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Research

Prenatal bed rest in developed and developing regions: a systematic review and meta-analysis

Brittany Matenchuk BSc, Rshmi Khurana MD, Chenxi Cai PhD, Normand G. Boulé PhD, Linda Slater MLIS, Margie H. Davenport PhD

Abstract

Background: Bed rest is prescribed by most maternity health care professionals for high-risk pregnancy complications, but the impact of bed rest at home and in hospital has not been explored. Our aim was to quantify the influence of bed rest on maternal/fetal health outcomes in developed and developing regions.

Methods: We conducted a systematic review and meta-analysis of randomized controlled trials. We conducted a structured search through MEDLINE, Embase, CINAHL, Web of Science and the Cochrane Library through Mar. 7, 2019. Trials comparing standard care to standard care plus bed rest after 20 weeks' gestation were assessed. Outcomes included infant birth weight, being small for gestational age, gestational age, premature or very premature birth, perinatal death, admission to the neonatal intensive care unit, preterm rupture of membranes, hypertensive disorders of pregnancy, preeclampsia and gestational diabetes mellitus.

Results: We identified 1191 publications, of which 43 were assessed for eligibility. Sixteen publications reporting on 14 unique studies (2608 women, 3328 infants) were included in the analysis. Overall, maternal/newborn outcomes were similar between women on bed rest and those not on bed rest. In subgroup analyses of developed and developing regions, length of gestation was shorter with bed rest (weighted mean difference –0.77 wk, 95% confidence interval [CI] –1.26 to –0.27, I^2 = 0%), and the risk of a very premature birth was increased (risk ratio 2.07, 95% CI 1.15 to 3.73, I^2 = 0%) in developed countries.

Interpretation: In developed regions, treatment of complicated pregnancies with more than 1 week of bed rest results in worse newborn outcomes. Additional studies are required to determine whether bed rest or hospital admission improves outcomes in developing regions. **PROSPERO Trial registration number:** CRD42018099237.

Bed rest and activity restriction is prescribed to about 20% of pregnant women with the intent of improving maternal/fetal health outcomes of high-risk pregnancies complicated by preterm labour, intrauterine growth restriction and hypertensive disorders of pregnancy.[1–3] Bed rest as a treatment is associated with an economic cost of up to US$7 billion per year in the United States alone (including hospital admission, lost wages and lost domestic productivity).[1,4] Previous meta-analyses focused on multiple or singleton pregnancy suggested there is little evidence to support a policy of routine hospital admission for bed rest.[5,6] However, high heterogeneity was highlighted as an issue for several outcomes. Despite the lack of evidence, bed rest continues to be prescribed by up to 95% of clinicians.[1,7] This has resulted in an urgent call for additional research to elucidate the potential benefits (or harms) of bed rest for the woman and her fetus by the World Health Organization and the American College of Obstetricians and Gynecologists.[7–9]

Previous meta-analyses are current to 2017[5,6,10,11] but do not include all available trials. There appears to be a dichotomy between studies on bed rest conducted in developing countries versus developed countries. Bed rest studies conducted in developing countries may be significantly confounded by hospital admission, which may provide patients with increased access to nutritious food and clean water and increased vigilance by medical personnel; this may have substantially less impact on health outcomes in the developed world. However, the influence of the study location's developmental status on the impact of bed rest at home and in hospital has not been explored. Therefore, we conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) that contrasted the effect on maternal/fetal health outcomes of bed rest or activity restriction in conjunction with standard care versus standard care alone (no bed rest) in pregnant women at 20 weeks' gestation or more.

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Correspondence to: Margie Davenport, margie.davenport@ualberta.ca

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Box 1: PICO framework

Population: The population of interest was pregnant women.

Intervention: The intervention was standard care (including tocolytics and antihypertensive medications) plus bed rest (including activity restriction, in hospital or at home). Bed rest was defined as a prescribed restriction of activity encompassing the majority of waking hours for 1 week or more.[12]

Comparison: The eligible comparator was standard care without activity restriction (no bed rest).

Outcomes:

- Fetal: birth weight, small at birth (birth weight < 1500 g and < 2500 g) or small for gestational age (< 10th percentile for gestational age and sex), gestational age, premature delivery (< 37 wk), very premature delivery (< 35 wk, < 34 wk or < 32 wk, as defined by the author), perinatal death and admission to the neonatal intensive care unit.
- Maternal: preterm rupture of membranes, hypertensive disorders of pregnancy, preeclampsia and gestational diabetes mellitus.

Methods

Eligibility criteria

We used the PICO (population, intervention, comparison, outcome[s]) framework to guide this review (Box 1).

Search strategy and study inclusion

We conducted this systematic review and meta-analysis in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions*.[13] We conducted a structured search through MEDLINE (1946 to Mar. 7, 2019), Embase (1974 to Mar. 7, 2019), CINAHL (1937 to Mar. 7, 2019), Scopus (inception to Mar. 7, 2019), Web of Science (1899 to Mar. 7, 2019) and the Cochrane Library (inception to Mar. 7, 2019). The complete search strategy is given in Appendix 1 (available at www.cmajopen.ca/content/7/3/E435/suppl/DC1). We searched for RCTs investigating the impact of bed rest versus standard care without activity restriction in pregnancy using controlled vocabulary (when available) and text words representing pregnancy/maternal/fetal outcomes or complications combined with terms representing bed rest. We modified the Cochrane RCT filter to exclude the drug therapy floating subheading and to include the term intervention*, and applied it to the searches with the exception of the Cochrane Library.[13] Studies were not excluded because of language of publication or publication format (e.g., abstracts only). The structured search was created by L.S. and reviewed by a second librarian with systematic review experience. Records identified by the search strategy were independently assessed in duplicate for inclusion by B.M. or C.C., and M.H.D., with N.G.B. acting as arbitrator in the event of disagreement.

