Article published online: 2022-07-13

Relationships between Women's and Men's Modifiable Preconception Risks and Health Behaviors and Maternal and Offspring Health Outcomes: An Umbrella Review

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Semin Reprod Med 2022;40:170–183

Abstract

Parental health before conception effects maternal and offspring health outcomes. Preconception care provides healthcare to prospective parents addressing modifiable preconception risks and health behaviors. This umbrella review aimed to consolidate evidence on women's and men's modifiable preconception risks or health behaviors associated with maternal and offspring health outcomes. MEDLINE, EMBASE, Maternity and Infant Care, CINAHL, and PsycINFO were searched from March 4, 2010, to March 4, 2020. Eligible studies were systematic reviews or meta-analyses of observational studies examining associations between modifiable preconception risks or health behaviors and maternal and offspring health outcomes. Screening, data extraction, and methodological quality assessment (AMSTAR 2) occurred independently by two reviewers. Degree of overlap was examined. Findings were summarized for evidence synthesis. Twenty-seven systematic reviews were included. Modifiable preconception risks and health behaviors were identified across categories: body composition (e.g., overweight, obesity), lifestyle behaviors (e.g., caffeine, smoking), nutrition (e.g., micronutrients), environmental exposures (e.g., radiation), and birth spacing (e.g., short interpregnancy intervals). Outcomes associated with exposures affected embryo (e.g., embryonic growth), maternal (e.g., gestational diabetes mellitus), fetal/neonate (e.g., preterm birth), and child (e.g., neurocognitive disorders) health. For real-world practice and policy relevance, evidence-based indicators for preconception care should include body composition, lifestyle, nutrition, environmental, and birth spacing.

Keywords
- preconception care
- risk factors
- health behavior
- maternal health
- pregnancy complications

Issue Theme Preconception (Part 1); Guest Editors, Kirsten I. Black, MBBS, MMed, FRANZCOG, PhD, FFSRH, DDU and Jacqueline A. Boyle, MBBS, FRANZCOG, MPH&TM, PhD

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0042-1744257.
ISSN 1526-8004.

The preconception health environment of prospective mothers and fathers has effects on maternal and offspring health outcomes.[1,2] The developmental origins of health and disease[3] model has fostered research efforts aimed at the prevention of disease by modifying risk exposures in the preconception period.[2,4–7] Consequently, preconception care[8] provided before women's first pregnancy (i.e., the preconception period) or between women's subsequent pregnancies (i.e., the interpregnancy period)[9] aims to address modifiable preconception risks and health behaviors—whereby exposure or risk can be prevented or reduced through behavior change or an intervention[5]—among prospective parents to improve maternal and offspring health.[8]

The substantive evidence describing preconception risks and health behaviors needs consolidation so that clear preconception care directives can be developed and translated into real-world applications. To date, Cochrane reviews have described routine pre-pregnancy health promotion for improving health outcomes,[10] preconception risks and interventions,[11] and the efficacy and safety of periconception folic acid for preventing birth defects.[12] Other systematic and scoping reviews have outlined the effects of preconception interventions on improving reproductive health and women's pregnancy outcomes delivered in primary care[13] and public health and community settings.[14,15] An additional review has examined preconception health interventions, knowledge, attitudes, behaviors, and intentions.[16] The largest body of research from these reviews focuses on folic acid supplementation to reduce the incidence of neural tube defects (NTDs).

Research is needed that addresses the broad determinants of preconception health[14] inclusive of all individuals of reproductive age (women and their partners).[14–16] From a public health policy and practice viewpoint, understanding modifiable preconception risks and health behaviors is crucial to promoting health across the life course through preconception care. However, to address these risks and behaviors requires individuals (reproductive-age women and their partners) and health professionals (e.g., general practitioners, obstetricians/gynecologists and pediatricians, nurses, midwives, public health workers, health educators, and other health professionals) that are aware of preconception modifiable risks and health behaviors throughout the reproductive life course.[17–23] As such, this review provides a summary of literature published in systematic reviews examining women's and men's preconception risks and health behaviors, and their association with maternal and offspring health outcomes.

Methods

Search Strategy

The protocol was developed in accordance with the PRISMA statement[24] and registered in PROSPERO on April 28, 2020 (CRD42020171244). Keyword and MeSH terms were employed into MEDLINE, EMBASE, Maternity and Infant Care, CINAHL, and PsycINFO on March 4, 2020. The full search strategy for each database can be downloaded from PROSPERO. ►**Table 1** provides an example of the search strategy as employed in MEDLINE (OVID) database.

Search limits included title and abstract, studies in humans, and articles published in the past 10 years, with no limits to language. Non-English articles were translated to the English language using Google Translate.[25] Abstracts were downloaded into EndNote X9[26] from each database and screened for duplicates before being imported into Covidence.[27]

Selection Criteria

Eligible studies were systematic reviews or meta-analyses of observational studies (i.e., cross-sectional, cohort—retrospective/prospective, case–control) that examined the association of a modifiable risk or health behavior (such as, but not limited to, dietary/nutritional, lifestyle, or environmental) with an embryo, maternal, fetal/neonate, or child health outcome and sampled individuals identified as being in the preconception period (i.e., exposure had occurred before conception). Articles (or results reported in articles) were excluded if the preconception period was not the primary topic of focus; the primary outcome was not related to a maternal or offspring health outcome; not on humans (i.e., animal studies); and intervention studies (i.e., trials) or were other types of reviews such as narrative reviews, commentary, or opinion articles.

Title and abstract and full-text screening occurred independently by two reviewers before inclusion for review. Disagreements were discussed until consensus was reached. If unresolved, a third reviewer was invited to adjudicate. The reason for article exclusion was documented. A PRISMA flow diagram was generated.

