

Prenatal bed rest: A meta-analysis

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Declaration of interests

The authors have no conflicts of interest to report.

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3 **42 ABSTRACT**

4 **43 BACKGROUND:** Bed rest is prescribed by 71-95% of maternity health care professionals for
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6 **44** high-risk pregnancy complications. We synthesized evidence from randomized controlled trials
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9 **45** to quantify the influence of maternal bed rest on maternal/fetal health outcomes in developed and
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11 **46** undeveloped regions.

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13 **47 METHODS:** A structured search was conducted through MEDLINE, EMBASE, CINAHL, Web
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16 **48** of Science, Ovid's Cochrane Central Register of Controlled Trials and Cochrane Database of
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18 **49** Systematic Reviews and ClinicalTrials.gov up to August 22, 2018. RCTs comparing standard
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20 **50** care to standard care plus bed rest after 20 weeks gestation were assessed.

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22 **51 RESULTS:** Our search identified 767 publications of which 71 were assessed for eligibility.
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25 **52** Sixteen publications reporting on fourteen unique studies (2,608 women, 3,328 fetuses) were
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27 **53** included in the analysis. Overall, maternal/newborn outcomes were similar between groups;
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29 **54** however, there was a 40g greater birth weight with bed rest (Weighted Mean Difference
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31 **55** [WMD]: 40g, 95% confidence interval [CI]: -30g, 110g, $I^2=31%$). In subgroup analyses between
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33 **56** developed and undeveloped regions, divergent effects were observed. Gestational length was
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35 **57** shorter with bed rest in developed regions (WMD: -0.77 weeks, 95% CI: -1.26, -0.27, $I^2=0%$).
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38 **58** The odds of a very premature birth (Odds Ratio [OR]: 2.69, 95% CI: 1.19, 6.07, $I^2=0%$) and
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40 **59** having a newborn <1500g (OR: 1.93, 95% CI: 1.00, 3.70, $I^2=0%$) were also increased in
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42 **60** developed regions.

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45 **61 INTERPRETATION:** In developed regions, treatment of complicated pregnancies with
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47 **62** prolonged bed rest results in worse newborn outcomes.
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66 **Introduction**

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68 Bed rest and activity restriction is prescribed to approximately 20% of pregnant women with the
69 intent of improving maternal/fetal health outcomes of high-risk pregnancies complicated by
70 preterm labour, intrauterine growth restriction and hypertension¹⁻³. It is associated with an
71 economic cost of up to 7 billion dollars per year in the United States alone (including
72 hospitalization, lost wages, and lost domestic productivity)^{1,4}. However, strong evidence
73 suggests prolonged bed rest negatively impacts maternal health (linked to anxiety, depression,
74 gestational diabetes, muscle atrophy, bone loss and venous thromboembolism) and there is little
75 evidence of improved pregnancy outcomes⁵⁻⁷. Despite the lack of evidence bed rest continues to
76 be prescribed by up to 95% of clinicians^{1,8}. This has resulted in an urgent call for additional
77 research to elucidate the potential benefits (or harms) of bed rest for the mother and fetus by the
78 World Health Organization and the American College of Obstetricians and Gynecologists⁸⁻¹⁰.
79 We conducted a systematic review and meta-analysis of randomized, controlled trials (RCTs)
80 which contrasted bed rest or activity restriction in conjunction with standard care versus standard
81 care alone (no bed rest) in pregnant women ≥ 20 weeks gestation on maternal/fetal health
82 outcomes.

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84 **Methods**

85 *Eligibility Criteria*

86 This review was conducted in accordance with the PRISMA guidelines¹¹ and registered with the
87 PROSPERO database (Registration number: CRD42018099237). Inclusion criteria (defined *a*
88 *priori*) were: RCTs in pregnant women comparing standard care (including tocolytics, anti-
89 hypertensive medications) plus bed rest (including activity restriction; hospitalized or at home)

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90 versus standard care without activity restriction (no bed rest). Trials were eligible if they
91 included women who were ≥ 20 weeks gestation. Bed rest was defined as a prescribed restriction
92 of activity encompassing the majority of waking hours for ≥ 1 week⁵. Fetal outcomes included
93 birth weight, small at birth (birth weight < 1500 g and < 2500 g), or small for gestational age
94 (SGA: less than the 10th percentile for gestational age and sex), gestational age, premature
95 delivery (< 37 weeks at birth), very premature delivery (as defined by the author < 35 , < 34 or < 32
96 weeks at birth), perinatal death and admission to the neonatal intensive care unit (NICU).
97 Maternal outcomes included preterm rupture of membranes (PROM), Pregnancy-Induce
98 Hypertension (PIH), pre-eclampsia, and gestational diabetes mellitus (GDM). Studies were not
99 excluded due to language of publication or publication format (e.g., abstracts only).

100 101 *Information sources*

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103 A structured search was conducted through MEDLINE, EMBASE, CINAHL, Web of Science,
104 Ovid's Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic
105 Reviews and ClinicalTrials.gov up to and including August 22, 2018 (see Online Supplement for
106 complete search strategy).

107 108 *Study selection and data extraction*

109 Records identified by the search strategy were independently assessed for inclusion by BAM or
110 CC and MHD, with NGB acting as arbitrator in the event of disagreement. The most recent or
111 complete version from multiple publications of the same trial was selected. Data from included
112 studies were extracted independently by BAM and MHD using a standardized data collection
113 form including: the above described outcomes of interest, as well as maternal age, height, body
114 mass index (BMI) at study entry, and existing conditions (i.e., GDM, maternal hypertension,

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3 115 PRM), sample size, indication for bed rest, duration of bed rest, location of bed rest and no bed
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5 116 rest groups (e.g., hospital versus home) and any co-interventions used.

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10 118 *Quality measures and risk of bias*

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12 119 The risk of bias in RCTs were assessed following the Cochrane Handbook¹². All studies were
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14 120 screened for potential sources of bias including selection bias, reporting bias, performance bias,
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16 121 detection bias, attrition bias and “other” sources of bias. Risk of bias across studies was rated as
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18 122 "serious" when studies having the greatest influence on the pooled result [assessed using weight
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20 123 (%) given in forest plots] presented “high” risk of bias. The quality of the evidence was assessed
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22 124 using the Grading of Recommendations Assessment, Development and Evaluation (GRADE)
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24 125 system. Evidence from RCTs began with a high quality evidence by default, and then were
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26 126 downgraded or upgraded based on pre-specified criteria. Criteria to downgrade included study
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28 127 limitations (weight of studies showed serious risk of bias), inconsistency (heterogeneity was high
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30 128 [$I^2 \geq 50\%$] or when only one study was assessed), indirectness (bed rest-only interventions and
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32 129 bed rest + co-interventions were combined for analysis), imprecision (the 95% CI crossed the
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34 130 line of no effect, and was wide) and publication bias (significant evidence of small-study
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36 131 effects).

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40 133 *Statistical analysis*

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42 134 Statistical analyses were conducted using Review Manager v5.2. (Cochrane Collaboration,
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44 135 Copenhagen, Denmark). For continuous outcomes, mean differences between bed rest and no
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46 136 bed rest groups were examined. For binary outcomes, odds ratios were calculated. Inverse-

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3 137 variance weighting was applied to obtain pooled weighted mean differences (WMD) and odds
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5 138 ratios (OR) using a random effect model.
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10 140 A sensitivity analysis was performed to evaluate whether the effects were different when
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12 141 examining relationships between the different indications for bed rest and maternal/infant
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14 142 outcomes. When possible, the following *a priori* determined subgroup analyses were conducted:
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16 143 1) developmental status of the region in the year the study took place based on the world Bank
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18 144 country definition in the World Development Indicators database. These definitions intend to
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20 145 reflect basic economic region conditions¹³. 2) Single versus multiple gestation pregnancies. Chi-
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22 146 squared tests were used to estimate heterogeneity between trials. The percent of total variability
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24 147 that is attributable to heterogeneity (i.e., not to chance) was expressed as the I-squared (I^2). When
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26 148 possible, missing standard deviations (SD) for outcomes were estimated from reported p-
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28 149 values¹⁴, according to Cochrane Handbook procedures (section 7.7.3.3¹²).
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35 151 **Results**

37 152 *Study selection*

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40 153 Sixteen articles from 14 individual randomized controlled trials met our inclusion criteria (see
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42 154 Figure 1). When multiple publications from the same trial were identified, the article with the
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44 155 most complete datasets was selected for extraction.
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49 157 *Study characteristics*

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52 158 The 14 studies assessed in our analysis included 2,608 pregnancies (3,328 newborns) including
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54 159 nine from developed and five from undeveloped regions. While the studies in developed regions
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3 160 were from diverse regions around the world, all five trials from undeveloped regions were
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5 161 conducted in Zimbabwe¹⁵⁻¹⁹. Indications for bed rest included multiple gestation pregnancy¹⁵⁻²⁰,
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7 162 maternal hypertension or pre-eclampsia¹⁵⁻¹⁹, and PROM¹⁵⁻¹⁷. Studies evaluating pregnancies in
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9 163 developed regions examined multiple gestation pregnancy²⁰⁻²², maternal hypertension^{20,22-24},
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11 164 preterm labour^{25,26}, suspected intrauterine growth restriction (IUGR)²⁷ and PROM, where women
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13 165 were not excluded if they had concurrent maternal hypertension or GDM²⁸.
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19 167 The length of the prescribed bed rest was reported in 9 studies and ranged from 1.0 to 9.7
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21 168 weeks^{15-19,22,24,26,28}. Five studies did not report the duration of bed rest^{20,21,23,25,27}. One study had
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23 169 two interventions, one involving a sedation component in both bed rested and non-bed rested
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25 170 groups and one without sedation in both groups²³. Women who were randomized to the non-bed
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27 171 rest group were not prescribed activity restriction but otherwise received standard prenatal care.
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29 172 A summary of study characteristics is provided in Online Supplement Table 1.
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34 35 174 *Quality of evidence*

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38 175 Overall, the quality of evidence ranged from “low” to “high” (See Online Supplement Table 2).
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40 176 The most common reasons for downgrading the quality of evidence were 1) serious risk of bias,
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42 177 and 2) serious imprecision of the interventions. Common sources of bias included selection bias
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44 178 due to inadequate generation of a randomised sequence and reporting bias due to selective
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46 179 outcome reporting.
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51 52 181 *Synthesis of results*

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3 182 Overall, there was “moderate” quality evidence from 14 RCTs (1,995 births: 782 in developed
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5 183 regions and 1,213 in undeveloped regions) regarding the association between bed rest and
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7 184 perinatal death. The quality of evidence was downgraded from “high” to “moderate” because of
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10 185 serious imprecision of the intervention. Bed rest did not decrease the overall risk of perinatal
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12 186 death (OR: 1.09, 95% CI: 0.50 to 2.37, $I^2 = 38\%$; See Figure 2), or when separated by
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14 187 developmental status of the country ($p=0.30$).
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19 189 When gestational age at birth was considered as a continuous variable, “high” quality evidence
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21 190 revealing there was no difference between bed rest and no bed rest groups (WMD: -0.28 weeks,
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23 191 95% CI: -0.61 to 0.05, $I^2 = 30\%$). However, in developed regions, mothers who were on bed rest
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25 192 delivered babies at an earlier gestational age (WMD: -0.77 weeks, 95% CI: -1.26 to -0.27, $I^2 =$
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27 193 0%; “moderate” evidence) but not undeveloped regions (WMD: -0.04 weeks, 95% CI: -0.35 to
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29 194 0.26, $I^2=6\%$; $P=0.01$ for subgroup differences see Figure 3; “high” evidence). Our analysis of
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31 195 prematurity (<37 weeks) included 2,476 pregnancies. No difference was found between rate of
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33 196 prematurity for women on bed rest versus no bed rest (OR: 1.00, 95% CI: 0.78 to 1.30, $I^2=12\%$;
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35 197 “low” evidence) and subgroup analyses were not significant (see Online Supplement Figure 1).
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38 198 No difference also was found between rate of very prematurity (<34 weeks) for women on bed
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40 199 rest versus no bed rest (OR: 1.26, 95% CI: 0.80 to 2.00, $I^2=0\%$; “moderate” evidence). However,
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42 200 bed rest increased the risk of very premature births for women in developed regions (OR: 2.69,
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44 201 95% CI: 1.19 to 6.07, $I^2=0\%$; “moderate” evidence) but not undeveloped regions (OR: 0.88,
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46 202 95% CI: 0.50 to 1.54, $I^2=0\%$; see Figure 4; $P=0.03$ for subgroup differences; “moderate”
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48 203 evidence).
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3 205 There was “high” quality evidence revealing bed rest was associated with a greater birth weight
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5 206 compared to the no bed rest group (WMD: 40g, 95% CI: -30g to 110g, $I^2=31%$; see Figure 5).
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7 207 Subgroup analysis identified bed rest had no impact on birth weight in developed regions
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9 208 (WMD: -40g, 95% CI: -140g to 60g, $I^2=17%$; “moderate” evidence) but increased birth weight in
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11 209 undeveloped regions (WMD: 100g, 95% CI: 40g to 170g, $I^2=0%$; $P=0.002$ for subgroup
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13 210 differences; “high” evidence).
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17 212 Overall, “moderate” quality evidence indicating bed rest did not decrease the risk of birth weight
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19 213 <2500 grams (OR: 0.84, 95% CI: 0.69 to 1.03, $I^2=0%$). However, in undeveloped regions bed
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21 214 rest decreased the risk of delivering a baby <2500 grams (OR: 0.78, 95% CI: 0.61 to 1.00,
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23 215 $I^2=0%$; see Online Supplement Figure 2; “high” evidence) but not developed regions (OR: 1.01,
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25 216 95% CI: 0.69 to 1.49, $I^2=8%$; $P=0.26$ for subgroup differences; “low” evidence)
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33 218 The risk of delivering a newborn <1500g was similar between the bed rest and no bed rest
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35 219 groups (OR: 1.29, 95% CI: 0.69 to 2.40, $I^2=19%$, see Online Supplement Figure 3; “low”
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37 220 evidence). Subgroup analyses were not statistically significant ($P=0.08$).
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42 222 The risk of having a SGA newborn was similar between bed rest and no bed rest groups (OR:
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44 223 0.84, 95% CI: 0.62 to 1.12, $I^2=0%$; see Online Supplement Figure 4; “moderate” evidence), even
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46 224 after examining pregnancies in developed (OR: 1.10, 95% CI: 0.43 to 2.81, $I^2=9%$; “moderate”
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48 225 evidence), or undeveloped regions (OR: 0.81, 95% CI: 0.59 to 1.10, $I^2=0%$; “moderate”
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50 226 evidence). Subgroup analyses were not statistically significant.
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3 228 Bed rest did not reduce the rate of admission to NICU (OR: 0.88, 95% CI: 0.67 to 1.16, $I^2=0\%$;
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5 229 see Online Supplement Figure 5; “moderate” evidence). Subgroup analyses were not statistically
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8 230 significant.