Data extraction

Studies were extracted independently and in duplicate by 2 researchers (B.M. and M.H.D.) using a standardized data collection form including indication for bed rest, duration of bed rest, location of bed rest (e.g., hospital v. home), and any cointerventions used, as well as fetal outcomes of interest (birth weight, being small at birth [birth weight < 1500 g and < 2500 g] or small for gestational age [< 10th percentile for gestational age and sex], gestational age, premature delivery [< 37 wk], very premature delivery [< 35 wk, < 34 wk or < 32 wk, as defined by the author], perinatal death and admission to the neonatal intensive care unit) and maternal outcomes of interest (preterm rupture of membranes, hypertensive disorders of pregnancy, preeclampsia and gestational diabetes mellitus). When multiple publications from the same trial were identified, data were extracted from all available articles.

Quality measures and risk of bias

The risk of bias in RCTs was assessed independently and in duplicate by C.C. and M.H.D. following the *Cochrane Handbook for Systematic Reviews of Interventions*.[13] All studies were screened for potential sources of bias including selection bias, reporting bias, performance bias, detection bias, attrition bias and "other" sources of bias. The risk of bias across studies was rated as "serious" when studies having the greatest influence on the pooled result (assessed by means of weight [percent] given in forest plots) presented "high" risk of bias.[14] The quality of the evidence was assessed by C.C. and M.H.D. using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.[14] Evidence from RCTs was rated as high quality by default and then downgraded based on prespecified criteria, including study limitations (weight of studies showed serious risk of bias), inconsistency (heterogeneity was high [$I^2 \geq 50\%$] or only 1 study was assessed), indirectness (bed-rest–only interventions and bed rest plus cointerventions were combined for analysis), imprecision (95% confidence interval [CI] crossed the line of no effect and was wide) and publication bias (substantial evidence of small-study effects).

Statistical analysis

We conducted statistical analyses using Review Manager v5.2. (Cochrane Collaboration). For continuous outcomes, we examined mean differences between bed-rest and no–bed-rest groups. For binary outcomes, we calculated risk ratios (RRs). We applied inverse-variance weighting to obtain pooled weighted mean differences (WMDs) and RRs using a random effect model. We performed a sensitivity analysis to evaluate whether the effects were different when examining relations between the different indications for bed rest and maternal/infant outcomes. We conducted the following subgroup analyses, determined a priori: 1) developmental status of the region in the year the study took place based on the World Bank country definition[15] and 2) single- versus multiple-gestation pregnancies. We used χ^2 tests to estimate heterogeneity between trials. The percent of total variability attributable to heterogeneity (i.e., not due to chance) was expressed as the I^2. We explored the source of heterogeneity when intersubgroup heterogeneity was significant ($p < 0.05$). We estimated missing standard deviations (SDs) for outcomes from reported p values and sample sizes,[16] according to procedures in the *Cochrane Handbook for Systematic Reviews of Interventions* (section 7.7.3.3).[13] We used

GRADEpro GDT (McMaster University and Evidence Prime) to evaluate and tabulate quality of evidence and strength of recommendations.[17]

Ethics approval

Ethics approval was not required for this systematic review and meta-analysis.

Results

Study selection

The literature search identified 1191 potentially relevant studies, 43 of which were assessed for eligibility. Sixteen articles from 14 individual RCTs met our inclusion criteria and were included in the review (Figure 1).

Study characteristics

The 14 studies assessed in our analysis included 2608 pregnancies (3328 newborns). Nine studies were from developed regions, and 5 were from a developing region (Zimbabwe[18–22]). Indications for bed rest in the Zimbabwe studies included multiple-gestation pregnancy[18–21] and hypertensive disorders of pregnancy.[22] Studies evaluating pregnancies in developed regions examined multiple-gestation pregnancy,[23–25] hypertensive disorders of pregnancy,[26,27] preterm labour,[28,29] suspected intrauterine growth restriction,[30] high risk of preterm birth[28] and preterm rupture of membranes.[31]

The length of the prescribed bed rest ranged from 1.0 to 9.7 weeks.[18–22,25,27,29,31] A summary of study characteristics is provided in Table 1.

Quality of evidence

Overall, the quality of evidence ranged from low to high (Supplementary Table S1, Appendix 2, available at www.cmajopen.ca/content/7/3/E435/suppl/DC1). The most common reasons for downgrading the quality of evidence were serious risk of bias and serious imprecision of the interventions. Common sources of bias included selection bias owing to inadequate generation of a randomized sequence and reporting bias owing to selective outcome reporting.

Synthesis of results

Fetal outcomes

Bed rest did not decrease the risk of perinatal death overall (12 RCTs, 1995 births: 782 in developed regions and 1213 in Zimbabwe; RR 1.09, 95% CI 0.52 to 2.28, I^2 = 37% (Figure 2) or when separated by developmental status of the country (p = 0.3 for subgroup differences).[18–26,29–31]

Preterm birth (< 37 wk) and very preterm birth are the leading causes of perinatal morbidity and mortality.[32] In our meta-analysis, "very premature" was defined as less than 32 weeks in 2 studies,[21,25] less than 34 weeks in 4 studies[18–20,23] and less than 35 weeks in 2 studies.[26,29] Our analysis of premature birth included 2511 women.[18–29,31] No difference was found in rates of premature birth between women on bed rest and those not on bed rest (RR 0.98, 95% CI 0.91 to 1.06, I^2 = 0%; low evidence), and subgroup analyses were not significant (Supplementary Figure S1, Appendix 2). High heterogeneity was interrogated in the meta-analysis of very premature birth owing to statistically significant heterogeneity in the developed regions subgroup, which led to the removal of 1 study with a 100% event rate in both study arms.[31] Bed rest doubled the risk of having a very premature baby in developed regions (prevalence 6.2% v. 12.8%) (RR 2.07, 95% CI 1.15 to 3.73, I^2 = 0%; moderate evidence) (Figure 3) but not the developing region. Subgroup differences were significant (p = 0.03).

