

Rapid Responses to “Mortality among contraceptive pill users...”

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Rapid Responses to:

RESEARCH:

Philip C Hannaford, Lisa Iversen, Tatiana V Macfarlane, Alison M Elliott, Valerie Angus, and Amanda J Lee

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Mortality among contraceptive pill users: cohort evidence from Royal College of General Practitioners’ Oral Contraception Study
BMJ 2010; 340: c927 [[Abstract](#)] [[Full text](#)]

RCGP Study draws wrong conclusions, again

4 April 2010

Joel Brind,
Professor
Baruch College, City University of New York, New York, NY 10010 USA

Once again, Hannaford et al.[1] have made headlines in the popular press with their claim of a health benefit of oral contraceptives (OC’s). This time [1] they tout a 12% decrease in the rate of death from any cause, echoing the same magnitude of significant reduction of overall cancer incidence claimed in their 2007 BMJ report [2] on the same Royal College of General Practitioners’ Oral Contraceptive Study cohort. Once again [3], a detailed look at the data analysis suggests no such benefit, and even troubling trends in the opposite direction, particularly when considering more current trends of oral contraceptive use.

The lack of any significant life saving benefit is easily discerned from the difference between results from the “full dataset” from the cohort of 46,112 women (including years of “flagged” followup of women lost to the study), and the “GP observation subset” (from which years of life after loss to GP observation were excluded). Both datasets are substantial and of similar magnitude, including approximately 1.2 million woman-years and 580,000 woman-years, respectively. Common sense is sufficient to dictate reliance upon the results obtained with the smaller, better dataset wherever there are material differences in statistical trends. In fact, the authors flatly state: “The pattern of relative risks was different when we used the smaller general practice observation subset. In this subset, the adjusted relative risk for any death between ever users and never users was very close to unity (0.98, 0.88 to 1.10).” Therefore, the lack of any

significant benefit from oral contraceptive use is obvious, contrary to the authors' claim in their official conclusion that "a net benefit was apparent."

Troubling trends of increased morbidity and mortality among OC users v. non-users are also apparent when considering the subset of women who constituted a small minority of users in this study cohort, but who predominate among current users, namely, young nulliparous women. Specifically, the RCGP cohort, recruited during the first decade of widespread OC use, were all married, had a median age of 29 years, most (83% of users and 80% of non-users) were parous, and had a median duration of OC use of less than 4 years (44 months). However, analysis of data on the small subsets of younger women in the RCGP cohort reveal troubling trends. For example, there was an almost threefold increase in death from any cause among those under 30 years, and a threefold increase in death from breast cancer for women under age 45 between 5 and 9 years after cessation of OC use. Moreover, despite the drop in breast cancer death risk 10 or more years after cessation of OC use in the recent report [1], the 2007 report [2] showed a dramatically increased breast cancer incidence (relative risk = 2.45) persisting out to 20 years after cessation of OC use. Such disturbing trends, however, are easily washed out by dilution of data from women who overwhelmingly used OC's only after bearing one or more children, and only for a few years, contrary to currently predominant patterns of OC use.

1 Hannaford PC, Iversen L, MacFarlane TV, et al. Mortality among contraceptive pill users: cohort evidence from Royal college of General Practitioners' oral contraception study. 2010;340:c927

2. Hannaford PC, Selvaraj S, Elliott AM, et al. Cancer risk among oral contraceptive users: cohort data from the Royal College of General Practitioner's Oral Contraception Study. BMJ 2007;335:651.