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12 232 Overall, there was “low” quality evidence from 10 RCTs (n=963) regarding the association
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14 233 between bed rest and C-section. The quality of evidence was downgraded from “high” to “low”
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16 234 because of serious risk of bias and serious imprecision of the intervention. The pooled estimate
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18 235 indicated bed rest did not reduce the rate of C-section (OR 1.04, 95% CI 0.66, 1.63, $I^2 = 32\%$; see
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20 236 Online Supplement Figure 6). Subgroup analyses were not statistically significant.
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26 238 Six RCTs (n=559) with “low” quality evidence indicating bed rest did not reduce odds of
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28 239 developing gestational hypertension (OR 0.74, 95% CI 0.28, 1.96, $I^2 = 0\%$; Online Supplement
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30 240 Figure 7). Subgroup analyses were not statistically significant. One “moderate” quality RCT
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32 241 (downgraded due to serious inconsistency), found bed rest also did not reduce the rate of pre-
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34 242 eclampsia (OR 0.57, 95% CI 0.16, 1.99; see Online Supplement Figure 8).
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40 244 Four RCTs with “moderate evidence” indicated bed rest did not reduce the rate of PRM (OR
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42 245 1.46, 95% CI 0.83, 2.57, $I^2 = 0\%$; Online Supplement Figure 9). Subgroup analyses were not
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44 246 statistically significant.
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49 248 One “moderate” quality RCT (downgraded due to serious inconsistency), found bed rest did not
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51 249 reduce the rate of GDM (OR 1.05, 95% CI 0.20, 5.37; see Online Supplement Figure 10).
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3 251 Eight out of 14 studies included multiple gestation pregnancies. When stratified for singleton or
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5 252 multiple gestation, perinatal death, prematurity <37 weeks, gestational age, birth weight <1500g,
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7 253 birth weight <2500g, small for gestational age, cesarean section, and admission to NICU were
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10 254 similar between non-bed rested and bed rested groups (see Online Supplement Figure 11).

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13 256 **Interpretation**

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16 257 This meta-analysis of 2,608 pregnancies (3,328 newborns) analyzed the influence of prenatal bed
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18 258 rest or activity restriction on maternal/fetal health outcomes. Overall, maternal and fetal
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20 259 outcomes were similar between bed rest and no bed rest. However, when stratified by
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22 260 developmental status of the region there was a divergent impact of bed rest between groups such
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24 261 that bed rest in developed regions decreased gestational age, increased the risk of delivering a
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26 262 very premature baby and increased the risk of delivering a baby <1500g. In contrast, bed rest in
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28 263 undeveloped regions increased birth weight by 100g and decreased the risk of delivering a baby
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30 264 <2500g.

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34 266 Preterm birth (<37 weeks) and very preterm birth are leading causes of perinatal morbidity and
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36 267 mortality²⁹. In the studies included in our meta-analysis, very premature was defined as <32
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38 268 weeks^{18,22}, <34 weeks^{15-17,20} and <35 weeks^{23,26}. Our analysis indicates that in developed
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40 269 regions, bed rest increases the odds of having a very premature baby by 169%. Further, women
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42 270 placed on prenatal bed rest in developed regions were twice as likely to deliver a baby <1500g
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44 271 compared to women who were not placed on bed rest. This finding is in line with other data that
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46 272 infants whose mothers were prescribed bed rest had an increased risk of fetal growth
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48 273 restriction.³³ The primary indication for bed rest is to prolong gestation and promote
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50 274 development towards term; however, the findings of our meta-analysis do not support the use of
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3 275 bed rest to improve those outcomes. In contrast to pregnancies in developed regions, our
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5 276 analysis demonstrated a modest increase in birth weight was associated with bed rest in
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7 277 Zimbabwe (100g). Concurrently, the risk of delivering a newborn <2500g was reduced by 22%.
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10 278 The association of positive outcomes with bed rest in undeveloped regions may be confounded
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12 279 by hospitalization.
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17 281 To examine the potential confounding effect of multiple versus single gestation pregnancies,
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19 282 additional sub-group analyses were conducted. Sub-group differences were non-significant and
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21 283 within-group heterogeneity was increased. Overall, bed rest increased birth weight by 80g in
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23 284 twin/triplet pregnancies compared to the no bed rest group. However, this modest improvement
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26 285 in birth weight was not associated with increased gestational age at birth in twin/triplet
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28 286 pregnancies (36.1 weeks for bed rest and 36.5 weeks for no bed rest groups).
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32 33 288 **Strengths and limitations**

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35 289 This study is the first of its kind to have sufficient power to assess the relationship between
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37 290 prenatal bed rest and maternal/fetal health outcomes. In order to achieve sufficient statistical
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39 291 power, all indications for bed rest were combined. This approach resulted in the inclusion of 14
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42 292 studies incorporating 2,608 pregnancies and 3,328 babies. We believe that this provides a
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44 293 valuable and relevant assessment of bed rest as a non-specific clinical intervention that is widely
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46 294 used in obstetric populations. As Zimbabwe has one of the highest rates of maternal and fetal
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48 295 morbidity and mortality in the world, our findings from undeveloped regions may not be
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50 296 generalizable to other developing regions.
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3 298 Between 71 and 95% of maternity health care professionals prescribe bed rest for high-risk
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5 299 pregnancy complications^{1,8}. However, our analyses demonstrated that instead of improving
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7 300 outcomes, prescription of bed rest have no effects on maternal outcomes, and may be associated
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9 301 with serious negative consequences for the newborn in developed regions. Based on the results
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11 302 of our meta-analysis, in developed regions one additional baby will be born very premature for
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13 303 every 5.9 women treated with bed rest and one additional baby will be born <1500 grams for
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15 304 every 20 women treated with bed rest. Due to the negative effects of bed rest on baby, prenatal
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17 305 bed rest in developed regions should be abandoned in standard clinical practice. In conjunction
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19 306 with the overwhelming evidence supporting negative maternal health consequences of prenatal
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21 307 bed rest, our results suggest there is no advantage for the newborns and the mothers, and that this
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23 308 practice should be abandoned in developed regions. Alternatively, hospitalized bed rest in
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25 309 Zimbabwe, the only undeveloped country represented in this review, has demonstrated health
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27 310 benefits for the newborn including increased birth weight and decreased risk of being born
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29 311 <2500g. As all women on bed rest in undeveloped regions were hospitalized and all women
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31 312 randomized to no bed rest were allowed to return home, it is difficult to determine if the
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33 313 improvement in health outcomes was due to bed rest per se, or hospitalization and better access
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35 314 to food, clean water and medical staff.
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44 316 **Conclusion**

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46 317 Prenatal bed rest in developed regions should be abandoned in clinical practice and used only in
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48 318 the context of further research. In undeveloped regions, bed rest appears to have a positive effect
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50 319 on birth weight but may be confounded by the effects of hospitalization.
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Confidential

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6 417 Figure 1: Study flow diagram.
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8 418 Figure 2: Effect of Bed rest (experimental) vs. non-bed rest (control) on perinatal death.
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10 419 Bed rest did not significantly decrease perinatal death in undeveloped regions or
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12 420 developed regions. OR = Odds Ratio; 95% confidence interval = [95% CI].
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15 421 Figure 3: Effect of Bed rest (experimental) vs. non-bed rest (control) on gestational age.
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17 422 Bed rest resulted in 0.77 weeks decreased in gestational age in developed regions. WMD =
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19 423 weighted mean difference; 95% confidence interval = [95% CI].
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22 424 Figure 4: Effect of Bed rest (experimental) vs. non-bed rest (control) on very preterm birth.
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24 425 Bed rest increased the rate of very preterm birth in pregnancies in developed regions. OR =
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26 426 Odds Ratio; 95% confidence interval = [95% CI].
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29 427 Figure 5: Effect of Bed rest (experimental) vs. non-bed rest (control) on birthweight. Bed
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31 428 rest resulted in 100g increased in birth weight in undeveloped regions. WMD = weighted
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33 429 mean difference; 95% confidence interval = [95% CI].
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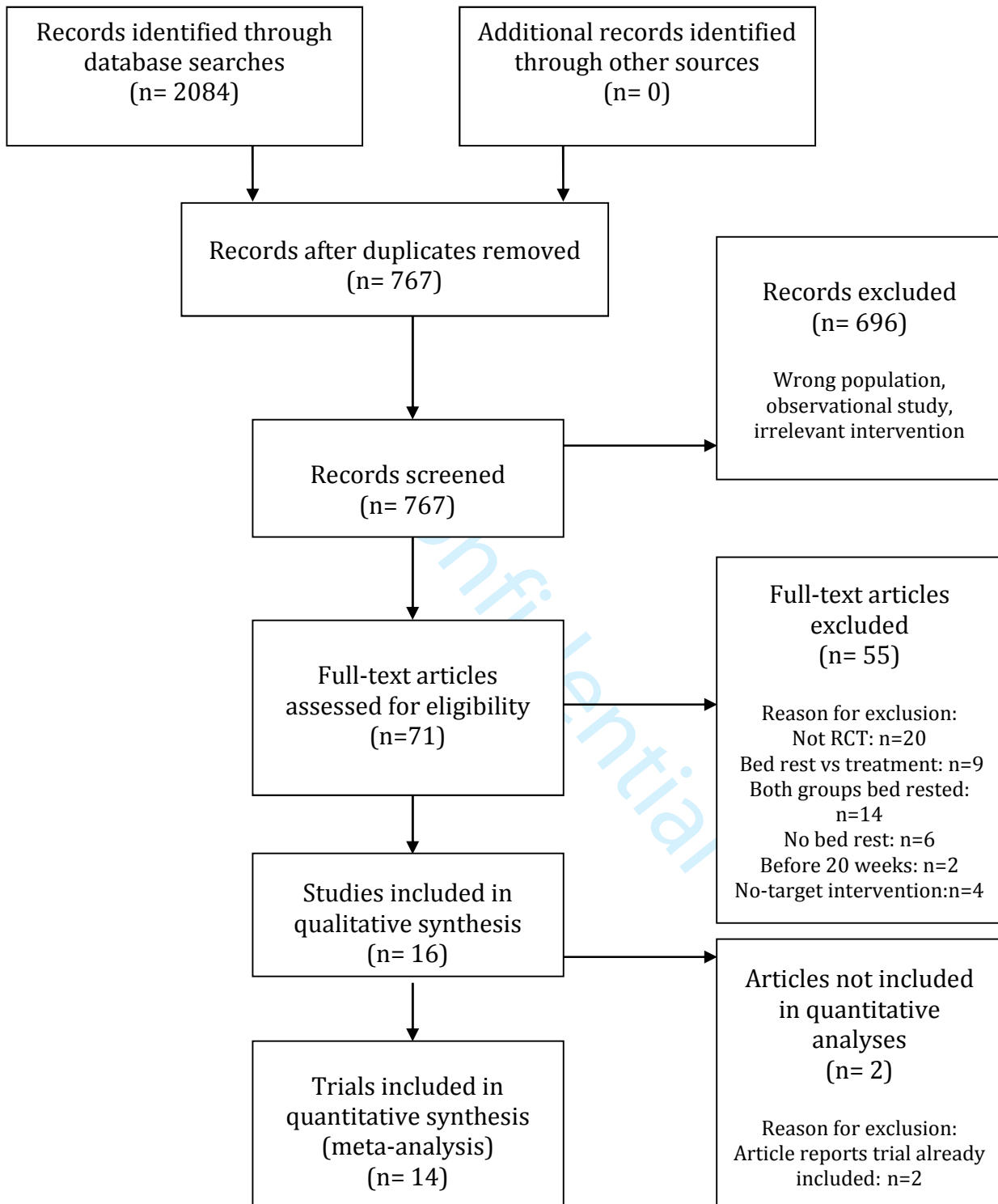


Figure 1. Study flow diagram.

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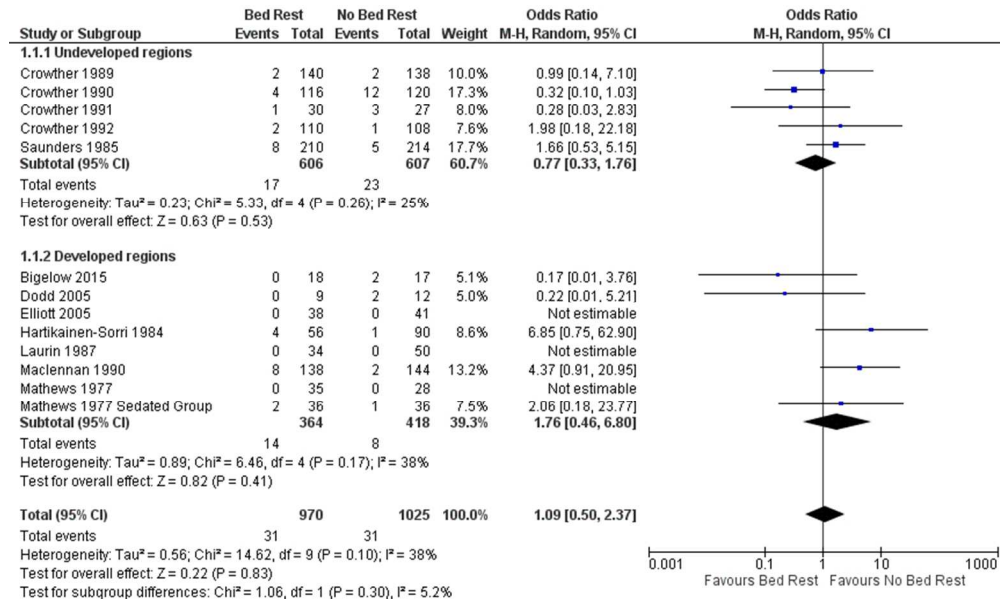
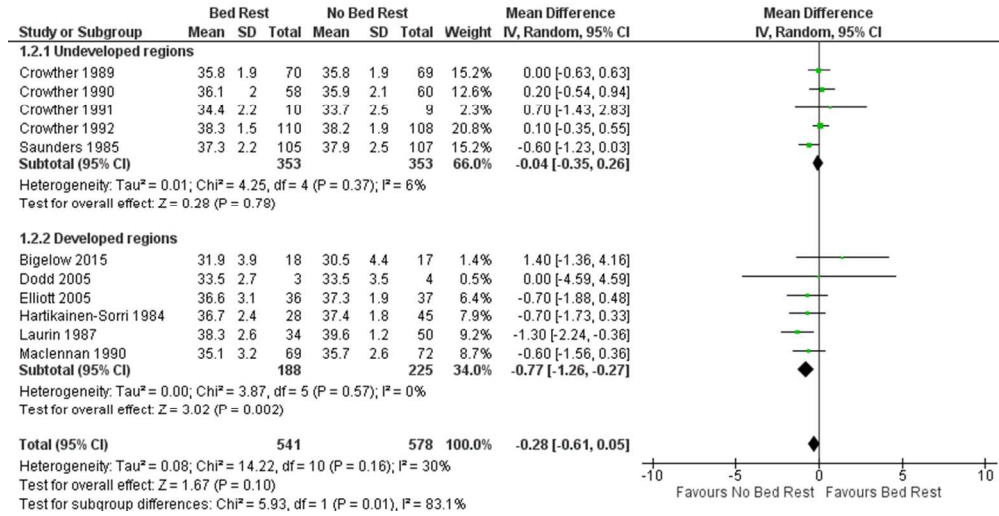


Figure 2: Effect of Bed rest (experimental) vs. non-bed rest (control) on perinatal death. Bed rest did not significantly decrease perinatal death in undeveloped regions or developed regions. OR = Odds Ratio; 95% confidence interval = [95% CI].