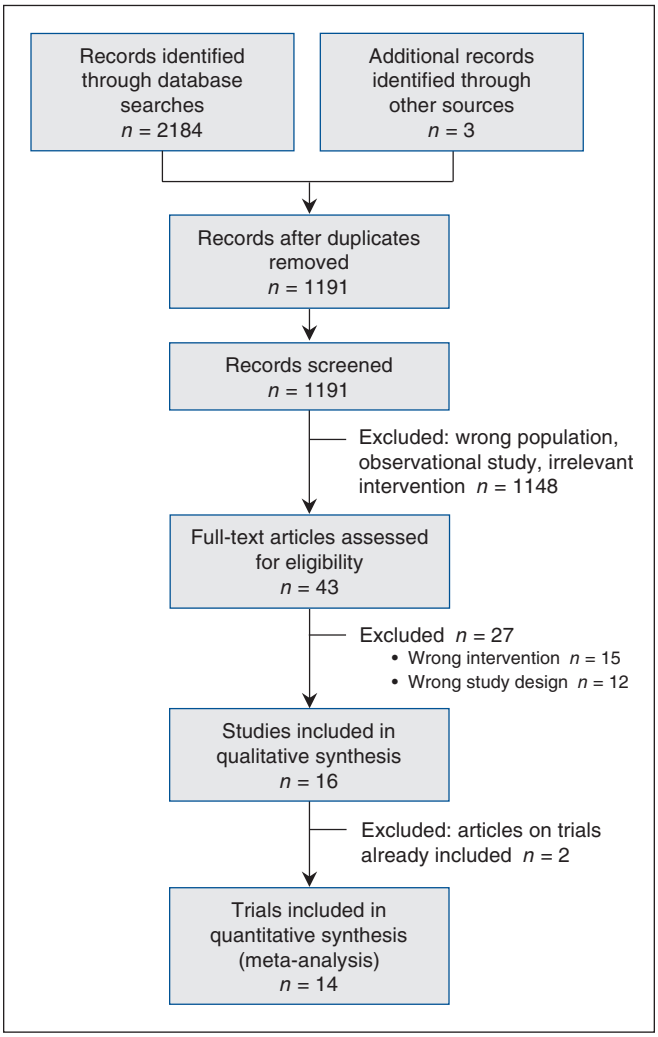

Figure 1: Flow diagram showing study selection.

Subgroup differences were significant for birth weight (p = 0.02) and gestational age (p = 0.01). Overall, there was high-quality evidence that bed rest was not associated with a greater birth weight compared to no bed rest (1492 births; WMD 40 g, 95% CI –30 g to 110 g, I^2 = 31%) (Supplementary Figure S2, Appendix 2).[18–20,22,23,25–27,29–31] However, subgroup analysis identified that bed rest modestly increased birth weight in Zimbabwe (WMD 100 g, 95% CI 40 g to 170 g, I^2 = 0%; p = 0.002 for subgroup differences; high evidence) but had no impact on birth weight in developed regions.

Table 1 (part 1 of 4): Study characteristics

Investigator	Country	Participants and methods	Intervention	Outcomes extracted
Developing country				
Crowther et al.,[20] 1989	Zimbabwe	139 women with twin pregnancies at < 34 weeks' gestation with cervical score ≥ –2 Randomization: block randomization Allocation concealment: consecutively numbered opaque, sealed envelopes Loss to follow-up: 2/70 women in experimental group were noncompliant Exclusion criteria: uncertain gestational age, cervical suture in place, antepartum hemorrhage, hypertension, previous cesarean delivery and in labour Recruitment dates: 1984 onward	**Experimental group:** in-hospital bed rest Mean gestational age at study start 33.3 (SD 1.8) wk Length: 2.5 wk *n* = 70 **Control group:** conventional outpatient management; admitted to hospital if pregnancy complications occurred Mean gestational age at study start 33.5 (SD 1.8) wk Length: 2.3 wk *n* = 69	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, birth weight < 2500 g, birth weight < 1500 g, SGA, admission to NICU **Maternal:** cesarean delivery, pregnancy-induced hypertension, PROM
Crowther et al.,[19] 1990	Zimbabwe	118 women with uncomplicated twin pregnancies between 28 and 30 weeks' gestation Randomization: block randomization Allocation concealment: numbered opaque, sealed envelopes Exclusion criteria: cervical suture, hypertension, cesarean delivery scar, antepartum hemorrhage or uncertain gestational age 15/58 in experimental group were noncompliant Recruitment dates: 1984–1986	**Experimental group:** in-hospital bed rest; participants were encouraged to rest in bed as much as possible, although voluntary ambulation was allowed Mean gestational age at study start 29.1 (SD 1.2) wk Length: 7.0 wk *n* = 58 **Control group:** advised to continue normal activities at home; admitted to hospital if pregnancy complications occurred Mean gestational age at study start 29.2 (SD 1.7) wk Length: 6.7 wk *n* = 60	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, birth weight < 2500 g, birth weight < 1500 g, SGA, admission to NICU **Maternal:** cesarean delivery, pregnancy-induced hypertension, PROM
Crowther et al.,[18] 1991	Zimbabwe	Multiple-gestation births Randomization: block randomization Allocation concealment: opaque, sealed envelopes Loss to follow-up: none	**Experimental group:** in-hospital bed rest Mean gestational age at study start 29.0 (SD 4.7) wk Length: 5.4 wk *n* = 10 **Control group:** advised to continue normal activities at home; admitted to hospital if pregnancy complications occurred Mean gestational age at study start 29.4 (SD 3.0) wk Length: 4.3 wk *n* = 9	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, birth weight < 2500 g, birth weight < 1500 g, SGA, admission to NICU **Maternal:** cesarean delivery, pregnancy-induced hypertension, PROM
Crowther et al.,[22] 1992	Zimbabwe	218 women with singleton pregnancies at 28–38 weeks' gestation with nonproteinuric hypertension (blood pressure > 140/90 mm Hg) Randomization: block randomization, stratified Allocation concealment: opaque, sealed envelopes Loss to follow-up: none Recruitment dates: 1985–1986	**Experimental group:** admission to hospital for rest Mean gestational age at study start 35.3 (SD 2.6) wk Length: 3.0 wk *n* = 110 **Control group:** normal activity at home Mean gestational age at study start 34.6 (SD 3.0) wk Length: 3.6 wk *n* = 108	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, birth weight < 2500 g, SGA, admission to NICU **Maternal:** cesarean delivery, preeclampsia

