Ramadan during pregnancy and offspring health outcomes over the life course:

A systematic review and meta-analysis

(Accepted Manuscript)

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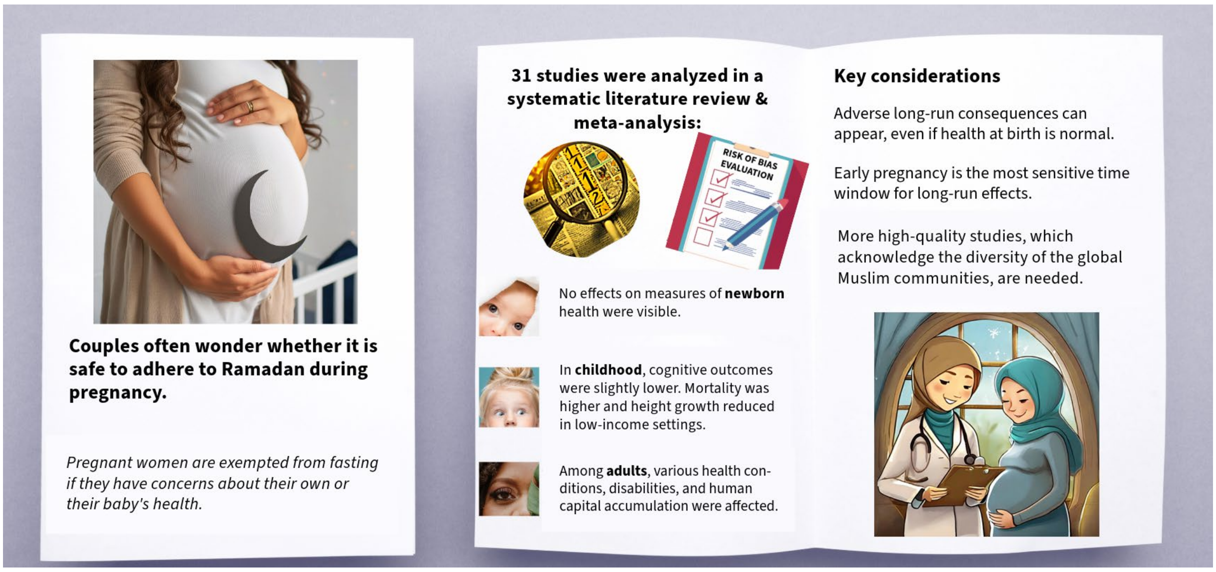
This document is the final draft author manuscript, as accepted for publication by the journal, including modifications based on referees' suggestions, before it has undergone copyediting, typesetting and proof correction.

Please cite this manuscript as:

Pradella F, Witte P, Van Ewijk R, Ramadan during pregnancy and offspring health outcomes over the life course: a systematic review and meta-analysis, *Human Reproduction Update*, 2024; dmae026, https://doi.org/10.1093/humupd/dmae026.

The published version can be found at https://doi.org/10.1093/humupd/dmae026.

Graphical abstract for a systematic review and meta-analysis on Ramadan during pregnancy and offspring health over the life course. The graphical abstract was prepared using Adobe Firefly.



Summary of the Graphical Abstract: Systematic review and meta-analysis suggest that Ramadan during pregnancy can have long-term adverse health consequences, even if health indicators at birth are not affected.

Abstract

Background: Intermittent fasting, such as during Ramadan, is prevalent among pregnant women. However, the association between Ramadan during pregnancy and offspring health along the life course has not been fully established.

Objective and rationale: Fetal programming research indicates that prenatal exposures, particularly during early pregnancy, can cause long-term structural and physiological changes that adversely affect offspring health. Our objective was to systematically identify and assess the evidence regarding Ramadan during pregnancy.

Search methods: 31 studies were sourced from PubMed, EMBASE, Web of Science, and EconLit. Included studies evaluated outcomes in individuals with prenatal Ramadan exposure, compared to unexposed Muslim controls. Main outcomes were birth weight, gestational length, and sex ratio in newborns; height, mortality, and cognition in children; and disabilities, chronic diseases, and human capital accumulation in adults. Each study was evaluated for bias risk. The overall quality of evidence was appraised using the GRADE system. Random-effects meta-analyses were conducted for outcomes analyzed in at least three primary studies.

Outcomes: The initial search identified 2933 articles, 1208 duplicates were deleted. 31 publications fulfilled the eligibility criteria for the qualitative synthesis; 22 studies were included in meta-analyses. The overall quality of the evidence was low to moderate and differed by study design and outcome. Among newborns, prenatal Ramadan exposure was not associated with birth weight (mean difference (MD) -3 grams (95% CI -18 to 11; I^2 = 70%) or the likelihood of prematurity (percentage point difference (PPD) 0.19 (95% CI -0.11 to 0.49; I^2 = 0%)). The probability that a newborn is male was reduced (PPD -0.14 (95% CI -0.28 to -0.00; I^2 = 0%)). This potentially reflects sex-specific mortality rates resulting from adverse in utero circumstances. In childhood, the exposed performed slightly poorer on cognitive tests (MD -3.10% of a standard deviation (95% CI -4.61 to -1.58; I^2 = 51%)). Height growth among the exposed was reduced, and this pattern was already visible at ages below 5 (height-for-age z-score MD -0.03 (95% CI -0.06 to -0.00; I^2 = 76%)). Qualitative literature synthesis revealed that childhood mortality rates were increased in low-income contexts. In adulthood, the prenatally exposed had an increased likelihood of hearing disabilities (odds ratio (OR) 1.26 (95% CI 1.09 to 1.45; I^2 = 32%)), while sight was not affected. Other impaired outcomes include chronic diseases or their symptoms, and indicators of human capital accumulation such as home ownership (qualitative literature synthesis). The first trimester emerged as a sensitive period for long-term impacts.

Wider implications: Despite the need for more high-quality studies to improve the certainty of the evidence, the synthesis of existing research demonstrates that Ramadan during pregnancy is associated with adverse offspring health effects in childhood and especially adulthood, despite an absence of observable effects at birth. Not all health effects may apply to all Muslim communities, which are diverse in backgrounds and behaviors. Notably, moderating factors like daytime activity levels, and dietary habits outside fasting hours have hardly been considered. It is imperative for future research to address these aspects.

Registration number: PROSPERO (CRD42022325770).

Introduction

The prenatal environment exerts profound impacts on fetal physiology. Adaptations to adverse circumstances may enhance short-term survival while coming at the cost of a predisposition toward worse long-run health outcomes. Fetal programming theory describes how epigenetic markers are altered in response to early life environments and how as a consequence of this, prenatal adversity may result in enduring health conditions. These conditions, often dormant at birth, may only surface as chronic ailments decades later (Almond and Currie, 2011, Almond et al., 2018, Gluckman et al., 2005, Ollikainen et al., 2010). Various exposures, such as instances of famine exposure during pregnancy, have been associated with negative outcomes for offspring health over the life course (De Rooij et al., 2022, Li et al., 2015, Lumey et al., 2011, Painter et al., 2005, Ross and Desai, 2005, Yang et al., 2008). Early developmental stages, characterized by significant plasticity in biological and epigenetic mechanisms, are particularly responsive to environmental stressors, with exposure being most detrimental during early pregnancy when DNA methylation is highly sensitive (Griffiths and Hunter, 2014, Harris and Seckl, 2011, Tobi et al., 2015). While extensive fetal programming research has identified health implications in response to severe shocks during pregnancy, there is a growing interest in investigating subtler prenatal exposures' impacts on offspring health due to their prevalence among pregnant women.

One subtler, and prevalent, form of nutritional deprivation during pregnancy is intermittent fasting, such as breakfast skipping (Mazumder and Seeskin, 2015, Shiraishi et al., 2019). Another manifestation of intermittent fasting is observed in the context of cultural and religious fasting, followed by adherents of various faiths (Trabelsi et al., 2022). This also includes daytime intermittent fasting during Ramadan, a period of important spiritual reflection for Muslims. During Ramadan, the ninth month of the Islamic calendar, healthy adult Muslims worldwide participate in a fasting regimen that spans 29-30 days, involving abstinence from food and drink from dawn to sunset. Other adjustments to Ramadan include the adaptation of sleep rhythms to the intake of food very early in the morning and late at night and changes in nutrient intake due to traditional meals being consumed at the breaking of the fast after sunset and before sunrise (Faris et al., 2020, Seiermann and Gabrysch, 2020). While for healthy non-pregnant adults, Ramadan may improve lipid profile, metabolic and cardiovascular health (Adawi et al., 2017, Al-Jafar et al., 2024, Al-Jafar et al., 2021, Ghashang et al., Madkour et al., 2023, Mirmiran et al., 2019, Su et al., 2021) as well as life satisfaction and prosocial behavior (Campante and Yanagizawa-Drott, 2015, Haruvy et al., 2018), vulnerable populations are exempted from adherence to the intermittent fasting regime. This includes children, the elderly and the sick. Pregnant women are exempted from Ramadan fasting if they have concerns about the health of the unborn child or their own health.

Ramadan is thought to have potential adverse effects on fetal growth and organ development particularly during early pregnancy, when cells are highly susceptible to epigenetic alterations (Heppe et al., 2013, Langley-Evans, 2015, Rifas-Shiman et al., 2006, Wu et al., 2004). During Ramadan, both maternal macronutrient intake and total calories consumed tend to be altered (Arab, 2004, Larijani et al., 2003, Savitri et al., 2018). Additionally, pregnant women following intermittent fasting regimes, including Ramadan, exhibit symptoms indicative of accelerated starvation, i.e. they rapidly reach a state that more generally occurs during starvation and which is marked by decreased serum levels of glucose and alanine, coupled with elevated concentrations of free fatty acids and ketones. These changes stem from a shift from glucose to fat metabolism (Arab, 2004, Burbos et al., 2009, Malhotra et al., 1989, Metzger et al., 1982, Prentice et al., 1983).

At the same time, empirical evidence shows that Muslim women in various settings fast during pregnancy. Fasting rates range from 43% in the UK and 54% in the Netherlands to 88% in Pakistan and 99% in Bangladesh (Mubeen et al., 2012, Petherick et al., 2014, Savitri et al., 2014, Seiermann et al., 2021) and are highest in the first trimester, when many women are not yet aware of their pregnancy. Surveys among pregnant Muslim women revealed that in some contexts, sensitization to potential health implications is absent, and sometimes pregnant women perceive fasting as recommended (“mustahabb”) during pregnancy (Hossain et al., 2021, Karimi et al., 2021). Main reasons for fasting are thus motivated by religious convictions and for some, fasting also serves as a means to attain spiritual and emotional well-being and fosters a sense of community (Firouzbakht et al., 2013, Leimer et al., 2018, Lou and Hammoud, 2016, Robinson and Raisler, 2005, Uludağ and Göral Türkcü, 2022).

Given that over 220 million offspring to Muslims are born each year (Pew Research Center, 2017) and of the pregnancies among Muslim women, over 80% overlap with Ramadan, a systematic qualitative and quantitative evaluation of the current evidence on effects of Ramadan during pregnancy, in particular Ramadan during early pregnancy, has become timely. Previous reviews did not evaluate the literature for risk of bias, did not include meta-analytical evidence, and/or covered only part of the literature. At the same time, advice for obstetricians is currently based on these reviews (Shahawy et al., 2023). The purpose of the current study was therefore to provide an all-encompassing systematic review and meta-analysis summarizing the effects of Ramadan during pregnancy on offspring health throughout their entire life course. Importantly, this review systematically differentiates effects by pregnancy trimester of Ramadan exposure with a focus on exposure in early pregnancy. Based on an extensive risk-of-bias assessment that is documented for each individual study, risk of bias is considered in both the literature synthesis as well as the meta-analysis. A nuanced life-course assessment of the effects of Ramadan during pregnancy is essential to provide pregnant women and healthcare professionals with objective evidence on the offspring health effects of intermittent fasting during pregnancy.

Methods

Protocol registration

The review protocol was registered with and is available on PROSPERO (CRD42022325770). The reporting adheres to the guidelines outlined in The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA), as well as Meta-analysis of Observational Studies in Epidemiology (MOOSE) protocols (Brooke et al., 2021, Moher et al., 2010).

Search strategy

We performed a systematic search of peer-reviewed original literature to identify the available evidence on Ramadan during pregnancy and health outcomes of Muslim offspring, independent of the life stage of the offspring, thus including studies on subjects aged ≥0. We consulted with a medical librarian who is an expert in search methodology to discuss the design of the search strategy and literature search.

Any study published before November 2, 2023 was included in the search. The systematic literature search was conducted in the PubMed, EMBASE, EconLit and Web of Science databases. For optimal precision, each database was searched individually. To streamline the search, a block search approach was used. Duplicates were excluded. The full search protocol is available in Supplementary Table S1. In addition, we conducted searches in Arabic, Persian, Turkish and Urdu to make sure to encompass literature published in languages other than English, which are prevalent within the Muslim community. This search in additional languages was carried out on Google Scholar, in consultation with the medical librarian. Google Scholar was selected due to the limitations of other databases in handling searches across various languages. This extension of our search methodology was targeted at identifying articles in the designated languages that lacked English abstracts, thereby ensuring the inclusiveness of our literature review. Upon consultation with the medical librarian, we screened the first 200 results for each Google Scholar search.

Eligibility criteria

This review used broad inclusion criteria to capture all studies with “Ramadan during pregnancy” as type of exposure. Full quantitative, peer-reviewed studies reporting on Ramadan during pregnancy and its associations with short- and long-run offspring health outcomes were considered eligible.

Studies were excluded if the study sample did not include a control group that was unexposed to Ramadan, such as studies comparing women fasting for more than 20 to women fasting one to ten days. Studies that reported on associations between Ramadan during pregnancy and maternal health outcomes (e.g. gestational diabetes) were also excluded.

After deduplication, two researchers conducted independent screening of studies that aligned with the search criteria by assessing their titles and abstracts. The studies that potentially fulfilled the inclusion criteria were retrieved as full versions. The reviewers then independently examined whether the studies met the selection criteria. In instances where there was a difference of opinion regarding a study's fulfillment of the inclusion criteria, a study was discussed and subsequently the third researcher was consulted. No automation tools were used in this process.

Data extraction

Two researchers independently collected data from the set of studies that met all inclusion criteria using a predefined data extraction table that covered bibliographical information, sample characteristics, measure of effects, methodology and outcomes.

Estimates of effects, including trimester-specific exposure results, were gathered for all health outcomes for which a study reported results. In case a study reported both unadjusted and adjusted results, we only extracted the adjusted results as these are considered superior (see also the Quality assessment section below). Effect estimates were extracted with the associated standard errors, confidence intervals and p-values. Associations were considered significant if the reported two-sided p-value was <0.05.

Quality assessment

This study incorporates a comprehensive risk of bias assessment, following the Cochrane and MOOSE guidelines. Quality criteria for all study designs were developed *a priori* against which all primary studies were assessed. All eligible studies were subsequently evaluated independently by two authors to assess risk of bias. Any discrepancies in ratings were discussed with the third author.

