in use, OCs remained the most popular method, accounting for more than 80% of all hormonal contraceptive use. In Study 2, incident use of CPA-EE declined throughout the study period. South Asian women and women with older physicians (65+) were more likely to receive a potentially inappropriate CPA-EE prescription.

Conclusion: This thesis contributes to a sparse body of literature on hormonal contraceptive use in Canada. While rates of OC use are declining, hormonal IUD use is increasingly widespread, particularly among younger women. Chinese and South Asian women are less likely to be prescribed OCs and may therefore be at greater risk for unintended pregnancy, although this warrants further investigation, as does the influence of provider characteristics on off-label prescribing patterns.

PREFACE

The work presented in this thesis was conducted and written by Suzanne Maginley (SM) at the University of British Columbia (UBC). SM developed the research objectives, study designs, and analytical approaches with the assistance of the thesis committee, which was comprised of Drs. Steve Morgan (UBC), Barbara Mintzes (University of Sydney), and Jean Shoveller (UBC).

The two empirical studies contained in this thesis were contributions to a broader Canadian Institutes of Health Research funded research project titled 'Sex, gender and equity in prescription drug access, appropriateness, and affordability,' led by Dr. Steve Morgan at UBC. Ethics approval was granted by UBC's Behavioural Research Ethics Board (H11-02273).

With the assistance of Dr. Steve Morgan and Emilie Gladstone (Policy Analyst, Centre for Health Services and Policy Research, UBC), SM completed the documentation for data access requests and data extractions from Population Data BC required for both empirical studies contained in this thesis. Sandra Peterson (Research Analyst, CHSPR), extracted relevant data according to SM's requests and removed all personal identifiers prior to providing the datasets to SM for analyses, as per confidentiality agreements. SM conducted all data analyses, compiled results, and drafted all written material relating to both studies. The thesis committee provided guidance at various steps in the research process and offered critical feedback on earlier drafts prior to submission of this thesis to the Faculty of Graduate and Postdoctoral Studies.

Versions of Chapters 2 and 3 of this thesis are currently undergoing co-author revision, and will be submitted for publication in the upcoming months. Key findings from Chapter 3 were disseminated

by SM as an oral presentation ('Trends and determinants of potentially inappropriate prescribing of Diane-35 for oral contraception among young women in British Columbia') at the 13th Canadian Association for Health Services and Policy Research Conference. May 9-12, 2016. Toronto, Canada.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
ATC	Anatomical Therapeutic Chemical
BC	British Columbia
CCS	Canadian Contraception Studies (1993, 1995, 1998, and 2002)
CFS	Canadian Fertility Survey (1984)
CPSBC	College of Physicians and Surgeons of British Columbia
CPA-EE	Cyproterone acetate–ethinyl estradiol
CI	Confidence interval
DMPA	Depot medroxyprogesterone acetate
EE	Ethinyl estradiol
ICD	International Classification of Diseases
IUD	Intrauterine device
LARC	Long-acting reversible contraceptive
LHA	Local Health Area
OC	Oral contraceptive
OR	Odds ratio
SOGC	Society of Obstetricians and Gynaecologists of Canada
VTE	Venous thromboembolism
UK	United Kingdom
US	United States

1 INTRODUCTION

1.1 Thesis overview

Choosing an appropriate method of contraception is an important element of reproductive health care for women and their health care providers around the world. Women who are educated about and have access to safe and effective contraception can make informed decisions about family planning, resulting in less unintended pregnancies and abortions (Peipert, Madden, Allsworth, & Secura, 2012; Singh, Sedgh, & Hussain, 2010). Infants and children also derive benefits from effective contraceptive use, as evidenced by decreased rates of infant mortality and improved health status of wanted versus unwanted children in countries where contraceptive use is high (Korenman, Kaestner, & Joyce, 2002). At the population level, patterns of contraceptive use can also affect the dynamics of population growth and the age structure of countries (United Nations, 2015).

The context in which women make decisions about contraception has changed dramatically since the introduction of the first hormonal method of birth control—the oral contraceptive pill—over 50 years ago. The advent of hormonal contraception in the early 1960s signaled the beginning of a new era where women could have greater autonomy over their own reproductive and sexual health (Liao & Dollin, 2012). Over the following decades, the popularization of oral contraceptives (OCs) gave rise to the development of non-oral hormonal methods, including hormone-releasing intrauterine devices (IUDs), injectable medications (depot medroxyprogesterone acetate, or DMPA), transdermal patches, subdermal implants, and intravaginal rings (Liao & Dollin, 2012).

Despite the availability of an expanded range of hormonal contraceptives, these newer, non-oral methods were infrequently used by North American women throughout the 1990s and 2000s (Balakrishnan, Krotki, & Lapierre-Adamcyk, 1985; Black et al., 2009; Fisher & Black, 2007; Mosher & Jones, 2010; United Nations, 2015). Previous studies of contraceptive use in Canada have consistently reported low uptake of non-oral hormonal contraceptives (Balakrishnan et al., 1985; Black et al., 2009; Fisher & Black, 2007; Mosher & Jones, 2010; Rotermann, Dunn, & Black, 2015; United Nations, 2015), although two non-oral methods—the hormonal IUD and injectable DMPA—are more effective than OCs at preventing unintended pregnancy (Trussell, 2007, 2011; Winner et al., 2012).

Historically, OCs have been one of the most commonly used methods of contraception in Canada (Balakrishnan et al., 1985; Black et al., 2009; Fisher & Black, 2007; Rotermann et al., 2015). OCs are also among the prescription drugs most frequently used by Canadian women (Rotermann, Sanmartin, Hennessy, & Arthur, 2014), three-quarters of whom will use OCs at some point in their lives (Rotermann et al., 2015). The widespread use of OCs in Canada and the expanding range of other hormonal contraceptive options underscores the need for comprehensive and timely estimates of contraceptive trends. Additionally, since different methods and formulations of hormonal contraceptives confer unique risk-benefit profiles to users, it may be important to review the appropriateness of different types of contraceptives for women with varied reproductive health needs. However, in contrast to many Western countries, including the United States (US) and the United Kingdom (UK), Canada does not routinely collect comprehensive data on contraceptive use

(Black & Guilbert, 2015). Consequently, there is a paucity of population-level data to inform current reproductive health research in Canada.

At present, the latest Canadian studies investigating contraceptive use at the population level are either outdated (Black et al., 2009) or exclusively focused on OCs (Rotermann et al., 2015). The most recently published Canadian study examining the use of all OCs and non-oral hormonal contraceptives was based on survey data collected more than 10 years ago (Black et al., 2009). In acknowledgement of this knowledge gap, women's health experts have publicly criticized Canada's lack of data on contraceptive use (Schwartz, 2013), and have stated that more current studies of contraceptive use in Canada are needed (Black et al., 2009). Studies of this nature are necessary to support current reproductive policy and planning, as well as to inform evidence-based practice (Black et al., 2009).

The goal of this thesis is to provide a comprehensive, updated overview of hormonal contraceptive use within a Canadian setting. Specifically, the two quantitative studies presented in this thesis will examine: (1) levels, trends, and determinants of hormonal contraceptive use by contraceptive type in reproductive-aged women, and (2) levels, trends, and determinants of potentially inappropriate use of cyproterone acetate and ethinyl estradiol (CPA-EE, more generally known by its brand name Diane-35), an acne drug that is also known to be prescribed to women as an oral contraceptive despite ongoing safety concerns.

1.2 Review of the literature

The purpose of this literature review is to expand upon ideas introduced in the previous section and clarify the reasoning behind the research questions and hypotheses, which will be presented in Section 1.3. The literature that is discussed in this section can be broadly classified into one of four areas of focus: (1) historical trends of hormonal contraceptives in Canada, (2) regulatory history and use of CPA-EE as an OC in Canada, (3) safety and efficacy of off-label prescribing and drug use, and (4) patient and physician characteristics associated with potentially inappropriate (including off-label) prescribing and drug use.

1.2.1 Hormonal contraception in Canada

Early history of hormonal contraceptives in Canada, 1960s–1980s

The availability of contraception and reproductive health services has changed dramatically over the past 50 years, with one of the most pivotal advances being the development of safe, effective, and reversible methods of hormonal contraception for women (Hatcher, 2008, 2011; Liao & Dollin, 2012). The oral contraceptive pill, introduced in Canada in 1961, gained prominence as the first available method of hormonal contraception (Black et al., 2004). Since contraception was illegal at the time, OCs could only be legally prescribed for purposes other than birth control, such as menstrual irregularity or cycle control (Liao & Dollin, 2012). Therefore, many Canadian women continued to rely on less effective, traditional methods of birth control, such as withdrawal and

rhythm, until contraception was eventually decriminalized in 1969 (Liao & Dollin, 2012). Although there are no reliable Canadian statistics on contraceptive use in the 1970s, US statistics show that at least one-third of American women were using OCs by 1973 (Watkins, 2012).

While the first OCs experienced an early surge in popularity throughout North America, serious safety concerns arose with regards to increased risk of potentially fatal venous thromboembolism (VTE) associated with OC use (Liao & Dollin, 2012). This serious adverse effect is rare, but occurred more frequently with early OC formulations containing estrogen doses that were considerably higher than what is used in modern OCs (Hatcher, 2008).

The first IUDs were introduced to the Canadian market in the 1970s. Since these IUDs did not contain an estrogen component, they served as an alternative for women concerned about the potential adverse effects of high-estrogen OCs (Liao & Dollin, 2012). However, shortly after IUDs were introduced in Canada, some users reported serious side effects, such as pelvic infections, ectopic pregnancies, perforated uteruses, and permanent infertility (Byrne, 1990). These adverse effects were found to occur more frequently among users of a specific IUD known as the Dalkon Shield, which was subsequently recalled by Health Canada in 1974. Other models of IUDs remained on the Canadian market, as the Dalkon Shield safety flaws were specific to its own unique design, and were not applicable to IUDs in general (Byrne, 1990; Sivin, 1993). Although similar adverse events occurred and continue to occur with other IUDs, serious complications arising from the use of modern IUDs are rare (Bayer Inc., 2014; Stoddard, McNicholas, & Peipert, 2011).

History and published research on contraceptive trends in Canada, 1980s–2000s

Much of what is known about Canadian contraceptive trends from the 1980s to the early 2000s comes from a small collection of population-based survey studies. The 1984 Canadian Fertility Survey (CFS) was the first major national study to provide a population-level overview of women's contraceptive use in Canada (Balakrishnan et al., 1985). The CFS was followed by four national Canadian Contraception Studies (CCSs), conducted in 1993, 1995, 1998, and 2002 (Boroditsky & Fisher, 2000; Boroditsky, Fisher, & Sand, 1995; Fisher, Boroditsky, & Bridges, 1999; Fisher, Boroditsky, & Morris, 2004a, 2004b).

According to the results of the 1984 CFS and the 1993 CCS, OC use among all Canadian women of reproductive age climbed from 19.2% in 1984 to 27% in 1993 (Balakrishnan et al., 1985; Boroditsky et al., 1995). During the same period, IUD use declined from 5.7% to 2% (Balakrishnan et al., 1985; Boroditsky et al., 1995), possibly due to lingering public mistrust following the Dalkon Shield recall in 1974 (Kerger, Bernal, Paustenbach, & Huntley-Fenner, 2016; Shaw, 1997). The rapid rise in popularity of OCs from the mid-1980s to 1990s was accompanied by the introduction of new OC formulations containing lower estrogen doses, new progestins, and different dosing regimens (Rotermann et al., 2015), which mitigated some of the adverse effects associated with earlier high-estrogen OCs (Liao & Dollin, 2012). As OCs continued to gain popularity throughout the 1990s, pharmaceutical companies developed new methods of hormonal contraception, such as the contraceptive implant and injectable DMPA, which offered innovative ways of delivering hormones to prevent pregnancy (Boroditsky & Fisher, 2000; Boroditsky et al., 1995; Fisher et al., 1999; Fisher et al., 2004a, 2004b).

Since all four successive Canadian Contraception Studies used similar research methodologies, sample sizes, and identical age ranges, we are able to draw comparisons and observe contraceptive trends over time for the period spanning 1993 to 2002. Based on these survey data, OC use continued to rise in Canada, with 32% of reproductive-aged women using OCs in 2002 (up from 27% in 1993) (Boroditsky et al., 1995; Fisher et al., 2004a, 2004b). In contrast, IUD use fell to 1% in 2002 (down from 2% in 1993) (Boroditsky et al., 1995; Fisher et al., 2004a, 2004b). The first injectable contraceptive, which was approved by Health Canada in 1997 and marketed under the brand name Depo-Provera, had little influence on the overall contraceptive market, as it was used by only 2% of reproductive-aged women in 1998 and 3% of reproductive-aged women in 2002 (Fisher et al., 1999; Fisher et al., 2004a, 2004b).

Since the early 2000s, a number of new OC brands and several non-oral hormonal contraceptives have been approved by Health Canada. There are currently over 40 brands of OCs on the Canadian market, with products differing in terms of estrogen dose, type of progestin, and dosing regimen. In addition, there are four non-oral hormonal contraceptive options available: the hormonal IUD, intravaginal ring, transdermal patch, and injectable DMPA (Health Canada, 2015).[1] Although new hormonal contraceptive options have become available, OCs have maintained a stronghold on the Canadian contraceptive market throughout the early 2000s, accounting for 43.7% of total contraceptive use (including both hormonal and non-hormonal methods) among reproductive-aged

[1] It should be noted that the subdermal implant, marketed under the name Norplant, was also available to Canadian women between 1994 and 2000 (Health Canada, 2015). Similar to the hormonal IUD, Norplant was a progestin-only method of birth control that provided long-acting contraceptive protection for up to 5 years with a single application. However, Norplant was recalled by Health Canada due to manufacturing problems that caused a lower-than-expected hormonal release rate in some product batches, which could have compromised contraceptive efficacy (Black et al., 2009).

women (Black et al., 2009). Conversely, non-oral hormonal contraception, including the hormonal IUD (2.0%), transdermal patch (1.2%), intravaginal ring (0.6%), and injectable DMPA (2.4%), accounted for dramatically lower proportions of total contraceptive use (Black et al., 2009).

Contraceptive safety and effectiveness

For both OCs and non-oral hormonal contraceptives, the use of different progestins confers different risk-benefit profiles (Stegeman et al., 2013). The risks and benefits associated with a given progestin vary depending on the estrogen dose (for combined estrogen-progestin contraceptives) or hormone delivery method (Arowojolu, Gallo, Lopez, & Grimes, 2012; Collier, 2013; Pini et al., 1996; Stegeman et al., 2013; Vasilakis-Scaramozza & Jick, 2001). Contraceptive methods also differ in effectiveness. The effectiveness of a given method is typically measured in terms of "failure rates," defined as the percentage of users who experience unintended pregnancy within the first 12 months of either "perfect use" or "typical use" (Hatcher, 2011). Perfect-use failure rates apply to users who always use a contraceptive method consistently and correctly, whereas typical-use failure rates provide a more realistic measure of true effectiveness by accounting for both inconsistent and incorrect use (Hatcher, 2011).

With perfect use, OCs are a highly effective contraceptive method. However, perfect adherence to a daily pill regimen is seldom achieved. Since OCs require daily compliance, typical OC users experience a 9% failure rate (i.e., 9% of OC users will experience unintended pregnancy within the first year of OC use) (Lopez, Grimes, Gallo, Stockton, & Schulz, 2013; Trussell, 2007, 2011). In a systematic review of randomized controlled trials, contraceptive effectiveness was not found to be

significantly different for the transdermal patch or intravaginal ring versus the comparison combined OCs (Lopez et al., 2013).[2] Comparatively, for longer-acting hormonal methods that are less reliant on routine user compliance, typical use closely approximates the effectiveness of perfect use (Trussell, 2007, 2011; Winner et al., 2012). For example, injectable DMPA, which requires a single injection once every 3 months, has a typical-use failure rate of 6%[3], while the hormonal IUD failure rate is 0.2% for both perfect and typical use, making it the most effective choice for reversible contraception (Trussell, 2007, 2011).

Unintended pregnancy in Canada

Unintended pregnancy is a significant public health concern that carries a substantial cost burden for the Canadian health care system. An estimated 40% of all pregnancies in Canada are unintended (University of Ottawa, 2015), translating to approximately $175 million per year in potentially unavoidable health care expenditures (Black et al., 2015). In Canada and worldwide, adolescent and young adult women disproportionately experience unintended pregnancy (United Nations, 2015). For instance, in the US, women aged 15 to 19 years had the highest proportion (82%) of unintended pregnancies (Finer, 2010; Finer & Zolna, 2014), and women aged 18 to 24 years had the highest

[2] According to Trussell (2011), the estimated typical-use failure rate for OCs (9%) was based on the 1995 and 2002 National Survey of Family Growth, while the perfect-use failure rate for OCs (0.3%) was based on clinical trials. For the transdermal patch and vaginal ring, estimates for typical and perfect use were set equal to those for OCs, as randomized trials had not shown superior efficacy of these non-oral methods over OCs.

[3] The estimated typical-use failure rate of DMPA (6%) accounts for women who returned late for the next injection, which is scheduled to occur at 3-month intervals. In a study of women using DMPA who returned consistently and on time for injections, the three-year cumulative failure rate for DMPA was 0.7%, which was comparable to the failure rate for women using IUDs or the contraceptive implant (Winner et al., 2012). In this study, the failure rate for DMPA was lower than other reported rates because the authors categorized a pregnancy as a contraceptive failure only in users who had returned for injections; thus, these rates represent perfect use rather than typical use of DMPA.

rates of both unintended pregnancy and unintended pregnancy ending in birth (Finer & Zolna, 2014).

Unintended pregnancies in Canada can be attributed to a number of factors, including but not limited to imperfect contraceptive adherence (Black et al., 2009, 2015) and contraceptive failure (Trussell 2007; 2011). Despite the wide availability of safe and effective contraception, only 65% of Canadian women who are sexually active and not trying to conceive "always" use a reliable method of birth control (Black et al., 2009). To address this public health concern, some women's health researchers have advocated for increased use of long-acting reversible contraceptives (LARCs), such as the hormonal IUD, which are more effective than OCs at preventing unintended pregnancy during typical use (Black et al., 2015; Hauck & Costescu, 2015; Stubbs & Schamp, 2008).[4]

Ethnicity and hormonal contraceptive use

Past studies of contraceptive use in Canada have shown that Canadian-born women are more likely to use OCs than immigrant women. This trend was initially identified in the 1984 CFS (Balakrishnan et al., 1985), and has only been sparsely investigated in subsequent studies (Martin & Wu, 2000; Rotermann et al., 2015). As Canada becomes increasingly reliant on immigration for population growth (Statistics Canada, 2016), there may be value in characterizing patterns of hormonal contraceptive use for Canadian women from diverse backgrounds.

[4] Worldwide, the only current LARC methods are the IUD (hormonal and non-hormonal) and the contraceptive implant (not available in Canada). In my review of the literature, injectable DMPA was not usually discussed as a LARC method. Injectable DMPA is administered intramuscularly at 3-month intervals, which is considerably shorter than the hormonal IUD and contraceptive implant that are both effective for up to 5 years. Thus, for the purpose of this thesis, I have chosen to not categorize injectable DMPA as a LARC.

Compared to all other member countries of the G8,[5] Canada has the largest net international migration as a proportion of population growth (Martel, 2012). Historically, most Canadian immigrants have come from Europe, but, more recently, the largest group of newcomers to Canada are from Asia and the Middle East (Chui, 2013). This has resulted in an ethnic minority population representing approximately 1 out of every 5 people (19.1%) in Canada's total population, predominately individuals of South Asian and Chinese ethnicity (Chui, 2013).

Although Canadian research on sociodemographic characteristics of hormonal contraceptive users is limited, there is an extensive body of literature from other Western countries investigating contraceptive use and pregnancy outcomes among different racial and ethnic minority groups. In the US, Black and Hispanic women have been shown to experience poorer reproductive health outcomes, including higher rates of unintended pregnancy and abortions, and are less likely to reliably use contraception compared to the general population (Jones, Mosher, & Daniels, 2012). Similarly, in the UK, researchers found that contraception use was significantly lower in all ethnic minority groups than in white women (Saxena et al., 2006). In light of these findings, it may be expected that ethnic minorities in Canada also demonstrate unique patterns of hormonal contraceptive use. However, little is known about the sociodemographic profiles of hormonal contraceptive users in Canada, nor about the current rates and trends of hormonal contraceptive use at the population level. In contrast to many other developed countries, and despite the prevalence of hormonal contraceptive use, Canada does not collect comprehensive national data on contraceptive trends (Black & Guilbert, 2015; Schwartz, 2013).

[5] G8 (Group of Eight) countries include Canada, France, Germany, Italy, Japan, Russia, the US, and the UK.

1.2.2 Regulatory history and off-label contraceptive use of CPA-EE in Canada

In 1998, Health Canada approved CPA-EE (cyproterone acetate 2 mg and ethinyl estradiol 35 mcg), more generally known as Diane-35[6], for the temporary treatment of severe acne in women who are unresponsive to oral antibiotics or other first-line acne treatments. Although CPA-EE was granted market authorization solely for this specific indication, it has been widely prescribed to women without acne as an OC because of its ability to suppress ovulation (Mintzes, Morgan, & Bassett, 2005).

In a 2005 study examining the impact of a nationally televised documentary on inappropriate prescribing patterns of CPA-EE, researchers found that initiation rates for the drug increased between 1998 and 2002 (Mintzes et al., 2005). Interestingly, nearly half of all new prescriptions for CPA-EE during that period were given to women who had no records of prior acne diagnosis or treatment (Mintzes et al., 2005). This finding is especially concerning as there is a growing body of evidence suggesting that CPA-EE is causally associated with increased risk of VTE compared to other approved OCs in Canada (de Bastos et al., 2014; Stegeman et al., 2013).[7]

[6] Following Diane-35's patent expiry, two new generic forms of CPA-EE were approved by Health Canada (Cyestra-35 in April 2007, followed by Novo-Cyproterone/Ethinyl Estradiol in September 2008). I was unable to determine the exact date of Diane-35's patent expiry, but estimate that it occurred shortly before market entry of the first generic competitor (i.e., in 2006 or early 2007).

[7] Stegeman et al. (2013) performed a systematic review and network meta-analysis to provide a comprehensive overview of the risk of VTE in women using different combined OCs, including CPA-EE. The effect size depended both on the progestogen used and the estrogen dose. CPA-EE was found to be among the formulations with the highest risk of VTE.

Between 2002 and 2005, Health Canada issued a series of safety warnings regarding the prescribing and use of CPA-EE for unapproved indications (Health Canada, 2002, 2003, 2005). In each of these advisories, Health Canada cited concerns about elevated VTE risk associated with CPA-EE use, and repeatedly emphasized that CPA-EE should not be prescribed solely for contraceptive use. An excerpt from Health Canada's letter to healthcare professionals states, "Based on an analysis, commissioned by [Diane-35's manufacturer] Berlex, of recently published information, users of Diane-35 appear to have an elevated risk of venous thromboembolic events compared to users taking low-dose combined oral contraceptives in some studies...Diane-35 should not be taken for the purpose of contraception alone" (Health Canada, 2003).

In February 2013, Health Canada publicly announced plans to launch a review of all available safety information on CPA-EE, following the decision by France to temporarily suspend marketing authorization for CPA-EE due to safety concerns. In a public information update released several months later, Health Canada reiterated, based on their review of the evidence, that the benefits of CPA-EE continue to outweigh the risks, as long as it is used according to the approved label (Health Canada, 2013).

1.2.3 Off-label and potentially inappropriate prescribing practices and drug use

When new drugs are approved for use in Canada, as in all countries with a functioning system of pharmaceutical regulation, they are accompanied by approved product information (the "Product Monograph"). A drug's Product Monograph stipulates its indication for use, the appropriate patient population, and recommended dosages and administration schedules (Canada Standing Senate

Committee on Social Affairs, 2014). The use of an approved drug beyond these specific criteria is referred to as "off-label" use.

While off-label prescribing by physicians may sometimes be clinically appropriate (American Academy of Pediatrics, 2002), it may also be potentially inappropriate when there is a lack adequate evidence to support a drug's safety and efficacy for off-label use (Abbott & Ayres, 2014; Dresser & Frader, 2009; Gazarian et al., 2006). Inappropriate prescribing can be defined as "the prescription of medications where risk outweighs benefit, failure to use a safer alternative drug, the misuse of a drug including incorrect dosage and duration of treatment, use of drugs with significant drug–drug and drug–disease interactions and, finally, the omission of beneficial drugs" (Spinewine et al., 2007).

In Canada, drug manufacturers cannot legally promote a product for off-label use. Physicians are, however, generally at liberty to prescribe off-label if they believe it is in their patients' best interests (Canada Standing Senate Committee on Social Affairs, 2014). Furthermore, there is no legal requirement for physicians to record the indication for which a given drug is prescribed, even if it is being prescribed off-label. Consequently, little is known about the prevalence of off-label prescribing in Canada, nor about adverse outcomes resulting from inappropriate off-label drug use.

Prevalence of off-label prescribing in Canada

In what has been regarded as "the most extensive and informative study to evaluate the safety of off-label drug use in an adult population to date" (Good & Gellad, 2016), a team of Canadian researchers examined off-label prescribing using data from over 250,000 prescriptions involving

approximately 46,000 patients (Eguale et al., 2012). The study followed 113 Quebec physicians practicing in urban centres whose offices were equipped with MOXXI, an electronic health record research network that includes prescribing records. The results showed that 11% of prescriptions given to patients were for off-label indications. This is likely a conservative estimate of the actual prevalence of off-label prescribing, as the study design did not account for appropriateness of dosing, suitability of patients' age or sex for a given drug, or recognition of other clinical issues included in the approved label**.**

Measures of appropriateness in off-label prescribing

One of the primary concerns with off-label prescribing is that it involves an information deficit and unknown level of patient risk (Abbott & Ayres, 2014), as most drugs are not adequately studied in terms of their efficacy or safety for unapproved indications. Before a drug is approved for a given indication, the manufacturer must first carry out clinical trials to test the drug's effectiveness and to assess safety for that specific indication. The regulatory agency will then determine whether or not the scientific evidence is strong enough to support approving the drug for that indication. Since off-label use often lacks such rigorous scientific evaluation (Abbott & Ayres, 2014), critics of off-label prescribing argue that the practice often fails to satisfy evidentiary standards of evidence-based medicine, and may lead to inappropriate prescribing decisions that could cause unnecessary harm to patients (Hebert & Stanbrook, 2007; Mackey & Liang, 2011).

In their study of off-label prescribing, Eguale et al. (2012) reported that 79% of drugs prescribed off-label lacked strong scientific evidence of efficacy, which was defined as at least one randomized

clinical trial supporting the drug's intended off-label use. Similar results were reported in a US study (Radley, Finkelstein, & Stafford, 2006), where 73% of drugs prescribed off-label had "uncertain or inadequate scientific evidence" to support off-label use. In a separate study of critical care patients in the US, 48% of all off-label prescriptions lacked adequate supporting evidence (Lat et al., 2011).

Beyond the lack of evidentiary basis for off-label drug use, another critical concern is the relatively unknown potential for adverse effects associated with unapproved use of off-label drugs. According to Eguale et al.'s 2012 study, off-label drugs were associated with a 43% increase in adverse drug reactions compared to on-label drugs. Based on the strength of these findings, the authors recommended that caution should be exercised in prescribing drugs for off-label uses that lack strong scientific evidence (Eguale et al., 2012).

In summary, current research on the potential risks associated with off-label prescribing suggests that a significant proportion of off-label prescribing is inconsistent with evidence-based practice, carries greater potential for harm, and may, therefore, be deemed potentially inappropriate.

1.2.4 Physician and patient knowledge of potentially inappropriate prescribing practices

In a US study published in the Journal of Pharmacoepidemiology and Drug Safety, 1,199 primary-care doctors and psychiatrists were asked to identify the approved treatment indication for a series of routinely prescribed drugs (Chen, Wynia, Moloney, & Alexander, 2009). The physicians provided correct responses for just over half (55%) of the cases, which suggests that some physicians lack

awareness or the required knowledge to differentiate between approved versus off-label use of commonly prescribed drugs.

The Senate of Canada Standing Committee on Social Affairs, Science and Technology has expressed concerns regarding the manner by which Canadian physicians acquire information about prescription drugs (Canada Standing Senate Committee on Social Affairs, 2014; Miller, 2014). The Standing Committee explained that many physicians are educated, or "detailed", about a drug's use(s) directly from pharmaceutical sales representatives (Canada Standing Senate Committee on Social Affairs, 2014; Miller, 2014). While physician detailing for approved treatment indications is common and legal, the promotion of drugs for off-label indications is illegal. A recent Canadian study found evidence to suggest that off-label indications were "detailed" to Vancouver- and Montreal-based primary care physicians by pharmaceutical sales representatives in 13% of drug-specific promotions, although this practice is strictly prohibited under the Food and Drugs Act (Canada Standing Senate Committee on Social Affairs, 2014; Mintzes et al., 2013). As such, these findings support the notion that some physicians may not be fully aware of the appropriate treatment indications (nor, perhaps, the contraindications) for some commonly prescribed drugs (Mintzes et al., 2013).

