**Influence and management of conflicts of interest in randomised clinical trials**

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*Cite this as: BMJ 2020;371:m3764
Find this at: http://dx.doi.org/10.1136/bmj.m3764*

**Study question** What are clinical trial researchers’ experiences regarding how they perceive conflicts of interests having unduly influenced trials, and what management strategies were used to minimise any potential influence?

**Methods** In a qualitative study, 20 experienced clinical trial researchers, with methodological or statistical expertise who differed by geographical location, educational background, and experience with different types of funders, were interviewed. The interview candidates were identified based on searches in Web of Science and snowball sampling. All interviews were conducted by telephone, recorded, transcribed verbatim, imported to NVivo 12, and analysed by systematic text condensation.

**Study answer and limitations** Perceived undue influence of conflicts of interest involved commercial funders (eg, drug and device companies) and non-commercial funders (eg, government agencies). Examples of undue influence were choice of comparator, manipulation of the randomisation process, prematurely stopping trials, fabrication of data, blocking access to data, and spin (eg, overly favourable interpretation of the results). Financial conflicts of interest related to non-commercial funders (eg, government health agencies with a political agenda) were considered important by some interviewees. The interviewees had used many strategies for managing conflicts of interest: disclosure procedures, exclusion of the funder from design and analysis, independent committees, contracts ensuring complete access to the data, and no restriction by the funder on analysis and reporting. The study could not establish how often the reported examples and events occur.

**What this study adds** This study describes how trial researchers perceive conflicts of interest having unduly influenced clinical trials. Considerable variability was found in researchers’ understanding of what are conflicts of interests and when they should be reported.

**Funding, competing interests, and data sharing**

The study received no funding.
The authors have no competing interests.
To preserve the anonymity of the interviewees, the transcribed interviews are not available for sharing.

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Covid-19: risks to healthcare workers and their families

ORIGINAL RESEARCH Nationwide linkage cohort study

Risk of hospital admission with coronavirus disease 2019 in healthcare workers and their households

Shah ASV, Wood R, Gribben C, et al

Cite this as: BMJ 2020;371:m3582

Find this at: http://dx.doi.org/10.1136/bmj.m3582

Study question What is the risk of hospital admission with coronavirus disease 2019 (covid-19) in patient facing and non-patient facing healthcare workers and their household members?

Methods This national record linkage study compared the risk of covid-19 related hospital admission among 158 445 healthcare workers (aged 18-65 years), their household members (n=229 905), and other members of the general population during the peak period for covid-19 infection in Scotland (1 March to 6 June 2020). For patient facing healthcare workers, the risk was also compared for “front door” (eg, paramedics or workers in acute receiving specialties), intensive care, non-intensive care aerosol generating procedures, and other settings.

Study answer and limitations Healthcare workers and their households contributed a sixth of all admissions with covid-19 in this age group (360/2097; 17.2%) in Scotland. The overall absolute risk was low, but compared with non-patient facing healthcare workers and their households it was threefold and twofold higher, respectively, among patient facing healthcare workers (3.30, 2.13 to 5.13) and their households (1.79, 1.10 to 2.91). Healthcare workers in front door roles were at highest risk. Healthcare workers were assigned into categories on the basis of their job titles and settings, not self-reported activity, so some misclassification is likely to have occurred, diluting differences between the groups.

What this study adds Findings from the “first wave” in Scotland show that healthcare workers overall are at low risk of admission to hospital with covid-19. However, those in patient facing roles, especially front door roles, are at an increased relative risk of admission, as are their households. Those in non-patient facing roles had similar risks to the general population. These findings should inform decisions about the organisation of health services, the use of personal protective equipment, and staff redeployment.

Funding, competing interests, and data sharing Funding was from the British Heart Foundation and the Wellcome Trust. No competing interest reported. The analytical code is available at https://github.com/ChronicDiseaseEpi/hcw.

COMMENTARY Mistakes made in the first wave must not be repeated in the second

Since the beginning of the coronavirus disease 2019 (covid-19) pandemic, healthcare workers have shown a remarkable resilience and professional dedication despite a fear of becoming infected and infecting others. In this issue, Shah and colleagues now report robust and concerning findings regarding the risks of covid-19 among healthcare workers and their households.

In a large register based cohort study, the authors compared the risk of covid-19 related hospital admission between patient facing and non-patient facing workers, their household members, and the general population. Absolute risks were low, but during the first three months of the pandemic, patient facing healthcare workers were three times more likely to be admitted to hospital with covid-19 than non-patient facing healthcare workers. Risk was doubled among household members of patient facing workers.

Previous work reported similar risks for covid-19 among healthcare workers, but the new study provides the most comprehensive estimate to date of the risk of more serious disease, and it is the first to report risk to household members. The reasons for the observed increase in risk—likely multifactorial—need to be explored to help to guide safety improvements in healthcare settings.

