

Systematic Reviews on the Prevention of Adverse Pregnancy Outcomes Related to Maternal Obesity to Improve Evidence-Based Counselling

Systematische Übersichtsarbeiten über die Verbesserung der evidenzbasierten Beratung zur Prävention von mütterlichen adipositasbezogenen ungünstigen Schwangerschaftsausgängen

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Keywords

maternal obesity, gestational diabetes, health literacy, evidence-based medicine, counselling

Schlüsselwörter

mütterliche Adipositas, Gestationsdiabetes, Gesundheitskompetenz, evidenzbasierte Medizin, Beratung

received 3.2.2024

accepted after revision 13.3.2024

Bibliography

Geburtsh Frauenheilk 2024; 84: 564–572

DOI 10.1055/a-2295-1725

ISSN 0016-5751

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ABSTRACT

Background

Health professionals and their patients should understand the importance of evidence. In the case of gestational diabetes mellitus, which is often associated with an abnormally high body mass index, the immediate and long-term outcome of women and their offspring depends in part on advice and implementation of lifestyle changes before, during and after pregnancy.

Methods

Up to September 2023, MEDLINE, CENTRAL, and WEB OF SCIENCE were used to identify systematic reviews and meta-analyses on the prevention of gestational diabetes. The ROBIS and AMSTAR criteria were analyzed for all systematic reviews.

Results

A total of 36 systematic reviews were identified. Dietary interventions, physical activity or a combined approach all reduced adverse pregnancy outcomes such as gestational diabetes, pregnancy-induced hypertension and related morbidities. Within the randomized controlled trials included in the 36 systematic reviews, the type, intensity and frequency of interventions varied widely. The primary outcomes, reporting and methodological quality of the 36 systematic reviews and meta-analyses also varied.

The meta-analysis with the highest ROBIS and AMSTAR-2 scores was selected to design an icon array based on a fact box simulating 100 patients.

Conclusions

We propose a methodology for selecting the best evidence and transforming it into a format that illustrates the benefits and harms in a way that can be understood by lay patients, even if they cannot read. This model can be applied to counselling for expectant mothers in low and high-income

countries, regardless of socioeconomic status, provided that women have access to appropriately trained healthcare providers.

ZUSAMMENFASSUNG

Hintergrund

Die Bedeutung von Evidenz sollte medizinische Fachkräften und ihren Patientinnen klar sein. Bei Gestationsdiabetes mellitus, der oft mit einem ungewöhnlich hohen Body-Mass-Index assoziiert ist, hängen sowohl die direkten Schwangerschaftsausgänge als auch die Langzeitergebnisse der Frauen und Kinder teilweise von der Beratung und den Lebensstiländerungen während und nach der Schwangerschaft ab.

Methoden

Bis September 2023 wurden Recherchen in MEDLINE, CENTRAL und WEB OF SCIENCE zur Identifizierung von systematischen Übersichtsarbeiten und Metaanalysen zur Prävention von Gestationsdiabetes durchgeführt. Alle systematischen Übersichtsarbeiten wurden anhand der ROBIS- und AMSTAR-Kriterien analysiert.

Ergebnisse

Es wurden insgesamt 36 systematische Übersichtsarbeiten identifiziert. Ernährungsinterventionen, körperliche Aktivität

ten oder eine Kombination beider Herangehensweisen konnten ungünstige Schwangerschaftsausgänge wie z.B. Gestationsdiabetes, schwangerschaftsinduzierte Hypertonie und die damit zusammenhängende Morbidität senken. In den randomisierten kontrollierten Studien, die in den 36 systematischen Übersichtsarbeiten eingeschlossen wurden, gab es starke Unterschiede in der Art, der Intensität und der Häufigkeit der Intervention. Die primären Endpunkte, die Berichterstattung und die methodologische Qualität der 36 systematischen Übersichtsarbeiten und Metaanalysen variierten ebenfalls stark.

Es wurde die Metaanalyse mit den höchsten ROBIS- und AMSTAR-2-Punktzahlen ausgewählt, um eine Reihe von Symbolen basierend auf einer 100 Patientinnen simulierenden Faktenbox zu entwerfen.