There is also evidence to suggest that patients themselves may be similarly unaware of the nature and extent of off-label prescribing practices. Results from a nationwide poll in the US showed that half of the 3,018 respondents falsely believed that a drug could be prescribed only for its approved treatment indication (Harris Interactive, 2006). This finding suggests that many patients who receive an off-label prescription may not be aware that they are using a drug for any purpose other than its

approved use. In such cases, concerns may be warranted if patients and physicians alike are not adequately informed of the increased risks, side effects, or possible adverse reactions associated with off-label use of a given drug.

1.2.5 Sociodemographic characteristics associated with potentially inappropriate and off-label prescribing

Sociodemographic factors, such as age and level of education, are often discussed in population-level studies of contraceptive trends (Black et al., 2009; Boroditsky & Fisher, 2000; Boroditsky et al., 1995; Fisher et al., 1999; Fisher et al., 2004a, 2004b; Rotermann et al., 2015), yet there has been minimal investigation of the influence of these factors on risk of exposure to potentially inappropriate contraceptive use. However, several studies have provided evidence of sex-specific differences in the risk of receiving a potentially inappropriate prescription. In a 2011 Scottish study of inappropriate prescribing involving 315 primary care physicians and 1.76 million patients, women were more likely than men to receive high-risk prescriptions (Guthrie et al., 2011). Similarly, Eguale et al.'s 2012 study of off-label drug use in Canada showed that women were more likely to receive off-label prescriptions than men. In a recent cohort study that examined sex differences in the risk of receiving a potentially inappropriate prescription among older adults in BC, women were at 16% higher odds of receiving a potentially inappropriate prescription than men (Morgan et al., 2016). Collectively, these studies provide compelling evidence to suggest that sex-specific patterns of prescribing exist and may adversely impact women, rendering them more vulnerable to risks associated with potentially inappropriate drug use.

Some studies have also examined the association between sociodemographic characteristics of physicians and patterns of potentially inappropriate or off-label prescribing. For example, in a 2007 Canadian study, researchers examined inappropriate prescribing of antibiotics by analyzing linked administrative data on infection diagnoses and respective treatments (Cadieux, Tamblyn, Dauphinee, & Libman, 2007). Their findings showed that international medical graduates, physicians with high-volume practices, and physicians who were in practice longer were more likely to prescribe inappropriately. Eguale et al. (2012) broadly explored the relationship between physician characteristics and off-label prescribing in a Canadian setting, and found that physicians with evidence-based orientations were less likely to prescribe off-label, particularly in cases where drugs lacked strong scientific evidence to support off-label use (Eguale et al., 2012). Thus, there is evidence to suggest that certain physician sociodemographic and clinical characteristics may be associated with differences in risk of potentially inappropriate prescribing.

1.3 Research objectives

This thesis consists of two separate, but related, quantitative studies. The objectives and research questions for each respective study are outlined below:

Study 1 objective: Identify and describe current levels, trends, and determinants of hormonal contraceptive use among reproductive-aged women (15 to 49 years) in a Canadian setting.

Research question 1: How have incidence and prevalence of hormonal contraceptive use changed over time (from 2006 to 2013) among reproductive-aged women residing in British Columbia (BC), Canada?

Research question 2: Which patient sociodemographic characteristics are associated with hormonal contraceptive use?

Study 2 objective: Investigate levels, trends, and determinants associated with potentially inappropriate use of CPA-EE as a contraceptive among young women (aged 15 to 34 years) in a Canadian setting.

Research question 1: How has both on-label and off-label incident use of CPA-EE changed over time (2006–2013) in BC, Canada?

Research question 2: Which sociodemographic characteristics of patients and physicians are associated with potentially inappropriate CPA-EE use?

Continuing from this introductory chapter, Chapters 2 and 3 present two separate, but related, quantitative studies on level, trends, and determinants of hormonal contraceptive use among women residing in the province of BC, Canada between 2006 and 2013. Finally, the concluding discussion (Chapter 4) contextualizes and integrates the findings of both studies, discusses the strengths and limitations of the study designs, and provides recommendations for future research.

2 LEVELS, TRENDS, AND DETERMINANTS OF HORMONAL CONTRACEPTIVE USE AMONG REPRODUCTIVE-AGED WOMEN IN BRITISH COLUMBIA

2.1 Introduction

Choosing an appropriate method of contraception is an important element of reproductive health care for women around the world. With the introduction of the first hormonal method—the oral contraceptive (OC) pill—over 50 years ago, women were granted greater autonomy over their own reproductive and sexual health (Liao & Dollin, 2012). Over time, a number of new OCs and non-oral hormonal contraceptives have been developed, and hormonal contraception has become increasingly widespread. It is estimated that approximately half of all contraceptive users in Canada opt for a hormonal method of birth control (Black et al., 2009).

There are currently over 40 different brands of OCs on the Canadian market, in addition to four non-oral hormonal methods: injectable medication, the intravaginal ring, the hormonal IUD, and the transdermal patch (Health Canada, 2015). Despite the availability of an expanded range of hormonal contraceptives in recent years, OCs are the predominant method of choice for Canadian women (Black et al., 2009; Rotermann et al., 2015; United Nations, 2015). Consequently, OC use in Canada has been more thoroughly investigated than non-oral hormonal methods (Balakrishnan et al., 1985; Boroditsky et al., 1995; Boroditsky, Fisher, & Sand, 1996; Fisher et al., 1999; Fisher et al., 2004a, 2004b; Rotermann et al., 2015), for which there is significantly less data on current patterns of use

(Black et al., 2009; Schwartz, 2013). At present, the latest Canadian study to investigate trends of use for the full range of oral and non-oral hormonal contraceptives was published in 2009, but was based on survey data collected over a decade ago (Black et al., 2009). Accordingly, reproductive health experts have publicly criticized Canada's lack of data on contraceptive use (Schwartz, 2013), and have stated that more current studies of contraceptive use in Canada are needed (Black et al., 2009).

The overarching objective of this study is to characterize current hormonal contraceptive use in a Canadian setting. Specifically, I will investigate levels, trends, and determinants of hormonal contraceptive use among reproductive-aged women in BC using population-based administrative data spanning the years 2006 to 2013.

2.2 Methods

This was a retrospective study of outpatient prescription drug purchases by residents of BC, Canada. All subjects were covered under BC's universal, public health insurance program for medical and hospital care; all subjects were also eligible for coverage under BC's universal, public drug benefit plan, under which deductibles are set in relation to household income.

2.2.1 Data sources and study cohort

Description of data sources

My analyses were based on de-identified, linked health datasets provided by Population Data BC with approval of relevant data stewards and the University of British Columbia's Behavioural Research Ethics Board (BC Ministry of Health, 2013). All inferences, opinions, and conclusions drawn in this chapter are my own, and do not reflect the opinions or policies of Population Data BC. The datasets included sociodemographic information and administrative records of all prescription drug dispensations, fee-for-service physician visits, and hospitalizations for all BC residents between 2004 and 2013, inclusive.

The datasets used for this study excluded military veterans, registered First Nations, and inmates of federal penitentiaries (who collectively make up approximately 4% of the population). To ensure complete data capture, I restricted analyses to include only those women who resided in BC for at least 275 days in a given observation year, or in each of three consecutive observation years when measuring incident contraceptive use. I determined length of residency in a given year using a "days registered" variable in the sociodemographic dataset for each calendar year.

I obtained records of prescription drug dispensations from PharmaNet, an information system that records every prescription filled at a pharmacy outside of acute care hospitals in BC, regardless of patient age or insurance status. Population Data BC uses personal identifiers to facilitate linkage of

records belonging to the same individual across datasets (i.e., PharmaNet, sociodemographic records, and administrative health files) and over time.

Description of study cohort

To compare prevalence of hormonal contraceptive use over time, I measured period prevalence in both 2006 and 2013 using two separate (though not mutually exclusive) cohorts of women: (1) those aged 15 to 49 in 2006 who had resided in BC for at least 275 days in that observation year and in each of the two years prior (n = 903,037); and (2) those aged 15 to 49 in 2013 who had resided in BC for at least 275 days in that observation year and in each of the two years prior *(*n = 909,890).

To measure incidence of hormonal contraceptive use over time, I constructed annual measures of incident use on rolling cohorts of women from 2006 to 2013, inclusive. I defined incident use as the first hormonal contraceptive purchase following at least two full years of residency in BC without records of any hormonal contraceptive purchases in the preceding two years. I restricted the cohort to women aged 15 to 49 (as of December 31 in the year of incident prescription) who had resided in BC for at least 275 days in the year of incident prescription, and in each of the two years prior (n = 301,055).[8]

[8] Incident use was ascertained using prescription dispensations data spanning the years 2004 to 2013, inclusive. To be considered an incident user in the 2006 cohort, a minimum "prescription naïve" period of two years (2004 to 2006) was required. In comparison, to be considered an incident user in the 2013 cohort, a minimum "prescription naïve" period of ten years (2004 to 2013) was required. Therefore, women who were identified as incident users later in the study period may have experienced a longer period of "prescription-naïvety" than those who were identified as incident users at the beginning of the study period.

2.2.2 Exposure measures

Measures of hormonal contraceptive use

In this study, I sought to estimate prevalent and incident hormonal contraceptive use by contraceptive type. I categorized hormonal contraceptives by mechanism of hormonal delivery (i.e., contraceptive type) in accordance with the World Health Organization's Anatomical Therapeutic Chemical (ATC) Classification System. Contraceptive types included combined estrogen-progestin OCs (ATC G03HB01, G03HB01, G03AA07, G03AB03, G03AA09, G03AB05, G03AA11, G03AB11, G03AA01, G03AA05, G03AA13, G03AB04), progestin-only OCs (G03AC01), injectable contraceptive medications with progestin (G03AC06), intravaginal rings with estrogen and progestin (G02BB01), transdermal hormonal patches with estrogen and progestin (G03AA13), and IUDs with progestin (G02BA03).

Since there are many different OC formulations available in Canada, I categorized OCs by the most frequently prescribed progestin types: levonorgestrel (ATCs G03AA07, G03AB03), drospirenone (ATC G03HB01), norgestimate (ATCs G03AA11, G03AB11), and desogestrel (ATCs G03AA09, G03AB05). Other OC formulations that were prescribed less frequently, including progestin-only OCs[9], were grouped into an 'other' category (ATCs G03AA01, G03AA05, G03AA13, G03AB04,

[9] Progestin-only OCs were grouped together with 'other' progestins only for analyses of incident OC use by progestin type (Figure 2-2). For all other analyses, progestin-only OCs and combined OCs are presented separately.

G03AC01, G03HB01).[10] Drospirenone, levonorgestrel, norgestimate, and desogestrel were chosen as standalone comparators to all other OCs and non-oral hormonal contraceptives because they accounted for the top-selling OC brands in Canada: Alesse (levonorgestrel), Yasmin and Yaz (drospirenone), Tri-Cyclen and Tri-Cyclen Lo (norgestimate), and Marvelon (desogestrel).

While CPA-EE (ATC G03HB01) is not indicated for contraceptive use in Canada, women who received a prescription for CPA-EE were still included in the "other progestin" category. CPA-EE is known to be prescribed off-label as an OC, and has been included in similar contraceptive trends studies in Canada and Denmark (Rotermann et al., 2015; Wilson, Laursen, & Lidegaard, 2012).

Sociodemographic characteristics

Age. Age in years was provided in the demographics data from Population Data BC. To account for any period trends, age was calculated as of December 31 for any given year. A categorical age variable was constructed based on the following age groupings: 15–19 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, and 40–49 years. For ease of comparison, these age groupings are identical or similar to those used in other recent Canadian studies of contraceptive use (Black et al., 2009; Rotermann et al., 2015).

Household income (quintile). Household income was measured using a validated combination of household-specific income data for those registered with BC's income-based drug benefit program

[10] In addition to progestin-only OCs containing northisterone (more generally known by the brand name Micronor), combined OC formulations containing ethynodiol, norethisterone, norgestrel, and cyproterone were included in the "other" category.

and neighbourhood-based proxy incomes for the remaining population (Hanley & Morgan, 2008). This information was used to construct a variable for income quintile, which was used as a proxy for socioeconomic status in the logistic regression analyses.

Marital status. Marital status was given as a binary variable (married/in-union or single) in the demographics dataset.

Ethnicity. Ethnicity was derived using a validated algorithm to identify surnames of the dominant ethnic minority groups in BC: Chinese (40% of ethnic minorities) and South Asians (from India, Pakistan, Bangladesh, and Sri Lanka; 26% of ethnic minorities) (British Columbia Government, 2008; Shah et al., 2010). Women who were not flagged as an ethnic minority were categorized as "European/other" in the results tables, and were also referred to as the "general population" in the discussion section.

Rurality. Neighbourhood urbanization ("rurality") was categorized based on the population density of the Local Health Area (LHA) in which women lived. LHAs are geographic units of analysis that are used for planning health services delivery in BC; each BC resident is assigned to one of 89 LHAs based on their home address. For ease of interpretation, LHAs were collapsed into three rurality categories: urban, rural, and mixed rural-urban.

2.2.3 Outcome measures

Rates of incident and prevalent hormonal contraceptive use are presented by contraceptive type. These rates were calculated as the number of women filling a relevant prescription divided by the population of all women satisfying the same age and residency requirements. Preliminary analyses suggested that age-adjusted rates did not significantly change the unadjusted results.

Since there were many different OC formulations available in BC throughout the study period, OC use was further stratified by progestin type to examine levels and trends of OC use in more detail.

2.2.4 Statistical analyses

Descriptive statistics were used to summarize overall and method-specific hormonal contraceptive use by age group, marital status, ethnicity, income, and rurality in 2006 and 2013. These method-specific analyses were conducted for combined OCs, progestin-only OCs, hormonal IUDs, the transdermal patch, and the intravaginal ring.

Multiple logistic regression was used to generate crude odds ratios (ORs) and adjusted ORs with 95% confidence intervals (CIs) for selected sociodemographic characteristics believed to be associated with hormonal contraceptive use. Selection of covariates was based on data availability,

the Andersen Model of Health Care Utilization (Andersen, 1995)[11], and existing literature on hormonal contraceptive use in Canada (Black et al., 2009; Boroditsky & Fisher, 2000; Boroditsky et al., 1995; Fisher et al., 1999; Fisher et al., 2004a, 2004b; Rotermann et al., 2015).

For all analyses, a value of $p<0.05$ was considered statistically significant. All analyses were performed using Stata version 13.1 (StataCorp, 2013).

2.2.5 Ethics approval

This study was approved by the University of British Columbia's Behavioural Research Ethics Board (H11-02273; October 2011).

[11] The Andersen Model of Health Care Utilization is one of the most widely acknowledged frameworks for identifying predictors of health care utilization. This model was initially developed in 1968 by Ronald M. Anderson, a US medical sociologist and health services researcher. It is a multilevel model that incorporates both individual and contextual determinants of health services use. The model suggests that an individual's use of health services is a function of their predisposition to use services, factors that enable or impede use, and their need for care, thus providing a way to conceptualize these variations in utilization rates and consumption of medical resources.

2.3 Results

2.3.1 Prevalence of hormonal contraceptive use

2006 prevalence

To compare differences in prevalent hormonal contraceptive use over time, I measured period prevalence using the earliest (2006) and latest (2013) years of administrative data. In 2006, 189,199 (21.0%) women aged 15 to 49 received at least one prescription for a hormonal contraceptive (Table 2-1). Contraceptive use was most prevalent among women aged 20 to 24 (26.0%), followed by those aged 25 to 29 (21.4%). Women aged 35 to 39 accounted for the lowest proportion (10.9%) of use. Hormonal contraceptive users tended to be unmarried (70.9%) and live in urban areas (65.7%). Ethnic minorities (Chinese and South Asian) accounted for a small proportion of users (5.3% and 3.0%, respectively). Women in the lowest income quintile represented the highest proportion (24.4%) of users, closely followed by those in the highest income quintile (22.7%).

Since sociodemographic characteristics are not independent of each other, I used multiple logistic regression to account for the simultaneous effects of these factors. Based on 2006 data, the adjusted odds of hormonal contraceptive use were highest in women aged 20 to 24 (OR=2.56, 95% CI 2.52–2.61) and 25 to 29 (OR=2.27, 95% CI 2.23–2.32), compared to the reference category of 15- to 19-year-olds (OR=1.00). Married women had lower odds of hormonal contraceptive use (OR=0.75, 95% CI 0.75–0.77) than unmarried women. Women belonging to the highest income quintile had slightly higher odds of hormonal contraceptive use (OR=1.17, 95% CI 1.15–1.19) compared to

those in the lowest income quintile (reference category, OR=1.0). Compared to European/other women, Chinese (OR=0.35, 95% CI 0.34–0.35) and South Asian (OR=0.46, 95% CI 0.45–0.48) women had significantly lower odds of hormonal contraceptive use. Living in a mixed (urban-rural) geographic area (compared to an urban area) was associated with a small but statistically significant increase in hormonal contraceptive use (OR=1.07, 95% CI 1.06–1.08).

Table 2-1. Sample characteristics of prevalent hormonal contraceptive users aged 15-49 in BC, 2006.

	Overall study sample		**Study sample by hormonal contraceptive use**				**Logistic regression odds ratios (95% CIs)**	
	903,037	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	116,883	(12.9)	88,850	(12.4)	28,033	(14.8)	Ref	Ref
20-24	113,454	(12.6)	64,314	(9.0)	49,140	(26.0)	2.42 (2.38-2.47)	2.56 (2.52-2.61)
25-29	108,037	(12.0)	67,635	(9.5)	40,402	(21.4)	1.89 (1.86-1.93)	2.27 (2.23-2.32)
30-34	113,714	(12.6)	85,436	(12.0)	28,278	(14.9)	1.05 (1.03-1.07)	1.32 (1.29-1.35)
35-39	133,391	(14.8)	112,790	(15.8)	20,601	(10.9)	0.58 (0.57-0.59)	0.73 (0.71-0.75)
40-49	317,558	(35.2)	294,813	(41.3)	22,745	(12.0)	0.24 (0.24-0.25)	0.30 (0.29-0.31)
Married								
No	487,422	(54.0)	353,319	(49.5)	134,103	(70.9)	Ref	Ref
Yes	415,615	(46.0)	360,519	(50.5)	55,096	(29.1)	0.40 (0.40-0.41)	0.75 (0.74-0.77)
Ethnicity								
European/other	758,713	(84.0)	585,239	(82.0)	173,474	(91.7)	Ref	Ref
Chinese	102,450	(11.3)	92,403	(12.9)	10,047	(5.3)	0.37 (0.36-0.37)	0.35 (0.34-0.35)
South Asian	41,874	(4.6)	36,196	(5.1)	5,678	(3.0)	0.53 (0.51-0.54)	0.46 (0.45-0.48)
Income quintile								
Lowest	187,231	(20.7)	141,152	(19.8)	46,079	(24.4)	Ref	Ref
2nd	157,523	(17.4)	126,275	(17.7)	31,248	(16.5)	0.76 (0.75-0.77)	0.88 (0.86-0.89)
3rd	182,410	(20.2)	148,492	(20.8)	33,918	(17.9)	0.70 (0.69-0.71)	0.82 (0.81-0.84)
4th	173,607	(19.2)	139,984	(19.6)	33,623	(17.8)	0.74 (0.72-0.75)	0.89 (0.87-0.91)
Highest	192,181	(21.3)	149,295	(20.9)	42,886	(22.7)	0.88 (0.87-0.89)	1.17 (1.15-1.19)
Rurality								
Urban	616,750	(68.3)	492,362	(69.0)	124,388	(65.7)	Ref	Ref
Mixed	229,551	(25.4)	176,344	(24.7)	53,207	(28.1)	1.19 (1.18-1.21)	1.07 (1.06-1.08)
Rural	53,374	(5.9)	42,085	(5.9)	11,289	(6.0)	1.06 (1.04-1.09)	0.98 (0.96-1.00)

2013 prevalence

In 2013, 196,169 (21.6%) women aged 15 to 49 received at least one prescription for a hormonal contraceptive (Table 2-2). Overall, the characteristics of women in the 2013 cohort were similar to

those of those in the 2006 cohort. Hormonal contraceptive use continued to be most prevalent in women aged 20 to 24 (24.1%), those who were unmarried (71.1%), and those living in urban areas (66.3%). Ethnic minorities continued to account for a very small proportion of users (6.0% and 3.3%, respectively). However, in 2013, women in the highest income quintile, as opposed to the lowest quintile, represented the highest proportion (24.0%) of users.

Table 2-2. Sample characteristics of prevalent hormonal contraceptive users aged 15-49 in BC, 2013.

	Overall study sample		Study sample by hormonal contraceptive use				Logistic regression odds ratios (95% CIs)	
	909,890	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	109,033	(12.0)	82,587	(11.6)	26,446	(13.5)	Ref	Ref
20-24	115,930	(12.7)	68,630	(9.6)	47,300	(24.1)	2.15 (2.11-2.19)	2.27 (2.23-2.31)
25-29	122,998	(13.5)	79,788	(11.2)	43,210	(22.0)	1.69 (1.66-1.72)	2.01 (1.98-2.05)
30-34	131,699	(14.5)	99,620	(14.0)	32,079	(16.4)	1.01 (0.99-1.02)	1.29 (1.26-1.32)
35-39	129,722	(14.3)	109,221	(15.3)	20,501	(10.5)	0.59 (0.57-0.60)	0.75 (0.73-0.77)
40-49	300,508	(33.0)	273,875	(38.4)	26,633	(13.6)	0.30 (0.30-0.31)	0.38 (0.37-0.39)
Married								
No	517,878	(56.9)	378,350	(53.0)	139,528	(71.1)	Ref	Ref
Yes	392,012	(43.1)	335,371	(47.0)	56,641	(28.9)	0.46 (0.45-0.46)	0.75 (0.74-0.76)
Ethnicity								
European/other	746,496	(82.0)	568,579	(79.7)	177,917	(90.7)	Ref	Ref
Chinese	111,887	(12.3)	100,198	(14.0)	11,689	(6.0)	0.37 (0.37-0.38)	0.39 (0.38-0.40)
South Asian	51,507	(5.7)	44,944	(6.3)	6,563	(3.3)	0.47 (0.45-0.48)	0.50 (0.49-0.51)
Income quintile								
Lowest	157,567	(17.3)	122,713	(18.1)	34,854	(18.5)	Ref	Ref
2nd	166,813	(18.3)	134,522	(19.9)	32,291	(17.1)	0.85 (0.83-0.86)	0.92 (0.90-0.93)
3rd	173,327	(19.0)	140,380	(20.7)	32,947	(17.5)	0.83 (0.81-0.84)	0.92 (0.91-0.94)
4th	199,794	(22.0)	156,746	(23.2)	43,048	(22.9)	0.97 (0.95-0.98)	1.09 (1.08-1.11)
Highest	167,906	(18.5)	122,675	(18.1)	45,231	(24.0)	1.30 (1.28-1.32)	1.50 (1.48-1.53)
Rurality								
Urban	640,604	(70.4)	510,943	(72.0)	129,661	(66.3)	Ref	Ref
Mixed	219,098	(24.1)	163,629	(23.0)	55,469	(28.3)	1.34 (1.32-1.35)	1.18 (1.16-1.19)
Rural	45,919	(5.0)	35,389	(5.0)	10,530	(5.4)	1.17 (1.15-1.20)	1.08 (1.06-1.11)

In 2013, the adjusted odds of hormonal contraceptive use were highest among women aged 20 to 24 (reference group: 15- to 19-year-olds), unmarried, and in the highest income quintile (reference group: lowest income quintile). Compared to European/other women, Chinese (OR=0.39, 95% CI 0.38–0.40) and South Asian (OR=0.50, 95% CI 0.49–0.51) women had significantly lower odds of

hormonal contraceptive use. Living in either a rural or mixed (urban-rural) geographic area (reference group: urban) was associated with small but statistically significant increases in hormonal contraceptive use.

Table 2-3. Contraceptive use by drug type (as % of all contraceptive use*), ages 15-49, 2006 versus 2013.

	Counts and percentages of women who received at least one hormonal contraceptive prescription, by contraceptive type				
	2006 (*n*=189,199)		**2013 (*n*=196,169)**		**Difference**
Contraceptive method					
Combined OC	163,718	86.5%	162456	82.8%	-3.7%
Injectable DMPA	11,881	6.3%	8553	4.4%	-1.9%
Transdermal patch	6,740	3.6%	3679	1.9%	-1.7%
Progestin-only OC	7,276	3.8%	9132	4.7%	0.9%
Intravaginal ring	3,783	2.0%	9098	4.6%	2.6%
Hormonal IUD	3,295	1.7%	12501	6.4%	4.7%

* Women are counted more than once if they received a prescription for more than one contraceptive type in a given year. Therefore, percentages do not add up to 100%.

Table 2-3 provides an overview of the changes in prevalent hormonal contraceptive use from 2006 to 2013. Combined OCs experienced the greatest decline in prevalent use: 86.5% of all hormonal contraceptive users filled at least one combined OC prescription in 2006, compared to only 82.8% of all users in 2013, representing a 3.7% decrease. Prevalent use also declined for injectable DMPA (1.9% decrease) and the transdermal patch (1.7% decrease). Conversely, the proportion of all hormonal contraceptive users receiving hormonal IUDs rose from 1.7% in 2006 to 6.4% in 2013—an increase of 4.7%. Smaller increases in prevalent use were observed for progestin-only OCs (0.9% increase) and the intravaginal ring (2.6% increase).

2.3.2 Incidence rates of new hormonal contraceptive users

A total of 1,396,778 women met the inclusion criteria for BC residency and were aged 15 to 49 years at some point between January 1, 2006 and December 31, 2013, inclusive. Of these women, 301,055 (21.6%) met the criteria for definition as an new contraceptive user (i.e., received an initial prescription for a hormonal contraceptive during the study period without any prior record of use). Annual[12] incidence (per 100,000 women aged 15 to 49) was measured for both overall and method-specific hormonal contraceptive use among new users. Overall, I observed a decline in hormonal contraceptive use among new users, from 5,259 per 100,000 women in 2006 to 3,279 per 100,000 in 2013 (Figure 2-1). This trend was primarily driven by declining rates of OC initiators, who represented the majority of new hormonal contraceptive users.

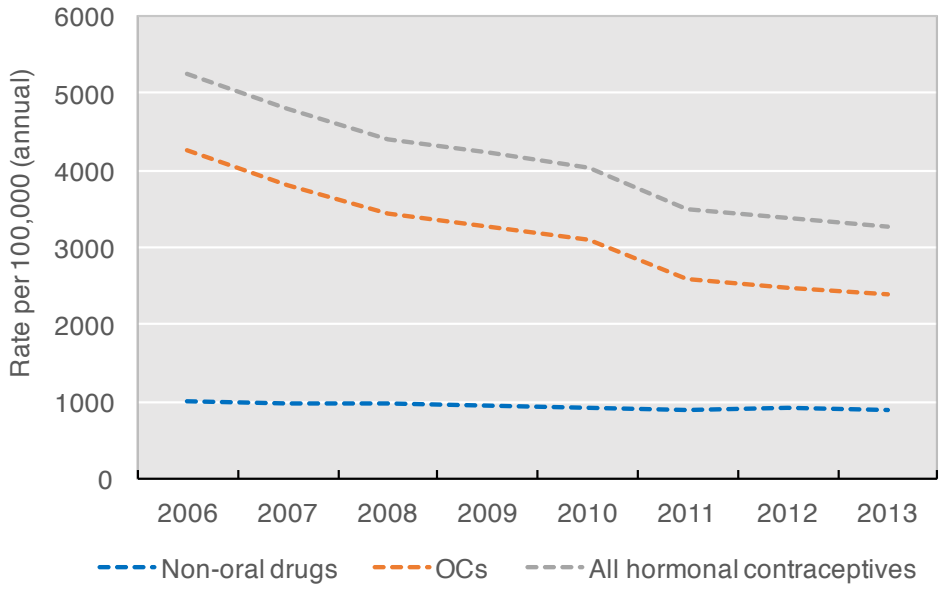

Figure 2-1. Incident hormonal contraceptives use (per 100,000 women), ages 15–49, OCs versus non-oral contraceptives, 2006–2013.

[12] Overall and method-specific quarterly incidence are provided in Appendix A, Figure A-1 and Figure A-2.

I observed a decline in incident use for all hormonal contraceptive methods, with the exception of the hormonal IUD (Figure 2-2). The hormonal IUD was the only method that became increasingly popular among new users, with incident use rising from 288 per 100,000 women in 2006 to 567 per 100,000 women by 2013. OCs containing the progestin levonorgestrel were the preferred choice for new contraceptive users, accounting for 39.9% (92,497/231,834) of all incident OC use. Despite the popularity of levonorgestrel-containing OCs, these formulations still experienced a decline in incident use throughout the study period, dropping from 1,623 per 100,000 women in 2006 to 1,240 per 100,000 women in 2013.

