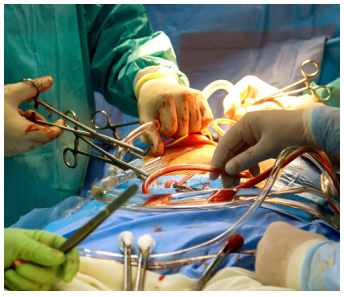
research



Antiplatelet therapy after coronary bypass p 189

Tranexamic acid and postpartum haemorrhage p 192

Effects of aluminium adjuvants p 194

Optimising antiplatelet therapy after coronary artery bypass grafting

ORIGINAL RESEARCH Multicentre, double blinded, randomised controlled trial

Dual antiplatelet therapy for three months versus 12 months after coronary artery bypass grafting

Yuan X, Li J, Lei L, et al; on behalf of the TOP-CABG Collaborative Group

Cite this as: *BMJ* 2026;393:e088939
Find this at doi: 10.1136/bmj-2025-088939

Study question Is three months' dual antiplatelet therapy (DAPT) as efficacious as 12 months' DAPT in preventing saphenous vein graft occlusion after coronary artery bypass grafting while reducing bleeding risk?

Methods A multicentre, double blind, non-inferiority randomised controlled trial was conducted in 13 cardiac surgery centres in China. A total of 2300 participants aged 18 to 80 years undergoing elective primary coronary artery bypass grafting with at least one saphenous vein graft were randomly assigned to receive ticagrelor plus aspirin either for 12 months or for three months followed by aspirin alone for nine months. The primary outcomes were saphenous vein graft occlusion at one year (non-inferiority) and Bleeding Academic Research Consortium (BARC) type 2, 3, or 5 bleeding (superiority). The number needed to treat to prevent one bleeding event was also determined.

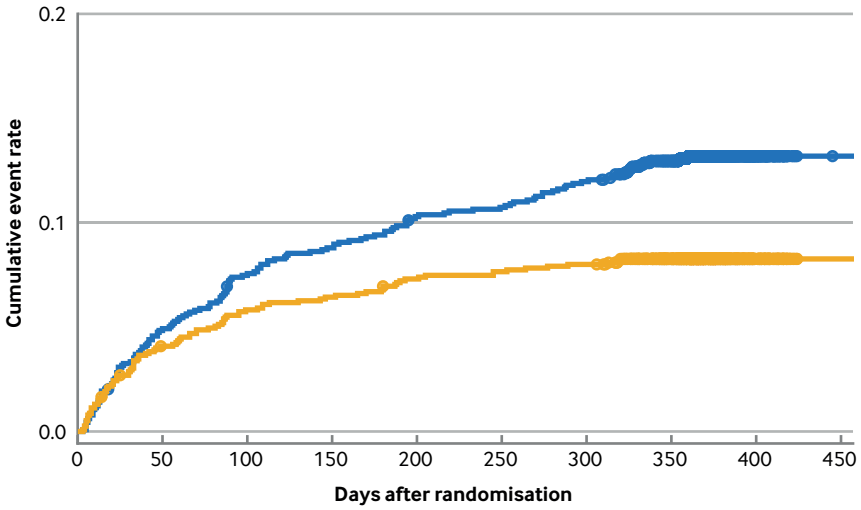
Study answer and limitations 2070 patients (90.4%) with a total of 5125 saphenous vein graft segments were assessed at one year. The mean number of saphenous vein graft segments was 2.5 (standard deviation 0.8). Saphenous vein graft occlusion occurred in 280 of 2596 (10.8%) saphenous vein graft segments in the three month DAPT group and 283 of 2529 (11.2%) in the 12 month DAPT group (absolute difference −0.31%, 95% confidence interval (CI) −3.13% to 2.52%; P=0.008 for non-inferiority). During a median follow-up of 368 (interquartile range 358-382) days, BARC type 2, 3, or 5 bleeding occurred in 95 patients (8.3%) in the three month DAPT group and 149 patients (13.2%) in the 12 month DAPT group (absolute difference −4.67%, 95% CI −7.18% to −2.16%; P<0.001). The number needed to treat was 21 (95% CI 13 to 46) to prevent one bleeding event. Pre-randomisation screening for DAPT intolerance excluded patients who were prone to bleeding during the early

postoperative phase, which could introduce survivor bias and limit the generalisability of the findings to patients at higher bleeding risk. Data on saphenous vein graft imaging were missing for 9.6% of participants.