Table 1 Keywords and MeSH terms for MEDLINE (OVID)

((preconception OR pre-conception OR periconceptional OR peri-conceptional OR pre-pregnancy OR prepregnancy OR interconception OR preconception care).tw. OR preconception care.sh) AND (risk factors OR risk taking OR exp health behavior OR exp attitude to health OR health knowledge, attitudes, practice OR exp life style OR exp diet OR exp dietary supplements OR nutrients OR micronutrients OR illicit drugs OR prescription drugs OR exp environmental exposure).sh) AND (infertility OR exp pregnancy outcome OR exp pregnancy complications OR maternal health OR maternal death OR maternal mortality OR exp fetal development OR perinatal death OR child mortality OR exp congenital abnormalities OR exp fetal diseases OR exp infant newborn diseases OR noncommunicable diseases).sh OR (maternal outcome OR infant outcome OR child outcome OR life course).tw.))

Methodological Quality

Two review authors independently assessed the quality of the included studies using AMSTAR 2.[28] Disagreements were discussed until consensus was reached.

Data Extraction

Data items were extracted independently by two reviewers. Disagreements were discussed between reviewers until consensus was reached.

Overlap

The degree of overlap of the included primary studies was examined from all reviews in our review by employing the method described by Pieper et al[29] The corrected cover area (CCA) was calculated as a measure of overlap and described as a value indicating the proportion and percentage of overlap.[29]

Data Synthesis

Characteristics and findings from included systematic review and meta-analyses were presented in tables, summarizing for evidence synthesis the population, timeframe, exposure, main outcomes measured, and results as presented in the articles.

Results

Database searches yielded 5,101 articles. After duplicate removal and title and abstract screening, 62 full-text articles were assessed against the eligibility criteria. Thirty-five articles[16,30–63] were excluded with reasons from the review. Reasons for exclusion from the review included: not a systematic review ($n = 16$),[16,30–44] exposure not defined or reported as occurring during the preconception timeframe ($n = 11$),[45–53,55,64] not eligible exposures (e.g., not modifiable) ($n = 3$),[37,57,63] ineligible study design ($n = 2$),[58,59] conference abstract ($n = 1$),[60] irrelevant outcomes ($n = 1$),[61] and not the relevant study population ($n = 1$).[62] A total of 27 systematic reviews were included (►**Fig. 1**), and of these 19 presented meta-analysis of at least one outcome and exposure of interest[64–82] and the remaining 8 presented a systematic review without meta-analysis.[83–90]

