Women's health

Removing organs "just in case"—is prophylactic removal of the ovaries a good thing?

Aileen Clarke, Yu Mei Chang, Klim McPherson

This papers highlights the issues and illustrates a research agenda for trying to disentangle the problems of the continuing use of an untested technbology—prophylactic oophorectomy—at the time of hysterectomy.

 $B_{(also known as ovariectomy) is}^{(also known as ovariectomy) is}$ nely as a prophylactic measure in women who are not at a known increased risk of ovarian cancer. In the UK in 2003, for example, about 41 000 women had an elective hysterectomy for benign conditions.1 Of these about 19 000 women aged less than 60 years, simultaneously had bilateral oophorectomy. Hysterectomy with bilateral oophorectomy is undertaken for a variety of conditions including; chronic pelvic pain, endometriosis, adenomyosis, uterine prolapse, and pelvic inflammatory disease. However, most women have a hysterectomy because of fibroids or menorrhagia (abnormal or heavy bleeding) and it has been estimated that in as many as 30% of these hysterectomies, oophorectomy is undertaken as an additional prophylactic measure against the possible future development of ovarian cancer.² Although these figures relate to the UK, prophylactic oophorectomy with hysterectomy for benign conditions is undertaken in many countries.3-6

Ovarian cancer is comparatively common and currently not easily treated. Some 6000 women each year in the UK develop ovarian cancer and worldwide only about 40% of women diagnosed with ovarian cancer are alive at five years.7-9 Although genetic markers for the likelihood of development of ovarian cancer exist, most women undergoing oophorectomy or ovariectomy at the time of their hysterectomy are not tested for those genetic markers. (A small number of women have a prophylactic oophorectomy usually without hysterectomy each year because of their genetic susceptibility to ovarian cancer.10) But genetic markers for ovarian cancer, while useful for considering the disease within families, are present in small percentages both in the general population and in the population of those who develop ovarian cancer, as a number of steps is required in a pathway of causality between known genetic markers and cancer.¹¹

All this suggests that currently oophorectomy may be being undertaken at an inappropriately high rate, especially in those not identified as at increased risk of disease. Oophorectomy at the time of hysterectomy certainly represents the highest population based rate of removal of any healthy organ for prophylactic reasons. (Colectomy, mastectomy, and appendicectomy are all undertaken prophylactically: but of those, only appendicectomy is also undertaken without evidence of increased susceptibility to disease, and there is some debate as to whether that is justified.¹²)

Why is prophylactic oophorectomy undertaken at the time of hysterectomy? There are three possible reasons. Firstly, ovaries are often considered unimportant once a woman's reproductive life is over; secondly, ovaries are seen as associated with the possibility of causing recurrent gynaecological symptoms (sometimes described as the retained ovary or ovarian remnant syndrome¹³); and thirdly, there is insufficient evidence available on which to base a decision, because although some work has been done, a full evaluation of the risks, costs, and benefits of prophylactic oophorectomy in the absence of genetic markers and at the time of hysterectomy has not been undertaken.14

So that proper evaluation can take place, further evidence is needed. For example, evidence is still needed on the natural history of the ovary. The ovaries do not die until a woman dies—but what functions do they fulfil postmenopausally? Androgens are produced that can be converted by aromatases into oestrogens¹⁵ but exactly how much of what kinds of hormones are produced by the ovary in the perimenopause and immediate postmenopause in the context of whether or not a woman has also had a hysterectomy, is unknown. And the relative benefits of those hormones on the cardiovascular system, the bones, or other health effects are likewise not clear. We know that ovaries tend to cease producing hormones within three to five years of a hysterectomy causing an earlier menopause than the natural age at menopause.16 17 And we know that women have a reduced likelihood of developing ovarian cancer after a hysterectomy even without a prophylactic oophorectomy-suggesting that the ability of the ovaries to continue production of ovarian hormones is compromised by hysterectomy.18

Since HRT prescription has become problematic it is not entirely clear how women should be treated after an oophorectomy.¹⁹ Particular risks and benefits for a number of common diseases with and without HRT need to be characterised for these women. The incidence of cardiovascular disease,²⁰ breast cancer,²¹ and fracture risk²² have all been reported as affected by oophorectomy and subsequent HRT and yet specific unequivocal evidence is not available to ensure that appropriate advice can be given to women for even these commonest of conditions.