The literature on Ramadan during pregnancy can be subdivided into two study designs. As both designs consist of observational studies, there is always a risk of bias. In order to judge the risk of bias in each study, we developed risk of bias criteria that addressed key components of each study design in the risk of bias assessment, as recommended by the MOOSE criteria (Stroup et al., 2000). An overview of all risk of bias assessment domains, including the minimum standards for classification as low risk of bias, is provided in Supplementary Table S2.

The “self-reported fasting” (SRF) design compares health outcomes among the offspring of fasting vs. non-fasting women, where self-declared fasting information is linked to offspring health data that mostly stem from hospitals. These studies must control for a broad set of confounders that influence both the maternal decision to fast and offspring health outcomes.

By contrast, the natural experiment (NE) design exploits large-scale datasets with Muslims with known birthdates. These studies classify all individuals whose time in utero overlapped with a Ramadan as exposed, without further information on maternal fasting during Ramadan. This means that NE studies provide intention-to-treat estimates, since not all pregnant women fast during pregnancy. An advantage of the NE design is that, in contrast to the fasting decision, the occurrence of a Ramadan during a pregnancy is not confounded with maternal background characteristics. However, NE studies need to include month of birth controls to separate the effects of Ramadan from season of birth effects. Otherwise, these studies cannot plausibly argue that the detected effects are attributable to Ramadan during pregnancy. Following Cochrane guidelines, our evaluation distinguished the risk of bias assessment by study design: while NE studies provide "intention-to-treat" effects, SRF effects are to be considered as "per-protocol", so that different domains of bias needed to be addressed (see Supplementary Table S2).

Meta-analysis

Outcomes that had been included in at least three primary studies that were classified as being at a low risk of bias were meta-analytically analyzed. Random-effects meta-analyses were run using Stata SE (version 17). Estimates were weighted by the inverses of their respective variances, which correspond to the squares of the standard errors to the regression coefficient or mean difference. If only confidence intervals or, in rare cases, only p-values were given, these were converted into standard errors (Altman and Bland, 2011). For binary outcome variables, the majority of studies reported results as percentage point differences (PPD), while others reported odds ratios. The latter were converted into the former metric using the probability in the control group and the adjusted odds ratio (see for example Liberman (2005)). Only when rates differed very strongly between studies so that weighted average PPDs would not be interpretable in a meaningful way, did we convert all results to odds ratios. When a study reported results from analyses on distinct samples, each sample was treated independently as if it were the result of a separate primary study. This was specifically applicable to Almond and Mazumder (2011).
Analyses were run separately for exposures that applied to the entirety of pregnancy, and exposures that specifically related to the first trimester of pregnancy. For studies that only reported a set of results by phase of pregnancy, these results were combined into a single effect estimate with corresponding standard error for the entirety of pregnancy, by running a fixed effects meta-analysis on the study's pregnancy phase-specific effect estimates. Between-study heterogeneity was assessed using χ^2-tests and I^2-statistics.
For outcomes on which more than seven studies could be included, publication bias was assessed using funnel plots, as well as an Egger's regression test. Furthermore, for outcomes analyzed by at least three SRF and three NE studies, we tested whether results differed by study design (SRF vs NE). As a sensitivity check, studies that were at a high risk of bias were included into the meta-analysis. This provides insights on how effect patterns change if studies judged to be at risk of bias are considered, as recommended by the Cochrane guidelines (Higgins et al., 2023).

Results

Study selection

Electronic database searches were conducted at two time points (original search on 15 March 2023, and an updated search on 2 November 2023 using EMBASE). The search identified 2933 studies. After deduplication and screening out irrelevant records based on the inclusion and exclusion criteria, full texts of 69 studies were assessed for eligibility. These were selected for quantitative or qualitative synthesis for the review. No additional eligible studies were identified based on a literature search in Arabic, Persian, Turkish and Urdu on 2 November 2023. Finally, 31 studies comprising several millions of subjects were included in the final review and qualitative trend synthesis. Of these, 22 studies were found eligible for the meta-analysis. Figure 1 visually depicts the process of selecting studies for inclusion in this systematic review according to PRISMA guidelines (Page et al., 2021).

Risk of bias of included studies

Supplementary Figure S1 shows the domain-based summary of the risk of bias for each individual study. The main reasons for classification as high risk of bias were: bias caused by uncontrolled or under-adjusted confounding factors (SRF studies) and biases caused by failure to adjust for confounding by season of birth (NE studies). Two out of the 21 NE studies and seven out of the eleven SRF studies were found to be at high risk of bias (note that one study contributed both NE and SRF estimates and hence appears twice). 14 high-quality studies contributed to the meta-analyses.

Overall certainty of the evidence

In examining the certainty of the evidence using the GRADE criteria (Ryan and Hill, 2016), it was decided that evidence on short-term (neonatal health), medium-term (childhood) and long-term (adulthood) outcomes should be evaluated separately. According to the GRADE framework, the quality of certainty rating had a baseline rating of 'low' for all outcomes, because no randomized controlled trials (RCT) were included in the analyses. Evidence on adulthood outcomes was upgraded to a moderate certainty rating. In these studies, all plausible confounding factors have been accounted for via the NE design, an important criterion in the GRADE rating system. For childhood and neonatal health outcomes, no upgrading of the certainty of evidence assessment was undertaken, since multiple SRF studies on neonatal health outcomes had a high risk of bias and there was a high degree of inconsistency in the results (i.e. effects in opposite directions such as in case of birth weight, cf. Table 1). However, when excluding the studies identified as being at a high risk of bias (Supplementary Figure S1), the evidence from the remaining studies on childhood and neonatal outcomes could be upgraded to a moderate certainty rating as well. All remaining childhood outcomes controlled for all plausible confounding factors via a NE design, while the neonatal outcome studies comprised NE studies and SRF studies that took care to minimize the risk for confounding.

Ramadan during pregnancy and offspring-health across the life course

Table 1 shows the characteristics and results of the 31 included studies by offspring life phase and health outcome (Almond and Mazumder, 2011, Almond et al., 2015, Awwad et al., 2012, Azizi et al., 2004, Chaudhry, 2022, Chaudhry and Mir, 2021, Chu et al., 2023, Denizli et al., 2023, Ghazal et al., 2020, Greve et al., 2017, Hızlı et al., 2012, Jürges, 2015, Karimi and Basu, 2018, Karimi et al., 2021, Kavehmanesh and Abolghasemi, 2004, Kunto and Mandemakers, 2019, Lee et al., 2020, Majid et al., 2019, Majid, 2015, Mirghani and Hamud, 2006, Petherick et al., 2014, Pradella et al., 2023, Pradella and van Ewijk, 2018, Savitri et al., 2018, Savitri et al., 2020, Savitri et al., 2014, Schoeps et al., 2018, Schultz-Nielsen et al., 2016, Tith et al., 2019, Van Ewijk, 2011, Van Ewijk et al., 2013). For ease of reference of the available evidence, studies with high risk of bias are highlighted in italics. The findings of these studies are summarized in Table 1, but not elaborated upon due to their high risk of bias.
The body of evidence is characterized by a diversity of outcome measures that often precludes their aggregation through meta-analysis. This most strongly applies to adulthood outcomes. For several newborn health outcomes and for one childhood outcome, meta-analyses could be conducted.

Effects of Ramadan during pregnancy on neonatal health

Anthropometrics

Studies on birth weight were based on diverse study populations, covering multiple regions of the world (Greve et al., 2017, Jürges, 2015, Kavehmanesh and Abolghasemi, 2004, Lee et al., 2020, Majid et al., 2019, Petherick et al., 2014, Savitri et al., 2018, Savitri et al., 2020, Savitri et al., 2014). As depicted in Figure 2 (for exposure irrespective of phase of pregnancy) and Supplementary Figure S2 (for trimester 1 exposure), among the studies that were not at a high risk of bias, birth weight was neither associated with Ramadan irrespective of phase of pregnancy (9 studies, mean difference (MD) -3 grams (95% CI -18 to 11), nor with Ramadan specifically during the first pregnancy trimester (7 studies, MD -69 grams (95% CI -173 to 34)). Heterogeneity tests suggested a moderately sized ($I^2 = 70\%; P = 0.06$) amount of effect heterogeneity for the overall analysis. However, for exposure during the first pregnancy trimester, heterogeneity was large ($I^2 = 99\%$, P <0.001). Two studies (Pradella et al., 2023, Savitri et al., 2014) reported negative effects of first trimester exposure of around 300 grams, while the five other studies reported effects that were close to zero. Pradella et al. (2023) considered maternal diet during Ramadan as a potential effect moderator for first trimester exposure. Birth weight was only found to be decreased among offspring to women who reduced their intake of foods with high fat content during Ramadan.

Four studies reported on associations between Ramadan during pregnancy and low birth weight as a binary outcome measure (Greve et al., 2017, Lee et al., 2020, Petherick et al., 2014, Savitri et al., 2020). The probability that newborns had a low birth weight, defined as <2500 grams, did not differ between exposed and non-exposed, neither for exposure irrespective of pregnancy phase (percentage point difference (PPD) -0.27 (95% CI: -2.39 to 1.85)), nor for trimester 1 exposure (PPD -0.08 (95% CI: -0.51 to0.35)). Similarly, the probability of a newborn being small for gestational age, or being "below average in size" was not found to be associated with Ramadan during pregnancy (Lee et al., 2020, Savitri et al., 2020).

Gestational duration

Four studies reported on associations between Ramadan during pregnancy and gestational duration (Petherick et al., 2014, Pradella et al., 2023, Savitri et al., 2020, Tith et al., 2019). No associations with the probability of a premature birth before 37 weeks were detected (PPD 0.19 (95% CI -0.11 to 0.49)). Two studies showed that gestational length as a continuous measure was affected neither (Pradella et al., 2023, Savitri et al., 2020). All studies on gestational duration cover high-income settings and countries in which Islam is a minority religion.

Sex ratio

The 'fragile male hypothesis' states that unfavorable prenatal conditions are more critical for male embryos and fetuses (Kraemer, 2000). Meta-analytical results (Figure 2, Supplementary Figure S2) show that the probability of a male birth is slightly lower after prenatal Ramadan exposure (4 studies, PPD -0.14 (95% CI -0.28 to -0.00)). Contrary to expectations, this effect is not centered around first trimester exposure (PPD 0.02 (95% CI -0.21 to 0.24)). The studies examining the likelihood of male births are exclusively on high-income settings, including the United States, Denmark, Germany, and the Netherlands.

The point that an adverse prenatal environment leads to a higher mortality rates among males is confirmed by Van Ewijk (2011), who finds that prenatally exposed respondents in Indonesia are less like to be male, for all pregnancy trimesters of exposure. This study can however not distinguish whether this pattern is due to effects of prenatal Ramadan exposure on sex ratio at birth, or to potential later-life changes in sex ratios due to sex-specific mortality patterns that are related to the prenatal exposure.

Mortality

Two studies investigated effects on neonatal or perinatal mortality (Lee et al., 2020, Savitri et al., 2020). While Lee et al. (2020) finds a higher mortality risk before 3 months upon first trimester exposure to Ramadan, both studies do not find effects on mortality before seven days. These studies had large to very large sample sizes and were based on study populations from Ethiopia and the Netherlands, respectively.

Other newborn health outcomes

With respect to other clinical newborn health outcomes, the evidence remains scarce, and all studies but one are at a high risk of bias. Savitri et al. (2020) report associations with an increased risk for severe congenital anomalies, in particular after third trimester exposure, but no associations with congenital anomalies (irrespective of severity) or APGAR scores were detected. This study is based on data from the Netherlands.

Effects of Ramadan during pregnancy on childhood health

Anthropometrics

Most studies on childhood anthropometric outcomes studied height growth, a proxy for long-term malnutrition. Four studies report on height outcomes among under 5-year-old children. The three studies using height-for-age z-scores (Chaudhry and Mir, 2021, Karimi and Basu, 2018, Kunto and Mandemakers, 2019) find a reduced height (MD -0.03 (95% CI -0.06 to -0.00)) among under 5-year-olds who had been exposed at any stage of pregnancy. This effect was not concentrated among those exposed during the first trimester (MD -0.02 (95% CI -0.09 to 0.05)) (Figure 2, Supplementary Figure S2). Chaudhry and Mir (2021) moreover find increased stunting rates among exposed Pakistani in this age group. Lee et al. (2020) use unstandardized height measurements and find a reduced height after third trimester exposure.

Three studies report on height growth among older than 5-year-old children, as well as (young) adults. Two of these studies report on associations between Ramadan during pregnancy with height growth from childhood to young adulthood (<18 year-olds). Both report significantly lower height-for-age z-scores from adolescence onwards (Karimi et al., 2021, Kunto and Mandemakers, 2019). Effects among adolescents were concentrated among those exposed in early and mid-pregnancy. One study reports that Ramadan during pregnancy is associated with a lower final attained height, in particular if exposure occurs in in early pregnancy (Van Ewijk, 2011).
In contrast to height, weight status is a proxy for short-term nutrition. The evidence on weight-for-age as well as BMI and being underweight mostly finds no significant associations between Ramadan during pregnancy and any of these outcomes (Kunto and Mandemakers, 2019, Lee et al., 2020). One large-scale study finds that Ramadan during pregnancy is associated with an increased risk of being underweight among under 5-year-olds, in particular upon exposure in early- and mid- pregnancy (Chaudhry and Mir, 2021).

Some of the variation in the results regarding whether and when anthropometric effects materialize might be because local circumstances such as nutritional diversity – during Ramadan and postnatally – play a role. All studies on anthropometric outcomes focused on countries in the Global South. There are no indications about whether similar effects occur in circumstances in which food insecurity is not an issue.

Mortality

Two studies on infant and childhood mortality report increased risks after prenatal exposure (Lee et al., 2020, Schoeps et al., 2018). Both studies find associations in particular when the overlap with a Ramadan occurred in early pregnancy. Reported effects range between 30% and 40% increases relative to baseline mortality. The study settings exhibited high baseline mortality rates: 75 per 1,000 children in Ethiopia for mortality before the first year of life, and 34 per 1,000 children in Burkina Faso for mortality before the fifth birthday. These baseline mortality rates underline the high mortality rates in the countries compared to global averages (Perin et al., 2022). There is no evidence about whether similar effects occur in more affluent settings.

Cognitive outcomes and schooling

Ramadan during pregnancy is found to be negatively associated with cognitive outcomes among school-aged children (-3.10% of a standard deviation, 95% CI (-4.61 to -1.58)) (Supplementary Figure S3). Two studies on cognitive outcomes among children used standardized national tests in schools (Almond et al., 2015, Greve et al., 2017), while one study reports on items from IQ tests and measurements of children's numeric abilities in a household survey (Majid, 2015). Effects on school performance are reported on multiple school subject domains, including math, reading, writing and foreign language learning. Majid (2015) reports that children who were prenatally exposed also perform worse on items from general intelligence tests. Please note that meta-analytical results on cognitive outcomes should be interpreted with some caution as school-based measurements of cognitive performance (Almond et al., 2015, Greve et al., 2017) are being combined with test items to measure children's numerical abilities in a household survey (Majid, 2015).

