research

Effects of genetic testing in male infertility p 33

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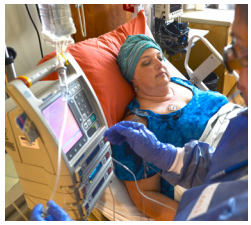
Food preservatives and risk of cancer p 36



Intensified chemotherapy in breast cancer p 38

ORIGINAL RESEARCH Multicentre, open label, randomised controlled trial

Preimplantation genetic testing for aneuploidy versus no genetic testing in couples undergoing intracytoplasmic sperm injection for severe male infertility

Lin X, Wu D, Zhang C, et al

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Find this at doi: 10.1136/bmj-2025-084050

Study question Does preimplantation genetic testing for aneuploidy (PGT-A) improve live birth rates in couples with severe male factor infertility undergoing intracytoplasmic sperm injection (ICSI)?

Methods A multicentre randomised controlled trial, conducted across four Chinese reproductive medicine centres, randomised 450 couples with severe male factor infertility (1:1) to ICSI with PGT-A (n=225) or ICSI without PGT-A (n=225). The PGT-A group received ICSI with blastocyst genetic testing before transfer, whereas the no PGT-A group received ICSI without. Primary outcomes were live birth after the first embryo transfer and cumulative live birth up to three transfer cycles within 12 months after randomisation.

Study answer and limitations 109 (48.4%) and 104 (46.2%) couples in the PGT-A and no PGT-A groups, respectively, had a live birth after the first embryo transfer (odds ratio 1.09 (95% confidence interval (CI) 0.76 to 1.58), P=0.64). Cumulative live birth rates per woman were 60.4% (136/225) and 60.9% (137/225) in the PGT-A and no PGT-A groups, respectively (odds ratio 0.98, 95% CI 0.67 to 1.43, P=0.92). The PGT-A group had a significantly lower pregnancy loss after the first embryo transfer (13 (5.8%) *v* 43 (19.1%); 0.26 (0.14 to 0.50), P<0.001) and cumulative pregnancy loss (25 (11.1%) *v* 51 (22.7%); 0.43 (0.25 to 0.72), P=0.001) than the no PGT-A group. However, further studies are needed with longer follow-up and populations yielding more embryos.

What this study adds This study found no improvement in the live birth rates but a lower rate of pregnancy loss with application of PGT-A for couples with severe male factor infertility undergoing ICSI.

Funding, competing interests, and data sharing Mainly supported by grants from the National Natural Science Foundation of China (82088102). Author BWM has received consultancy, travel support, and research funding from Merck, and consultancy fees from Organon and Norgine. BWM holds stock in ObsEva. Deidentified individual data will be available on request.

Study registration ClinicalTrials.gov NCT02941965.

Weight regain after cessation of GLP-1 drugs

ORIGINAL RESEARCH Systematic review and meta-analysis

Weight regain after cessation of medication for weight management

West S, Scragg J, Aveyard P, et al

Cite this as: *BMJ* 2026;392:e085304
Find this at doi: 10.1136/bmj-2025-085304

Study question What is the rate of weight regain after stopping weight management medication (WMM) in adults with overweight or obesity?

Methods This review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. Medline, Embase, PsycINFO, CINAHL, Cochrane, Web of Science, and trial registries were searched from inception until February 2025 for randomised controlled trials, non-randomised trials, and observational studies that included WMM (≥8 weeks) with follow-up for ≥4 weeks after cessation of WMM in adults (≥18 years) with overweight or obesity. Data were analysed using mixed effect, meta-regression, and time-to-event models. Weight regain after cessation of WMM was compared with that reported after cessation of behavioural weight management programmes. The primary outcome was rate of weight regain from baseline. The secondary outcome was associated changes in cardiometabolic markers: glycated haemoglobin, fasting glucose, total cholesterol, triglycerides, and systolic and diastolic blood pressure.