The rate of hysterectomy is said to be decreasing, as newer interventions for menorrhagia and dysfunctional uterine available.23 bleeding become Simultaneously the rate of prophylactic oophorectomy with hysterectomy is also said to be decreasing.24 But there are equity issues, in that there are socioeconomic disparities in who is exposed to which surgeries.25 And a proportion of women undergoing less invasive interventions go on to have hysterectomy subsequently.²⁶ It may not therefore be possible, or prudent, just to wait until hysterectomy and with it the practice of prophylactic oophorectomy dies a natural death.

If the rate at which prophylactic oophorectomy has been undertaken until recently has been necessary to reduce the rate of ovarian cancer in the population, then means should be found to continue with ovarian removal while less invasive methods of dealing with dysfunctional uterine bleeding are found.²⁷ On the other hand, it may be wise to gather the appropriate evidence and to make a considered decision about this technology.

There are some important immediate research needs. Perhaps the most

Policy implications

There are policy implications for:

- research funders to fund definitive research on whether prophylactic oophorectomy should be undertaken at the time of hysterectomy for benign conditions.
- for health care funders or payers to consider whether prophylactic ophorectomy should be undertaken routinely under these circumstances for the populations they cover.
- for individual practitioners and patients to consider carefully choices to be made at the time of hysterectomy.

important is to elucidate the best combination of strategies to reduce the incidence of ovarian cancer. (Examples might include gathering evidence and developing models to assess population risks and benefits of: genetic screening, screening for biomarkers, screening for early disease, and removal of either one or two ovaries prophylactically at the time of gynaecological surgery). The other pressing research need is to gather evidence on the risks and benefits for common diseases (cardiovascular disease, breast cancer, and osteoporosis) affected by oophorectomy and subsequent HRT. Certainly better evidence is needed on the functioning of the ovaries after a hysterectomy.

Is prophylactic oophorectomy a public or community health issue? The answer is yes. In many countries of the world, women are undergoing an untested technology each year, with potentially serious consequences. Women on average live for 30 years after the menopause (either natural or surgical) in the UK, and large numbers of women are affected by the common conditions whose incidence and prevalence are changed by hysterectomy and oophorectomy. Viewed in terms of loss of quality adjusted life years (QALYs), even a small change in quality of life for a large number of women will translate into a lot of QALYs over a period of 30 years. Undoubtedly this is a public health issue. We need to start taking this aspect of women's health in the peri-menopause and post-menopause far more seriously.

J Epidemiol Community Health 2006;**60**:186–187. doi: 10.1136/jech.2005.035170

Authors' affiliations

A Clarke, Y M Chang, Public Health and Policy Research Unit, Barts and the London School of Medicine and Dentistry, University of London, UK; aileen.clarke@qmul.ac.uk K McPherson, Department of Obstetrics and Gynaecology, University of Oxford, UK

Correspondence to: Dr A Clarke, Public Health and Policy Research Unit, Barts and the London School of Medicine and Dentistry, University of London, UK; aileen.clarke@qmul.ac.uk

Funding: none.

Competing interests: none declared.

REFERENCES

- 1 UK Department of Health. Hospital episode
- Group and the statistical statistics of the statistics and the statistics of the statisti
- 3 Fignon A. Bilateral ovarian removal during hysterectomy: what is done and what should be done. Eur J Obstet Gynecol Reprod Biol 1998;76:201–5.
- 4 Vuorma S, Teperi J, Hurskainen R, et al. Hysterectomy trends in Finland in 1987–1995–a register based analysis. Acta Obstet Gynecol Scand 1998;77:770–6.
- 5 Progetto Menopausa Italia Study Group. Determinants of hysterectomy and oophorectomy in women attending menopause clinics in Italy. *Maturitas* 2000;**36**:19–25.
- 6 Lewis CE, Groff JY, Herman CJ, et al. Overview of women's decision making regarding elective hysterectomy, oophorectomy, and hormone replacement therapy. J Womens Health Gend Based Med 2000;9[suppl 2]:55–14.
- Ries LAG, Eisner MP, Kosary CL, et al, eds. SEER Cancer Statistics Review, 1975–2000. Bethesda, MD: National Cancer Institute. http:// seer.cancer.gov/CSR/1975_2002/ (based on Nov 2004 SEER data submission, posted to the SEER web site 2005.
- 8 Office for National Statistics. Cancer statistics registrations: registrations of cancer diagnosed in 2001. London: National Statistics, 2004.
- 9 Office for National Statistics. Mortality statistics: cause, England and Wales. London: National Statistics, 2005.