304x180mm (72 x 72 DPI)



Effect of Bed rest (experimental) vs. non-bed rest (control) on gestational age. Bed rest resulted in 0.77 weeks decreased in gestational age in developed regions. WMD = weighted mean difference; 95% confidence interval = [95% CI].

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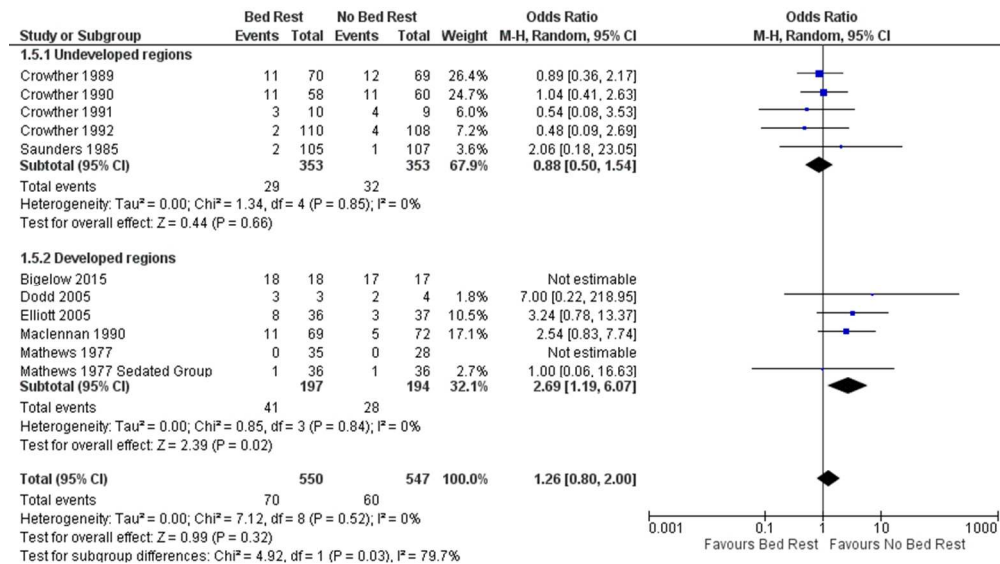


Figure 4: Effect of Bed rest (experimental) vs. non-bed rest (control) on very preterm birth. Bed rest increased the rate of very preterm birth in pregnancies in developed regions. OR = Odds Ratio; 95% confidence interval = [95% CI].

304x169mm (72 x 72 DPI)

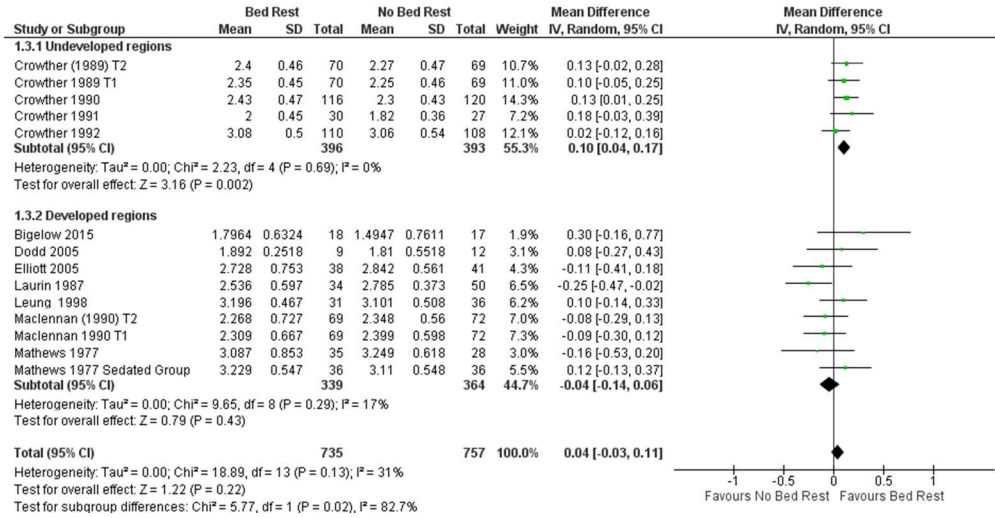


Figure 5: Effect of Bed rest (experimental) vs. non-bed rest (control) on birthweight. Bed rest resulted in 100g increased in birth weight in undeveloped regions. WMD = weighted mean difference; 95% confidence interval = [95% CI].

332x169mm (72 x 72 DPI)

ONLINE SUPPLEMENT TABLE 1. Study Characteristics.

Author, Year, Country	Sample Size, n	Age±SD, y	Study Start BMI, kg/m ² (or 28weeks #)	Indication for Bed Rest	Bed Rest Intervention		Complications				
					Gestational age at Start of Bed Rest or study entry ± SD	Length of Bed Rest or length in study (weeks)	Maternal Hypertension or Pre-eclampsia	GDM	PROM	Preterm Labour	Misc.
Bigelow 2015, USA	HBR: 18 NBR: 17	30.5±20.0 32.0±17.8	NA NA	PROM	29.2±5.7 28.9±7.6	2.7 1.6			18 17		latency antibiotics - =ampicillin/amoxicillin and erythromycin for up to 7 days and a 48 hr course of IM betamethasone
Crowther 1989, Zimbabwe	HBR: 70 NBR: 69	27.1±5.9 27.0±5.7	26.60 27.47	Multiple Gestation	33.3±1.8 33.5±1.8	2.5 2.3	7 6		13 8		
Crowther 1990, Zimbabwe	HBR: 58 NBR: 60	26.5±5.7 26.7±5.4	26.57 27.52	Multiple Gestation	29.1±1.2 29.2±1.7	7.0 6.7	3 9		7 5		
Crowther 1986/91, Zimbabwe	BR: 10 NBR: 9	25.2±5.5 29.3±7.4	27.02 28.24	Multiple Gestation	29.0±4.7 29.4±3.0	5.4 4.3	1 3		1 3		
Crowther 1992, Zimbabwe	HBR: 110 NBR: 108	28.9±6.6 28.7±6.3	30.36 30.55	Hypertension/ Preeclampsia	35.3±2.6 34.6±3.0	3.0 3.6	15‡25* 18‡45*				
Dodd 2005, Australia	HBR: 3 NBR: 4	33.2±0.8 36.2±13.2	21.57 22.65	Multiple Gestation	23.4±1.7 22.0±1.8	NA NA	1 1				
Elliot 2005, USA	AR: 36 NBR: 37	24.8±5.5 24.9±5.2	NA NA	Preterm Labour	30.7±2.7 31.0±2.5	5.9 6.3				36 37	Tocolysis with MgSO4
Hartikainen-Sorri 1984, Finland	HBR: 28 NBR: 45	NA NA	NA NA	Multiple Gestation	NA NA	NA NA	unknown§ unknown§				
Hobel 1994, USA	HBR: 432 NBR: 422 NBRP:412	NA NA NA	NA NA NA	Preterm Labour	NA NA NA	NA NA NA				34 41 30	
Laurin 1987, Sweden	HBR: 34 NBR: 50	25.6±4.4 25.8±5.0	NA NA	Suspected IUGR	NA NA	NA NA				2 4	
Leung 1998, Hong Kong	HAR: 44 NBR: 44	31.0±5.2 32.5±5.3	22.64 23.92	Hypertension	33.2±2.9 33.1±3.0	1.0 0.4	31 36				
Maclennan 1990, Australia	HBR: 69 NBR: 72	29.5±3.1 28.4±3.6	27.43 27.39	Multiple Gestation	26.0±2.1 26.0±2.1	9.1 9.7	9 31	3 3	13 9		

Mathews 1977/82, UK	BR S: 36 NBR S: 36	NA NA	NA NA	Multiple Gestation	>28 >28	NA NA	36 36					Sedation with phenobarbitone 15 mg three times a day
	BR: 35 NBR: 28	NA NA	NA NA		>28 >28	NA NA	35 28					
Saunders 1985, Zimbabwe	HBR: 105 NBR: 107	26.6±6.7 27.3±6.0	NA NA	Multiple Gestation	32.7 32†	4.6 0.5	4 5					
Totals:	2,608	27.9 	27.6 		31.5 	4.2 	386	10	94	184		

†were recruited before 32 weeks gestation; ‡chronic hypertension; *severe hypertension; §both groups had similar numbers of complications including hypertension; ||weighted averages; HBR = hospitalized bed rest; NBR = no bed rest; BR = bed rest; AR = activity restriction; NBRP = no bed rest, participants treated with placebo ; NAR = no activity restriction; BR S = bed rest with sedation; NBR S = no bed rest with sedation; PROM = premature rupture of membranes; GDM = gestational diabetes mellitus; IM = intra-muscular; SD = standard deviation; BMI = body mass index (kg/m²).

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ONLINE SUPPLEMENT TABLE 2. GRADE table for study quality evaluation.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
Association between bed rest (intervention) and perinatal death												
12	randomised trials	not serious	not serious	not serious	serious ^a	none	31/970 (3.2%)	31/1025 (3.0%)	OR 1.09 (0.50 to 2.37)	3 more per 1,000 (from 15 fewer to 39 more)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and perinatal death in undeveloped regions												
5	randomised trials	not serious	not serious	not serious	serious ^a	none	17/606 (2.8%)	23/607 (3.8%)	OR 0.77 (0.33 to 1.76)	8 fewer per 1,000 (from 25 fewer to 27 more)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and perinatal death in developed regions												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
7	randomised trials	serious ^b	not serious	not serious	serious ^c	none	14/364 (3.8%)	8/418 (1.9%)	OR 1.76 (0.46 to 6.80)	14 more per 1,000 (from 10 fewer to 98 more)	⊕⊕ LOW	CRITICAL
Association between bed rest (intervention) and gestational age												
11	randomised trials	not serious	not serious	not serious	not serious	none	541	578	-	MD 0.28 wks lower (0.61 lower to 0.05 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and gestational age in undeveloped regions												
5	randomised trials	not serious	not serious	not serious	not serious	none	353	353	-	MD 0.04 wks lower (0.35 lower to 0.26 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and gestational age in developed regions												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
6	randomised trials	serious ^d	not serious	not serious	not serious	none	188	225	-	MD 0.77 wks lower (1.26 lower to 0.27 lower)	⊕⊕⊕ MODERATE	CRITICAL
Association between bed rest (intervention) and birth weight												
11	randomised trials	not serious	not serious	not serious	not serious	none	735	757	-	MD 0.04 kg higher (0.03 lower to 0.11 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and birth weight in undeveloped regions												
4	randomised trials	not serious	not serious	not serious	not serious	none	396	393	-	MD 0.1 kg higher (0.04 higher to 0.17 higher)	⊕⊕⊕⊕ HIGH	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
Subgroup analysis: Association between bed rest (intervention) and birth weight in developed regions												
7	randomised trials	serious ^d	not serious	not serious	not serious	none	339	364	-	MD 0.04 kg lower (0.14 lower to 0.06 higher)	⊕⊕⊕ MODERATE	CRITICAL
Association between bed rest (intervention) and prematurity												
13	randomised trials	serious ^e	not serious	not serious	serious ^a	none	265/1045 (25.4%)	306/1466 (20.9%)	OR 1.00 (0.78 to 1.30)	0 fewer per 1,000 (from 38 fewer to 47 more)	⊕⊕ LOW	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and prematurity in undeveloped regions												
5	randomised trials	not serious	serious ^f	not serious	serious ^a	none	140/353 (39.7%)	148/353 (41.9%)	OR 0.82 (0.44 to 1.50)	47 fewer per 1,000 (from 101 more to 178 fewer)	⊕⊕ LOW	CRITICAL