What this study adds A three month DAPT strategy was non-inferior to the 12 month DAPT strategy in saphenous vein graft occlusion and was superior in reducing bleeding risk.

Funding, competing interests, and data sharing
Funded by the National Clinical Research Centre for Cardiovascular Diseases, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College. Nanjing Zhengda Tianqing Pharmaceutical provided the study drugs. No competing interests declared. Deidentified data and analytical code are publicly available in Dryad (doi:10.5061/dryad.jsxksn0qs).

Study registration ClinicalTrials.gov NCT05380063.



Kaplan-Meier curve of Bleeding Academic Research Consortium type 2, 3, or 5 bleeding within one year after coronary artery bypass grafting surgery by treatment group. DAPT=dual antiplatelet therapy

COMMENTARY Shorter regimens may be more appropriate for some patients

Coronary artery bypass grafting (CABG) remains a cornerstone intervention for multivessel coronary artery disease, offering durable relief of symptoms and improved long term survival for patients worldwide.[1] Yet the success of CABG depends heavily on the patency of bypass conduits, particularly saphenous vein grafts, which are vulnerable to early thrombotic occlusion.[2] Antiplatelet therapy is therefore central to postoperative care, but the optimal regimen and duration continue to be debated.[3] In this context, Yuan and colleagues' trial provides timely and important evidence on whether shorter duration dual antiplatelet therapy (DAPT) can offer comparable graft protection with fewer harms.[4]

Yuan and colleagues conducted a multicentre, double blind, randomised controlled trial comparing DAPT for 12 months or the same dual antiplatelet regimen for the first three months, followed by placebo plus aspirin for nine months in patients undergoing elective CABG with saphenous vein grafts. The study showed that a three month regimen was non-inferior to a 12 month regimen for saphenous vein graft occlusion at one year (10.8% *v* 11.2%; absolute difference −0.31%, 95% confidence interval (CI) −3.13% to 2.52%; P=0.008 for non-inferiority). Importantly for both patients and clinicians, shorter therapy was associated with statistically significantly fewer bleeding events (Bleeding Academic Research Consortium (BARC) type 2, 3, or 5 bleeding: 8.3% *v* 13.2%; hazard ratio 0.62, 95% CI 0.48 to 0.81). These findings were consistent across prespecified subgroups, including those stratified by ischaemic complexity (SYNTAX score) and graft failure risk (SAFINOUS score), suggesting that a shorter course of DAPT may be appropriate for many patients undergoing routine CABG.[4]