For most outcomes, effects are mainly observed among children who had been exposed to Ramadan in early pregnancy. According to two studies that investigate heterogeneities, the effects are concentrated among those with the weakest cognitive performance (Majid et al., 2019), or those with the lowest socioeconomic status (Greve et al., 2017). The available evidence covers Muslim populations from the UK, Denmark and Indonesia.

Two studies used binary measures for actual school attendance in countries with very low schooling levels. Almond and Mazumder (2011) for Uganda find no effects on years of schooling, and some evidence for reduced illiteracy rates for early pregnancy exposure. In this regard, it should be noted that in low-income settings, the opportunity costs of schooling are high, since children often contribute to the household income, particularly in lower-income households. School enrolment status thus proxies for factors beyond cognitive ability in low-income contexts. Majid (2015) finds that in Indonesia, Muslim children whose time in utero overlapped with a Ramadan are more likely to be engaged in child labor.

At the same time, in other contexts, impaired physical health might even have positive effects on school enrolment due to decreased productivity of child labor among the physically impaired children (Almond and Mazumder, 2011). For example, during the time frame covered by this study (Almond and Mazumder, 2011), access to school was not universal in Uganda, with two thirds of children leaving school without completing the fifth grade, while primary education consists of seven years of schooling. Another particularity of the setting is that many children start school with a delay and the percentage of age-appropriate enrolled children is low (Kan and Klasen, 2021). Lee et al. (2020) for Ethiopia, where only about a quarter of children graduate primary school, neither find Ramadan during pregnancy to be associated with the current school enrolment status of a child nor with the probability of having graduated primary school. It remains unknown if Ramadan during pregnancy is associated with school attendance in settings with a higher share of students graduating primary school.

Other childhood health outcomes

Other childhood health outcomes were only investigated by Van Ewijk (2011), reporting associations between Ramadan during pregnancy and a decreased general health, as rated by nurses after taking various health measurements, among children. This study reports on Indonesia.

Effects of Ramadan during pregnancy on health in adulthood

General health

A broad range of adulthood outcomes has been studied. Some of these can be grouped into disabilities and human capital outcomes. All other outcomes are covered here under the header "general health". The studies concerned have in common that they used the same Indonesian data source. Van Ewijk (2011) reports on an overall measure of health compared to other of the same age and sex, as rated by nurses. Health among the prenatally exposed was found to be worse irrespective of the pregnancy phase of exposure, and effects were larger among adults aged 45+ (19% of a standard deviation) than among younger adults (5% of a standard deviation). Additionally, exposed individuals aged 50+ more often reported symptoms that are indicative of coronary heart problems or type 2 diabetes. Similarly, evidence of an increased prevalence of anemia was only detected among older individuals. Hypertension rates were not affected. Van Ewijk et al. (2013) report lower BMIs among those who were exposed in early pregnancy. Pradella and van Ewijk (2018) find an increased occurrence of breathing difficulties. This pattern increased in strength with age.

Disabilities

Two studies report on Ramadan during pregnancy and the risks of various types of disabilities in adulthood, using samples from Uganda, Iraq and Pakistan (Chaudhry, 2022). Meta-analytical results suggest that Ramadan during pregnancy is associated with an increased likelihood of hearing impairments (OR 1.26 (95% CI 1.09 to 1.45)), while no overall effect was found for sight impairments (OR 1.00 (95% CI 0.94 to 1.08)) (Supplementary Figure S3). Note that these results should be treated with some caution as the underlying variables may have been measured in different ways across studies and samples, as is suggested by the different base rates of hearing impairments (0.38% for Uganda, 0.02% for Iraq and 0.6% for Pakistan) (Almond and Mazumder, 2011, Chaudhry, 2022) .

Other outcomes could be synthesized only qualitatively, as each one had been analyzed in no more than two independent samples. Almond and Mazumder (2011) reported increased rates of mental/learning disabilities among those exposed in the first trimester in Uganda, and increased rates of psychological disabilities (which included mental/learning disabilities) for trimester 1 exposure in Iraq. These effects were especially pronounced if exposure occurred in the month of conception, with effect sizes of 0.25 and 0.23 percentage points against base rates of 0.14% and 0.36%, respectively. In contrast, Chaudhry (2022) finds no significant effects on memory impairments in Pakistan.

Finally, Almond and Mazumder (2011) find no effects on psychological disabilities (which exclude mental/learning disabilities) for Uganda, and for both Iraq and Uganda report increased likelihoods of “any disability” after exposure in the month of conception, with effect sizes of 0.8 and 0.3 percentage points against base rates of 3.8% and 1.5%, respectively.

Human capital

The available evidence consistently reports negative associations between Ramadan during pregnancy and human capital outcomes (Almond and Mazumder, 2011, Majid et al., 2019, Majid, 2015, Schultz-Nielsen et al., 2016). Majid (2015) reports that in Indonesia, the prenatally exposed are more likely to be employed in the informal sector, particularly when exposure occurred in early pregnancy. In many low-income settings, people working in the informal sector tend to be less educated, and informal sector jobs generally pay lower wages (Charmes, 2012).

Two studies report on employment likelihood in the formal sector in three settings which can only be compared with caution. In high-income countries such as Denmark, employment is an indicator of a high human capital. In contrast, in Iraq, which is a middle-income country with a large informal sector, formal sector employment is considered as an indicator of low socio-economic status. Schultz-Nielsen et al. (2016) finds that Ramadan exposure in late pregnancy is associated with a lower employment likelihood in Denmark. Almond and Mazumder (2011) find mixed evidence on employment rates in Iraq and Uganda. . A less equivocal measure of human capital is wealth accumulation. In both Iraq and Uganda, Almond and Mazumder (2011) find that prenatally exposed males tend to accumulate less wealth, as proxied by home ownership. In both countries, about 75% of males were home owners and this rate was about 1 to 2 percentage points lower among the exposed, dependent on the gestational month during which exposure occurred.

For Indonesia, Majid (2015) finds that Ramadan during pregnancy is associated with a lower number of weekly worked hours, mainly among those exposed in the earlier stages of pregnancy. For Denmark, Schultz-Nielsen et al. (2016) does not find effects on hours worked. These findings might again be attributable to the very different economic circumstances in the two countries on which these studies were conducted since hours worked are substantially higher in low-and-middle income countries (LMIC) (Bick et al., 2018). For Denmark, Schultz-Nielsen et al. (2016) report that those who were exposed in early pregnancy receive lower hourly wages, while Majid et al. (2019) do not report effects on monthly wages in Indonesia. In high-income countries, lower wages are more strongly associated with employees having a lower education than in LMIC, where the informal sector is larger and job opportunities as well as human capital accumulation opportunities are limited also for the better-educated (Pritadrajati et al., 2021).

Publication bias and sensitivity tests

As a sensitivity test, the studies that were at a high risk of bias were added to the meta-analyses. This was only possible for the outcomes birth weight, low birth weight and prematurity. For trimester 1 exposure, this analysis could only be conducted for birth weight as most high risk of bias studies did not report trimester-specific results. These were outcomes on which no significant effect had been found. Adding studies that were at a high risk of bias would not have changed this, and weighted average effect sizes would not have changed in a relevant way when adding these studies (Supplementary Figure S4, Supplementary Figure S5).

For the outcome birth weight, a funnel plot and an Egger's test showed no evidence for publication bias (P=0.12; Supplementary Figure S6). For other outcomes, no test on publication bias could be conducted since none had been included by more than seven studies.

The only outcome for which results from SRF and NE studies could be compared was birth weight. NE studies find neither effects for exposure irrespective of phase of pregnancy (5 studies, MD -0.84 grams (95% CI -13.98 to 12.30)), nor for trimester 1 exposure (MD -1-13 grams (95% CI -15.13 to 12.87)), see Supplementary Figure S7. But SRF studies on average do find significant negative effects for both irrespective of phase of pregnancy (4 studies, MD -93.52 grams (95% CI -182.57 to -4.47)), and for trimester 1 exposure (MD -221.07 grams (95% CI -431.55 to -10.58)).

Discussion

The current systematic review revealed that Ramadan during pregnancy is associated with multiple adverse health outcomes in adulthood as well as several worse outcomes in childhood. At the same time, the influence on neonatal health appears to be minimal or absent. At birth, there are few if any indications that the health of the prenatally exposed is worse. There is no overall evidence of effects on variables ranging from birth weight and gestational duration to perinatal mortality and APGAR. Only some evidence for a lower share of males at birth, which is hypothesized to be an indication of adverse prenatal conditions (Kraemer, 2000), is reported.

In childhood, effects become apparent across a range of outcomes. Mortality among children under 5 and infants who had been prenatally exposed is considerably increased. This finding was reported for settings in the Global South with high overall mortality rates, so that this result may not be generalizable to all parts of the world. What causes the increased mortality rates is not known. One hypothesis is that this may be due to a higher vulnerability to infections in these environments that are characterized by undernutrition and high infection rates (Schoeps et al., 2018). Fitting to this hypothesis is the result that height-for-age is on average lower, and stunting rates are higher among exposed children in various countries in the Global South. Height proxies for long-term undernutrition, and recurrent infections in childhood (such as episodes of diarrhea and respiratory disease) are a main risk factor for impaired height growth (Dewey and Mayers, 2011, Hedges et al., 2017, Salam et al., 2015, Stephensen, 1999). A lower-rated general health among exposed children in Indonesia fits to this pattern as well (Van Ewijk, 2011). Adverse effects at this age do not remain limited to developing countries. Evidence from studies on poorer and richer countries alike reported poorer performances on measures of cognitive and schooling performance, such as mathematics and language tests, after prenatal Ramadan exposure.

The pattern of adverse outcomes after prenatal exposure is clearest and widest in scope during adulthood. The exposed are reported to have worse general health conditions, higher risks of having disabilities including visual and auditory, as well as psychological ones. They more often suffer from breathing difficulties, anemia, and symptoms that may indicate diabetes 2 or coronary heart problems. Moreover, their human capital outcomes are worse as they tend to have worse employment situations (in poorer as well as richer countries) and (at least in two LMIC countries) are less likely to own homes. The worse performance in the educational system during childhood potentially co-drives the impaired labor market and economic outcomes among adults. However, these outcomes might also be driven by the impaired health outcomes of the prenatally exposed, respectively a combination of impairments along the health and education domains. The available evidence does not allow conclusions about the effect pathway. One study reports that the negative effects on labor market performance in adulthood are concentrated among those who work the fewest hours (Majid et al., 2019).

Interpretation of results in light of the fetal programming hypothesis

This pattern of results is in agreement with the long-known predictions of the fetal programming hypothesis: Prenatal exposures can have long-run adverse health effects, even though offspring health may be without pathological findings at birth (Almond and Currie, 2011, Gluckman et al., 2005, Godfrey and Barker, 2000, Metcalfe and Monaghan, 2001). While many studies have investigated exposures during pregnancy and their associations with offspring health, most focus on severe deprivations. By synthesizing the literature on Ramadan during pregnancy as a more subtle form of nutritional restriction during pregnancy, the findings of this review suggest that the predictions of the fetal programming theory also hold for more subtle prenatal shocks.

From a biological viewpoint, it has been documented that when a pregnant woman skips meals, her body enters a state of "accelerated starvation" while it begins to use stored fat as a source of energy instead of glucose (Metzger et al., 1982). Such shifts in metabolism already occur after skipping single meals (‘breakfast skipping’). Pregnant women who fast during Ramadan experience similar biochemical changes (Malhotra et al., 1989). Epigenetic research predicts that such prenatal exposures can trigger long-term structural adaptations. From an evolutionary standpoint, health consequences of these adaptations however often remain latent until the post-reproductive phase of life, a mechanism thought to support species survival (Bateson et al., 2004, Godfrey and Barker, 2000).

Since the initial research on the fetal origins hypothesis, empirical evidence has shown associations between prenatal shocks and chronic diseases that are prevalent among adults, often after mid-age (Godfrey and Barker, 2001). Our results corroborate this pattern of effects that become more visible as the prenatally exposed become older. Among adults, Ramadan during pregnancy was consistently found to be associated with worse outcomes, in particular among older age groups.

Our synthesis of the literature by the timing of the Ramadan-pregnancy overlap provided further insights into the underlying dynamics. While exposure to Ramadan at any stage of pregnancy appears to exert harmful health effects, long-term effects most consistently appear for exposure during the earliest stages of pregnancy. This is in accordance with medical theory: The prenatal period is characterized by critical growth phases of the embryo/fetus, which occur at different times and at different paces throughout gestation. Many critical growth phases are concentrated in early pregnancy, when rapid cell divisions contribute to the formation and genesis of body parts and organs, as well as neurological, cognitive, and metabolic functions (Gale et al., 2004, Mone et al., 2004, Sandman et al., 2011, Uylings, 2006). Additionally, gestation is a time window characterized by tissue plasticity, and marked by epigenetic adaptations. Cells are most prone to epigenetic adaptations in early gestation, and adverse prenatal circumstances are therefore thought to be particularly harmful if they occur during the early stages of gestation (Almond et al., 2018, Fleming et al., 2018, Langley-Evans, 2015, Tobi et al., 2015).

If the associations between Ramadan during pregnancy and long-term health outcomes are to a large extent driven by fetal programming and epigenetic alterations, then this might also explain why effects on birth weight are rarely found. Fetuses gain in weight especially fast during the final stages of pregnancy, whereas long-run effects tend to be most strongly linked to early pregnancy exposures. Alterations at the epigenetic level, as well as some disruptions to the early formational stages of specific organs such as the brain, are difficult to measure in newborns. While in many studies, birth weight is used as proxy for general health, its predictive power for adulthood health is limited (Almond and Currie, 2011, Belbasis et al., 2016). Consequently, considering longer-run outcomes in the assessment of pregnancy-related exposures seems particularly relevant in the context of more subtle prenatal exposures, in response to which birth weight effects might be less likely.

Strengths and limitations

The current systematic review should be interpreted considering a few limitations. First, the review was limited to published studies, potentially excluding additional research that remains unpublished. At the same time, no evidence for publication bias was detected. Second, while the total number of outcomes that has been studied is large, most of these outcomes have only been analyzed by one, or only a few studies. This heightened the challenge in synthesizing the evidence, meaning that only a relatively small portion of outcomes could be meta-analyzed. Future research on comparable outcomes is imperative to enhance the evidence base and allow for more conclusive data on the health effects in response to Ramadan during pregnancy, particularly concerning later-life outcomes. Definitions of outcomes across the life course should ideally be standardized for uniformity across studies. Third, the evidence on Ramadan during pregnancy stems from very diverse settings. For example, the included studies on child mortality mainly report on settings with high child mortality rates as well as a high infectious disease pressure, and effect patterns could be different non-LMIC settings. Moreover, Ramadan during pregnancy is an exposure that varies by cultural setting. Muslim communities differ in their cultures and traditions (Bulliet, 2003), including the practice of Ramadan (Alghafli et al., 2019, Beck, 2022, Possamai et al., 2022). This implies that context-specific knowledge is pivotal to the choice of an appropriate set of control variables in SRF studies. Also meals consumed at the breaking of the fast differ from region to region, ranging from foci on soups to an increased intake of sweets during non-fasting hours (Beck, 2022, Shatila et al., 2021). Similarly, dietary adjustment to Ramadan among pregnant women is highly context-specific (Pradella et al., 2023, Savitri et al., 2018, Seiermann et al., 2021).

