RESEARCH

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Is it safe to drive stoned?

Simulated laboratory studies suggest a dose-response relation between cannabis use and reduced driving skills, explain Mark Ashbridge and colleagues in the introduction to their full length paper on bmj.com. But it is not clear whether this observation translates to real life. Various cross-sectional, cohort, case-control, and culpability studies (which compare drivers responsible for the collision with those who were not) have produced mixed results. Ashbridge's team undertook a systematic review and meta-analysis to investigate, and their findings suggest cannabis use was associated with a near doubling of the risk of collision (p 14).

DAVID KENDALL/PA

What does the study mean for policy, legislation, and personal freedom? Readers of the national papers, bloggers, campaigners, and doctors have been considering these questions and sharing links to the story online, "liking" it on Facebook, and Tweeting. Writing a rapid response on bmj.com, Malcolm Vandenburg asks what the results mean for those patients who are prescribed cannabinoids for medical conditions. In an accompanying editorial Wayne Hall considers whether roadside testing for cannabis works, 10 years after its introduction in some countries (p 7). Although roadside alcohol testing has proved effective, he writes, it has been helped by a clear link between alcohol breath levels and impairment, and major, sustained publicity campaigns that have rendered drink driving increasingly socially unacceptable. The case for cannabis seems more complicated.

You can hear the authors discussing the study in a *BMJ* podcast at http://bit.ly/xgvMjT.

Predicting the severity of menopausal symptoms?

The menopause is associated with a range of symptoms that vary widely in their severity and duration. To get a clearer picture of the condition, Gita Mishra and Diana Kuh used longitudinal data from the MRC National Survey of Health and Development to characterise the symptoms experienced by 695 women who had a natural menopause at age 48 to 54 (p 16). They found four stable groups of symptoms—psychological, somatic, vasomotor, and sexual discomfort—and the profiles for all except the somatic symptoms showed a clear relation to the menopausal transition.

For example, half the women had mild vasomotor symptoms, whereas 10% were classified as very severe, with chronic bothersome symptoms. The other two profiles were of early severe symptoms that then diminished and increasing moderate symptoms. The authors hope that if these symptom profiles are confirmed, the key points where they diverge might allow health professionals to distinguish the most likely profile for an individual woman's symptoms.

In her linked editorial (p 8), Susan Davis points out the limitations of the study—such as exclusion of hormone therapy users, and thereby probably of many highly symptomatic women—which limit the conclusions that can be drawn. However, the main message seems clear: women with minimal symptoms around the time of their final menstrual period are unlikely to develop severe symptoms later, whereas women with moderate to severe menopausal symptoms are likely to have them for several years.

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Ocular safety of sildenafil citrate when administered chronically for pulmonary arterial hypertension

Sildenafil, developed for intermittent use in the management of erectile dysfunction, is also approved in the United States and Europe for long term treatment of pulmonary arterial hypertension. Evidence suggests (albeit inconsistently) that the drug may have ocular effects, and these were investigated by Barbara M Wirostko and colleagues.

Their multicentre randomised controlled trial included 277 patients with pulmonary arterial hypertension who received different doses of sildenafil (up to four times the usual recommended dose for erectile dysfunction) or placebo daily for 12 weeks. The study was then extended, with open label dosing, to collect data through 18 months of treatment.

The findings of the objective assessments—intraocular pressure and visual function tests (visual acuity, colour vision, and visual field)—were similar across all the groups. With respect to subjective visual function, the study found a modest, dose dependent increase in transient phosphodiesterase type 6 mediated effects such as chromatopsia, cyanopsia, photophobia, visual brightness, and visual disturbances. The investigators conclude that daily sildenafil is safe and well tolerated from an ocular perspective in this population. The study was funded by Pfizer UK (doi: 10.1136/bmj.e554).

CME

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Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies

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EDITORIAL by Hall

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Cite this as: *BMJ* 2012;344:e536
doi: 10.1136/bmj.e536

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:e536

STUDY QUESTION

Does the acute consumption of cannabis (cannabinoids) among drivers increase the risk of a motor vehicle collision?

SUMMARY ANSWER

n a systematic review and meta-analysis, we found that driving while under the influence of cannabis was associated with an almost doubling of risk of being involved in a motor vehicle collision that resulted in serious injury or death.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The scientific literature on acute cannabis use and motor collision risk in real life settings is scarce, with little consensus on the association as a whole. Our results indicate an increase in collision risk while driving under the influence of cannabis, and provide a more definitive statement on the direction that public policy and intervention efforts should take in tackling road safety.