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
Subgroup analysis: Association between bed rest (intervention) and prematurity in developed regions												
8	randomised trials	serious ^e	not serious	not serious	serious ^a	none	125/692 (18.1%)	158/1113 (14.2%)	OR 1.11 (0.81 to 1.50)	13 more per 1,000 (from 24 fewer to 57 more)	⊕⊕ LOW	CRITICAL
Association between bed rest (intervention) and very premature birth												
10	randomised trials	not serious	not serious	not serious	serious ^c	none	70/550 (12.7%)	60/547 (11.0%)	OR 1.26 (0.80 to 2.00)	25 more per 1,000 (from 20 fewer to 88 more)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and very premature birth in undeveloped regions												
5	randomised trials	not serious	not serious	not serious	serious ^a	none	29/353 (8.2%)	32/353 (9.1%)	OR 0.88 (0.50 to 1.54)	10 fewer per 1,000 (from 42 more to 43 fewer)	⊕⊕⊕ MODERATE	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
Subgroup analysis: Association between bed rest (intervention) and very premature birth in developed regions												
5	randomised trials	serious ^g	not serious	not serious	not serious	none	41/197 (20.8%)	28/194 (14.4%)	OR 2.69 (1.19 to 6.07)	168 more per 1,000 (from 23 more to 362 more)	⊕⊕⊕ MODERATE	CRITICAL
Association between bed rest (intervention) and birth weight <2500g												
10	randomised trials	not serious	not serious	not serious	serious ^a	none	384/899 (42.7%)	431/938 (45.9%)	OR 0.84 (0.69 to 1.03)	43 fewer per 1,000 (from 7 more to 90 fewer)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and birth weight <2500g in undeveloped regions												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
5	randomised trials	not serious	not serious	not serious	not serious	none	265/606 (43.7%)	298/607 (49.1%)	OR 0.78 (0.61 to 1.00)	62 fewer per 1,000 (from 0 fewer to 121 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and birth weight <2500g in developed regions												
5	randomised trials	serious ^g	not serious	not serious	serious ^a	none	119/293 (40.6%)	133/331 (40.2%)	OR 1.01 (0.69 to 1.49)	2 more per 1,000 (from 85 fewer to 98 more)	⊕⊕ LOW	CRITICAL
Association between bed rest (intervention) and birth weight <1500g												
8	randomised trials	serious ^g	not serious	not serious	serious ^c	none	41/740 (5.5%)	32/786 (4.1%)	OR 1.29 (0.69 to 2.40)	11 more per 1,000 (from 12 fewer to 52 more)	⊕⊕ LOW	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and birth weight <1500g in undeveloped regions												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
4	randomised trials	not serious	not serious	not serious	serious ^c	none	13/496 (2.6%)	15/499 (3.0%)	OR 0.76 (0.34 to 1.73)	7 fewer per 1,000 (from 20 fewer to 21 more)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and birth weight <1500g in developed regions												
4	randomised trials	serious ^g	not serious	not serious	not serious	none	28/244 (11.5%)	17/287 (5.9%)	OR 1.93 (1.00 to 3.70)	49 more per 1,000 (from 0 fewer to 130 more)	⊕⊕⊕ MODERATE	CRITICAL
Association between bed rest (intervention) and small for gestational age												
6	randomised trials	not serious	not serious	not serious	serious ^a	none	129/498 (25.9%)	143/493 (29.0%)	OR 0.84 (0.62 to 1.12)	35 fewer per 1,000 (from 24 more to 88 fewer)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and small for gestational age in undeveloped regions												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
4	randomised trials	not serious	not serious	not serious	serious ^a	none	115/396 (29.0%)	131/393 (33.3%)	OR 0.81 (0.59 to 1.10)	45 fewer per 1,000 (from 22 more to 106 fewer)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and small for gestational age in developed regions												
2	randomised trials	not serious	not serious	not serious	serious ^c	none	14/102 (13.7%)	12/100 (12.0%)	OR 1.10 (0.43 to 2.81)	10 more per 1,000 (from 65 fewer to 157 more)	⊕⊕⊕ MODERATE	CRITICAL
Association between bed rest (intervention) and admission to NICU												
8	randomised trials	not serious	not serious	not serious	serious ^a	none	184/621 (29.6%)	197/631 (31.2%)	OR 0.88 (0.67 to 1.16)	27 fewer per 1,000 (from 33 more to 79 fewer)	⊕⊕⊕ MODERATE	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
Subgroup analysis: Association between bed rest (intervention) and admission to NICU in undeveloped regions												
4	randomised trials	not serious	not serious	not serious	serious ^a	none	128/396 (32.3%)	143/393 (36.4%)	OR 0.79 (0.57 to 1.10)	53 fewer per 1,000 (from 22 more to 118 fewer)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and admission to NICU in developed regions												
4	randomised trials	serious ^g	not serious	not serious	serious ^a	none	56/225 (24.9%)	54/238 (22.7%)	OR 1.12 (0.69 to 1.84)	20 more per 1,000 (from 58 fewer to 124 more)	⊕⊕ LOW	CRITICAL
Association between bed rest (intervention) and birth weight in multiple gestation pregnancies												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
5	randomised trials	serious ^g	not serious	not serious	not serious	none	433	441	-	MD 0.08 kg higher (0.01 higher to 0.15 higher)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and birth weight in multiple gestation pregnancies in undeveloped regions												
3	randomised trials	not serious	not serious	not serious	not serious	none	286	285	-	MD 0.13 kg higher (0.06 higher to 0.2 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and birth weight in multiple gestation pregnancies in developed regions												
2	randomised trials	serious ^g	not serious	not serious	not serious	none	147	156	-	MD 0.06 kg lower (0.02 lower to 0.08 higher)	⊕⊕⊕ MODERATE	CRITICAL
Association between bed rest (intervention) and C-section												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
10	randomised trials	serious ^d	not serious	not serious	serious ^a	none	109/474 (23.0%)	109/489 (22.3%)	OR 1.04 (0.66 to 1.63)	7 more per 1,000 (from 64 fewer to 96 more)	⊕⊕ LOW	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and C-section in undeveloped regions												
4	randomised trials	not serious	not serious	not serious	serious ^a	none	38/248 (15.3%)	38/246 (15.4%)	OR 0.92 (0.44 to 1.93)	11 fewer per 1,000 (from 80 fewer to 106 more)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and C-section in developed regions												
6	randomised trials	serious ^d	not serious	not serious	serious ^a	none	71/226 (31.4%)	71/243 (29.2%)	OR 1.11 (0.58 to 2.11)	22 more per 1,000 (from 99 fewer to 173 more)	⊕⊕ LOW	CRITICAL
Association between bed rest (intervention) and pregnancy induced hypertension												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
6	randomised trials	not serious	serious ^f	not serious	serious ^c	none	36/281 (12.8%)	56/278 (20.1%)	OR 0.74 (0.28 to 1.96)	44 fewer per 1,000 (from 129 more to 135 fewer)	⊕⊕ LOW	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and pregnancy induced hypertension in undeveloped regions												
3	randomised trials	not serious	not serious	not serious	serious ^a	none	11/138 (8.0%)	18/138 (13.0%)	OR 0.55 (0.19 to 1.55)	54 fewer per 1,000 (from 58 more to 103 fewer)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and pregnancy induced hypertension in developed regions												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
3	randomised trials	not serious	serious ^f	not serious	serious ^c	none	25/143 (17.5%)	38/140 (27.1%)	OR 1.16 (0.20 to 6.64)	30 more per 1,000 (from 202 fewer to 441 more)	⊕⊕ LOW	CRITICAL
Association between bed rest (intervention) and pre-eclampsia												
1	randomised trials	not serious	serious ^h	not serious	not serious ⁱ	none	4/105 (3.8%)	7/107 (6.5%)	OR 0.57 (0.16 to 1.99)	27 fewer per 1,000 (from 54 fewer to 57 more)	⊕⊕⊕ MODERATE	CRITICAL
Association between bed rest (intervention) and preterm rupture of membranes												
4	randomised trials	not serious	not serious	not serious	serious ^c	none	34/219 (15.5%)	25/219 (11.4%)	OR 1.46 (0.83 to 2.57)	44 more per 1,000 (from 18 fewer to 135 more)	⊕⊕⊕ MODERATE	CRITICAL

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
Subgroup analysis: Association between bed rest (intervention) and preterm rupture of membranes in undeveloped regions												
3	randomised trials	not serious	not serious	not serious	serious ^c	none	21/150 (14.0%)	16/147 (10.9%)	OR 1.32 (0.60 to 2.93)	30 more per 1,000 (from 41 fewer to 155 more)	⊕⊕⊕ MODERATE	CRITICAL
Subgroup analysis: Association between bed rest (intervention) and preterm rupture of membranes in developed regions												
1	randomised trials	not serious	serious ^h	not serious	not serious ⁱ	none	13/69 (18.8%)	9/72 (12.5%)	OR 1.63 (0.65 to 4.09)	64 more per 1,000 (from 40 fewer to 244 more)	⊕⊕⊕ MODERATE	CRITICAL
Association between bed rest (intervention) and GDM												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bed rest	control	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	serious ^h	not serious	not serious ⁱ	none	3/69 (4.3%)	3/72 (4.2%)	OR 1.05 (0.20 to 5.37)	2 more per 1,000 (from 33 fewer to 148 more)	⊕⊕⊕ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio; **MD:** Mean difference

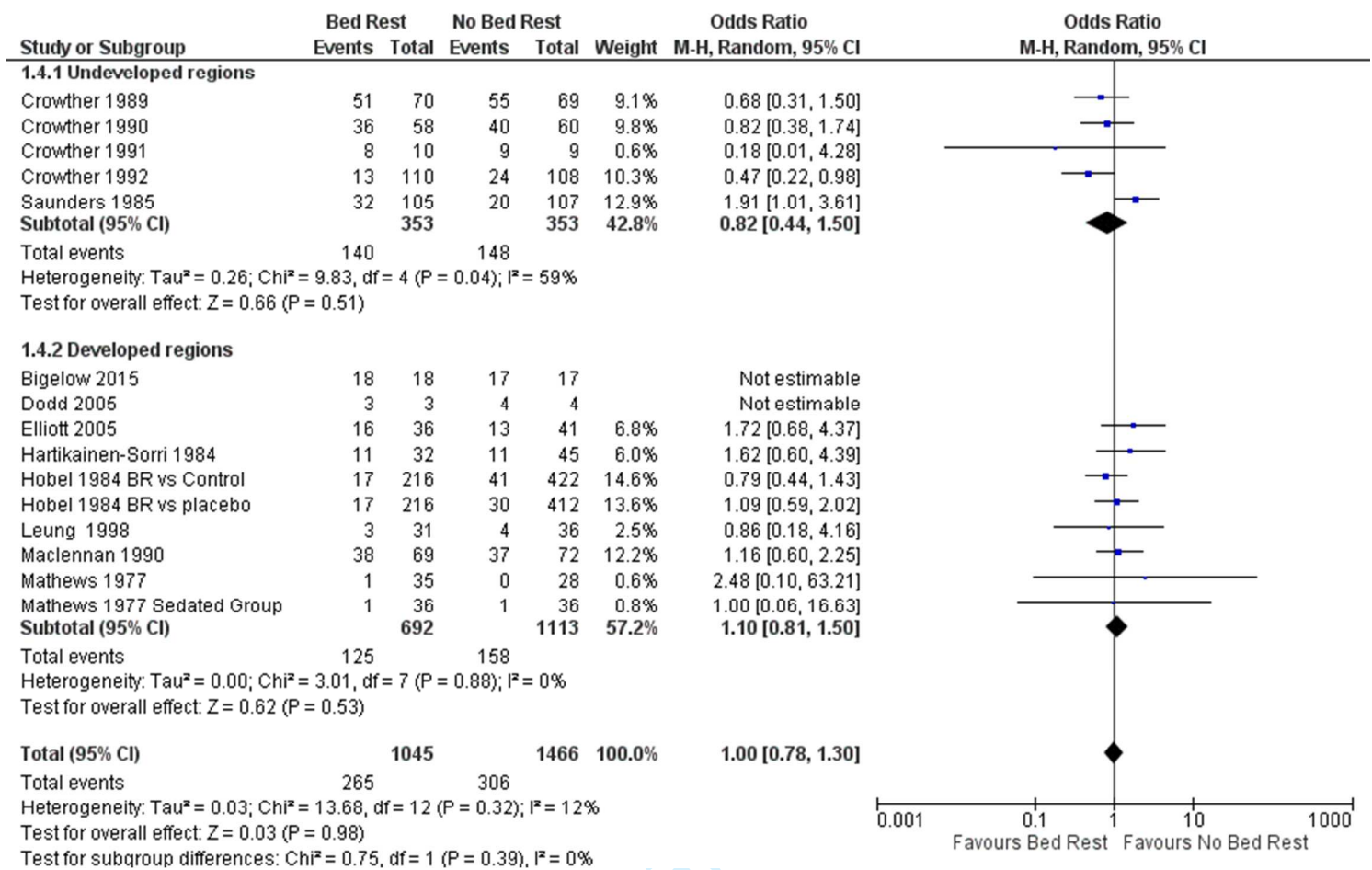
Explanations

- a. Serious imprecision. The 95% CI crosses the line of no effect.
- b. Serious risk of bias. High risk of selection bias. Unclear risk of detection bias; it was unknown if the outcome assessments were blinded.
- c. Serious imprecision. The 95% CI crosses the line of no effect, and is wide, such that our recommendation would be different if the true effect were at one end of the CI or the other.
- d. Serious risk of bias. High risk of selection and reporting bias. Unclear risk of detection bias; it was unknown if the outcome assessments were blinded.
- e. Serious risk of bias. High risk of reporting bias. Unclear risk of selection bias; it was unknown if allocation concealment was adequate. Unclear risk of detection bias; it was unknown if the outcome assessment were blinded.
- f. Serious inconsistency because the heterogeneity was high ($I^2 \geq 50\%$)
- g. Serious risk of bias. High risk of reporting bias. Unclear risk of detection bias; it was unknown if the outcome assessments were blinded.
- h. Serious inconsistency because only one study

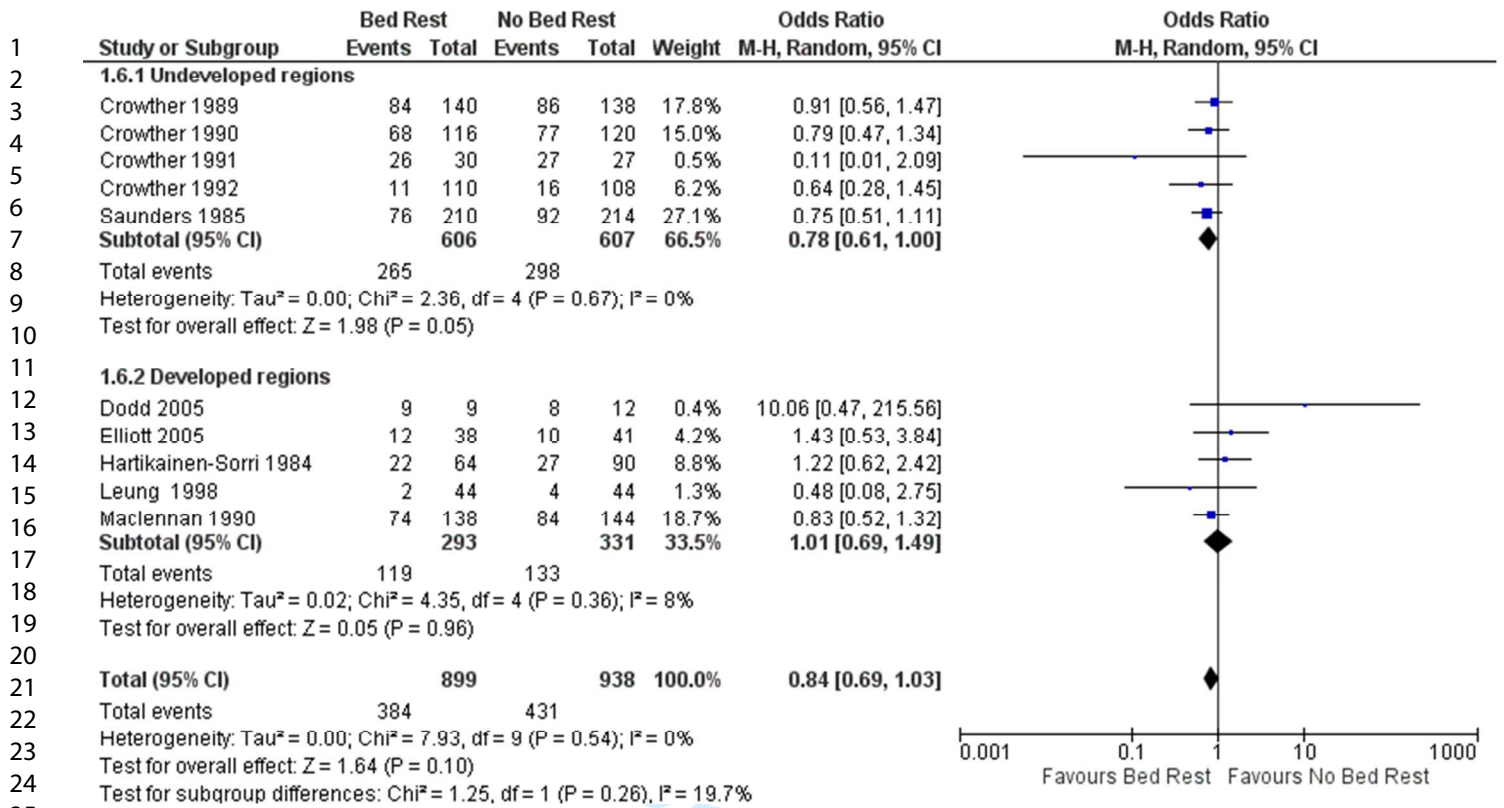
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i. No serious imprecision; only one study but already downgraded for serious inconsistency for this reason