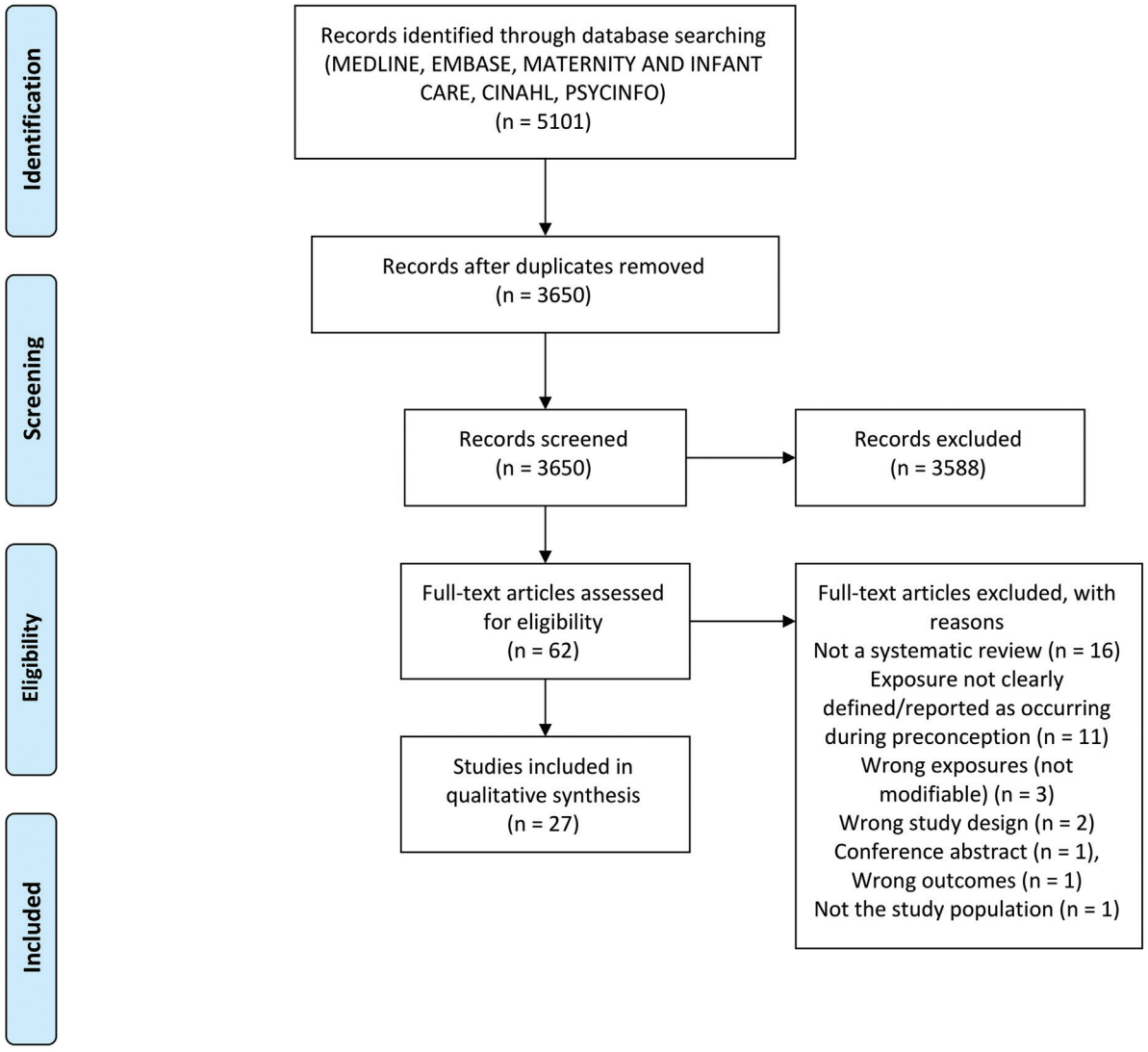

Fig. 1 PRISMA flow diagram.

Table 2 Summary of findings of included systematic reviews with meta-analysis

	Reference	Population	Timeframe	Exposure	Embryo	Maternal	Fetal/ Neonate	Child
Body composition	Dean et al 2014	Reproductive-age women	Preconception	Underweight			+	
	Liu et al 2016							
	Álvarez-Bueno et al 2017			Overweight and obesity		+	+/−	+
	Liu et al 2016							
	Najafi et al 2019							
	Sanchez et al 2018							
	Zhang et al 2015							
	Dean et al 2014			Overweight		+	+	
	Dai et al 2018			Obesity		+	+	+
	Zhang et al 2019							
	Kanadys et al 2012							
	Liu et al 2016							
	Sanchez et al 2018							
	Teulings et al 2019	Parous reproductive-age women	Interpregnancy	ΔBMI kg/m^2 (weight gain: 1 and 2, 2–3, or > 3 BMI units)		+		
	Teulings et al 2019			ΔBMI kg/m^2 (weight gain: >3 BMI units)		+	+	
	Teulings et al 2019			ΔBMI kg/m^2 (weight loss: >1 BMI unit)			+	
	Teulings et al 2019			ΔBMI kg/m^2 (weight gain: > 3 BMI units, normal BMI at index pregnancy)		+	+	
	Teulings et al 2019			ΔBMI kg/m^2 (weight gain: 2–3, >3 BMI units; normal BMI at index pregnancy)		+		
Lifestyle	Karalexi et al 2017	Male partners	Preconception	Alcohol intake				−
	Lassi et al 2014	Reproductive-age women	Periconception	Caffeine intake	+			
	Lassi et al 2014		Preconception	Alcohol intake	+		+	
	Patra et al 2011			Alcohol consumption (average of between 2 and 4 drinks or more per day)			+	
	Lassi et al 2014			Smoking			+	−
	Lassi et al 2014	Male partners		Illicit drug use (heroin)			+	
	Lassi et al 2014	Reproductive-age women	Periconception	Illicit drug use			−	
	Lassi et al 2014			Illicit drug use			+	
	Lassi et al 2014		Preconception	Illicit drug use		+		
	Mijatovic-Vukas et al 2018			Physical activity (any type and >90 min/wk in leisure time physical activity)		+		
	Tobias et al 2011			Physical activity		+		
Nutrition	Crider et al 2013	Reproductive-age women	Preconception	Folic acid supplementation (range 400–700 μg daily)				−
			Periconception					
	Hodgetts et al 2015		Preconception	Folic acid supplementation (400–500 μg daily)			+	
	Dean et al 2014			Multivitamin supplementation		+	+	

(*Continued*)

Table 2 (*Continued*)

	Reference	Population	Timeframe	Exposure	Embryo	Maternal	Fetal/ Neonate	Child
Environment	Lassi et al 2014			Occupational radiation	+			
	Lassi et al 2014	Reproductive-age women Male partners		Occupational radiation				+
	Lassi et al 2014	Male partners		Non-occupational radiation			+	+
	Lassi et al 2014	Reproductive-age women		Pesticides	+			
	Lassi et al 2014	Male partners		Pesticides				+
	Lassi et al 2014	Reproductive-age women Male partners		Chemicals (paints, solvents, industrial products, etc.)				+
	Lassi et al 2014			Dermal hydrocarbons and metal				+
	Lassi et al 2014			Lead			+	
	Lassi et al 2014	Reproductive-age women	Periconception	Cooking with wood, coal, and/or tires			+	
	Lassi et al, 2014		Preconception	Particulate air pollution	+			
	Zhang et al 2020			Ambient air pollution and ozone (O3)		+		

Abbreviations: BMI, body mass index; +, association found; −, no association found.
Notes: The analysis includes only observational study findings from the review.
Main associated health outcomes: embryo (e.g., reduced fecundity, miscarriage, prolonged time to pregnancy, reduced embryonic growth trajectories), maternal (e.g., antenatal/postnatal depression, maternal obesity, preeclampsia, gestational diabetes mellitus, caesarean, pregnancy-induced hypertension, shoulder dystocia, labor dystocia, precipitous labor, placental abruption, uterine rupture), fetal/neonate (e.g., congenital heart defects, neural tube defects, congenital abnormalities, anencephaly, large for gestational age, macrosomia, intensive care neonatal admission, stillbirth, low birth weight, preterm birth, small for gestational age, gastroschisis, reduced intrauterine growth, cryptorchidism, oesophageal atresia), and child (e.g., reduced neurocognitive development, attention-deficit hyperactivity disorder, autism spectrum disorder, developmental delay, emotional/behavioral problems, cerebral palsy, asthma, leukemia, acute lymphoblastic leukemia, childhood cancers, childhood overweight).

