# **External article**

## Ovarian cancer population screening and mortality after long-term follow-up in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial

This page provides information about a publication describing research funded by the Health Technology Assessment programme under award number 16/46/01, which has been published in a third-party journal. For information about copyright and reproduction of the original publication, please see the publisher's website.

## **Publication**

Menon U, Gentry-Maharaj A, Burnell M, Singh N, Ryan A, Karpinskyj C, *et al.* Ovarian cancer population screening and mortality after long-term follow-up in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. *Lancet* 2021;**397**:2182–93. https://doi.org/10.1016/S0140-6736(21)00731-5

## Abstract

#### Summary

#### Background

Ovarian cancer continues to have a poor prognosis with the majority of women diagnosed with advanced disease. Therefore, we undertook the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) to determine if population screening can reduce deaths due to the disease. We report on ovarian cancer mortality after long-term follow-up in UKCTOCS.

#### Methods

In this randomised controlled trial, postmenopausal women aged 50–74 years were recruited from 13 centres in National Health Service trusts in England, Wales, and Northern Ireland. Exclusion criteria were bilateral oophorectomy, previous ovarian or active non-ovarian malignancy, or increased familial ovarian cancer risk. The trial management system confirmed eligibility and randomly allocated participants in blocks of 32 using computer generated random numbers to annual multimodal screening (MMS), annual transvaginal ultrasound screening (USS), or no screening, in a 1:1:2 ratio. Follow-up was through national registries. The primary outcome was death due to ovarian or tubal cancer (WHO 2014 criteria) by June 30, 2020. Analyses were by intention to screen, comparing MMS and USS separately with no screening using the versatile test. Investigators and participants were aware of screening type, whereas the outcomes review committee were masked to randomisation group. This study is registered with ISRCTN, 22488978, and ClinicalTrials.gov, NCT00058032.

#### Findings

Between April 17, 2001, and Sept 29, 2005, of 1243282 women invited, 202638 were recruited and randomly assigned, and 202562 were included in the analysis:  $50625 (25 \cdot 0\%)$  in the MMS group,  $50623 (25 \cdot 0\%)$  in the USS group, and  $101314 (50 \cdot 0\%)$  in the no screening group. At a median follow-up of  $16 \cdot 3$  years (IQR  $15 \cdot 1 - 17 \cdot 3$ ), 2055 women were diagnosed with tubal or ovarian cancer:  $522 (1 \cdot 0\%)$  of 50625 in the MMS group,  $517 (1 \cdot 0\%)$  of 50623 in the USS group, and  $1016 (1 \cdot 0\%)$  of 101314 in the no screening group. Compared with no screening, there was a  $47 \cdot 2\%$  (95% CI  $19 \cdot 7$  to  $81 \cdot 1$ ) increase in stage I and  $24 \cdot 5\%$  ( $-41 \cdot 8$  to  $-2 \cdot 0$ ) decrease in stage IV disease incidence in the MMS group than in the no screening group, whereas the incidence of stage III or IV disease was  $10 \cdot 2\%$  ( $-21 \cdot 3$  to  $2 \cdot 4$ ) lower. 1206 women died of the disease: 296 ( $0 \cdot 6\%$ ) of 50625 in the MMS group, 291 ( $0 \cdot 6\%$ ) of 50623 in the USS group, and  $619 (0 \cdot 6\%)$ 

of 101314 in the no screening group. No significant reduction in ovarian and tubal cancer deaths was observed in the MMS (p=0.58) or USS (p=0.36) groups compared with the no screening group.

#### Interpretation

The reduction in stage III or IV disease incidence in the MMS group was not sufficient to translate into lives saved, illustrating the importance of specifying cancer mortality as the primary outcome in screening trials. Given that screening did not significantly reduce ovarian and tubal cancer deaths, general population screening cannot be recommended.

### Funding

National Institute for Health Research, Cancer Research UK, and The Eve Appeal.

### Funding

This publication was funded by the Health Technology Assessment programme as a part of award number 16/46/01.

This article reports on one component of the research award Long term impact of screening on ovarian cancer mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS). For more information about this research please view the award page [https://fundingawards.nihr.ac.uk/award/16/46/01]

## DOI

https://doi.org/10.1016/S0140-6736(21)00731-5

2