Table 1 (part 2 of 4): Study characteristics

Investigator	Country	Participants and methods	Intervention	Outcomes extracted
Saunders et al.,[21] 1985	Zimbabwe	212 women with twin pregnancies at about 30 weeks' gestation Randomization: randomized; method not described Allocation concealment: consecutively numbered sealed envelopes Loss to follow-up: 11/105 in experimental group declined hospital admission, and 2/105 delivered before intervention start; 1/107 in control group delivered before intervention start Recruitment dates: not specified	**Experimental group:** in-hospital bed rest from 32 weeks' gestation until labour Mean gestational age at study start 32.7 wk Length: 4.6 wk *n* = 105 **Control group:** no activity restriction, at home; admitted to hospital if pregnancy complications occurred Gestational age at study start about 32 wk Length: > 5 wk *n* = 107	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, gestational age, birth weight < 2500 g, birth weight < 1500 g **Maternal:** preeclampsia
Developed countries				
Bigelow et al.,[31] 2016	US	36 women aged 18–55 yr with singleton pregnancies at < 34 weeks' gestation with PPROM Randomization: computer-generated randomization scheme Allocation concealment: sealed envelopes Exclusion criteria: actively receiving magnesium sulfate, footling breech presentation, or maternal or fetal indication for immediate delivery Loss to follow-up: 1/18 withdrew from control allocation Recruitment dates: not specified	**Experimental group:** in-hospital bed rest; instructed to spend majority of day in bed in reclined or sleeping position Mean gestational age at study start 29.2 (SD 5.7) wk Length: 2.7 wk *n* = 18 **Control group:** admitted to hospital; asked to walk for minimum of 20 min 3 times daily Mean gestational age at study start 28.9 (SD 7.6) wk Length: 1.6 wk *n* = 17 **Participants in both groups** given latency antibiotics ± ampicillin/amoxicillin and erythromycin for up to 7 d and 48-h course of intramuscularly administered betamethasone	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, admission to NICU **Maternal:** cesarean delivery
Dodd et al.,[23] 2005	Australia	7 women with triplet pregnancies Randomization: randomization schedule used variable blocks with stratification by parity Allocation concealment: third party opened consecutively numbered opaque, sealed envelopes and reported allocation over telephone Loss to follow-up: none Recruitment dates: 1996–2003	**Experimental group:** in hospital from 24 to 30 weeks' gestation; biweekly assessment; allowed to leave ward during weekends; encouraged to rest at home following discharge Mean gestational age at study start 23.4 (SD 1.7) wk Length: about 6 wk *n* = 3 **Control group:** advised to continue normal activity at home; biweekly in-clinic assessment Mean gestational age at study start 22.0 (SD 1.8) wk Length: about 6 wk *n* = 4	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, birth weight < 2500 g, birth weight < 1500 g **Maternal:** cesarean delivery, pregnancy-induced hypertension

When gestational age at birth was considered as a continuous variable, women who were on bed rest delivered babies at an earlier gestational age in developed regions (WMD –0.77 wk, 95% CI –1.26 to –0.27, I^2 = 0%; moderate evidence) (Figure 4) but not in the developing region (WMD –0.04 wk, 95% CI –0.35 to 0.26, I^2 = 6%; high-quality evidence).[18–25,29,30,31]

Overall, moderate-quality evidence indicated that bed rest did not decrease the risk of birth weight less than 2500 g (1837 births; RR 0.92, 95% CI 0.85 to 1.00, I^2 = 0% [Supplementary Figure S3, Appendix 2]).[18–25,27,29] Bed rest decreased the risk of delivering a baby weighing less than 2500 g in Zimbabwe (RR 0.89, 95% CI 0.81 to 0.98, I^2 = 0%; high-quality evidence) but not in developed regions.

Table 1 (part 3 of 4): Study characteristics

Investigator	Country	Participants and methods	Intervention	Outcomes extracted
Elliott et al.,[29] 2005	US	73 women with singleton pregnancies experiencing preterm labour with negative fetal fibronectin recruited from 4 tertiary hospitals in southwestern United States Randomization: computer-generated randomization schedule Allocation concealment: reported to study coordinator by third party, who opened opaque, sealed envelopes Inclusion criteria: > 14 yr of age, intact membranes, documented uterine contractions of > 6/h at admission, 23–33 6/7 weeks' gestation, < 3 cm cervical dilatation Recruitment dates: November 1997–September 2000	**Experimental group:** activity restriction at home; 2 weekly clinic visits, followed by biweekly clinic visits Mean gestational age at study start 30.7 (SD 2.7) wk Length: 5.9 wk *n* = 36 **Control group:** instructed to resume normal activities, including work responsibilities, at home; 2 weekly clinic visits followed by biweekly clinic visits Mean gestational age at study start 31.0 (SD 6.3) wk Length: 6.6 wk *n* = 37	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, birth weight < 2500 g, birth weight < 1500 g, admission to NICU **Maternal:** none
Hartikainen-Sorri et al.,[24] 1984	Finland	73 women with twin pregnancies Randomization: based on year of birth Allocation concealment: not mentioned Loss to follow-up: 5 women excluded from experimental group owing to program refusal Recruitment dates: 1979–1980	**Experimental group:** routine hospital rest Gestational age at study start > 29 wk Length: until delivery (mean 36.7 [SD 2.4] wk) *n* = 28 **Control group:** specialized outpatient antenatal care; weekly clinic visits; admitted to hospital if complications occurred Gestational age at study > 29 wk Length: until delivery (mean 37.4 [SD 1.8] wk) *n* = 45	**Infant:** perinatal death, preterm birth (< 37 wk), gestational age, birth weight < 2500 g, birth weight < 1500 g **Maternal:** pregnancy-induced hypertension
Hobel et al.,[28] 1994	US	1774 women at high risk for preterm birth based on scoring of risk factors at < 31 weeks' gestation Women in intervention hospitals were randomized to 1 of 5 interventions Randomization: method not described Allocation concealment: not described Loss to follow-up: not described	**1. Experimental group:** bed rest at home **2. Control group 1:** placebo **3. Progestin:** women administered progestin; not included in meta-analyses **4. Social support:** women given social support; not included in meta-analyses **5. Control group 2:** no intervention Length: < 31 wk until birth **All participants in intervention hospitals** were given education intervention consisting of identification of preterm labour, steps to take if signs of preterm labour occurred and prevention strategies	**Infant:** preterm birth (< 37 wk) **Maternal:** none
Laurin et al.,[30] 1987	Sweden	Women with singleton pregnancies with estimated weight deviation (suspected intrauterine growth restriction) of > 20% at 32 weeks' gestation or > 15% at 34 weeks' gestation Randomization: quasi-random based on even and odd year of birth (maternal) Allocation: not described Loss to follow-up: 15/49 in experimental group and 8/58 in control group did not fulfill requirements of their allocation Recruitment dates: 1982–1983	**Experimental group:** admitted to hospital; advised to rest in bed 22 h per day; allowed to rest at home on weekends Gestational age at study start < 35 wk Length: > 3 wk on average *n* = 34 **Control group:** normal activity at home; discontinuation of work duties Gestational age at study start < 35 wk Length: > 4 wk on average *n* = 50	**Infant:** perinatal death, birth weight, gestational age **Maternal:** cesarean delivery

