

Report to Supportive Physicians on the Health Effects of Hormonal Contraception

Medical Ethics Council
Archdiocese of Kansas City

Context

Contraception is widespread, including among Catholics.

Medical experts seem to advocate contraception for its “health benefits.”

To dispel this concept would not be a panacea, but could substantially impact contraception.

What Is the Potential Impact of Our Report?

Hasson & Hill (2012) polled 824 church-going Catholic women.

- Only 44% wanted to learn more about Church teaching on family planning.
- But, of those women open to learning more, health is an important topic.
 - Fifty-two percent want to hear about health & relationship benefits of NFP.
 - Forty-five percent (non-exclusive) want to hear why NFP is pro-woman for health, self-image, and equality in relationships.

Obstacles to Overcome

Numerous obstacles are implicit in the above; some moral, some social, some intellectual.

Intellectual Obstacles

- Incredible volume of data, over many years.
- Is the data biased?
- We are not “experts” in the eyes of the world.

Volume, timeliness, & bias of data.

- We used all relevant articles of the last 5 years, from the journal of the Catholic Medical Association.
- In order to assure quality and rigor, we compared with the latest editions of the foremost texts by the experts, as well as many of their citations.
 - *Contraceptive Technology* (Hatcher et al., 2011).
 - *Clinical Gynecologic Endocrinology & Infertility* (Fritz & Speroff, 2011).
- Providentially, a new study published better information, just in time for our report.

- The *Danish Sex Hormone Register Study* is one of the largest and most complete studies to date.
- It provides new data on the risks, contradicting previous expert reassurances.

Countering the experts

We are not “experts” but the following are true.

- We have expertise in NFP.
- Of those open to learning more about Catholic teachings on NFP, significant numbers are interested in hearing from others, not just experts (Hasson & Hill, 2012):
 - fifty-two percent want to hear about NFP health benefits from other couples;
 - fifty percent want to hear an NFP recommendation from doctors;
 - thirty-one percent want to hear a homily encouraging NFP.
- We have the truth on our side.
- This is true for the medical evidence, as this report intends to show.

Cancer

Risks of Contraception

- Breast cancer (Br Ca) risk is increased with hormonal contraception (HC) by 20% (Mørch et al., 2017).
 - Note this says HC rather than oral contraception (OC). That is because this study showed Br Ca risk also with the levonorgestrel IUD; previous studies included mostly OC.
 - OC is particularly associated with triple-negative (no estrogen or progesterone receptors, low human epidermal growth factor) breast cancer, a subtype with high mortality and limited therapeutic options. OC use for 1 year increases the risk of triple negative breast cancer 150%. In young women, the risk of having used OC for 1 year is even higher, a 320% increase in triple negative breast cancer in women 40 and younger (Dolle et al., 2009).
- Cervical cancer risk is increased with oral contraception (OC) for 5 yrs' use by 10%.
 - Risk is increased with 10 yrs' use by 120% (Hatcher et al., 2011, pp. 283-4).
- The World Health Organization regards OC as a carcinogen (International Agency for Research on Cancer, 2018);
 - group 2A is “probably carcinogenic,” group 2B is “possibly carcinogenic.”
 - though OC is in group 1, the same as asbestos, radon, and tobacco, WHO states carcinogens in the same group may not have the same level of risk; just the same level of proof.
 - WHO also states OC is protective against cancer of endometrium and ovary.

Benefits of Contraception

- Ovarian cancer risk is said to be decreased with OC, possibly by 47% (Hatcher et al., 2011, pp. 265-6).
- Uterine cancer risk is said to be decreased with OC, possibly by 40-50% (Hatcher et al., 2011, p. 266; Fritz and Speroff, 2011, p. 995).

Risk-Benefit Comparison

Br Ca is 3 to 4 (if in situ Br Ca is included) times more common than ovarian and uterine cancer combined (Siegel, Miller, and Jemal, 2018).

- So, of the cancers affected by contraception, the most common one is increased.

The Development of Hormonal Contraception Might Help Explain a Demographic Trend

Breast cancer has increased at an alarming rate (426%) since the release of the birth control pill. “The American Cancer Society reported in 1973, ‘In women less than 65 years of age,’ the breast cancer death rate has ‘shown little fluctuation’ and is ‘almost unchanged since 1914’” (Schneider

et al., 2014, p. 246). Some of this is related to delayed childbearing and post-menopausal hormone replacement, factors not unrelated to hormonal contraception.