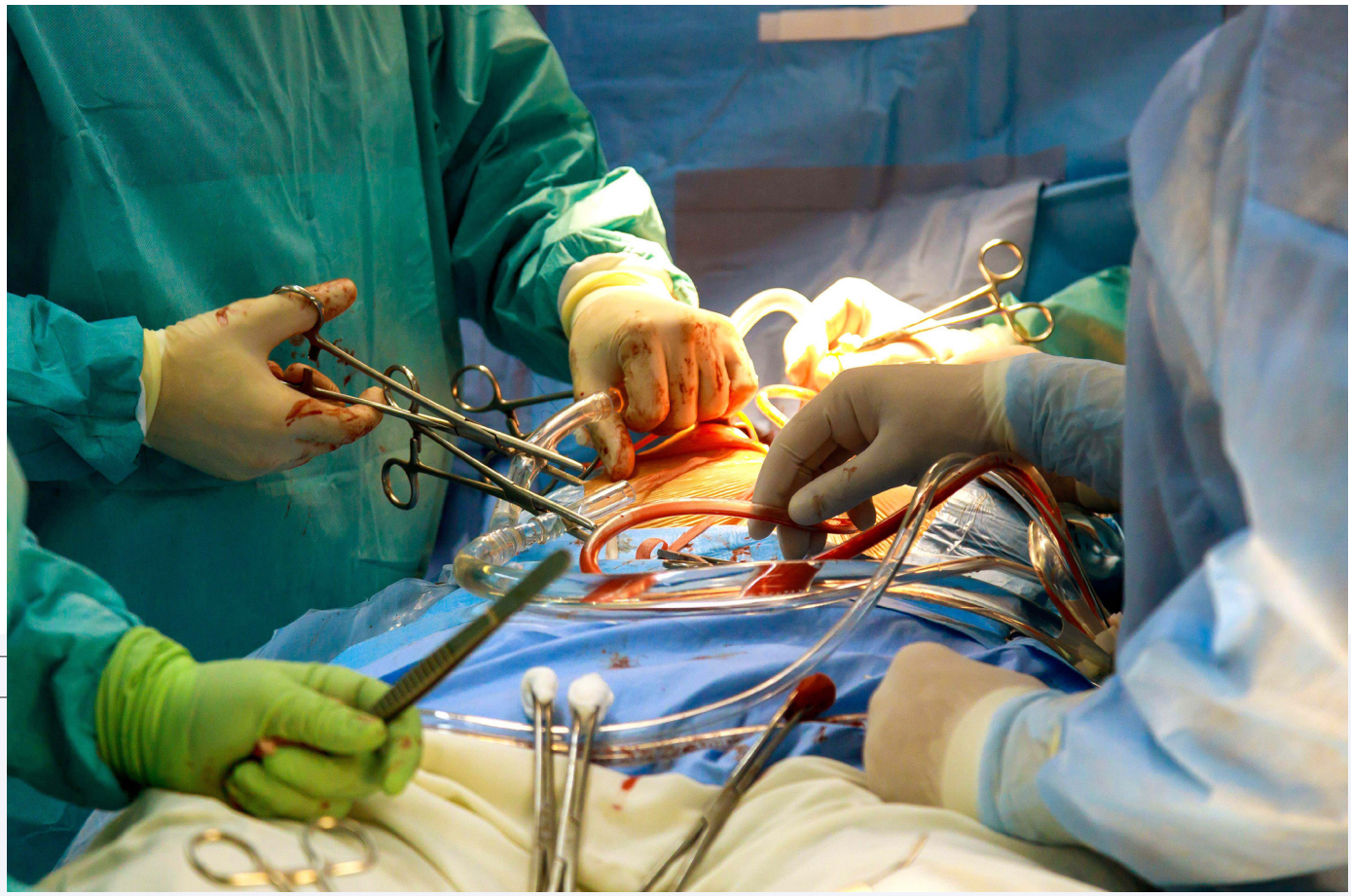
For appropriately selected patients, a three month DAPT regimen can preserve graft patency while reducing bleeding complications

Study limitations

Although the trial offers compelling evidence, several limitations warrant careful consideration. About 11% of participants did not adhere to the assigned regimen, although per protocol and as treated analyses supported the primary findings. The study population largely comprised individuals at low to moderate bleeding risk, limiting generalisability to patients with frailty, anaemia, renal dysfunction, or those requiring long term anticoagulation—groups frequently encountered in real world practice. The focus on enrolment at a single high volume centre might also restrict applicability to more diverse surgical settings. Finally, although the trial was adequately powered for graft patency, it was underpowered to detect differences in major adverse cardiovascular and cerebrovascular events, rendering secondary clinical outcomes exploratory rather than definitive.[4]

For patients and their families, the implications of these findings are meaningful. Bleeding complications after cardiac surgery can prolong recovery, increase anxiety, and reduce quality of life.[5] A shorter DAPT regimen that maintains graft patency while reducing bleeding risk may therefore offer a more tolerable and reassuring postoperative experience. For clinicians, the results provide a pragmatic option that aligns with the growing emphasis on minimising the burden from treatment without compromising efficacy.