- 10 Kauff ND, Satagopan JM, Robson ME, et al. Riskreducing salpingo-oophorectomy in women with a BRCA1 or BRCA2 mutation. N Engl J Med 2002;346:1609–15.
- 11 Esashi F, Christ N, Gannon J, et al. CDKdependent phosphorylation of BRCA2 as a regulatory mechanism for recombinational repair. Nature 2005;434:598–604.
- 12 Salom EM, Schey D, Penalver M, et al. The safety of incidental appendectomy at the time of abdominal hysterectomy. Am J Obstet Gynecol 2003;189:1563–7.
- 13 Mahdavi A, Berker B, Nezhat C, et al. Laparoscopic management of ovarian remnant. Obstet Gynecol Clin North Am 2004;31:593–7.
- 14 Pell I, Dowie J, Clarke A, et al. Development and preliminary evaluation of a clinical guidance programme for the prophylactic oophorectomy decision. Quality in Health Care 2002;11:32–9.
- 15 Simpson ER. Sources of estrogen and their importance. J Steroid Biochem Mol Biol 2003;86:223–30.
- 16 Siddle N, Sarrel P, Whitehead M. The effect of hysterectomy on the age at ovarian failure: identification of a subgroup of women with premature loss of ovarian function and literature review. *Fertil Steril* 1987;47:94–100.
- 17 Oldenhave A, Jaszmann LBJ, Everaard TAM, et al. Hysterectomised women with ovarian conservation report more severe climacteric complaints than do normal climacteric women of similar age. Am J Obstet Gynecol 1993:68:765–71.
- 18 Chiaffarino F, Parazzini F, Decarli A, et al. Hysterectomy with or without unilateral oophorectomy and risk of ovarian cancer. *Gyneco I Oncol* 2005;97:318–22.
- 19 Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the women's health initiative randomized controlled trial. JAMA 2002;288:321–33.
- Hsia J, Barad D, Margolis K, et al, for Women's Health Initiative Research Group. Usefulness of prior hysterectomy as an independent predictor of Framingham risk score (The Women's Health Initiative). Am J Cardiol 2003;92:264-9.
 Beral V. Million Women Study Collaborators.
- 21 Beral V. Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the million women study. *Lancet* 2003;362:419–27.
- 22 Melton LJ 3rd, Khosla S, Malkasian GD, et al. racture risk after bilateral oophorectomy in elderly women. J Bone Miner Res 2003;18:900–5.
- 23 Reid PC, Mukri F. Trends in number of hysterectomies performed in England for menorrhagia: examination of health episode statistics, 1989 to 2002–3. BMJ 2005;330:938–9.
- 24 Chan LY, Yuen PM. Influence of the Women's Health Initiative trial on the practice of prophylactic oophorectomy and the prescription of estrogen therapy. (Letter). *Fertil Steril* 2004;81:1699–700.
- 25 Kuh D, Stirling S. Socioeconomic variation in admission for diseases of female genital system and breast in a national cohort aged 15–43. BMJ 1995;311:840–3.
- 26 Clarke A, Judge A, Herbert A, et al. Readmission to hospital 5 years after hysterectomy or endometrial resection in a national cohort study. Quality and Safety in Health care 2005;1:41–7.
- Quality and Safety in Health care 2005;1:41-7.
 Sizzi O, Paparella P, Bonito C, et al. Laparoscopic assistance after vaginal hysterectomy and unsuccessful access to the ovaries or failed uterine mobilization: changing trends. Journal of the Society of Laparoendoscopic Surgeons 2004;8:339-46.