Degree of Overlap

The included articles cited 655 primary publications in 738 unique instances across all reviews representing a CCA of 0.5% ($\text{CCA} = 738–655/(655 \times 27) - 655 = 0.005$) indicating only a slight overlap. We further examined 10 reviews containing more than five articles cited more than once across all included reviews[65,68,70,73–75,77,83,86,88] and their exposure(s) and outcome(s) of interest. Three reviews[65,77,83] studied preconception obesity and reported on childhood neurocognitive development. Two reviews[68,73] examined preconception underweight and reported on preterm birth, small for gestational age, and low birthweight, and two reviews[68,86] studied preconception multivitamin supplementation (including folic acid) and reported on preeclampsia, congenital abnormalities, and NTDs. One review[88] studied folic acid supplementation and NTDs. The remainder of reviews[70,73–75] had examined different exposures and outcomes. We determined the impact any occurrence of overlap would have on our review findings was negligible.

Critical Appraisal

The methodological quality of the included studies ranged between critically low ($n = 11$),[68,70–74,76,79,82,85,86] low ($n = 10$),[64–66,69,77,78,80–82,87,90] and moderate ($n = 6$).[67,75,83,84,88,89] Of the seven AMSTAR 2 critical domains, 23 studies failed to register a study protocol before commencement of the review, five studies failed in adequacy of the literature search, 24 studies failed in providing justification for excluding individual studies, 10 studies failed to describe risk of bias from individual studies being included in the review, and 13 studies failed in appropriateness of meta-analytical methods (e.g., the use of unadjusted odds ratios [ORs] or risk ratios [RRs]). Where meta-analysis was performed, nine studies failed in consideration of risk of bias when interpreting the results of the review, and six studies failed to adequately assess the presence and likely impact of publication bias. The individual assessment for each of the studies against the 16 items of the AMSTAR 2 critical appraisal tool can be requested from the corresponding author.

Study Characteristics

►**Table 2** and ►**Table 3** summarize findings by population, timeframe, exposure, and main associated outcome(s) as embryo, maternal, fetal/neonate, and child health outcomes. The data extraction tables describing detailed characteristics of the included studies can be requested from the corresponding author.

Table 3 Summary of findings of included systematic reviews

	Reference	Population	Timeframe	Exposure	Embryo	Maternal	Fetal/ Neonate	Child
Body composition	Adane et al 2016	Reproductive-age women	Preconception	Obesity				+
	Oostingh et al 2019	Reproductive-age women		BMI	+			
	Steinig et al 2017	Reproductive-age women		Obesity (BMI >30 kg/m^2)		+		
	Weng et al 2012	Children aged 2 to 16 y		Maternal overweight				+
	Woo Baidal et al 2016	Children aged 6 mo to 18 y		Maternal pre-pregnancy BMI				+
	Woo Baidal et al 2016	Children aged 6 mo to 18 y		Paternal BMI				+
Nutrition	Oostingh et al 2019	Reproductive-age women		Diet (Mediterranean dietary pattern)	+			
	Oostingh et al 2019	Reproductive-age women		Folic acid and multivitamin supplement	+			
	Oostingh et al 2019	Reproductive-age women	Periconception	Vitamin B6 levels	+			
	Oostingh et al 2019	Reproductive-age women		Folic acid levels	+			
	Oostingh et al 2019	Reproductive-age women		Vitamin B12 levels	+			
	Ramakrishnan et al 2012	Reproductive-age women	Preconception	Multivitamin			+	
	Ramakrishnan et al 2012	Reproductive-age women		Multivitamin		+		
	Viswanathan et al 2017	Reproductive-age women	Preconception	Folic acid supplementation			+	
Lifestyle	Oostingh et al 2019	Reproductive-age women	Periconception	Smoking	+			
	Oostingh et al 2019	Reproductive-age women		Alcohol	+			
	Oostingh et al 2019	Reproductive-age women		Caffeine				
	Oostingh et al 2019	Reproductive-age women	Preconception Periconception	Physical activity (moderate)	+			
	Woo Baidal et al 2016	Children aged 6 mo to 18 y	Preconception	Paternal smoking				−
Birth spacing	Hutcheon et al 2019	Parous reproductive-age women	Interpregnancy (<24 mo)	Short interpregnancy interval (<6 and 6–11 mo)		+		
	Hutcheon et al 2019	Parous reproductive-age women		Short interpregnancy interval (<6 vs. 18–23 mo)		+		
	Hutcheon et al 2019	Parous reproductive-age women		Short interpregnancy interval (6–11 vs. 18–23 mo)		+		
	Hutcheon et al 2019	Parous reproductive-age women		Short interpregnancy interval (<12 vs. 12–43 mo and <24		+		

(*Continued*)

Table 3 (*Continued*)

	Reference	Population	Timeframe	Exposure	Embryo	Maternal	Fetal/ Neonate	Child
				vs. 24–47 mo and <24 vs. ≥120 mo)				
	Hutcheon et al 2019	Parous reproductive-age women		Short interpregnancy interval (<6 vs. 18–60 mo and 6–12 vs. 18–60 mo and 12–18 vs. 18–60 mo)		+		
	Hutcheon et al 2019	Parous reproductive-age women		Short interpregnancy interval (<6 vs. 24–59 mo)		+		
	Hutcheon et al 2019	Parous reproductive-age women		Short interpregnancy interval (<6 vs. 18–59 mo) in women attempting vaginal birth after caesarean		+		
Environment	Oostingh et al 2019	Reproductive-age women	Preconception	Diet (fish contaminated with organochlorine compounds)	+			