Selection criteria for studies

We did a systematic review of observational studies, with meta-analysis. We searched 19 electronic databases, unrestricted by year or language of publication. We also did manual searches of reference lists, conducted a search for unpublished studies, and reviewed personal libraries of the research team. We included observational epidemiology studies of motor vehicle collisions with an appropriate control group. Selected studies measured recent cannabis use in drivers via toxicological analysis of whole blood or self reports. We excluded experimental or simulator studies.

Primary outcome(s)

The primary outcome was involvement in a motor vehicle collision, defined by the World Health Organization as: "a collision or incident that may or may not lead to injury, occurring on a public road and involving at least one moving vehicle."

Main results and role of chance

We selected nine studies for inclusion in the review and meta-analysis. Driving under the influence of cannabis was associated with a significantly increased risk of motor vehicle collisions (odds ratio 1.92 (95% confidence interval 1.35 to 2.73); P=0.0003). Estimates of increased collision risk were higher in case-control studies (2.79 (1.23 to 6.33); P=0.01) and studies of fatal collisions (2.10 (1.31 to 3.36); P=0.002) than in culpability studies (1.65 (1.11 to 2.46); P=0.07) and studies of non-fatal collisions (1.74 (0.88 to 3.46); P=0.11).

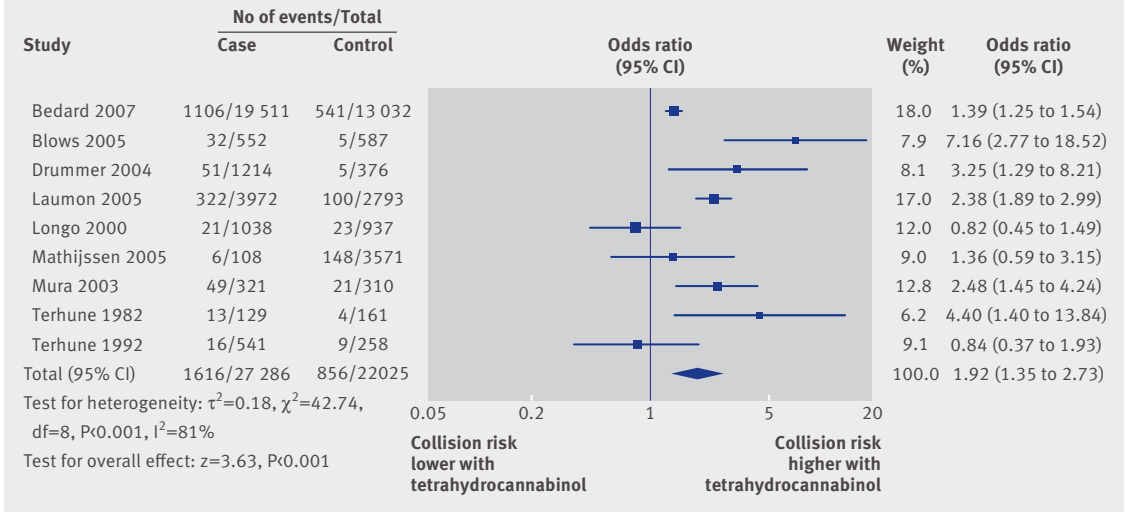
Bias, confounding, and other reasons for caution

We found considerable heterogeneity across the nine included studies (I^2=81%). Insufficient data were available for tetrahydrocannabinol concentrations in the nine studies to allow an examination of dose-response effects in this review. Although we selected only studies of motor vehicle collisions resulting in serious injuries and deaths, cannabis might also be a risk factor for minor collisions.

Study funding/potential competing interests

All authors received financial support from Dalhousie University and the Canadian Institutes of Health Research for the submitted work. The study sponsors had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit this article for publication. All researchers worked independently of the funding bodies.

Vehicle collision risk and acute cannabis consumption



Effect of specific exercise strategy on need for surgery in patients with subacromial impingement syndrome: randomised controlled study

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Cite this as: *BMJ* 2012;344:e787
doi: 10.1136/bmj.e787

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:e787

STUDY QUESTION

Can a specific exercise strategy improve shoulder function and pain in patients with subacromial impingement syndrome, thereby decreasing the need for arthroscopic subacromial decompression?