Fourth, study designs were restricted. No RCTs are available on Ramadan during pregnancy due to the impossibility of randomizing pregnant women into fasting vs. non fasting groups. Sample sizes of many SRF studies were small. A substantial share of studies were classified as being at a high risk of confounding. The literature review and meta-analysis concentrated on the remaining studies. We could only compare the results from studies using different research designs for one outcome, birth weight. NE studies found no effect, while SRF studies found a statistically significant negative effect. One needs to be cautious in the interpretation of this difference in results. By construction, there is an underestimation in NE studies as they use an intention-to-treat design, while SRF studies may be subject to residual confounding. At the same time, other factors such as differences in study setting may also have played a role as only a handful of studies of either type could be compared. The results leave open the possibility (but provide no proof) that under certain circumstances, there may be effects of Ramadan observance on birth weight. This is something for future studies to address.

Despite these limitations, the current systematic review and meta-analysis has several notable strengths. First, this review includes all published studies (prior to 2 November 2023) fulfilling a priori defined criteria using a systematic and transparent search of the literature. Our search strategy for this was discussed with a medical librarian. Second, we did not limit the literature search to English, but included other languages that are commonly spoken in Muslim communities. Third, our protocol was pre-registered on PROSPERO and followed the guidelines published by Cochrane, including the use of the risk of bias assessment tool. Unlike previous reviews, we performed a rigorous test of risk of bias for each original study, using pre-defined study-design specific criteria. This approach makes our review the first to comprehensively integrate insights from both NE and SRF study designs that are prevalent in Ramadan pregnancy research. As such, it stands as the first review to encompass the entire body of literature on short- and long-term outcomes of Ramadan during pregnancy. Previous reviews did not assess the quality of the included studies (Noshili et al., 2022), or developed quality scores that provided only limited information regarding the risk of bias (Mahanani et al., 2021, Oosterwijk et al., 2021). Mahanani et al. (2021) only reviewed literature on long-term outcomes, while the review by Ong et al. (2023) and the meta-analysis by Glazier et al. (2018)

only covered literature on birth outcomes. The latter two studies excluded some of the studies with the highest sample sizes. We acknowledged the risk of bias assessment in the analyses, by setting apart studies with high risk of bias. In this way, the current review was able to provide a comprehensive overview while focusing on the results from those studies that were not at a high risk of bias. This approach still left us with studies from around the globe, that covered outcomes throughout the life course, and that together had sample sizes numbering in the millions.

Recommendations for future research

Islam, being the second-largest faith in the world, is practiced by populations that are diverse in their economic circumstances, composition of nutrition and religious customs. While this review showed that adverse effects of prenatal Ramadan exposure occur in populations around the globe, specific effects may differ considerably according to population characteristics. For example, increased child mortality rates were reported in Ethiopia and Burkina Faso (Lee et al., 2020, Schoeps et al., 2018), and reduced height growth has been reported in various LMIC. But this does not automatically imply that similar effects occur among richer populations that grow up in very different environments. It is possible that certain effects are more pronounced in populations with poorer nutritional and health conditions. Future research will need to answer the question whether this is the case. An increased body of evidence on Ramadan during pregnancy and offspring health covering Muslim populations across the globe, acknowledging diverse cultural and geographical backgrounds, will allow important insights into how the effects of Ramadan during pregnancy vary across settings.

Similarly, there is a dearth of research investigating whether daytime activity levels and nutritional patterns outside of the fasting hours may moderate the effects of prenatal Ramadan. If activity levels and nutritional intake are important effect moderators, this may mean that effects of Ramadan during pregnancy will differ between, as well as within countries. For instance, considerable variation exists in the types of meals consumed at Iftar (Beck, 2022, Shatila et al., 2021), while daytime life adapts to Ramadan much more in some countries than in others. Moreover, since fasting occurs from dawn to sunset, the duration of fasting varies substantially depending on the calendar month in which Ramadan fell and the region of the world. It is important to understand whether this leads to differences in how the health of the child is affected.

Knowledge on moderating factors is vital for pregnant women who wish to fast. It is possible that adverse effects on the child could be alleviated by adjusting the composition of nutrition outside of fasting hours or by enabling pregnant women to reduce their activity levels while fasting. To our knowledge, only one study has offered insights into this matter and this study found evidence suggesting that adverse effects on neonatal health are potentially reduced when pregnant women increase the intake of foods with high-fat contents during Ramadan (Pradella et al., 2023). Increasing the knowledge base on such effect moderators can provide important insights for recommendations for pregnant women wishing to fast during Ramadan.

To understand if nutrition while fasting also alleviates longer-term health consequences for the offspring, there is a need for longitudinal studies that track Muslim women and their offspring over time, beginning during pregnancy. Such studies should measure activity levels during Ramadan and incorporate food diaries to provide insights into the roles of specific (micro-)nutrients.

More generally speaking, from a methodological viewpoint, the risk of bias assessment (Supplementary Figure S1) revealed that future studies on Ramadan during pregnancy should aim to improve methodological practices. Priority should be given to the separation of Ramadan during pregnancy from confounders related to maternal background characteristics in SRF designs. The risk of bias assessment showed that 64% of all SRF studies did not fulfill this criterion and therefore had to be classified as being at high risk of bias. Since fasting during pregnancy is a choice – and therewith not random – a sufficient set of control variables must be included in any SRF study to allow conclusions on offspring health. The quality criteria provided here for NE and SRF study designs (Supplementary Table S2), in combination with

knowledge on local context, can be used to design and evaluate the quality of future studies on Ramadan during pregnancy, which are needed to fill the evidence gaps identified in this systematic review..
Lastly, studies on fasting rates among pregnant Muslims are encouraged particularly in regions of the world for which no data on this are yet available. This includes the entire continents of Africa and North America, as well as the Arabian peninsula.

Conclusions and implications for practice

Intermittent fasting is prevalent among pregnant women. Besides fasting for religious reasons which is common in many faiths (Trabelsi et al., 2022), also breakfast skipping and dieting are common practices during pregnancy (Loo et al., 2022, Mazumder and Seeskin, 2015, Pinho-Pompeu et al., 2020, Shiraishi et al., 2019). In this systematic review and meta-analysis, we found consistent evidence for associations between Ramadan intermittent fasting during pregnancy and long-term offspring adverse health outcomes, while neonatal health was shown to be unaffected.

This systematic review underlines that it is particularly relevant to bring together the evidence on short- and long-term effects in response to prenatal exposures. There seem to be no or only minor influences of Ramadan during pregnancy on birth outcomes, while the evidence on long-term effects suggests adverse effects along multiple health dimensions on outcomes in childhood, and adulthood. The absence of observable effects at birth thus does not justify concluding that intermittent fasting during pregnancy is safe for the offspring. This finding is in accordance with the predictions of the fetal programming hypothesis. A central aspect of the fetal programming hypothesis is that health effects can remain latent for a long time. This pattern of effects was also found for other prenatal exposures including more extreme prenatal nutritional deprivations such as famines (Lau et al., 2011, Lumey et al., 2011). From a practical viewpoint, this finding is pertinent to the design of recommendations for counselling. Health practitioners who are informed about the risks for long-term health outcomes even if health birth is not pathological can support patients in making informed decisions about Ramadan and other forms of intermittent fasting during pregnancy.

The synthesis of the available evidence suggests that the first pregnancy trimester is a particular critical and susceptible time window for several effects on offspring health. Health practitioners should consider pre-pregnancy counselling on intermittent fasting, as many pregnancies go unnoticed during the early stages (Young and Ramakrishnan, 2021). Moreover, given that Ramadan is a religious practice, it is important to recognize that many pregnant women may desire to fast for religious and cultural reasons. Further research is essential, focusing not only on evaluating the health effects of Ramadan during pregnancy, but also identifying potential effect moderators that can lead to comprehensive guidelines on Ramadan during pregnancy.

Data availability

This study is based on secondary aggregate data extracted from previously published studies; no primary data were collected specifically for this research. All data underpinning the findings of this article can be found within the tables and figures presented in the main text, the online supplementary material, and within the source references cited at the end of the article. The dataset used for the meta-analysis is available in the supplementary materials.

Acknowledgements

The authors thank Floyd van der Zee for his exceptional research assistance in the literature search and management process. Our appreciation extends to Dr. Sarah Al-Maawi and Asiye Balci for their thorough review of the manuscript and for providing essential guidance on cultural sensitivities pertinent to the Muslim perspective. We also acknowledge the valuable insights provided by medical librarian Lorena Cascant Ortolano (Medical University Library, Johannes-Gutenberg University Mainz) which ensured the quality of our search strategy. Last but not least, we thank Nicholas Kyei (Heidelberg University) for his time and expertise in setting up the search on EMBASE.

Authors‘ roles

F.P. and R.v.E. conceptualized the study and oversaw all aspects of conduct. F.P., R.v.E., and P.W. contributed to the design of the study. The management of the literature search, including the development of eligibility and risk of bias assessment criteria, was jointly handled by F.P. and R.v.E. R.v.E. and F.P. also supervised the systematic database search and data extraction for the qualitative literature review, which was executed by F.P. and P.W., with support from a research assistant. F.P. and R.v.E. were responsible for conducting the risk of bias assessment. P.W. was responsible for data extraction for the meta-analysis and also carried out the analysis. R.v.E. gave statistical advice. F.P. wrote the first version of the manuscript revised by R.v.E. with input from all authors. F.P. and R.v.E. were responsible for creating the tables and figures for the qualitative literature synthesis, including the risk of bias assessment. The figures for the meta-analysis were a collaborative effort between P.W., R.v.E and F.P. All authors were actively involved in interpreting the results, deciding to submit the manuscript, and approved the final version. The corresponding author confirms that all individuals who meet the authorship criteria are listed and no eligible authors have been omitted. All authors agree to be accountable for all aspects of the work.

Funding

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. We acknowledge the financial support from Johannes Gutenberg-University Mainz, Faculty of Law & Economics, which provided funds to support the authors during the study period and the preparation of the manuscript.

Conflict of interest

The authors hereby declare that there are no conflicts of interest regarding the content of this manuscript.

Figure 1. PRISMA 2020 flowchart for the selection of studies in a systematic review and meta-analysis of Ramadan during pregnancy and offspring health outcomes over the life course.

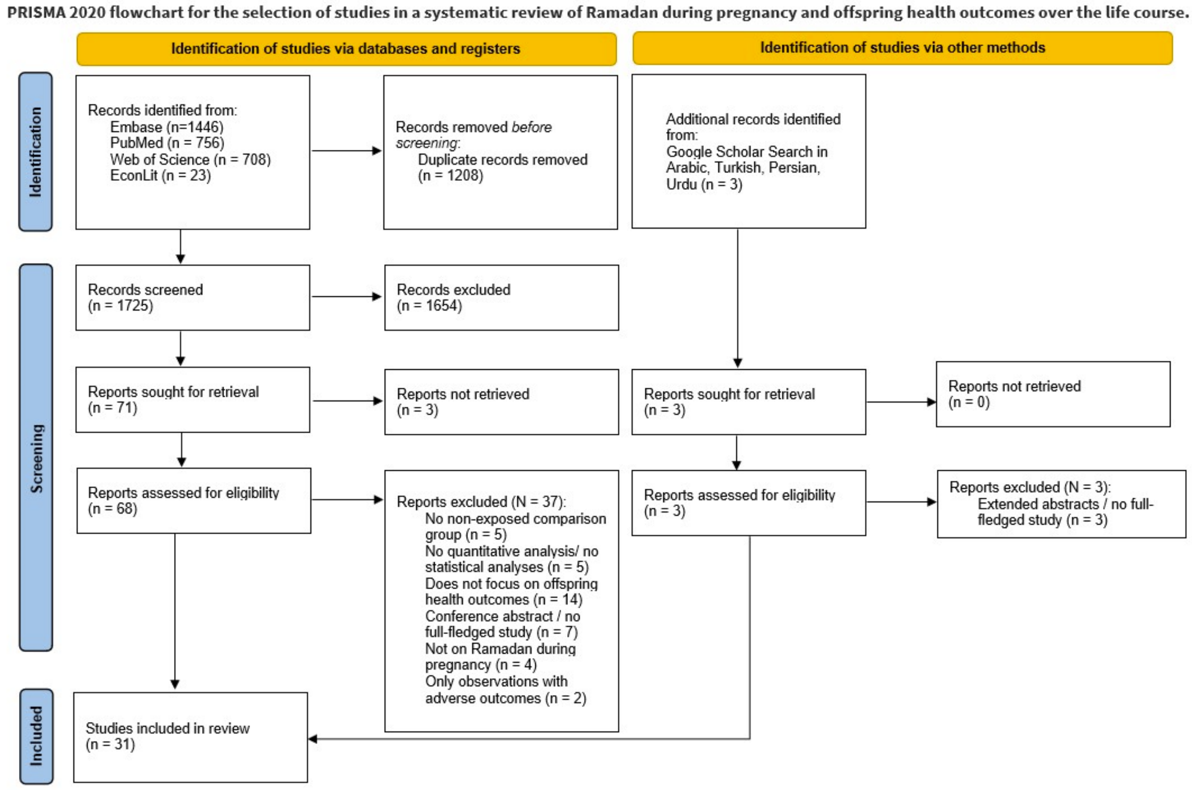


Figure 2. Meta-analytical results: Associations between prenatal exposure to Ramadan and offspring health outcomes, irrespective of pregnancy phase of exposure.

