Jacobs IJ, Menon U, Ryan A, et al. **Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial.** Lancet. 2015 Dec 16. pii: S0140-6736(15)01224-6. doi: 10.1016/S0140-6736(15)01224-6. *(Original)* PMID: 26707054

BACKGROUND: Ovarian cancer has a poor prognosis, with just 40% of patients surviving 5 years. We designed this trial to establish the effect of early detection by screening on ovarian cancer mortality.
METHODS: In this randomised controlled trial, we recruited postmenopausal women aged 50-74 years from 13 centres in National Health Service Trusts in England, Wales, and Northern Ireland. Exclusion criteria were previous bilateral oophorectomy or ovarian malignancy, increased risk of familial ovarian cancer, and active non-ovarian malignancy. The trial management system confirmed eligibility and randomly allocated participants in blocks of 32 using computer-generated random numbers to annual multimodal screening (MMS) with serum CA125 interpreted with use of the risk of ovarian cancer algorithm, annual transvaginal ultrasound screening (USS), or no screening, in a 1:1:2 ratio. The primary outcome was death due to ovarian cancer by Dec 31, 2014, comparing MMS and USS separately with no screening, ascertained by an outcomes committee masked to randomisation group. All analyses were by modified intention to screen, excluding the small number of women we discovered after randomisation to have a bilateral oophorectomy, have ovarian cancer, or had exited the registry before recruitment. Investigators and participants were aware of screening type. This trial is registered with ClinicalTrials.gov, number NCT00058032.
FINDINGS: Between June 1, 2001, and Oct 21, 2005, we randomly allocated 202 638 women: 50 640 (25.0%) to

MMS, 50 639 (25.0%) to USS, and 101 359 (50.0%) to no screening. 202 546 (>99.9%) women were eligible for analysis: 50 624 (>99.9%) women in the MMS group, 50 623 (>99.9%) in the USS group, and 101 299 (>99.9%) in the no screening group. Screening ended on Dec 31, 2011, and included 345 570 MMS and 327 775 USS annual screening episodes. At a median follow-up of 11.1 years (IQR 10.0-12.0), we diagnosed ovarian cancer in 1282 (0.6%) women: 338 (0.7%) in the MMS group, 314 (0.6%) in the USS group, and 630 (0.6%) in the no screening group. Of these women, 148 (0.29%) women in the MMS group, 154 (0.30%) in the USS group, and 347 (0.34%) in the no screening group had died of ovarian cancer. The primary analysis using a Cox proportional hazards model gave a mortality reduction over years 0-14 of 15% (95% CI -3 to 30; p=0.10) with MMS and 11% (-7 to 27; p=0.21) with USS. The Royston-Parmar flexible parametric model showed that in the MMS group, this mortality effect was made up of 8% (-20 to 31) in years 0-7 and 23% (1-46) in years 7-14, and in the USS group, of 2% (-27 to 26) in years 0-7 and 21% (-2 to 42) in years 7-14. A prespecified analysis of death from ovarian cancer of MMS versus no screening with exclusion of prevalent cases showed significantly different death rates (p=0.021), with an overall average mortality reduction of 20% (-2 to 40) and a reduction of 8% (-27 to 43) in years 0-7 and 28% (-3 to 49) in years 7-14 in favour of MMS.

INTERPRETATION: Although the mortality reduction was not significant in the primary analysis, we noted a significant mortality reduction with MMS when prevalent cases were excluded. We noted encouraging evidence of

a mortality reduction in years 7-14, but further follow-up is needed before firm conclusions can be reached on the efficacy and cost-effectiveness of ovarian cancer screening.
FUNDING: Medical Research Council, Cancer Research UK, Department of Health, The Eve Appeal.