Table 1 (part 4 of 4): Study characteristics

Investigator	Country	Participants and methods	Intervention	Outcomes extracted
Leung et al.,[27] 1998	Hong Kong	88 women with singleton pregnancies at 28–38 weeks' gestation with diastolic blood pressure 90–100 mm Hg Randomization: not described Allocation concealment: consecutively numbered opaque, sealed envelopes Loss to follow-up: infant outcomes for 13 pregnancies in experimental group and 8 pregnancies in control group not presented owing to lack of hypertension Exclusion criteria: proteinuria or symptoms of severe preeclampsia Recruitment dates: May 1995–November 1996	**Experimental group:** admitted to hospital and advised to rest in bed as much as possible Mean gestational age at study start 33.2 (SD 2.9) wk *n* = 44 **Control group:** normal activity at home; daily proteinuria testing at home and weekly clinic visits; admitted to hospital if proteinuria, severe preeclampsia or fetal growth restriction developed Mean gestational age at study 33.1 (SD 3.0) wk *n* = 44	**Infant:** birth weight, birth weight < 2500 g, SGA, admission to NICU (reported only for pregnancies in which hypertension developed [31 inpatients and 36 outpatients]) **Maternal:** cesarean delivery, pregnancy-induced hypertension
MacLennan et al.,[25] 1990	Australia	141 women with multiple-gestation pregnancies (twins) Randomization: computer-generated list of random numbers Allocation concealment: patient and research coordinator blinded to allocation number meaning Exclusion criteria: hypertension, polyhydramnios, antepartum hemorrhage, preterm labour or rupture of membranes. Loss to follow-up: 13/69 participants allocated to experimental group did not complete study Recruitment dates: not specified	**Experimental group:** in hospital from 26 to 30 weeks' gestation; allowed to leave on weekends Mean gestational age at study start 26.0 (SD 2.1) wk Length: 4 wk *n* = 69 **Control group:** advised to continue normal activities at home and visit clinic every 2 wk Mean gestational age at study start 26.0 (SD 2.1) wk Length: 4 wk *n* = 72	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, birth weight < 2500 g, birth weight < 1500 g, admission to NICU **Maternal:** cesarean delivery, pregnancy-induced hypertension, PROM, GDM
Mathews,[26] 1977	UK	135 women with singleton pregnancies complicated by mild nonalbuminuric and nonsymptomatic hypertension (diastolic blood pressure 90–109 mm Hg) after 28 weeks' gestation Randomization: randomized; method not described Allocation concealment: previously prepared cards in envelopes Loss to follow-up: patients excluded from trial if they refused hospital admission	**Sedated group** *Experimental group:* admitted to hospital and kept in bed aside from meals and toileting; administered phenobarbitone, 15 mg 3 times daily Gestational age at study start > 28 wk Length: 97.2% delivered after 37 wk *n* = 36 *Control group:* advised to resume normal activity at home; administered phenobarbitone, 15 mg 3 times daily Gestational age at study start > 28 wk Length: 97.2% delivered after 37 wk *n* = 36 **Nonsedated group** *Experimental group:* admitted to hospital and kept in bed aside from meals and toileting Gestational age at study start > 28 wk Length: 97.1% delivered after 37 wk *n* = 35 *Control group:* advised to resume normal activity at home Gestational age at study start > 28 wk Length: 100% delivered after 37 wk *n* = 28	**Infant:** perinatal death, preterm birth (< 37 wk), very preterm birth, birth weight, gestational age, birth weight < 2500 g, SGA **Maternal:** cesarean delivery, pregnancy-induced hypertension

Notes: GDM = gestational diabetes mellitus, NICU = neonatal intensive care unit, PPROM = preterm premature rupture of membranes, PROM = premature rupture of membranes, SD = standard deviation, SGA = small for gestational age.