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Competing interests: None declared

The oral contraceptive pill and longevity

12 March 2010

Hany Lashen,
Senior Clinical Lecturer / Honorary Consultant in Reproductive Medicine
University of Sheffield
Send response to journal:
[Re: The oral contraceptive pill and longevity](#)

Dear Sir I read with interest the findings of this paper prompted by the immediate media attraction this paper has received. There is a magnificent amount of data in this study that renders it worthy of publication however, despite addressing the weakness of the study the authors have neglected 2 major weaknesses; the first is the self selection which lies in the reason for not taking the pill in the first place. Did the never users want to and were deemed not suitable for health reasons, strong family history or obesity. In such case the 2 groups started the study on unequal footing with regard to their health and disease risk. Some of them may have suffered infertility problems and had no reason to take to take the pill in the first place, which explains the difference in parity between the groups. Such group have their pertinent health risk such as ovarian and endometrial cancer. Second, there is no mention of body weight or any other anthropometric measures in the data collected. Given that obesity is a strong confounder of most of the diseases assessed by the study and a contraindication to taking the pill, I consider neglecting to collect such data a major flaw in the study. The study was started in the late 60s and obesity has only become a major problem relatively recently therefore the chance of including equal number of obese and overweight women in the 2 groups is very unlikely and the chance of selection bias is subsequently high. In fact, the contra-indications to prescribing the pill would have been more adhered to in those days when obesity and overweight were less common than under the current climate allowing more opportunity that the non-users were more likely to be either overweight or obese. Another issue in support of selection bias, albeit inadvertent in this case, is the significantly higher risk of violent death which reflects common personality traits or environmental exposure pertinent to those who chose the combined contraceptive which is mentioned in a pure scientific context and not meant in any negative sense. The drop out rate reach one third of the population which was commented upon by the authors nevertheless, its significance was conveniently played down. I do not wish to reduce the significance of the study, in fact I applaud the authors for the magnificent work which offers a justifiable reassurance that the pill does not carry the once thought high risk of disease and cancer. Furthermore, despite the inferiority of this evidence compared to a prospective randomised trial, it is cost effective and offers a reasonable degree of comprehensibility.

Competing interests: None declared

Contraceptive pill use and violent death

13 March 2010

S. Craig Roberts,
Senior Lecturer

School of Biological Sciences, University of Liverpool, Liverpool L69 7ZB

Send response to journal:

[Re: Contraceptive pill use and violent death](#)

Hannahford et al. (2010)[1] report convincing evidence for reduction in mortality from several forms of cancer and other disease in women who have used oral contraception compared to never users. However, they also find a higher rate of violent death among ever users, and that the rate of violent death increases with longer duration of oral contraceptive use, but they are unable to explain these intriguing results. I suggest that recent evolutionary insights into human partner choice may provide a clue.

There is evidence that use of oral contraception alters women's baseline preferences for men[2,3] such that pill users prefer men who are relatively similar to themselves at loci in the major histocompatibility complex (MHC). One consequence of being partnered with relatively MHC-similar men is that such women express lower sexual responsivity toward their long-term partner compared with women in relatively MHC-dissimilar couples, reject sexual advances from their partner more frequently, and report having had more extra-pair partners[4]. Other evidence points to MHC-similar couples being more likely to experience problems conceiving children, and having less healthy children due to lower MHC-heterozygosity[5]. Cumulatively, these effects could have real impact on the quality of spousal relationships[3,5].

It is not unreasonable to suspect that such effects could also influence rates of intimate partner violence. This is the most common cause of nonfatal injury among women[6] and accounts for more than a third of women murdered in the US[7]. Furthermore, ex-partners are a key risk factor[6], which could further emphasise the risk for pill users if the behavioural effects of pill use ultimately influence rates of marital breakdown[3,5].

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Competing interests: None declared

Royal College of General Practitioners Pill study reports three times more deaths in young contraceptive pill users

13 March
2010

Ellen CG Grant,
Physician and medical gynaecologist
Kingston-upon-Thames, KT2 7JU

Send response to journal:

[Re: Royal College of General Practitioners Pill study reports three times more deaths in young contraceptive pill users](#)

My colleagues and I have contributed many publications since 1962 describing and explaining the harmful effects of oral contraceptives. These include 14 electronic responses at www.bmj.com which point out numerous deep flaws in the large “observational” Royal College of General Practitioners Pill study such as very large drop out rates and losses. As usual Hannaford and colleagues make unsubstantiated claims of benefit.¹ It would need a Magic Pill and not a Bitter Pill to confer benefit up to 40 years later after an average “observed” use of 44 months!