Schlussfolgerungen

Es wird hier eine Methode vorgeschlagen, mit der die beste Evidenz ausgewählt und in ein Format überführt werden kann, das die Vorteile und Schäden so veranschaulicht, dass sie von Patientinnen ohne medizinische Vorbildung verstanden werden können, selbst wenn diese Frauen nicht lesen können. Dieses Modell kann bei der Beratung werdender Mütter in Ländern mit niedrigem und hohem Einkommen eingesetzt werden, unabhängig vom sozioökonomischen Status der Frauen, sofern sie Zugang zu entsprechend ausgebildeten Gesundheitsdienstleistern haben.

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first diagnosed in pregnancy [1]. In 2020, the pooled global prevalence of GDM was 14% with a range of 13.97% to 14.04%, whereby high-income countries had the highest standardized prevalence of GDM [2]. GDM is associated with elevated immediate risks for pre-eclampsia, perinatal mortality, preterm delivery, fetal macrosomia, shoulder dystocia or cesarean delivery [3]. Metzger et al. reported on abnormal maternal postpartum glucose tolerance requiring continuous follow-up of all women with GDM [4]. During the life course of these women, increased hyperinsulinemia, dyslipidemia, type-2 diabetes mellitus (DM), hypertension, and cardiovascular disease (CVD) were described [5]. Glucose resistance appears earlier in obese women due to pre-existing impaired insulin resistance. Overweight, obesity and excessive gestational weight gain (GWG) [6] are all associated with increased risks of GDM. First-trimester algorithms allow an individualized prediction with a sensitivity of up to 80% [7, 8, 9, 10] pointing towards pre-existing risk profiles that lower the threshold for the disease [11, 12, 13]. The risk of developing overt diabetes mellitus after a pregnancy with GDM increases with age resulting in a cumulative 15-year risk of 25% [14].

Barker et al. postulated that the global incidence of GDM depends on a mismatch between the pre-and postnatal environment

[15] explaining the increasing prevalence in regions with previously low rates of GDM. There is a U-shaped relation between low (Odds ratio [OR] 2.15, 95% Confidence Interval [CI] 1.29–3.50) and high birth weight (OR: 1.97, 95% CI: 1.12–3.45) and subsequent GDM in females [16]. Prenatal famine exposure and fetal growth restriction (FGR) were associated with impaired glucose tolerance, proinsulin and insulin secretion in adulthood [17, 18, 19]. In addition, GDM associated with fetal macrosomia increases the risk of childhood obesity [20]. Gestational diabetes and gestational hypertension both significantly increase the odds of childhood overweight with a high maternal BMI being the main driver for this association [21]. Ultrasound measurements have shown that fetal overgrowth already starts at 20 weeks of gestation and remains until adulthood [22]. Hypertriglyceridemia was diagnosed in 14/68 children (21%) before puberty [23]. At the age of 11 years, the risk for metabolic syndrome is 3.6-fold higher [24]. As adults, the risks of insulin resistance and metabolic syndrome [23, 25], CVD, insulin-dependent DM and early mortality [18] are increased.

The rising global rates of overweight, obesity, GDM and type 2 DM require urgent consideration by policymakers and awareness of physicians and future parents. Therefore, healthcare providers should translate the evidence into formats recognizable for lay people. In other fields of medicine, it has been shown that fact

boxes and icon arrays can enable patients to make informed decisions [26, 27] recognizing benefits and harms [28, 29, 30] and to understand the evidence independently of the opinion of their healthcare providers [31]. In this umbrella review, we evaluated current systematic reviews (SRs) and meta-analyses to reduce GDM and present a framework for counselling.

Material and Methods

A literature search was conducted up to September 2023 using MEDLINE, Web of Science and the Cochrane Library on the prevention of GDM using the following search terms: pregnancy, overweight, obesity, weight gain, diabetes, GDM, perinatal mortality, systematic reviews and meta-analyses. Data on primary and secondary outcomes, participant characteristics, intervention details, frequency and compliance were collected using a standardized Excel spreadsheet (► Fig. 1).