Study answer and limitations Overall, 37 studies (63 intervention arms, 9341 participants) were included. The average monthly rate of weight regain was 0.4 kg (95% confidence interval 0.3 to 0.5) (mixed model 0.3 kg (0.2 to 0.4) monthly versus control in randomised controlled trials). All cardiometabolic markers were projected to return to baseline within 1.4 years after cessation of WMM. The monthly rate of weight regain was faster after WMM than after behavioural weight management programmes (by 0.3 kg, 0.22 to 0.34), independent of initial weight loss. Key limitations included the limited number of studies using newer and more effective incretin mimetic treatments and the short follow-up duration after cessation of treatment.

What this study adds This review found that cessation of WMM was followed by rapid weight regain and reversal of beneficial effects on cardiometabolic markers. Regain after WMM was faster than after behavioural weight management programmes.

COMMENTARY Weight management drugs are no magic bullets for treating obesity

Obesity is one of the major public health and clinical concerns globally, including in industrialised countries, as well as lower middle income countries such as India and Egypt. For example, the prevalence of obesity among adults has reached 40.3% in the US[1] and 26.2% in the UK.[2] Obesity and excess weight gain predispose people to an increased risk of developing numerous chronic diseases, including type 2 diabetes, cardiovascular conditions, and certain types of cancer, along with decline in cognitive function, dementia, and premature death.[3]

Unfortunately, obesity is not a disease that can be easily treated and managed. Numerous dietary and lifestyle modifications are recommended to help clinicians manage this condition in patients. It is, however, well known that the effects vary among individuals, and weight regain is almost inevitable for most people who initially lose weight. Procedures such as bariatric surgery seem to be more effective in achieving substantial, sustained weight loss, although the invasive nature of such surgeries and other concerns limit their application for the treatment of obesity.[4]

The rise of GLP-1s

More recently, medications such as glucagon-like peptide-1 (GLP-1) receptor agonists have gained popularity as the preferred drug treatments for obesity and related conditions. The efficacy of these medications has been demonstrated in clinical trials, which collectively showed that, on average, the use of GLP-1 receptor agonists may lead to a 4.6 kg weight loss or >2 unit reduction of body mass index.[5] Although the efficacy of these medications is highly encouraging, the consequences of the cessation of treatment have not been previously systematically reviewed, until the systematic review and meta-analysis by West and colleagues.[6] This is a timely investigation because, as the authors pointed out, real world observations suggested that a large proportion of people would discontinue use of a GLP-1 receptor agonist within 12 months of initiation.[7] The results from West and colleagues' meta-analysis indicated that, after an average of 39 weeks' treatment, cessation led to 0.4 kg/month weight regain, resulting in a

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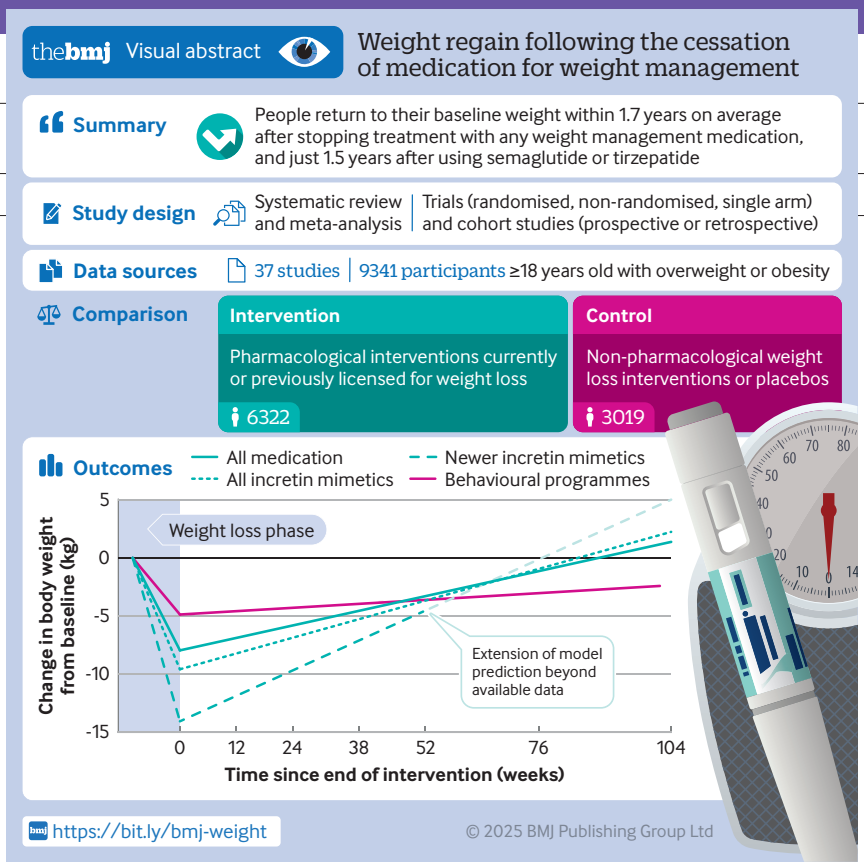