Abbreviations: BMI, body mass index; +, association found; −, no association found.
Notes: The analysis includes only observational study findings from the review.
Main associated health outcomes: embryo (e.g., reduced fecundity, miscarriage, prolonged time to pregnancy, reduced embryonic growth trajectories), maternal (e.g., antenatal/postnatal depression, maternal obesity, preeclampsia, gestational diabetes mellitus, caesarean, pregnancy-induced hypertension, shoulder dystocia, labor dystocia, precipitous labor, placental abruption, uterine rupture), fetal/neonate (e.g., congenital heart defects, neural tube defects, congenital abnormalities, anencephaly, large for gestational age, macrosomia, intensive care neonatal admission, stillbirth, low birth weight, preterm birth, small for gestational age, gastroschisis, reduced intrauterine growth, cryptorchidism, oesophageal atresia), and child (e.g., reduced neurocognitive development, attention deficit hyperactivity disorder, autism spectrum disorder, developmental delay, emotional/behavioral problems, cerebral palsy, asthma, leukemia, acute lymphoblastic leukemia, childhood cancers, childhood overweight).

Summary of Findings

Body Composition

Maternal

Underweight

Preconception underweight significantly increases the odds of preterm birth (OR: 1.30 [95% confidence interval [CI], 1.13–1.49]),[73] and (OR: 1.32 [95% CI, 1.22, 1.43]),[68] small for gestational age (OR: 1.67 [95% CI, 1.49–1.87])[73] and (RR: 1.64 [95% CI, 1.22–2.21]),[68] and low birth weight infants (OR: 1.67 [95% CI, 1.39–2.02]).[73]

Overweight

Preconception overweight prolongs the time to pregnancy in comparison to normal weight women and increases the risk of miscarriage.[85] Overweight women have increased odds of preeclampsia (OR: 2.28 [95% CI, 2.04–2.55]), gestational diabetes mellitus (GDM) (OR: 1.91 [95% CI, 1.58, 2.32][68]; adjusted OR [aOR]: 2.01 [95% CI, 1.75–2.26]),[75] and an increased likelihood of a caesarean birth (OR: 1.42 [95% CI, 1.21–1.66]).[68] Overweight women significantly increase their odds for large-for-gestational-age infants (OR: 1.45 [95% CI, 1.29–1.63]), infant admission to neonatal intensive care unit (OR: 1.29 [95% CI, 1.12–1.48]), stillbirth (OR: 1.27 [95% CI, 1.18–1.36]),[73] and infant macrosomia (OR: 1.70 [95% CI, 1.55–1.87])[73]; aOR: 1.93 [95% CI, 1.65, 2.27]).[67]

Dean et al found a significant association between preconception overweight and birth defects (NTDs, congenital heart defects) (OR: 1.15 [95% CI, 1.07–1.24]).[68] Sanchez et al reported preconception overweight increased the odds for compromised neurodevelopmental outcomes in children (OR: 1.17 [95% CI, 1.11–1.24).[77] A higher maternal prepregnancy body mass index (BMI) was found to have a consistent relationship with childhood overweight.[90] In another systematic review by Weng et al, one study found that the children of mothers' who were overweight before pregnancy were 1.37 times (95% CI, 1.18–1.58) more likely to be overweight at 3 years of age than children of normal-weight mothers.[89]

Obesity

Obese women compared with normal-weight women prolong their time to pregnancy and have higher miscarriage risk.[85] Women with obesity were shown to have an increased likelihood of GDM (aOR: 3.98 [95% CI, 3.42–4.53]; pooled aRR: 2.24 [95% CI, 1.97–2.51]),[75] premature births (OR: 1.18 [95% CI, 1.07–1.30]), medically induced preterm births (OR: 1.72 [95% CI, 1.45–2.04]),[70] and shoulder dystocia (RR: 1.63 [95% CI, 1.33–1.99]).[80] Obese women significantly increase their odds of large-for-gestational-age infants (OR: 1.88 [95%

CI, 1.67–2.11]), infant admission to neonatal intensive care unit (OR: 1.91 [95% CI, 1.60–2.29]), stillbirth (OR: 1.81 [95% CI, 1.69–1.93]), and giving birth to low birth weight infants (OR: 1.24 [95% CI, 1.09–1.41]).[73] Conversely, obesity also increases the odds for infant macrosomia (OR: 2.92 [95% CI, 2.67–3.20][73]; OR: 1.63 [95%, 1.51–1.76]).[68]

An adverse association was found between childhood cognitive development and gross motor function in children and mothers with preconception obesity.[83] In a meta-analysis by Álvarez-Bueno et al, preconception obesity was more likely to have negative influences on a child's neurocognitive development (Effect Size [ES]: 0.06 [95% CI, −0.09 to −0.03]).[65] Similarly, Sanchez et al reported that preconception obesity increased odds for compromised neurodevelopmental outcomes in children (OR: 1.51 [95% CI, 1.35–1.69]), attention-deficit hyperactivity disorder (OR: 1.62 [95% CI, 1.23–2.14]), autism spectrum disorder (OR: 1.36 [95% CI, 1.08–1.70]), developmental delay (OR: 1.58 [95% CI, 1.39–1.79]), and emotional/behavioral problems (OR: 1.42 [95% CI, 1.26–1.59).[77] Zhang et al found a significant association between preconception obesity and an increased odd of cerebral palsy in children (aOR: 1.51 [95% CI, 1.24–1.84]).[64] Children of mothers who were obese before pregnancy were 4.25 times (95% CI, 2.86–6.32) more likely to be overweight at 7 years of age compared with children of nonobese mothers.[89] Another study found that children of mothers who were obese before pregnancy were 2.36 times (95% CI, 2.36–8.85) more likely to be overweight between 9 and 14 years of age compared with children of nonobese mothers.[89] The review by Steinig et al found a positive association between preconception obesity and antenatal and postnatal depression.[87]