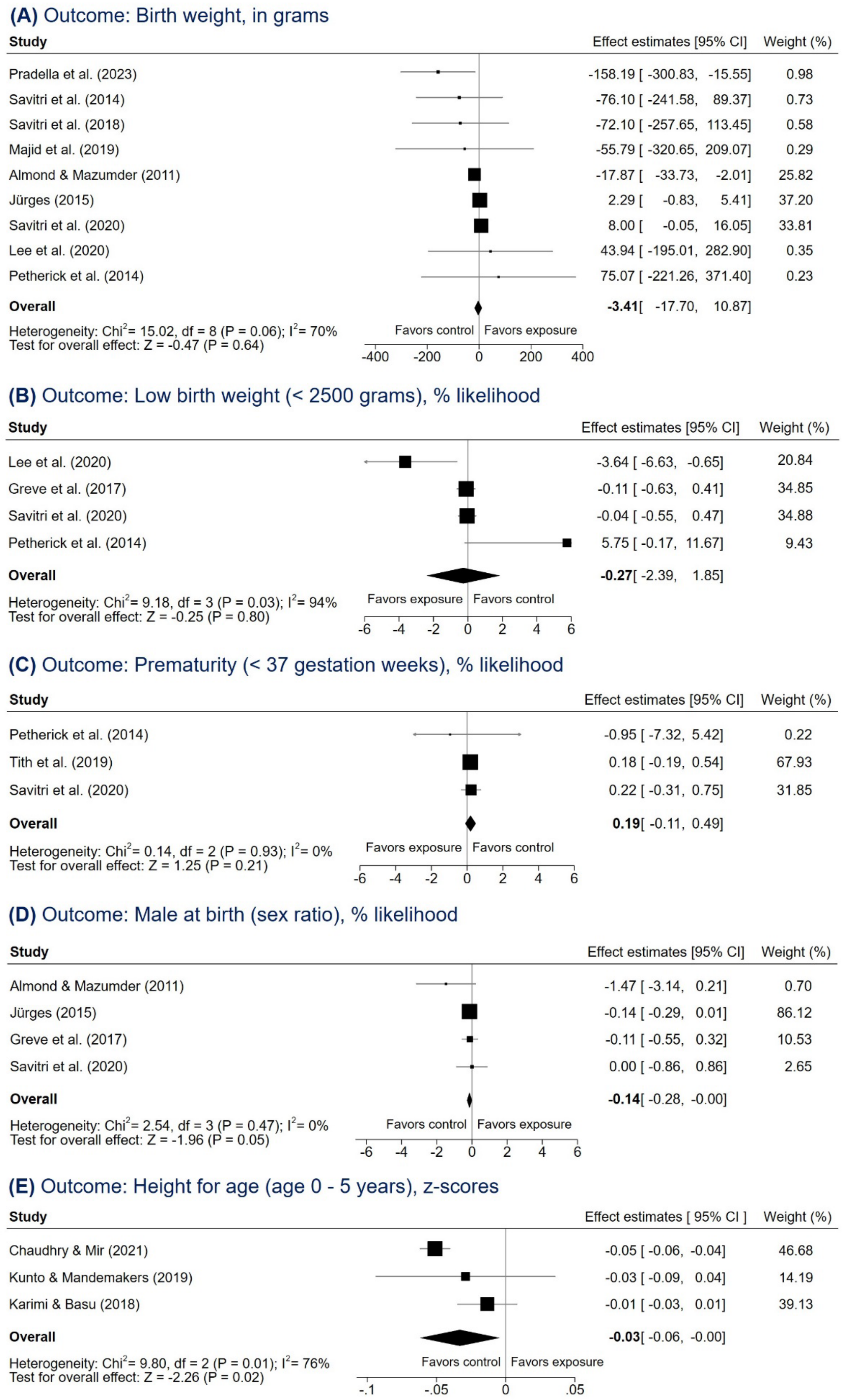


Table 1. Study characteristics and qualitative literature synthesis for associations between prenatal Ramadan exposure and offspring health outcomes at birth, in childhood, and in adulthood.

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
Neonatal health												
Anthropometrics	Birth weight	Almond & Mazumder (2011)	USA	Michigan Natality Microdata	1986-2006	>950 000	NE	↓*	↓*	↓*	↓	0
	Birth weight	*Awwad et al. (2012)*	*Lebanon*	*Medical centers in Beirut*	*2008*	*402*	*SRF*	↓*	*not reported*	*not reported*	*not reported*	**1**
	Birth weight	*Ghazal et al. (2020)*	*Lebanon*	*Private clinic in Beirut*	*2010-2019*	*502*	*SRF*	↑*	*not reported*	*not reported*	*not reported*	**1**
	Birth weight	*Hizli et al. (2012)*	*Turkey*	*Fatih University and Zekai Tahir Burak Hospitals*	*2010*	*110*	*SRF*	↑	*not reported*	*not reported*	*not reported*	**1**
	Birth weight	Jürges (2015)	Germany	German birth registers	1996-2010	>1 000 000	NE	↑	↑	↑	↑	0
	Birth weight	*Kavehmanesh & Abolghasemi (2004)*	*Iran*	*Najmieh and Baqiyatallah hospitals in Tehran*	*2000*	*539*	*SRF*	↑	*not reported*	*not reported*	*not reported*	**1**

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of association	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Birth weight	Lee et al. (2020)	Ethiopia	Demographic and Health Survey	1988-2003	>21 000	NE	*not reported*	↑	↑	↓	0
	Birth weight	Majid, Behrman & Mani (2019)	Indonesia	Indonesian Family Life Survey	1993	559 (females), 624 (males)	NE	↓ (males), ↔ (females)	not reported	not reported	not reported	0
	Birth weight	*Mirghani & Hamud (2006)*	*United Arab Emirates*	*Al-Ain Hospital, Al-Ain District*	*2002-2004*	*324*	*SRF*	↑	*not reported*	*not reported*	*not reported*	**1**
	Birth weight	Petherick, Tuffnell & Wright (2014)	United Kingdom	Born in Bradford Cohort Study	2010	310	SRF	↑	not reported	not reported	not reported	0
	Birth weight	Pradella et al. (2023)	Germany	Hospitals in Mainz	2017-2018	326	SRF	↓*	↓**	↓	↓	0
	Birth weight	Savitri et al. (2020)	Netherlands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↑	↑	↑	↑	0
	Birth weight	Savitri et al. (2018)	Indonesia	Budi Kamuliaan Hospital in Jakarta	2012-2014	139	SRF	↓	↓	↓	↓	0
	Birth weight	*Savitri et al. (2018)*	*Indonesia*	*Budi Kamuliaan Hospital in Jakarta*	*2012-2014*	*1351*	*NE*	↑	↑	↑	↑	**1**

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Birth weight	Savitri et al. (2014)	Nether-lands	Medical centers in Amsterdam and Zaanstad	2010	130	SRF	*not reported*	↓	↑	↑	0
	Low birth weight (<2500 g)	*Awwad et al. (2012)*	*Lebanon*	*Medical centers in Beirut*	*2008*	*402*	*SRF*	↑	*not reported*	*not reported*	*not reported*	**1**
	Low birth weight (<2500 g)	*Denizli et al. (2023)*	*Turkey*	*Ankara City Hospital*	*2021*	*92*	*SRF*	*not reported*	*not reported*	*not reported*	↓	**1**
	Low birth weight (<2500 g)	Greve, Schultz-Nielsen & Tekin (2017)	Denmark	Danish administrative registers	1985-1995	9268	NE	↔	↔	↔	↔	0
	Low birth weight (<2500 g)	Lee et al. (2020)	Ethiopia	Demographic and Health Survey	1988-2003	>21 000	NE	not reported	↓	↓	↓	0
	Low birth weight (<2500 g)	Petherick, Tuffnell & Wright (2014)	United Kingdom	Born in Bradford Cohort Study	2010	310	SRF	↑	not reported	not reported	not reported	0
	Low birth weight (<2500 g)	Savitri et al. (2020)	Nether-lands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↓	↓	↓	↓	0
	Low birth weight (<1500 g)	*Awwad et al. (2012)*	*Lebanon*	*Medical centers in Beirut*	*2008*	*402*	*SRF*	↔	*not reported*	*not reported*	*not reported*	**1**

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Small for gestational age (birth weight <10th percentile)	Savitri et al. (2020)	Netherlands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↓	↓	↓	↔	0
	Small for gestational age (birth weight <10th percentile)	*Awwad et al. (2012)*	*Lebanon*	*Medical centers in Beirut*	*2008*	*402*	*SRF*	↓	*not reported*	*not reported*	*not reported*	**1**
	Size at birth below average	Lee et al. (2020)	Ethiopia	Demographic and Health Survey	1988-2003	>21 000	NE	*not reported*	↑	↓	↑	0
Gestational duration	*Gestational age*	*Denizli et al. (2023)*	*Turkey*	*Ankara City Hospital*	*2021*	*92*	*SRF*	*not reported*	*not reported*	*not reported*	↓	**1**
	Gestational age	*Hizli et al. (2012)*	*Turkey*	*Fatih University and Zekai Tahir Burak Hospitals*	*2010*	*110*	*SRF*	↑	*not reported*	*not reported*	*not reported*	**1**
	Gestational age	*Mirghani & Hamud (2006)*	*United Arab Emirates*	*Al-Ain Hospital, Al-Ain District*	*2002-2004*	*324*	*SRF*	↑	*not reported*	*not reported*	*not reported*	**1**
	Gestational age	Pradella et al. (2023)	Germany	Hospitals in Mainz	2017-2018	326	SRF	↔	↓	↑	↑	0
	Gestational age	Savitri et al. (2020)	Netherlands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↑	↑	↓	↔	0

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Prematurity (<37 wk)	*Awwad et al. (2012)*	*Lebanon*	*Medical centers in Beirut*	*2008*	*402*	*SRF*	↔	*not reported*	*not reported*	*not reported*	**1**
	Prematurity (<37 wk)	*Denizli et al. (2023)*	*Turkey*	*Ankara City Hospital*	*2021*	*92*	*SRF*	*not reported*	*not reported*	*not reported*	↓	**1**
	Prematurity (<37 wk)	Petherick, Tuffnell & Wright (2014)	United Kingdom	Born in Bradford Cohort Study	2010	310	SRF	↓	not reported	not reported	not reported	0
	Prematurity (<37 wk)	Savitri et al. (2020)	Netherlands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↑	↑	↑	↑	0
	Prematurity (<37 wk)	Tith et al. (2019)	Canada	Birth registry of Quebec	1981-2017	>78 000	NE	not reported	↔	↑	not reported	0
	Prematurity (<32 wk)	*Awwad et al. (2012)*	*Lebanon*	*Medical centers in Beirut*	*2008*	*402*	*SRF*	↑	*not reported*	*not reported*	*not reported*	**1**
Sex ratio	Share of male births	Almond & Mazumder (2011)	USA	Michigan Natality Microdata	1986-2006	>950 000	NE	↓	↓*	↓	↓	0
	Share of male births	Greve, Schultz-Nielsen & Tekin (2017)	Denmark	Danish administrative registers	1985-1995	9268	NE	not reported	↔	↓	↔	0
	Share of male births	Jürges (2015)	Germany	German birth registers	1996-2010	>1 000 000	NE	not reported	↔	↓	↓	0

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of association	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Share of male births	Savitri et al. (2020)	Nether-lands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↔	↑	↑	↑	0
	Probability of male respondent	Van Ewijk (2011)	Indonesia	Indonesian Family Life Survey	2000	>23 000	NE	↓**	↓*	↓*	↓	0
Mortality	Death <1 day	Lee et al. (2020)	Ethiopia	Demographic and Health Survey	1988-2003	>21 000	NE	*not reported*	↔	↔	↔	0
	Death <7 days	*Mirghani & Hamud (2006)*	*United Arab Emirates*	*Al-Ain Hospital, Al-Ain District*	*2002-2004*	*324*	*SRF*	↔	*not reported*	*not reported*	*not reported*	**1**
	Death <7 days	Savitri et al. (2020)	Nether-lands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↓	↓	↓	↓	0
	Death <3 months	Lee et al. (2020)	Ethiopia	Demographic and Health Survey	1988-2003	>21 000	NE	not reported	↑*	↔	↔	0
Newborn health monitoring	Apgar score <7	Savitri et al. (2020)	Nether-lands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↑	↑	↓	↔	0
	Apgar at 1 min	*Denizli et al. (2023)*	*Turkey*	*Ankara City Hospital*	*2021*	*92*	*SRF*	*not reported*	*not reported*	*not reported*	↔	**1**

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of association	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Apgar at 1 min	*Mirghani & Hamud (2006)*	*United Arab Emirates*	*Al-Ain Hospital, Al-Ain District*	*2002-2004*	*324*	*SRF*	↔	*not reported*	*not reported*	*not reported*	**1**
	Apgar at 5 min	*Denizli et al. (2023)*	*Turkey*	*Ankara City Hospital*	*2021*	*92*	*SRF*	*not reported*	*not reported*	*not reported*	↔	**1**
	Apgar at 5 min	*Mirghani & Hamud (2006)*	*United Arab Emirates*	*Al-Ain Hospital, Al-Ain District*	*2002-2004*	*324*	*SRF*	↔	*not reported*	*not reported*	*not reported*	**1**
	Congenital anomalies	Savitri et al. (2020)	Nether-lands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↑	↑	↑	↑	0
	Severe congenital anomalies	Savitri et al. (2020)	Nether-lands	Perinatal Registry of the Netherlands	2000-2010	>1 600 000	NE	↑*	↑	↑	↑*	0
	Caesarian delivery	*Awwad et al. (2012)*	*Lebanon*	*Medical centers in Beirut*	*2008*	*402*	*SRF*	↓*	*not reported*	*not reported*	*not reported*	**1**
	Caesarian delivery	*Azizi et al. (2004)*	*Iran*	*Islamic Schools in Iran*	*2001*	*191*	*SRF*	↓*	*not reported*	*not reported*	*not reported*	**1**
	Caesarian delivery	*Hizli et al. (2012)*	*Turkey*	*Fatih University and Zekai Tahir Burak Hospitals*	*2010*	*110*	*SRF*	↔	*not reported*	*not reported*	*not reported*	**1**

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of association	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Admission to NICU	*Denizli et al. (2023)*	*Turkey*	*Ankara City Hospital*	*2021*	*92*	*SRF*	*not reported*	*not reported*	*not reported*	↔	**1**
	Admission to NICU	*Hizli et al. (2012)*	*Turkey*	*Fatih University and Zekai Tahir Burak Hospitals*	*2010*	*110*	*SRF*	↑	*not reported*	*not reported*	*not reported*	**1**
	Admission to NICU	*Mirghani & Hamud (2006)*	*United Arab Emirates*	*Al-Ain Hospital, Al-Ain District*	*2002-2004*	*324*	*SRF*	↑**	*not reported*	*not reported*	*not reported*	**1**
Childhood												
Anthropometrics height-for-age	<5 years, z-scores	Chaudhry & Mir (2021)	Pakistan	Multiple Indicator Cluster Survey	2007-2018	>170 000	NE	↓*	↓**	↓**	↔	0
	<5 years, z-scores	Karimi & Basu (2018)	37 countries	Demographic and Health Survey	1994-2014	>300 000	NE	↓ (boys) ↔ (girls)	↓** (boys) ↔ (girls)	↓** (boys) ↔ (girls)	↓ (boys) ↔ (girls)	0
	<5 years, z-scores	Kunto & Mandemakers (2019)	Indonesia	Indonesian Family Life Survey	1993-2015	>21 000	NE	↔	↑	↑	↓	0
	<5 years, non-standardized	Lee et al. (2020)	Ethiopia	Demographic and Health Survey	1988-2003	>21 000	NE	↓	↓	↓	↓*	0