Funding, competing interests, and data sharing This project was funded in part by the National Institute of Health and Care Research Oxford Biomedical Research Centre. See full paper on bmj.com for competing interests. Data may be made available to investigators upon request by email to the corresponding author.

Systematic review registration PROSPERO CRD42024532069.

RETRACTION

Intraosseous versus intravenous vascular access in upper extremity among adults with out-of-hospital cardiac arrest: cluster randomised clinical trial (VICTOR trial)

This research article by Ko and colleagues has been retracted by the journal owing to problems with randomisation and allocation that may affect the validity of the paper's findings. For more details please go to: doi.org/10.1136/bmj-2024-079878

body weight that would return to baseline values in less than two years.

The results are not surprising given that it is well documented that reduced adherence to, or cessation of, dietary and lifestyle interventions leads to similar patterns of weight regain. Nevertheless, the study findings casted doubt on the notion that GLP-1 receptor agonists are a perfect cure for obesity. Issues such as high costs, side effects, and the inconvenience of injections are among some common reasons for discontinuing the medications.[7 8] How shall we deal with the weight regain after treatment is discontinued? One strategy is perhaps to switch to healthy diets and healthy lifestyles that have been robustly and consistently proven to be effective in preventing excess weight regain in observational studies with extended follow-up,[9] although further research is needed to study weight regain in individuals who adopt a heathier lifestyle after the cessation of GLP-1 receptor agonists.

Healthy dietary and lifestyle practices should remain the foundation for obesity treatment and management

Lasting benefits

Considerable weight loss, even if followed by weight regain, can still lead to beneficial long term consequences for people living with obesity.[10] Participants in the Diabetes Prevention Program trial achieved 5-7% weight loss through a structured healthy lifestyle intervention.[11] Even though the lifestyle intervention group eventually regained weight, the cumulative incidence of developing diabetes was lower in the lifestyle intervention group compared with the placebo group. In observational studies, individuals with obesity who intentionally lost ≥4.5 kg of body weight through various strategies, ranging from dietary modifications to commercial weight loss programmes, had a statistically significantly lower incidence of diabetes than their counterparts without weight loss attempts.[12] One caveat, however, is that individuals in the healthy body mass index range (18.5-24.9), when intentionally losing weight through these strategies (except for exercise), had an increased risk of developing diabetes compared with their counterparts who did not seek to lose weight. This phenomenon is probably due to the mechanism of "fat overshooting," whereby individuals with a healthy body mass index lose more lean mass than people with obesity and, upon regaining weight, experience a faster increase in fat mass than lean mass.[13]

GLP-1 receptor agonists should not be relied on as a magic cure for treating obesity. While considerable weight loss, even if temporary, may still bring some health benefits for those with obesity, people using GLP-1 receptor agonists should be aware of the high discontinuation rate and the consequences of cessation of medications. Healthy dietary and lifestyle practices should remain the foundation for obesity treatment and management, with medications such as GLP-1 receptor agonists used as adjuncts. Such practices not only help prevent excess weight gain but can also lead to numerous health benefits that go beyond weight control. Effective public health measures, such as taxation on sugary beverages, clear food labelling, and subsidies for fresh fruit and vegetables, should be in place to facilitate the adherence and improvement of diet quality.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.r2586