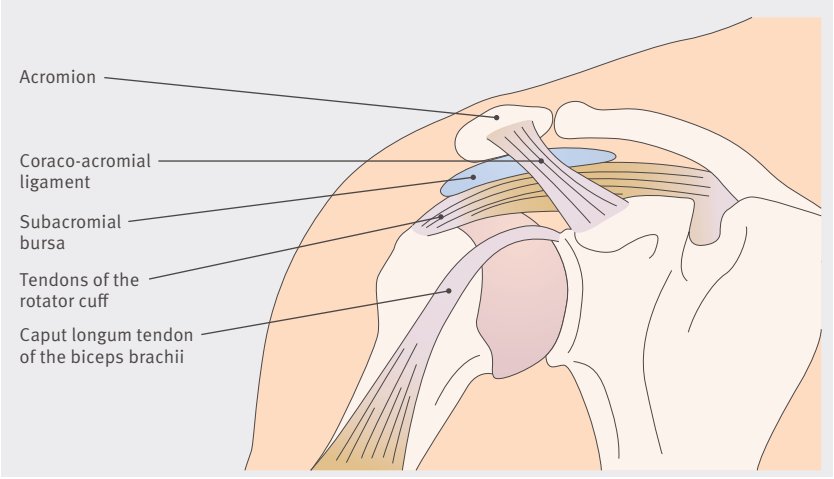
SUMMARY ANSWER

Compared with a control exercise group, patients in the specific exercise group had significantly greater improvements in shoulder function and pain and fewer patients needed surgery at the three month assessment.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Different exercise programmes are used as first line treatment in patients with subacromial impingement syndrome, but conclusive evidence to support the efficacy for these programmes is lacking. This specific exercise strategy proved effective in improving shoulder function and pain in patients in whom earlier conservative treatment had failed.

Anatomy of shoulder



Design

This was a randomised, participant and single assessor blinded, controlled study. Patients were randomised to a specific exercise strategy, targeting the rotator cuff and scapula stabilisers, or to control exercises for 12 weeks. Patients in both groups received five to seven individual sessions with a physiotherapist during this period.

Participants and setting

From the department of orthopaedics, Linköping University Hospital, Sweden, we recruited 102 patients with long standing (more than six months) subacromial impingement syndrome in whom earlier conservative treatment had failed and who were on a waiting list for surgery.

Primary outcomes

The primary outcome was change in the Constant-Murley shoulder score between baseline and an assessment at three months. Secondary outcomes included patients' global impression of change because of treatment and their decision regarding surgery.

Main results and the role of chance

Overall, 97 (95%) participants completed the 12 week study. The specific exercise group had a significantly (P<0.001) greater improvement in the Constant-Murley score than the control exercise group (between group mean differences 15, 95% confidence interval 8.5 to 20.6). Significantly more patients in the specific exercise group reported a successful outcome (defined as a large improvement or recovered) in the patients' global impression of change because of treatment (69% (35/51) *v* 24% (11/46); odds ratio 7.6, 3.1 to 18.9; P<0.001). A significantly lower proportion of patients in the specific exercise group chose to undergo surgery (20% (10/51) *v* 63% (29/46); 7.7, 3.1 to 19.4; P<0.001).

Harms

None reported.

Bias, confounding, and other reasons for caution

Only one physiotherapist was involved in all the treatment and was not blinded to group assignment, which might have influenced the results. There was, however, a strict standardised study protocol and a blinded assessor.

Generalisability to other populations

All patients were recruited from the surgical waiting list of one orthopaedic clinic. This might affect the external validity of the results, but, as patients were referred from all primary care units in the region of Östergötland (population 427 106) we think that the included patients are representative of the studied population. The severity of symptoms and duration might be more heterogeneous in patients with subacromial impingement syndrome attending primary care than in the studied population. Therefore this positive effect of treatment needs to be confirmed in a primary care setting, with longer follow-up, before further implementation of this specific exercise strategy.

Study funding/potential competing interests

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. TH is funded in part by the research council in the south east of Sweden (FORSS).

Trial registration number

Clinical trials NCT01037673

Health symptoms during midlife in relation to menopausal transition: British prospective cohort study

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EDITORIAL by Davis

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Cite this as: *BMJ* 2012;344:e402
doi: 10.1136/bmj.e402

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:e402

STUDY QUESTION

Can women be classified into groups of symptoms experienced through the menopausal transition?

SUMMARY ANSWER

Four stable symptom groups were identified: psychological, vasomotor, sexual, and somatic; within these we identified several profiles based on severity, which clearly related to the timing of menopause for psychological, vasomotor, and sexual symptoms but not for somatic symptoms.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Vasomotor symptoms are some of the few health symptoms reported by women during midlife that have established links with the menopausal transition, with many studies on other symptoms reporting mixed findings. This study provides a detailed account of symptom groups and their relation to the timing of menopause for women with specific profiles of symptoms.

