RESEARCH

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CATHERINE POUEDRAS/SPL

WHAT OUR READERS ARE SAYING

Assessing the risk of venous thromboembolic events in women taking progestin-only contraception

In this meta-analysis of eight observational studies (p 12), the use of progestin-only contraception was not associated with a higher risk of venous thromboembolism than non-use of hormonal contraception. A rapid respondent says:

"In 1995 the UK Committee on Safety of Medicines 'informed' the public that third generation oral contraceptive pills double the risk of thromboembolism. Scared women refrained from taking the pill, and pill sales fell. This probably led to 13 000 additional abortions and 13 000 additional births in England and Wales in the following year. Presumably the pill scare would not have happened if the public had been informed about the underlying tiny difference in absolute risk. I therefore ask the authors in due respect of their work to add an estimate of the absolute risk difference to the increase of risk associated with injectable progestin."

BSIP, LAURENT/SPL

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The health and development of children born to older mothers in the United Kingdom
In this observational study using longitudinal cohort data, increasing maternal age was associated with improved health and development for children up to 5 years of age. The results of this study are relevant to concerns raised about older people seeking to use fertility treatments and possible risks posed to children delivered by older mothers, say the authors.

Reporting of conflicts of interest from drug trials in Cochrane reviews
According to this cross sectional study, most Cochrane reviews of drug trials published in 2010 did not provide information on trial funding sources or trial author-industry financial ties or employment. When this information was reported, location of reporting was inconsistent across reviews, say the authors.

Effect of assertive outreach after suicide attempt in the AID (assertive intervention for deliberate self harm) trial
In this randomised controlled trial including 243 patients with a suicide attempt within the past 14 days who were admitted to hospitals in Copenhagen, assertive outreach showed no significant effect on subsequent suicide attempt. The difference in rates of events between register data and self reported data could indicate detection bias, say the authors.

Contribution of modifiable risk factors to social inequalities in type 2 diabetes
In the Whitehall II cohort study, modifiable risk factors such as health behaviours and obesity, when measured repeatedly over time, explained almost half of the social inequalities in the incidence of type 2 diabetes. This is more than was seen in previous studies based on single measurement of risk factors, say the authors.

Time trends in drug resistant HIV-1 infections in the United Kingdom up to 2009
According to this multicentre observational study, the previously observed decline in the prevalence of transmitted drug resistance in HIV-1 infections probably acquired in the UK seems to have stabilised. The continued high prevalence of thymidine analogue mutations suggests that the source of this resistance may be increasingly from patients who have not had antiretroviral therapy and who harbour resistant viruses. The authors recommend that testing of all newly diagnosed HIV-1 positive people should be continued.

Physiotherapy intervention in Parkinson's disease: systematic review and meta-analysis

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STUDY QUESTION How effective is physiotherapy in treating patients with Parkinson's disease?

SUMMARY ANSWER Compared with no intervention, physiotherapy has short term benefits in Parkinson's disease, but further large, well designed, randomised controlled trials are needed to assess the efficacy of physiotherapy in the longer term.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Two reviews of exercise and treadmill based interventions reported potential benefits of physiotherapy for people with Parkinson's disease, although the methodological quality of the trials was generally not high. This review not only found a short term benefit of the overall effect of physiotherapy in these patients but also made an indirect comparison of the different physiotherapy methods used.

Selection criteria for studies

We identified relevant trials by electronic searching literature databases and trial registers (including Medline, Embase, REHABDATA, Latin American and Caribbean Health Sciences Literature, Electronic Theses Online Service) and hand searching major journals, conference proceedings, and reference lists of retrieved publications. The literature search included trials published up to the end of January 2012. Our selection criteria were randomised controlled trials of physiotherapy versus no intervention or placebo in patients with Parkinson's disease. Our definition of physiotherapy interventions included general physiotherapy, exercise, treadmill training, cueing, dance, and martial arts.

Main results and the role of chance

Of 39 trials of 1827 participants included in this review, 29 trials provided data for inclusion in the quantitative meta-analyses. Significant benefit from physiotherapy was reported for nine of 18 outcomes assessed. The results for speed (0.04 m/s, 95% confidence interval 0.02 to 0.06, P<0.001), the Berg balance scale (3.71 points, 2.30 to 5.11, P<0.001), and the unified Parkinson's disease rating scale (total score, −6.15 points, −8.57 to −3.73, P<0.001; activities of daily living subscore, −1.36, −2.41 to −0.30, P=0.01; motor subscore, −5.01, −6.30 to −3.72, P<0.001) may translate into clinically relevant improvements in a person's functional mobility. Indirect comparisons of the different physiotherapy interventions found no evidence that the treatment effect differed across the interventions for any outcomes assessed, with the exception of the motor subscores on the unified Parkinson's disease rating scale (in this instance, one trial was found to be the cause of the heterogeneity).