Interpregnancy Weight Change

Women with interpregnancy weight gain, compared with normal weight women, increase their odds of developing GDM in a subsequent pregnancy that is proportionate to their BMI increase (1–2 BMI units: aOR: 1.51 [95% CI, 1.22–1.80]; 2–3 BMI units: aOR: 1.81 [95% CI, 1.20–2.41]; >3 BMI units: aOR: 2.37 [95% CI, 1.50–3.34]); the highest odds was reported for women with a BMI <25 kg/m^2 in their previous pregnancy and an interpregnancy weight gain of >3 BMI units (aOR: 4.36 [95% CI, 2.29–6.44]).[78] Women with an interpregnancy weight gain of >3 BMI units increase their likelihood of hypertension (aOR: 1.70 [95% CI, 1.50–1.91]) and preeclampsia (aOR: 1.71 [95% CI, 1.51–1.91]) in a subsequent pregnancy.[78] There is increased odds of developing pregnancy-induced hypertension in women with a previous pre-pregnancy BMI <25 kg/m^2 if their weight increases more than 2 BMI units(2–3 BMI units, aOR: 1.60 [95% CI, 1.04–2.16]; >3 BMI units, aOR: 2.21 [95% CI, 1.81–2.60]).[78] An interpregnancy weight gain of >3 BMI units increases the odds of giving birth to a large-for-gestational-age neonate by 63% (aOR: 1.63 [95% CI, 1.30–1.97]) in a subsequent pregnancy.[78] The likelihood is highest when the women's BMI was <25 kg/m^2 in her previous pregnancy and her interpregnancy weight gain is >3 BMI units (aOR: 1.80 [95% CI, 1.24–2.35]).[78] However, interpregnancy weight loss of >1 BMI unit was associated with lowering the odds of giving birth to a large-for-gestational-age neonate in a subsequent pregnancy (aOR: 1.63 [95% CI, 1.30–1.97]).[78]

Paternal

Body Mass Index

One systematic review reports paternal preconception BMI,[90] finding an association between fathers with a higher preconception BMI and having children who are overweight.[90]

Lifestyle

Maternal

Smoking

Women smoking in the preconception period have poorer fecundity ratios, prolonged time to pregnancy, reduced embryonic growth trajectories, and increased miscarriage risk.[85] Compared with no smoking, preconception smoking has significantly higher odds of preterm birth (OR: 2.2 [95% CI, 1.29–3.75]),[72] and periconceptional smoking increases the likelihood of congenital heart defects threefold (OR: 2.80 [95% CI, 1.76–4.47]).[72]

Alcohol

Women consuming alcohol in the preconception and periconceptional period may experience lower conception rates and an increased risk of miscarriage.[85] In the systematic review by Oostingh et al, three out of seven studies found greater than three drinks per week was associated with miscarriage.[85] In the meta-analysis by Lassi et al, preconception alcohol consumption increased the risk of miscarriage by 30% (pooled RR: 1.30 [0.85–1.97]).[72] Periconception alcohol consumption is also associated with reduced embryonic growth trajectories.[85] Preconception alcohol consumption increased the odds of NTDs, with binge drinking increasing the risk by 20% more compared with one drink per day (OR: 1.24 [95% CI, 0.92–1.68]).[72] Periconceptional alcohol consumption is associated with an increased risk of oesophageal atresia with or without tracheo-oesophageal fistula (RR: 1.26 [95% CI, 1.03–1.56]) and periconceptional alcohol intake once weekly increased the risk of congenital heart defects compared with no intake (OR: 0.96 [95% CI, 0.91–1.01]).[72] The risk of low birth weight increased when an average of three drinks or more per day are consumed during the periconceptional period (RR: 1.07 [95% CI, 0.79–1.45]), and the risk of preterm birth is increased when an average of five drinks or more per day are consumed (RR: 1.04 [95% CI, 0.65–1.68]).[76] Compared with no alcohol intake during the periconceptional period, consuming an average of two drinks or more per day increases risk of small-for-gestational-age infant (RR: 1.02 [95% CI, 0.82–1.27]).[76]

Caffeine

Women consuming more than 501 mg caffeine per day in the periconceptional period significantly increased their time to

pregnancy and had a higher risk of miscarriage.[85] In the meta-analysis by Lassi et al, periconception caffeine intake increased risk of miscarriage with greater than 300 mg/day (pooled RR: 1.77 [95% CI, 0.83–3.78]).[72] In addition, reduced embryonic growth trajectories were observed in women consuming caffeine during preconception.[85]

Physical Activity

Women undertaking vigorous physical activity in preconception have been associated with prolonging the time to pregnancy; however, moderate physical activity was shown to significantly decrease the risk of miscarriage.[85] Engaging in any type of physical activity compared with none during the preconception period is associated with approximately 30% reduced odds of GDM (pooled OR: 0.70 [95% CI, 0.57–0.85]).[74] While engaging in physical activity levels >90 minute/week or higher physical activity levels during preconception was associated with 46 and 55% reduced odds of GDM (pooled OR: 0.54 [95% CI, 0.34–0.87][74] and pooled OR: 0.45 [95% CI, 0.28–0.75]),[79] respectively.