Overstretched

During the first wave of the pandemic, overstretched healthcare systems left healthcare workers in hard hit countries struggling with long working hours, fatigue, and extreme psychological stress. Rapidly vanishing supplies, national lockdowns, and a feeding frenzy on the open market for personal protective equipment (PPE) led to shortages. Healthcare workers often had to care for patients with suspected or confirmed covid-19 infection without proper training or adequate PPE. This contributed to an increased risk to healthcare workers during the initial phase.

Most countries struggled with insufficient testing capacity in the first months of the pandemic, which hampered early detection of emerging outbreaks and implementation of infection control measures. Increasing experience now suggests that every suspected healthcare associated infection should trigger a bundle of immediate infection control measures, including extensive screening for SARS-CoV-2, quarantining of all patients on the affected ward, physical distancing between personnel, and use of reinforced PPE during all contact with patients on the affected ward.

Most, but not all, studies report increased risks for healthcare workers caring for patients with covid-19. Working in intensive care units is not associated with an increased risk of infection, possibly owing to the protection afforded by high level PPE or to the decrease in infectivity that occurs in the later stages of the illness, even among critically ill patients. The greatest risk to healthcare workers may be their
own colleagues or patients in the early stages of unsuspected infections when viral loads are high.\textsuperscript{12}

Most studies to date, including Shah and colleagues’ study, have evaluated risks to healthcare workers during the early phases of the pandemic. Advances since then may have reduced the risks, although further confirmatory studies are needed. Such advances include greater knowledge of transmission dynamics and the impact of asymptomatic and pre-symptomatic infections;\textsuperscript{16} better access to effective PPE; improved testing capabilities; optimised triage systems; implementation of new infection control measures such as continuous mask use in hospitals;\textsuperscript{17,18} and faster outbreak alerts and responses.

High quality prospective studies evaluating new prevention and control practices will be important to guide improvements in our approach to protecting healthcare workers and their families,\textsuperscript{19} including those from ethnic minority communities who have the highest risks of infection and poor outcomes, widening workplace inequality.\textsuperscript{3}

The international community must support efforts by the World Health Organization to secure adequate supplies of PPE and covid-19 tests for low and middle income countries. An effective vaccine, if and when available, must be distributed fairly, and healthcare workers must be prioritised globally. In accordance with United Nations Sustainable Development Goals, we must ensure the protection and security of all healthcare workers in all settings.\textsuperscript{20}

Cite this as: BMJ 2020;371:m3944

Find the full version with references at http://dx.doi.org/10.1136/bmj.m3944
Study question
What are the risks of breast cancer in women using different types of hormone replacement therapy (HRT)?

Methods
Data were extracted from the two largest databases in UK primary care, QRResearch and Clinical Practice Research Datalink (CPRD), both of which have links to hospital, mortality, cancer registry, and social deprivation records. Identical case-control studies were run on each extraction and the findings combined. Overall, between 1998 and 2018, 98,611 incident cases of breast cancer were diagnosed in women aged 50 to 79 years, and these cases were matched to 457,498 female controls by age, general practice, and date of diagnosis (index date). Data for all prescriptions for HRT prior to one year before the index date were analysed. Recent use was defined as exposure within the past five years and long term use as exposure of five years’ duration or more. Findings were adjusted for personal characteristics, smoking status, alcohol consumption, relevant comorbidities, family history, and other prescribed drugs.

Study answer and limitations
Compared with never use, in recent users (<5 years; prescription >1 year and <5 years before the index date) with long term use (≥5 years; last prescription ended before that period), oestrogen only therapy and combined oestrogen and progesterone therapy were both associated with increased risks of breast cancer (adjusted odds ratio 1.15 (95% confidence interval 1.09 to 1.21) and 1.79 (1.73 to 1.85), respectively). For combined progestogens, the increased risk was highest for norethisterone (1.88, 1.79 to 1.99) and lowest for dydrogesterone (1.24, 1.03 to 1.48). The increases varied across progestogen types, patient age, and body mass index categories. In recent oestrogen only users, between three (in younger women) and eight (in older women) extra cases per 10,000 women years would be expected, and in oestrogen-progestogen users between nine and 36 extra cases per 10,000 women years.

Incident breast cancer rate per 10,000 women years for women unexposed and exposed for different durations to different HRTs by age range. Rates were estimated using rates in unexposed populations multiplied by adjusted odds ratios derived from subgroup analyses for different age categories.

For past oestrogen-progestogen users, the results would suggest between two and eight extra cases per 10,000 women years. The study’s main limitations derive from imprecise indications for prescribing and a lack of information on patient adherence to treatment.

What this study adds
The findings suggest increased risks of breast cancer associated with longer term HRT use, and a noticeable decline in risks once treatment is stopped.

Funding, competing interests, and data sharing
Details of funding, data sharing, and competing interests are in the full paper on bmj.com.