The genuine proof from the randomised controlled Women’s Health Initiative Study, that progestogen and oestrogen hormones (given as combined HRT) increase cancers and vascular diseases and mortality from lung cancer, is apparently disregarded.² Combined HRT is the same biochemically and physiologically as the Pill. Although most deaths in this RCGP Pill study were in women over age 49, whether or not they were taking HRT is largely unknown.

It is remarkable that Hannaford is unable to explain the increased risk of violent and accidental deaths among users of oral contraceptives. Has he not read our 1968 proof that progesterone dominant oral contraceptives raise endometrial monoamine oxidase levels and increase depressive mood changes and loss of libido?³ This study was quoted in the RCGP 1974 publication which reported observations in the Pill study from 1968 to 1972. By then the RCGP study found increases among Pill users in about 60 conditions including mental illnesses and marriage break ups. ⁴

We also noted in our 1968 paper that increased violent events were seen with a dose combination which particularly increased both vascular arteriolar development and dilatation of

sinusoids. Now the immediate progesterone stimulated increase in Vascular Endothelial Growth Factor is thought to be a contributory cause of increases in metastatic breast, lung and ovarian cancers as well as vascular diseases.^{2,5}

Even if the results are taken at face value, it is absurd to claim a net benefit if nearly three times more women in the main pill taking age group, younger than age 30, are likely to die (RR 2.85). CNS and pituitary tumours increased with over 3 years of Pill use. Also Pill ever takers under age 45 had a 1.76 increased risk of cancer and vascular death 5 -9 years after stopping use. This is enough time to find the increase in breast cancer mortality but after this risk estimates would be meaningless due to widespread HRT taking. These hormones in the form of HRT are the main cause of premature cancer death in menopausal women whether or not they took the hormones as the Pill at the beginning of this or any other study 40 years ago.

It is now surely inconceivable that any medical scientist who has some understanding of basic mechanisms could believe that widespread hormone use, especially of progesterones, is not a major health problem.

1 Hannaford PC, Iverson L, MacFarlane TV, et al. Mortality among contraceptive pill users: cohort evidence from Royal College of General Practitioners' oral contraception study. *BMJ* 2010;340:c927.

2 Chlebowski RT, Schwartz AG, Wakelee H, Anderson GL, Stefanick ML, Manson JE, Rodabough RJ, Chien JW, Wactawski-Wende J, Gass M, Kotchen JM, Johnson KC, O'Sullivan MJ, Ockene JK, Chen C, Hubbell FA; Women's Health Initiative Investigators. Oestrogen plus progestin and lung cancer in postmenopausal women (Women's Health Initiative trial): a post-hoc analysis of a randomised controlled trial. *Lancet*. 2009 Oct 10;374(9697):1243-51

3 Grant ECG, Pryse-Davies J. Effect of oral contraceptives on depressive mood changes and on endometrial monoamine oxidase and phosphatases. *BMJ* 1968;3:777-80.

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Competing interests: None declared

Understanding Statistics

13 March 2010

Elizabeth A Johnswood,
Allied Health Professional
Kingscote South Australia, 5223

Send response to journal:
[Re: Understanding Statistics](#)

I include a quote from the article published on [www](#) and then picked up and published on many other websites. Can you please explain how 2864 deaths (ever users) is LOWER than 1747 deaths (never users)?

"1747 deaths occurred in never users of oral contraception and 2864 in ever users. Compared with never users, ever users of oral contraception had a significantly lower rate of death from any cause (adjusted relative risk 0.88, 95% confidence interval 0.82 to 0.93)."

sincerely elizabeth johnswood
Competing interests: None declared

Re: Understanding Statistics

14 March 2010

L Sam Lewis,
GP
Surgery, Newport, Pembrokeshire, SA42 0TJ
Send response to journal:
[Re: Re: Understanding Statistics](#)

Hi Elizabeth,

I had assumed the answer to this unfortunately ambiguous statement must lie in the word 'rate'.

"1747 deaths occurred in never users of oral contraception and 2864 in ever users....