Bias, confounding, and other reasons for caution

The methodological quality and reporting of most trials was variable, and often inadequate. Of the 39 trials, only 18 provided information on the randomisation method, and only five used a central randomisation procedure to ensure concealment of treatment allocation. Blinded assessors were used in 24 studies, and only nine reported using intention to treat analysis. In addition, the included trials were relatively small, and most assessed the effect of physiotherapy intervention versus no intervention over a short period of time (<three months). In a long term disease such as Parkinson's disease, future research should investigate the effect of therapy over a much longer period. In the trial data available, we found little focus on patient oriented outcomes, without which studies cannot necessarily capture the difficulties experienced by patients in everyday life or their opinions on treatment acceptability and personal improvements.

Study funding/potential competing interests

The study received funding from Parkinson's UK, and the Department of Health, which provided core support to the University of Birmingham Clinical Trials Unit. SP, CM, CEC, CS, KW, and NI are either recruiting to or involved in the running of the UK PD REHAB trial.

Summary of outcomes

	Intervention *v* no intervention	
Outcome	Mean difference (95% CI)	P
Speed (m/s)	0.04 (0.02 to 0.06)	P<0.001
2 or 6 min walk test (m)	13.37 (0.55 to 26.20)	P=0.04
Freezing of gait questionnaire	−1.41 (−2.63 to −0.19)	P=0.02
Timed up and go test (s)	−0.63 (−1.05 to −0.21)	P=0.003
Functional reach test (cm)	2.16 (0.89 to 3.43)	P<0.001
Berg balance scale	3.71 (2.30 to 5.11)	P<0.001
Unified Parkinson's disease rating scale		
Total score	−6.15 (−8.57 to −3.73)	P<0.001
Activities of daily living subscore	−1.36 (−2.41 to −0.30)	P=0.01
Motor subscore	−5.01 (−6.30 to −3.72)	P<0.001

All results favoured physiotherapy intervention.

Assessing the risk of venous thromboembolic events in women taking progestin-only contraception: a meta-analysis

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STUDY QUESTION

Is use of progestin-only contraception associated with an increased risk of venous thromboembolism?

SUMMARY ANSWER

No, the use of progestin-only contraception was not associated with an increased risk of thrombosis.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

The risk of venous thromboembolic events with hormone contraceptives is influenced by the dose of oestrogen and formulation of progestin. This meta-analysis of eight observational studies did not identify an association between oral progestin-only contraception and venous thromboembolic risk. Subgroup analysis suggests that injectable progestin contraception is associated with an approximately doubled venous thromboembolic risk.

Selection criteria for studies

We performed a literature search of journal articles using PubMed, Embase, and the Cochrane Database of Systematic Reviews, searching for "progestin" and related terms, "contraceptive", and "thrombosis" and related terms. Studies were included if they met all of the following conditions: randomised trial, case-control or cohort or cross sectional study (prospective or retrospective); presence of an arm featuring progestin-only users and a control arm with no hormone use; use of progestin for the purpose of contraception only (excluding post-coital contraception); independent analysis of pre-menopausal women; incidence of venous thromboembolic episodes (defined as deep venous thrombosis or pulmonary embolism) reported; study featured human data only; one or more of three possible administration routes (oral, injectable, and intrauterine) were considered.

Primary outcomes

We estimated the risk ratio of venous thromboembolic episodes for users of progestin-only oral contraceptives versus non-users. As a secondary analysis, we estimated the adjusted risk ratio of venous thromboembolism according to route of administration of progestin-only contraceptives (oral, injectable, and intrauterine).

Main results and role of chance

Our literature search identified eight observational studies that fulfilled the inclusion criteria. A total of 147 women across all studies were diagnosed with a venous thromboembolic event while taking progestin-only contraception. The summary measure for the adjusted relative risk of a venous thromboembolic episode for users versus non-users of a progestin-only contraceptive using the random effects model was 1.03 (95% CI 0.76 to1.39). Subset analysis was performed on the adjusted results with a random effects model. A total of 54 women developed a venous thromboembolic event while taking a progestin-only pill, and there was no significant increase in risk of venous thromboembolism compared with non-users (relative risk 0.90 (95% CI of 0.57 to 1.45)). However, the relative risk of an event for users of an injectable progestin formulation versus non-users was 2.67 (1.29 to 5.53).

Bias, confounding, and other reasons for caution

A potential limitation of this study is the paucity of published literature on the topic, with a total of eight studies available for analysis and no randomised trials. Control for confounding in the individual studies was usually limited, and selection bias cannot be excluded as the basis of a significant association between depot administration and venous thrombosis.