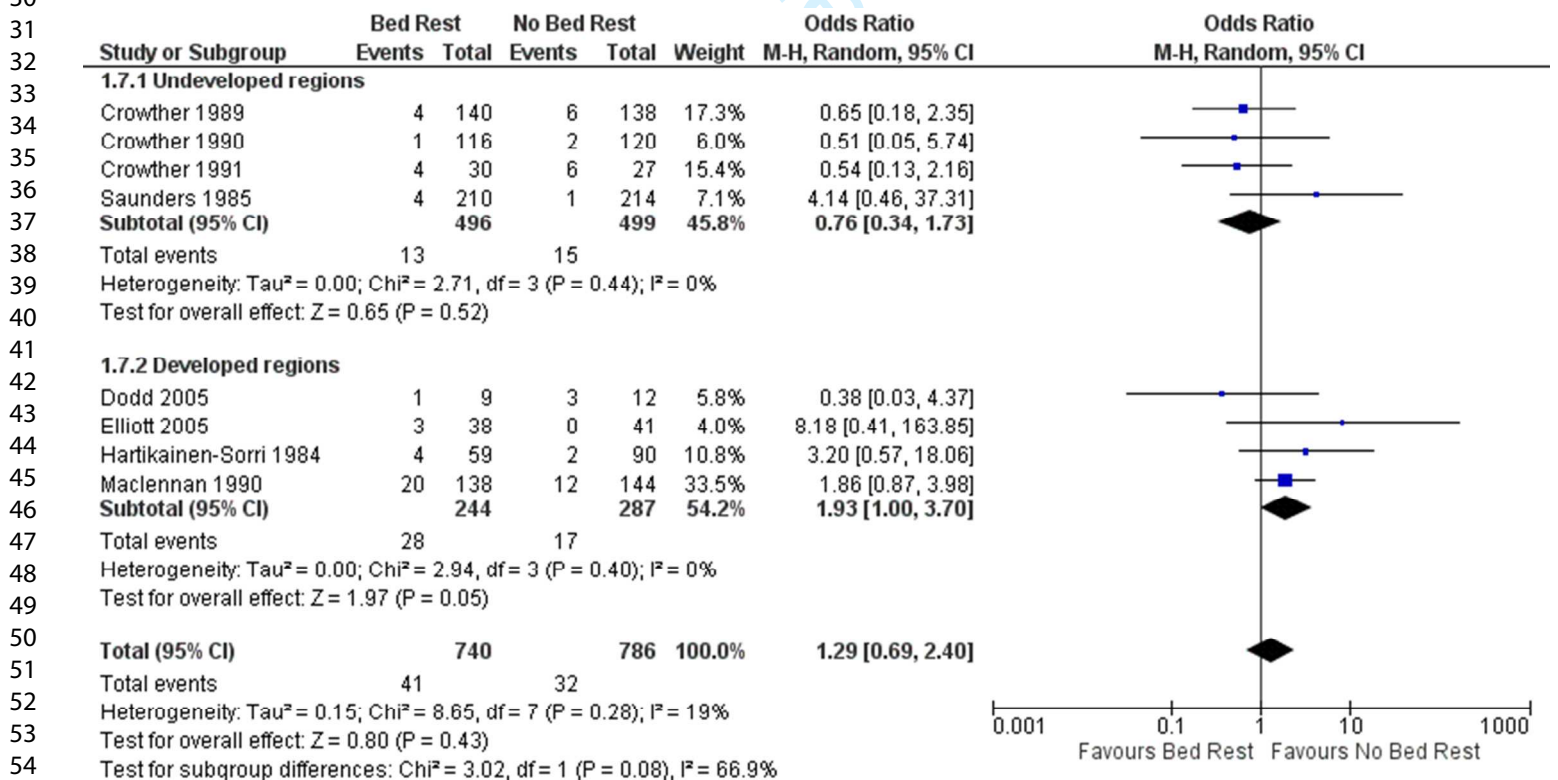
Confidential



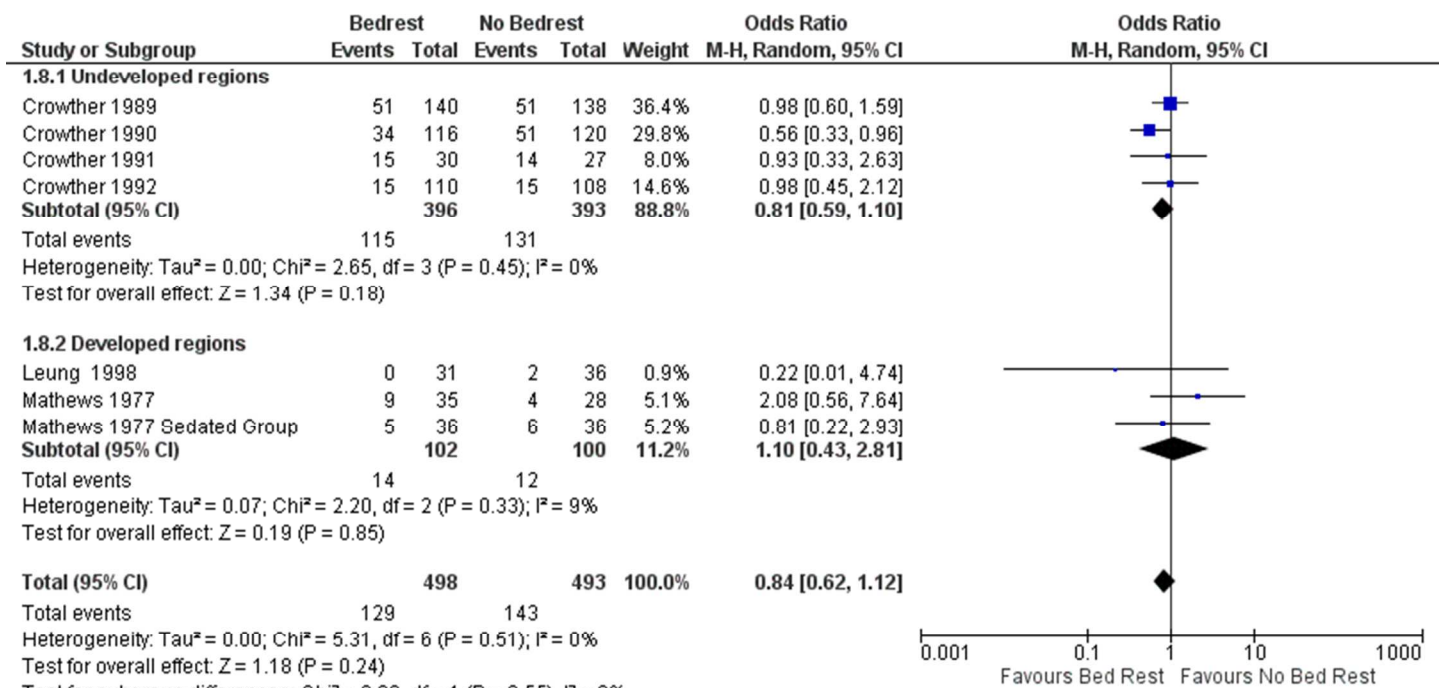
ONLINE SUPPLEMENT FIGURE 1. Effect of Bed rest (experimental) vs. non-bed rest (control) on prematurity <37 weeks. Bed rest did not significantly decrease prematurity <37 weeks in undeveloped regions or developed regions. OR = Odds Ratio; 95% confidence interval = [95% CI].



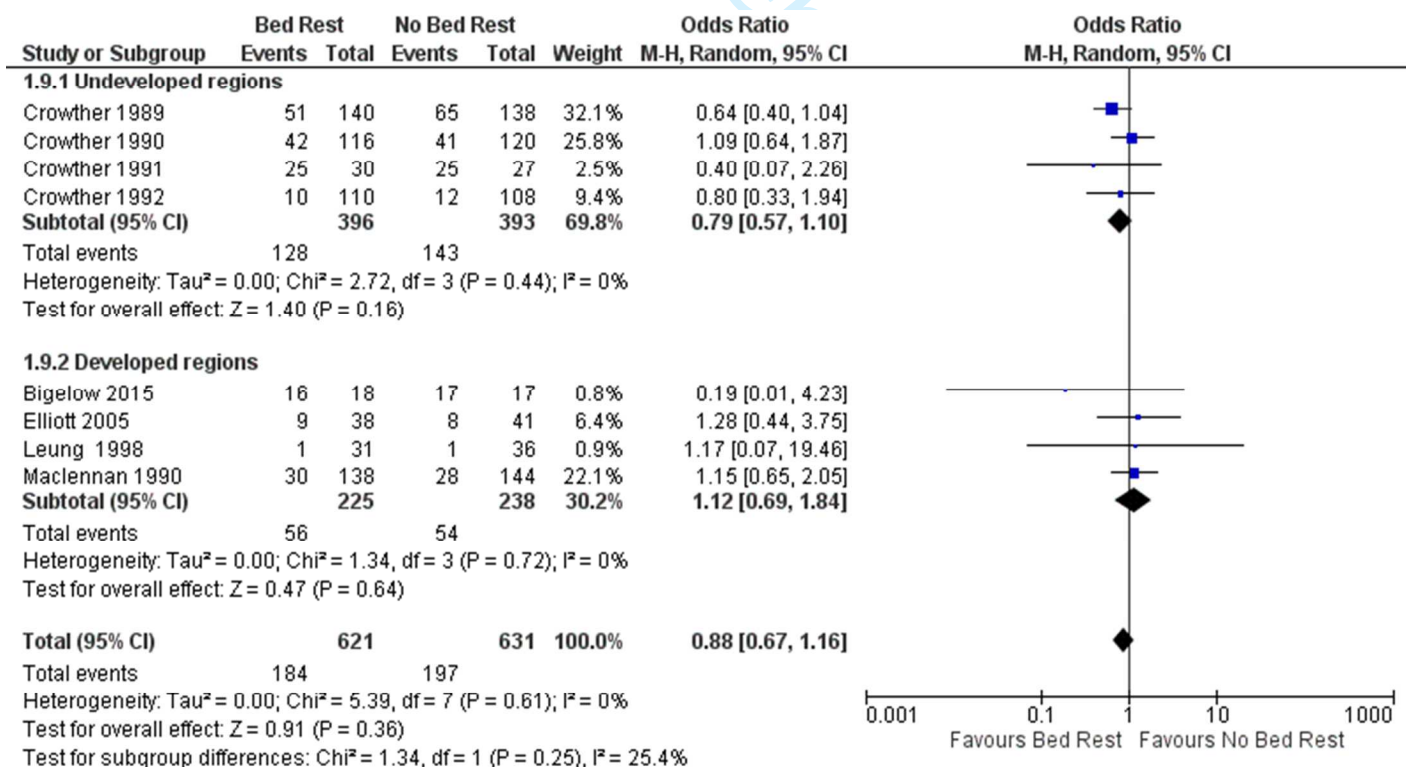
ONLINE SUPPLEMENT FIGURE 2. Effect of Bed rest (experimental) vs. non-bed rest (control) on birth weight <2500 grams. Bed rest decreased the rate of birth weight <2500 grams in pregnancies in undeveloped regions. OR = Odds Ratio; 95% confidence interval = [95% CI].



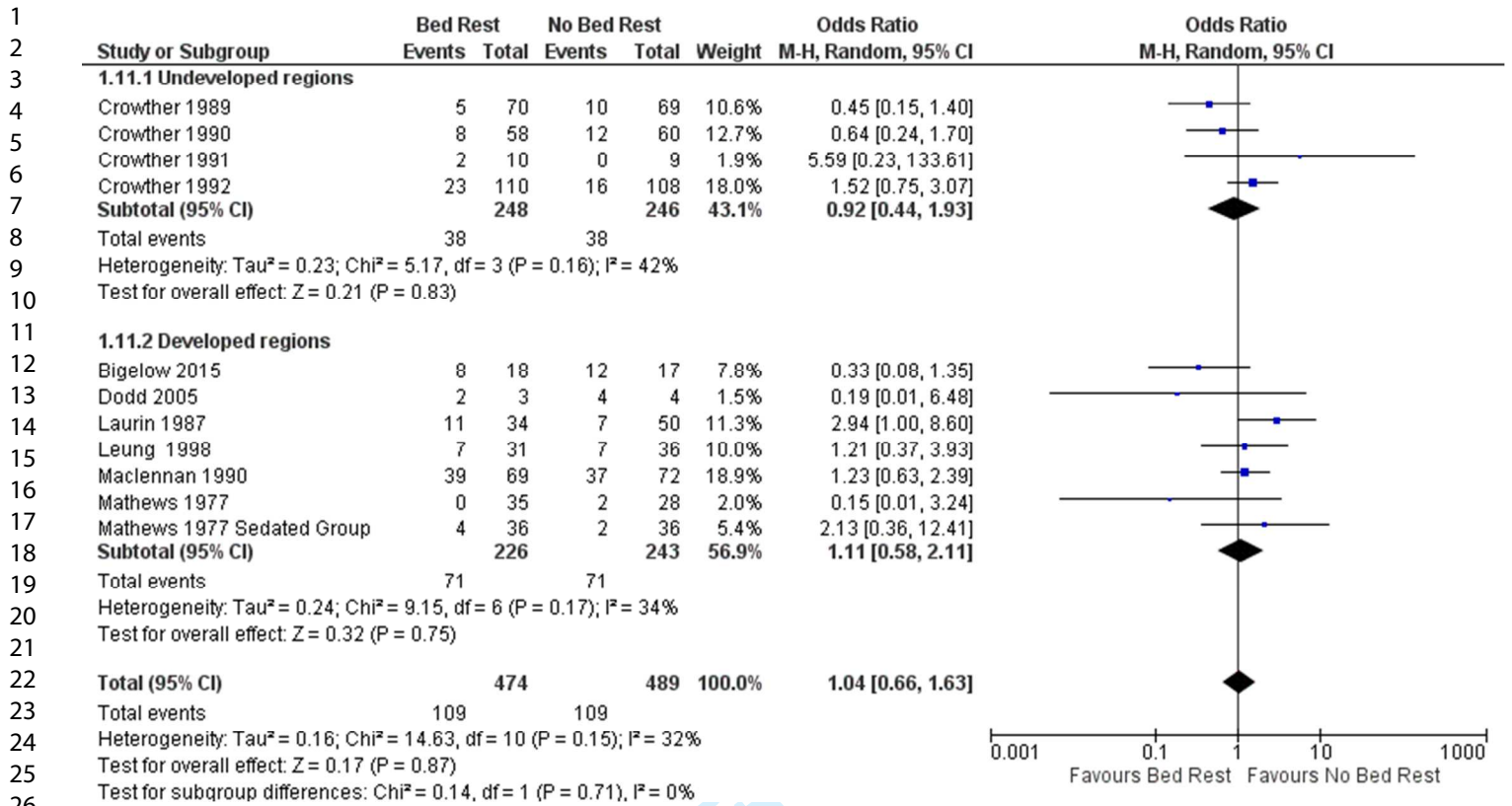
ONLINE SUPPLEMENT FIGURE 3. Effect of bed rest (experimental) vs. non-bed rest (control) on risk of birth weight <1500 grams. Bed rest significantly increased the risk of birth weight <1500 grams in pregnancies in developed regions. OR = Odds Ratio; 95% confidence interval = [95% CI].