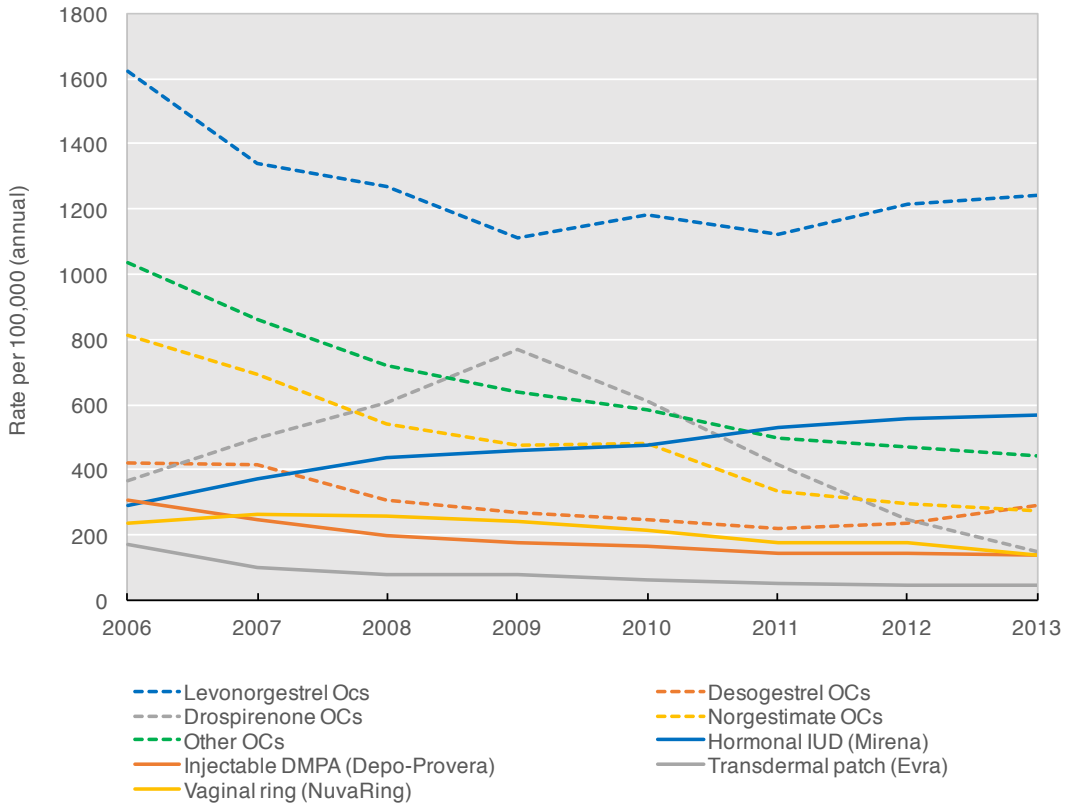

Figure 2-2. Incident hormonal contraceptive use (per 100,000 women) in BC, ages 15–49, by contraceptive type, 2006–2013.

Since age is an important determinant of method-specific contraceptive use (Black et al., 2009), I stratified incident use by age group (15–24, 25–34, and 35–49 years) to examine differences in trends over time. The results showed a decline in OC use (Figure 2-3) and increased hormonal IUD use (Figure 2-4) across all age groups.[13] Women aged 25 to 34 had the most significant differences in incident use over time: OC use dropped from 4,974 to 1,754 per 100,000 women, while IUD use rose from 391 to 754 per 100,000 women throughout the study period (as summarized in Table 2-4).

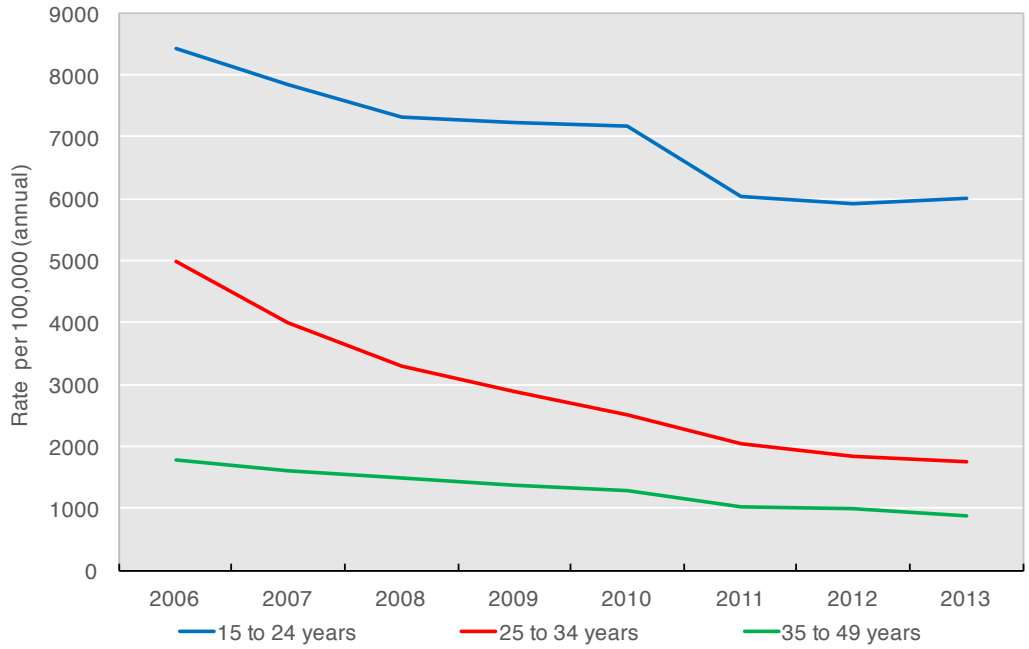

Figure 2-3. Declining rates of incident OC use (per 100,000 women) in BC, by age group, 2006–2013.

[13] Figures showing age-specific incident use of other non-oral hormonal contraceptives are provided in Appendix A, Figure A-3.

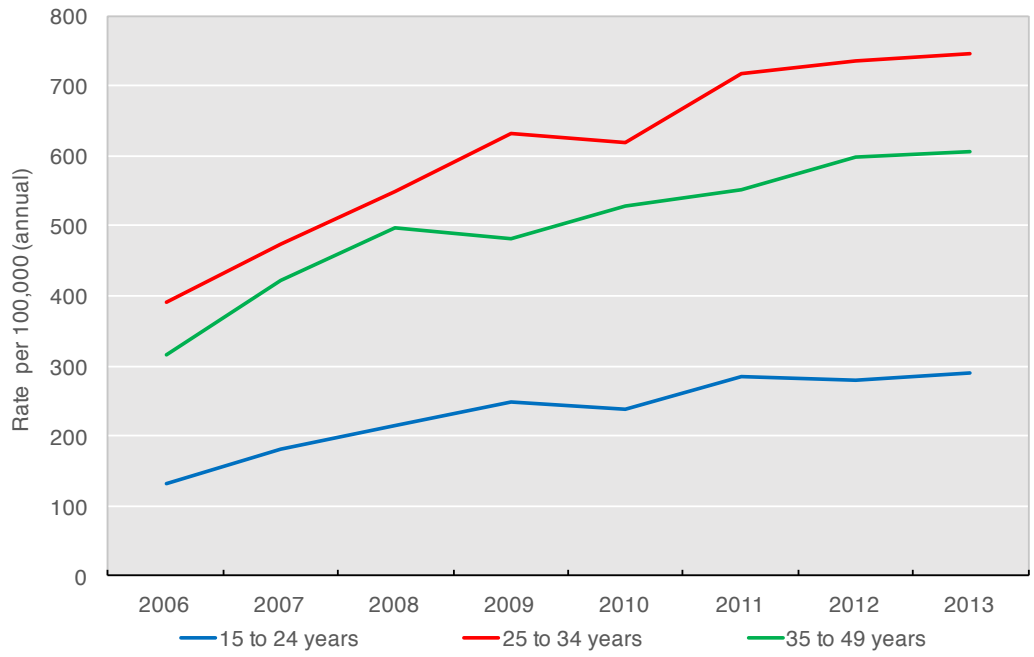

Figure 2-4. Increasing rates of incident IUD use (per 100,000 women) in BC, by age group, 2006–2013.

Table 2-4. Summary table of incidence rates of new IUD and OC users (per 100,000 women), by age group, 2006 versus 2013.

	New IUD users (per 100,000)		New OC users (per 100,000)	
Age group, yrs	**2006**	**2013**	**2006**	**2013**
15-24	133	291	8,429	6,008
25-34	391	745	4,974	1,754
35-49	317	607	1,776	881

2.3.3 Characteristics of method-specific hormonal contraceptive use

An overview of the sociodemographic characteristics of women aged 15 to 49 years who filled a prescription for a specific type of hormonal contraceptive in 2013 is provided in Appendix A, Table A-1. Women who filled a prescription for more than one type of contraceptive were counted once in each respective category.

Combined OCs

In 2013, 162,456 (17.9%) women aged 15 to 49 received at least one prescription for a combined OC (Table 2-5). Combined OCs were most prevalent among women aged 20 to 24 (25.4%), followed by women aged 25 to 29 (22.0%). Women aged 35 to 39 accounted for the lowest proportion (9.7%) of users. Combined OC users tended to be unmarried (73.4%) and live in urban areas (67.1%). Ethnic minorities accounted for a small proportion of users (6.1% and 3.4%, respectively). Women in the highest income quintile represented the highest proportion (24.8%) of users. Overall, these characteristics are very similar to those presented for all hormonal contraceptive users in 2013 (Table 2-2), with the exception of some variation in the distribution of users by age group.

Table 2-5. Characteristics of women aged 15-49 residing in BC in 2013, by combined OC use.

	Overall study sample		Study sample by combined OC use				Logistic regression odds ratios (95% CIs)	
	909,890	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	109,033	(12.0)	85,053	(11.4)	23,980	(14.8)	Ref	Ref
20-24	115,930	(12.7)	74,643	(10.0)	41,287	(25.4)	1.96 (1.93-2.00)	2.06 (2.02-2.10)
25-29	122,998	(13.5)	87,184	(11.7)	35,814	(22.0)	1.46 (1.43-1.48)	1.76 (1.73-1.80)
30-34	131,699	(14.5)	106,492	(14.2)	25,207	(15.5)	0.84 (0.82-0.86)	1.11 (1.09-1.14)
35-39	129,722	(14.3)	113,973	(15.2)	15,749	(9.7)	0.49 (0.48-0.50)	0.65 (0.64-0.67)
40-49	300,508	(33.0)	280,089	(37.5)	20,419	(12.6)	0.26 (0.25-0.26)	0.34 (0.33-0.35)
Married								
No	517,878	(56.9)	398,636	(53.3)	119,242	(73.4)	Ref	Ref
Yes	392,012	(43.1)	348,798	(46.7)	43,214	(26.6)	0.41 (0.41-0.42)	0.70 (0.69-0.71)
Ethnicity								
European/other	746,496	(82.0)	599,529	(80.2)	146,967	(90.5)	Ref	Ref
Chinese	111,887	(12.3)	101,953	(13.6)	9,934	(6.1)	0.40 (0.39-0.41)	0.42 (0.41-0.43)
South Asian	51,507	(5.7)	45,952	(6.1)	5,555	(3.4)	0.49 (0.48-0.51)	0.53 (0.52-0.55)
Income quintile								
Lowest	157,567	(17.3)	129,147	(18.2)	28,420	(18.2)	Ref	Ref
2nd	166,813	(18.3)	140,594	(19.8)	26,219	(16.8)	0.85 (0.83-0.86)	0.93 (0.91-0.95)
3rd	173,327	(19.0)	146,438	(20.6)	26,889	(17.2)	0.83 (0.82-0.85)	0.94 (0.92-0.96)
4th	199,794	(22.0)	163,924	(23.1)	35,870	(23.0)	0.99 (0.98-1.01)	1.13 (1.11-1.15)
Highest	167,906	(18.5)	129,088	(18.2)	38,818	(24.8)	1.37 (1.34-1.39)	1.58 (1.55-1.61)
Rurality								
Urban	640,604	(70.4)	531,954	(71.5)	108,650	(67.1)	Ref	Ref
Mixed	219,098	(24.1)	174,071	(23.4)	45,027	(27.8)	1.27 (1.25-1.28)	1.12 (1.11-1.14)
Rural	45,919	(5.0)	37,554	(5.1)	8,365	(5.2)	1.09 (1.06-1.12)	1.01 (0.98-1.04)

Since sociodemographic characteristics are not independent of each other, I used multiple logistic regression to account for the simultaneous effects of these characteristics. Compared to women aged 15 to 19 years, the adjusted odds of combined OC use were highest among women aged 20 to 24 (OR=2.06, 95% CI 2.02–2.10), and declined with older age. Significantly lower odds of use (OR=0.70, 95% CI 0.69–0.71) were observed among women who were married or in-union compared to single women. Compared to European/other women, Chinese (OR=0.42, 95% CI 0.41–0.43) and South Asian (OR=0.53, 95% CI 0.52–0.55) women had significantly lower odds of use. Women in the highest income quintile had higher odds of use (OR=1.58, 95% CI 1.55–1.61) compared to women in the lowest income quintile. In addition, living in a mixed (urban-rural)

geographical area was associated with slightly higher odds of use (OR=1.12, 95% CI 1.11–1.14) compared to urban areas, although there was no significant difference between urban and rural.

I compared the characteristics of combined OC users in 2006 and 2013 in an effort to characterize any changes in use over time. In 2006, 163,718 (18.1%) women aged 15 to 49 received at least one prescription for a combined OC (Appendix A, Table A-2[14]), which was only slightly higher than in 2013 (17.9%). Overall, the characteristics of combined OC users and adjusted odds ratios in 2006 and 2013 were very similar, except for a higher proportion (24.1%) of lower income users in 2006.

Hormonal IUDs

In 2013, 12,501 (1.4%) women aged 15 to 49 received at least one prescription for a hormonal IUD (Table 2-6). Hormonal IUDs were most prevalent among the oldest age group (26.8% of users were aged 40 to 49), while the youngest age group (15 to 19 years) accounted for the lowest proportion (5.3%) of users. The proportion of hormonal IUD use by age ranged from 15.3% to 18% across the other age groups. The distribution of users by marital status was approximately equal (51.8% unmarried, 48.2% married or in-union), which differs from the results for combined OC use. However, similar to combined OCs, ethnic minorities accounted for a small proportion of hormonal IUD users (4.9% and 3.8%, respectively). Women in the highest income quintile represented the highest proportion (24.5%) of hormonal IUDs users, followed by women in the second highest

[14] For analyses where I found no significant differences between 2006 and 2013 for a given contraceptive method, summary tables of characteristics and associated odds ratios for the 2006 comparators are included in Appendix A rather than in the body of this chapter.

income quintile (22.8% of users). Women living in urban areas represented 61.8% of users, while women in rural areas accounted for only 6.2% of users.

Overall, the characteristics of hormonal IUD users in 2013 are similar to those presented for all hormonal contraceptive users in the same year (Table 2-2) with respect to ethnicity, income, and rurality. However, there are notable differences between the distribution of age and marital status for hormonal IUD users compared to all hormonal contraceptive users, with a higher proportion of older and married women, and fewer younger women, using hormonal IUDs.

Compared to women aged 15 to 19, the adjusted odds of hormonal IUD use were highest among women aged 25 to 29 (OR=3.02, 95% CI 2.76–3.31), after adjusting for other factors, such as marital status, ethnicity, income, and rurality (Table 2-6). Married women had significantly higher odds (OR=1.24, 95% CI 1.19–1.30) of hormonal IUD use than unmarried women. Compared to European/other women, Chinese (OR=0.41, 95% CI 0.38–0.45) and South Asian (OR=0.63, 95% CI 0.57–0.69) women had significantly lower odds of use. Women in the highest income quintile had significant higher odds of use (OR=1.27, 95% CI 1.20–1.35) compared to those in the lowest income quintile. Women living in mixed urban-rural and rural areas also had significantly higher odds of hormonal IUD use compared to urban women.

Table 2-6. Characteristics of women aged 15-49 residing in BC in 2013, by hormonal IUD use.

	Overall study sample		Study sample by hormonal IUD use				Logistic regression odds ratios (95% CIs)	
	909,890	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	109,033	(12.0)	108,375	(12.1)	658	(5.3)	Ref	Ref
20-24	115,930	(12.7)	114,012	(12.7)	1,918	(15.3)	2.77 (2.53-3.03)	2.81 (2.56-3.08)
25-29	122,998	(13.5)	120,773	(13.5)	2,225	(17.8)	3.03 (2.78-3.31)	3.02 (2.76-3.31)
30-34	131,699	(14.5)	129,406	(14.4)	2,293	(18.3)	2.92 (2.68-3.18)	2.86 (2.60-3.14)
35-39	129,722	(14.3)	127,665	(14.2)	2,057	(16.5)	2.65 (2.43-2.90)	2.49 (2.26-2.74)
40-49	300,508	(33.0)	297,158	(33.1)	3,350	(26.8)	1.86 (1.71-2.02)	1.68 (1.54-1.85)
Married								
No	517,878	(56.9)	511,404	(57.0)	6,474	(51.8)	Ref	Ref
Yes	392,012	(43.1)	385,985	(43.0)	6,027	(48.2)	1.23 (1.19-1.28)	1.24 (1.19-1.30)
Ethnicity								
European/other	746,496	(82.0)	735,084	(81.9)	11,412	(91.3)	Ref	Ref
Chinese	111,887	(12.3)	111,269	(12.4)	618	(4.9)	0.36 (0.33-0.39)	0.41 (0.38-0.45)
South Asian	51,507	(5.7)	51,036	(5.7)	471	(3.8)	0.59 (0.54-0.65)	0.63 (0.57-0.69)
Income quintile								
Lowest	157,567	(17.3)	155,421	(18.2)	2,146	(18.0)	Ref	Ref
2nd	166,813	(18.3)	164,796	(19.3)	2,017	(16.9)	0.89 (0.83-0.94)	0.87 (0.81-0.92)
3rd	173,327	(19.0)	171,192	(20.1)	2,135	(17.9)	0.90 (0.85-0.96)	0.89 (0.83-0.94)
4th	199,794	(22.0)	197,078	(23.1)	2,716	(22.8)	1.00 (0.94-1.06)	0.97 (0.91-1.03)
Highest	167,906	(18.5)	164,986	(19.3)	2,920	(24.5)	1.28 (1.21-1.36)	1.27 (1.20-1.35)
Rurality								
Urban	640,604	(70.4)	632,897	(70.9)	7,707	(61.8)	Ref	Ref
Mixed	219,098	(24.1)	215,112	(24.1)	3,986	(32.0)	1.52 (1.46-1.58)	1.35 (1.30-1.41)
Rural	45,919	(5.0)	45,148	(5.1)	771	(6.2)	1.40 (1.30-1.51)	1.30 (1.20-1.40)

I compared the characteristics of hormonal IUD users in 2006 and 2013 to identify any significant differences in use over this period. In 2006, 3,285 (0.4%) women aged 15 to 49 received at least one prescription for a hormonal IUD (Table 2-7), which is significantly lower than the proportion of women using hormonal IUDs in 2013 (1.4%). In addition, younger women represented fewer hormonal IUD users in 2006; for example, women aged 20 to 24 accounted for only 10.6% of users in 2006, compared to 15.3% of users in 2013.

Table 2-7. Characteristics of women aged 15-49 residing in BC in 2006, by hormonal IUD use.

	Overall study sample		Study sample by hormonal IUD use				Logistic regression odds ratios (95% CIs)	
	903,037	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	116,883	(12.9)	116,793	(13.0)	90	(2.7)	Ref	Ref
20-24	113,454	(12.6)	113,104	(12.6)	350	(10.6)	4.02 (3.18-5.06)	1.71 (1.61-1.82)
25-29	108,037	(12.0)	107,519	(11.9)	518	(15.7)	6.25 (5.00-7.82)	1.57 (1.47-1.68)
30-34	113,714	(12.6)	113,070	(12.6)	644	(19.5)	7.39 (5.93-9.22)	1.36 (1.27-1.47)
35-39	133,391	(14.8)	132,646	(14.7)	745	(22.6)	7.29 (5.86-9.07)	1.13 (1.05-1.22)
40-49	317,558	(35.2)	316,610	(35.2)	948	(28.8)	3.89 (3.13-4.82)	0.55 (0.51-0.59)
Married								
No	487,422	(54.0)	486,044	(54.0)	1,378	(41.8)	Ref	Ref
Yes	415,615	(46.0)	413,698	(46.0)	1,917	(58.2)	1.63 (1.52-1.75)	0.57 (0.55-0.60)
Ethnicity								
European/other	758,713	(84.0)	755,826	(84.0)	2,887	(87.6)	Ref	Ref
Chinese	102,450	(11.3)	102,196	(11.4)	254	(7.7)	0.65 (0.57-0.74)	0.28 (0.25-0.31)
South Asian	41,874	(4.6)	41,720	(4.6)	154	(4.7)	0.97 (0.82-1.14)	0.45 (0.40-0.52)
Income quintile								
Lowest	187,231	(20.7)	186,532	(20.7)	699	(21.2)	Ref	Ref
2nd	157,523	(17.4)	156,996	(17.4)	527	(16.0)	0.90 (0.80-1.00)	0.79 (0.75-0.83)
3rd	182,410	(20.2)	181,745	(20.2)	665	(20.2)	0.98 (0.88-1.09)	0.67 (0.64-0.71)
4th	173,607	(19.2)	172,990	(19.2)	617	(18.7)	0.95 (0.85-1.06)	0.66 (0.62-0.70)
Highest	192,181	(21.3)	191,420	(21.3)	761	(23.1)	1.06 (0.96-1.18)	0.56 (0.53-0.59)
Rurality								
Urban	616,750	(68.3)	614,511	(68.3)	2,239	(68.0)	Ref	Ref
Mixed	229,551	(25.4)	228,697	(25.4)	854	(25.9)	1.02 (0.95-1.11)	1.63 (1.56-1.69)
Rural	53,374	(5.9)	53,177	(5.9)	197	(6.0)	1.02 (0.88-1.18)	1.76 (1.65-1.88)

With respect to ethnicity, Chinese women represented a slightly higher proportion of users in 2006 (7.7%) than in 2013 (4.9%), although the adjusted odds of hormonal IUD use among Chinese women, as compared with European/other women, was lower in 2006 (OR=0.28, 95% CI 0.25–0.31). Similarly, South Asian women accounted for a slightly higher proportion of users in 2006 (4.7%) than in 2013 (3.8%), with lower adjusted odds of hormonal IUD use in 2006 (OR=0.45, 95% CI 0.40–0.52) compared to 2013.

Finally, I observed interesting differences in the adjusted odds of income associated with hormonal IUD use in 2006 compared to 2013. In 2013, I reported that women in the highest income quintile had significantly higher odds of hormonal IUD use compared to those in the lowest quintile.

Conversely, in 2006, I observed an inverse income gradient associated with hormonal IUD use, with higher income associated with decreased odds of use.

Injectable DMPA

In 2013, 8,553 (0.9%) women aged 15 to 49 received at least one prescription for DMPA (Table 2-8). There was a relatively equal distribution of DMPA use across all age groups. DMPA use was more prevalent in unmarried (78.2%) and lower-income (27.0%) women. Ethnic minorities accounted for a small proportion of users (2.5% and 1.9%, respectively). Women living in rural areas accounted for a small proportion of users (8.9%), compared to women in urban (52.0%) and mixed urban-rural (39.1%) areas.

The adjusted odds of DMPA use were slightly lower for older women in the 35–39 and 40–49 age groups (compared to the reference category of 15- to 19-year-olds). In particular, women aged 40 to 49 had almost half the odds of DMPA use (OR=0.62, 95% CI 0.57–0.67) compared to women aged 15 to 19. Married women had significantly lower odds of use (OR=0.49, 95% CI 0.46–0.52) compared to unmarried women. Compared to European/other women, Chinese (OR=0.20, 95% CI 0.18–0.24) and South Asian (OR=0.39, 95% CI 0.33–0.45) women had significantly lower odds of use. I also observed an income gradient for DMPA, with lower income associated with increased odds of use. Women in the lowest income category (reference category, OR=1.00) had approximately twice the odds of DMPA use compared to women in the highest income category (OR=0.50, 95% CI 0.46–0.54). Although women living in rural areas accounted for a small

proportion of DMPA users, their odds of use were double (OR=2.01, 95% CI 2.01–1.86) those of urban women (reference category, OR=1.00).

Table 2-8. Characteristics of women aged 15-49 residing in BC in 2013, by injectable DMPA use.

	Overall study sample		Study sample by injectable DMPA use				Logistic regression odds ratios (95% CIs)	
	909,890	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	109,033	(12.0)	107,567	(11.9)	1,466	(17.1)	Ref	Ref
20-24	115,930	(12.7)	114,268	(12.7)	1,662	(19.4)	1.07 (0.99-1.15)	1.07 (1.00-1.15)
25-29	122,998	(13.5)	121,593	(13.5)	1,405	(16.4)	0.85 (0.79-0.91)	1.00 (0.92-1.08)
30-34	131,699	(14.5)	130,395	(14.5)	1,304	(15.2)	0.73 (0.68-0.79)	0.99 (0.91-1.07)
35-39	129,722	(14.3)	128,647	(14.3)	1,075	(12.6)	0.61 (0.57-0.66)	0.89 (0.82-0.97)
40-49	300,508	(33.0)	298,867	(33.2)	1,641	(19.2)	0.40 (0.38-0.43)	0.62 (0.57-0.67)
Married								
No	517,878	(56.9)	511,191	(56.7)	6,687	(78.2)	Ref	Ref
Yes	392,012	(43.1)	390,146	(43.3)	1,866	(21.8)	0.37 (0.35-0.38)	0.49 (0.46-0.52)
Ethnicity								
European/other	746,496	(82.0)	738,315	(81.9)	8,181	(95.7)	Ref	Ref
Chinese	111,887	(12.3)	111,676	(12.4)	211	(2.5)	0.17 (0.15-0.20)	0.20 (0.18-0.24)
South Asian	51,507	(5.7)	51,346	(5.7)	161	(1.9)	0.28 (0.24-0.33)	0.39 (0.33-0.45)
Income quintile								
Lowest	157,567	(17.3)	155,374	(18.1)	2,193	(27.0)	Ref	Ref
2nd	166,813	(18.3)	165,068	(19.3)	1,745	(21.5)	0.75 (0.70-0.80)	0.79 (0.74-0.84)
3rd	173,327	(19.0)	171,813	(20.0)	1,514	(18.6)	0.62 (0.58-0.67)	0.70 (0.66-0.75)
4th	199,794	(22.0)	198,150	(23.1)	1,644	(20.2)	0.59 (0.55-0.63)	0.67 (0.63-0.72)
Highest	167,906	(18.5)	166,871	(19.5)	1,035	(12.7)	0.44 (0.41-0.47)	0.50 (0.46-0.54)
Rurality								
Urban	640,604	(70.4)	636,161	(70.9)	4,443	(52.0)	Ref	Ref
Mixed	219,098	(24.1)	215,761	(24.1)	3,337	(39.1)	2.21 (2.12-2.32)	1.83 (1.75-1.92)
Rural	45,919	(5.0)	45,161	(5.0)	758	(8.9)	2.40 (2.22-2.60)	2.01 (1.86-2.18)

I also compared the characteristics of DMPA users in 2006 and 2013. In 2006, 11,881 (1.3%) women aged 15 to 49 received at least one prescription for DMPA (Appendix A, Table A-3). Overall, the characteristics of DMPA users in 2006 and 2013 were similar, except for slightly higher adjusted odds of use among younger age groups in 2006.

Intravaginal ring

In 2013, 9,098 (1.0%) women aged 15 to 49 received at least one prescription for the intravaginal ring (Table 2-9). The intravaginal ring was most prevalent among women aged 20 to 24 (29.1%) and women aged 25 to 29 (31.4%). The majority of intravaginal ring users were unmarried (76.6%) and living in urban areas (64.4%). As with other hormonal contraceptive methods, ethnic minorities accounted for a small proportion of users (4.3% and 1.5%, respectively). Women in the highest income quintile represented the highest proportion (22.6%) of users by a small margin, although the distribution of intravaginal ring use was relatively even across all income quintiles.

Table 2-9. Characteristics of women aged 15-49 residing in BC in 2013, by intravaginal ring use.