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	<5 years, stunting	Chaudhry & Mir (2021)	Pakistan	Multiple Indicator Cluster Survey	2007-2018	>170 000	NE	↑*	↑**	↑**	↔	0
	<5 years, stunting	*Chu, Goli & Rammohan (2023)*	*56 countries*	*Demographic and Health Survey*	*2003-2020*	*>900 000*	*NE*	↓**	↔	↓*	↓**	**1**
	5-9 years, z-scores	Kunto & Mandemakers (2019)	Indonesia	Indonesian Family Life Survey	1993-2015	>21 000	NE	↓	↓	↑	↓	0
	3-14 years, z-scores	*Azizi et al. (2004)*	*Iran*	*Islamic Schools in Iran*	*2001*	*191*	*SRF*	↔	*not reported*	*not reported*	*not reported*	**1**
	10-14 years, z-scores	Kunto & Mandemakers (2019)	Indonesia	Indonesian Family Life Survey	1993-2015	>21 000	NE	↓	↓	↓	↓	0
	<18 years, z-scores	Karimi, Little & Mokhtari (2021)	Iran	Urban Health Equity and Assessment Response Tool Survey, Tehran	2011	4931	NE	↓	↔	↓*	↔	0
	15-18 years, z-scores	Kunto & Mandemakers (2019)	Indonesia	Indonesian Family Life Survey	1993-2015	>21 000	NE	↓	↓*	↓	↓	0

Outcome domain	Outcome measure	Author (Year)	Locatio n	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Final attained height, unstandardized	Van Ewijk, Painter & Roseboom (2013)	Indonesia	Indonesian Family Life Survey	2000	>12 000	NE	↓	↓**	↓	↓	0
Anthropometrics weight-for-age	<5 years, z-scores	Kunto & Mandemakers (2019)	Indonesia	Indonesian Family Life Survey	1993-2015	>21 000	NE	↑	↑	↑	↑	0
	5-9 years, z-scores	Kunto & Mandemakers (2019)	Indonesia	Indonesian Family Life Survey	1993-2015	>21 000	NE	↓	↓	↑	↓	0
	3-14 years, z-scores	*Azizi et al. (2004)*	*Iran*	*Islamic Schools in Iran*	*2001*	*191*	*SRF*	↓	*not reported*	*not reported*	*not reported*	**1**
	10-14 years, z-scores (BMI)	Kunto & Mandemakers (2019)	Indonesia	Indonesian Family Life Survey	1993-2015	>21 000	NE	↓	↓	↑	↓	0
	15-18 years, z-scores (BMI)	Kunto & Mandemakers (2019)	Indonesia	Indonesian Family Life Survey	1993-2015	>21 000	NE	↑	↑	↑	↑	0
	<5 years, underweight (<5th percentile of same age and sex)	Lee et al. (2020)	Ethiopia	Demographic and Health Survey	1988-2003	>21 000	NE	not reported	↔	↔	↔	0
	<5 years, underweight (z-score <-2)	Chaudhry & Mir (2021)	Pakistan	Multiple Indicator Cluster Survey	2007-2018	>170 000	NE	↑*	↑**	↑**	↔	0

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	<5 years, underweight	*Chu, Goli & Rammohan (2023)*	*56 countries*	*Demographic and Health Survey*	*2003-2020*	*>900 000*	*NE*	↓*	↔	↔	↓*	**1**
Mortality	Death <1 year	Lee et al. (2020)	Ethiopia	Demographic and Health Survey	1988-2003	>21 000	NE	*not reported*	↑*	↔	↔	0
	Death <5 years	Schoeps et al. (2018)	Burkina Faso	Nouna Health and Demographic Surveillance System		>41 000	NE	↑	↑*	↑	↔	0
General health		Van Ewijk (2011)	Indonesia	Indonesian Family Life Survey	2000	9343	NE	↓*	↓*	↓*	↓	0
Cognitive outcomes and schooling	IQ (items from Raven's CPM)	Majid (2015)	Indonesia	Indonesian Family Life Survey	1993 - 2008	3521	NE	↓**	↓	↑	↓	0
	IQ (full-scale)	*Azizi et al. (2004)*	*Iran*	*Islamic Schools in Iran*	*2001*	*191*	*SRF*	↔	*not reported*	*not reported*	*not reported*	**1**
	Math test performance	Almond, Mazumder & Van Ewijk (2015)	England	Pupil Level Annual School Census (PLASC)	1998-2007	>4 600 000	NE	↓	↓*	↓	↓	0

Outcome domain	Outcome measure	Author (Year)	Locatio n	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Math test performance	Greve, Schultz-Nielsen & Tekin (2017)	Denmark	Danish administ-rative registers	1985-1995	9268	NE	not reported	↑	↑	↔	0
	Math (numeracy)	Majid (2015)	Indonesia	Indonesian Family Life Survey	1993 - 2008	3521	NE	↓**	↓	↓*	↓	0
	Reading test performance	Almond, Mazumder & Van Ewijk (2015)	England	Pupil Level Annual School Census (PLASC)	1998-2007	>4 600 000	NE	↓	↓*	↓	↓	0
	Writing test performance	Almond, Mazumder & Van Ewijk (2015)	England	Pupil Level Annual School Census (PLASC)	1998-2007	>4 600 000	NE	↓	↓*	↓	↓	0
	Danish (native language) test performance	Greve, Schultz-Nielsen & Tekin (2017)	Denmark	Danish administ-rative registers	1985-1995	9268	NE	not reported	↓* (girls) ↑* (boys)	↓ (girls) ↑ (boys)	↓* (girls) ↓* (boys)	0
	English (foreign language) test performance	Greve, Schultz-Nielsen & Tekin (2017)	Denmark	Danish administ-rative registers	1985-1995	9268	NE	not reported	↓* (girls) ↔ (boys)	↓* (girls) ↔ (boys)	↓ (girls) ↔ (boys)	0
	Science test performance	Greve, Schultz-Nielsen & Tekin (2017)	Denmark	Danish administ-	1985-1995	9268	NE	not reported	↓ (girls) ↑ (boys)	↓ (girls) ↔ (boys)	↓ (girls) ↔ (boys)	0

Outcome domain	Outcome measure	Author (Year)	Locatio n	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
				rative registers								
	Enrolled in school, 7-11 year-olds	Lee et al. (2020)	Ethiopia	Demographi c and Health Survey	1988-2003	>21 000	NE	not reported	↑	↑	↑	0
	Graduated primary school	Lee et al. (2020)	Ethiopia	Demographi c and Health Survey	1988-2003	>21 000	NE	not reported	↑	↑	↑	0
	No schooling	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↔	↔	↔	0
	Years of schooling	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↔	↔	↔	0
	Illiteracy	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↑	↔	↔	0
	Child labor	Majid (2015)	Indonesia	Indonesian Family Life Survey	1993 - 2008	2036	NE	↑**	↑	↔	↑	0
Adulthood												
General health	Impaired general health	Van Ewijk (2011)	Indonesia	Indonesian Family Life Survey	2000	>23 000	NE	↑**	↑*	↑*	↑*	0
	Anthropometrics / BMI	Van Ewijk, Painter & Roseboom (2013)	Indonesia	Indonesian Family Life Survey	2000	>12 000	NE	↓*	↓*	↓**	↓**	0

Outcome domain	Outcome measure	Author (Year)	Locatio n	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Anthropometrics / Weight	Van Ewijk, Painter & Roseboom (2013)	Indonesia	Indonesian Family Life Survey	2000	>12 000	NE	↓*	↓*	↓*	↓*	0
	Breathing difficulties	Pradella & Van Ewijk (2018)	Indonesia	Indonesian Family Life Survey	1997-2008	>28 000	NE	↑*	↑*	↑	↑*	0
	Anemia among >45 year-olds	Van Ewijk (2011)	Indonesia	Indonesian Family Life Survey	2000	>23 000	NE	↑	↑	↑*	↔	0
	Chest pain as a symptom of coronary heart problems, >50 year-olds	Van Ewijk (2011)	Indonesia	Indonesian Family Life Survey	2000	>23 000	NE	↑*	↑	↑*	↑	0
	Time to wound healing as a symptom of diabetes 2, >50 year-olds	Van Ewijk (2011)	Indonesia	Indonesian Family Life Survey	2000	>23 000	NE	↑**	↑	↑**	↑**	0
	High blood pressure	Van Ewijk (2011)	Indonesia	Indonesian Family Life Survey	2000	>23 000	NE	↔	↔	↔	↔	0
	Pulse pressure among ≤45 year olds	Van Ewijk (2011)	Indonesia	Indonesian Family Life Survey	2000	>23 000	NE	↑	↑**	↑**	↑	0
Disabilities	Any Disability	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↑*	↑	↔	0

Outcome domain	Outcome measure	Author (Year)	Locatio n	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Any Disability	Almond & Mazumder (2011)	Iraq	Iraqi Census	1997	>250 000	NE	not reported	↑*	↑	↑	0
	Sight impairment/ Blindness	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000;	NE	not reported	↔	↔	↔	0
	Sight impairment/ Blindness	Almond & Mazumder (2011)	Iraq	Iraqi Census	1997	>250 000	NE	not reported	↔	↑*	↔	0
	Sight impairment/ Blindness	Chaudhry (2022)	Pakistan	Multiple Indicator Cluster Survey	2017-2019	>270 000	NE	not reported	↔	↔	↔	0
	Hearing impairment/ Deafness	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↑*	↑	↑	0
	Hearing impairment/ Deafness	Almond & Mazumder (2011)	Iraq	Iraqi Census	1997	>250 000	NE	not reported	↔	↔	↔	0
	Hearing impairment/ Deafness	Chaudhry (2022)	Pakistan	Multiple Indicator Cluster Survey	2017-2019	>270 000	NE	not reported	↑(* for males)	↔	↔	0
	Mental/Learning disability	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↑**	↑	↑*	0

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of asso-ciation	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Memory impairments	Chaudhry (2022)	Pakistan	Multiple Indicator Cluster Survey	2017-2019	>270 000	NE	not reported	↔	↔	↔	0
	Psychological disability (incl. mental/learning)	Almond & Mazumder (2011)	Iraq	Iraqi Census	1997	>250 000	NE	not reported	↑**	↑	↔	0
	Psychological disability	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↓	↓	↓	0
Human capital	Formal sector employment (signal for low SES in the context)	Almond & Mazumder (2011)	Iraq	Iraqi Census	1997	>250 000	NE	not reported	↑*	↑*	↓*	0
	Employment (not further defined)	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↓	↓*	↔	0
	Formal sector employment (signal for high SES in the context)	Schultz-Nielsen, Tekin & Greve (2016)	Denmark	Register-based Labor Force Statistics	2008	<25 000	NE	↔	↔	↔	↓*	0
	Employment in informal sector (proxy for low SES in the context)	Majid (2015)	Indonesia	Indonesian Family Life Survey	1993 - 2008	7780	NE	↑*	↑*	↑	↑	0
	Hours worked	Majid (2015)	Indonesia	Indonesian Family Life Survey	1993 - 2008	7780	NE	↓*	↓*	↓*	↓	0

Outcome domain	Outcome measure	Author (Year)	Location	Data source	Study period	Sample size	Study design	Overall direction of association	Trimester-specific effect concentrations			High risk of bias
									First trimester	Second trimester	Third trimester	
	Hours worked	Schultz-Nielsen, Tekin & Greve (2016)	Denmark	Register-based Labor Force Statistics	2008	<25 000	NE	↔	↑	↔	↓	0
	Income / monthly	Majid, Behrman & Mani (2019)	Indonesia	Indonesian Family Life Survey	1993 - 2008	6438	NE	↔	not reported			0
	Income / hourly wage	Schultz-Nielsen, Tekin & Greve (2016)	Denmark	Register-based Labor Force Statistics	2008	<25 000	NE	↔	↓*	↔	↔	0
	Income / annual	Schultz-Nielsen, Tekin & Greve (2016)	Denmark	Register-based Labor Force Statistics	2008	<25 000	NE	not reported	↔	↔	↔	0
	Wealth / Home ownership	Almond & Mazumder (2011)	Iraq	Iraqi Census	1997	>250 000	NE	not reported	↓**	↓**	↓**	0
	Wealth / Home ownership	Almond & Mazumder (2011)	Uganda	Ugandan Census	2002	>80 000	NE	not reported	↓*	↔	↔	0

↑ Increase (in case of binary outcome measures: increased risk); ↓ Decrease (in case of binary outcome measures: decreased risk); ↔ No effects detected / no clear direction.

* P-value <0.05

** P-value <0.01

Note that all arrows that are not accompanied by asterisks show effect directions that were not statistically significant and should be interpreted with caution.

Bias: 1 = high risk of bias, 0 = no high risk of bias. Studies identified as high risk of bias are additionally marked in *italics* for clarity.

SRF, self-reported fasting design

NE, natural experiment design

wk, gestational week

NICU, neonatal intensive care unit

IQ, intelligence quotient

Raven's CPM, Raven's Coloured Progressive Matrices

Supplementary Table S1: Electronic search strategy using PubMed®, EMBASE®, EconLit® and Web of Science® online facilities.

Filters: from inception

PubMed® search

(((pregnan*[Title/Abstract]) OR (in utero[Title/Abstract]) OR (gestation*[Title/Abstract])) AND (Ramadan[Title/Abstract])) OR (((pregnan*[Title/Abstract]) OR (in utero[Title/Abstract]) OR (gestation*[Title/Abstract])) AND ((Muslim[Title/Abstract]) OR (Islam*[Title/Abstract])))

EMBASE® search

(((pregnan*[.ti,ab,kf.]) OR (in utero[.ti,ab,kf.]) OR (gestation*[.ti,ab,kf.])) AND (Rama*[.ti,ab,kf.])) OR (((pregnan*[.ti,ab,kf.]) OR (in utero[.ti,ab,kf.]) OR (gestation*[.ti,ab,kf.])) AND ((Muslim[.ti,ab,kf.]) OR (Islam*[.ti,ab,kf.])))

EconLit ® search

((AB pregnan* OR AB in utero OR AB gestation*) AND (AB Ramadan)) OR ((TI pregnan* OR TI in utero OR TI gestation*) AND (TI Ramadan)) OR ((AB pregnan* OR AB in utero OR AB gestation*) AND (AB Muslim OR AB Islam*)) OR ((TI pregnan* OR TI in utero OR TI gestation*) AND (TI Muslim OR TI Islam*))

Web of Science® search

((AB = pregnan* OR AB = in utero OR AB = gestation*) AND (AB = Ramadan)) OR ((TI = pregnan* OR TI = in utero OR TI = gestation*) AND (TI = Ramadan)) OR ((KP = pregnan* OR KP = in utero OR KP = gestation*) AND (KP = Ramadan)) OR ((AB = pregnan* OR AB = in utero OR AB = gestation*) AND (AB = Muslim OR AB = Islam*)) OR ((TI = pregnan* OR TI = in utero OR TI = gestation*) AND (TI = Muslim OR TI = Islam*)) OR ((KP = pregnan* OR KP = in utero OR KP = gestation*) AND (KP = Muslim OR KP = Islam*))

Supplementary Table S2. Risk of bias assessment domains based on which all included studies were evaluated for risk of bias.