[how many women were at risk in each group ? 15559 and 25942 - gleaned from the first figure "Flow chart of RCGP Oral Contraception Study"]

.. Compared with never users, ever users of oral contraception had a significantly lower RATE of death from any cause (adjusted relative risk 0.88, 95% confidence interval 0.82 to 0.93). "

So imagine my surprise to find that the crude death rate of 2864/25942 (0.1104) is just a little lower than 1747/15559 (0.1123). This 0.98 crude ratio must have undergone considerable manipulation to yield an "adjusted" relative risk of 0.88.

But observational studies, flawed by way of selection biases, are simply not scientifically capable of showing the mortality benefits that authors may claim, crude or adjusted !

Competing interests: None declared

Miguel A. Martinez-Gonzalez,
Professor and Chair, Dpt. of Public Health,
University of Navarra, Spain

Send response to journal:

[Re: The need to avoid bias and to define an induction period](#)

As for any study with such a long follow-up (39 years), the cohort of the Royal College of General Practitioners is to be commended without reservations (1).

However, several issues deserve further thought and consideration. When they are pondered together, the results and conclusions of this study probably need to be substantially toned down.

It is surprising why the authors did not give greater importance to the fact that such a huge proportion of participants (one third) were lost to follow-up. Usually, a great restraint is needed when interpreting a cohort study attaining a retention rate lower than 80%.

They used mortality instead of using incidence of disease. It is well known that mortality, especially total mortality, is not only related to the incidence of major chronic diseases but also to the quality and timeliness of medical care. If the quality of medical care is associated with the exposure to oral contraceptives, the use of mortality as outcome would lead to severe bias. It is true that by standardizing the rates for socioeconomic status they might have partially attenuate this bias. However, there is much room for residual confounding.

They acknowledge the possibility of bias due to a "healthy survivor" effect. This potential bias may provide an alternative explanation of their results and it calls for caution before broadcasting conclusions about a net benefit.

Hypertension has a high potential to be a major confounder not accounted for. It is well known that physicians use to take routine measurements of blood pressure in their clinics and, because of the synergy of cardiovascular risk factors, they tend to not prescribe oral contraceptives to hypertensive women. This could be another alternative non-causal explanation of the reported findings. If hypertensive women are more likely to be present in the never users group, a higher age-, smoking -, parity- and socioeconomic-adjusted mortality is to be expected in them under the null hypothesis of no association. This is so because hypertension is one of the most powerful predictors of early death (2). No analysis in this report has controlled for hypertension.

It is intriguing why they have not used Cox proportional hazards regression (showing the Kaplan-Meier curves) to appropriately tackle the issue of the time to event structure of their cohort. Cox regression is nowadays the standard approach to analyze prospective studies,

especially if mortality is the outcome. Would the overall estimate (RR= 0.82) had been the same using a fully- adjusted Cox regression?

More importantly, a mandatory tenet in epidemiology is to define meaningfully the exposure (and the non-exposure) under study. Any study is expected to set the minimums for the duration, frequency, and assumed length of the induction period for the exposed group and would set maximums (e.g., how many days or weeks after contraceptive use are considered as negligible?) for these same characteristics to define the unexposed group.

Otherwise, the blurred definition of the compared groups would lead to a diluted effect. It is difficult to understand the apparent underlying assumption that the effect of contraceptives on mortality may linger for several decades. No specific and meaningful induction period is stated. This vagueness undermines the study interpretation.

Should they have restricted the induction period only to 9 years after exposure (a more realistic assumption), a relative risk showing a harmful effect had been apparent.

All these methodological concerns might explain why the present results are not consistent with the available meta-analyses of observational studies about major causes of death (3-6) and neither with the more important results of the Women's Health Initiative (WHI) randomised trial (7,8). It rigorously tested the effect of estrogens and progestogens (the hormones contained in oral contraceptives) on cancer and cardiovascular disease and found a harmful effect. The randomized design of the WHI prevents most of the above-mentioned potential biases and should be considered as the gold standard for assessing the effects of combined female hormones (estrogens and progestogens).