However, the broader challenge of optimising antiplatelet therapy after CABG extends beyond treatment duration. Variability in platelet responsiveness between individuals remains a major obstacle. Standard agents such as aspirin and $P2Y_{12}$ inhibitors exhibit heterogeneous effects due to genetic polymorphisms, metabolic differences, drug



VALENTYN SEMENOV/ALAMY

interactions, and comorbidities.[6] This variability means that some patients may be overtreated—exposed to unnecessary bleeding risk—whereas others may be under-protected against thrombotic events. Emerging evidence suggests that perioperative testing of platelet function could help identify patients with heightened platelet reactivity who might benefit from intensified therapy, while sparing others from prolonged DAPT.[7] Yet these approaches remain exploratory and their integration into routine care is limited by logistical, economical, and evidentiary gaps.

Future research

Although Yuan and colleagues' trial represents an important step towards more personalised antiplatelet strategies, it is not the final destination. Future research should prioritise diverse, international populations, including those at high bleeding risk or with complex comorbidities. Trials incorporating platelet function testing, pharmacogenomic profiling, or predictive modelling could help identify subgroups who would benefit from shorter or longer therapy. Longitudinal studies examining graft patency beyond one year, as well as patient centred outcomes such as functional recovery and quality of life, would further strengthen the evidence base.

Yuan and colleagues' trial provides robust evidence that, for appropriately selected patients, a three month DAPT regimen can preserve graft patency while reducing bleeding complications. This represents a meaningful advance for patients, clinicians, and health systems seeking to balance efficacy with safety. Yet the broader goal—true precision in post-CABG antiplatelet therapy—remains on the horizon. Achieving it will require integrating trial evidence with individualised assessment tools that capture each patient's unique thrombotic and haemorrhagic profile. As the discipline moves forward, the challenge is not merely to shorten or lengthen therapy but also to tailor it, ensuring that every patient receives the right treatment at the right intensity and for the right duration.

Shahzad G Raja
drrajashahzad@hotmail.com
See bmj.com for author details

Cite this as: *BMJ* 2026;393:s815

Find the full version with references at http://dx.doi.org/10.1136/bmj.s815

PCPEXCLUSIVE/ALAMY

Tranexamic acid for preventing severe bleeding in caesarean births

ORIGINAL RESEARCH Multicentre, double blind, randomised, placebo controlled, phase 3 trial

Prophylactic tranexamic acid for the prevention of postpartum haemorrhage in women with placenta praevia

Zhang L, Bi S, Chen L, et al; on behalf of the study's collaborator group

Cite this as: *BMJ* 2026;393:e089636
File this at doi: 10.1136/bmj-2026-089636

Study question Does prophylactic treatment with tranexamic acid reduce the incidence of postpartum haemorrhage in women with placenta praevia undergoing caesarean delivery compared with placebo?

Methods A randomised, double blind, placebo controlled, phase 3 study was conducted across 24 maternity units in China between July 2023 and March 2025, involving a total of 1732 women with placenta praevia who were scheduled for caesarean delivery. 38 women were excluded because they withdrew consent or were determined to be ineligible after randomisation. 1694 participants received prophylactic oxytocin and were randomly assigned in a 1:1 ratio to receive either intravenous tranexamic acid (1 g in 10 mL, diluted with 40 mL normal saline) or placebo (10 mL normal saline diluted with 40 mL normal saline) over 10 minutes, starting within five minutes after umbilical cord clamping. The primary outcome was postpartum haemorrhage, defined as calculated estimated blood loss ≥1000 mL or as red cell transfusion within two days after delivery. Serious adverse events included thromboembolic events and acute kidney or liver injury.