Natural Experiment (NE) Study Design *NE studies compare Muslims whose time in utero did vs did not overlap with a Ramadan as exposed in an intention-to-treat design*					
Risk of bias: Domain number	**Rationale**	**Implementation requirement**	**Justification**	**Minimum criterion**	**Additional quality measure**
1	Avoiding bias due to confounding by separation of Ramadan during pregnancy from month/season of birth effects	Controlling for month of birth	Ramadan progresses through the Gregorian calendar in 33-year cycles because the Islamic lunar calendar is approximately 11 days shorter than the Gregorian calendar. Regressions that adjust for month of birth enable the separation of the effects associated with the season of birth from those specifically attributable to Ramadan during pregnancy.	X	
2	Avoiding bias due to confounding by separation of Ramadan during pregnancy from month/season of birth effects	Birth years cover at least 15 years	To adequately implement D1, the birth years of the study participants must encompass a significant portion of the 33-year cycle	X	
3	Avoiding bias due to	Difference-in-differences analysis	If the sample encompasses only a limited range of birth cohorts, a difference-in-differences analysis is required. This involves adjusting for the season of birth	X	

	confounding by separation of Ramadan during pregnancy from month/season of birth effects		patterns observed in Non-Muslims by subtracting these from the corresponding patterns in their Muslim counterparts, thereby isolating the effect of Ramadan. *(D3 is deemed satisfied if D1* ***and*** *D2 are met)*		
4	Precision of the effect estimate	Exposure calculated based on exact date of birth	Estimates of the effects are more accurate when exposure is determined using the exact birth dates of study participants. Ramadan spans only 29-30 days, and the specific exposure of interest is the overlap between Ramadan and pregnancy. Reliance on the broader month of birth to ascertain exposure introduces a greater attenuation bias by adding noise to the exposure variable. D4 Is considered an extra quality metric, acknowledging that while using month of birth data for exposure calculation is less precise, it does not invalidate results.		X
5	Ensuring the stability of research findings	Sensitivity checks	Sensitivity checks include placebo tests on Non-Muslim samples and balancing tests to assess the quasi-randomness of Ramadan during pregnancy. Note that the ITT approach relies on the assumption that the occurrence of Ramadan during pregnancies is quasi-random, meaning that it is not systematically related to parental characteristics. Several studies from different settings have shown in balancing tests that pregnancy overlap with Ramadan is not correlated with parental characteristics such as education, income, or maternal smoking behavior in various Muslim populations, so that selective fertility does not seem to play a role. Placebo tests: If the occurrence of a Ramadan during pregnancy is correlated with health outcomes in Non-Muslims, this would raise worries that Ramadan-health associations in Muslims, too, are driven by residual confounding. Multiple studies have shown that no associations between Ramadan-during-pregnancy and health occur among Non-Muslims. Since various studies have shown that balancing tests and placebo tests hold in various settings, it is not deemed necessary for each individual study to		X

			demonstrate the same. Doing so was therefore not included among the set of minimum quality criteria, but was recorded as an additional indicator of a study's quality.		
Self-Reported Fasting (SRF) Study Design *SRF studies compare offspring born to fasting vs non-fasting mothers, based on self-reported fasting behavior*					
Risk of bias: Domain number	**Rationale**	**Implementation requirement**	**Justification**	**Minimum criterion**	**Additional quality measure**
1	Avoiding confounding by correlated maternal background characteristics	Statistical comparison of fasting vs non-fasting women for differences in pre-pregnancy characteristics	Inferential statistics used to determine significant differences between two groups allow insights into the comparability of two groups. Studies should investigate whether fasting and non-fasting women differ in their pre-pregnancy characteristics and subsequently adjust for covariates.	X	
2	Avoiding confounding by correlated maternal background characteristics	Adjusting for covariates/matching	Confounders must be controlled for in order to separate the effect of maternal Ramadan fasting from correlated maternal background characteristics such as education, immigration or the living environment, which might both influence the maternal decision (not) to fast during Ramadan as well as her offspring's health outcomes. As an alternative for regression-based adjusting for covariates, matching on background characteristics can be used.	X	

3	Avoiding confounding by correlated maternal background characteristics	Adequate adjusting for covariates/matching	Adjusting is considered to be inadequate if not more than 3 pre-pregnancy characteristics are included.	X	
4	Ensuring data accuracy and validity	Reliable recall period	Accurate detection of fasting effects depends on mothers reliably reporting their Ramadan fasting practices, which is less likely in studies conducted long after the pregnancy in question.	X	
5	Ensuring the stability of research findings	Sensitivity checks	Studies were evaluated to determine if they conducted formal statistical tests for residual confounding or tested result robustness, such as through alternative statistical models. This mainly concerns a detailed examination of the included covariates, and the extent to which these are able to address the risk of confounding, and was therefore not set as a minimum quality criterion.		X

This table provides details on the risk of bias assessment domains that were developed for assessment of each individual study included in the systematic literature review. Studies that do not meet the minimum criteria for classification as low risk of bias are classified as being at high risk of bias.

Supplementary Figure S1. Domain-levels judgement for each individual study and of the distribution of risk-of-bias judgements within each bias domain.

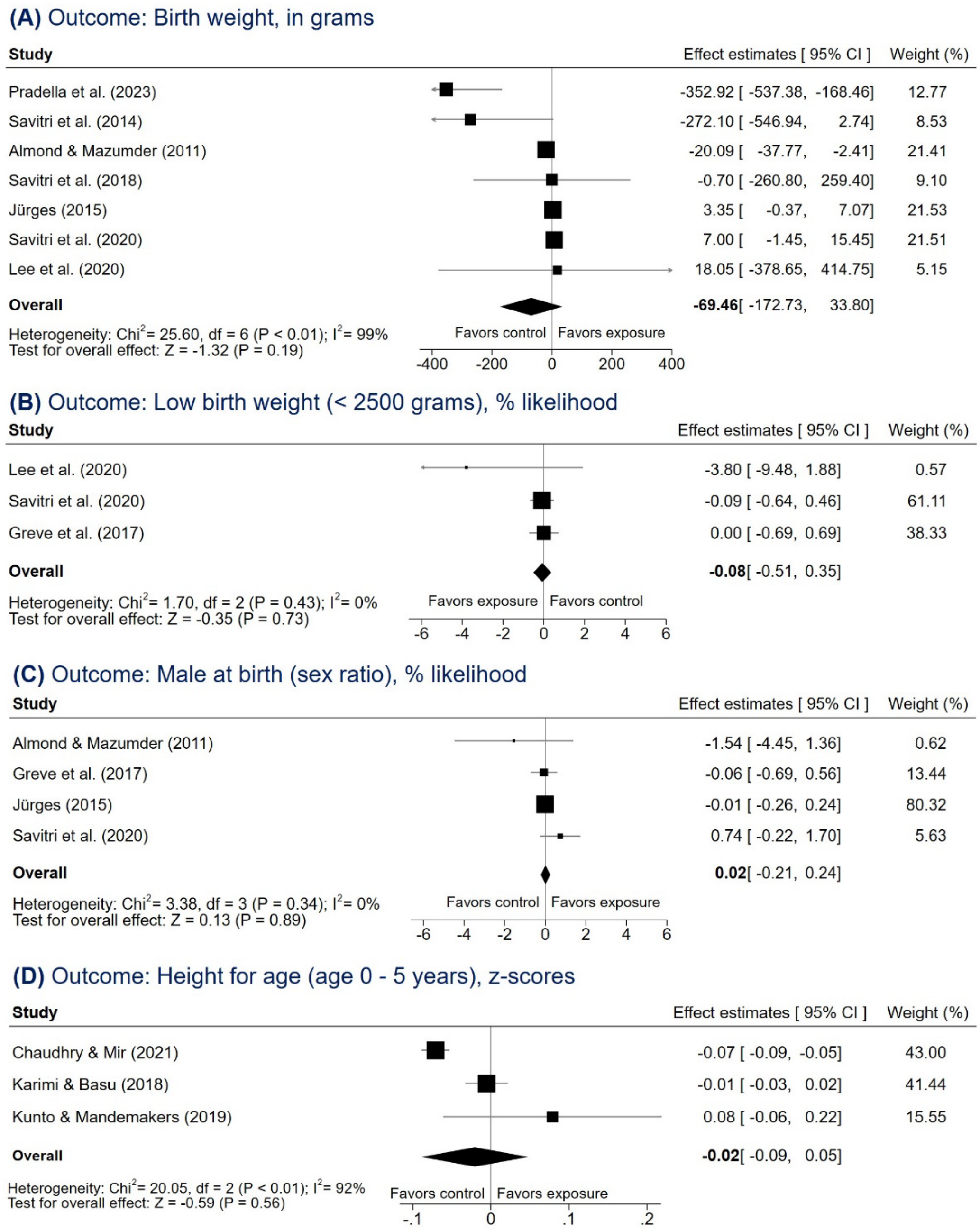
Natural Experiment Studies							
Study / Risk of bias domain	1	2	3	4	5	Overall	Notes
Almond & Mazumder (2011)	+	+	+	·	+	+	D4: For Uganda and Iraq, only month of birth is known. For US exact date of birth
Almond, Mazumder & Van Ewijk (2015)	+	N/A	+	+	+	+	
Chaudhry (2022)	+	+	+	·	·	+	
Chaudhry & Mir (2021)	+	+	+	+	+	+	
Chu, Goli & Rammohan (2023)	!	+	+	·	+	!	D4: Exact date of birth (which is available only for a subsample) is used in a robustness check
Greve, Schultz-Nielsen & Tekin (2017)	+	N/A	+	+	+	+	
Jürges (2015)	+	+	+	+	+	+	
Karimi, Little & Mokhatari (2021)	+	+	+	+	+	+	
Karimi & Basu (2018)	+	+	+	+	+	+	
Kunto & Mandemakers (2019)	+	+	+	+	+	+	
Lee et al. (2020)	+	+	+	·	+	+	
Majid, Behrman & Mani (2019)	+	·	·	+	+	·	D2: 33 year cycle covered for adult outcomes, but not for children. Children: No additional difference-in-differences analysis

Study / Risk of bias domain	1	2	3	4	5	Overall	Notes
Majid (2015)	+	·	·	+	+	·	D2: 33 year cycle covered for adult outcomes, but not for children. Children: No additional difference-in-differences analysis
Pradella & Van Ewijk (2018)	+	+	+	+	+	+	
Savitri et al. (2018)	!	!	!	+	+	!	D4: Ramadan exposure calculated based on last menstrual period, which is even more exact than birth date
Savitri et al. (2020)	+	N/A	+	+	+	+	
Schoeps et al. (2018)	+	+	+	+	+	+	
Schultz-Nielsen, Tekin & Greve (2016)	+	+	+	+	+	+	
Tith et al. (2019)	·	+	+	+	+	·	D1: Control for season instead of month of conception
Van Ewijk, Painter & Roseboom (2013)	+	+	+	+	+	+	
Van Ewijk (2011)	+	+	+	+	+	+	
Self-Reported Fasting Studies							
Study / Risk of bias domain	**1**	**2**	**3**	**4**	**5**	**Overall**	**Notes**
Awwad et al. (2012)	+	!	!	+	·	!	
Azizi et al. (2004)	!	!	!	!	·	!	
Denizli et al. (2023)	+	!	!	+	·	!	
Ghazal et al. (2020)	+	+	!	+	·	!	

Study / Risk of bias domain	1	2	3	4	5	Overall	Notes
Hizli et al. (2012)	!	!	·	+	·	!	
Kavehmanesh & Abolghasemi (2004)	!	!	+	+	·	!	D3: The study also presents some results on height at birth based on analyses without covariates (not considered here)
Mirghani & Hamud (2006)	!	!	!	+	·	!	
Petherick, Tuffnell & Wright (2014)	+	+	+	+	·	+	
Pradella et al. (2023)	+	+	+	+	+	+	
Savitri et al. (2014)	+	+	+	+	·	+	
Savitri et al. (2018)	+	+	+	+	·	+	

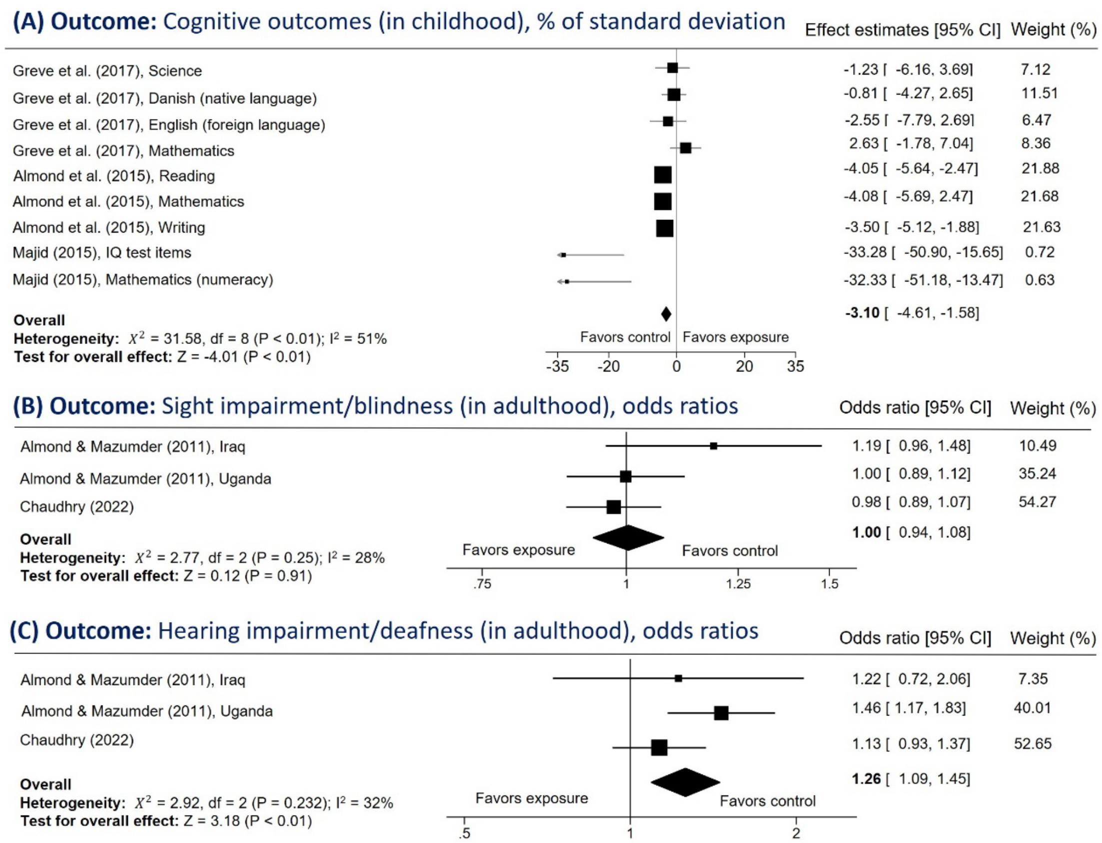
Judgement: ! High concerns · Some concerns + Low concerns

Supplementary Figure S2. Meta-analytical results: Associations between prenatal exposure to Ramadan and offspring health outcomes, Ramadan exposure in trimester 1.



Supplementary Figure S2. Meta-analytical results: Associations between prenatal exposure to Ramadan and offspring health outcomes, Ramadan exposure in trimester 1.
Results from random effects meta-analyses that include studies not classified as being at a high risk of bias. Black diamond markers represent overall estimates.
(A) Associations between prenatal Ramadan exposure and birth weight (in grams).
(B) Associations between prenatal Ramadan exposure and percent likelihood for low birth weight (defined as birth weight less than 2500 grams).
(C) Associations between prenatal Ramadan exposure and share of male births (in percent).
(D) Associations between prenatal Ramadan exposure and height-for-age among 0 to 5 year-old children (z-scores).