	Overall study sample		**Study sample by intravaginal ring use**				**Logistic regression odds ratios (95% CIs)**	
	909,890	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	109,033	(12.0)	108,338	(12.0)	695	(7.6)	Ref	Ref
20-24	115,930	(12.7)	113,282	(12.6)	2,648	(29.1)	3.64 (3.35-3.96)	3.75 (3.44-4.09)
25-29	122,998	(13.5)	120,140	(13.3)	2,858	(31.4)	3.71 (3.41-4.03)	4.36 (4.00-4.76)
30-34	131,699	(14.5)	130,157	(14.4)	1,542	(16.9)	1.85 (1.69-2.02)	2.40 (2.18-2.64)
35-39	129,722	(14.3)	128,985	(14.3)	737	(8.1)	0.89 (0.80-0.99)	1.19 (1.07-1.33)
40-49	300,508	(33.0)	299,890	(33.3)	618	(6.8)	0.32 (0.29-0.36)	0.43 (0.38-0.48)
Married								
No	517,878	(56.9)	510,912	(56.7)	6,966	(76.6)	Ref	Ref
Yes	392,012	(43.1)	389,880	(43.3)	2,132	(23.4)	0.40 (0.38-0.42)	0.68 (0.64-0.72)
Ethnicity								
European/other	746,496	(82.0)	737,924	(81.9)	8,572	(94.2)	Ref	Ref
Chinese	111,887	(12.3)	111,500	(12.4)	387	(4.3)	0.30 (0.27-0.33)	0.34 (0.30-0.38)
South Asian	51,507	(5.7)	51,368	(5.7)	139	(1.5)	0.23 (0.20-0.28)	0.27 (0.22-0.32)
Income quintile								
Lowest	157,567	(17.3)	155,926	(18.2)	1,641	(18.9)	Ref	Ref
2nd	166,813	(18.3)	165,223	(19.3)	1,590	(18.3)	0.91 (0.85-0.98)	1.03 (0.96-1.11)
3rd	173,327	(19.0)	171,783	(20.1)	1,544	(17.8)	0.85 (0.80-0.92)	1.01 (0.94-1.09)
4th	199,794	(22.0)	197,843	(23.1)	1,951	(22.4)	0.94 (0.88-1.00)	1.12 (1.04-1.19)
Highest	167,906	(18.5)	165,938	(19.4)	1,968	(22.6)	1.13 (1.06-1.20)	1.32 (1.24-1.42)
Rurality								
Urban	640,604	(70.4)	634,770	(70.8)	5,834	(64.4)	Ref	Ref
Mixed	219,098	(24.1)	216,365	(24.1)	2,733	(30.2)	1.37 (1.31-1.44)	1.21 (1.15-1.27)
Rural	45,919	(5.0)	45,424	(5.1)	495	(5.5)	1.19 (1.08-1.30)	1.08 (0.98-1.19)

After adjusting for all factors, women aged 25 to 29 were more than four times as likely (OR=4.36, 95% CI 4.00–4.76) to use the intravaginal ring compared to the reference group of 15- to 19-year-olds. Women aged 20 to 24 were more than three times as likely (OR=3.75, 95% CI 3.44–4.09), and those aged 30 to 34 were more than twice as likely (OR=2.40, 95% CI 2.18–2.64), to use the intravaginal ring compared to women aged to 15 to 19. Married women had lower odds of use (OR=0.68, 95% CI 0.64–0.72) compared to unmarried women. Compared to European/other women, Chinese (OR=0.34, 95% CI 0.30–0.38) and South Asian (OR=0.27, 95% CI 0.22–0.32) women had significantly lower odds of intravaginal ring use. Women in the lowest income quintile had slightly lower odds of use than those in higher income quintiles, although the association between income and intravaginal ring use was not as statistically significant as what I have reported for other contraceptive methods, such as injectable DMPA. Differences in the adjusted odds of intravaginal ring use by rurality were also minimal.

In 2006, 3,783 (0.4%) women aged 15 to 49 received at least one intravaginal ring prescription (Appendix A, Table A-4). Overall, I did not identify any significant differences in the characteristics of intravaginal ring users between 2006 and 2013.

Progestin-only OCs

In 2013, 9,132 (1.0%) women aged 15 to 49 received at least one prescription for a progestin-only OC (Table 2-10). Progestin-only OCs were most prevalent among women aged 30 to 34 (30.5%) and women aged 25 to 29 (23.3%). Women aged 15 to 19 accounted for a very small proportion of users (4.1%). The majority of users were married (58.2%) and living in urban areas (64.8%). Ethnic

minorities (Chinese and South Asian) accounted for a small proportion of users (4.8% and 3.1%, respectively). Women in the two highest income quintiles represented just under half (46.6%) of all progestin-only OC users.

Table 2-10. Characteristics of women aged 15-49 residing in BC in 2013, by progestin-only OC use.

	Overall study sample		Study sample by progestin-only OC use				Logistic regression odds ratios (95% CIs)	
	909,890	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	109,033	(12.0)	108,661	(12.1)	372	(4.1)	Ref	Ref
20-24	115,930	(12.7)	114,802	(12.7)	1,128	(12.4)	2.87 (2.55-3.23)	2.89 (2.56-3.26)
25-29	122,998	(13.5)	120,867	(13.4)	2,131	(23.3)	5.15 (4.61-5.75)	3.88 (3.46-4.36)
30-34	131,699	(14.5)	128,917	(14.3)	2,782	(30.5)	6.30 (5.66-7.03)	4.12 (3.66-4.63)
35-39	129,722	(14.3)	128,177	(14.2)	1,545	(16.9)	3.52 (3.14-3.94)	2.07 (1.83-2.34)
40-49	300,508	(33.0)	299,334	(33.2)	1,174	(12.9)	1.15 (1.02-1.29)	0.64 (0.56-0.72)
Married								
No	517,878	(56.9)	514,060	(57.1)	3,818	(41.8)	Ref	Ref
Yes	392,012	(43.1)	386,698	(42.9)	5,314	(58.2)	1.85 (1.77-1.93)	2.29 (2.17-2.42)
Ethnicity								
European/other	746,496	(82.0)	738,077	(81.9)	8,419	(92.2)	Ref	Ref
Chinese	111,887	(12.3)	111,453	(12.4)	434	(4.8)	0.34 (0.31-0.38)	0.40 (0.36-0.44)
South Asian	51,507	(5.7)	51,228	(5.7)	279	(3.1)	0.48 (0.42-0.54)	0.41 (0.36-0.46)
Income quintile								
Lowest	157,567	(17.3)	156,093	(18.2)	1,474	(16.8)	Ref	Ref
2nd	166,813	(18.3)	165,234	(19.3)	1,579	(18.0)	1.01 (0.94-1.09)	0.94 (0.87-1.01)
3rd	173,327	(19.0)	171,690	(20.0)	1,637	(18.7)	1.01 (0.94-1.08)	0.92 (0.86-0.99)
4th	199,794	(22.0)	197,711	(23.1)	2,083	(23.8)	1.12 (1.04-1.19)	1.00 (0.93-1.07)
Highest	167,906	(18.5)	165,909	(19.4)	1,997	(22.8)	1.27 (1.19-1.36)	1.23 (1.14-1.32)
Rurality								
Urban	640,604	(70.4)	634,698	(70.8)	5,906	(64.8)	Ref	Ref
Mixed	219,098	(24.1)	216,414	(24.1)	2,684	(29.5)	1.33 (1.27-1.40)	1.16 (1.11-1.22)
Rural	45,919	(5.0)	45,398	(5.1)	521	(5.7)	1.23 (1.13-1.35)	1.10 (1.00-1.20)

After adjusting for all factors, women aged 30 to 34 were more than four times as likely (OR=4.12, 95% CI 3.66–4.63) to use progestin-only OCs compared to the reference group of 15- to 19-year-olds. Women aged 25 to 29 were more than three times as likely (OR=3.88, 95% CI 3.46–4.36) to use progestin-only OCs compared to women aged to 15 to 19. The only age group with lower odds of progestin-only OC use compared to the reference group were women aged 40 to 49 (OR=0.64, 95% CI 0.56–0.72). Married women had more than double the odds of use (OR=2.29, 95% CI

2.17–2.42) compared to unmarried women. Compared to European/other women, Chinese (OR=0.40, 95% CI 0.36–0.44) and South Asian (OR=0.41, 95% CI 0.36–0.46) women had significantly lower odds of progestin-only OC use. Women in the highest income quintile had slightly greater odds of use than those in lowest income quintile, although the association between income and progestin-only OC use was minimal. Differences in the odds of progestin-only OC by urban or rural geography were also minimal.

In 2006, 7,276 (0.8%) women aged 15 to 49 received at least one prescription for a progestin-only OC (Appendix A, Table A-5). Overall, the characteristics of progestin-only OC users in 2006 were very similar to those in 2013, except for increased odds of use in age groups 20-24, 25-29, 30-34, and 35-39 years (compared to 15- to 19-year-olds).

Transdermal patch

In 2013, 3,679 women (0.4%) aged 15 to 49 received at least one prescription for the transdermal patch (Table 2-11). Combined, women aged 20 to 29 accounted for nearly half (48.9%) of all transdermal patch use. Women using the transdermal patch tended to be unmarried (71.3%) and living in urban areas (68.1%). Income was relatively evenly distributed across all quintiles. Ethnic minorities (Chinese and South Asian) accounted for a small proportion of users (12.8% and 4.5%, respectively). However, the proportion of Chinese women using the transdermal patch (12.8%) is notable in comparison to other hormonal contraceptive methods, since Chinese women accounted for 12.3% of the overall study population, but represented only 2.5% to 7.7% of other method-specific users.

Table 2-11. Characteristics of women aged 15-49 residing in BC in 2013, by transdermal patch use.

	Overall study sample		Study sample by transdermal patch use				Logistic regression odds ratios (95% CIs)	
	909,890	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	109,033	(12.0)	108,506	(12.0)	527	(14.3)	Ref	Ref
20-24	115,930	(12.7)	114,988	(12.7)	942	(25.6)	1.69 (1.52-1.88)	1.70 (1.52-1.90)
25-29	122,998	(13.5)	122,141	(13.5)	857	(23.3)	1.44 (1.30-1.61)	1.45 (1.29-1.62)
30-34	131,699	(14.5)	131,063	(14.5)	636	(17.3)	1.00 (0.89-1.12)	0.98 (0.86-1.12)
35-39	129,722	(14.3)	129,357	(14.3)	365	(9.9)	0.58 (0.51-0.66)	0.58 (0.50-0.68)
40-49	300,508	(33.0)	300,156	(33.1)	352	(9.6)	0.24 (0.21-0.28)	0.24 (0.21-0.28)
Married								
No	517,878	(56.9)	515,254	(56.9)	2,624	(71.3)	Ref	Ref
Yes	392,012	(43.1)	390,957	(43.1)	1,055	(28.7)	0.53 (0.49-0.57)	1.00 (0.91-1.10)
Ethnicity								
European/other	746,496	(82.0)	743,454	(82.0)	3,042	(82.7)	Ref	Ref
Chinese	111,887	(12.3)	111,415	(12.3)	472	(12.8)	1.04 (0.94-1.14)	1.09 (0.99-1.21)
South Asian	51,507	(5.7)	51,342	(5.7)	165	(4.5)	0.79 (0.67-0.92)	0.82 (0.70-0.96)
Income quintile								
Lowest	157,567	(17.3)	156,775	(18.2)	792	(22.5)	Ref	Ref
2nd	166,813	(18.3)	166,152	(19.3)	661	(18.8)	0.79 (0.71-0.87)	0.85 (0.76-0.94)
3rd	173,327	(19.0)	172,628	(20.0)	699	(19.9)	0.80 (0.72-0.89)	0.88 (0.79-0.97)
4th	199,794	(22.0)	199,027	(23.1)	767	(21.8)	0.76 (0.69-0.84)	0.84 (0.76-0.93)
Highest	167,906	(18.5)	167,309	(19.4)	597	(17.0)	0.71 (0.64-0.79)	0.78 (0.70-0.87)
Rurality								
Urban	640,604	(70.4)	638,101	(70.7)	2,503	(68.1)	Ref	Ref
Mixed	219,098	(24.1)	218,162	(24.2)	936	(25.5)	1.09 (1.01-1.18)	1.07 (0.99-1.16)
Rural	45,919	(5.0)	45,685	(5.1)	234	(6.4)	1.31 (1.14-1.49)	1.32 (1.15-1.52)

Compared to the reference category of 15- to 19-year-olds, women aged 20 to 24 had the highest odds of transdermal patch use (OR=1.70, 95% CI 1.52–1.90), and odds decreased with each age category. There were no significant differences in transdermal patch use by marital status. The transdermal patch was the only hormonal contraceptive that was not associated with significantly decreased odds of use in Chinese women (OR=1.09, 95% CI 0.99–1.21). Women in the lowest income quintile had slightly increased odds of use, as did women living in rural areas.

In 2006, 6,740 (0.7%) women aged 15 to 49 received at least one prescription for the transdermal patch (Appendix A, Table A-6), compared to 0.4% of women in 2013. Overall, the characteristics of

transdermal patch users were very similar in 2006 compared to 2013. The only notable difference was that Chinese women did not have increased odds of transdermal patch use compared to European/other women in 2006.

2.4 Discussion

My results suggest that prevalent use of hormonal contraceptives remained stable throughout the study period, with 21.0% of women in 2006 and 21.6% of women in 2013 filling at least one prescription. However, I observed a decline in the incident use of hormonal contraceptives from 2006 to 2013. The only exception to this trend was the hormonal IUD, with annual incidence rising from 288 per 100,000 women in 2006 to 567 per 100,000 women in 2013. Similar increases in IUD use have been seen in recent studies from the United States (Finer, Jerman, & Kavanaugh, 2012; Kavanaugh, Jerman, & Finer, 2015), however, to my knowledge, this is the first Canadian study to report this trend. As expected, and in line with findings from previous Canadian studies (Black et al., 2009; Rotermann et al., 2015), OCs remained the predominant method of hormonal contraception for reproductive-aged women, while non-oral hormonal contraceptives were considerably less popular.

In the following sections, I discuss key findings related to (1) OCs, (2) hormonal IUDs, (3) the transdermal patch and intravaginal ring, (4) injectable DMPA, (5) income as a potential determinant of hormonal contraceptive use, and (6) ethnicity as a potential determinant of hormonal contraceptive use.

2.4.1 Oral contraceptives

Combined OC users were more likely to be unmarried, higher income, and living in mixed urban-rural areas. Women aged 20 to 29 accounted for nearly half of all combined OC users. Overall, these results are consistent with the sociodemographic characteristics of OC users identified in other Canadian studies (Black et al., 2009; Rotermann et al., 2015). This study was the first in Canada to characterize contraceptive use by ethnicity. I found that ethnic minorities (Chinese and South Asian) represented a very small proportion of combined OC users. In comparison, progestin-only OC users were represented by a larger proportion of married women and women aged 25 to 34, likely due to the popularity of progestin-only OCs among postpartum women and those who are breastfeeding (Hall, Trussell, & Schwarz, 2012).

OCs, specifically combined OCs, have remained the most popular method of hormonal contraception for Canadian women based on both prevalence and incidence measures. However, this is the first Canadian study to report a significant decline in the rate of incident OC use among new users. This downward trend was predominantly driven by declining rates of combined OC use rather than progestin-only OC use, as the latter only accounted for a small (10%) proportion of incident OC use. The proportion of the population using combined OCs remained stable (18.1% of the population in 2006, compared to 17.9% in 2013). However, combined OCs experienced the largest drop in prevalent use as a percentage of all hormonal contraceptive use, from 86.5% in 2006 to 82.8% in 2013—a decrease of 3.7%. Collectively, these results suggest that OCs are declining in popularity among new hormonal contraceptive users in Canada, while prevalent use has remained consistent over time.

At present, there are over 40 brands of OCs available in Canada (Health Canada, 2015). My results showed that combined OC formulations containing the progestin levonorgestrel were the preferred choice for new users, which is consistent with Canada-wide patterns of OC use (Rotermann et al., 2015). In a systematic review (Stegeman et al., 2013), the relative risk of VTE for low-dose estrogen OCs containing gestodene, desogestrel, cyproterone, or drospirenone was 50 to 80% higher than for low-dose estrogen OCs containing levonorgestrel. It should be noted that all estrogen-progestin contraceptives, including combined OCs, increase the risk of VTE, which is not the case for progestin-only methods, such as the hormonal IUD, injectable DMPA, and progestin-only OCs (Stegeman et al., 2013). However, for those women who opt for OCs, levonorgestrel-containing OCs may represent a safer option than other alternatives (Stegeman et al., 2013).

While levonorgestrel-containing formulations were overwhelmingly popular among new users, drospirenone-containing formulations experienced a period of rapid growth beginning in 2006 and peaking in late 2008 to early 2009. Interestingly, this rise in popularity was followed by a sharp decline in new users beginning in 2009 and continuing throughout the latter half of the study period. The early growth of drospirenone likely reflects the popularity of the brand name drug Yasmin, which was approved by Health Canada in December 2004. However, Yasmin and its lower-estrogen variant, Yaz (approved in January 2009), were subsequently linked to several VTE-related deaths in the late 2000s that were well-documented in the media (CBC News, 2011, 2013). In 2010, a class-action lawsuit was filed against the manufacturer, Bayer Inc., with respect to drosperinone-containing contraceptives (CBC News, 2011). Subsequently, Health Canada issued an Advisory in 2011 that stated, "Overall, the body of current evidence suggests that the risk of blood clots is 1.5 to

3 times higher with oral contraceptives that contain drospirenone relative to those that contain levonorgestrel, a different hormone" (Health Canada, 2011). It is likely that these events contributed to the observed decline in new drospirenone users after 2009. It should be noted, however, that despite the decline in incident use observed in this study, drospirenone-containing formulations continue to be among the most commonly used OCs in Canada.

2.4.2 Hormonal IUDs

I observed an increased uptake of hormonal IUDs among reproduced-aged women, as evidenced by a steady increase in rates of hormonal IUD use. The percentage of hormonal contraceptive users who received a hormonal IUD increased from 1.7% in 2006 to 6.4% in 2013, representing the largest increase of any contraceptive method. Similarly, the hormonal IUD was the only method to experience an upward trend in incident use, from 288 per 100,000 women in 2006 to 567 per 100,000 women in 2013. The increase of hormonal IUD users appears to be largely due to greater uptake among younger women. Collectively, the proportion of users who opted for the hormonal IUD from the younger age groups (ages 15–19, 20–24, and 25–29) increased by 9.4% from 2006 to 2013, with the largest increase observed among 20- to 24-years-olds (from 10.6% to 15.3%). It should be noted that due to the relatively small sample size of hormonal IUD users in 2006 (n = 3,285), it is possible that marital status and/or income may have confounded the association between hormonal IUD use and age, resulting in adjusted ORs that were significantly different from the crude ORs.

These findings suggest a significant uptake of hormonal IUDs between 2006 and 2013, although I cannot be certain that BC-specific trends are generalizable to the rest of Canada. These findings do, however, help to explain the stable prevalence of overall hormonal contraceptive use observed in this study. Since hormonal IUDs can be used for an extended period of time, greater uptake of this method would result in more ongoing (i.e., prevalent) contraceptive users over time, and fewer women refilling prescriptions on a routine monthly basis.

It is important to acknowledge that I have provided a conservative estimate of total IUD use in BC because of two limitations in the data. Firstly, the most recent Canadian study that examined IUD prevalence used measures of total IUD use (i.e., hormonal IUD combined with copper IUD use).[15] Unfortunately, I was unable to account for copper IUD use in this study. Since it is a non-hormonal device, the copper IUD does not have an assigned drug identification number (DIN), and was not captured in the prescription dispensations data. Secondly, I restricted my analyses to include only those women who received a hormonal IUD prescription in 2013, although I recognize that this contraceptive method is effective at preventing pregnancy for up to 5 years (Hatcher, 2008). Thus, a woman who began using the hormonal IUD (Mirena) as early as 2009 could have been using the same device in 2013, but would not have been captured as a current IUD user in my analyses unless she received a new hormonal IUD prescription in 2013.

Prior to this study, the most recent estimates of total IUD use were based on survey data collected in 2006 (Black et al., 2009), which estimated total IUD use at 5.8% of sexually active women aged 15

[15] By province, Black et al. (2009) combined estimates of hormonal IUD and copper IUD use into a single statistic. Estimates of hormonal IUD and copper IUD use were only separated at the national level. Thus, my estimates of hormonal IUD use in BC may not directly comparable due to these differences in study methodology.

to 50 in BC. As expected, my 2006 estimates of IUD use in BC were more conservative (1.7% of women aged 15 to 49), as the previous study included copper IUD users. Furthermore, my findings may not be directly comparable to those from Black et al.'s (2009) study due to differences in research methodology. While my retrospective study sampled nearly the entire population of reproductive-aged women in BC using administrative data, Black et al. (2009) performed a cross-sectional internet survey, sampling sexually active females across Canada.

Implications of increased uptake of hormonal IUDs

At present, the hormonal IUD is the only hormonal LARC available in Canada.[16] The hormonal IUD is inserted into the uterus by a trained practitioner and releases a small amount of progestin, which prevents sperm from entering the uterus and also alters the lining of the uterus to prevent implantation (Bayer Inc., 2014). Like other LARCs, including the copper IUD, the hormonal IUD can provide effective contraception for an extended period without requiring further action by the user. Consequently, this method may appeal to women who value the convenience of LARCs over shorter-acting hormonal methods, such as OCs, which require daily adherence to ensure consistent and correct use (Hatcher, 2008). Furthermore, while hormonal IUDs have a higher upfront cost for users compared to other methods, their long period of effective use makes them the most cost-

[16] Throughout the majority of the study period (2006–2013), Mirena was the only hormonal IUD available in Canada, and was also the only hormonal IUD dispensed to women in the study cohort. A second hormonal IUD (Jaydess) was approved by Health Canada in October 2013 (Health Canada, 2015), but no dispensation records for this product appeared in my dataset. Both Mirena and Jaydess contain the progestin levonorgestrel. Mirena is effective for up to 5 years, while Jaydess can be used for up to 3 years.

effective method of reversible hormonal contraception over time.[17] Cost may be especially important in the context of Canada where, barring only a few exceptions, the cost of hormonal contraception is almost exclusively borne by the user or their private insurer, rather than by the public health system (Black et al., 2009; Morgan et al., 2014).

Historically, IUD use in North America has lagged behind other developed regions of the world (Stubbs & Schamp, 2008; United Nations, 2015). According to a recent United Nations report on worldwide contraceptive use, IUDs account for only 4.7% (US) and 1% (Canada) of married or partnered women of reproductive age who use contraceptives in North America, which is comparable to prevalence rates in some of the least developed countries in the world (United Nations, 2015). Further, estimates of IUD use in North America are significantly lower than the prevalence of IUD use worldwide (13.7%) and in Western Europe (11.7%), and are extremely low in comparison to countries such as China (39.9%) and Egypt (30.6%), where IUDs are widely available and used by women (United Nations, 2015).

The historically low prevalence of IUD use in Canada may be due to lingering public mistrust following the Dalkon Shield recall in 1974 (Kerger et al., 2016). When the Dalkon Shield was discontinued due to safety concerns, estimates of IUD use in Canada plummeted (Byrne, 1990; Kerger et al., 2016; Shaw, 1997). The flaws in the Dalkon Shield were specific to its unique design, and were not applicable to IUDs in general (Sivin, 1993). Nevertheless, IUD use in Canada declined throughout the following decades (Balakrishnan et al., 1985; Black et al., 2009; Martin & Wu, 2000).

[17]As of January 1, 2017, Mirena costs $385.00 at sexual health clinics in BC (Options for Sexual Health, 2017). Since Mirena can be used for up to 5 years, the approximate monthly cost is less than $6.50. In comparison, OCs cost $13.00 for a one-month supply.

By the 1990s to the early 2000s, estimates of IUD use among reproductive-aged women in Canada reached a low of just 1% (Boroditsky et al., 1995; Fisher et al., 2004a, 2004b).[18] Thus, my study may be the first to signal a reversal of the apparent downward trend in IUD use that has been occurring in Canada since the mid-1970s.

Despite strong clinical evidence of the safety of modern IUDs[19] (Stoddard et al., 2011), the notion that IUDs carry a higher risk of adverse effects still persists among physicians in some countries where IUD use is low, including Canada and the US (Hauck & Costescu, 2015). For example, in a Canadian survey of family physicians, many believed the side effects of IUDs were more severe than is currently supported by clinical guidelines (Stubbs & Schamp, 2008). Furthermore, IUDs have not typically been considered an appropriate first-line contraceptive method for young, nulliparous, and unmarried women (Suhonen, Haukkamaa, Jakobsson, & Rauramo, 2004). These findings suggest that, even in countries where IUDs are available, some women may experience barriers to equitably accessing this contraceptive method (Black, Lotke, Buhling, & Zite, 2012; Black, Lotke, Lira, Peers, & Zite, 2013; Buhling, 2014; Dunn, Anderson, & Bierman, 2009; Fisher et al., 2004a; Goertzen, 2006; Hauck & Costescu, 2015; Stanwood, Garrett, & Konrad, 2002; Stubbs & Schamp, 2008). Consequently, some reproductive health experts are calling for improved education to users, care providers, and health care systems to help facilitate greater IUD uptake among a broader range of Canadian women (Hauck & Costescu, 2015; Stubbs & Schamp, 2008).

[18] This estimate of 1% accounted for total (hormonal plus copper) IUD use.

[19] Use of the term "modern IUDs" in this section is in reference to both hormonal and copper IUDs.

Currently, clinical practice guidelines from the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the American College of Obstetricians and Gynecologists (ACOG) recommend that LARCs, including the hormonal IUD, be presented as a contraceptive option to any woman of reproductive age, as these methods are more effective and have higher continuation rates than other contraceptives (American College of Obstetricians and Gynecologists, 2015; Black & Guilbert, 2015).[20] With failure rates of 0.2% for both perfect and typical use, hormonal IUDs are more effective than other hormonal methods that rely on continued user compliance (Trussell 2007, 2011; Winner et al., 2012). Comparatively, OCs are associated with a 9% failure rate within the first year of typical use (Trussell, 2007, 2011). With perfect use, the failure rate of OCs is only 0.3% (Trussell, 2007, 2011), but effectiveness is significantly reduced after accounting for the challenges associated with adhering to a daily pill regimen (Hatcher, 2011; Trussell, 2011). Hormonal IUDs also have higher continuation rates at one year compared to other hormonal contraceptive methods (Peipert et al., 2011; Trussell, 2011). Consequently, hormonal IUDs are associated with a significant decrease in the number of method failures and unintended pregnancies compared to other hormonal contraceptive methods (Hatcher, 2011; Trussell, 2007, 2011; Winner et al., 2012).

LARCs and unintended pregnancy:

Unintended pregnancy is an important public health issue that poses significant maternal and perinatal health risks (Hauck & Costescu, 2015; Korenman et al., 2002; Peipert et al., 2012).

[20] It should be noted that this is in contrast to the current product monograph in Canada for the hormonal IUD (Mirena), which states, "MIRENA is not the contraceptive method of first choice for young, nulligravid women. Controlled clinical trials were done in previously parous women aged mainly over 18 years. Use of this product before menarche is not indicated" (Bayer Inc., 2014).

Unintended pregnancies can be attributed to a number of factors, including imperfect contraceptive adherence (Black et al., 2009, 2015) and contraceptive failure (Trussell 2007; 2011), which is more common among users of short-acting hormonal contraceptives, such as OCs (Black et al., 2009). The direct cost of unintended pregnancies in Canada is estimated at over $320 million per year, with 82% of this cost ($143 million) attributable to imperfect contraceptive adherence (Black et al., 2015). However, it is estimated that the annual cost of unintended pregnancies in Canada could be decreased by as much as $35 million with an increase in LARC use, with cost savings being realized if just 10% of current OC users switched to LARCs for at least one year (Black et al., 2015).

I observed a significant increase in hormonal IUD use, particularly among women aged 20 to 24. This age group also has the highest rate of unintended pregnancy (104/1000 women aged 15 to 44 years) (Finer & Zolna, 2014).[21] Thus, given the potential cost savings and improved health outcomes associated with reducing unintended pregnancies, my finding of increased hormonal IUD uptake suggests a positive trend for women's reproductive health in BC. Many experts in this field have previously acknowledged that IUDs are underutilized in Canada (Harper et al., 2008; Harper, Brown, Foster-Rosales, & Raine, 2010; Hauck & Costescu, 2015; Stubbs & Schamp, 2008), with some stating that IUDs should be recognized as a suitable contraceptive option for the majority of women (Black et al., 2015; Stoddard et al., 2011).

[21] Based on US estimates. Age-specific rates of unintended pregnancy have not been researched in a Canadian context.

2.4.3 Transdermal patch and intravaginal ring

Two newer non-oral hormonal contraceptives, the transdermal patch and intravaginal ring, were used by a small percentage of women in this cohort. The transdermal patch, introduced in Canada in 2003 under the brand name Evra (Health Canada, 2015), was used by only 1.9% of women aged 15 to 49 in 2013. Meanwhile, 4.6% of women opted for the intravaginal ring, which has been available in Canada since 2004 under the brand name NuvaRing (Health Canada, 2015). Low rates of use for both methods have been reported in a previous Canadian study, estimating prevalence of the transdermal patch and the intravaginal ring at only 1.2% and 0.6% of sexually active women, respectively (Black et al., 2009).