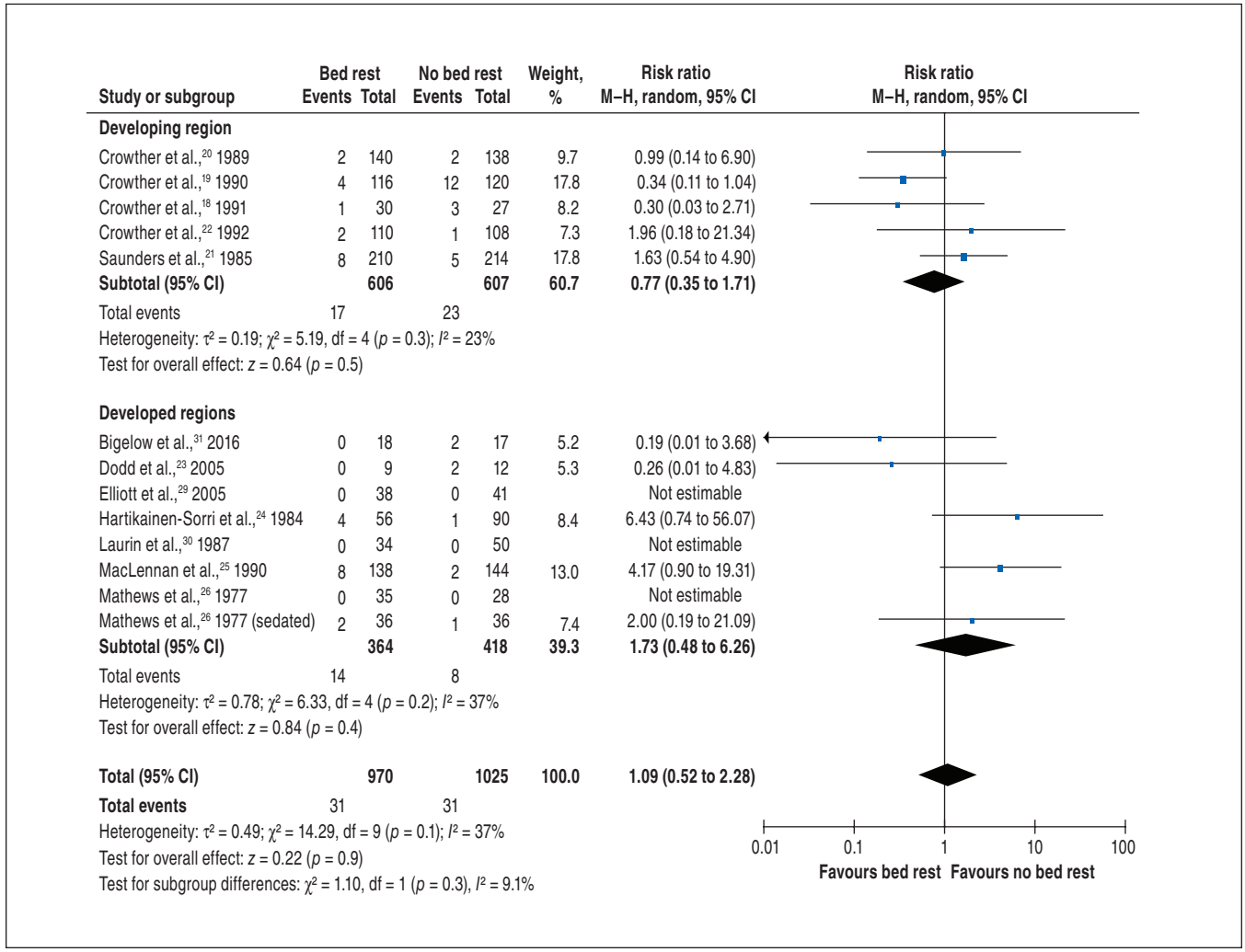

Figure 2: Effect of bed rest (experimental) versus no bed rest (control) on perinatal death. Note: CI = confidence interval, df = degrees of freedom, M–H = Mantel–Haenszel.

The risk of delivering a newborn weighing less than 1500 g (Supplementary Figure S4, Appendix 2),[18–21,23–25,29] being small for gestational age (Supplementary Figure S5, Appendix 2)[18–20,22,26,27] or being admitted to the neonatal intensive care unit (Supplementary Figure S6, Appendix 2)[18–20,22,25,27,29,31] was similar between the bed-rest and no–bed-rest groups. Subgroup analyses were not statistically significant.

Maternal outcomes

Overall, there was low-quality evidence from 10 RCTs (963 women) regarding the association between bed rest and cesarean birth.[18–20,22,23,25–27,30,31] The pooled estimate indicated that bed rest did not reduce the rate of cesarean delivery (RR 1.00, 95% CI 0.74 to 1.34, I^2 = 31%) (Supplementary Figure S7, Appendix 2). Subgroup analyses were not statistically significant.

Six RCTs (559 women) with low-quality evidence indicated that bed rest did not reduce the risk of hypertensive disorders of pregnancy (RR 0.85, 95% CI 0.51 to 1.42, I^2 = 25%) (Supplementary Figure S8, Appendix 2).[18–20,23–26] Bed rest also did not reduce the rate of preeclampsia (RR 0.98, 95% CI 0.80 to 1.19) (Supplementary Figure S9, Appendix 2) or preterm rupture of membranes (438 women; RR 1.38, 95% CI 0.85 to 2.26, I^2 = 0%) (Supplementary Figure S10, Appendix 2).[18–20,25]

One moderate-quality RCT[25] (downgraded owing to serious inconsistency) (141 women) showed that bed rest did not reduce the rate of gestational diabetes (RR 1.04, 95% CI 0.22 to 4.99) (Supplementary Figure S11, Appendix 2). Funnel plots showed that the outcomes examined were not influenced by publication bias (Supplementary Figures S12 and S13, Appendix 2).

Sensitivity analyses

Eight of the 14 studies included multiple-gestation pregnancies.[18–21,23,25–27] When stratified for singleton or multiple gestation, perinatal death, premature birth at less than 37 weeks, gestational age, birth weight less than 1500 g, birth weight less than 2500 g, being small for gestational age, admission to neonatal intensive care unit, cesarean delivery, preterm