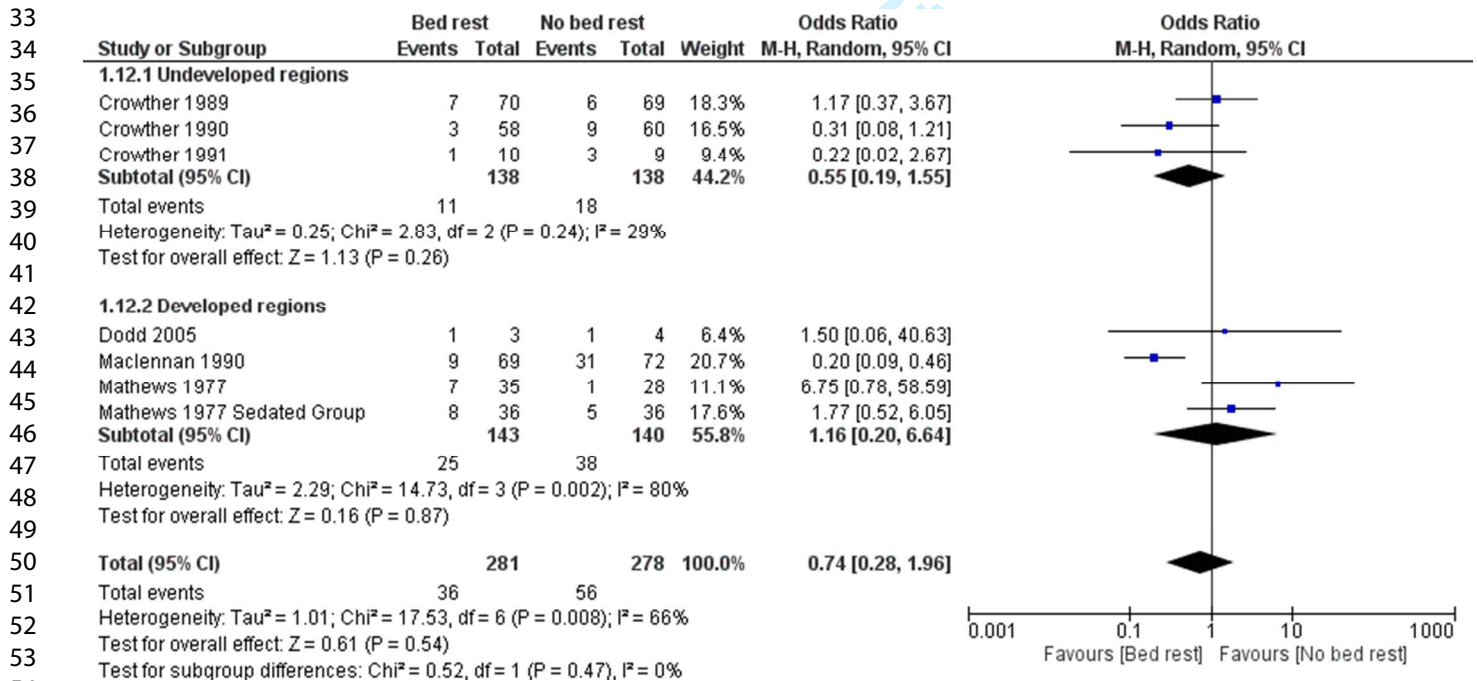
ONLINE SUPPLEMENT FIGURE 4. Effect of Bed rest (experimental) vs. non-bed rest (control) on small for gestational age. Small for gestational age was not different between groups in developed or undeveloped regions. OR = odds ratio; 95% confidence interval = [95% CI].



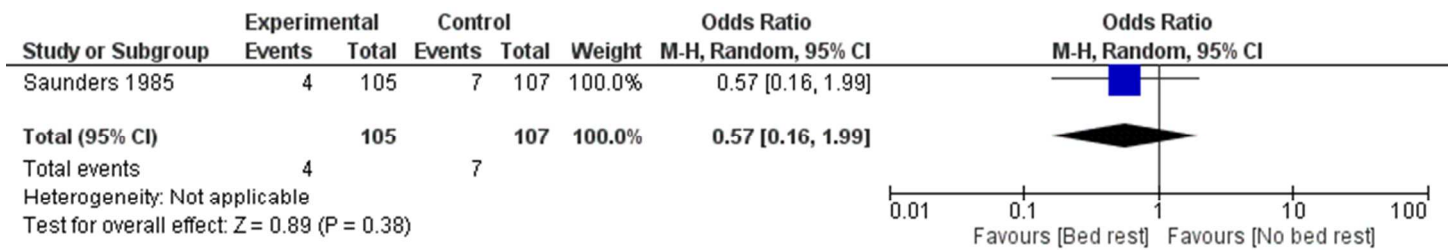
ONLINE SUPPLEMENT FIGURE 5. Effect of Bed rest (experimental) vs. non-bed rest (control) on admission to neonatal intensive care unit (NICU). Bed rest did not significantly decrease risk of admission to NICU in developed or undeveloped regions. OR = Odds Ratio; 95% confidence interval = [95% CI].



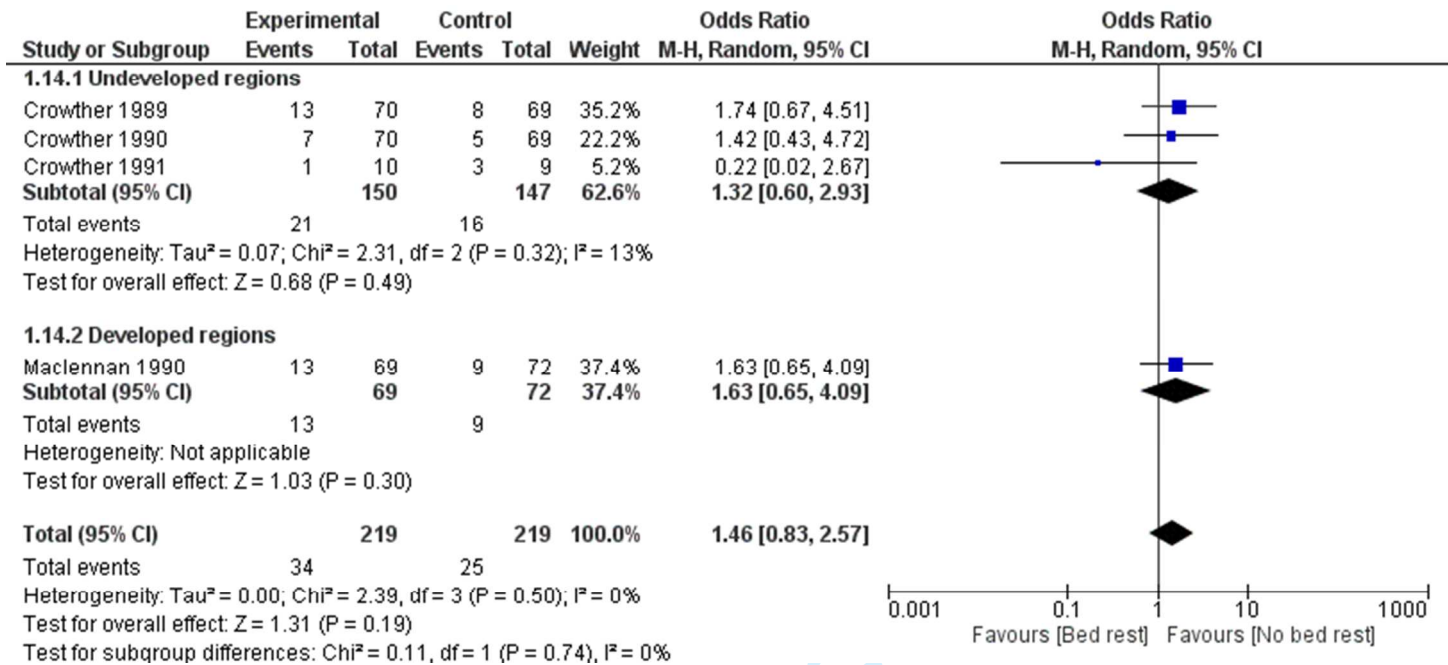
ONLINE SUPPLEMENT FIGURE 6. Effect of Bed rest (experimental) vs. non-bed rest (control) on C-section. Bed rest did not significantly decrease risk of C-section in developed or undeveloped regions. OR = Odds Ratio; 95% confidence interval = [95% CI].



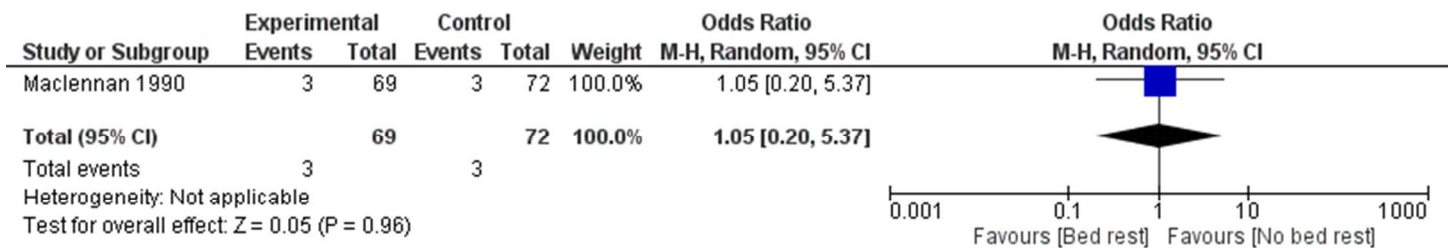
ONLINE SUPPLEMENT FIGURE 7. Effect of Bed rest (experimental) vs. non-bed rest (control) on pregnancy induce-hypertension. Bed rest significant reduce the risk of pregnancy induce-hypertension compared to non-bed rest. OR = Odds Ratio; 95% confidence interval = [95% CI].



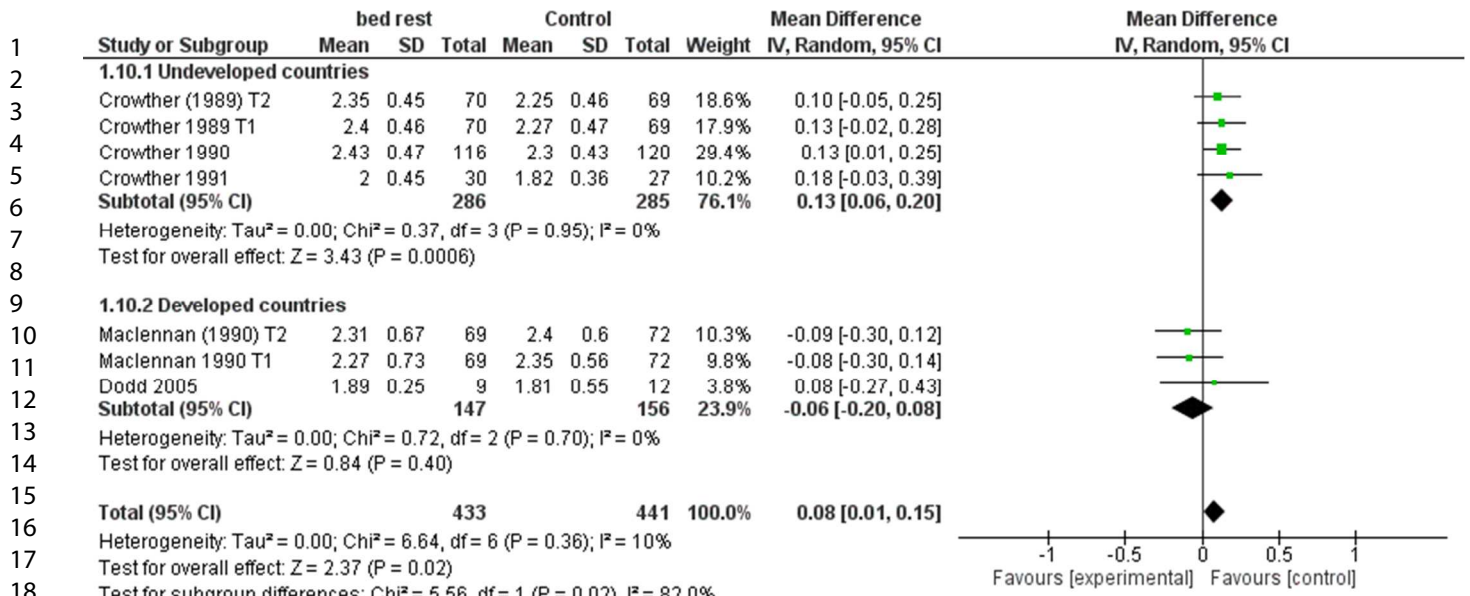
ONLINE SUPPLEMENT FIGURE 8. Effect of Bed rest (experimental) vs. non-bed rest (control) on pre-eclampsia. Bed rest did not significantly decrease risk of pre-eclampsia. OR = Odds Ratio; 95% confidence interval = [95% CI].



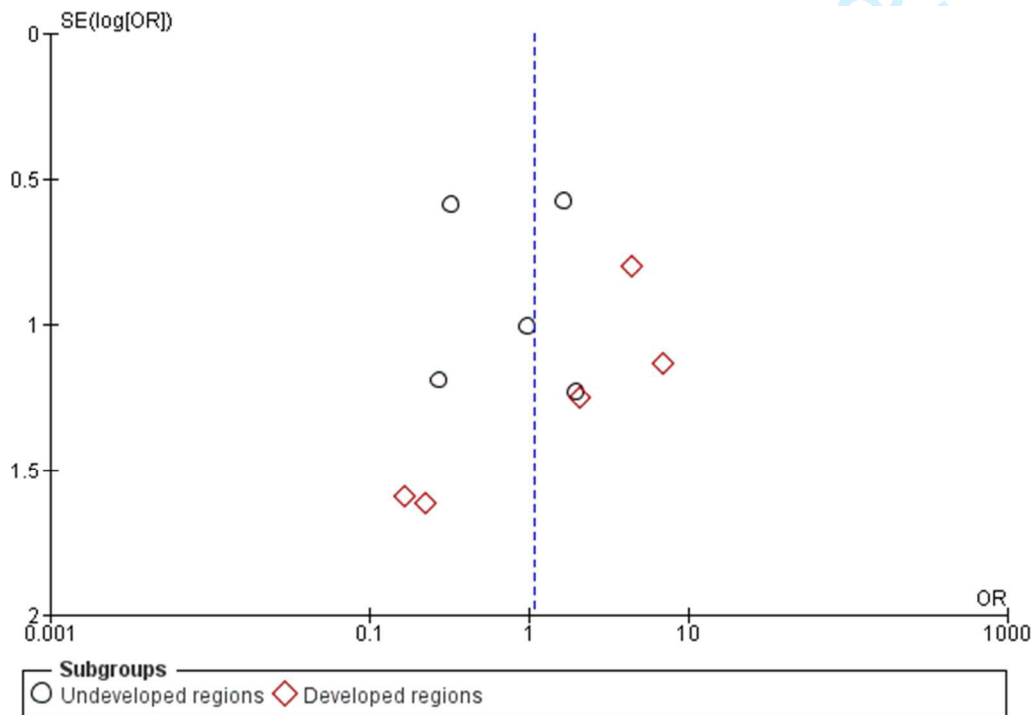
ONLINE SUPPLEMENT FIGURE 9. Effect of Bed rest (experimental) vs. non-bed rest (control) on PRM. Bed rest did not significantly decrease risk of PRM in developed or undeveloped regions. OR = Odds Ratio; 95% confidence interval = [95% CI].