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Competing interests: None declared

Does it mean that OC is always safe?

18 March 2010

Edoardo Cervoni,
Primary Care Doctor
Central Lancashire PCT NHS,
PR9 9JA

Send response to journal:

[Re: Does it mean that OC is always safe?](#)

As I expected, the paper had International resonance and as I was reading an (Italian) GP daily news magazine, the message taken home has been: contraceptive use does not increase mortality. Besides to compliment Prof Hannford and colleagues for the "titanic" work always associated with such big cohort studies, I must remember that the paper does not strongly support that conclusion. Its very likely, in my opinion, that there are differences between the 2 groups other than the use of contraceptive. We may argue that some patient not taking contraceptive may have done so as they were not engaged in relationship(s) because of health related issues. It may be assumed that some patients may have not taken contraception because of already known important risk factors or established medical problems.

Regards,

E Cervoni, MD

Competing interests: None declared

Large long term increases in mortality in oral contraceptive takers in RCGP study

23 March
2010

Ellen CG Grant,
Physician and medical gynaecologist
Kingston-upon-Thames, KT2 7JU

Send response to journal:

Re: [Large long term increases in mortality in oral contraceptive takers in RCGP study](#)

It is a great pity that so much international publicity was given to the claim by the authors of the Royal College of General Practitioner's study that oral contraceptives are not associated with an increased long term risk of death.¹ A closer look at the flow chart does indeed reveal evidence of large long term increases in mortality in "ever" takers.

In 1977 the RCGP oral contraceptive pill study flagged deaths for 35 104 women (out of 47 173 recruited since 1968) but did not flag any later hormone use including fertility drugs or HRT in relation to these deaths. In fact, 3 in 4 deaths reported happened after GP observations were stopped from 1996 to 2007. By this time median ages of the study groups were increasing from 49 to 60 – ages when many women would be taking HRT.

Overall the study flow chart shows that the number of deaths increased by 4.3 times (664 increased to 2864) in 28 142 "ever" takers and by 3.4 times (520 increased to 1747) in 16 786 "never" takers between 1996 and 2007.

Deaths increased 9.3 times in "ever" takers (62 to 578) but only by 5.5 times in "never" takers (73 to 405) for women still under GP observation from 1996 to 2007.

Importantly also from 1996 to 2007 there was an 8 times increase in flagged deaths in "ever" takers who left the study before age 38. 74/7761 (0.9%) increased to 567/ 7687 (7.4%).

In contrast, there were no more deaths in "never" takers who left the study under age 38. 23/4154 (0.55%) remained 23 deaths from 1996 to 2007.

I think the crucial mistake, of flagging deaths but not hormone use, contributed to the authors' apparent inability to define an expected large overall increase in mortality because combined HRT contains progestogens and oestrogens as do oral contraceptives. Even so, there were no significant differences for colorectal cancer or uterine body cancer deaths among ever and "never" takers. The only significant difference in individual cancer mortality risk was for ovarian cancer with 14 deaths in ever takers and 29 deaths in "never" takers who might have taken fertility drugs or HRT, both of which have been related to increases in ovarian cancer.^{2,3} The latest data from the prestigious WHI randomised control study found no protective effect on colorectal cancer mortality in the progestin plus estrogen trial over an 8-year intervention and follow-up period.⁴

These important facts demonstrate that the Royal College's mortality net benefit claim is likely to be wrong.

1 Hannaford PC, Iverson L, MacFarlane TV, et al. Mortality among contraceptive pill users: cohort evidence from Royal College of General Practitioners' oral contraception study. *BMJ* 2010;340:c927.

2 Zhou B, Sun Q, Cong R, Gu H, Tang N, Yang L, Wang B. Hormone replacement therapy and ovarian cancer risk: a meta-analysis. *Gynecol Oncol.* 2008;108:641-51.