Preservatives and risk of cancer

ORIGINAL RESEARCH Emulation of a target trial

Intake of food additive preservatives and incidence of cancer

Hasenböhler A, Javaux G, Payen de la Garanderie M, et al

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Find this at doi: 10.1136/bmj-2025-084917

Study question What is the association between long term intake of food preservatives and cancer incidence?

Methods This study included 105 260 adults (78.7% women) from the French NutriNet-Santé prospective cohort, 2009-23. Dietary intakes, including industrial food brands, were assessed using repeated 24 hour dietary records. Cumulative time dependent intake of preservatives was evaluated through multiple composition databases and quantification of additive doses by ad hoc laboratory assays in food products for the most frequently consumed additive-food pairs. Multivariable proportional hazards Cox models adjusted for potential confounders characterised the associations between intake of preservatives (three categories: defined as sex specific thirds if preservative was consumed by at least a third of participants, otherwise defined as non-consumers and lower or higher consumers separated by the sex specific median) and cancer incidence.

Study answer and limitations Participants completed a mean of 21 (standard deviation (SD) 18) dietary records. During a mean follow-up of 7.57 (SD 4.56) years) 4226 participants received a diagnosis of incident cancer (1208 breast, 508 prostate, 352 colorectal, and 2158 other cancers). Higher intakes of several preservatives were associated with higher cancer incidence: total non-antioxidants with overall cancer (hazard ratio for higher consumers versus non-consumers or lower consumers 1.16 (95% confidence interval (CI) 1.07 to 1.26)); absolute risk of cancer at age 60 years, respectively, (13.3%, 12.1%) and breast cancer (1.22 (1.05 to 1.41); 5.7%, 4.8%); total sorbates, specifically potassium sorbate, with overall cancer (1.14 (1.04 to 1.24); 13.4%, 11.8%) and breast cancer (1.26 (1.07 to 1.49); 5.7%, 4.6%); total sulfites with overall cancer (1.12 (1.02 to 1.24); 13.4%, 11.9%); potassium metabisulfite with overall cancer (1.11 (1.03 to 1.20); 13.5%, 12.0%) and breast cancer (1.20 (1.04 to 1.38); 5.7%, 4.9%); sodium nitrite with prostate cancer (1.32 (1.02 to 1.70); 4.2%, 3.4%); potassium nitrate with overall cancer (1.13 (1.05 to 1.23); 14.0%, 12.0%) and breast cancer (1.22 (1.05 to 1.41); 5.9%, 4.8%); total acetates with overall cancer (1.15 (1.06 to 1.25); 14.3%, 12.2%) and breast cancer (1.25 (1.07 to 1.45); 6.1%, 4.9%); acetic acid with overall cancer (1.12 (1.01 to

COMMENTARY Potential carcinogenic effects of preservative food additives require further validation

Preservative food additives are extensively used in the modern food industry to extend shelf life by inhibiting microbial growth and slowing chemical changes that lead to spoilage.[1] Growing concerns have emerged about the potential health effects of some preservatives. For example, experimental studies have shown that nitrates and nitrites (preservatives added to processed meats) can be converted endogenously to N-nitroso compounds—proven carcinogens in animals and potential carcinogens in humans.[2] Recognising the risks, the European Food Safety Authority has established acceptable daily intake levels for nitrates and nitrites.[3] However, epidemiological evidence linking preservative additives to cancer risk remains scarce, largely because of limited data on the specific industrial food products consumed and the considerable variation in additive levels across brands.