Illicit Drugs

Illicit drug use in the periconceptional period increases the incidence of gastroschisis in infants (OR: 1.76 [95% CI, 0.99–3.13]).[72] Preconception illicit drug use increases the likelihood of postnatal depression for the mother (OR: 9.60 [95% CI, 1.80–51.20]).[72]

Paternal

Illicit Drugs

One meta-analysis measured paternal preconception illicit drug use, finding that paternal preconception heroin use significantly increases the risk of NTDs (RR: 1.63 [95% CI, 1.23–2.16]).[72]

Nutrition

Maternal

Dietary Pattern

A stronger adherence to the Mediterranean dietary pattern during preconception was associated with significantly lower odds of attending an infertility consultation, reported in the review by Oostingh et al.[85]

Multivitamins and Nutrients

Supplementing multivitamins and folic acid during preconception was significantly associated with increased fecundity.[85] Lower vitamin B12 and lower and higher folic acid concentrations during periconception were associated with reduced morphological development of the embryo,[85] whereas higher vitamin B6 status was associated with a reduction in miscarriage risk.[85] Dean et al reported a 27% risk reduction of preeclampsia with preconception multivitamin supplementation (pooled OR: 0.73 [95% CI, 0.58–0.92]).[68] Preconception and/or periconception multivitamin supplementation was negatively associated with low birth weight, small-for-gestational-age infants, and preterm birth in the systematic review by Ramakrishnan et al.[86]

Folic Acid

The systematic review by Viswanathan et al reported that preconception folic acid supplementation demonstrated a negative association with NTDs and a 43% risk reduction of multiple congenital abnormalities (pooled OR: 0.57 [95% CI, 0.34–0.82]).[88] An earlier meta-analysis reported that folic acid supplementation during preconception had a 49% decreased risk of NTDs (pooled RR: 0.51 [95% CI, 0.31–0.82]).[68] Preconception folic acid supplementation (400–500 µg daily) also has significantly lower odds for small-for-gestational-age births (aOR: 0.75 [95% CI, 0.61–0.92]).[69]

Environmental

Maternal

Radiation

Maternal periconceptional occupational radiation exposure increased risk of early miscarriage (RR: 1.32 [95% CI, 1.04–1.66]).[72] Maternal preconception occupational exposure to ionizing radiation increased risk of childhood cancers (RR: 1.19 [95% CI, 0.92–1.54]).[72]

Pesticides

In women, a significantly lower pregnancy success rate was reported with periconceptional consumption of fish contaminated with organochlorine compounds compared with no consumption of organochlorines.[85] Maternal preconception pesticide exposure was associated with miscarriage.[72]

Air Pollution

Maternal preconception exposure to high levels of traffic-related particulate air pollution increases risk of early pregnancy loss as reported by Lassi et al.[72]

Chemicals and Metal

Maternal exposure to excess lead increased the odds of congenital heart defects (OR: 2.59 [95% CI, 1.68–3.82]).[72] Use of wood when cooking increased the risk of NTDs threefold (95% CI, 1.70–6.21), and women cooking or heating with wood, coal, or tires in their homes increase the odds of infant anencephaly (OR: 2.04 [95% CI, 1.29–3.23]).[72] Maternal preconception exposure to chemicals (e.g., paints, solvents, industrial products) increased risk of acute lymphoblastic leukemia in offspring[72] and exposure to dermal hydrocarbons and metal increased risk of leukemia and acute lymphoblastic leukemia.[72]

Paternal

Radiation

Paternal preconception occupational exposure to ionizing radiation increased risk of childhood cancers (RR: 1.29 [95% CI, 1.02–1.63]).[72] Paternal nonoccupational ionizing radiation exposure from X-rays was associated with increased risk

of low birth weight (MD: −73.00 [95% CI, −78.97, −67.03]) and increased risk of reduced intrauterine growth (MD: −53.00 [95% CI, −58.21, −47.79]).[72] Father's exposed to abdominal X-ray during preconception was associated with an increased risk of leukemia in offspring.[72]

Chemicals and Metal

Paternal exposure to pesticides in the year before conception increased the risks of hematological malignancies in offspring.[72] Paternal preconception exposure to chemicals (e.g., paints, solvents, industrial products) increased risk of acute lymphoblastic leukemia in offspring[72] and exposure to dermal hydrocarbons and metal increased risk of leukemia and acute lymphoblastic leukemia.[72] Paternal preconception exposure to excess lead increased the odds of congenital heart defects (OR: 2.59 [95% CI, 1.68–3.82]).[72]

Birth Spacing

Maternal

Short Interpregnancy Interval

Short interpregnancy intervals (<6 and 6–11 months) were associated with increased likelihood of maternal obesity compared with intervals of 18 to 23 months (aOR: 1.61 [95% CI, 1.05–2.45], and aOR: 1.43 [95% CI, 1.10–1.87]).[84] The odds of GDM were also higher with shorter interpregnancy intervals <6 versus 18 to 23 months (aOR: 1.35 [95% CI, 1.02–1.80]),[84] whereas the odds of preeclampsia were lower with shorter interpregnancy intervals of 6 to 11 versus 18 to 23 months (OR: 0.71 [95% CI, 0.54–0.94]).[84] The likelihood of labor dystocia was lower with shorter interpregnancy intervals <12 versus 12 to 43 months (aOR: 0.91 [95% CI, 0.85–0.97]), <24 versus 24 to 47 months (aOR: 0.94 [95% CI, 0.93–0.96]), and <24 versus ≥120 months (aOR: 0.66 [95% CI, 0.64–0.68]).[84] The odds of precipitous labor were higher with shorter interpregnancy intervals <6 versus 18 to 60 months (aOR: 1.30 [95% CI, 1.11–1.51]), 6 to 12 versus 18 to 60 months (aOR: 1.19 [95% CI, 1.04–1.36]), and 12 to 18 versus 18 to 60 months (aOR: 1.25 [95% CI, 1.10–1.41]).[84] The likelihood of placental abruption was higher with shorter interpregnancy intervals <6 versus 24 to 59 months (aOR: 1.9 [95% CI, 1.3–3.0]).[84] Uterine rupture was more likely with short interpregnancy intervals <6 versus 18 to 59 months in women attempting vaginal birth after caesarean birth (aOR: 3.05 [95% CI, 1.36–6.87]).[84]

Discussion

Main Findings

Modifiable preconception risks and health behaviors across multiple categories (body composition, lifestyle, nutrition, environmental, and birth spacing) were found to be associated with numerous maternal and offspring health outcomes.

