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

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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, 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, P = 0%), and the risk of a very premature birth was increased (risk ratio 2.07, 95% CI 1.15 to 3.73, P = 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, intraterine 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 201716,30,11 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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Research

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.13

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.11 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.cmaopen.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 RCT filter to exclude the drug therapy floating subheading.

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 [I² ≥ 50%] or only 1 study was assessed), indirectness (bed-rest-only interventions and bed rest plus co-interventions 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 definition15 and 2) single- versus multiple-gestation pregnancies. We used χ² tests to estimate heterogeneity between trials. The percent of total variability attributable to heterogeneity (i.e., not due to chance) was expressed as the I². We explored the source of heterogeneity when intergroup 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
GRADEpro GDT (McMaster University and Evidence Prime) to evaluate and tabulate quality of evidence and strength of recommendations.  

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). Indications for bed rest in the Zimbabwe studies included multiple-gestation pregnancy and hypertensive disorders of pregnancy. Studies evaluating pregnancies in developed regions examined multiple-gestation pregnancy, hypertensive disorders of pregnancy, preterm labour, suspected intrauterine growth restriction, high risk of preterm birth and preterm rupture of membranes.

The length of the prescribed bed rest ranged from 1.0 to 9.7 weeks. 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 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). 

Preterm birth (< 37 wk) and very preterm birth are the leading causes of perinatal morbidity and mortality. In our meta-analysis, “very premature” was defined as less than 32 weeks in 2 studies, less than 34 weeks in 4 studies and less than 35 weeks in 2 studies. Our analysis of preterm birth included 2511 women. No difference was found in rates of preterm birth between women on bed rest and those not on bed rest (RR 0.98, 95% CI 0.91 to 1.06, $I^2 = 31\%$) (Supplementary Figure S2, Appendix 2).

Preterm birth 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) but not the developing region. Subgroup differences were significant ($p = 0.03$).

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). However, subgroup analysis identified that bed rest modestly increased birth weight in Zimbabwe (WMD 100 g, 95% CI 40 g to 170 g, $F = 0\%$; $p = 0.002$ for subgroup differences; high evidence) but had no impact on birth weight in developed regions.
| Investigator | Country | Participants and methods | Intervention | Outcomes extracted |
|--------------|---------|--------------------------|--------------|--------------------|
| **Developing country** | | | | |
| Crowther et al., 1989 | Zimbabwe | 139 women with twin pregnancies at < 34 weeks' gestation with cervical score ≥ -2 | Experimental group: in-hospital bed rest | 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 |
| | | 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 | 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 | |
| | | Experimental group: in-hospital bed rest |  | |
| | | Control group: conventional outpatient management; admitted to hospital if pregnancy complications occurred |  | |
| | | 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 | |
| | | Recruitment dates: 1984 onward |  | |
| | | Mean gestational age at study start 33.5 (SD 1.8) wk  
Length: 2.3 wk  
n = 69 | |
| Crowther et al., 1990 | Zimbabwe | 118 women with uncomplicated twin pregnancies between 28 and 30 weeks' gestation | Experimental group: in-hospital bed rest; participants were encouraged to rest in bed as much as possible, although voluntary ambulation was allowed | 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 |
| | | 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 | Mean gestational age at study start 29.1 (SD 1.2) wk  
Length: 7.0 wk  
n = 58 | |
| | | Recruitment dates: 1984–1986 | Control group: advised to continue normal activities at home; admitted to hospital if pregnancy complications occurred | |
| | | 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 | |
| | | Mean gestational age at study start 29.2 (SD 1.7) wk  
Length: 6.7 wk  
n = 60 | |
| | | 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 1.7) wk  
Length: 6.7 wk  
n = 60 | |
| | | Mean gestational age at study start 29.4 (SD 1.7) wk  
Length: 6.7 wk  
n = 60 | |
| Crowther et al., 1991 | Zimbabwe | Multiple-gestation births | Experimental group: in-hospital bed rest | 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 |
| | | Randomization: block randomization  
Allocation concealment: opaque, sealed envelopes  
Loss to follow-up: none | Mean gestational age at study start 29.0 (SD 4.7) wk  
Length: 5.4 wk  
n = 10 | |
| | | Recruitment dates: 1985–1986 | Control group: advised to continue normal activities at home; admitted to hospital if pregnancy complications occurred | |
| | | 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 | |
| | | Mean gestational age at study start 29.4 (SD 3.0) wk  
Length: 4.3 wk  
n = 9 | |
| | | 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 | |
| | | Mean gestational age at study start 29.4 (SD 3.0) wk  
Length: 4.3 wk  
n = 9 | |
| Crowther et al., 1992 | Zimbabwe | 218 women with singleton pregnancies at 28–38 weeks' gestation with nonproteinuric hypertension (blood pressure > 140/90 mm Hg) | Experimental group: admission to hospital for rest | 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, pre eclampsia |
| | | Randomization: block randomization, stratified  
Allocation concealment: opaque, sealed envelopes  
Loss to follow-up: none  
Recruitment dates: 1985–1986 | Mean gestational age at study start 35.3 (SD 2.6) wk  
Length: 3.0 wk  
n = 110 | |
| | | 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, pre eclampsia | |
| | | Mean gestational age at study start 34.6 (SD 3.0) wk  
Length: 3.6 wk  
n = 108 | |
| | | Control group: normal activity at home |  | |
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]). 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.