Findings from NutriNet-Santé may prompt regulatory agencies to revisit existing policies

In this context, Hasenböhler and colleagues comprehensively examined the association between exposure to preservative food additives and the risk of cancer in a linked study among 105 260 adults in NutriNet-Santé, a large prospective cohort study in France.[4] Total intake of non-antioxidant preservatives was associated with a modestly increased risk of overall cancer (hazard ratio of 1.16 comparing highest versus lowest sex specific thirds of consumption). A major strength of this study was its detailed assessment of preservative intake, through repeated 24 hour dietary records linked dynamically to food composition databases and supplemented by ad hoc laboratory assays. Adjustment for nutritional profiles, preservatives from natural sources, and other food additives associated with cancer[5 6] enabled a clearer assessment of the independent association of preservative additives. However, given the modest increased risk estimates, causality cannot be established and unmeasured or residual confounding cannot be ruled out, especially considering the strong correlations between some preservatives and their food vectors. For example, nitrites and nitrates were consumed mainly through processed meats, whereas sulfites were consumed predominantly from alcoholic beverages—both classified as carcinogenic to humans.[7 8] It is uncertain to what extent the observed associations (hazard ratio 1.32 between sodium nitrite and prostate cancer, 1.22 between potassium nitrate and breast cancer) may be attributed to other constituents and metabolites of processed meat (eg, heterocyclic amines and polycyclic aromatic hydrocarbons) and alcohol beverages (eg, acetaldehyde) implicated in carcinogenesis.[9-11]

Natural is better

Rising consumer demand for "more natural" preservation methods has driven a shift from artificial towards natural alternatives.[1] In Hasenböhler and colleagues' study, the natural preservatives assessed were limited to a few compounds: plant derived (eg, rosemary extract), animal derived (eg, lysozyme), and microorganism derived (eg, nisin). The authors reported an inverse association between rosemary extract and colorectal

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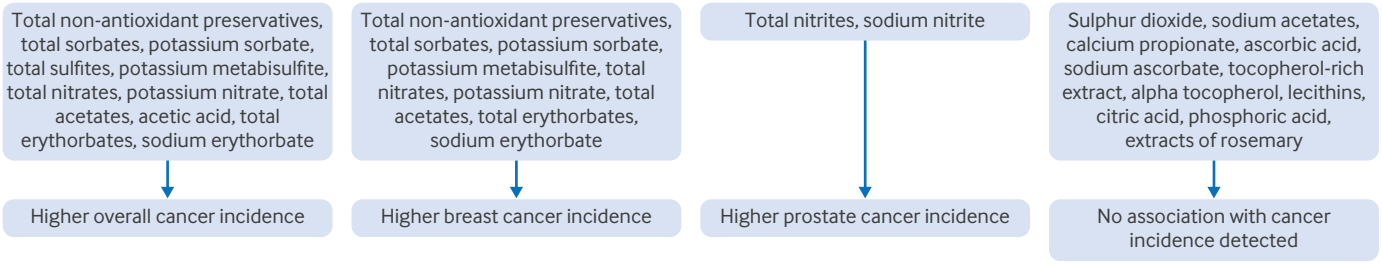

Summary of main associations between preservative food additives and cancer incidence

1.25); 14.4%, 12.4%); and sodium erythorbate with overall cancer (1.12 (1.04 to 1.22); 13.5%, 11.9%) and breast cancer (1.21 (1.04 to 1.41); 5.7%, 4.8%). Although these findings were adjusted for a wide range of potential confounders and were robust to multiple sensitivity analyses, residual confounding cannot be entirely ruled out. Additional epidemiological and experimental studies are needed to confirm these results.

What this study adds Multiple positive associations between intake of preservatives widely used in industrial foods and higher cancer incidence (overall, breast, and prostate) were observed in this large prospective cohort.

If confirmed, these new data call for the re-evaluation of regulations governing the use of preservatives by the food industry, to improve consumer protection. In the meantime, the findings support recommendations for consumers to favour freshly made, minimally processed foods.