Study answer and limitations Primary outcome data were available for 99.8% (1691/1694) of participants. Placenta accreta spectrum was diagnosed in 303 participants (17.9%). The primary outcome occurred in 29.7% (251/845) of participants in the tranexamic acid group and 35.1% (297/846) in the placebo group (relative risk 0.85, 95.2% confidence interval (CI) 0.75 to 0.96; P=0.01). The rates of serious adverse events were similar between the tranexamic acid group and placebo group (0.5% (4 of 837) *v* 0.5% (4 of 845); relative risk 1.01, 95% CI 0.25 to 4.00). A limitation of the study is that the findings are specific to women with placenta praevia receiving prophylactic oxytocin and may not be generalisable to other obstetric populations.

What this study adds This study provides evidence that adding tranexamic acid to prophylactic oxytocin modestly reduces the risk of postpartum haemorrhage in women with placenta praevia undergoing caesarean delivery, with no signal of increased serious adverse events.

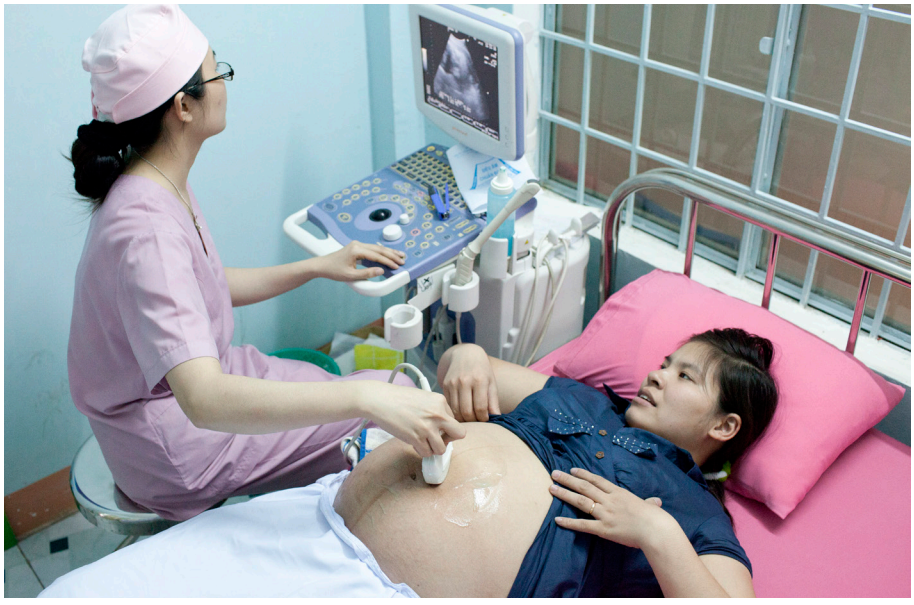
Funding, competing interests, and data sharing
Funded by the National Key Research and Development Program of China, National Natural Science Foundation of China, General Program of Guangdong Province Natural Science Foundation, Plan on Enhancing Scientific Research in Guangzhou Medical University, and China Postdoctoral Science Foundation. No competing interests declared. The code used to analyse the data in the paper are available in the supplementary file on bmj.com. The data underlying the findings in this paper are openly and publicly available and can be found at https://github.com/ChenDunjin-GZHMU.

Study registration ClinicalTrials.gov NCT05811676.

Primary and selected secondary and safety outcomes in women with placenta praevia undergoing caesarean delivery, by treatment group. Values are number (percentage) unless stated otherwise

Outcomes	Tranexamic acid (n=845)	Placebo (n=849)	Relative risk (95% CI)
Primary outcome			
Postpartum haemorrhage	251 (29.7)	297 (35.1)*	0.85 (0.75 to 0.96)†
Calculated estimated blood loss ≥1000 mL	217 (25.7)	267 (31.6)	0.81 (0.70 to 0.93)
Red cell transfusion <2 days after delivery	159 (18.8)	183 (21.6)	0.88 (0.74 to 1.03)
Secondary outcomes			
Mean (SD) gravimetrically estimated blood loss within 24 hours after delivery (mL)	790 (767)	813 (688)	–
Gravimetrically estimated blood loss ≥1000 mL	127 (15.0)	175 (20.6)	0.80 (0.66 to 0.96)
Serious adverse event‡:	4 (0.5)	4 (0.5)	1.01 (0.25 to 4.00)
Thromboembolic event (venous or arterial)	1 (0.1)	3 (0.4)	0.34 (0.04 to 3.23)
Acute kidney or liver injury	3 (0.4)	1 (0.1)	3.05 (0.32 to 29.13)