Study funding/potential competing interests

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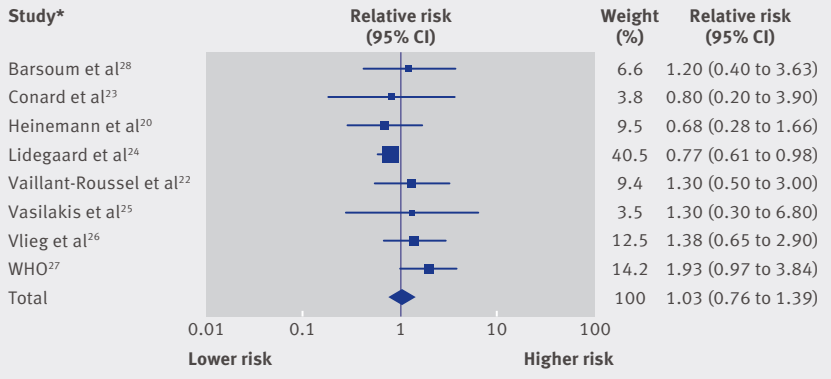
Adjusted relative risks of venous thromboembolism for users *v* non-users of progestin-only contraceptive



Test for heterogeneity: Q=9.21, df=7, I^2=24%, P=0.24
*See full article for details of studies

Effectiveness of rotavirus vaccination in prevention of hospital admissions for rotavirus gastroenteritis among young children in Belgium: case-control study

The RotaBel Study Group

EDITORIAL by Patel

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See full article for list of authors and group members

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STUDY QUESTION How effective is rotavirus vaccine in young children, as measured by admissions to hospital for rotavirus gastroenteritis?

SUMMARY ANSWER The effectiveness of two doses of the monovalent rotavirus vaccine against admissions to hospital for rotavirus gastroenteritis in young children was 90% (95% confidence interval 81% to 95%).

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Rotavirus vaccine effectiveness during routine use has been reported mainly in low-middle income settings. Rotavirus vaccination is effective for the prevention of admissions for rotavirus gastroenteritis in infants in Belgium, providing protection equivalent to that seen in clinical trial settings. The effectiveness of the vaccine was relatively stable across age groups, viral co-infection status, rotavirus vaccination status, and rotavirus genotype.

Effectiveness of monovalent rotavirus vaccine against admission for rotavirus gastroenteritis in young children (Belgium, February 2008-June 2010) (confirmed cohort who met all criteria defined in protocol)

	Vaccine effectiveness (% (95% CI))	Sensitivity (%)	
		–	+
Received two doses of monovalent vaccine			
Overall	90 (81 to 95)	76	93
Age (months):			
3-11	91 (75 to 97)	69	94
≥12	90 (76 to 96)	82	91
Received at least one dose of any rotavirus vaccine			
Overall	91 (82 to 95)	78	93
By age (months):			
3-11	93 (80 to 97)	75	95
≥12	89 (75 to 95)	81	90

Participants and setting

We included 215 children admitted to hospital with community acquired rotavirus gastroenteritis confirmed by polymerase chain reaction. All children were of an eligible age to receive the rotavirus vaccine and had no contraindications for vaccination. We identified 276 age and hospital matched controls without gastroenteritis and without contraindications for rotavirus vaccination.

Design, size, and duration

This was a prospective hospital based multicentre matched case-control study. Cases and controls were recruited from a random sample of 39 (about a third) Belgian hospitals with paediatric beds between February 2008 and June 2010.

Primary outcome, risks, exposures

Effectiveness of two doses of the monovalent rotavirus vaccine (compared with unvaccinated) on the occurrence of severe rotavirus gastroenteritis confirmed by polymerase chain reaction in children admitted to hospital.

Main results and the role of chance

For the primary analysis, we included 160 informative case-control pairs (70 fully vaccinated and 90 unvaccinated cases with their 179 fully vaccinated and 19 unvaccinated matched controls) in the logistic regression analysis. Effectiveness of two doses of the monovalent rotavirus vaccine for the prevention of admission for rotavirus gastroenteritis was 90% (95% confidence interval 81% to 95%). Results of the sensitivity analysis for this primary objective (assuming cases and controls with missing/unknown vaccination history were vaccinated and unvaccinated, respectively) ranged from 76% to 93%.

Bias, confounding, and other reasons for caution

Despite our efforts to minimise bias in the selection of cases and controls, there were a few significant differences in some demographic and socioeconomic parameters between the groups. We carried out a multivariate analysis to control for some of these factors, which resulted in similar estimates of vaccine effectiveness.

Another major concern was the validity of the obtained history of rotavirus vaccination. There is, however, an equal risk of misclassification for cases and controls and, as controls already had a high reported vaccine uptake (>90%), this possible underestimate was probably minimal and will have little effect on the current estimates of effectiveness. Finally, although a third of all paediatric departments in Belgium were included as study sites, our cases might not represent the full spectrum of severe cases of rotavirus gastroenteritis in the population in Belgium.

Generalisability to other populations

Our findings should prove useful for public health officers and policy makers to help their decision making on the implementation of rotavirus vaccine in other similar high income countries.

Study funding/potential competing interests

This study was funded by GlaxoSmithKline Biologicals, which helped with study design, data collection, and analysis. GlaxoSmithKline Biologicals also funded Jennifer Coward (independent medical writer, Bollington, UK) to help with writing the paper.