Participants and setting

695 women from England, Scotland, and Wales who experienced natural menopause and reported on 20 common health symptoms.

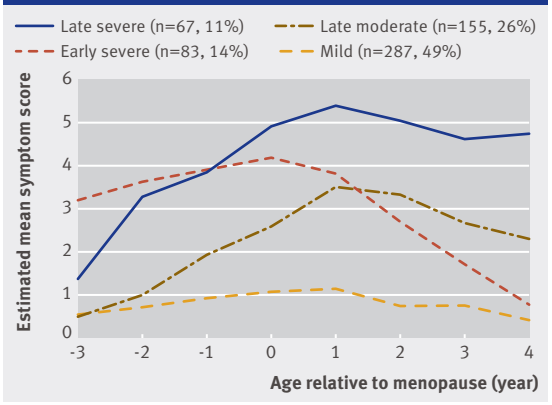
Design, size, and duration

Nationally representative cohort study followed up since birth in 1946 and annually from age 47 to 54.

Main results and the role of chance

Nearly two out of three women (65%, n=394) reported mild and moderate psychological symptoms through the menopausal transition, whereas 10% (n=63) had a severe psychological symptom profile that peaked at or in the year after menopause. Almost half of the women (n=287) were classified as having mild vasomotor symptoms, although in this analysis a slight peak occurred in the year after menopause; 14% (n=83) had the early severe profile that also peaked around early postmenopause and then declined noticeably; and 11% (n=67) had the late severe profile of bothersome symptoms that increased rapidly in perimenopause and remained high for four years or more after menopause. Women were less likely to have a severe profile for vasomotor symptoms if they were from a non-manual social class (odds ratio 0.79, 95% confidence interval 0.57 to 1.01) or had degree level qualifications (0.37, 0.18 to 0.77). The 14% of women (n=85) who had the late severe profile for sexual discomfort showed a similar increase in symptoms until menopause, with symptoms persisting after menopause. Married women were more likely to have the late severe or late moderate profile than women of other marital status (2.40, 1.30 to 4.41). The four profiles for somatic symptoms (mild, moderate, severe, and very severe), did not vary by chronological age or age at menopause.

Profiles for vasomotor symptoms according to age relative to menopause



Bias, confounding, and other reasons for caution

This longitudinal study of the symptoms experienced through midlife was limited to women with natural menopause. All the symptoms were reported, with no use of biomarkers. The links between some sociodemographic factors and health behaviours and bothersome symptoms may result from the differential attrition of the women with hysterectomy or those taking hormone treatment who were excluded from the analyses. Stronger relations may exist between symptom profiles and contemporaneous measures of sociodemographic and health behaviours (rather than baseline measures at age 43 years). Factor analysis and latent class analysis are exploratory techniques, in that they are data driven and do not assume a priori symptom groupings. Confidence in the symptom groupings identified here was strengthened by the confirmatory analysis that indicated their stability over time. The classification of symptoms according to profiles is probabilistic, representing the likelihood of a woman following one or other profile. They should be used only as a general guide, rather than for individual prediction.

Generalisability to other populations

The results are generalisable to women born in Britain in the 1940s.

Study funding/potential competing interests

The Medical Research Council provided funding for the National Survey of Health and Development and financial support for DK and GDM. GDM also received funding from the Australian National Health and Medical Research Council. We have no competing interests.

Impact of single centre status on estimates of intervention effects in trials with continuous outcomes: meta-epidemiological study

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Cite this as: *BMJ* 2012;344:e813
doi: 10.1136/bmj.e813

This is a summary of a paper that was published on bmj.com as *BMJ* 2012;344:e813

STUDY QUESTION

Do single centre and multicentre randomised controlled trials of continuous outcomes produce different estimates of intervention effects?