Funding, competing interests, and data sharing The NutriNet-Santé study is funded by French and European public grants and institutions. No competing interests declared. Researchers from public institutions can submit a request to have access to the data for strict reproducibility analysis (systematically accepted) or for a new collaboration (reviewed by the steering committee of the NutriNet-Santé study) to collaboration@etude-nutrinet-sante.fr.

Study registration ClinicalTrials.gov NCT03335644.

CORRECTION

Analysis of peer reviewers' response to invitations by gender and geographical region: cohort study of manuscripts reviewed at 19 biomedical journals before and during covid-19 pandemic

This research paper by Ben Messaoud and colleagues (*BMJ* 2023;381:e075719, published in print issue of 17 June 2023) has a correction notice. For more details please go to doi:10.1136/bmj-2023-075719.

cancer, although based on limited cases. A prior analysis of the same database[12] found that only nitrite and nitrate additives were associated with cancer risk, with no associations observed for total nitrite or nitrate intake or for intakes from natural sources. The authors hypothesised that the high antioxidant content of vegetables may reduce the carcinogenic potential of naturally occurring nitrites and nitrates. It remains unclear whether synthetic preservatives are more harmful than natural ones.

Hasenböhler and colleagues' study was constrained by limited statistical power for certain site specific cancers, such as colorectal cancer. Future research priorities include conducting larger and longer term prospective studies in diverse populations; randomised trials exploring dietary modifications, such as manipulating the intake of preservatives; and mechanistic investigations to elucidate the

biological pathways through which potential risks may arise. A promising direction is to integrate multi-omics approaches such as the metabolome[13] and microbiome[14 15] with traditional dietary assessments to identify sensitive and specific biomarkers of preservative intakes.[16] Moreover, because various additives and food chemicals often coexist in processed foods, further epidemiological and experimental studies are needed to elucidate the combined and interactive effects of preservatives with other chemical components.

Balance is needed

From a policy perspective, preservatives offer clear benefits by extending shelf life and lowering food costs, which can be particularly important for populations with lower incomes. However, the widespread and often insufficiently monitored use of these additives, with uncertainties of their long term health effects, call for a more balanced approach. Currently, the US Food and Drug Administration evaluates the premarket safety of food additives, but a formal approach for reviewing food additives already present in the food supply is lacking.[17] Findings from NutriNet-Santé may prompt regulatory agencies to revisit existing policies, such as setting stricter limits on use, requiring clearer labelling, and mandating disclosure of additive contents. Furthermore, collaborative global monitoring initiatives, similar to those implemented for trans fatty acids and sodium, could also support evidence based risk assessments and guide reformulation by the food industry.[18 19] At the individual level, public health guidance is already more definitive about the reduction of processed meat and alcohol intake, offering actionable steps even as evidence on the carcinogenic effects of preservatives is evolving.

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Find the full version with references at http://dx.doi.org/10.1136/bmj.r2613

ORIGINAL RESEARCH Phase 3 randomised trial

Effect of adjuvant carboplatin intensified chemotherapy versus standard chemotherapy on survival in women with high risk, early stage, triple negative breast cancer (CITRINE)

Liu Y, Gong Y, Zhu XZ, et al

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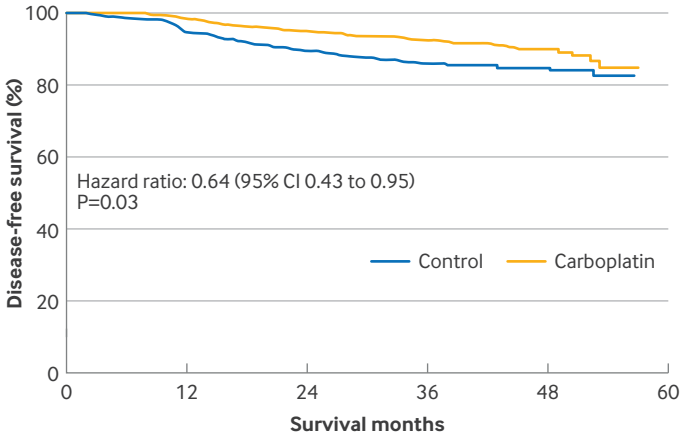
Find this at doi: 10.1136/bmj-2025-085457

Study question Does incorporation of carboplatin into adjuvant anthracycline/taxane based chemotherapy for high risk, early stage, triple negative breast cancer confer survival benefits?