Supplementary Figure S3. Meta-analytical results: Associations between prenatal exposure to Ramadan and offspring health outcomes at later life stages, irrespective of pregnancy phase of exposure.

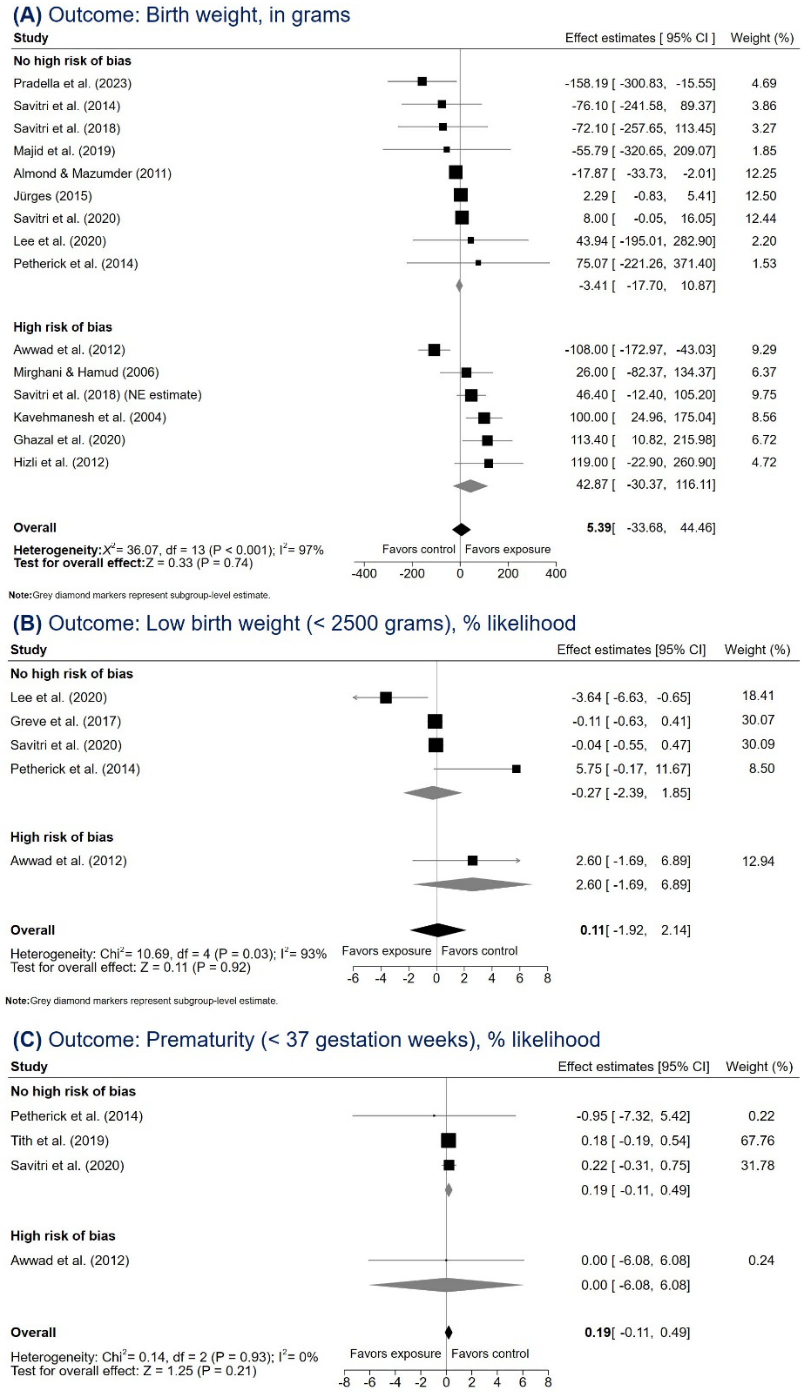


Supplementary Figure S3. Meta-analytical results: Associations between prenatal exposure to Ramadan and offspring health outcomes at later life stages, irrespective of pregnancy phase of exposure.

Results from random effects meta-analyses that include studies not classified as being at high risk of bias. Black diamond markers represent overall estimates.

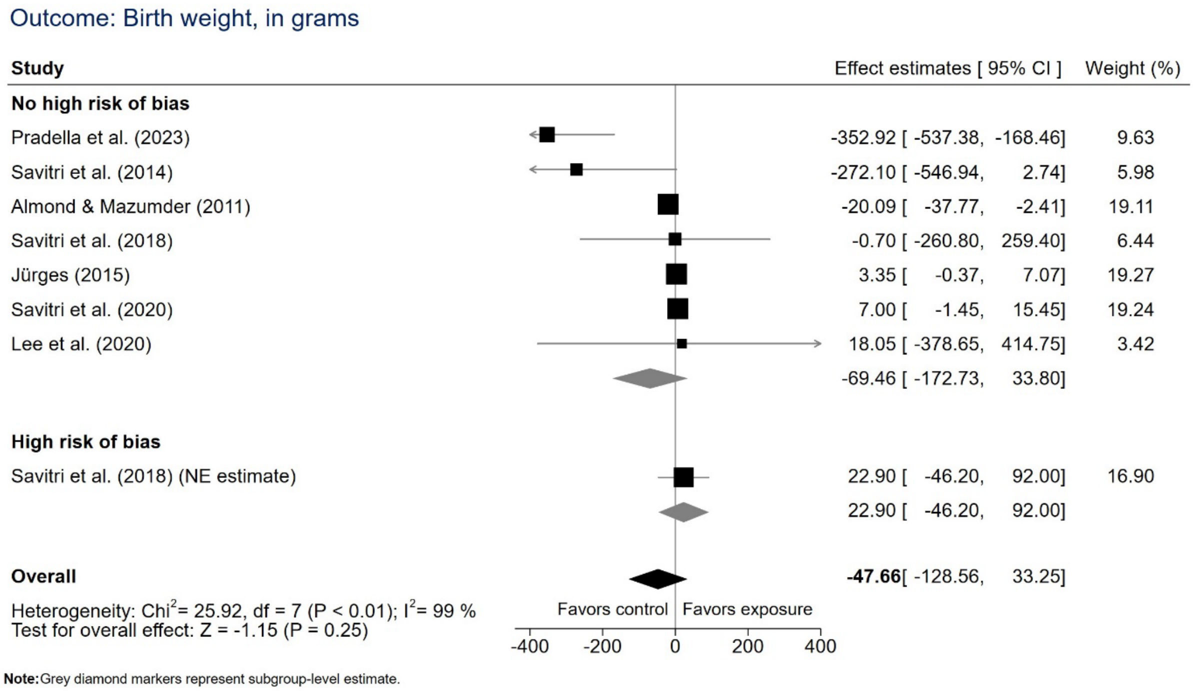
(A) Associations between Ramadan during pregnancy and cognitive outcomes in childhood (percent of standard deviation of test scores).
(B) Associations between Ramadan during pregnancy and likelihood for sight impairments/blindness in adulthood (in odds ratios).
(C) Associations between Ramadan during pregnancy and likelihood for hearing impairments/deafness in adulthood (in odds ratios).

Supplementary Figure S4. Meta-analytical results: Associations between prenatal exposure to Ramadan and offspring health outcomes, irrespective of pregnancy phase of exposure.



Supplementary Figure S4. Meta-analytical results: Associations between prenatal exposure to Ramadan and offspring health outcomes, irrespective of pregnancy phase of exposure. Analysis based on the full sample of included studies eligible for meta-analysis, including studies classified as being at high risk of bias. Grey diamond markers represent subgroup overall estimates. Black diamond markers represent overall estimates. NE, natural experiment study.
(A) Associations between prenatal Ramadan exposure and birth weight (in grams).
(B) Associations between prenatal Ramadan exposure and percent likelihood for low birth weight (defined as birth weight less than 2500 grams).
(C) Associations between prenatal Ramadan exposure and percent likelihood for premature birth (defined as birth at less than 37 weeks of gestation).

Supplementary Figure S5. Meta-analytical results: Associations between prenatal exposure to Ramadan and birth weight (in grams), exposure in trimester 1.

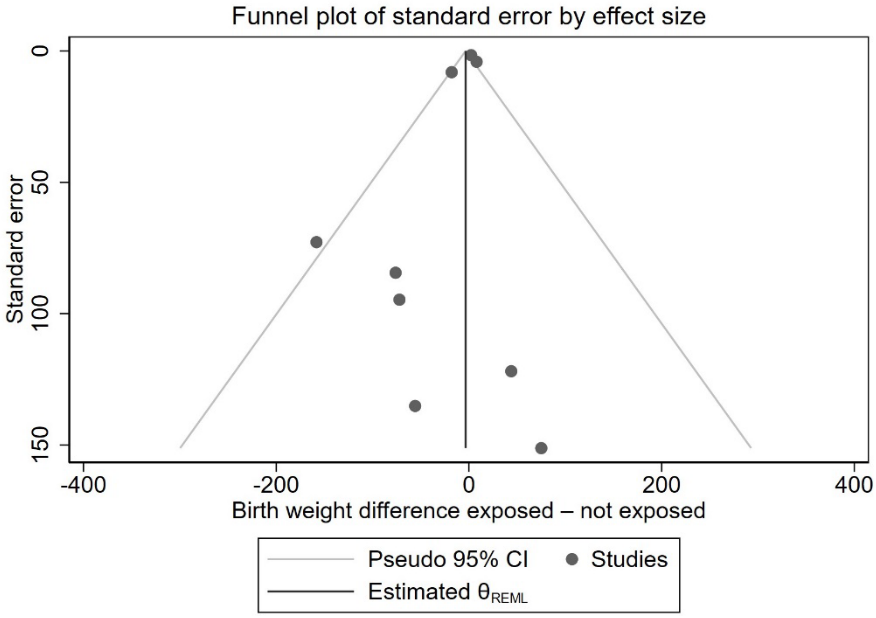


Supplementary Figure S5. Meta-analytical results: Associations between prenatal exposure to Ramadan and birth weight (in grams), exposure in trimester 1.

Analysis based on the full sample of included studies eligible for meta-analysis, including studies classified as being at high risk of bias.

Grey diamond markers represent subgroup overall estimates. Black diamond markers represent overall estimates.

Supplementary Figure S6. Funnel plot for the outcome birth weight (for associations irrespective of pregnancy phase of exposure).

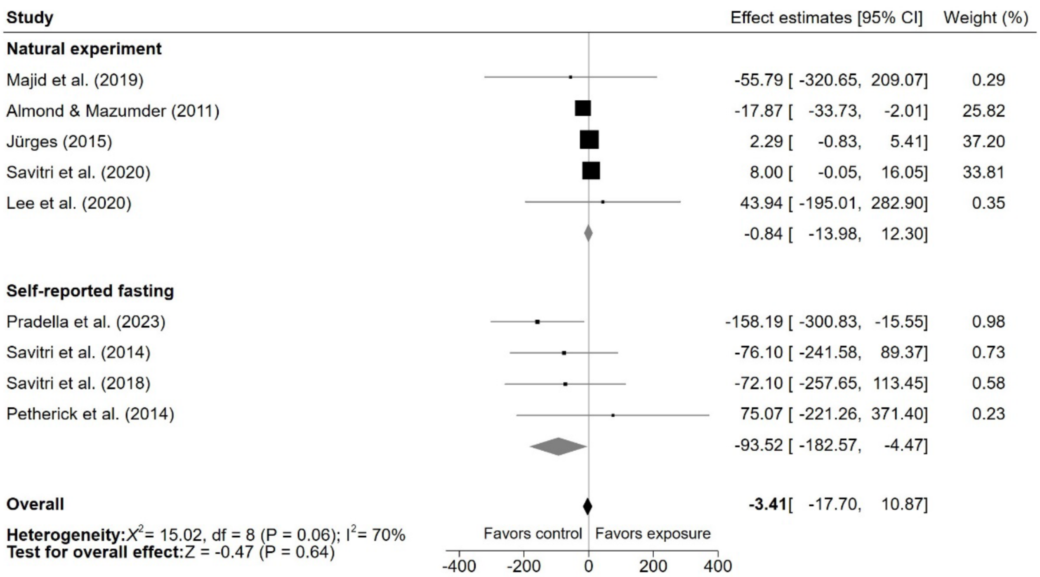


Supplementary Figure S6. Funnel plot for the outcome birth weight (for associations irrespective of pregnancy phase of exposure).

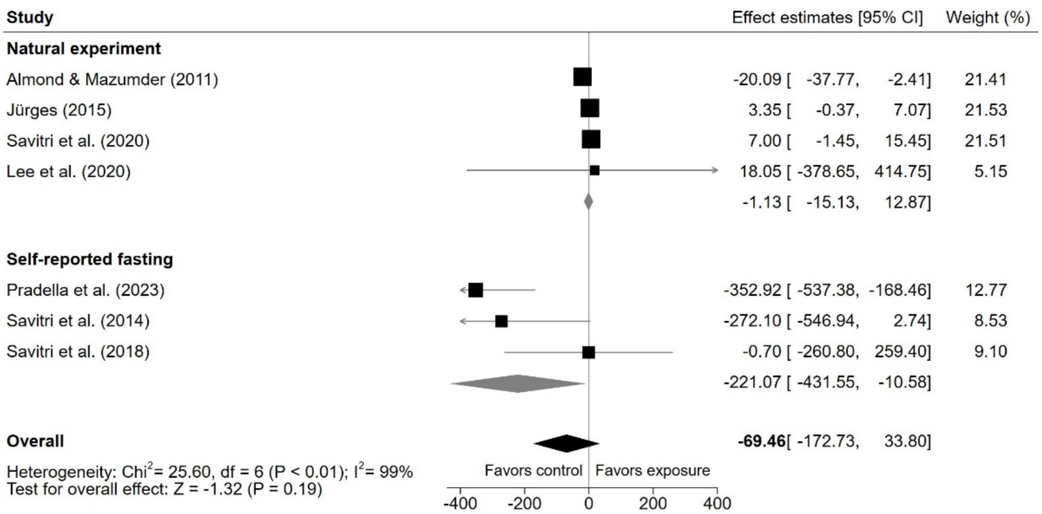
Results based on studies not classified as being at a high risk of bias. Egger's regression test did not indicate asymmetry (P=0.12).

Supplementary Figure S7. Meta-analytical results: Comparison of results by study design for the outcome birth weight.

(A)



(B)



Supplementary Figure S7. Meta-analytical results: Comparison of results by study design for the outcome birth weight.

Results from random effects meta-analyses that include studies not classified as being at high risk of bias.
Grey diamond markers represent subgroup overall estimates for each study design.
Black diamond markers represent overall estimates.

(A) Associations between Ramadan during pregnancy and birth weight (in grams), irrespective of pregnancy phase of exposure.
(B) Associations between Ramadan during the first pregnancy trimester and birth weight (in grams).

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