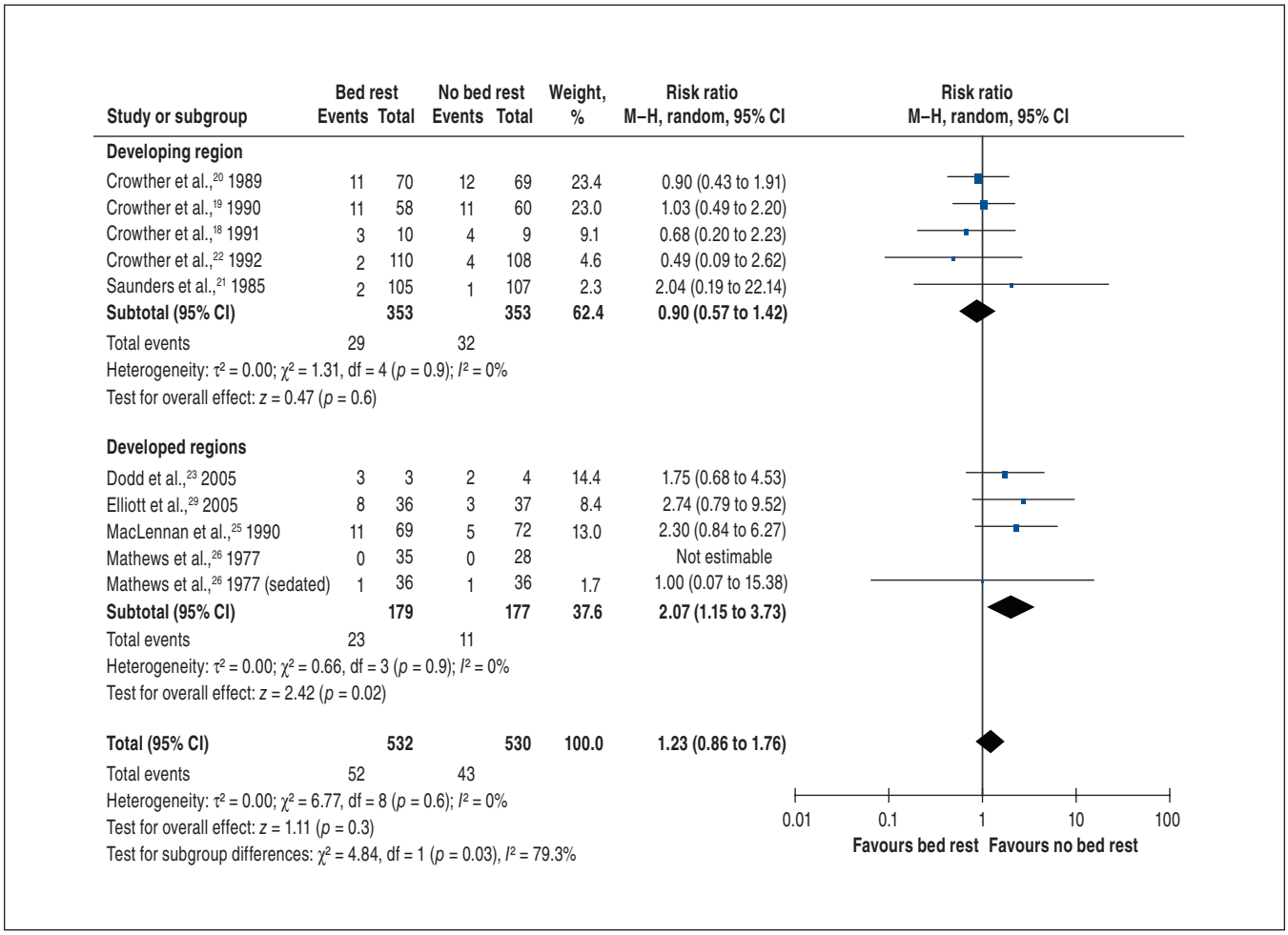

Figure 3: Effect of bed rest (experimental) versus no bed rest (control) on very preterm birth. The study by Bigelow and colleagues[31] was removed owing to its influence on heterogeneity (heterogeneity of developed regions subgroup $p < 0.001$; 100% event rate in both study arms). Note: CI = confidence interval, df = degrees of freedom, M–H = Mantel–Haenszel.

rupture of membranes, gestational diabetes, pregnancy-induced hypertension and preeclampsia were all similar between the no–bed-rest and bed-rest groups (Supplementary Figures S14–S27, Appendix 2). Although RCTs examining bed rest for multiple births were more common in the developing region than in developed regions, stratification by singleton- versus multiple-gestation birth explained significantly less heterogeneity than stratification by developmental status of the region.

Interpretation

Overall, maternal and fetal outcomes were similar between women on bed rest and those not on bed rest. However, stratification by the developmental status of the region explained a significant amount of heterogeneity; this has been noted in previous meta-analyses on this topic.[5,10,11] Stratification identified a divergent impact of bed rest between groups such that bed rest in developed regions decreased gestational age by 5.4 days and increased the risk of delivering a very premature baby. In contrast, bed rest in the developing region increased birth weight by 100 g and decreased the risk of delivering a baby weighing less than 2500 g.

Six Cochrane reviews have previously examined the impact of bed rest on maternal and fetal outcomes including the prevention of preeclampsia (2 studies, $n = 106$),[33] improving outcomes of pregnancies complicated by hypertension (4 studies, $n = 449$),[10] the prevention of preterm birth (1 study, $n = 1266$),[3] impaired fetal growth (1 study, $n = 107$)[34] and multiple gestation (7 studies combining complicated and uncomplicated pregnancies, $n = 713$;[5] 6 studies including strict or partial bed rest, $n = 636$).[11] In all cases, the investigators concluded that there was insufficient evidence for or against the use of bed rest to improve maternal/fetal health outcomes as a result of small samples and high heterogeneity. In nonpregnant populations, the physiological effects of bed rest are not altered by the indication for bed rest;[35] thus, we combined all indications for bed rest during pregnancy. Stratification by developmental status of the region resulted in subgroup heterogeneity of 40% or less for all but 1 subgroup analysis (55%). Hospital admission may explain some of the differences observed between the influence of bed rest in developed versus developing regions.