3 Grant ECG. Increased risk of serous ovarian cancer following clomifene fertility treatment.http://bmj.com/cgi/eletters/338/feb05_2/b249#208597, 11 Feb 2009

4 Prentice RL, Pettinger M, Beresford SA, Wactawski-Wende J, Hubbell FA, Stefanick ML, Chlebowski RT. Colorectal cancer in relation to postmenopausal estrogen and estrogen plus progestin in the Women's Health Initiative clinical trial and observational study. *Cancer Epidemiol Biomarkers Prev.* 2009;18:1531-7.

Competing interests: None declared

Confirming long term safety of oral contraception

31 March 2010

Jai. B Sharma,
Associate Professor of Obstetrics and Gynaecology
All India Institute of Medical Sciences, New Delhi, India 110029
Send response to journal:
[Re: Confirming long term safety of oral contraception](#)

This very large and long term study on safety of oral contraception once again confirms long term safety and efficacy of oral contraceptives. The results are very promising that ever users of oral contraceptives had in fact a lower mortality rate as compared to never users. This should silence any critics once for all. The results also highlight that most cancers including gynaecological and bowel cancers were less common in oral pill users as compared to never users. This is especially relevant as there has been question mark over safety of estrogens on human health after their adverse effects were noted with estrogen replacement therapy in elderly women. In fact oral pills also increase bone mineral density and should reduce fracture rates amongst users as compared to never users.

Traditionally it is believed that oral pills may increase incidence of cervical cancer but the present study found its lower incidence in the users. However, the authors did not mention about breast cancer which many sceptics still feel may be increased with use of oral pills as most breast cancers are estrogen receptors positive and this cancer is the commonest cancer amongst women in the world.

The results of this large study are really welcome and promising to highlight long term safety of oral pills which are the most effective method of contraception and save many women's lives

from complications of unwanted pregnancies. In fact not using them causes many unwanted pregnancies especially in developing countries with unsafe abortions causing preventable maternal mortality. There is a real need to remove the various false myths about oral pills in developing countries to increase their use in which direction this study is a huge step.

Competing interests: None declared

RCGP OC study mortality increases underestimated by unknown HRT use 4 April 2010

Ellen CG Grant,
Physician and medical gynaecologist
Kingston-upon-Thames, KT2 7JU

Send response to journal:

[Re: RCGP OC study mortality increases underestimated by unknown HRT use](#)

Unfortunately the partly drug funded Royal College of General Practitioner (RCGP) contraceptive pill report makes claims of reduced mortality which are flawed and difficult to entangle.¹

Contraceptive pills cannot magically prevent deaths.

Data omissions include the following: the RCGP pill study was designed in 1968 to have 23 000 “ever” and “never” takers but deaths were flagged for 21 936 users and only in 13 168 never takers; by 1972 more pill takers had been lost than controls so more takers were added; some “never” takers were moved into the taker group; when deaths were flagged in 1977 most current use (average age 29 for 44 months) would have already stopped; information on fertility drugs or HRT (also progesterones and oestrogens) were not revealed for the whole duration of the study; some HRT use was known until 1996 but 3 out of 4 deaths occurred in the next 10 years. Although more deaths were in “never” pill takers over age 50, these women were significantly older when recruited and a larger proportion would have taken HRT which causes increases in mortality.

Deaths increased three times more in “ever” takers under age 30 than in young “never” takers. GP observed “ever” takers had significant increased mortality rates compared with “never” takers for all circulatory diseases, cerebrovascular disease, other circulatory diseases (thrombosis), and violence (perhaps reflecting previously increases in mental illness and marital break ups in “ever” takers). A much vaunted ovarian cancer reduction depended on 14 deaths in “ever” takers and 29 deaths in “never” takers and 75 deaths in each group in the full data set. Whether these women were taking fertility drugs or HRT, which can increase the risk of ovarian cancer, is unknown.^{2,3}

The study Flow Chart shows that from 1996 to 2007 “ever” pill takers in the GP observation set deaths had 10.3 times more deaths compared with 6.5 times in “never” takers. Women who left GP observation younger than age 38 had 8.7 times more deaths if “ever” users but no increase in deaths occurred in “never” takers. “Ever” takers of oral contraceptives had 2864 deaths; 1312 from all cancers including 312 breast and 258 lung cancers; 763 from circulatory diseases; and 156 deaths from violence.