The safety population included all participants who received either tranexamic acid or placebo.
CI=confidence interval; SD=standard deviation.
*Data on calculated estimated blood loss were available for 846 participants.
†For postpartum haemorrhage, a 95.2% CI was used with a predefined threshold of P<0.048. For postpartum haemorrhage the adjusted P=0.01. CIs for outcomes other than the primary outcome were not adjusted for multiplicity and therefore should not be used for hypothesis testing.
‡Other serious adverse events included myocardial infarction, seizure, and any other unexpected serious adverse events.



CHAU DOAN/LIGHTROCKET/GETTY IMAGES

COMMENTARY Less blood loss, but uncertainty remains about outcomes that matter to women

Caesarean section is one of the most common major surgical procedures worldwide, accounting for about 25 million surgeries every year.[1 2] Bleeding can be substantial, with average blood losses of 700-1000 mL, and may be considerably greater if surgery is complex or underlying conditions such as placental abnormalities exist.[3] Severe bleeding is a common cause of maternal death after caesarean section in low and middle income countries, and although mortality is rare in high income countries, important non-fatal outcomes such as anaemia, fatigue, and postpartum depression are common.[4 5]

Tranexamic acid is an effective treatment for reducing bleeding.[6] The benefits are time dependent and greatest when given early.[7] These findings have prompted growing interest in whether earlier tranexamic acid use could prevent progression to severe haemorrhaging rather than treating the bleeding once established.

Several trials have assessed tranexamic acid for preventing severe postpartum bleeding, but the results are inconsistent.[8] Zhang and colleagues' trial adds to this evidence by examining the effect of tranexamic acid in women with placenta praevia, a group at high risk of severe bleeding.

The trial included 1732 women from 24 maternity units across China. The described methods are robust, with prospective registration, good concealment of allocation, objective outcome assessment, and minimal missing data.

Katharine Ker
Katharine.Ker@lshtm.ac.uk
Ian Roberts
See bmj.com for author details

MALCOLM WILLETT

Women with placenta praevia having a caesarean birth were randomly allocated to receive 1 g tranexamic acid or matching placebo within five minutes of cord clamping. Tranexamic acid reduced the primary haemorrhage outcome, defined as calculated blood loss ≥1000 mL or as blood transfusion within two days of giving birth, by 15%. No evidence was found for an increase in serious adverse effects.

Severe bleeding is a common cause of maternal death after caesarean section in low and middle income countries

Positive impact

These are important findings. Although the authors describe the reduction in bleeding as modest, this understates the impact, particularly in women at high risk of harm from bleeding for whom even modest relative risk reductions translate into worthwhile benefits. As highlighted in "The missing evidence: anaemia, postpartum bleeding and maternal death" report, women with moderate or severe anaemia can become seriously ill despite losing much less than 1000 mL of blood.[9] This is highly relevant given that one third of pregnant women worldwide experience anaemia.[10] Data on maternal wellbeing, including depression, were collected, but the trial had low power for these outcomes.

Zhang and colleagues interpreted their results in the context of other trials on caesarean section, but evidence from surgery more broadly is also relevant. The ATACAS,[11] POISE-3,[12] and TRACTION[13] trials assessed the effects of tranexamic acid before incision and observed large reductions in bleeding. Although these trials did not include participants undergoing caesarean section, they nevertheless inform our understanding of the effects of tranexamic acid, which are likely to be widely applicable.