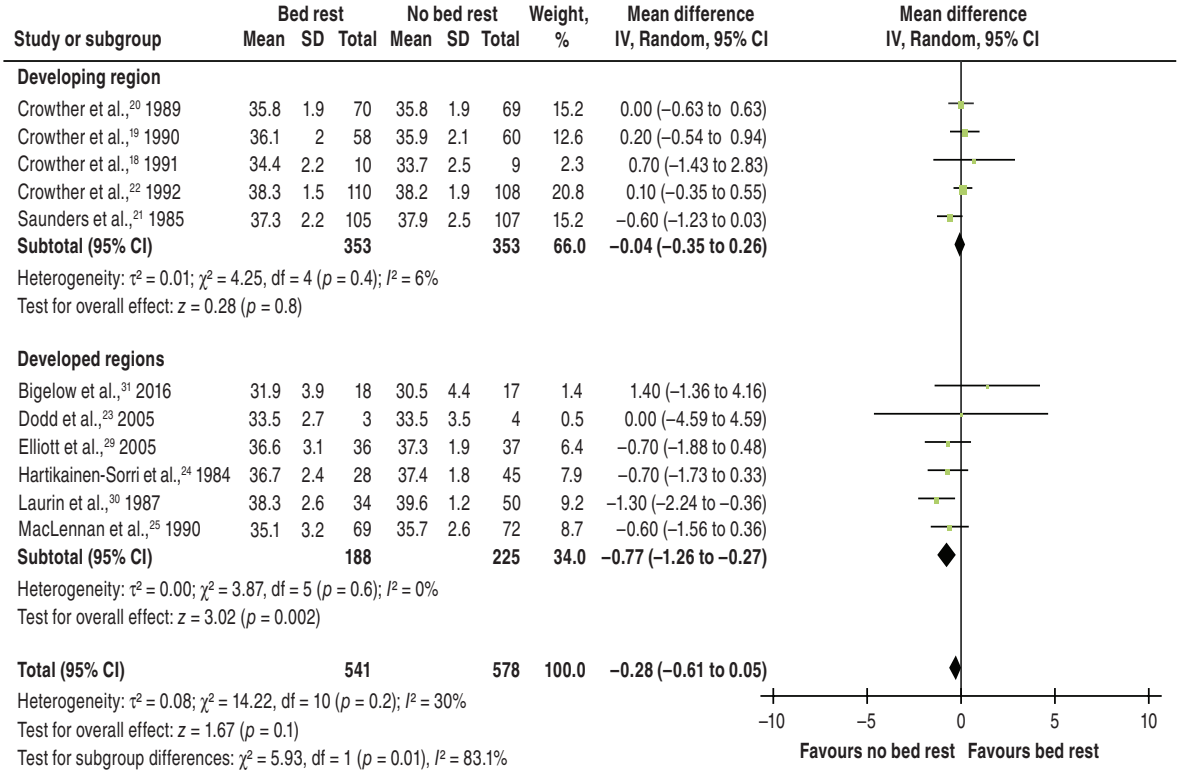

Figure 4: Effect of bed rest (experimental) versus no bed rest (control) on gestational age. Note: CI = confidence interval, df = degrees of freedom, IV = inverse variance, SD = standard deviation.

Although bed rest has been shown to decrease maternal weight gain in developed countries,[36] admission to hospital in developing countries may afford access to proper nutrition, sanitation, clean water and medical professionals. These factors may overcome some of the negative physiological effects of bed rest in selected populations.

It is beyond the scope of this review to determine whether bed rest or hospital admission itself improved birth weight in studies in Zimbabwe. Additional work is required to dissect the influence of hospital admission versus bed rest in developing regions. Bed rest is likely to drive inflammation, which may increase the risk of preterm birth, necessitating further research on the levels of inflammatory cytokines in pregnant women on bed rest. Although there is a reduction in blood pressure during bed rest,[37] other mechanisms of harm such as endothelial dysfunction may lead to further negative effects in pregnancies complicated by hypertension or preeclampsia. As a result, further research may be required in developed regions on the influence of bed rest on pregnancies complicated by hypertension.

Limitations

All trials of bed rest in developing regions were conducted in Zimbabwe. As the rates of maternal and fetal morbidity and mortality in Zimbabwe are among the highest in the world,[38,39] our findings from this country may not be generalizable to other developing regions. Furthermore, as all the Zimbabwe studies were conducted between 1984 and 1992, this may limit the applicability of the results for developing countries, as obstetrical practice will have changed over time. In the Zimbabwe studies, bed rest was conducted in hospital, and no bed rest was conducted at home. In developing countries, low birth weight is associated with hypertensive disorders of pregnancy, preeclampsia, nutritional status of the woman, anemia and access to health care.[40] Hospital admission may afford improved access to skilled health care workers, sanitation and nutritional status monitoring, thereby reducing the risk of low birth weight.[40]

Conclusion

Our analyses showed that, in developed regions, 1 additional baby was born very premature for every 15.1 women treated with bed rest. In conjunction with the overwhelming evidence of negative maternal health consequences of prenatal bed rest, our results suggest that bed rest increases the risk of serious negative consequences for newborns in developed regions. In developing regions, bed rest appears to have a minimal positive effect on birth weight, but this finding may be confounded by the effects of hospital admission.

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Affiliations: Program for Pregnancy and Postpartum Health (Matenchuk, Cai, Davenport) and Physical Activity and Diabetes Laboratory (Boulé, Davenport), Faculty of Kinesiology, Sport, and Recreation, University of Alberta; Departments of Medicine (Khurana) and Obstetrics & Gynecology (Khurana), University of Alberta; Women and Children's Health Research Institute (Cai, Davenport), University of Alberta; John W. Scott Health Sciences Library (Slater), University of Alberta; Alberta Diabetes Institute (Boulé, Davenport), University of Alberta, Edmonton, Alta.

Contributors: Margie Davenport led the review. Rshmi Khurana conceived the project. Margie Davenport, Normand Boulé and Linda Slater designed the search strategy. Margie Davenport, Brittany Matenchuk and Chenxi Cai performed the review. Margie Davenport and Brittany Matenchuk analyzed and interpreted the data. Brittany Matenchuk drafted the manuscript, and Margie Davenport, Rshmi Khurana, Chenxi Cai and Normand Boulé critically revised it for important intellectual content. All of the authors approved the version to be published and agreed to be accountable for all aspects of the work.

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