Strengths and Limitations

This review—employing a thorough, rigorous search strategy and overlap assessment to minimize amplifying findings from one study—is the most comprehensive examination of research investigating preconception modifiable risks and health behaviors to date. The review identified variable amounts of evidence for a range of exposures. Greater quantities of evidence may be due to a research focus on health priority areas, such as obesity. However, limited research examining environmental exposures and paternal exposures in humans may reflect a need to broaden the current gaze among preconception epidemiological research. Given this umbrella review included only systematic reviews, it does not include primary research on these topics not already reviewed. As such, there is potential that non-reviewed topic areas have been excluded. For example, research on men's preconception health has received attention over the last decade on various types of paternal exposure and offspring health outcomes[91–94]; however, this has not yet been comprehensively summarized, although further work is underway.[95] Heterogeneity existed between the data (e.g., OR/RR); therefore, further analyses to determine the strength of the association between an exposure and outcome was not possible.

Interpretation

The vast amount of evidence outlined in this review emphasizes preconception care's critical role in the prevention of noncommunicable diseases through modification of preconception risk exposure,[2,6,7] and providing primary prevention for adverse maternal and offspring health outcomes. The review identified a list of modifiable preconception risks and health behaviors that could be applied to improve screening for preconception risks, enabling the timely initiation of preconception counseling and education where needed.[96] These modifiable risk factors can be scaffolded by existing conceptual frameworks that outline the critical timing to commence preconception care.[97] For example, addressing body composition through adopting a healthy diet and increased physical activity should be considered as early as 3 years prior to conception,[97] whereas cessation of smoking and alcohol consumption should commence at least 3 months before conception or when intending to become pregnant.[97]

Particularly given the lack of consensus regarding the best way to provide preconception care in healthcare systems,[96] one of the challenges for preconception care is identifying opportunities for population-level delivery that aims to benefit the whole population and is equitable, considering the unique needs of low socioeconomic, adolescent, LGBTQIA+, men, ethnic minority, and culturally and linguistically diverse populations.[98] Barker et al propose a preconception care framework that identifies preconception health awareness and intervention opportunities throughout the reproductive life course.[21] Another approach reflects differing aspects of preconception care healthcare delivery models, including screening, education and intervention in primary care, hospital, community, and community outreach settings.[96] The findings of this review may help inform future planning for preconception care initiatives in the community.

The modifiable preconception risks identified in the review may be best ameliorated by both population- and individual-level behavioral change strategies. Behavior change interventions such as preconception counseling and education delivered in primary care, public health, and community settings are effective at reducing risks and encouraging health-promoting behaviors including supplementing with folic acid and/or folic acid–containing multivitamin, consumption of a healthy diet, physical activity, and reduction in use of harmful substances (caffeine, smoking, alcohol, and illicit drugs).[10,11,13,15,16,99] Some preconception care initiatives, programs, and clinical practice guidelines have been developed;[9,100–107] however, these efforts need to be wider spread.

A range of health professionals can assist with preconception care delivery such as physicians (e.g., general practitioners, obstetricians/gynecologists, and pediatricians) and other health professionals (e.g., nurses, midwives, public health workers, social workers, health educators, pharmacists, nutritionists, naturopaths, and acupuncturists).[108,109] One of the known barriers to implementing preconception care is health professionals' confidence in, and capacity to deliver, preconception care.[22,110] Consequently, identifying and addressing barriers to providing preconception care requires close attention to health professionals' time constraints, limited resources, and knowledge of preconception care.[96,110] There is a need to develop preconception care resources to support health professionals in their role and policies to support preconception care implementation across a wide range of private and public health settings.[23,111] For this to be achieved, the development and application of a validated preconception care health literacy instrument can be used to undertake assessment of health professionals' preconception care knowledge to determine the next steps needed for preconception care education and evaluation of preconception care delivery.[112]

Conclusion

For real-world practice and policy relevance, evidence-based indicators for preconception care should include body composition, lifestyle, nutrition, environmental, and birth spacing. Identifying the effects of modifiable risk factors on maternal and offspring health outcomes can help inform future public health messages, clinical guidelines, and preconception care interventions to confirm whether modifying preconception risks and exposures affects maternal and offspring outcomes. Future research attention on the effects of preconception environmental exposures and paternal exposures is needed.

Ethical Statement

Ethics approval was not required for this umbrella review.

Authors' Contributions

C.C. designed the protocol and performed the searches, screening, quality appraisal, overlap assessment, data extraction, and data analysis and drafted, reviewed, and edited the manuscript. A.S. was second reviewer for article screening at the title and abstract stage; D.S. was second reviewer for article screening at the full-text stage; A.G. was second reviewer for quality appraisal; D.V. was second reviewer for data extraction; and A.S., D. S., and E.M. reviewed and edited the manuscript.

Funding

The lead reviewer was financially supported by an Australian Government Research Training Program Scholarship. This project is funded by a project grant from Endeavor College of Natural Health (grant approval number: PRO19–7927). Funding sources have not had any role in conducting the umbrella review.

Conflict of Interests

The authors have no conflicts of interest to declare.

Acknowledgments

The authors have no acknowledgments to make.

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