One reason why the transdermal patch and intravaginal ring may have experienced low uptake in Canada is that both methods have been subject to media scrutiny and class action lawsuits in Canada and the US. As a result, some women may have safety concerns about the possibility of increased VTE risk associated with the progestins used in these methods (Health Canada, 2009, 2014). Another possible explanation is that Health Canada approval of a contraceptive, or any prescription drug, does not guarantee equitable access for all users. With the exception of Quebec, which reimburses the cost of all hormonal contraceptives, provincial drug formularies provide coverage for a limited selection of drugs (Morgan et al., 2014). Unfortunately, the transdermal patch and intravaginal ring are not generally covered by provincial drug formularies, so many Canadian women must pay the total cost of these methods out-of-pocket unless they have coverage under a private insurance plan (Black et al., 2009; Morgan et al., 2014). While the price of the transdermal patch and the intravaginal ring is comparable to combined OCs (Every Woman's Health Centre, 2017; Options

for Sexual Health, 2017), most Canadian insurance plans provide coverage only for OCs (HealthQuotes.ca, 2017). Thus, there may be little incentive for some Canadian women to choose the transdermal patch or the intravaginal ring as their preferred method of contraception.

2.4.4 Injectable DMPA

I observed a decrease in prevalent use of DMPA as a percentage of total hormonal contraceptive use between 2006 (6.0%) and 2013 (4.2%). My results also showed a decline in incident use of DMPA, from 308 per 100,000 women in 2006 to 136 per 100,000 women in 2013. The low prevalence of DMPA was expected, since this method was previously estimated to account for only 2.4% of all contraceptive use among sexually active women in Canada (Black et al., 2009). Despite its low prevalence in Canada, DMPA is a highly effective contraceptive method, with low failure rates associated with perfect use (0.2%) (Trussell, 2007, 2011). With a typical use failure rate of 6%, DMPA is more effective than OCs, the transdermal patch, and the intravaginal ring (9%) (Trussell, 2007, 2011). Similar to LARCs, DMPA has the benefit of demanding less user compliance, since the injection is administered once every 3 months. Therefore, DMPA may be an appropriate contraceptive method for women who have difficulty adhering to a daily OC regimen, or a monthly transdermal patch or intravaginal ring regimen. Furthermore, since DMPA does not contain estrogen, it serves as a suitable alternative for those who have contraindications[22] to estrogen (Black, 2007; Black et al., 2004).

[22] Some common examples of contraindications to estrogen include postpartum women who are breastfeeding, current or past history of VTE, hypertension, smokers over the age of 35, and history of heart disease (Black et al., 2004).

While the underlying reasons for the declining use of DMPA in this population are not fully understood, it is possible that concerns about bone density loss associated with DMPA use have contributed to its low prevalence among Canadian women (Black, 2007). However, although DMPA is causally associated with a decrease in bone mineral density, recent studies have shown this decrease is most rapid in the first two years of use, and is substantially or fully reversible in both adults and adolescents after discontinuation of DMPA (Clark, Sowers, Levy, & Nichols, 2006; Clark, Sowers, Nichols, & Levy, 2004; Harel et al., 2010; Kaunitz, Darney, Ross, Wolter, & Speroff, 2009; Lopez, Chen, Mullins Long, Curtis, & Helmerhorst, 2015; Scholes, LaCroix, Ichikawa, Barlow, & Ott, 2005). Furthermore, bone mineral density loss experienced by both adult and adolescent DMPA users has never been shown to be more than one standard deviation below normal density levels, even after 5 years of DMPA use (for comparison, osteoporosis is defined as 2.5 standard deviations below normal density levels) (Guilbert et al., 2009). The World Health Organization, the ACOG, and the SOGC have all stated that, based on current evidence, women aged 18 to 45 should be able to use DMPA without restrictions (Black, 2007; The American College of Obstetricians and Gynecologists, 2014; World Health Organization, 2007). Current clinical practice guidelines from the SOGC emphasize that "the advantages of using DMPA outweigh the theoretical concerns regarding fracture risk" for younger and older (perimenopausal) women (Black, 2007).

The results of my regression analyses revealed a clear income gradient associated with DMPA use, with higher odds of use among lower-income women. This finding may be partially explained by the age distribution of DMPA users, since younger women (15-24 years) had higher odds of DMPA use than older women (40-49 years), and younger age may also be associated with lower income status. However, the underlying reason for the observed gradient in DMPA use by income is unlikely to be

explained by age alone. Economic incentive is not a likely causal factor, since DMPA is similar in cost to that of combined OCs (Options for Sexual Health, 2017). It is more likely that there are other mediating factors influencing the association between income and DMPA use that are beyond the scope of this study.

In a recent study of female sex workers in Vancouver, Canada, the authors observed disproportionately higher rates of DMPA use among the most vulnerable women, including younger women, women with indigenous ancestry, those with lower educational levels, and women living with HIV (Socías et al., 2016). This finding may help to explain the income gradient observed in my study. Furthermore, it raises concerns about the provision of sexual health care to marginalized women.

Similar to my findings for OCs, IUDs, and other non-oral hormonal contraceptives, ethnicity was associated with non-use of DMPA, with Chinese and South Asian women having significant lower odds of use compared to the general population. This may be partially explained by the exceptionally low prevalence of injectable contraceptive drugs in both China and South Asia. According to a recent United Nations report on worldwide contraceptive trends, less than 1% of married or in-union women aged 15 to 49 used injectable contraceptives in these regions (United Nations, 2015).

Since the implementation of China's one-child policy in 1979, Chinese women have heavily relied on IUDs as their preferred method of reversible contraception (Wang, 2012). Meanwhile, in some South Asian countries, injectable contraceptives have been a highly contentious issue in recent decades. In India, for example, DMPA has been available on the private drug market since 1993,

although the federal Drugs Technical Advisory Board recommended against inclusion of DMPA in the publicly-funded National Family Planning Program, which was established in 1995 (Ved & Visaria, 2016). It was not until August 2015 that the Board revised their earlier stance and approved coverage for DMPA under India's public healthcare system (Drugs Technical Advisory Board, 2015). Since Chinese and South Asian immigrants account for a significant percentage of the ethnic minorities in BC, it is possible that certain cultural attitudes or beliefs about DMPA may be impacting contraceptive use within these ethnic groups.

2.4.5 Income and hormonal contraceptive use

In this study, income was associated with the use of hormonal contraception overall and for method-specific use. I found that women in the lowest income quintile were less likely to use hormonal contraceptives than those in the highest quintile. Regarding method-specific use, I found that lower-income women were less likely to use OCs, the hormonal IUD and the intravaginal ring. Similar income disparities related to contraceptive use in general have been observed in previous research. For example, Black et al.'s (2009) study found significantly lower odds of "always" using contraception among women with incomes under $100,000. Predictably, findings from a more recent Canadian study saw that women with unintended pregnancies were more often of lower income compared to those with planned pregnancies (Metcalfe, Talavlikar, du Prey, & Tough, 2016).

Collectively, these findings highlight the importance of cost in the context of contraceptive use in Canada. While this factor likely intersects with a multitude of other variables, the results do support

the notion that cost is an existing barrier, due to the lack of coverage for contraceptives within our public health care system, that may contribute to inequitable access to effective hormonal contraception for some Canadian women.

2.4.6 Ethnicity and hormonal contraceptive use

My results consistently showed that Chinese and South Asian women had lower odds of overall and method-specific hormonal contraceptive use compared to the general population, after adjusting for other factors. The only exception to this trend was the transdermal patch, which had similar odds of use among Chinese women compared to the general population. Although Canadian research examining ethnicity and hormonal contraceptive use is limited (Wiebe, 2013; Wiebe, Janssen, Henderson, & Fung, 2004; Wiebe, Sent, Fong, & Chan, 2002), my findings are consistent with population-based studies from the US and the UK that have reported lower odds of contraceptive use among ethnic minorities compared to white women (Jones et al., 2012; Saxena et al., 2006). However, since cultural factors may affect attitudes toward contraception and the use of hormones, it is important to acknowledge that some Chinese and South Asian women may be opting for non-hormonal methods of contraception, such as condoms, which were not captured in the current study.

As a nation, Canada has experienced tremendous growth in its ethnic minority population in recent years, rising from 13% in 2001 to 19% in 2011 (Statistics Canada, 2001, 2011b). This rapid period of growth has been largely driven by an influx of Chinese and South Asian immigrants (Statistics Canada, 2001, 2011b). While increased use of hormonal IUDs may account for some of the trends

observed in this study, significantly lower odds of hormonal contraceptive use among BC's dominant ethnic minority groups may also be influencing overall contraceptive trends within the province. Chinese and South Asians constitute two of the largest ethnic minority groups in Canada, and represent approximately 18% of the BC population (Statistics Canada, 2011b). Thus, it is possible that decreased hormonal contraceptive use among Chinese and South Asian women contributed to the decline in overall hormonal contraceptive use observed in this study.

To my knowledge, this is the first population-based contraceptive study in Canada to include a measure of ethnicity, and I consider it an important step in the investigation of inequities in reproductive health. Previously, some researchers have sought to identify and describe ethnic disparities in contraceptive use among Canadian women using qualitative methods. The findings from these studies have offered insight into some of the potential factors that may be impacting patterns of hormonal contraceptive use among women from ethnic minority groups. For example, in a Vancouver-based study of ethnic differences in attitudes towards contraception, researchers interviewed Chinese women and discovered widespread negative attitudes associated with OC use (Wiebe et al., 2002). Many of these women cited a fear of being perceived as "bad" (promiscuous) and concerns about OC use leading to permanent infertility, highlighting the influence of culture-based attitudes and misconceptions on reproductive decision-making in this ethnic minority group.

Another Vancouver-based study explored knowledge and attitudes of Asian immigrant women towards emergency contraception (which was not included in my study, but may be considered a contraceptive drug) (Shoveller, Chabot, Soon, & Levine, 2007). Participants self-identified as either Asian or South Asian, but were purposively sampled to consist primarily of Chinese (Asian) and

Indian (South Asian) women, effectively mirroring the ethnic minority groups used in my study. Similar to findings from Wiebe et al.'s (2002) study, the authors observed general misperceptions and a lack of knowledge about reproductive physiology and contraceptive methods in their sample of Chinese and Indian women, and also noted that participants routinely expressed fear of negative judgment from others, particularly health care providers from within their own ethnic community.

Collectively, the observations from these qualitative studies suggest that sociodemographic characteristics, such as ethnicity, can affect access to and preference for certain contraceptive methods. Further, these findings provide insight into the sociocultural context of contraceptive decision-making, which may help to explain my findings of lower odds of hormonal contraceptive use among ethnic minorities. These previous qualitative findings imply that some Chinese and South Asian women in BC face sociocultural barriers (e.g., lack of reproductive knowledge, concerns about safety, or fear of judgement) to hormonal contraceptive use, despite the availability of various safe and effective contraceptive methods. Consequently, women from these ethnic minority groups may be at greater risk for unintended pregnancy and its associated adverse health outcomes.

Further investigation of possible sociodemographic or sociocultural barriers to contraceptive use in Canada may help to support our understanding of existing inequities within reproductive health care in Canada. However, it is important to note that there are some inherent challenges in attempting to establish empirical links between ethnicity and health. For example, earlier studies of contraceptive use in Canada have reported lower odds of OC use among immigrant women (Balakrishnan et al., 1985; Rotermann et al., 2015). While immigrants and ethnic minorities may share some similarities with respect to contraceptive use, it is important to recognize that immigrant status is not

synonymous with ethnicity: for example, approximately one-third of ethnic minorities living in Canada in 2011 were also born in Canada (Statistics Canada, 2011a). Furthermore, by homogenizing various ethnicities into a single immigrant group, we lose the ability to detect potentially important differences between ethnic minority groups. It would be valuable to continue the characterization of hormonal contraceptive users in Canada through future studies, which would contribute to a greater understanding of the unique reproductive needs of women from diverse sociocultural backgrounds.

2.5 Conclusion

The purpose of this study was to provide a comprehensive, updated overview of hormonal contraceptive use within a Canadian setting. Specifically, the objective was to investigate levels, trends, and determinants of hormonal contraceptive use among reproductive-aged women in BC using population based administrative data spanning the years 2006 to 2013. During this period, OCs remained the most popular form of hormonal contraception among reproductive-aged women. However, my findings have also provided novel evidence of (1) stable prevalence, but declining incidence of overall hormonal contraceptive use, (2) declining popularity of OCs, (3) a growing preference for hormonal IUDs, and (4) decreased odds of hormonal contraceptive use among ethnic minorities (Chinese and South Asian women). Collectively, these findings suggest that contraceptive trends in Canada have shifted over the past decade. As Canada's population becomes increasingly diverse, more current research of reproductive health, with a focus on contraceptive patterns of use, may be necessary in order to better understand and appropriately address the unique reproductive needs of all Canadian women.

3 LEVELS, TRENDS, AND DETERMINANTS OF POTENTIALLY INAPPROPRIATE PRESCRIBING OF DIANE-35 FOR ORAL CONTRACEPTION AMONG YOUNG WOMEN IN BRITISH COLUMBIA

3.1 Introduction

In 1998, Health Canada approved CPA-EE (more commonly known by the brand name Diane-35) for the temporary treatment of severe acne in women who are unresponsive to oral antibiotics or other first-line acne treatments. Although CPA-EE was granted market authorization only for this specific indication, it has been widely prescribed to women without acne as an OC because of its ability to suppress ovulation (Mintzes et al., 2005). Off-label use of CPA-EE in this manner may be considered an inappropriate prescribing practice, as Diane-35 and other generic CPA-EE formulations are causally associated with increased risk of VTE compared to other estrogen-progestin combinations that have been approved for contraceptive use in Canada (de Bastos et al., 2014; Stegeman et al., 2013).

In response to this safety concern, Health Canada has repeatedly stated that CPA-EE should not be prescribed solely for contraceptive use (Health Canada, 2002, 2003, 2005, 2013). However, since Health Canada does not regulate the practice of medicine, physicians are generally at liberty to prescribe off-label if they believe it is in their patients' best interests (Canada Standing Senate Committee on Social Affairs, 2014).

While off-label prescribing of drugs may sometimes be clinically appropriate (American Academy of Pediatrics, 2002), the practice is often controversial when the safety and efficacy of a treatment intervention is unknown or poorly documented, as is the case with a substantial proportion of off-label drug use (Abbott & Ayres, 2014; Eguale et al., 2012; Hebert & Stanbrook, 2007; Mackey & Liang, 2011). According to a recent Canadian study, off-label drugs were associated with a 43% increase in adverse drug reactions compared to on-label drugs, and over three-quarters of drugs prescribed off-label lacked strong evidence of efficacy (Eguale et al., 2012). As there are no formal mechanisms to monitor off-label prescribing and drug use in Canada, these findings highlight the need for further investigation of potentially inappropriate prescribing practices, particularly when there is a lack adequate evidence to support a drug's safety and efficacy for off-label use. Research of this nature may be especially valuable to help monitor the effect of off-label drug use on population subgroups, including women, that are known to be more susceptible to risk of exposure to potentially inappropriate prescribing and related adverse drug reactions (Canada Standing Senate Committee on Social Affairs, 2014; Eguale et al., 2012; Guthrie et al., 2011). To my knowledge, no other study has investigated patterns of potentially inappropriate use of CPA-EE as an OC since 2005 (Mintzes et al., 2005), although Diane-35 and its generics are still available in Canada.

The purpose of this study is to provide a comprehensive, current overview of potentially inappropriate contraceptive use of CPA-EE within a Canadian context. Specifically, this study investigates levels, trends, and determinants of off-label CPA-EE use among reproductive-aged women in BC using population-based administrative data spanning the years 2006 to 2013.

3.2 Methods

This is a retrospective study of outpatient prescription drug purchases by residents of BC, Canada. All subjects were covered under BC's universal, public health insurance program for medical and hospital care; all subjects were also eligible for coverage under BC's universal, public drug benefit plan, under which deductibles are set in relation to household income.

3.2.1 Data sources and study cohort

Description of data sources

My analyses are based on de-identified, linked health datasets provided by Population Data BC with approval of relevant data stewards and the University of British Columbia's Behavioural Research Ethics Board (BC Ministry of Health, 2013). All inferences, opinions, and conclusions drawn in this chapter are my own, and do not reflect the opinions or policies of Population Data BC. The datasets included sociodemographic information and administrative records of all prescription drug dispensations, fee-for-service physician visits, and hospitalizations for all BC residents from 2006 to 2013, inclusive.

The datasets used for this study excluded military veterans, registered First Nations, and inmates of federal penitentiaries (who collectively make up approximately 4% of the population). To ensure complete data capture, I restricted the cohort to only those individuals who resided in BC for at least

275 days in a given observation year, or in each of three consecutive observation years when measuring incident use of CPA-EE or OCs. I determined an individual's length of residency in a given year using a "days registered" variable in the sociodemographic dataset for each calendar year.

Records of prescription drug dispensations were retrieved from PharmaNet, an information system that records every prescription filled at a pharmacy outside of acute care hospitals in BC, regardless of patient age or insurance status. Physician characteristics data were obtained from the College of Physicians and Surgeons of British Columbia (CPSBC) registry. Population Data BC uses personal identifiers to facilitate linkage of records belonging to the same individual across datasets (i.e., PharmaNet, sociodemographic records, administrative health files, and CPSBC) and over time.

Description of study cohort

The study cohort consisted of all female residents in BC aged 15 to 34 years[23] who received an initial prescription for CPA-EE or an OC between January 1, 2006 and December 31, 2013. I included only those women who had resided in BC for at least 275 days in the year of incident prescription, and in each of the two consecutive years prior (n = 185,296).[24] An overview of the analytic sample selection process is provided in Figure 3-1.

[23] In my dataset, OC initiation rates (i.e., prescribing to first-time OC users) were low among women aged 35 and older. Since the current study is focused on CPA-EE and OC initiators, I limited the study cohort to women aged 15 to 34 years.

[24] Incident use was ascertained using prescription dispensations data spanning the years 2004 to 2013, inclusive. To be considered an incident user in the 2006 cohort, a minimum "prescription naïve" period of two years (2004 to 2006) was required. In comparison, to be considered an incident user in the 2013 cohort, a minimum "prescription naïve" period of ten years (2004 to 2013) was required. Therefore, women who were identified as incident users later in the study period may have experienced a longer period of "prescription-naïvety" than those who were identified as incident users at the beginning of the study period.

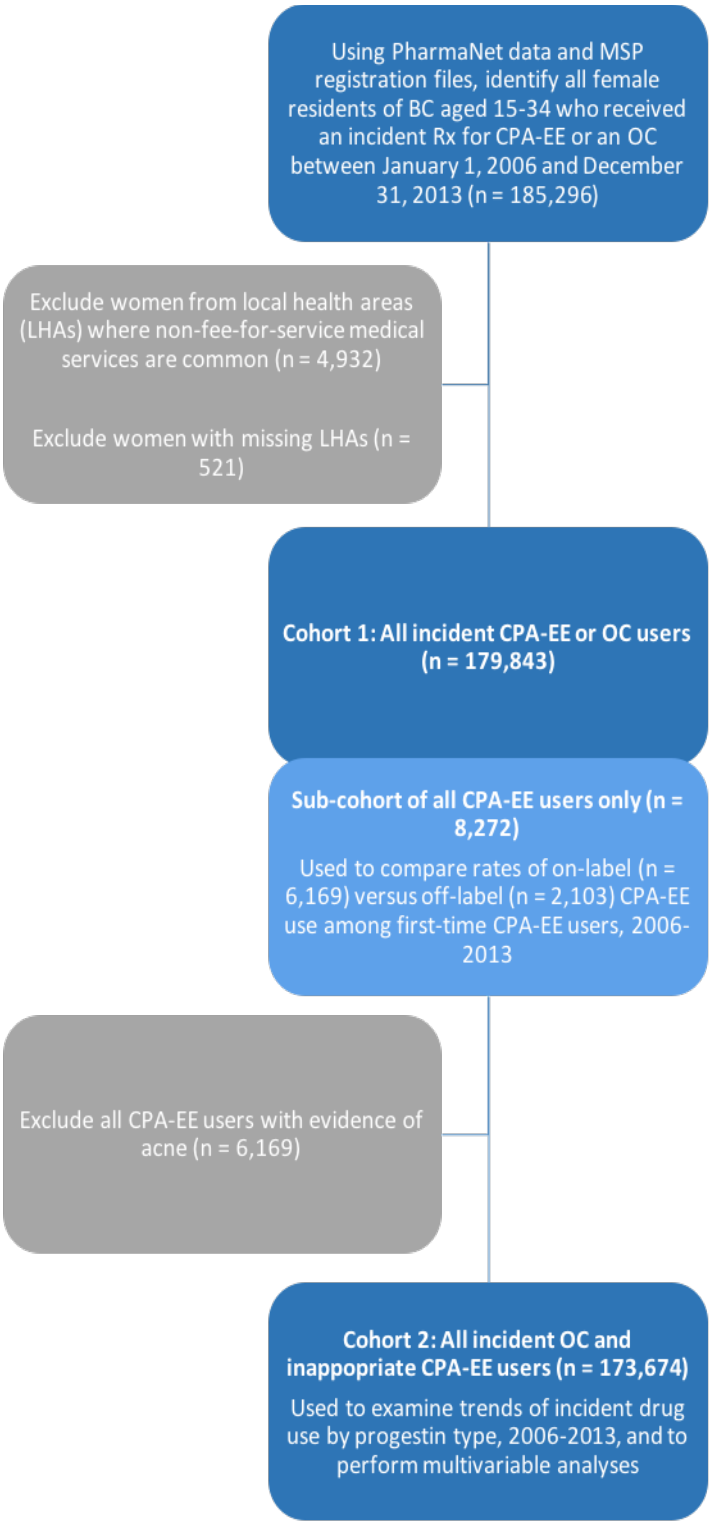

Figure 3-1. Flowchart detailing selection process of analytical sample to examine the levels, trends, and determinants of OC and off-label CPA-EE use, women aged 15–34 years residing in BC, 2006–2013.

In order to differentiate between on-label and off-label (i.e., potentially inappropriate) CPA-EE use, I created a flag for women who had evidence of medically diagnosed or treated acne. Women were classified as having either "possible acne" or "no acne" based on their medical history from 1 year prior to 3 months after the initial CPA-EE prescription date. All "possible acne" cases met at least one of following criteria: diagnosis with an ICD-9 (International Classification of Diseases, 9th Revision) (Slee, 1978) code starting with 706 (diseases of sebaceous glands); at least one consultation with a dermatologist; a prescription for topical anti-infectives (ATC D10A), retinoids (ATC D10B), or aldosterone agonists (ATC C03DA); or use of tetracycline (ATC J01A), sulfonamide combination (ATC J01EE), or macrolide (ATC J01F) antibiotics for 30 days or longer. I flagged all "possible acne" cases (n = 6,169). These women were included in my analyses of on-label versus off-label use, but were excluded from all other analyses.

Finally, to reduce the extent to which use of medical services is undercounted, I excluded residents of LHAs wherein greater than 30% of all medical services are provided non-fee-for-service, which fall outside the scope of the dataset (n = 4,932). For the same reason, I also excluded any remaining individuals with missing demographic information about area of residence (n = 521).

3.2.2 Exposure measures

Measures of CPA-EE and OC use

All CPA-EE and OC prescriptions were identified in the PharmaNet data by their drug identification number (DIN). I further categorized these drugs by progestin category based on the World Health Organization's ATC Classification System code corresponding to each DIN as follows: cyproterone (ATC G03HB01), drospirenone (ATC G03AA12), levonorgestrel (ATCs G03AA07, G03AB03), desogestrel (ATCs G03AA09, G03AB05), norgestimate (ATCs G03AA11, G03AB11), or other progestins (ATCs G03AA01, G03AA05, G03AA13, G03AB04, G03AC01). Drospirenone, levonorgestrel, norgestimate, and desogestrel were chosen as standalone comparators to cyproterone because these progestins accounted for the top-selling OCs in Canada: Yasmin and Yaz (drospirenone), Alesse (levonorgestrel), Tri-Cyclen and Tri-Cyclen Lo (norgestimate), and Marvelon (desogestrel).

Sociodemographic characteristics

Age group. Age in years was given as an existing variable in the demographics data provided by Population Data BC. To account for any period trends, age was calculated as of December 31 for a given year. For the logistic regression analyses, I constructed a categorical age variable containing the following age groupings: 15–19 years, 20–24 years, 25–29 years, and 30–34 years.

Household income (quintile). I measured household income using a validated combination of household-specific income data for those registered for BC's income-based drug benefit program and neighbourhood-based proxy incomes for the remaining population (Hanley & Morgan, 2008). This information was used to construct a variable for income quintile, which was used as a proxy for socioeconomic status in the logistic regression analyses.

Marital status. Marital status was given as a binary variable (married/in-union or single) in the demographics dataset.

Ethnicity. Ethnicity was determined using a validated algorithm to identify surnames of the dominant ethnic minority groups in BC: Chinese (40% of visible minorities) and South Asians (from India, Pakistan, Bangladesh, and Sri Lanka; 26% of visible minorities) (British Columbia Government, 2008; Shah et al., 2010). Women who were not flagged as an ethnic minority were categorized as "European/other" in the results, and were also referred to as the "general population" in the discussion section.

Rurality. Neighbourhood urbanization ("rurality") was categorized based on the population density of the LHA in which women lived. For ease of interpretation, LHAs were further classified into three rurality categories: urban, rural, and mixed rural-urban.

Physician age group. Physician age group was given as a categorical variable in the CPSBC dataset. Age groupings from the original dataset were collapsed into fewer categories (25–44 years, 45–54 years, 55–64 years, >65 years) for the purpose of this study.

Physician sex. Physician sex was given as a binary variable (male or female) in the CPSBC dataset.

3.2.3 Outcome measures

I constructed annual measures of incident CPA-EE use (excluding on-label use) and OC use on rolling cohorts of women satisfying similar inclusion criteria. Specifically, incident use was defined as the first CPA-EE or OC purchase following at least two full years of residency in BC without records of any prior CPA-EE or OC purchases. Rates of incident use were calculated as the number of women filling a relevant prescription divided by the population of women satisfying the same age and residency requirements. Preliminary analyses suggested that age-adjusted rates (to account for potential differences in the age structure of the population over time) did not significantly change the unadjusted results.

3.2.4 Statistical analyses

Descriptive statistics were used to present CPA-EE and OC use by age group, marital status, ethnicity, income, rurality, physician sex, and physician age group. I used multiple logistic regression to generate crude odds ratios (ORs) and adjusted ORs with 95% confidence intervals for selected sociodemographic characteristics believed to be associated with potentially inappropriate CPA-EE use. Adjusted ORs were calculated using a mixed-effects logistic regression model. I adjusted for clustering at the level of the physician because patients with similar characteristics may cluster within certain clinical practices (Thompson, Fernald, & Mold, 2012).

Selection of covariates for regression analyses was based on data availability, the Andersen Model of Health Care Utilization (Andersen, 1995), and existing literature on hormonal contraceptive use in Canada (Black et al., 2009; Boroditsky & Fisher, 2000; Boroditsky et al., 1995; Fisher et al., 1999; Fisher et al., 2004a, 2004b; Rotermann et al., 2015).

For all analyses, a value of $p<0.05$ was considered statistically significant. All analyses were performed using Stata version 13.1 (StataCorp, 2013).

3.2.5 Ethics approval

This study was approved by the University of British Columbia's Behavioural Research Ethics Board (H11-02273; October 2011).

3.3 Results

In total, 179,843 women met the inclusion criteria and received an initial prescription for either an OC or CPA-EE between January 1, 2006, and December 31, 2013. Of these women, 8,272 (4.6%) were first-time CPA-EE users, including 2,103 (1.2%) who initiated treatment on CPA-EE without evidence of acne (Figure 3-1).

Table 3-1. Comparison of on-label versus off-label* initiators of CPA-EE in BC, ages 15–34, 2006–2013.