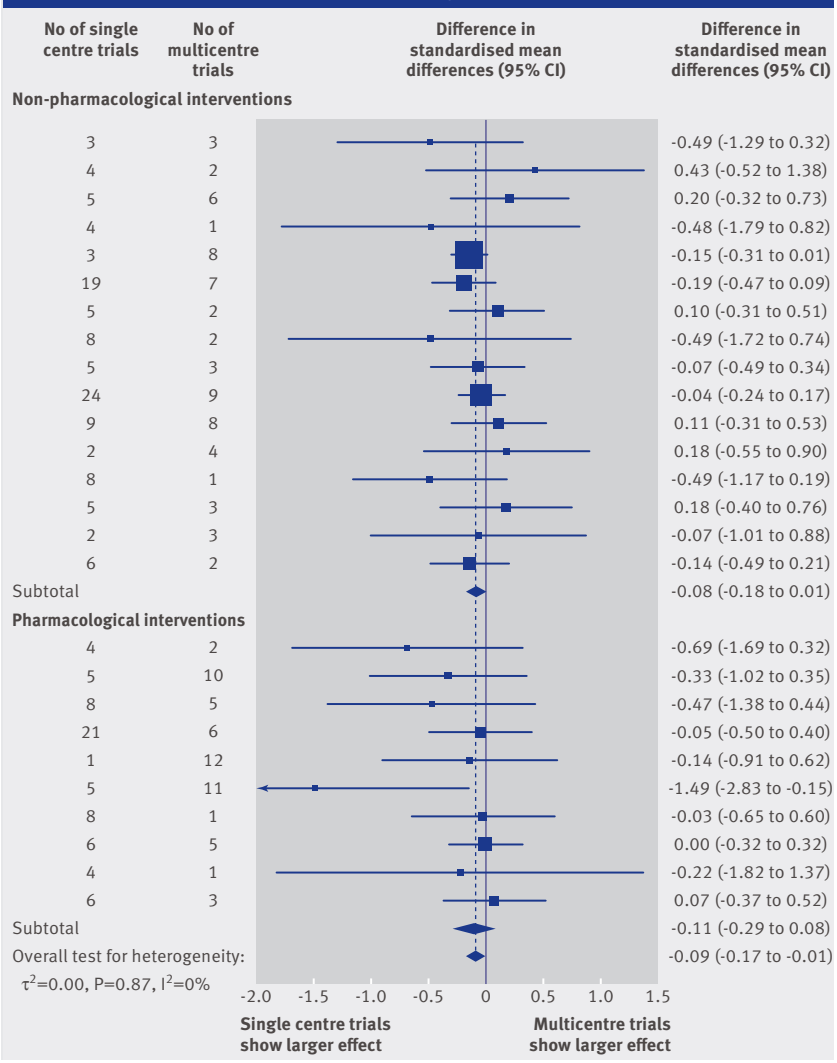
SUMMARY ANSWER

Intervention effects were on average slightly larger with single centre than with multicentre trials.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

A recent meta-epidemiological study of binary outcomes found intervention effects larger with single centre than with multicentre trials. We found a similar result for trials of continuous outcomes.

Differences in intervention effects between single centre and multicentre trials



Selection criteria for studies

This meta-epidemiological study assessed 26 meta-analyses including 292 randomised controlled trials (177 single centre, 115 multicentre) with continuous outcomes published between January 2007 and January 2010 in the Cochrane database of systematic reviews. The intervention effects were estimated with standardised mean differences. For each meta-analysis, we used random effects regression to assess the difference in standardised mean differences between single centre and multicentre trials. We then pooled differences in standardised mean differences across meta-analyses by a random effects meta-analysis model. A combined difference in standardised mean differences of less than 0 indicated that treatment effects were on average larger with single centre than with multicentre trials.

Primary outcome

Difference in standardised mean differences between single centre and multicentre trials.

Main results and role of chance

Intervention effect estimates were on average larger with single centre than with multicentre trials (difference in standardised mean differences −0.09, 95% confidence interval −0.17 to −0.01, P=0.04). Of 26 meta-analyses, 19 exhibited larger intervention effect estimates in single centre than in multicentre trials. Adjustment for sample size slightly attenuated the difference (combined difference in standardised mean differences −0.08, 95% confidence interval −0.17 to 0.01). Adjustment for risk of bias yielded similar estimates with wider confidence intervals (−0.09, 95% confidence interval −0.17 to 0.00 for overall risk of bias).

Bias, confounding, and other reasons for caution

Single centre trials had smaller sample sizes than did multicentre trials. Our results were slightly attenuated after adjusting for sample size, so "small study effect" (the tendency for small trials to show larger treatment effect than larger trials) might have contributed to the observed differences. Publication bias could also have contributed to the observed differences in treatment effect estimates between single centre and multicentre trials. The association of single centre and multicentre trials and intervention effect estimates may also be confounded by methodological quality. After adjusting for risk of bias, we obtained similar estimates, with slightly wider confidence intervals. Further studies are needed to explore the role and impact of these different mechanisms.

Study funding/potential competing interests

This study received no funding. We have no competing interests.