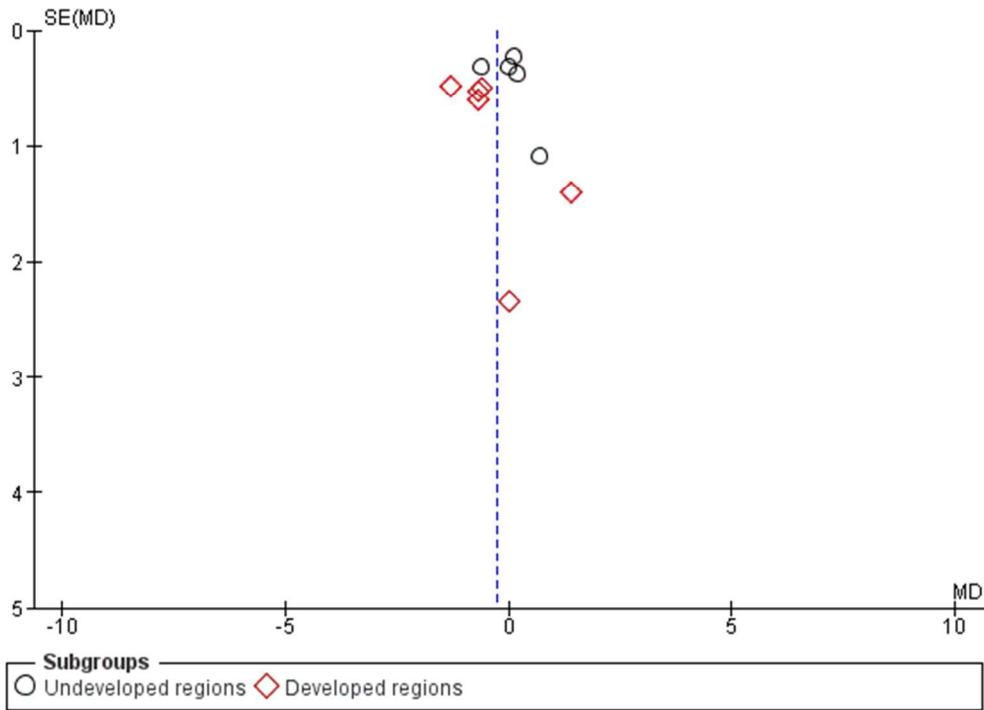
ONLINE SUPPLEMENT FIGURE 10. Effect of Bed rest (experimental) vs. non-bed rest (control) on GDM. Bed rest did not significantly decrease risk of GDM. OR = Odds Ratio; 95% confidence interval = [95% CI].



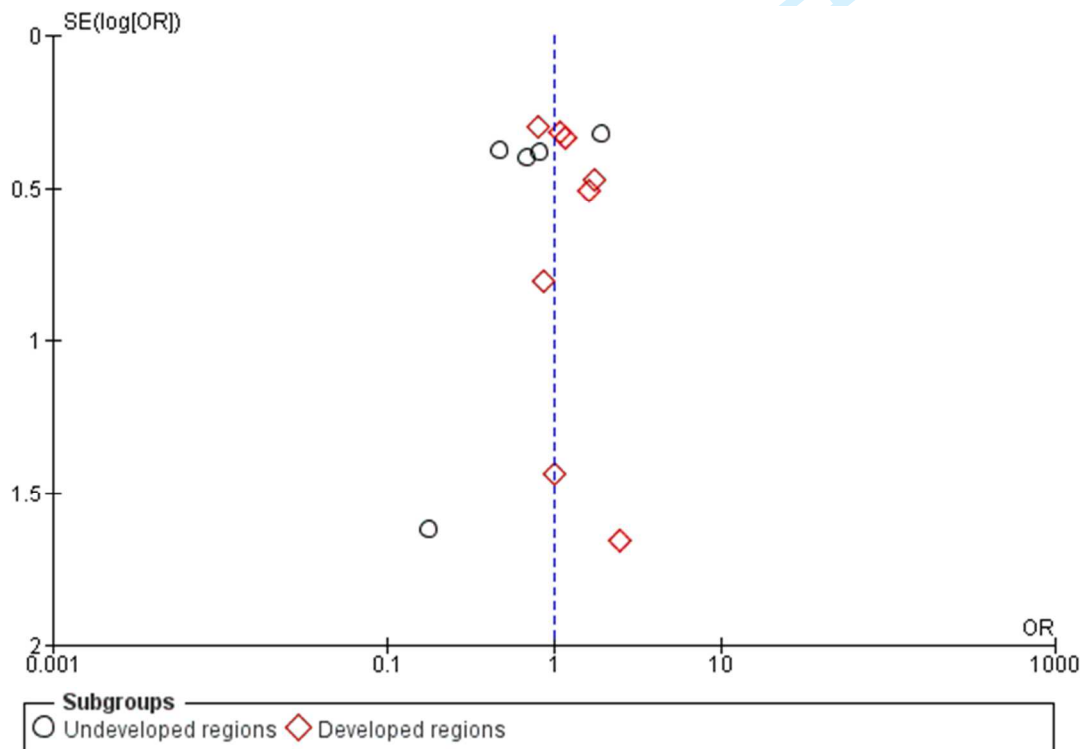
ONLINE SUPPLEMENT FIGURE 11. Effect of Bed rest (experimental) vs. non-bed rest (control) on birth weight in multiple gestation pregnancies. Bed rest resulted in a 130 gram increase in birth weight in undeveloped regions. WMD = weighted mean difference; 95% confidence interval = [95% CI].



1 **ONLINE SUPPLEMENT FIGURE 12.** Funnel plot using 12 studies on perinatal death following maternal
 2 prenatal
 3 bedrest.
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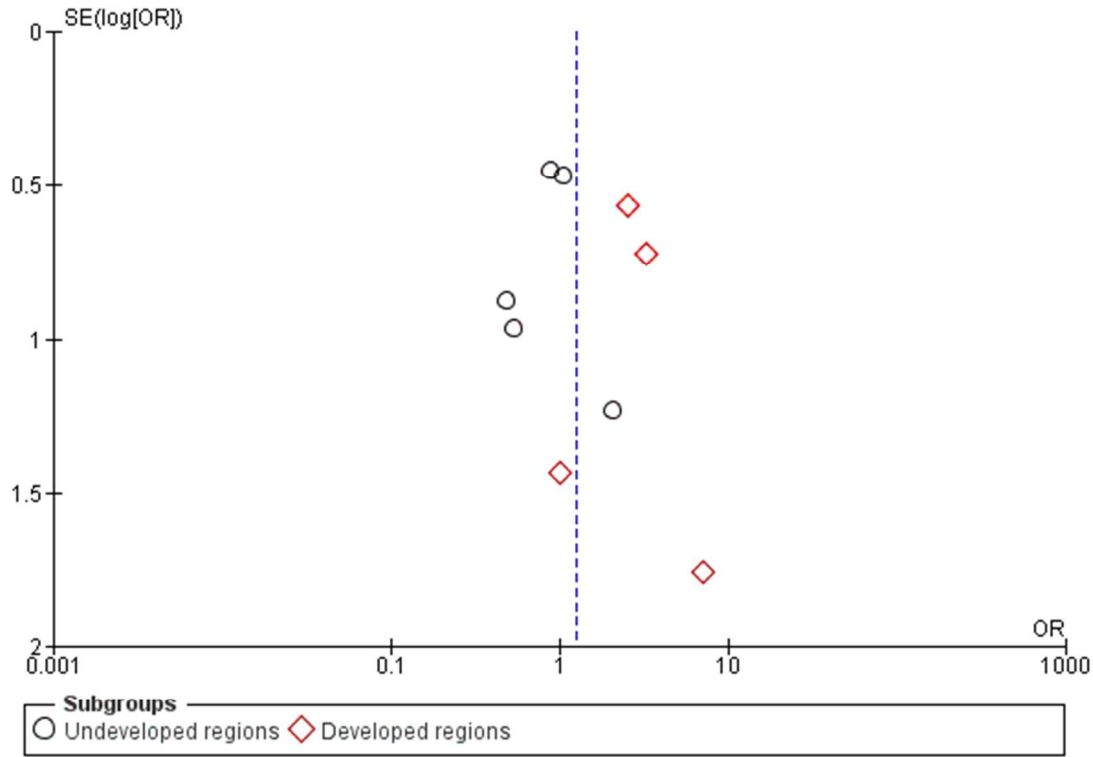


29 **ONLINE SUPPLEMENT FIGURE 13.** Funnel plot using 11 studies on gestational age at birth following
 30 maternal prenatal bedrest.
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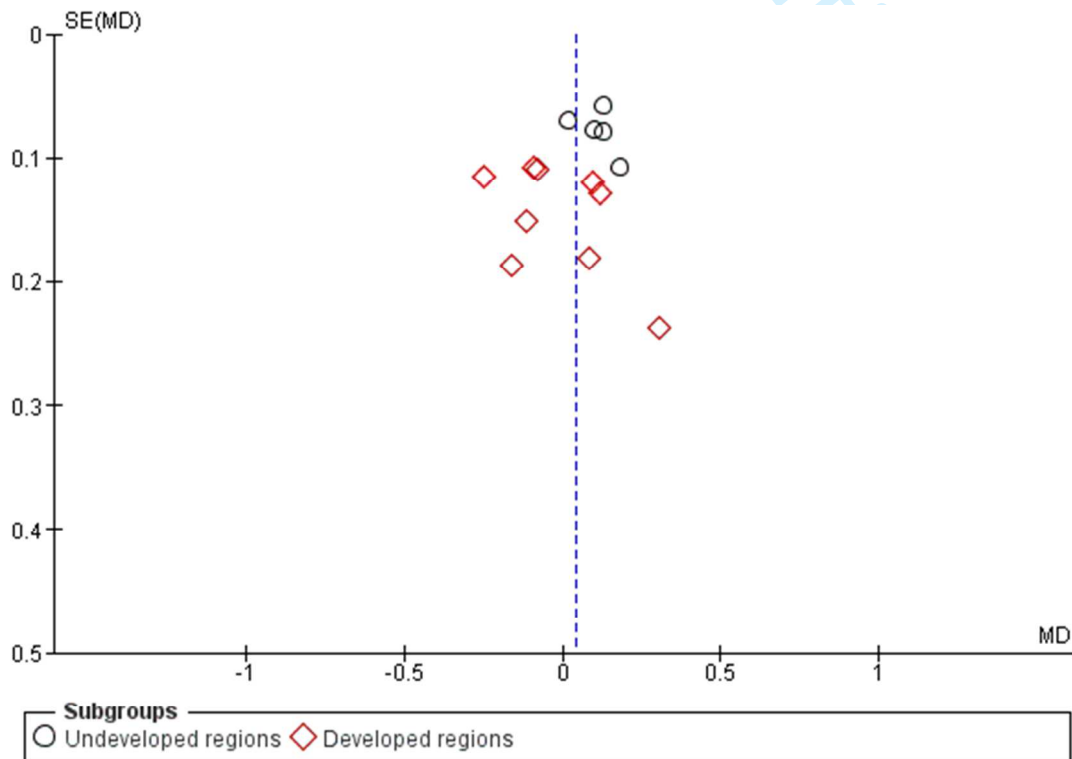


58 **ONLINE SUPPLEMENT FIGURE 14.** Funnel plot using 13 studies on premature birth (gestational age <37
 59 weeks) following maternal prenatal bedrest.
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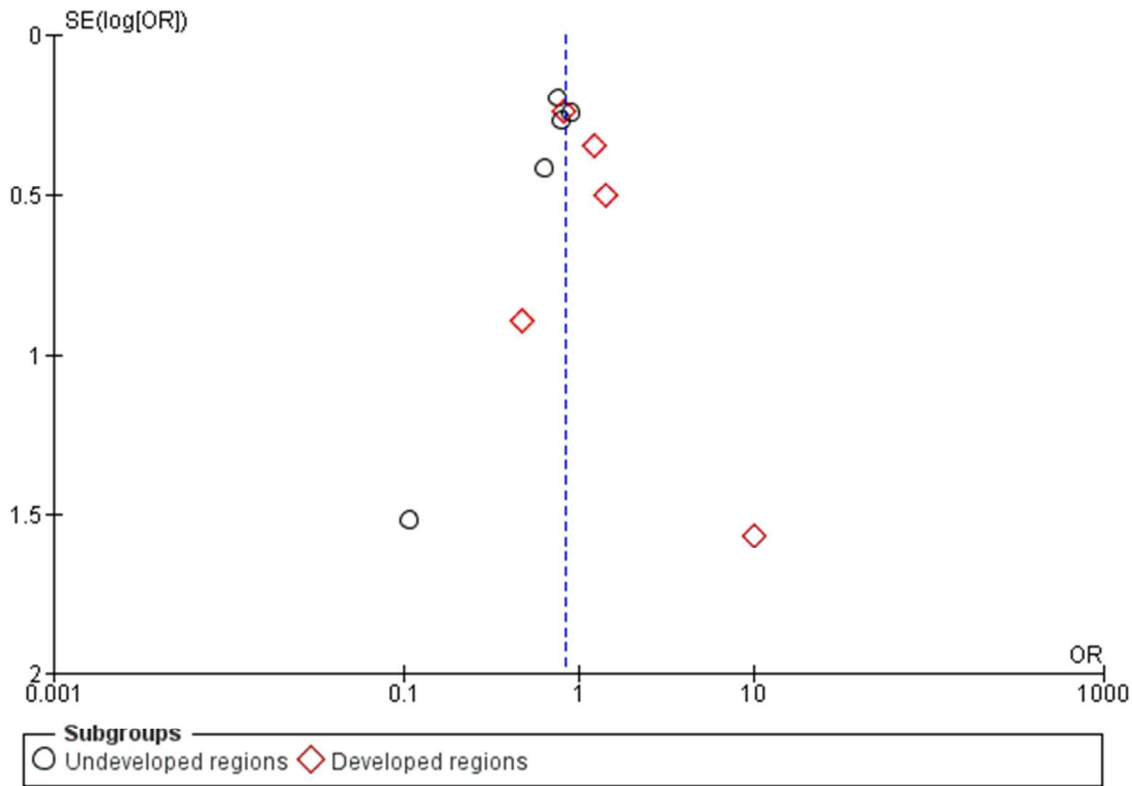
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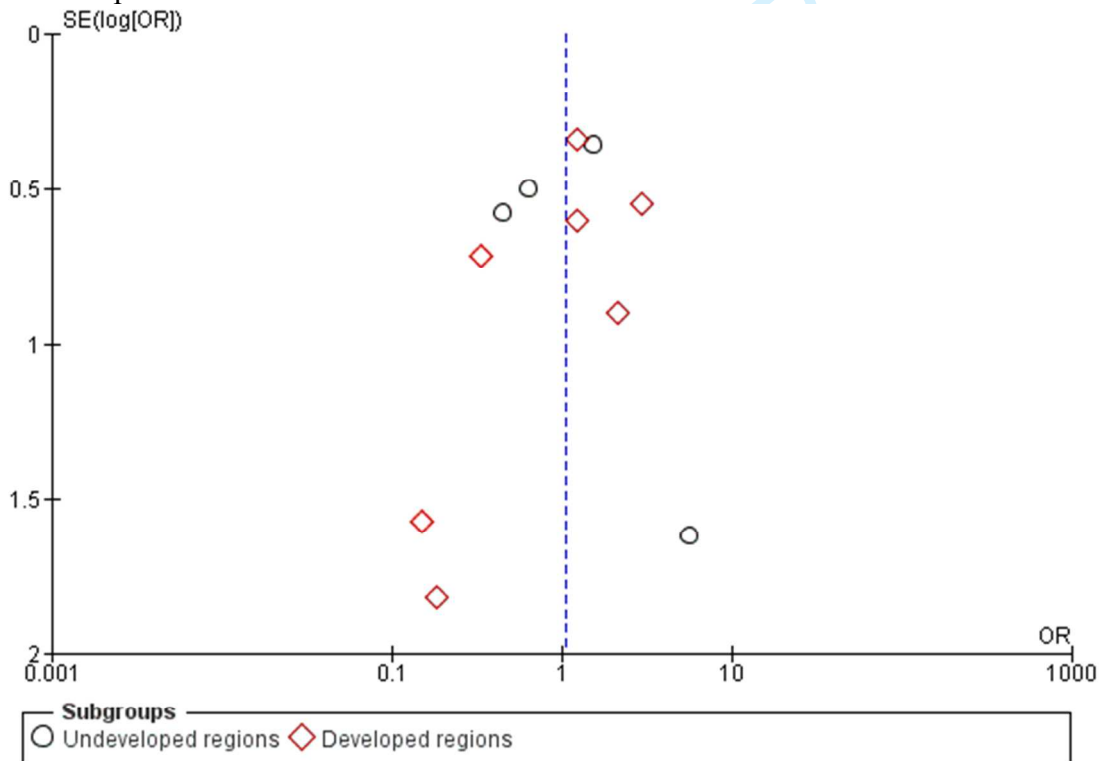
ONLINE SUPPLEMENT FIGURE 15. Funnel plot using 10 studies on very premature birth (author defined <35, 34, or 32 weeks gestational age) following maternal prenatal bedrest.