	Group, no. (%)						Logistic regression odds ratios (95% CIs) for potentially inappropriate CPA-EE use	
	OC user (*n* = 171,571)		CPA-EE with acne (*n* = 6,169)		CPA-EE without acne (*n* = 2,103)		Unadjusted	Adjusted
Age, yr								
15-19	76,290	(44.5)	3,727	(60.4)	908	(43.2)	Ref	Ref
20-24	44,625	(26.0)	1,333	(21.6)	589	(28.0)	1.11 (1.00, 1.23)	1.07 (0.96-1.20)
25-29	27,517	(16.0)	685	(11.1)	355	(16.9)	1.08 (0.96-1.23)	1.16 (1.00-1.33)
30-34	23,139	(13.5)	424	(6.9)	251	(11.9)	0.91 (0.79-1.05)	1.13 (0.95-1.34)
Married								
No	147,433	(85.9)	5,820	(94.3)	1,915	(91.1)	Ref	Ref
Yes	24,138	(14.1)	349	(5.7)	188	(8.9)	0.60 (0.52-0.70)	0.48 (0.39-0.57)
Ethnicity								
European/other	152,684	(89.0)	5,124	(83.1)	1,826	(86.8)	Ref	Ref
Chinese	11,352	(6.6)	569	(9.2)	138	(6.6)	1.02 (0.85-1.21)	0.95 (0.78-1.17)
South Asian	7,535	(4.4)	476	(7.7)	139	(6.6)	1.54 (1.30-1.84)	1.44 (1.18-1.75)
Income quintile								
Lowest	32,063	(19.0)	1,014	(16.6)	413	(19.9)	Ref	Ref
2nd	26,506	(15.7)	842	(13.8)	329	(15.9)	0.96 (0.83-1.11)	1.02 (0.88-1.19)
3rd	30,275	(17.9)	992	(16.2)	393	(19.0)	1.01 (0.88-1.16)	1.11 (0.96-1.28)
4th	37,977	(22.4)	1,325	(21.7)	440	(21.2)	0.90 (0.79-1.03)	1.00 (0.87-1.15)
Highest	42,407	(25.1)	1,938	(31.7)	496	(23.9)	0.91 (0.80-1.04)	1.00 (0.87-1.16)
Rurality								
Metro	109,950	(64.1)	4,307	(69.8)	1,393	(66.2)	Ref	Ref
Mixed	52,060	(30.3)	1,613	(26.2)	613	(29.1)	0.93 (0.84-1.02)	0.97 (0.85-1.10)
Rural	9,561	(5.6)	249	(4.0)	97	(4.6)	0.80 (0.65-0.98)	0.78 (0.61-1.00)
Practitioner sex								
Female	75,713	(45.2)	2,706	(44.4)	850	(41.1)	Ref	Ref
Male	91,645	(54.8)	3,395	(55.7)	1,218	(58.9)	1.18 (1.08-1.29)	1.12 (0.98-1.28)
Practitioner age, yr								
25-44	57,611	(34.4)	1,865	(30.6)	652	(31.5)	Ref	Ref
45-54	59,300	(35.4)	2,205	(36.1)	693	(33.5)	1.03 (0.93-1.15)	1.08 (0.94-1.23)
55-64	40,583	(24.2)	1,524	(25.0)	541	(26.1)	1.18 (1.05-1.32)	1.15 (0.98-1.35)
65+	9,923	(5.9)	509	(8.3)	183	(8.8)	1.63 (1.38-1.92)	1.66 (1.32-2.09)

*CPA-EE use without acne is considered "off-label" or "potentially inappropriate" use.

The characteristics of the study sample are presented in Table 3-1. New initiators of CPA-EE and OCs tended to be younger, unmarried, and live in an urban area. Overall, ethnic minorities

constituted a small percentage of CPA-EE and OC users. Specifically, Chinese women accounted for 6.6% of off-label CPA-EE users, 9.2% of on-label CPA-EE users, and 6.6% of OC users, while South Asian women represented 6.6% of off-label CPA users, 7.7% of on-label CPA-EE users, and 4.4% of OC users. Overall, the characteristics of on-label and off-label CPA-EE users were similar, although on-label users tended to be slightly younger (60.4% aged 15 to 19, compared to 43.2% of off-label users) and have higher income (31.7% in the highest income quintile, compared to 23.9% of off-label users).

I observed a downward trend in incident CPA-EE use for both on-label and off-label indications between 2006 and 2013 (Figure 3-2). Off-label CPA-EE initiations, which were of particular interest to this study, declined from 110 per 100,000 women in 2006 to 33 per 100,000 women in 2013. Among all new users of CPA-EE, the proportion of off-label users decreased from 29.5% in 2006 to 23.3% in 2013 (Table 3-2).

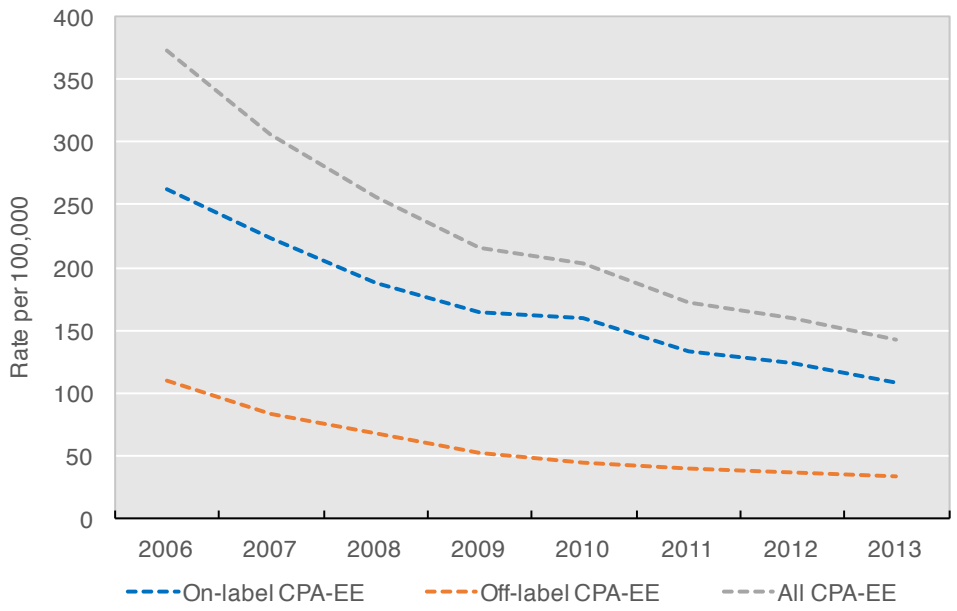

Figure 3-2. Annual trends in incidence rates (per 100,000 women) of on-label, off-label, and total CPA-EE use over time in BC, ages 15–34, 2006–2013.

Table 3-2. Proportion of on-label versus off-label CPA-EE use (as a percentage of total CPA-EE use) in women in BC, ages 15–34, 2006–2013.

	Count of CPA-EE initiators with evidence of acne	Count of CPA-EE initiators without evidence of acne	Total CPA-EE initiators	Appropriate use (%)	Inappropriate use (%)
2006	1,143	478	1,621	70.5	29.5
2007	983	366	1,349	72.9	27.1
2008	844	306	1,150	73.4	26.6
2009	748	234	982	76.2	23.8
2010	739	203	942	78.5	21.5
2011	634	190	824	76.9	23.1
2012	575	173	748	76.9	23.1
2013	503	153	656	76.7	23.3

I also observed a decline in incident use of OCs between 2006 and 2013, regardless of progestin type (Figure 3-3). Levonorgestrel- and desogestrel-containing OC formulations experienced a slight upturn around 2011, which continued throughout the remainder of the study period. Drospirenone-containing formulations were increasingly popular among new users from 2006 (582 per 100,000 women) to 2009 (1,290 per 100,000 women), but dropped sharply between 2009 and 2013 (248 per 100,000 women).

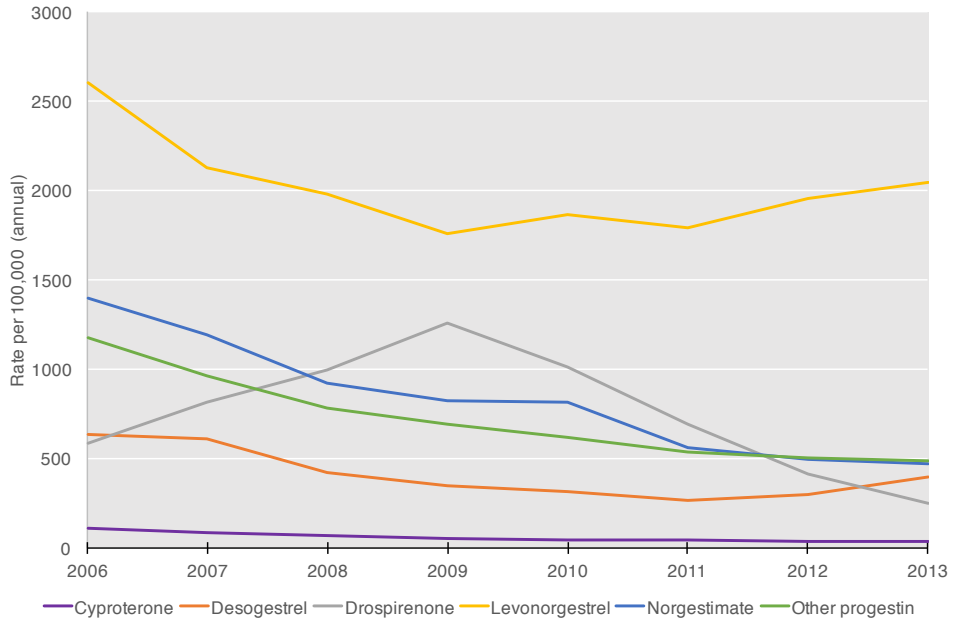

Figure 3-3. Rates (per 100,000 women) of incident CPA-EE* and OC use by progestin type in BC, ages 15–34, 2006–2013.

*CPA-EE users with on-label indications (i.e., evidence of prior acne diagnosis or treatment) were excluded from this analysis.

Overall, levonorgestrel-containing formulations were the predominant choice for new OC users. Despite an overall decline in incident use throughout the study period, the rate of levonorgestrel initiators in 2013 (2,046 per 100,000 women) remained significantly higher than the peak rate

reached by any other OC throughout the study period. In comparison, off-label CPA-EE accounted for the smallest proportion of new users among all progestin categories. Incidence rates of off-label CPA-EE were highest at the beginning of the study period (110 per 100,000 women), and gradually declined to a low of 33 per 100,000 women by 2013.

To examine the association between sociodemographic characteristics and risk of initiating treatment with CPA-EE for off-label indications, I calculated crude and adjusted odds ratios using multivariable logistic regression techniques (Table 3-1). Among all patient characteristics considered, only ethnicity was significantly associated with potentially inappropriate CPA-EE use, with South Asian women having greater odds of receiving a potentially inappropriate prescription (OR=1.44, 95% CI 1.18–1.75) than European/other women. In addition, women who had a physician aged 65 or older had higher odds (OR=1.66, 95% CI 1.32–2.09) of potentially inappropriate CPA-EE use compared to women with younger physicians (aged 25 to 44). Women who were married or in common-law relationships had significantly lower odds of receiving a potentially inappropriate CPA-EE prescription (OR 0.48, 95% CI 0.39–0.57). Age, rurality, income, and practitioner sex were not significantly associated with potentially inappropriate CPA-EE use.

3.4 Discussion

This study served to provide a comprehensive, current overview of patterns of potentially inappropriate use of CPA-EE within a Canadian context. Several novel results were identified in this study. Of particular note, the findings showed (1) declining rates of incident CPA-EE use between 2006 and 2013 for both on-label and off-label use, (2) declining incidence rates for all OCs between

2006 and 2013, and (3) higher odds of receiving a potentially inappropriate CPA-EE prescription among South Asian women and women who had older prescribing physicians (>65 years).

3.4.1 Trends in incident CPA-EE and OC use

As a first step, I identified women who received a new prescription for CPA-EE without prior evidence of acne diagnosis or treatment, which is indicative of potentially inappropriate CPA-EE use. Of the 179,843 women who met the inclusion criteria and received an initial prescription for either an OC or CPA-EE during the study period, 2,103 (1.2%) were identified as potentially inappropriate users of CPA-EE. Thus, potentially inappropriate CPA-EE represented only a small proportion of incident contraceptive use in this cohort.

In a previous study of potentially inappropriate contraceptive use among Canadian women, nearly half (45.5%) of the women who received an incident prescription for CPA-EE between 1998 and 2003 had no record of acne diagnosis or treatment (Mintzes et al., 2005). In this study, the proportion of women without acne among those initiating CPA-EE in 2006 was significantly lower (29.5%) than 2003 estimates, and continued to decline as expected throughout the study period (to 23.3% in 2013). The substantial decrease in the proportion of off-label CPA-EE use between 2003 and 2006 may have been prompted by safety advisories issued by Health Canada during this time period (Health Canada, 2002, 2003, 2005). In these advisories, which were targeted at health care professionals as well as the general public, Health Canada explicitly discouraged all off-label use of CPA-EE due to evidence of increased VTE risk. Thus, it is possible that the subsequent drop in off-label CPA-EE use (as a percentage of total CPA-EE use), up to and including 2013, was in response

to lingering safety concerns and public scrutiny, thereby affecting patient or physician preferences for certain contraceptives.

I observed a downward trend in incident use not only for CPA-EE, but also for all OCs, from 2006 to 2013. As previously discussed in Chapter 2, the observed decline in incidence rates for all OCs was unexpected, but may be partially explained by a growing preference for alternative contraceptive methods—specifically non-oral hormonal products, such as the hormonal IUD—among reproductive-aged women in BC. Although OCs are the most popular method of hormonal contraception in Canada (Black et al., 2009; Rotermann et al., 2015), LARCs confer several unique advantages over OCs that may be attractive to many hormonal contraceptive users. These methods provide effective contraception for an extended period (3 to 5 years for hormonal IUDs) without requiring further action by the user, which may appeal to women who value the convenience of LARCs over shorter-acting hormonal methods, such as OCs, which require daily adherence to ensure consistent and correct use (Hatcher, 2008; Peipert et al., 2011; Stubbs & Schamp, 2008).

Among all OCs approved for contraceptive use, formulations containing the progestin levonorgestrel were the most popular choice for first-time OC users, which is consistent with Canada-wide patterns of OC use (Rotermann et al., 2015). Based on evidence from a systematic review (Stegeman et al., 2013), the relative risk of VTE for low-dose estrogen OCs containing gestodene, desogestrel, cyproterone, or drospirenone was 50 to 80% higher than for low-dose estrogen OCs containing levonorgestrel. It should be noted that all estrogen-progestin contraceptives, including combined OCs, increase the risk of VTE, which is not the case for progestin-only methods, such as the hormonal IUD, injectable DMPA, and progestin-only OCs

(Stegeman et al., 2013). However, for women who opt for OCs, levonorgestrel-containing OCs may represent a safer option than other alternatives (Stegeman et al., 2013).

3.4.2 Characteristics associated with potentially inappropriate CPA-EE use

Of all patient characteristics included in the regression analyses, ethnicity had the strongest association with increased risk of potentially inappropriate CPA-EE use. Among South Asian women, the odds of receiving CPA-EE without evidence of acne were approximately 1.5 times that of the general population. This finding is an interesting contrast to the results from my other study of contraceptive use (Chapter 2), in which I reported that South Asian women had significantly lower odds of OC use compared to the general population. Interpreting the results of both studies together, South Asian women may be less likely to use OCs, and those who do may be more likely receive a potentially inappropriate prescription, despite the availability of safer alternatives. However, it is also possible that the higher odds of potentially inappropriate CPA-EE use among South Asian women could reflect underlying cultural differences between members of this ethnic subgroup compared to the general population. For example, some South Asian women may believe that acne treatment is more culturally and socially acceptable than hormonal contraception, and may therefore view CPA-EE as an attractive option because it has contraceptive benefits without being classified as a hormonal contraceptive. Collectively, my findings underscore the need for further studies to better characterize how factors such as ethnicity and culture can influence access to and preference for different contraceptive methods.

With respect to physician characteristics, women with older physicians (>65 years) were at greater risk of receiving a potentially inappropriate CPA-EE prescription. This is consistent with findings from another Canadian study that reported higher rates of inappropriate prescribing among physicians who had been in practice for longer periods of time (Cadieux et al., 2007). Given that similar findings have been previously reported, this potential determinant of inappropriate prescribing may warrant further investigation. The association between physician age and potentially inappropriate prescribing may be due to fundamental differences between age groups that were not adjusted for in the analyses. Due to the nature of administrative data, I was limited in my selection of physician characteristics. Future studies may benefit from examining a broader set of physician characteristics, such as ethnicity, location or type of practice, or years since graduation from medical school (which has been used as a proxy for physicians' knowledge of drugs in other studies) (Cadieux et al., 2007; Eguale et al., 2012). Information of this nature may allow for more rigorous analyses and offer valuable insight into the factors that influence off-label prescribing decisions in clinical practice.

3.4.3 Limitations

To my knowledge, this is the first population-level study to examine associations between potentially inappropriate CPA-EE use and patient and physician characteristics. This study has several limitations that should be discussed. Firstly, although CPA-EE has been shown to be associated with increased VTE risk compared to other estrogen-progestin OC formulations, its appropriateness for use as an OC may be a point of some contention for some physicians. Consequently, these physicians may decide that the benefits of CPA-EE outweigh the risks when prescribing off-label.

While physicians are generally at liberty to prescribe federally approved drugs in any manner that they believe is in their patients' best interests (Canada Standing Senate Committee on Social Affairs, 2014), Health Canada has explicitly and repeatedly stated that CPA-EE should not be used as first-line contraceptive due to the elevated risk of VTE. It is within this context that I have defined off-label use of CPA-EE as potentially inappropriate for the purposes of this study.

Secondly, it should be noted that I elected to use a conservative definition of potentially inappropriate CPA-EE use by excluding all women with any evidence of possible acne, which was similar to the criteria used in a previous study involving off-label CPA-EE use (Mintzes et al., 2005). Although CPA-EE is only indicated for severe acne that has failed to respond to other treatments, some women with very mild to moderate acne may have been misclassified as appropriate CPA-EE users in this study. Conversely, few cases of severe, treatment unresponsive acne would have gone undiagnosed, so it is very unlikely that I failed to detect truly appropriate CPA-EE cases. Nevertheless, this form of differential misclassification would have inflated the number of appropriate CPA-EE users and reduced the number of inappropriate CPA-EE users, thereby biasing the estimates of potentially inappropriate CPA-EE use toward the null. Consequently, the results likely represent an underestimate of the true rate of potentially inappropriate CPA-EE use in this study population.

Lastly, since my analyses were limited to only those variables that were included in the linked health datasets, the patient and physician characteristics used to identify determinants of potentially inappropriate CPA-EE use represent only a selection of possible important factors. This limitation

reflects the difficulty of capturing the full complexity of prescribing and drug use using administrative data, since information of this nature is not collected for research purposes.

3.5 Conclusion

The purpose of this study was to provide a comprehensive, current overview of potentially inappropriate use of CPA-EE as an OC within a Canadian context. Specifically, my objective was to investigate levels, trends, and determinants of potentially inappropriate CPA-EE use among reproductive-aged women in BC using population-based administrative data from 2006 to 2013. During this period, incident use declined for both CPA-EE and OCs. South Asian women and women with older prescribing physicians (>65 years) had significantly higher odds of receiving a potentially inappropriate CPA-EE prescription. Collectively, these findings contribute population-level knowledge about the patterns and risk of potentially inappropriate use of CPA-EE among young Canadian women.

4 CONCLUSION

This final chapter will be divided into four sections: (1) a brief summary of the key findings from the two research studies presented in this thesis, (2) a discussion of the scientific contributions of these studies, (3) a discussion of strengths and limitations associated with the selected research methodology, and (4) recommendations for future research in related research areas.

4.1 Summary and implications of research findings

This thesis had two primary objectives: (1) to characterize current patterns of hormonal contraceptive use in a Canadian context, and (2) to provide a comprehensive, current overview of potentially inappropriate contraceptive use of CPA-EE within a Canadian context. These objectives were investigated through two separate, but related, quantitative studies: (1) a study of levels, trends, and determinants of hormonal contraceptive use among reproductive-aged women in BC, and (2) a study of levels, trends, and determinants of potentially inappropriate CPA-EE use in BC.

4.1.1 Levels, trends, and determinants of hormonal contraceptive use among reproduced-aged women in British Columbia

In Chapter 2, 'Levels, trends, and determinants of hormonal contraceptive use among reproductive-aged women in British Columbia,' I provided evidence of a shift in patterns of hormonal

contraceptive use in a Canadian context. Similar to previous Canadian studies of contraceptive use (Black et al., 2009; Rotermann et al., 2015), I found that OCs remained the most popular method of reversible contraception among reproductive-aged women. However, I also identified several novel results, notably (1) stable prevalence, but declining incidence of overall hormonal contraceptive use, (2) declining popularity of OCs, (3) a growing preference for hormonal IUDs, and (4) decreased odds of hormonal contraceptive use among ethnic minorities (Chinese and South Asians).

Collectively, these findings suggest that OCs have recently declined in popularity among new contraceptive users in BC, while more women appear to be favouring hormonal IUDs as their preferred method of contraception. Historically, hormonal IUDs have been infrequently used by Canadian women, despite being the most effective and having the highest continuation rates of any hormonal contraceptive (Black & Guilbert, 2015; Trussell 2007, 2011). While my results showed a greater uptake of hormonal IUDs in BC, ethnic minority groups exhibited significantly lower odds use of all hormonal contraceptive use compared to the general population. Specifically, I observed consistently lower odds of hormonal contraceptive use among Chinese and South Asian women. These patterns of use may reflect the ways that sociodemographic characteristics, such as ethnicity, can affect access to and preference for certain contraceptive methods. Further investigation of these factors may help to strengthen our understanding of the barriers to contraceptive access that exist within potentially vulnerable populations, such as ethnic minorities.

4.1.2 Levels, trends, and determinants of potentially inappropriate prescribing of CPA-EE for oral contraception among young women in British Columbia

Chapter 3, 'Levels, trends, and determinants of potentially inappropriate prescribing of Diane-35 for oral contraception among young women in British Columbia,' provided evidence of declining rates of incident CPA-EE use between 2006 and 2013 for both on-label and off-label users. Of particular interest to this study were those women who received a new prescription for CPA-EE without prior diagnosis or treatment for acne (i.e., off-label use), which I defined as potentially inappropriate use within the context of this study.

Throughout the study period, potentially inappropriate CPA-EE use declined from 110 per 100,000 women in 2006 to 33 per 100,000 women in 2013. This decline may be partially explained by ongoing safety concerns and public scrutiny, which could affect patient or physician preferences for certain contraceptives. Another factor contributing to this decline may be a decrease in promotional spending following Diane-35's patent expiry. However, in comparing CPA-EE to other OCs, I observed a similar trend of declining incident use for all OC formulations between 2006 and 2013. Therefore, these declining trends may also reflect a growing preference for alternative contraceptive methods, such as hormonal IUDs, within this population of women.

Among all OC formulations, those containing the progestin levonorgestrel, including the popular brand-name drug Alesse, were the most popular choice for first-time OC users. Current evidence suggests that levonorgestrel-containing drugs may have a lower risk of VTE compared to other OC formulations (Stegeman et al., 2013).

Using large, population-based datasets, I identified two sociodemographic characteristics that were significantly associated with potentially inappropriate CPA-EE use. Specifically, women of South Asian ethnicity and women with older prescribing physicians had greater odds of receiving an off-label prescription for CPA-EE. These results suggest the possibility of unique risk profiles for certain subgroups of women, such as ethnic minorities, who may be at greater risk of exposure to potentially inappropriate prescribing practices.

4.2 Contribution of research

In the context of public health research in Canada, the study of hormonal contraception is relatively limited, particularly in comparison to other Western countries. Reproductive health experts have stated that there is an urgent need for high-quality data on current patterns of contraceptive use, which could be used to inform effective health policy and planning, support evidence-based clinical practice, and facilitate improved post-market surveillance of approved drugs (Black et al., 2009; Reid et al., 2011; Rotermann et al., 2015).

The results presented in Chapter 2 represent the most recent investigation of all hormonal contraceptive use in a Canadian setting since Black et al.'s 2009 study. My study benefitted from the use of comprehensive linked administrative health datasets containing sociodemographic information and administrative records of all prescription drug dispensations, fee-for-service physician visits, and hospitalizations for all BC. The previous study by Black et al. (2009), while significant in its contribution to the field of reproductive health in Canada, relied on survey data

collected over a decade ago, which pre-dates regulatory approval of several OCs and non-oral hormonal contraceptives that are commonly used today. The findings from my study provide a more current assessment of similar trends and analyses that were previously reported in the literature, with the added benefit of access to a study sample that encompassed nearly the entire population of reproductive-aged women in BC.

Through the investigation of off-label contraceptive use of CPA-EE (Chapter 3), this thesis also contributes to a greater understanding of the sociodemographic determinants that may influence risk of exposure to potentially inappropriate prescribing and drug use. Additionally, my research adds to existing evidence regarding sex-specific patterns of potentially inappropriate drug use (Eguale et al., 2012; Guthrie et al., 2011; Morgan et al., 2016).

Overall, this thesis builds on a relatively sparse body of literature on levels, trends, and determinants of hormonal contraceptive use in Canada. The collective results from both studies may be of interest to public health authorities and healthcare providers who are interested in identifying and addressing possible gaps in our current delivery of reproductive health care in Canada.

4.3 Strengths and limitations

While the two research studies presented in this thesis provide valuable information regarding patterns of hormonal contraceptive use in Canada, it is important to interpret these findings in light of their limitations. Some study-specific limitations were discussed within their respective chapters.

However, broader limitations, generally pertaining to the research methodology, are discussed below.

Limitations

There are limitations associated with the secondary use of administrative data for health care research, as this data is collected for administrative rather than for research purposes. Firstly, the selection and quality of data collection are not under the researchers' control, and can be difficult to validate (Groen, 2012).

Secondly, the outcomes that were measured in both studies were based on prescription drug claims, which is a variable that may overestimate the prevalence of drug use and underestimate the number of actual prescriptions issued by physicians. This is due to the possibility that some patients may not comply with treatment for prescriptions that they have filled, or may not fill their prescriptions that have been issued to them a physician. Despite this limitation, drug claims do serve to accurately represent the prescriptions an individual has purchased with the intention of use, and those that a health care provider has made the decision to prescribe.

Thirdly, surnames were used as a proxy for analyzing ethnic subgroups. Using a validated surname algorithm, I was able to accurately identify individuals with South Asian and Chinese origins from administrative data where information on race and ethnicity was excluded. However, this measure of ethnicity would, by necessity, not always be comprehensive or representative of the entire South Asian or Chinese population in BC (Shah et al., 2010). In particular, this algorithm has poorer

positive predictive value for individuals who are Canadian-born, including those who have adopted a different ethnic surname by marriage or those whose parents belonged to mixed ethnic backgrounds. However, it should be noted that, in Canada, individuals of South Asian or Chinese ethnicity are the least likely to report being married to someone from outside their ethnic group (Statistics Canada, 2011c). Furthermore, this particular surname algorithm has excellent predictive value overall, with approximately 90% positive predictive value (Shah et al., 2010).

Lastly, this research was conducted using BC-specific data, so inferences made may be limited to the context of this province. Since existing literature on Canadian contraceptive trends is limited, it is difficult to determine whether BC typically has distinctly different patterns of contraceptive use compared to the general Canadian population. Furthermore, the datasets used in both studies excluded individuals with declared First Nations status, members of the Canadian Forces, veterans, and inmates in federal penitentiaries, so it is not possible to generalize findings to members of these groups.

Strengths

In spite of these limitations, there are several notable strengths in the two studies that should be acknowledged. These strengths primarily relate to the use of population-based administrative data for a large, geographically and ethnically diverse province. Firstly, by relying on administrative data for prescription drug claims, I eliminated common biases associated with the use of self-report data, such as recall, non-response, and social-desirability biases (Groen, 2012).

Secondly, the use of large, linked datasets allowed me to sample nearly the entire population of reproductive-aged women in BC. This confers a unique advantage compared to survey-based sampling, which is limited by selection bias and typically only captures information for a small sample of the population (Groen, 2012). Furthermore, by utilizing data that is representative of the majority of the population, I was able to capture information about individuals who may be underrepresented in deliberately sampled cohorts, such as ethnic minorities or those of lower income. The de-identified data provided by Population Data BC ensured confidentiality for any individuals or subgroups of the population for whom factors such as privacy or stigma might otherwise interfere with their participation.

Finally, both studies benefitted from a relatively long observation period, from the beginning of 2004 to the end of 2013, which allowed me to conduct trend analyses spanning the years 2006 to 2013 (after accounting for a two-year washout period from 2004 to 2006). A study of this length would typically not be financially or logistically achievable through survey methods.

4.4 Recommendations for future research

The collective findings from this thesis underscore the need for more current studies on hormonal contraception within Canada. Specifically, attempts should be made to provide timely and comprehensive estimates of hormonal contraceptive use at the provincial, territorial, and national levels. This is especially warranted given the ongoing evolution of contraceptive methods, as well as the shifting reproductive needs of an increasingly diverse Canadian population.

This thesis produced novel findings using linked administrative datasets. Analyzing data of this nature is a promising strategy for health services research. This is particularly true in the field of reproductive health, which is currently limited by an absence of nationally-representative data on hormonal contraceptive use. However, the use of administrative data for research purposes should be part of a more comprehensive investigative process, as the use of administrative data alone typically cannot explain the underlying causes for the observed results. Survey-based and qualitative research may be especially important to help address existing knowledge gaps in this field.

Additional research is needed to explicate reasons for the observed ethnic disparity in hormonal contraceptive use reported in Chapter 2. My results showed that Chinese and South Asian women were less likely to use hormonal contraceptives compared to the general population, which may put these women at greater risk of experiencing unintended pregnancy or other adverse health outcomes. Further research in this area could offer valuable insight regarding knowledge, attitudes, and perceptions about contraception that may create barriers to or influence patterns of contraceptive use for certain ethnic minority groups.