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**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                             | Experimental group: in-hospital bed rest from 32 weeks' gestation until labour | Infant: perinatal death, preterm birth (<37 wk), very preterm birth, gestational age, birth weight < 2500 g, birth weight < 1500 g, Maternal: preeclampsia |
|                         |             | Randomization: randomized; method not described                                           | Mean gestational age at study start 32.7 wk                                   |                                                                                   |
|                         |             | Allocation concealment: consecutively numbered sealed envelopes                          | Length: 4.6 wk \( n = 105 \)                                                |                                                                                   |
|                         |             | 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                                                          |                                                                              |                                                                                   |
| Bigelow et al.,31 2016  | US          | 36 women aged 18–55 yr with singleton pregnancies at < 34 weeks' gestation with PPROM   | Experimental group: in-hospital bed rest; instructed to spend majority of day in bed in reclined or sleeping position | Infant: perinatal death, preterm birth (<37 wk), very preterm birth, birth weight, gestational age, admission to NICU, Maternal: cesarean delivery |
|                         |             | Randomization: computer-generated randomization scheme                                    | Mean gestational age at study start 29.2 (SD 5.7) wk                         |                                                                                   |
|                         |             | Allocation concealment: sealed envelopes                                                  | Length: 2.7 wk \( n = 18 \)                                                 |                                                                                   |
|                         |             | 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                                                          |                                                                              |                                                                                   |
| Dodd et al.,23 2005     | Australia   | 7 women with triplet pregnancies                                                         | 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 | 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 |
|                         |             | Randomization: randomization schedule used variable blocks with stratification by parity | Mean gestational age at study start 23.4 (SD 1.7) wk                         |                                                                                   |
|                         |             | Allocation concealment: third party opened consecutively numbered opaque, sealed envelopes and reported allocation over telephone | Length: about 6 wk \( n = 3 \)                                            |                                                                                   |
|                         |             | Loss to follow-up: none                                                                  |                                                                              |                                                                                   |
|                         |             | Recruitment dates: 1996–2003                                                             |                                                                              |                                                                                   |
Table 1 (part 3 of 4): Study characteristics