Methods This randomised, open label, phase 3 clinical trial conducted in China included female patients with operable high risk triple negative breast cancer (defined as either regional node positive or node negative with a Ki-67 labelling index of ≥50%) after definitive surgery. Patients were randomised to either the carboplatin arm comprising four cycles of two weekly epirubicin and cyclophosphamide followed by four cycles of weekly paclitaxel combined with carboplatin (n=404) or the control arm of four cycles of three weekly or two weekly epirubicin and cyclophosphamide followed by four cycles of weekly paclitaxel (n=404). The primary endpoint was disease-free survival at three years.

Study answer and limitations Three year disease-free survival was 92.3% for patients in the carboplatin arm and 85.8% for those in the control arm (hazard ratio 0.64, 95% confidence interval 0.43 to 0.95; P=0.03). Carboplatin was also associated with improvements in three year recurrence-free survival, three year distant disease-free survival, and three year overall survival. The incidence of grade 3-4 treatment related adverse events was 66.7% (n=269) in the carboplatin arm and 55.0% (n=222) in the control arm. Limitations include the open label design and inclusion of only Chinese patients.

What this study adds This is the first study to add carboplatin to an anthracycline/taxane based adjuvant chemotherapy regimen for patients with high risk, early stage triple negative breast cancer and suggests that carboplatin intensified chemotherapy significantly improved disease-free survival primarily by reducing early recurrence risk, without new safety concerns.



No at risk

Control	404	384	361	306	122
Carboplatin	404	396	383	329	133

No of disease trials/total No of participants (%)

	0 to 12 months	12 to 36 months	>36 months
Control	62/404 (15.3)	22/404 (5.4)	35/381 (9.2)	5/302 (1.7)
Carboplatin	42/404 (10.4)	7/404 (1.7)	24/396 (6.1)	11/327 (3.4)
	HR= 0.31 (95% CI 0.13 to 0.73)	HR= 0.65 (95% CI 0.39 to 1.09)	HR= 1.98 (95% CI 0.69 to 5.69)

Kaplan-Meier plot showing disease-free survival for patients. CI=confidence interval; HR=hazard ratio

Funding, competing interests, and data sharing This work was supported by grants from organisations such as the National Key Research and Development Project of China (see full paper on bmj.com). No competing interests declared. The data underlying the findings in this paper are openly and publicly available and can be found at http://117.72.180.52:8081 (search for CT2025-00002).

Study registration ClinicalTrials.gov NCT04296175.

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Hospital performance and real estate acquisitions

Bruch JD, et al. Changes in hospital financial performance and quality of care after real estate investment trust acquisition: quasi-experimental difference-in-differences study

BMJ 2025;391:e086226. http://dx.doi.org/10.1136/bmj-2025-086226

Effect of a brain cytoprotectant on functional outcomes after thrombectomy

Wang C, et al. Edaravone dexborneol versus placebo on functional outcomes in patients with acute ischaemic stroke undergoing endovascular thrombectomy (TASTE-2): randomised controlled trial

BMJ 2026;392:e086850. http://dx.doi.org/ bmj-2025-086850

Treaments for classic scabies

Boralevi F, et al. Oral ivermectin versus 5% permethrin cream to treat children and adults with classic scabies: multicentre, assessor blinded, cluster randomised clinical trial

BMJ 2026;392:e086277. http://dx.doi.org/10.1136/bmj-2026-e086277

Effects of lifestyle interventions on gestational diabetes

Allotey J, et al. Effects of lifestyle interventions in pregnancy on gestational diabetes: individual participant data and network meta-analysis

BMJ 2026;392:e084159. http://dx.doi.org/10.1136/bmj-2026-084159