In Chapter 3, I investigated potentially inappropriate use of CPA-EE as a contraceptive in BC, which is one of many examples of a prescription drug used off-label in Canada. The importance of conducting research on off-label drug use has been emphasized by Health Canada's Standing Committee on Social Affairs, Science and Technology, which recently published findings from a two-year, four-phase study on off-label prescribing in Canada (Canada Standing Senate Committee on Social Affairs, 2014). Due to the potential for harm and the lack of evidentiary basis commonly associated with off-label prescribing, future Canadian studies in this area should investigate the

appropriateness (including safety and effectiveness) of off-label drugs in comparison to approved alternatives. In addition, since my results suggest an association between ethnicity and potentially inappropriate drug use, future investigation may be warranted to identify issues facing potentially vulnerable subgroups, such as visible minorities, who may be at greater risk of exposure to adverse effects associated with off-label prescribing. As ethnic minorities represent an increasingly large proportion of the Canadian population, future studies exploring these topics may be useful to help understand how risk might be modified by social as well as structural factors. This may be valuable to health authorities and care providers who strive to meet the reproductive health care needs of an increasingly diverse population of Canadian women.

REFERENCES

Abbott, R., & Ayres, I. (2014). Evidence and extrapolation: Mechanisms for regulating off-label uses of drugs and devices. *Duke Law Journal, 64*(3), 377-435.

American Academy of Pediatrics. (2002). Uses of drugs not described in the package insert (off-label uses). *Pediatrics, 110*(1), 181-183. doi:10.1542/peds.110.1.181

American College of Obstetricians and Gynecologists. (2015). Committee opinion no. 642: Increasing access to contraceptive implants and intrauterine devices to reduce unintended pregnancy. *Obstetrics and Gynecology, 126*(4), e44-e48. doi:10.1097/AOG.0000000000001106

Andersen, R. M. (1995). Revisiting the behavioral model and access to medical care: Does it matter? *Journal of Health and Social Behavior, 36*(1), 1-10.

Arowojolu, A. O., Gallo, M. F., Lopez, L. M., & Grimes, D. A. (2012). Combined oral contraceptive pills for treatment of acne. *Cochrane Database of Systematic Reviews, 7*, CD004425. doi:10.1002/14651858.CD004425.pub6

Balakrishnan, T. R., Krotki, K., & Lapierre-Adamcyk, E. (1985). Contraceptive use in Canada, 1984. *Family Planning Perspectives, 17*(5), 209-215.

Bayer Inc. (2014). Mirena® product monograph. Retrieved from http://www.bayer.ca/omr/online/mirena-pm-en.pdf

BC Ministry of Health. (2013). *BC Ministry of Health. PharmaNet. Data extract. Data Stewardship Committee.* Retrieved from: http://www.popdata.bc.ca/data

Black, A. (2007). Canadian contraception consensus—update on depot medroxyprogesterone acetate (DMPA). *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 28*(4), 305-308. doi:http://dx.doi.org/10.1016/S1701-2163(16)32125-9

Black, A., Francoeur, D., Rowe, T., Collins, J., Miller, D., Brown, T., . . . Henneberg, E. (2004). Canadian contraception consensus. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 26*(4), 347-387, 389-436.

Black, A., & Guilbert, E. (2015). Canadian contraception consensus (part 1 of 4). *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 37*(10), 936-942.

Black, A., Guilbert, E., Costescu, D., Dunn, S., Fisher, W., Kives, S., . . . Whelan, A. M. (2016). Canadian contraception consensus (part 3 of 4): Chapter 8 - progestin-only contraception. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 38*(3), 279-300. doi:10.1016/j.jogc.2015.12.003

Black, A., Guilbert, E., Hassan, F., Chatziheofilou, I., Lowin, J., Jeddi, M., . . . Trussell, J. (2015). The cost of unintended pregnancies in Canada: Estimating direct cost, role of imperfect adherence, and the potential impact of increased use of long-acting reversible contraceptives. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 37*(12), 1086-1097. doi:10.1016/s1701-2163(16)30074-3

Black, A., Yang, Q., Wu Wen, S., Lalonde, A. B., Guilbert, E., & Fisher, W. (2009). Contraceptive use among Canadian women of reproductive age: Results of a national survey. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 31*(7), 627-640.

Black, K. I., Lotke, P., Buhling, K. J., & Zite, N. B. (2012). A review of barriers and myths preventing the more widespread use of intrauterine contraception in nulliparous women. *European Journal of Contraception and Reproductive Health Care*, 17(5), 340-350. doi:10.3109/13625187.2012.700744

Black, K. I., Lotke, P., Lira, J., Peers, T., & Zite, N. B. (2013). Global survey of healthcare practitioners' beliefs and practices around intrauterine contraceptive method use in nulliparous women. *Contraception*, 88(5), 650-656. doi:10.1016/j.contraception.2013.06.005

Boroditsky, R., & Fisher, W. (2000). Sexual activity, contraceptive choice, and sexual and reproductive health indicators among single Canadian women, age 15-29: Additional findings from the Canadian contraception study. *The Canadian Journal of Human Sexuality, 9*(2), 79.

Boroditsky, R., Fisher, W., & Sand, M. (1995). The Canadian contraception study. *Journal of Obstetrics and Gynaecology Canada. Journal d'Obstétrique et Gynécologie du Canada, 17*, 1-28.

Boroditsky, R., Fisher, W., & Sand, M. (1996). The 1995 Canadian contraception study. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC*(Spec No), 1-31.

British Columbia Government, Multiculturalism & Immigration Branch. (2008). The diversity of visible minorities and ethnic origins in BC. Retrieved from http://www.llbc.leg.bc.ca/public/pubdocs/bcdocs/444122/visible_minorities_ethnic_origins.pdf

Buhling, K. J., Hauck, B., Dermout, S., Ardaens, K., & Marions, L. (2014). Understanding the barriers and myths limiting the use of intrauterine contraception in nulliparous women: Results of a survey of european/Canadian healthcare providers. *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, 183, 146-154. doi:10.1016/j.ejogrb.2014.10.020

Byrne, K. (1990). Medical records in litigation: The Dalkon Shield story. *Health Information Management Journal, 20*(2), 62-65. doi:10.1177/183335839002000205

Cadieux, G., Tamblyn, R., Dauphinee, D., & Libman, M. (2007). Predictors of inappropriate antibiotic prescribing among primary care physicians. *Canadian Medical Association Journal, 177*(8), 877-883. doi:10.1503/cmaj.070151

Canada Standing Senate Committee on Social Affairs, Science and Technology. (2014). *Prescription pharmaceuticals in Canada: Off-label use*. Retrieved from http://www.parl.gc.ca/Content/SEN/Committee/412/soci/rep/rep05jan14-e.pdf

CBC News. (2011). Yasmin birth control lawsuit a 1st in Canada. Retrieved from http://www.cbc.ca/news/health/yasmin-birth-control-lawsuit-a-1st-in-canada-1.1029298

CBC News. (2013). Yaz, Yasmin birth control pills suspected in 23 deaths. Retrieved from http://www.cbc.ca/news/canada/british-columbia/yaz-yasmin-birth-control-pills-suspected-in-23-deaths-1.1302473

Chen, D. T., Wynia, M. K., Moloney, R. M., & Alexander, G. C. (2009). US physician knowledge of the FDA-approved indications and evidence base for commonly prescribed drugs: Results of a national survey. *Pharmacoepidemiology and Drug Safety, 18*(11), 1094-1100. doi:10.1002/pds.1825

Chui, T. (2013). *Immigration and ethnocultural diversity in Canada: National household survey, 2011*. Ottawa: Statistics Canada.

Clark, M., Sowers, M., Levy, B., & Nichols, S. (2006). Bone mineral density loss and recovery during 48 months in first-time users of depot medroxyprogesterone acetate. *Fertility and Sterility, 86*(5), 1466-1474. doi:10.1016/j.fertnstert.2006.05.024

Clark, M., Sowers, M., Nichols, S., & Levy, B. (2004). Bone mineral density changes over two years in first-time users of depot medroxyprogesterone acetate. *Fertility and Sterility, 82*(6), 1580-1586. doi:10.1016/j.fertnstert.2004.04.064

Collier, R. (2013). Scrutiny of Diane-35 due to potential dangers of off-label prescribing. *Canadian Medical Association Journal, 185*(5), E217-218. doi:10.1503/cmaj.109-4414

de Bastos, M., Stegeman, B. H., Rosendaal, F. R., Van Hylckama Vlieg, A., Helmerhorst, F. M., Stijnen, T., & Dekkers, O. M. (2014). Combined oral contraceptives: Venous thrombosis. *Cochrane Database of Systematic Reviews*(3), CD010813. doi:10.1002/14651858.CD010813.pub2

Dresser, R., & Frader, J. (2009). Off-label prescribing: A call for heightened professional and government oversight. *Journal of Law, Medicine & Ethics, 37*(3), 476-486, 396. doi:10.1111/j.1748-720X.2009.00408.x

Drugs Technical Advisory Board. (2015). Minutes of the 70th meeting of Drugs Technical Advisory Board (India). Retrieved from http://www.cdsco.nic.in/writereaddata/70th DTAB minutes.pdf

Dunn, S., Anderson, G. M., & Bierman, A. S. (2009). Temporal and regional trends in IUD insertion: A population-based study in Ontario, Canada. *Contraception*, 80(5), 469-473. doi:10.1016/j.contraception.2009.04.004

Eguale, T., Buckeridge, D. L., Winslade, N. E., Benedetti, A., Hanley, J. A., & Tamblyn, R. (2012). Drug, patient, and physician characteristics associated with off-label prescribing in primary care. *Archives of Internal Medicine, 172*(10), 781-788. doi:10.1001/archinternmed.2012.340

Every Woman's Health Centre. (2017). Birth control pricing. Retrieved from http://everywomanshealthcentre.ca/birth-control/

Finer, L. B. (2010). Unintended pregnancy among US adolescents: Accounting for sexual activity. *Journal of Adolescent Health, 47*(3), 312-314. doi:10.1016/j.jadohealth.2010.02.002

Finer, L. B., Jerman, J., & Kavanaugh, M. L. (2012). Changes in use of long-acting contraceptive methods in the United States, 2007-2009. *Fertility and Sterility*, *98*(4), 893-897. doi:10.1016/j.fertnstert.2012.06.027

Finer, L. B., & Zolna, M. R. (2014). Shifts in intended and unintended pregnancies in the United States, 2001-2008. *American Journal of Public Health, 104*(1), S43-S48. doi:10.2105/AJPH.2013.301416

Fisher, W., & Black, A. (2007). Contraception in Canada: A review of method choices, characteristics, adherence and approaches to counselling. *Canadian Medical Association Journal, 176*(7), 953-961. doi:10.1503/cmaj.060851

Fisher, W., Boroditsky, R., & Bridges, M. (1999). The 1998 Canadian contraception study. *Canadian Journal of Human Sexuality, 8*(3), 161.

Fisher, W., Boroditsky, R., & Morris, B. (2004a). The 2002 Canadian contraception study: Part 1. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 26*(6), 580-590.

Fisher, W., Boroditsky, R., & Morris, B. (2004b). The 2002 Canadian contraception study: Part 2. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 26*(7), 646-656.

Gazarian, M., Kelly, M., McPhee, J. R., Graudins, L. V., Ward, R. L., & Campbell, T. J. (2006). Off-label use of medicines: Consensus recommendations for evaluating appropriateness. *Medical Journal of Australia, 185*(10), 544-548.

Goertzen, J. (2006). Learning procedural skills in family medicine residency: Comparison of rural and urban programs. *Canadian Family Physician*, 52(5), 622-623.

Good, C. B., & Gellad, W. F. (2016). Off-label drug use and adverse drug events: Turning up the heat on off-label prescribing. *JAMA Internal Medicine, 176*(1), 63-64. doi:10.1001/jamainternmed.2015.6068

Groen, J. A. (2012). Sources of error in survey and administrative data: The importance of reporting procedures. *Journal of Official Statistics, 28*(2), 173-198.

Guilbert, E., Brown, J., Kaunitz, A., Wagner, M., Berube, J., Charbonneau, L., . . . Morin, R. (2009). The use of depot-medroxyprogesterone acetate in contraception and its potential impact on skeletal health. *Contraception, 79*(3), 167-177. doi:10.1016/j.contraception.2008.10.016

Guthrie, B., McCowan, C., Davey, P., Simpson, C. R., Dreischulte, T., & Barnett, K. (2011). High risk prescribing in primary care patients particularly vulnerable to adverse drug events: Cross sectional population database analysis in scottish general practice. *BMJ, 342*, d3514. doi:10.1136/bmj.d3514

Hall, K. S., Trussell, J., & Schwarz, E. B. (2012). Progestin-only contraceptive pill use among women in the United States. *Contraception, 86*(6), 653-658. doi:10.1016/j.contraception.2012.05.003

Hanley, G. E., & Morgan, S. (2008). On the validity of area-based income measures to proxy household income. *BMC Health Services Research, 8*, 79. doi:10.1186/1472-6963-8-79

Harel, Z., Johnson, C. C., Gold, M. A., Cromer, B., Peterson, E., Burkman, R., . . . Bachrach, L. K. (2010). Recovery of bone mineral density in adolescents following the use of depot medroxyprogesterone acetate contraceptive injections. *Contraception, 81*(4), 281-291. doi:10.1016/j.contraception.2009.11.003

Harper, C. C., Blum, M., de Bocanegra, H. T., Darney, P. D., Speidel, J. J., Policar, M., & Drey, E. A. (2008). Challenges in translating evidence to practice: The provision of intrauterine contraception. *Obstetrics and Gynecology, 111*(6), 1359-1369. doi:10.1097/AOG.0b013e318173fd83

Harper, C. C., Brown, B. A., Foster-Rosales, A., & Raine, T. R. (2010). Hormonal contraceptive method choice among young, low-income women: How important is the provider? *Patient Education and Counseling, 81*(3), 349-354. doi:10.1016/j.pec.2010.08.010

Harris Interactive. (2006). U.S. Adults ambivalent about the risks and benefits of off-label prescription drug use [Press release]. Retrieved from http://www.prnewswire.com/news-releases/us-adults-ambivalent-about-the-risks-and-benefits-of-off-label-prescription-drug-use-56012072.html

Hatcher, R. A. (2008). *Contraceptive technology* (Vol. 19th rev.). New York, N.Y: Ardent Media.

Hatcher, R. A. (2011). *Contraceptive technology* (Vol. 20th rev.). New York, N.Y.: Ardent Media.

Hauck, B., & Costescu, D. (2015). Barriers and misperceptions limiting widespread use of intrauterine contraception among Canadian women. *Journal of Obstetrics and Gynaecology Canada: JOGC = Journal d'Obstétrique et Gynécologie du Canada : JOGC, 37*(7), 606-616.

Health Canada. (2002). Important safety concerns on the use of Diane-35. *Dear Healthcare Professional.* Retrieved from http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2002/14699a-eng.php

Health Canada. (2003). Diane-35 and the risk of venous thromboembolism. *Public Communication.* Retrieved from http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2003/13992a-eng.php

Health Canada. (2005). Health Canada advises consumers of new warning for Diane-35. *Advisory.* Important Safety Information, Labelling and Packaging. Retrieved from http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2005/13690a-eng.php

Health Canada. (2009). Drug release information for the Evra transdermal contraceptive system - for health professionals. Retrieved from http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2009/14546a-eng.php

Health Canada. (2011). Yasmin and Yaz (drospirenone): Updated information on increased risk of blood clots [Press release]. Retrieved from http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2011/13563a-eng.php

Health Canada. (2013). Health Canada's review of Diane-35 supports current labelling and use. *Information Update: Drugs.* Important Safety Information. Retrieved from http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/29283a-eng.php

Health Canada. (2014). NuvaRing (etonogestrel/ethinyl estradiol slow release vaginal ring) - new usage restrictions - for the public. Retrieved from http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/40841a-eng.php

Health Canada. (2015). Drug product database. from Health Canada http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php

HealthQuotes.ca. (2017). Individual health insurance FAQ. Retrieved from https://www.healthquotes.ca/Individual/Health-Insurance-Questions.aspx

Hebert, P. C., & Stanbrook, M. (2007). Indication creep: Physician beware. *Canadian Medical Association Journal, 177*(7), 697, 699. doi:10.1503/cmaj.071223

Jones, J., Mosher, W., & Daniels, K. (2012). Current contraceptive use in the United States, 2006-2010, and changes in patterns of use since 1995. *National Health Statistics Reports*(60), 1.

Kaunitz, A., Darney, P., Ross, D., Wolter, K., & Speroff, L. (2009). Subcutaneous DMPA vs. Intramuscular DMPA: A 2-year randomized study of contraceptive efficacy and bone mineral density. *Contraception, 80*(1), 7-17. doi:10.1016/j.contraception.2009.02.005

Kavanaugh, M. L., Jerman, J., & Finer, L. B. (2015). Changes in use of long-acting reversible contraceptive methods among u.S. Women, 2009-2012. *Obstetrics and Gynecology*, *126*(5), 917-927. doi:10.1097/AOG.0000000000001094

Kerger, B. D., Bernal, A., Paustenbach, D. J., & Huntley-Fenner, G. (2016). Halo and spillover effect illustrations for selected beneficial medical devices and drugs. *BMC Public Health, 16*, 979. doi:10.1186/s12889-016-3595-7

Korenman, S., Kaestner, R., & Joyce, T. (2002). Consequences for infants of parental disagreement in pregnancy intention. *Perspectives on Sexual and Reproductive Health, 34*(4), 198-205.

Lat, I., Micek, S., Janzen, J., Cohen, H., Olsen, K., & Haas, C. (2011). Off-label medication use in adult critical care patients. *Journal of Critical Care, 26*(1), 89-94. doi:10.1016/j.jcrc.2010.06.012

Liao, P. V., & Dollin, J. (2012). Half a century of the oral contraceptive pill: Historical review and view to the future. *Canadian Family Physician, 58*(12), e757-e760.

Lopez, L. M., Grimes, D. A., Gallo, M. F., Stockton, L. L., & Schulz, K. F. (2013). Skin patch and vaginal ring versus combined oral contraceptives for contraception. *Cochrane Database of Systematic Reviews*(4), CD003552. doi:10.1002/14651858.CD003552.pub4

Lopez, L., Chen, M., Mullins Long, S., Curtis, K., & Helmerhorst, F. (2015). Steroidal contraceptives and bone fractures in women: Evidence from observational studies. *Cochrane Database of Systematic Reviews*(7), CD009849. doi:10.1002/14651858.CD009849.pub3

Mackey, T., & Liang, B. A. (2011). Off-label promotion reform: A legislative proposal addressing vulnerable patient drug access and limiting inappropriate pharmaceutical marketing. *University of Michigan Journal of Law Reform, 45*(1), 1.

Martel, L. (2012). *The Canadian population in 2011, population counts and growth: Population and dwelling counts, 2011 census*. Ottawa: Statistics Canada.

Martin, K., & Wu, Z. (2000). Contraceptive use in Canada: 1984-1995. *Family Planning Perspectives, 32*(2), 65-73.

Metcalfe, A., Talavlikar, R., du Prey, B., & Tough, S. C. (2016). Exploring the relationship between socioeconomic factors, method of contraception and unintended pregnancy. *Reprod Health, 13*(1), 28. doi:10.1186/s12978-016-0151-y

Miller, A. (2014). Off-label prescribing of antipsychotic drug highlights lack of oversight: Experts. *CTV News*. Retrieved from http://www.ctvnews.ca/health/off-label-prescribing-of-antipsychotic-drug-highlights-lack-of-oversight-experts-1.2053426

Mintzes, B., Lexchin, J., Sutherland, J. M., Beaulieu, M. D., Wilkes, M. S., Durrieu, G., & Reynolds, E. (2013). Pharmaceutical sales representatives and patient safety: A comparative prospective study of information quality in Canada, France and the United States. *Journal of General Internal Medicine, 28*(10), 1368-1375. doi:10.1007/s11606-013-2411-7

Mintzes, B., Morgan, S., & Bassett, K. L. (2005). Medicine by media: Did a critical television documentary affect the prescribing of cyproterone-estradiol (Diane-35)? *Canadian Medical Association Journal, 173*(11), 1313-1315. doi:10.1503/cmaj.050567

Morgan, S. G., Smolina, K., Mooney, D., Raymond, C., Bowen, M. L., Gorczynski, C., & Basham, K. A. R. (2014). The Canadian Rx atlas, 3rd edition.

Morgan, S. G., Weymann, D., Pratt, B., Smolina, K., Gladstone, E. J., Raymond, C., & Mintzes, B. (2016). Sex differences in the risk of receiving potentially inappropriate prescriptions among older adults. *Age and Ageing, 45*(4), 535-542. doi:10.1093/ageing/afw074

Mosher, W. D., & Jones, J. (2010). Use of contraception in the United States: 1982-2008. *Vital and Health Statistics. Series 23: Data from the National Survey of Family Growth*(29), 1-44.

Options for Sexual Health. (2017). Products and pricing. Retrieved from https://www.optionsforsexualhealth.org/clinic-services/products-pricing

Peipert, J. F., Madden, T., Allsworth, J. E., & Secura, G. M. (2012). Preventing unintended pregnancies by providing no-cost contraception. *Obstetrics and Gynecology, 120*(6), 1291-1297. doi:http://10.1097/AOG.0b013e318273eb56

Peipert, J. F., Zhao, Q., Allsworth, J. E., Petrosky, E., Madden, T., Eisenberg, D., & Secura, G. (2011). Continuation and satisfaction of reversible contraception. *Obstetrics and Gynecology, 117*(5), 1105-1113. doi:10.1097/AOG.0b013e31821188ad

Pini, M., Scoditti, U., Caliumi, F., Manotti, C., Quintavalla, R., Pattacini, C., . . . Bernardi, F. (1996). Risk of venous thromboembolism and stroke associated with oral contraceptives. Role of congenital thrombophilias. *Recenti Progressi in Medicina, 87*(7-8), 331-337.

Radley, D. C., Finkelstein, S. N., & Stafford, R. S. (2006). Off-label prescribing among office-based physicians. *Archives of Internal Medicine, 166*(9), 1021-1026. doi:10.1001/archinte.166.9.1021

Reid, R., Leyland, N., Wolfman, W., Allaire, C., Awadalla, A., Best, C., . . . Senikas, V. (2011). SOGC clinical practice guidelines: Oral contraceptives and the risk of venous thromboembolism: An update: No. 252, December 2010. *International Journal of Gynaecology and Obstetrics, 112*(3), 252-256. doi:10.1016/j.ijgo.2010.12.003

Rotermann, M., Dunn, S., & Black, A. (2015). Oral contraceptive use among women aged 15 to 49: Results from the Canadian health measures survey. *Health Reports, 26*(10), 21.

Rotermann, M., Sanmartin, C., Hennessy, D., & Arthur, M. (2014). Prescription medication use by Canadians aged 6 to 79. *Health Reports, 25*(6), 3.

Saxena, S., Copas, A. J., Mercer, C., Johnson, A. M., Fenton, K., Eren, B., . . . Wellings, K. (2006). Ethnic variations in sexual activity and contraceptive use: National cross-sectional survey. *Contraception, 74*(3), 224-233. doi:10.1016/j.contraception.2006.03.025

Scholes, D., LaCroix, A. Z., Ichikawa, L. E., Barlow, W. E., & Ott, S. M. (2005). Change in bone mineral density among adolescent women using and discontinuing depot medroxyprogesterone acetate contraception. *Archives of Pediatrics and Adolescent Medicine, 159*(2), 139-144. doi:10.1001/archpedi.159.2.139

Schwartz, D. (2013). Birth control trends in Canada not tracked. *CBC News*. Retrieved from http://www.cbc.ca/news/health/birth-control-trends-in-canada-not-tracked-1.1339896

Shah, B. R., Chiu, M., Amin, S., Ramani, M., Sadry, S., & Tu, J. V. (2010). Surname lists to identify South Asian and Chinese ethnicity from secondary data in Ontario, Canada: A validation study. *BMC Medical Research Methodology, 10*(1), 42-42. doi:10.1186/1471-2288-10-42

Shaw, D. (1997). Contraception: Special considerations in the mature woman. *Journal of Obstetrics and Gynaecology Canada, 20*(2), 133-138. doi:10.1016/S0849-5831(98)80004-9

Shoveller, J., Chabot, C., Soon, J. A., & Levine, M. (2007). Identifying barriers to emergency contraception use among young women from various sociocultural groups in British Columbia, Canada. *Perspectives on Sexual and Reproductive Health, 39*(1), 13-20. doi:10.1363/3901307

Singh, S., Sedgh, G., & Hussain, R. (2010). Unintended pregnancy: Worldwide levels, trends, and outcomes. *Studies in Family Planning, 41*(4), 241-250.

Sivin, I. (1993). Another look at the Dalkon Shield: Meta-analysis underscores its problems. *Contraception, 48*(1), 1-12. doi:10.1016/0010-7824(93)90060-K

Slee, V. N. (1978). The international classification of diseases: Ninth revision (ICD-9). *Annals of Internal Medicine, 88*(3), 424-426. doi:10.7326/0003-4819-88-3-424

Socías, M. E., Duff, P., Shoveller, J., Montaner, J., Nguyen, P., Ogilvie, G., & Shannon, K. (2016). Use of injectable hormonal contraception and HSV-2 acquisition in a cohort of female sex workers in Vancouver, Canada. *Sexually Transmitted Infections*. doi:10.1136/sextrans- 2016-052838.

Spinewine, A., Schmader, K. E., Barber, N., Hughes, C., Lapane, K. L., Swine, C., & Hanlon, J. T. (2007). Appropriate prescribing in elderly people: How well can it be measured and optimised? *Lancet, 370*(9582), 173-184. doi:10.1016/S0140-6736(07)61091-5

Stanwood, N. L., Garrett, J. M., & Konrad, T. R. (2002). Obstetrician-gynecologists and the intrauterine device: A survey of attitudes and practice. *Obstetrics and Gynecology*, *99*(2), 275-280. doi:10.1016/S0029-7844(01)01726-4

StataCorp. (2013). Stata statistical software: Release 13. College Station, TX, USA: StataCorp LP.

Statistics Canada. (2001). 2001 census of population, Statistics Canada catalogue no. 95f0489xcb2001002.

Statistics Canada. (2011a). 2011 national household survey, Statistics Canada catalogue no. 99-010-x2011030.

Statistics Canada. (2011b). 2011 national household survey, Statistics Canada catalogue no. 99-010-x2011038.

Statistics Canada. (2011c). Immigration and ethnocultural diversity: mixed unions in Canada. Rerieved from http://www12.statcan.gc.ca/nhs-enm/2011/as-sa/99-010-x/2011003/tbl/tbl1-eng.cfm

Statistics Canada. (2016). Population growth: Migratory increase overtakes natural increase. Retrieved from http://www.statcan.gc.ca/pub/11-630-x/11-630-x2014001-eng.htm

Stegeman, B. H., de Bastos, M., Rosendaal, F. R., van Hylckama Vlieg, A., Helmerhorst, F. M., Stijnen, T., & Dekkers, O. M. (2013). Different combined oral contraceptives and the risk of venous thrombosis: Systematic review and network meta-analysis. *BMJ, 347*, f5298. doi:10.1136/bmj.f5298

Stoddard, A., McNicholas, C., & Peipert, J. F. (2011). Efficacy and safety of long-acting reversible contraception. *Drugs, 71*(8), 969-980. doi:10.2165/11591290-000000000-00000

Stubbs, E., & Schamp, A. (2008). The evidence is in. Why are IUDs still out? Family physicians' perceptions of risk and indications. *Canadian Family Physician, 54*(4), 560-566.

Suhonen, S., Haukkamaa, M., Jakobsson, T., & Rauramo, I. (2004). Clinical performance of a levonorgestrel-releasing intrauterine system and oral contraceptives in young nulliparous women: A comparative study. *Contraception, 69*(5), 407-412. doi:10.1016/j.contraception.2003.11.008

The American College of Obstetricians and Gynecologists. (2014). Committee opinion no. 602: Depot medroxyprogesterone acetate and bone effects. *Obstetrics and Gynecology, 123*(6), 1398-1402. doi:10.1097/01.AOG.0000450758.95422.c8

Thompson, D. M., Fernald, D. H., & Mold, J. W. (2012). Intraclass correlation coefficients typical of cluster-randomized studies: Estimates from the Robert Wood Johnson prescription for health projects. *Annals of Family Medicine, 10*(3), 235-240. doi:10.1370/afm.1347

Trussell, J. (2007). Contraceptive efficacy. In: R. A. Hatcher, T. J. Nelson, F. Guest, & D. Kowal (Eds.), *Contraceptive technology* (Vol. 19th rev.) (pp. 747-826). New York, N.Y: Ardent Media.

Trussell, J. (2011). Contraceptive failure in the United States. *Contraception, 83*(5), 397-404. doi:10.1016/j.contraception.2011.01.021

United Nations. (2015). *Trends in contraceptive use worldwide 2015*. Retrieved from http://www.un.org/en/development/desa/population/publications/pdf/family/trendsContraceptiveUse2015Report.pdf

University of Ottawa. (2015). Society, the individual, and medicine. Facts and figures on abortions in Canada. Retrieved from http://www.med.uottawa.ca/sim/data/Abortion_e.htm

Vasilakis-Scaramozza, C., & Jick, H. (2001). Risk of venous thromboembolism with cyproterone or levonorgestrel contraceptives. *Lancet, 358*(9291), 1427-1429. doi:10.1016/S0140-6736(01)06522-9

Ved, R. R., & Visaria, L. (2016). *India's family planning programme: Policies, practices and challenges*: Routledge India.