| Investigator          | Country | Participants and methods                                                                 | Intervention                                                                 | Outcomes extracted                                           |
|-----------------------|---------|------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------|
| Elliott et al., 29    | US      | 73 women with singleton pregnancies experiencing preterm labour with negative fetal fibronectin recruited from 4 tertiary hospitals in southwestern United States | Experimental group: activity restriction at home; 2 weekly clinic visits, followed by biweekly clinic visits | 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 |
|                       |         | Randomization: computer-generated randomization schedule                                  | Mean gestational age at study start 30.7 (SD 2.7) wk                           |                                                             |
|                       |         | Allocation concealment: reported to study coordinator by third party, who opened opaque, sealed envelopes | Length: 5.9 wk                                                               |                                                             |
|                       |         | Inclusion criteria: > 14 yr of age, intact membranes, documented uterine contractions of > 6 hr at admission, 23–33 6/7 weeks’ gestation, < 3 cm cervical dilatation | *n* = 36                                                                    |                                                             |
|                       |         | Recruitment dates: November 1997–September 2000                                          |                                                                              |                                                             |
|                       |         |                                                                                          | **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                                                                    |                                                             |
| Hartikainen-Sorri et al., 24 | Finland | 73 women with twin pregnancies                                                          | Experimental group: routine hospital rest                                     | Infant: perinatal death, preterm birth (< 37 wk), gestational age, birth weight < 2500 g, birth weight < 1500 g Maternal: pregnancy-induced hypertension |
|                       |         | Randomization: based on year of birth                                                     | Gestational age at study start > 29 wk                                        |                                                             |
|                       |         | Allocation concealment: not mentioned                                                     | Length: until delivery (mean 36.7 [SD 2.4] wk)                               |                                                             |
|                       |         | Loss to follow-up: 5 women excluded from experimental group owing to program refusal     | *n* = 28                                                                    |                                                             |
|                       |         | Recruitment dates: 1979–1980                                                             | **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                                                                    |                                                             |
| Hobel et al., 28      | US      | 1774 women at high risk for preterm birth based on scoring of risk factors at < 31 weeks’ gestation | 1. **Experimental group:** bed rest at home                                 | Infant: preterm birth (< 37 wk) Maternal: none |
|                       |         | Women in intervention hospitals were randomized to 1 of 5 interventions                   | 2. **Control group 1:** placebo                                                |                                                             |
|                       |         | Randomization: method not described                                                      | 3. **Progestin:** women administered progestin; not included in meta-analyses |                                                             |
|                       |         | Allocation concealment: not described                                                    | 4. **Social support:** women given social support; not included in meta-analyses |                                                             |
|                       |         | Loss to follow-up: not described                                                         | 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* |                                                             |
|                       |         |                                                                                          |                                                                             |                                                             |
| Laurin et al., 30     | 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 | **Experimental group:** admitted to hospital; advised to rest in bed 22 h per day; allowed to rest at home on weekends | Infant: perinatal death, birth weight, gestational age Maternal: cesarean delivery |
|                       |         | Randomization: quasi-random based on even and odd year of birth (maternal)               | Gestational age at study start < 35 wk                                         |                                                             |
|                       |         | Allocation: not described                                                                | Length: > 3 wk on average                                                      |                                                             |
|                       |         | Loss to follow-up: 15/49 in experimental group and 8/58 in control group did not fulfill requirements of their allocation | *n* = 34                                                                    |                                                             |
|                       |         | Recruitment dates: 1982–1983                                                             |                                                                             |                                                             |
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 | **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 start 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: May 1995–November 1996 | **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 **Non sedated 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.
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.18–20,22,23–27,30,31 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, F = 31%) (Supplementary Figure S6, 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, F = 25%) (Supplementary Figure S8, Appendix 2).16–20,23–26 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 0.98, 95% CI 0.80 to 1.19) (Supplementary Figure S9, Appendix 2). Bed rest also 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...
rapture 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.4,10,11 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),13 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)14 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;15 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.

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**Table 1: Meta-analysis of bed rest versus no bed rest on very preterm birth.**