How Might Hormonal Contraception Increase Breast and Cervical Cancer?

Estrogen, and to a greater extent progestins induce breast cell proliferation (Schneider et al., 2014, p. 258).

OC appears to accelerate cervical cell proliferation also, and may affect gene expression and persistence of the cancer-causing human papilloma virus (Peck and Norris, 2012, p. 49).

Blood Clots

Venous thromboembolic risk is increased with OC by 100% (Fritz and Speroff, 2011, p. 981).

- OC in those with thrombophilic mutations have VTE risk increased 500 to 9,900% (Hatcher et al., 2011, p. 277).

How Might Hormonal Contraception Increase Heart Attack and Stroke?

Estrogen induces the liver to produce greater amounts of clotting Factors VII, VIII, and X, and less TPA and antiplasmin, as well as protein C resistance (Hatcher et al., 2011, pp. 277-278).

Heart Attack and Stroke

Heart attack and stroke are increased with many types of OC, by 30 to 130% (Lidegaard, Løkkegaard, Jensen, Skovlund, and Keiding, 2012).

- Though the confidence interval for 20 mcg ethinyl estradiol (EE) OC included 1.0, the authors stated that there were “only small differences in risk” between 20 mcg EE OC and 30 to 40 mcg EE OC.
- This study also showed a risk for the HC vaginal ring.

How Might Hormonal Contraception Increase Heart Attack and Stroke?

Estrogen's pro-thrombotic effects, listed above.

Ethinyl estradiol raises angiotensinogen.

Estrogen & progestins increase aldosterone activity.

(Hatcher et al., 2011, pp. 280-281).

Depression and Suicide

- Antidepressant medication use is increased with HC, by 23% (Skovlund, Mørch, Kessing, and Lidegaard, 2016).
 - The risk is increased even more in adolescents, by 80% (ibid.).

- Risk was found from combined estrogen-progestin OC, progestin-only OC, progestin patch, progestin vaginal ring, and progestin IUD.
- Suicide is increased with HC, by 208% (Skovlund, Mørch, Kessing, Lange, and Lidegaard, 2018).
 - Suicide attempts are increased with HC, by 97%.
 - Risk was found from combined OC, progestin-only OC, vaginal ring, and patch.

How Might Hormonal Contraception Increase Depression and Suicide?

Sex hormones influence brain areas linked to emotional processing.

Progesterone metabolites act on the GABA receptor.

Progestins increase MAO levels.

(Skovlund, Mørch, Kessing, and Lidegaard, 2016, p. 1155).

Q & A

How Good Are the Data Showing Contraceptive Risk?

Cancer

Breast cancer

The Mørch et al. study (2017) was published in *The New England Journal*, consistently one of the highest impact journals in the world.

n = 1.8 million women.

Cervical cancer

From Hatcher et al.'s *Contraceptive Technology* (2011), the “bible of contraception.”

Cancer hazard rating

The website of the World Health Organization (International Agency for Research on Cancer, 2018).

Thrombosis

Venous Thromboembolism

From Fritz and Speroff's *Clinical Gynecologic Endocrinology and Infertility* (2011), a leading text in the field.

Myocardial Infarction and Stroke

From *The New England Journal*.

n = 1.6 million women.

Mental illness

Depression

n = 1 million women.

Suicide

n = 476 thousand women.

Can't Statistics Be Twisted to Show Anything?

There are criteria by which to judge the quality of a study showing harm (Levine, Ioannidis, Haines, and Guyatt, 2008). Studies showing HC/OC harm met the following criteria of this AMA publication.

<u>Study</u>	<u>Adjustment for Confounding Factors at Baseline</u>	<u>Accuracy of Measuring Exposure to Risk Factor</u>	<u>Completeness of Ascertaining Outcome & Follow-up</u>
Mørch et al. (2017) on breast cancer	age, BMI, age at 1st birth, parity, tobacco, family history	pharmacy barcodes when purchasing HC/OC	national cancer registry
Lidegaard et al. (2012) on MI & CVA	age, hypertension, diabetes, lipids, smoking	pharmacy barcodes when purchasing HC/OC	national registries
Skovlund et al. (2016) on depression	Excluded those with a psychiatric history. Adjusted for age, education. Same effect with internal controls.	pharmacy barcodes when purchasing HC/OC	national registries
Skovlund et al. (2018) on suicide	Excluded those with a psychiatric history. Adjusted for age, education. Did a quantitative bias analysis.	pharmacy barcodes when purchasing HC/OC	national registries

Can There Be Doubt About the Data Showing Health Benefits of Hormonal Contraceptives?