Wang, C. (2012). Trends in contraceptive use and determinants of choice in China: 1980-2010. *Contraception, 85*(6), 570-579. doi:10.1016/j.contraception.2011.10.014

Watkins, E. (2012). How the pill became a lifestyle drug: The pharmaceutical industry and birth control in the United States since 1960. *American Journal of Public Health, 102*(8), 1462-1472. doi:10.2105/AJPH.2012.300706

Wiebe, E. (2013). Contraceptive practices and attitudes among immigrant and nonimmigrant women in Canada. *Canadian Family Physician, 59*(10), e451-455.

Wiebe, E., Janssen, P., Henderson, A., & Fung, I. (2004). Ethnic Chinese women's perceptions about condoms, withdrawal and rhythm methods of birth control. *Contraception, 69*(6), 493-496. doi:10.1016/j.contraception.2004.01.006

Wiebe, E., Sent, L., Fong, S., & Chan, J. (2002). Barriers to use of oral contraceptives in ethnic Chinese women presenting for abortion. *Contraception, 65*(2), 159-163. doi:10.1016/s0010-7824(01)00297-9

Wilson, N. M., Laursen, M., & Lidegaard, O. (2012). Oral contraception in Denmark 1998-2010. *Acta Obstetricia et Gynecologica Scandinavica, 91*(7), 810-815. doi:10.1111/j.1600-0412.2012.01416.x

Winner, B., Peipert, J. F., Zhao, Q., Buckel, C., Madden, T., Allsworth, J. E., & Secura, G. M. (2012). Effectiveness of long-acting reversible contraception. *New England Journal of Medicine, 366*(21), 1998-2007. doi:10.1056/NEJMoa1110855

World Health Organization. (2007). *Technical consultation on the effects of hormonal contraception on bone health: Summary report*. Retrieved from http://www.who.int/reproductivehealth/publications/family_planning/WHO_RHR_07_8/en/

APPENDIX A. ADDITIONAL TABLES AND FIGURES FROM CHAPTER 2: 'LEVELS, TRENDS, AND DETERMINANTS OF HORMONAL CONTRACEPTIVE USE AMONG REPRODUCTIVE-AGED WOMEN IN BRITISH COLUMBIA'

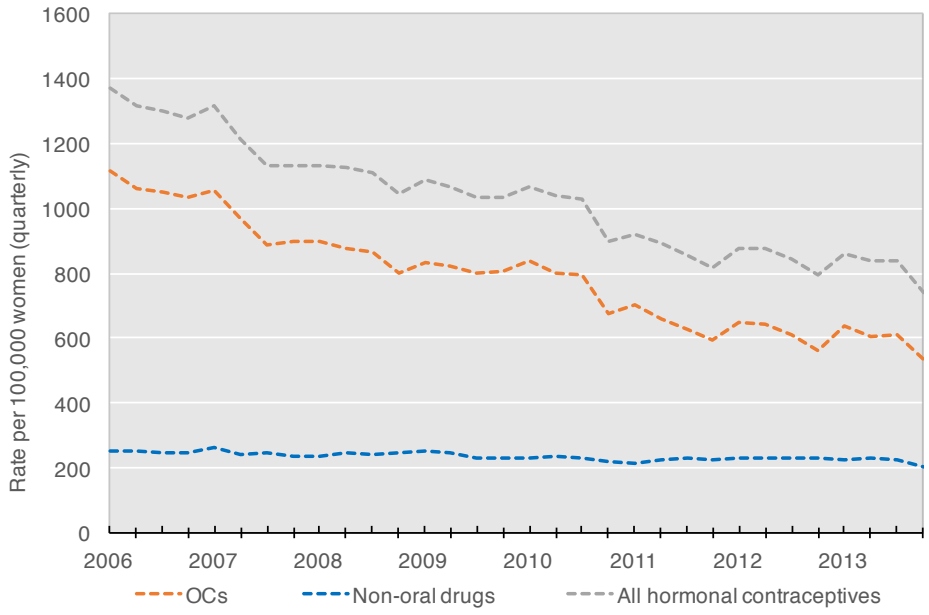

Figure A-1. Incident hormonal contraceptives use (per 100,000 women), ages 15–49, OCs versus non-oral contraceptives, 2006–2013, quarterly.

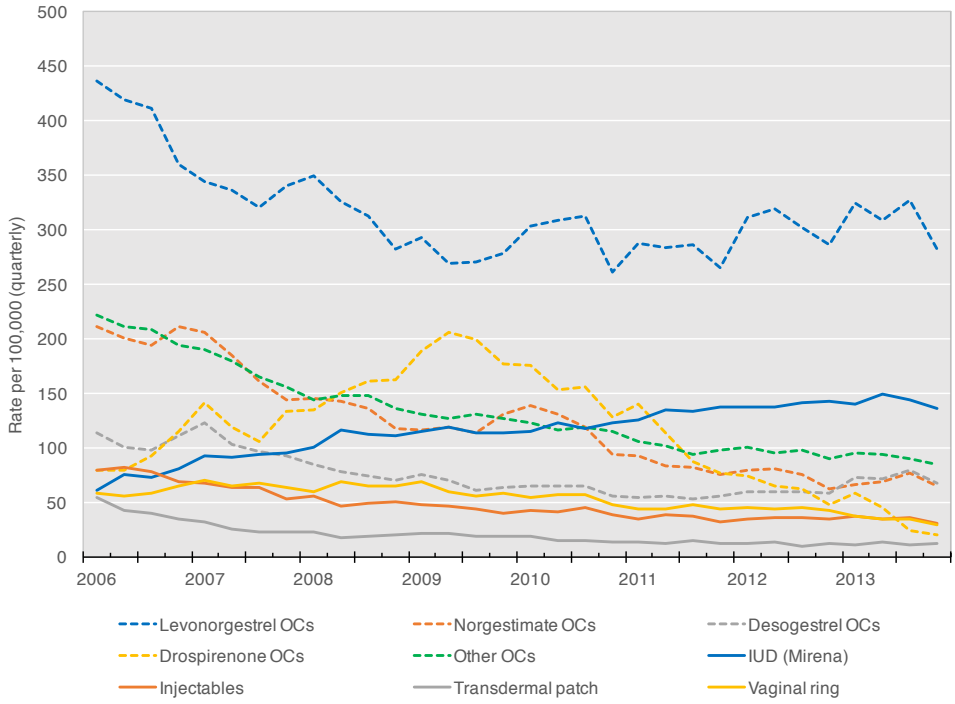

Figure A-2. Incident hormonal contraceptive use (per 100,000 women) in BC, ages 15–49, by contraceptive type, 2006–2013, quarterly.

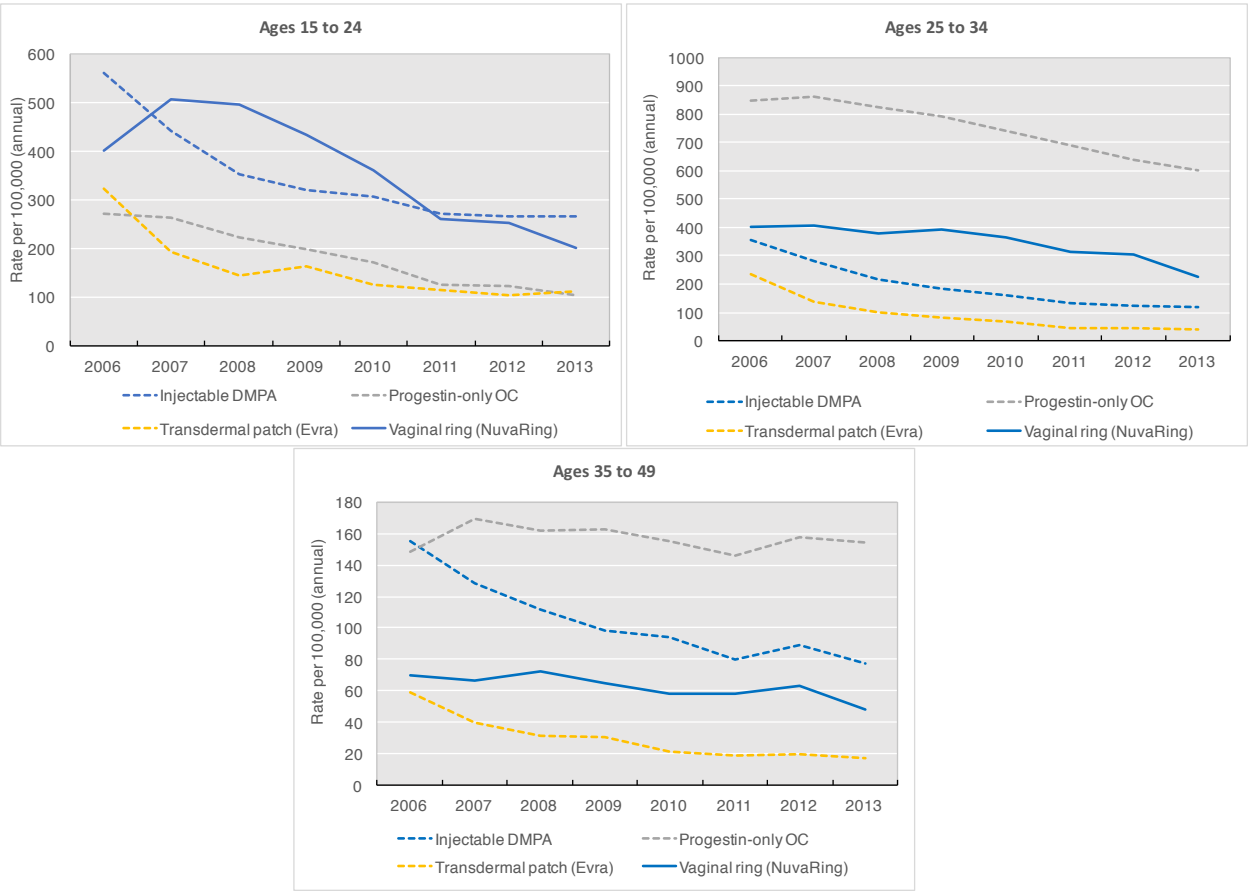

Figure A-3. Age-specific incident use of other non-oral hormonal contraceptives among women aged 15–49 in BC, 2006–2013.

Table A-1. Sample characteristics of prevalent hormonal contraceptive users* aged 15-49 residing in BC in 2013.

	Group, no. (%)													
	Did not fill a hormonal contraceptive prescription (*n* = 713,721)		**Filled at least one combined OC prescription (*n* = 162,456)**		**Filled at least one progestin-only OC prescription (*n* = 9,132)**		**Filled at least one injectable prescription (*n* = 8,553)**		**Filled at least one hormonal IUD prescription (*n* = 12,501)**		**Filled at least one intravaginal ring prescription (*n* = 9,098)**		**Filled at least one transdermal patch prescription (*n* = 3,679)**	
Age, yr														
15-19	82,587	(11.6)	23,980	(14.8)	372	(4.1)	1,466	(17.1)	658	(5.3)	695	(7.6)	527	(14.3)
20-24	68,630	(9.6)	41,287	(25.4)	1,128	(12.4)	1,662	(19.4)	1,918	(15.3)	2,648	(29.1)	942	(25.6)
25-29	79,788	(11.2)	35,814	(22.0)	2,131	(23.3)	1,405	(16.4)	2,225	(17.8)	2,858	(31.4)	857	(23.3)
30-34	99,620	(14.0)	25,207	(15.5)	2,782	(30.5)	1,304	(15.2)	2,293	(18.3)	1,542	(16.9)	636	(17.3)
35-39	109,221	(15.3)	15,749	(9.7)	1,545	(16.9)	1,075	(12.6)	2,057	(16.5)	737	(8.1)	365	(9.9)
40-49	273,875	(38.4)	20,419	(12.6)	1,174	(12.9)	1,641	(19.2)	3,350	(26.8)	618	(6.8)	352	(9.6)
Married														
No	378,350	(53.0)	119,242	(73.4)	3,818	(41.8)	6,687	(78.2)	6,474	(51.8)	6,966	(76.6)	2,624	(71.3)
Yes	335,371	(47.0)	43,214	(26.6)	5,314	(58.2)	1,866	(21.8)	6,027	(48.2)	2,132	(23.4)	1,055	(28.7)
Ethnicity														
European/other	568,579	(79.7)	146,967	(90.5)	8,419	(92.2)	8,181	(95.7)	11,412	(91.3)	8,572	(94.2)	3,042	(82.7)
Chinese	100,198	(14.0)	9,934	(6.1)	434	(4.8)	211	(2.5)	618	(4.9)	387	(4.3)	472	(12.8)
South Asian	44,944	(6.3)	5,555	(3.4)	279	(3.1)	161	(1.9)	471	(3.8)	139	(1.5)	165	(4.5)
Income quintile														
Lowest	122,713	(18.1)	28,420	(18.2)	1,474	(16.8)	2,193	(27.0)	2,146	(18.0)	1,641	(18.9)	792	(22.5)
2nd	134,522	(19.9)	26,219	(16.8)	1,579	(18.0)	1,745	(21.5)	2,017	(16.9)	1,590	(18.3)	661	(18.8)
3rd	140,380	(20.7)	26,889	(17.2)	1,637	(18.7)	1,514	(18.6)	2,135	(17.9)	1,544	(17.8)	699	(19.9)
4th	156,746	(23.2)	35,870	(23.0)	2,083	(23.8)	1,644	(20.2)	2,716	(22.8)	1,951	(22.4)	767	(21.8)
Highest	122,675	(18.1)	38,818	(24.8)	1,997	(22.8)	1,035	(12.7)	2,920	(24.5)	1,968	(22.6)	597	(17.0)
Rurality														
Urban	510,943	(72.0)	108,650	(67.1)	5,906	(64.8)	4,443	(52.0)	7,707	(61.8)	5,834	(64.4)	2,503	(68.1)
Mixed	163,629	(23.0)	45,027	(27.8)	2,684	(29.5)	3,337	(39.1)	3,986	(32.0)	2,733	(30.2)	936	(25.5)
Rural	35,389	(5.0)	8,365	(5.2)	521	(5.7)	758	(8.9)	771	(6.2)	495	(5.5)	234	(6.4)

* Women who filled a prescription for more than one type of contraceptive were counted once in each respective group. Of the *n* = 205,419 prevalent users represented in this table across all groups, *n* = 9,250 (4.5%) appeared in more than one group.

Table A-2. Characteristics of women aged 15-49 residing in BC in 2006, by combined OC use.

	Overall study sample		Study sample by combined OC use				Logistic regression odds ratios (95% CIs)	
	903,037	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	116,883	(12.9)	91,360	(12.4)	25,523	(15.6)	Ref	Ref
20-24	113,454	(12.6)	69,795	(9.4)	43,659	(26.7)	2.24 (2.2-2.28)	2.36 (2.32-2.41)
25-29	108,037	(12.0)	72,985	(9.9)	35,052	(21.4)	1.72 (1.69-1.75)	2.09 (2.04-2.13)
30-34	113,714	(12.6)	90,224	(12.2)	23,490	(14.3)	0.93 (0.91-0.95)	1.19 (1.16-1.22)
35-39	133,391	(14.8)	116,484	(15.8)	16,907	(10.3)	0.52 (0.51-0.53)	0.67 (0.65-0.68)
40-49	317,558	(35.2)	298,471	(40.4)	19,087	(11.7)	0.23 (0.22-0.23)	0.29 (0.28-0.29)
Married								
No	487,422	(54.0)	369,303	(50.0)	118,119	(72.1)	Ref	Ref
Yes	415,615	(46.0)	370,016	(50.0)	45,599	(27.9)	0.39 (0.38-0.39)	0.73 (0.72-0.74)
Ethnicity								
European/other	758,713	(84.0)	608,633	(82.3)	150,080	(91.7)	Ref	Ref
Chinese	102,450	(11.3)	93,768	(12.7)	8,682	(5.3)	0.38 (0.37-0.38)	0.36 (0.35-0.37)
South Asian	41,874	(4.6)	36,918	(5.0)	4,956	(3.0)	0.54 (0.53-0.56)	0.48 (0.47-0.5)
Income quintile								
Lowest	187,231	(20.7)	147,726	(20.0)	39,505	(24.1)	Ref	Ref
2nd	157,523	(17.4)	130,782	(17.7)	26,741	(16.3)	0.76 (0.75-0.78)	0.89 (0.88-0.91)
3rd	182,410	(20.2)	153,411	(20.8)	28,999	(17.7)	0.71 (0.7-0.72)	0.84 (0.83-0.86)
4th	173,607	(19.2)	144,482	(19.5)	29,125	(17.8)	0.75 (0.74-0.77)	0.92 (0.9-0.94)
Highest	192,181	(21.3)	153,986	(20.8)	38,195	(23.3)	0.93 (0.91-0.94)	1.23 (1.21-1.25)
Rurality								
Urban	616,750	(68.3)	508,039	(68.7)	108,711	(66.4)	Ref	Ref
Mixed	229,551	(25.4)	184,279	(24.9)	45,272	(27.7)	1.15 (1.13-1.16)	1.03 (1.01-1.04)
Rural	53,374	(5.9)	43,914	(5.9)	9,460	(5.8)	1.01 (0.98-1.03)	0.93 (0.91-0.95)

Table A-3. Characteristics of women aged 15-49 residing in BC in 2006, by injectable DMPA use.

	Overall study sample		Study sample by injectable DMPA use				Logistic regression odds ratios (95% CIs)	
	903,037	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	116,883	(12.9)	115,138	(12.9)	1,745	(14.7)	Ref	Ref
20-24	113,454	(12.6)	110,594	(12.4)	2,860	(24.1)	1.71 (1.61-1.81)	1.71 (1.61-1.82)
25-29	108,037	(12.0)	105,841	(11.9)	2,196	(18.5)	1.37 (1.28-1.46)	1.57 (1.47-1.68)
30-34	113,714	(12.6)	111,988	(12.6)	1,726	(14.5)	1.02 (0.95-1.09)	1.36 (1.27-1.47)
35-39	133,391	(14.8)	131,846	(14.8)	1,545	(13.0)	0.77 (0.72-0.83)	1.13 (1.05-1.22)
40-49	317,558	(35.2)	315,749	(35.4)	1,809	(15.2)	0.38 (0.35-0.4)	0.55 (0.51-0.59)
Married								
No	487,422	(54.0)	478,487	(53.7)	8,935	(75.2)	Ref	Ref
Yes	415,615	(46.0)	412,669	(46.3)	2,946	(24.8)	0.38 (0.37-0.4)	0.57 (0.55-0.6)
Ethnicity								
European/other	758,713	(84.0)	747,444	(83.9)	11,269	(94.8)	Ref	Ref
Chinese	102,450	(11.3)	102,086	(11.5)	364	(3.1)	0.24 (0.21-0.26)	0.28 (0.25-0.31)
South Asian	41,874	(4.6)	41,626	(4.7)	248	(2.1)	0.4 (0.35-0.45)	0.45 (0.4-0.52)
Income quintile								
Lowest	187,231	(20.7)	183,499	(20.8)	3,732	(31.9)	Ref	Ref
2nd	157,523	(17.4)	155,295	(17.6)	2,228	(19.1)	0.71 (0.67-0.74)	0.79 (0.75-0.83)
3rd	182,410	(20.2)	180,286	(20.5)	2,124	(18.2)	0.58 (0.55-0.61)	0.67 (0.64-0.71)
4th	173,607	(19.2)	171,705	(19.5)	1,902	(16.3)	0.54 (0.52-0.58)	0.66 (0.62-0.7)
Highest	192,181	(21.3)	190,486	(21.6)	1,695	(14.5)	0.44 (0.41-0.46)	0.56 (0.53-0.59)
Rurality								
Urban	616,750	(68.3)	610,358	(69.3)	6,392	(54.7)	Ref	Ref
Mixed	229,551	(25.4)	225,151	(25.5)	4,400	(37.7)	1.87 (1.8-1.94)	1.63 (1.56-1.69)
Rural	53,374	(5.9)	52,303	(5.9)	1,071	(9.2)	1.96 (1.83-2.09)	1.76 (1.65-1.88)

Table A-4. Characteristics of women aged 15-49 residing in BC in 2006, by intravaginal ring use.

	Overall study sample		Study sample by intravaginal ring use				Logistic regression odds ratios (95% CIs)	
	903,037	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	116,883	(12.9)	116,524	(13.0)	359	(9.5)	Ref	Ref
20-24	113,454	(12.6)	112,199	(12.5)	1,255	(33.2)	3.63 (3.23-4.08)	3.71 (3.3-4.18)
25-29	108,037	(12.0)	107,072	(11.9)	965	(25.5)	2.93 (2.59-3.3)	3.37 (2.97-3.83)
30-34	113,714	(12.6)	113,114	(12.6)	600	(15.9)	1.72 (1.51-1.96)	2.11 (1.84-2.43)
35-39	133,391	(14.8)	133,044	(14.8)	347	(9.2)	0.85 (0.73-0.98)	1.06 (0.9-1.24)
40-49	317,558	(35.2)	317,301	(35.3)	257	(6.8)	0.26 (0.22-0.31)	0.32 (0.27-0.39)
Married								
No	487,422	(54.0)	484,587	(53.9)	2,835	(74.9)	Ref	Ref
Yes	415,615	(46.0)	414,667	(46.1)	948	(25.1)	0.39 (0.36-0.42)	0.75 (0.68-0.82)
Ethnicity								
European/other	758,713	(84.0)	755,142	(84.0)	3,571	(94.4)	Ref	Ref
Chinese	102,450	(11.3)	102,295	(11.4)	155	(4.1)	0.32 (0.27-0.38)	0.31 (0.27-0.37)
South Asian	41,874	(4.6)	41,817	(4.7)	57	(1.5)	0.29 (0.22-0.37)	0.26 (0.2-0.34)
Income quintile								
Lowest	187,231	(20.7)	186,267	(20.9)	964	(25.7)	Ref	Ref
2nd	157,523	(17.4)	156,875	(17.6)	648	(17.3)	0.8 (0.72-0.88)	0.96 (0.87-1.06)
3rd	182,410	(20.2)	181,716	(20.4)	694	(18.5)	0.74 (0.67-0.81)	0.92 (0.84-1.02)
4th	173,607	(19.2)	172,999	(19.5)	608	(16.2)	0.68 (0.61-0.75)	0.87 (0.78-0.96)
Highest	192,181	(21.3)	191,340	(21.5)	841	(22.4)	0.85 (0.77-0.93)	1.16 (1.05-1.27)
Rurality								
Urban	616,750	(68.3)	614,204	(69.1)	2,546	(67.8)	Ref	Ref
Mixed	229,551	(25.4)	228,515	(25.7)	1,036	(27.6)	1.09 (1.02-1.18)	0.97 (0.9-1.04)
Rural	53,374	(5.9)	53,181	(6.0)	193	(5.1)	0.88 (0.76-1.01)	0.81 (0.7-0.94)

Table A-5. Characteristics of women aged 15-49 residing in BC in 2006, by progestin-only OC use.

	Overall study sample		Study sample by progestin-only OC use				Logistic regression odds ratios (95% CIs)	
	903,037	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	116,883	(12.9)	116,647	(13.0)	236	(3.2)	Ref	Ref
20-24	113,454	(12.6)	112,444	(12.6)	1,010	(13.9)	4.44 (3.85-5.12)	4.66 (4.03-5.37)
25-29	108,037	(12.0)	106,177	(11.9)	1,860	(25.6)	8.66 (7.56-9.92)	6.44 (5.58-7.42)
30-34	113,714	(12.6)	111,594	(12.5)	2,120	(29.1)	9.39 (8.21-10.74)	5.64 (4.88-6.52)
35-39	133,391	(14.8)	132,097	(14.7)	1,294	(17.8)	4.84 (4.21-5.56)	2.65 (2.28-3.08)
40-49	317,558	(35.2)	316,802	(35.4)	756	(10.4)	1.18 (1.02-1.37)	0.61 (0.52-0.71)
Married								
No	487,422	(54.0)	484,602	(54.1)	2,820	(38.8)	Ref	Ref
Yes	415,615	(46.0)	411,159	(45.9)	4,456	(61.2)	1.86 (1.78-1.95)	2.45 (2.3-2.61)
Ethnicity								
European/other	758,713	(84.0)	751,922	(83.9)	6,791	(93.3)	Ref	Ref
Chinese	102,450	(11.3)	102,197	(11.4)	253	(3.5)	0.27 (0.24-0.31)	0.31 (0.27-0.35)
South Asian	41,874	(4.6)	41,642	(4.6)	232	(3.2)	0.62 (0.54-0.70)	0.45 (0.39-0.51)
Income quintile								
Lowest	187,231	(20.7)	185,883	(21.0)	1,348	(18.6)	Ref	Ref
2nd	157,523	(17.4)	156,398	(17.7)	1,125	(15.6)	0.99 (0.92-1.07)	0.92 (0.85-1.00)
3rd	182,410	(20.2)	180,899	(20.4)	1,511	(20.9)	1.15 (1.07-1.24)	1.02 (0.95-1.11)
4th	173,607	(19.2)	172,071	(19.4)	1,536	(21.2)	1.23 (1.14-1.32)	1.10 (1.02-1.19)
Highest	192,181	(21.3)	190,468	(21.5)	1,713	(23.7)	1.24 (1.15-1.33)	1.29 (1.19-1.39)
Rurality								
Urban	616,750	(68.3)	612,123	(69.1)	4,627	(64.0)	Ref	Ref
Mixed	229,551	(25.4)	227,384	(25.7)	2,167	(30.0)	1.26 (1.2-1.33)	1.15 (1.09-1.21)
Rural	53,374	(5.9)	52,900	(6.0)	474	(6.6)	1.19 (1.08-1.3)	1.10 (1.00-1.22)

Table A-6. Characteristics of women aged 15-49 residing in BC in 2006, by transdermal patch use.

	Overall study sample		Study sample by transdermal patch use				Logistic regression odds ratios (95% CIs)	
	903,037	100%	No	%	Yes	%	Unadjusted	Adjusted
Age, yr								
15-19	116,883	(12.9)	115,721	(12.9)	1,162	(17.2)	Ref	Ref
20-24	113,454	(12.6)	111,365	(12.4)	2,089	(31.0)	1.87 (1.74-2.01)	1.85 (1.72-1.99)
25-29	108,037	(12.0)	106,530	(11.9)	1,507	(22.4)	1.41 (1.30-1.52)	1.41 (1.30-1.53)
30-34	113,714	(12.6)	112,746	(12.6)	968	(14.4)	0.86 (0.78-0.93)	0.88 (0.80-0.97)
35-39	133,391	(14.8)	132,790	(14.8)	601	(8.9)	0.45 (0.41-0.50)	0.47 (0.42-0.53)
40-49	317,558	(35.2)	317,145	(35.4)	413	(6.1)	0.13 (0.12-0.15)	0.14 (0.12-0.15)
Married								
No	487,422	(54.0)	482,393	(53.8)	5,029	(74.6)	Ref	Ref
Yes	415,615	(46.0)	413,904	(46.2)	1,711	(25.4)	0.40 (0.38-0.42)	0.96 (0.90-1.03)
Ethnicity								
European/other	758,713	(84.0)	752,821	(84.0)	5,892	(87.4)	Ref	Ref
Chinese	102,450	(11.3)	101,823	(11.4)	627	(9.3)	0.79 (0.72-0.85)	0.82 (0.76-0.90)
South Asian	41,874	(4.6)	41,653	(4.6)	221	(3.3)	0.68 (0.59-0.78)	0.63 (0.55-0.73)
Income quintile								
Lowest	187,231	(20.7)	185,378	(20.7)	1,853	(27.5)	Ref	Ref
2nd	157,523	(17.4)	156,318	(17.4)	1,205	(17.9)	0.77 (0.72-0.83)	0.91 (0.84-0.97)
3rd	182,410	(20.2)	181,121	(20.2)	1,289	(19.1)	0.71 (0.66-0.76)	0.84 (0.78-0.90)
4th	173,607	(19.2)	172,487	(19.2)	1,120	(16.6)	0.65 (0.60-0.70)	0.78 (0.72-0.84)
Highest	192,181	(21.3)	190,963	(21.3)	1,218	(18.1)	0.64 (0.59-0.69)	0.80 (0.74-0.86)
Rurality								
Urban	616,750	(68.3)	612,415	(68.3)	4,335	(64.3)	Ref	Ref
Mixed	229,551	(25.4)	227,651	(25.4)	1,900	(28.2)	1.18 (1.12-1.24)	1.12 (1.06-1.18)
Rural	53,374	(5.9)	52,879	(5.9)	495	(7.3)	1.32 (1.20-1.45)	1.28 (1.17-1.41)