| Study or subgroup | Bed rest | No bed rest | Weight, % | Risk ratio M–H, random, 95% CI |
|-------------------|----------|-------------|-----------|-------------------------------|
| Developing region |          |             |           |                               |
| Crowther et al., 20 1989 | 11 | 70 | 12 | 69 | 23.4 | 0.90 (0.43 to 1.91) |
| Crowther et al., 19 1990 | 11 | 58 | 11 | 60 | 23.0 | 1.03 (0.49 to 2.20) |
| Crowther et al., 18 1991 | 3 | 10 | 4 | 9 | 9.1 | 0.68 (0.20 to 2.23) |
| Crowther et al., 22 1992 | 2 | 110 | 4 | 108 | 4.6 | 0.49 (0.09 to 2.62) |
| Saunders et al., 21 1985 | 2 | 105 | 1 | 107 | 2.3 | 2.04 (0.19 to 22.14) |
| Subtotal (95% CI) | 353 | 353 | 62.4 | 0.90 (0.57 to 1.42) |
| Developed regions |          |             |           |                               |
| Dodd et al., 23 2005 | 3 | 3 | 2 | 4 | 14.4 | 1.75 (0.68 to 4.53) |
| Elliott et al., 24 2005 | 8 | 36 | 3 | 37 | 8.4 | 2.74 (0.79 to 9.52) |
| MacLennan et al., 25 1990 | 11 | 69 | 5 | 72 | 13.0 | 2.30 (0.84 to 6.27) |
| Mathews et al., 29 2005 | 0 | 35 | 0 | 28 | Not estimable |
| Mathews et al., 26 1977 (sedated) | 1 | 36 | 1 | 36 | 1.7 | 1.00 (0.07 to 15.38) |
| Subtotal (95% CI) | 179 | 177 | 37.6 | 2.07 (1.15 to 3.73) |
| Total events | 23 | 11 |
| Heterogeneity: \( \chi^2 = 0.00; \chi^2 = 0.66, df = 3 (p = 0.9); I^2 = 0% \) |
| Test for overall effect: \( z = 2.42 (p = 0.02) \) |
| Total (95% CI) | 532 | 530 | 100.0 | 1.23 (0.86 to 1.76) |
| Total events | 52 | 43 |
| Heterogeneity: \( \chi^2 = 0.00; \chi^2 = 6.77, df = 8 (p = 0.6); I^2 = 0% \) |
| Test for overall effect: \( z = 1.11 (p = 0.3) \) |
| Test for subgroup differences: \( \chi^2 = 4.84, df = 1 (p = 0.03), I^2 = 79.3% \) |

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**Figure 3:** Effect of bed rest (experimental) versus no bed rest (control) on very preterm birth. The study by Bigelow and colleagues31 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.
Although bed rest has been shown to decrease maternal weight gain in developed countries, 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, 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, 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. Hospital admission may afford improved access to skilled health care workers, sanitation and nutritional status monitoring, thereby reducing the risk of low birth weight.

**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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**Table:**

| Study or subgroup | Bed rest Mean | Bed rest SD | Bed rest Total | No bed rest Mean | No bed rest SD | No bed rest Total | Weight, % | Mean difference IV, Random, 95% CI | Mean difference IV, Random, 95% CI |
|------------------|--------------|------------|---------------|-----------------|---------------|------------------|-----------|----------------------------------|----------------------------------|
| Developing region |              |            |               |                 |               |                  |           |                                   |                                   |
| Crowther et al., 1989 | 35.8 | 1.9 | 70 | 35.8 | 1.9 | 69 | 15.2 | 0.00 (–0.63 to 0.63) |                                   |
| Crowther et al., 1990 | 36.1 | 2.0 | 58 | 35.9 | 2.1 | 60 | 12.6 | 0.20 (–0.54 to 0.94) |                                   |
| Crowther et al., 1991 | 34.4 | 2.2 | 10 | 33.7 | 2.5 | 9 | 2.3 | 0.70 (–1.43 to 2.83) |                                   |
| Crowther et al., 1992 | 38.3 | 1.5 | 110 | 38.2 | 1.9 | 108 | 20.8 | 0.10 (–0.35 to 0.55) |                                   |
| Saunders et al., 1985 | 37.3 | 2.2 | 105 | 37.9 | 2.5 | 107 | 15.2 | –0.60 (–1.23 to 0.03) |                                   |
| Subtotal (95% CI) | 353 | 188 | 541 | 353 | 225 | 578 | 100.0 | –0.28 (–0.61 to 0.05) |                                   |

**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.
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