Randomized controlled trials are the surest way to infer therapeutic benefit. According to the AMA's *Users' Guides to the Medical Literature*, "fewer and fewer promising interventions retain their postulated claims to effectiveness as we move...to RCTs" (Lacchetti, Ioannidis, and Guyatt, 2008, p. 114). On the other hand, non-randomized trials are usually used to demonstrate side effects; "traditionally, harms...have been studied with observational study designs" (ibid., p. 131). This is what we have done in this document.

We sought to evaluate the type of studies that contraception proponents use when inferring health benefit. Did they use randomized controlled studies, as is recommended by the AMA? We investigated this for contraception's strongest claim of health benefit.

Ovarian cancer

Contraception's strongest leg to stand on, in the assertion of health benefits other than contraception, is a claim of reducing ovarian cancer. The assertion that oral contraception (OC) does this is so well established that it has reached the level of a medical dogma. If not true, it would be shocking to the medical community.

The quality of studies upon which this particular assertion rests is not strong. Of the 25 studies cited by contraception experts Hatcher et al., Fritz & Speroff, none were randomized. (17 were original observational studies; 8 were reviews, re-analyses, or meta-analyses of observational studies.)

Considering biological mechanism, it is relevant to consider that the Danish Sex Hormone Registry, studying 900,000 women, found that post-menopausal hormone therapy is associated with an increased risk of ovarian cancer (Mørch et al., 2009); a possible mechanism is through the hormonal stimulation of cancerous cells (Fritz and Speroff, 2011, p. 842).

General

“Fundamentally, hormonal contraceptives, like all extrinsic interventions in the body, affect the undisturbed normal behavior of the biological systems. Therefore, in addition to the effects discussed, there may be other as yet unidentified effects. In general, unless necessary, extrinsic medical intervention in the natural functioning of the body should only be undertaken when there is a clear and compelling benefit that outweighs the risks. The risks clearly are not zero” (S. Caughron, June 21, 2018).

Did Contraception Proponents Previously Underestimate Risk?

<u>Contraception Proponents Stated</u>	<u>Subsequent Data Showed</u>
Br Ca risk from OC may not be real; Br Ca from low dose OC is a “myth” (Hatcher et al., pp. 63, 285).	HC raises Br Ca risk 20% (Mørch et al., 2017) Low dose OC was generally associated with increased Br Ca risk (p. 2234).
Any Br Ca risk from OC affects only the young, particularly < 35 yo (Fritz and Speroff, 2011, p. 1001).	Br Ca risk is no lower for older pts, though it may be higher if HC initiated before 20 yo (Mørch et al., 2017, p. 2233).
No effect upon Br Ca with increasing duration of OC use (Hatcher et al., 2011, p. 63).	Br Ca risk increased with longer durations of use (Mørch et al., 2017, p. 2228).
No effect upon Br Ca of past OC use - even implying a reduced risk with past use (Fritz and Speroff, 2011, p. 1001).	After 5+ yrs of HC use, higher Br Ca risk persists at least 5 years after HC discontinuation (Mørch et al., 2017, p. 2233).
No MI risk if no smoking/hypertension/diabetes (Hatcher et al., 2011, p. 61). No MI risk for < 50 mcg EE OC in healthy non-smokers (Fritz and Speroff, 2011, p. 987).	MI risk after adjustment for age, smoking, hypertension, diabetes, and lipids, from 30-40 mcg EE OC (Lidegaard et al., 2012).
No CVA risk from low dose OC under 35 yo (Hatcher et al., 2011, p. 61). No substantial CVA risk from low dose OC in healthy young (Fritz and Speroff, 2011, p. 987).	CVA risk after adjustment for age, hypertension, diabetes, lipids, and smoking, from 30-40 mcg EE OC (Lidegaard et al., 2012).
“Myths: The pill causes depression” (Hatcher et al., 2011, p. 251). “Low-dose oral contraceptives have minimal, if any, impact on mood” (Fritz and Speroff, 2011, p. 1030).	HC increases depression (Skovlund, Mørch, Kessing, and Lidegaard, 2016) and suicide (Skovlund, et al., 2018). “The use of all types of hormonal contraceptives was positively associated with a subsequent use of antidepressants and a diagnosis of depression” (Skovlund, Mørch, Kessing, and Lidegaard, 2016, p. 1159). Progestin-only products were also associated with suicide (Skovlund et al., 2018).

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