Maximising benefit

As to future research, the question is no longer whether tranexamic acid reduces bleeding—the evidence from randomised trials in obstetrics and surgery more broadly confirm this. Rather it is how tranexamic acid should be used to maximise patient benefit, specifically ensuring rapid administration in women with established bleeding, targeting preventive use in women most likely to benefit, and generating reliable evidence on the effects on outcomes that matter to women. As regards timing, tranexamic acid in non-obstetric surgery is given before incision. In most trials on caesarean section, however, administration is delayed until after cord clamping to avoid placental transfer. Although tranexamic acid crosses the placenta, with fetuses exposed to an estimated half of maternal concentrations, there is no evidence of any neonatal adverse effects.[14] Pre-incision administration, as with non-obstetric surgery, warrants evaluation in caesarean section, with careful monitoring of maternal and neonatal outcomes. Large, pragmatic randomised controlled trials of pre-incision tranexamic acid in caesarean section that prioritise patient centred outcomes are urgently needed.

Cite this as: *BMJ* 2026;393:s818

Find the full version with references at http://dx.doi.org/10.1136/bmj.s818

Aluminium adjuvants in vaccines and potential health effects

Doyon-Plourde P, Chong J, Abrams EM, et al

Cite this as: *BMJ* 2026;393:e088921
Find this at doi: 10.1136/bmj-2025-088921

Study question What does the available human evidence show about potential health effects of aluminium adjuvants in vaccines?

Methods For this systematic review, six databases were searched from inception to November 2025. Eligibility criteria were human studies reporting health outcomes after aluminium adjuvanted vaccination and study designs included randomised controlled trials, cohort studies, case series, and ecological studies. Risk of bias was assessed using validated tools, and certainty of evidence was rated using GRADE (Grading of Recommendations Assessment, Development and Evaluation).

Study answer and limitations The review included 59 studies (37 case series, 11 randomised controlled trials, nine cohort studies, two ecological studies). High quality evidence from randomised controlled trials and large cohort studies consistently showed no association between aluminium adjuvanted vaccines and serious or long term health outcomes, including autism spectrum disorder, type 1 diabetes, asthma, and other chronic conditions. The only consistent observed effects were uncommon, localised hypersensitivity reactions at the injection site (ie, persistent nodules and granulomas) affecting less than 1% of children after vaccination. These reactions are self-limited and carry a favourable long term prognosis. Evidence on macrophagic myofasciitis was limited to small, highly selected populations and does not establish a causal association with systemic symptoms. For common adverse events (eg, headache, myalgia), high certainty randomised controlled trials found no consistent increase in risk with aluminium adjuvanted formulations. The evidence base was dominated by methodologically limited studies, predominantly uncontrolled case series. Conclusions are primarily supported by higher quality randomised controlled trial and cohort evidence.

What this study adds This review provides a comprehensive synthesis of cumulative human evidence on the health effects of aluminium adjuvants in vaccines across several outcomes and study designs, and no support was found for causal associations with serious or long term harm.

TEK IMAGE/SPL

Funding, competing interests, and data sharing
Supported by the Public Health Agency of Canada as part of routine activities. No external funding. No personal competing interests declared. Reconciled extracted data available from the corresponding author on request.

Systematic review registration PROSPERO CRD42023462831.

Summary of findings on aluminium adjuvants in vaccines and potential health effects

Outcome	Type of evidence	Certainty of evidence	Causal association (conclusion)
Autism spectrum disorder	1 large cohort, 2 ecological studies	Moderate, very low (ecological studies)	Not in favour of a causal association
Asthma	2 large cohorts	Moderate	Not in favour of a causal association
Chronic conditions	1 randomised controlled trial, 3 cohorts, 1 case series	Moderate, low (neurofunctional symptoms)	Not in favour of a causal association
Macrophagic myofasciitis	12 case series, 1 cohort	Very low	Not in favour of a causal association
Headache	9 randomised controlled trials, 1 single arm cohort, 1 case series	High	Not in favour of a causal association for most studies (risk may vary by vaccine)
Myalgia	5 randomised controlled trials, 1 case series	High	Not in favour of a causal association
Wells syndrome	1 case series	Low	Insufficient evidence
Persistent nodules	12 case series, 1 cohort	Low	Consistent with a causal association
Granulomas	10 case series, 3 cohorts	Moderate	Consistent with a causal association