ONLINE SUPPLEMENT FIGURE 16. Funnel plot using 11 studies on infant birthweight following maternal prenatal bedrest.



ONLINE SUPPLEMENT FIGURE 17. Funnel plot using 10 studies on birthweight <2500g following maternal prenatal bedrest.



ONLINE SUPPLEMENT FIGURE 18. Funnel plot using 10 studies on C-section following maternal prenatal bedrest.

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Search Strategy Employed

Ovid Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Ovid MEDLINE 1946 to Present

1. exp Pregnancy Outcome/ or exp Fetus/ or exp Congenital Abnormalities/ or exp PrEGnancy Complications/ or exp PrEGnancy, High Risk/
2. ((pregnancy or birth or fetus or fetal or labo?r or deliver* or maternal) adj3 outcome*).ti,ab,kf.
3. (preterm or prematur* or birth weight or small for gestational age or large for gestational age or miscarriage* or spontaneous abortion* or pre eclampsia or ((fetal or fetus or neonat* or newborn* or infant* or congenital) adj3 abnormalit*)).ti,ab,kf.
4. (high risk adj3 pregnancy).ti,ab,kf.
5. (gestational diabetes or (membrane* adj2 ruptur*) or ((perinatal or fetal or maternal or infant* or neonat* or newborn*) adj2 (death or morality)) or polyhydramnios or caesarean or c-section).ti,ab,kf.
6. or/1-5
7. bone density/ or exp muscle strength/ or muscle tonus/ or exp Muscular Atrophy/
8. Depression/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or exp Anxiety disorders/
9. ((bone adj2 density) or muscl* or muscular or depress* or anxiety or metabolic).ti,ab,kf.
10. or/7-9
11. (pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum).ti,ab,hw.
12. 10 and 11
13. 6 or 12
14. bed rest/ or (bed rest or bedrest or (activit* adj3 restrict*)).ti,ab,kf.
15. 13 and 14
16. ((pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum) and (bed rest or bedrest or (activit* adj3 restrict*))).ti.
17. ((pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum) adj3 (bed rest or bedrest or (activit* adj3 restrict*))).ab.
18. 15 or 16 or 17
19. (clinical trial or randomized controlled trial).pt.
20. (randomi?ed or placebo* or randomly or trial or groups).ab.
21. intervention*.mp.
22. 19 or 20 or 21
23. 18 and 22
24. animals/ not (humans/ and animals/)
25. 23 not 24

Ovid Cochrane Central Register of Controoled Trials

1. exp Pregnancy Outcome/ or exp Fetus/ or exp Congenital Abnormalities/ or exp Pregnancy Complications/ or exp Pregnancy, High Risk/
2. ((pregnancy or birth or fetus or fetal or labo?r or deliver* or maternal) adj3 outcome*).ti,ab.

3. (preterm or prematur* or birth weight or small for gestational age or large for gestational age or miscarriage* or spontaneous abortion* or pre eclampsia or ((fetal or fetus or neonat* or newborn* or infant* or congenital) adj3 abnormalit*)).ti,ab.
4. (high risk adj3 pregnancy).ti,ab.
5. (gestational diabetes or (membrane* adj2 ruptur*) or ((perinatal or fetal or maternal or infant* or neonat* or newborn*) adj2 (death or morality)) or polyhydramnios or caesarean or c-section).ti,ab.
6. or/1-5
7. bone density/ or exp muscle strength/ or muscle tonus/ or exp Muscular Atrophy/
8. Depression/ or depressive disorder/ or depression, postpartum/ or depressive disorder, major/ or depressive disorder, treatment-resistant/ or dysthymic disorder/ or exp Anxiety disorders/
9. ((bone adj2 density) or muscl* or muscular or depress* or anxiety or metabolic).ti,ab.
10. or/7-9
11. (pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum).ti,ab,hw.
12. 10 and 11
13. 6 or 12
14. bed rest/ or (bed rest or bedrest or (activit* adj3 restrict*)).ti,ab.
15. 13 and 14
16. ((pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum) and (bed rest or bedrest or (activit* adj3 restrict*))).ti.
17. ((pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum) adj3 (bed rest or bedrest or (activit* adj3 restrict*))).ab.
18. 15 or 16 or 17

Ovid Cochrane database of SRs

1. ((pregnancy or birth or fetus or fetal or labo?r or deliver* or maternal) adj3 outcome*).ti,ab,kw.
2. (preterm or prematur* or birth weight or small for gestational age or large for gestational age or miscarriage* or spontaneous abortion* or pre eclampsia or ((fetal or fetus or neonat* or newborn* or infant* or congenital) adj3 abnormalit*)).ti,ab,kw.
3. (high risk adj3 pregnancy).ti,ab,kw.
4. (gestational diabetes or (membrane* adj2 ruptur*) or ((perinatal or fetal or maternal or infant* or neonat* or newborn*) adj2 (death or morality)) or polyhydramnios or caesarean or c-section).ti,ab,kw.
5. or/1-4
6. ((bone adj2 density) or muscl* or muscular or depress* or anxiety or metabolic).ti,ab,kw.
7. (pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum).ti,ab,kw.
8. 6 and 7
9. 5 or 8
10. (bed rest or bedrest or (activit* adj3 restrict*)).ti,ab,kw.
11. 9 and 10
12. ((pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum) and (bed rest or bedrest or (activit* adj3 restrict*))).ti.

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3 13. ((pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum)
4 adj3 (bed rest or bedrest or (activit* adj3 restrict*))).ab,kw.
5 14. 11 or 12 or 13
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8 **Ovid Embase**

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10 1. exp Pregnancy Outcome/ or exp Fetus/ or exp Congenital Disorder/ or exp Pregnancy
11 Complication/ or exp High Risk Pregnancy/
12 2. ((pregnancy or birth or fetus or fetal or labo?r or deliver* or maternal) adj3 outcome*).ti,ab.
13 3. (preterm or prematur* or birth weight or small for gestational age or large for gestational age
14 or miscarriage* or spontaneous abortion* or pre eclampsia or ((fetal or fetus or neonat* or
15 newborn* or infant* or congenital) adj3 abnormalit*)).ti,ab.
16 4. (high risk adj3 pregnancy).ti,ab.
17 5. (gestational diabetes or (membrane* adj2 ruptur*) or ((perinatal or fetal or maternal or infant*
18 or neonat* or newborn*) adj2 (death or morality)) or polyhydraminos or caesarean or c-
19 section).ti,ab.
20 6. or/1-5
21 7. bone density/
22 8. muscle strength/ or muscle atrophy.mp. [mp=title, abstract, original title, name of substance
23 word, subject heading word, keyword heading word, protocol supplementary concept word, rare
24 disease supplementary concept word, unique identifier]
25 9. exp muscle tone/
26 10. exp depression/
27 11. ((bone adj2 (density or deminerali*)) or muscl* or muscular or depress* or anxiety or
28 metabolic).ti,ab.
29 12. exp anxiety disorder/
30 13. or/7-12
31 14. (pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre
32 partum).ti,ab,hw.
33 15. 13 and 14
34 16. 6 or 15
35 17. bed rest/ or (bed rest or bedrest or (activit* adj3 restrict*)).ti,ab.
36 18. 16 and 17
37 19. ((pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum)
38 and (bed rest or bedrest or (activit* adj3 restrict*))).ti.
39 20. ((pregnan* or antenatal or prenatal or antepartum or prepartum or ante partum or pre partum)
40 adj3 (bed rest or bedrest or (activit* adj3 restrict*))).ab.
41 21. 18 or 19 or 20
42 22. limit 21 to (clinical trial or randomized controlled trial or controlled clinical trial)
43 23. (randomi?ed or placebo* or randomly or trial or groups).ab.
44 24. intervention*.mp.
45 25. 23 or 24
46 26. 21 and 25
47 27. 22 or 26
48 28. animals/ not (humans/ and animals/)
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ClinicalTrials.gov

1. Bed rest
2. Bedrest

Recruitment: Closed Studies

Study Results: Studies with Results

Scopus

(TITLE-ABS-KEY ((pregnancy OR birth OR maternal OR fetus OR fetal OR perinatal) W/2 (complication* OR outcome* OR "high risk")) OR ((fetus OR fetal OR perinatal OR neonat* OR infant* OR maternal) W/2 (death OR mortality)) OR ((fetus OR fetal OR perinatal OR neonat* OR infant* OR congenital) W/2 (abnormalit*)) OR (membrane* W/2 ruptur*) OR preterm OR prematur* OR "birth weight" OR "small for gestational age" OR "large for gestational age" OR miscarriage* OR "spontaneous abortion*" OR "pre eclampsia" OR "gestational diabetes") OR TITLE-ABS-KEY ((bone W/2 (density OR demineralization)) OR muscl* OR muscular OR depression OR depressive OR anxiety) AND TITLE-ABS-KEY (pregnan* OR deliver* OR prenatal OR antenatal OR perinatal OR prepartum OR antepartum OR "pre partum" OR "ante partum")) AND TITLE-ABS-KEY ((bedrest OR "bed rest" OR "activity restriction" OR "restricted activity")) OR TITLE-ABS-KEY ((bedrest OR "bed rest" OR "activity restriction" OR "restricted activity")) AND (pregnan* OR prenatal OR antenatal OR perinatal OR prepartum OR antepartum OR "pre partum" OR "ante partum")) AND TITLE-ABS-KEY (random* OR groups OR placebo* OR trial OR intervention*)

Web of Science Core Collection

((TS=((pregnancy OR birth OR maternal OR fetus OR fetal OR perinatal) NEAR/2 (complication* OR outcome* OR "high risk")) OR TS=((fetus OR fetal OR perinatal OR neonat* OR infant* OR congenital) NEAR/2 abnormalit*) OR TS=(preterm OR prematur* OR "birth weight" OR "small for gestational age" OR "large for gestational age" OR miscarriage* OR "spontaneous abortion*" OR "pre eclampsia" OR "gestational diabetes") OR TS=(bone NEAR/2 (density OR demineralization) OR muscl* OR muscular OR depression OR depressive OR anxiety) AND TS=(pregnan* OR prenatal OR antenatal OR perinatal OR prepartum OR antepartum OR "pre partum" OR "ante partum")) AND TS=(bedrest or "bed rest" or activit* near/2 restrict*) OR TS=(bedrest or "bed rest" or activit* near/2 restrict*) AND TS=(pregnancy OR birth OR maternal OR fetus OR fetal OR perinatal)) AND TS=(random* OR groups OR placebo* OR trial OR intervention*)

EBSCO Host CINAHL Plus

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3 S1 –(MH "Bed Rest") or "bed rest" or bedrest activit* n3 restrict*

4 S2 – ((MH "Pregnancy Outcomes") OR (MH "Pregnancy Complications+") OR (MH "Fetus+")
5 OR (MH "Fetal Abnormalities") OR (MH "Pregnancy, High Risk")) OR ((pregnancy or birth or
6 fetus or fetal or labo?r or deliver* or maternal) n3 outcome*) OR (preterm or prematur* or birth
7 weight or small for gestational age or large for gestational age or miscarriage* or spontaneous
8 abortion* or "pre eclampsia" or "gestational diabetes" or ((fetal or fetus or neonat* or newborn*
9 or infant* or congenital) n3 abnormalit*) OR high risk w3 pregnancy

10 S3 – S1 AND S2

11 S4 – ((MH "Bone Density") OR (MH "Depression+") OR (MH "Anxiety Disorders+") OR (MH
12 "Muscle Strength+") OR (MH "Muscle Weakness") OR (MH "Muscular Atrophy+") OR (MH
13 "Muscle Tonus")) OR (muscul* or muscular or depress* or anxiety or metabolic)

14 S5 - pregnan* or antenatal or prenatal or antepartum or prepartum or "ante partum" or "pre
15 partum"

16 S6 - S4 AND S5

17 S7 - S2 OR S6

18 S8 – S1 AND S7

19 S9 – TI (((pregnan* or antenatal or prenatal or antepartum or prepartum or "ante partum" or "pre
20 partum") and ("bed rest" or bedrest or (activit* n3 restrict*))) OR ((pregnan* or antenatal or
21 prenatal or antepartum or prepartum or "ante partum" or "pre partum") w3 ("bed rest" or bedrest
22 or (activit* n3 restrict*)))

23 S10 – S8 OR S9
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