Breast cancer incidence and mortality increases and decreases over the last 50 years match similar changes in progestogen plus oestrogen use.⁴

For 50 years studies have shown adverse biological effects including blood vessel and enzyme changes. In addition numerous epidemiological studies, including the prestigious Women’s Health Initiative randomised study, have confirmed that taking progestogens and oestrogens increases risks of cancers, vascular and mental diseases.⁵ Previous RCGP publications found deaths increased from breast, cervical, lung and liver cancers and vascular diseases in takers. However, most studies underestimate risks because of drop outs, losses and confusion about the effects of taking hormones for different reasons at different ages.

Hormone use for any reason does cause major public health problems. Omissions in study data give false reassurance to young women who are particularly at risk.

1 Hannaford PC, Iverson L, MacFarlane TV, et al. Mortality among contraceptive pill users: cohort evidence from Royal College of General Practitioners’ oral contraception study. *BMJ* 2010;340:c927.

2 Grant ECG. Increased risk of serous ovarian cancer following clomifene fertility treatment. http://bmj.com/cgi/eletters/338/feb05_2/b249#208597, 11 Feb 2009

3 Zhou B, Sun Q, Cong R, Gu H, Tang N, Yang L, Wang B. Hormone replacement therapy and ovarian cancer risk: a meta-analysis. *Gynecol Oncol.* 2008;108:641-51.

4 Colditz GA. Decline in breast cancer incidence due to removal of promoter: combination estrogen plus progestin. *Breast Cancer Res.* 2007;9:108.

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Competing interests: None declared

Table with data from RCGP Contraceptive Pill Flow chart. Flagged Deaths in 1996 and 2007

	Numbers of Deaths/Total women	
(Increases)	1996	2007

	Ever	Never	Ever	Never
Under GP observation in 1996	62/6538	73/3956	640 (x10.3)	478 (x6.5)
Had left GP observation age <38	74/7761	23/4154	641 (x8.7)	23 (x0)

RCGP Pill study – false mortality reduction claim

12 April 2010

Ellen CG Grant,
Physician and medical gynaecologist
Kingston-upon-Thames. KT2 7JU, UK
Send response to journal:
[Re: RCGP Pill study – false mortality reduction claim](#)

In 1968 the RCGP study was originally designed so that each Pill Taker was paired with a similar aged Control at recruitment for accuracy of future results. In 1968 the age distribution for 5 year age groups from age 15 to 45+ was very similar. The average age for both Takers and Controls was 29. In both groups about 60% of women were age <30. 1

Hannaford's Table 1 now shows that recruitment ages have been changed.2

RCGP 1968 Age <30 Takers 14 391/23 611 (61%) Controls 13 528/22 766 (59.5%)

RCGP 2007 Age <30 Takers 18 323/28 806(63.6%) Controls 8922/17 306 (51.6%)

In 2007 the full data set "at recruitment" lists 18 323 Ever users and 8922 Never users age <30. Now younger Takers outnumber younger Controls by 2 to 1. A transfer of 4000 younger Controls to the Taker group resulted in the "Never" users group becoming significantly older. An older group has a higher mortality. An older group would reach the menopause sooner be more likely to die from taking pill-type hormones as HRT. It is very misleading to rename Controls as Never users as any type of hormone use was unknown between 1996 and 2007 when most study deaths occurred.

Large scale dilution of the Taker group, with double the number of younger women than originally planned to give the most accurate results, falsely reduces overall long term mortality risks. Not recording all progesterone-type hormone use, whether taken as Pills, IUDs, creams or HRT, when 3 out of 4 deaths occurred, also makes nonsense of Hannaford's latest claim.

1 Royal College of General Practitioners. Oral contraceptives and Health. Pitman Medical, London 1974

2 Hannaford PC, Iversen L , Macfarlane TV, et al. Mortality among contraceptive pill users: cohort evidence from Royal College of General Practitioners' Oral Contraception Study BMJ 2010; 340: c927

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