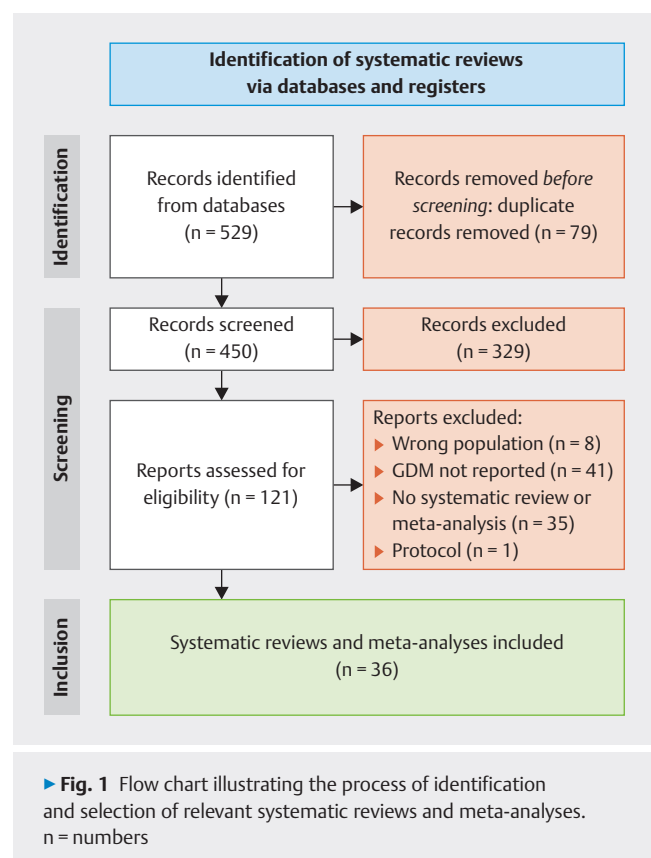
To extract the best evidence we analyzed the reporting and methodological quality of the publications. In the second step, the evidence with the highest ROBIS and AMSTAR-2 rating was selected to design a fact box with a corresponding icon array for those who are less familiar with a tabular format. Fact boxes contain a description of the reference class, a comparison of at least two groups, the effects in absolute numbers, and a summary of benefits and harms by relating the data to a group of 100 or 1000 participants [32]. Their development follows the evidence-based medicine models of Sackett et al. [33].

Results

Defining the occurrence of GDM as a primary outcome we identified 36 meta-analyses and systematic reviews whereby the following interventions were investigated:

- 8/36 with *only dietary counselling* [34, 35, 36, 37, 38, 39, 40, 41],
- 16/36 with *supervised exercise programs* [42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57],
- 6/36 with combined dietary and physical exercise interventions [58, 59, 60, 61, 62, 63],
- 6/36 whereby *only dietary, respectively exercise interventions were compared with a combination of both* [64, 65, 66, 67, 68, 69].

All of the participants included in the trial had been tested against groups receiving standard care. Only 9/36 studies used macrosomia or large for gestational age (LGA) as a primary or secondary outcome, 6/36 investigated perinatal mortality, and 2/36 NICU admission. In 27/36 publications all maternal BMI categories were considered, whereby two provided subgroup analyses for different BMI categories: 8 SRs exclusively concentrated on pregnant women with overweight and obesity [34, 59], only 2/36 on normal weight women. As several RCTs were cited within several SRs, summing patients would have induced bias. Therefore, instead of aggregating patient numbers, we categorized lifestyle interventions as follows:



1. Among 8/36 SRs investigating *only dietary advice* one SR including women with a BMI > 25 kg/m² reported that the intervention significantly reduced GDM. This was in accordance with a sub-analysis of women with the same BMI class within another publication [36]. Two meta-analyses specified the type of diet showing that a plant-based approach, respectively a Mediterranean diet significantly reduced GDM [40, 41]. One SR investigating a low-glycemic index diet found a decreased rate of LGA children [39]. Other significant outcome variables were a reduction of maternal weight gain (5/8 SRs), pregnancy-induced hypertension (PIH) (2/8 SRs), fasting and postprandial glucose and post-partum weight retention (both in 1/8 SRs).
2. Among 20/36 SRs investigating *physical activity and exercise programs* during pregnancy 13/20 found a significant reduction of GDM. A further SR reports that two RCTs showed a successful intervention in preventing GDM in contrast to eight RCTs with no statistical significance [54]. Exercise interventions were also able to reduce the incidence of preeclampsia, respectively PIH in 3/20 SRs [46, 52, 53]; 7/20 SRs showed a significant reduction of GWG in exercising mothers and 2/20 a significant reduction of LGA infants.
3. Among 6/36 SRs investigating the implementation of *both physical exercise and diet*, 2/6 found a significant reduction of GDM when the interventions started early and 4/6 described a significant reduction of maternal GWG during pregnancy.

4. Out of the 6/36 SRs comparing diet, exercise alone and a combination of both, two SRs showed a significant reduction of GDM in all three intervention arms [65, 68]. One SR indicated a benefit of only exercise, whereas another suggested a benefit of a singular diet or singular exercise in contrast to a combined approach which was not successful [64, 66]; 2/6 SRs did not prove a significant effect on GDM by any intervention although all three intervention types were successful in limiting GWG or PIH [67, 69].

All 36 SRs were analyzed according to ROBIS and AMSTAR criteria to determine the quality of the reviews. The overall risk of bias according to the ROBIS tool ranged from low in 12 reviews to high in 13 reviews with additionally 11 reviews showing an unclear risk. The overall confidence, rated using the ASTAR 2 criteria, was low, respectively critically low in six, 22 SRs, whereas six SRs had a moderate level of confidence. Only two SRs fulfilled all criteria of being a high-quality review [38, 60]. Therefore, we chose one of the latter for our counselling model.

► **Fig. 2** illustrates that dietary counselling in pregnant women had no significant impact on the prevention of GDM, although there was a trend to reduce GDM. Nevertheless, the model explains that 10/100 pregnant women without, but only 3/100 women with nutritional counselling developed PIH. This can easily be translated that in about 7/100 women PIH could be prevented (► **Fig. 2**).

Calculations were based on the absolute number of the control groups.

Dietary interventions

Apart from the general information of the icon array, the information for patients can be specified: The detailed components of women's diets influence GDM risks [70]. Consumption of sugar-sweetened drinks, potatoes [71], animal fat and cholesterol [72], high glycemic load and low-cereal fiber diets [73] are associated with an increased risk for GDM. Alternatively, a high-fiber diet [73], a plant-based diet [40], a Mediterranean diet [41], intake of vegetables, a substitution of red meat for poultry, fish, or legumes [74] and of potatoes by vegetables [71] and adherence to "healthful" dietary patterns [75] are also associated with a lower risk of GDM.

Physical exercise

There are large differences in the proportion of women performing regular exercise before and during pregnancy. In Norway, the rate before pregnancy was 46.4% but declined to 28% and 20% at 17 and 30 gestational weeks respectively [76]. Studies in Denmark [77], the USA [78] and Brazil [79] showed a more pronounced reduction in physical activity even in uncomplicated pregnancies whereby activity positively correlated with income. Most women do not meet recommendations for physical activity [79]. The meta-analyses varied in reporting and analyzing details of the interventions. Seven meta-analyses performed detailed subgroup analyses indicating that an early initiation, high intensity and frequent performances were essential for a successful intervention [46, 47, 48, 53, 54, 66, 67]. Women should be motivated to accu-

mulate at least 600 MET (metabolic equivalent of task) minutes of supervised moderate-intensity training which equals e.g. 140 min of brisk walking, water aerobics, stationary cycling or resistance training per week [46, 47]. Other authors emphasize the benefit of low-intensity mind-body exercises such as yoga or pilates [49]. Only 6/20 SRs considered the participant's compliance [46, 47, 50, 51, 64, 67]. Six meta-analyses reported details of the interventions without considering them for separate subgroup analyses [41, 50, 51, 55, 56, 69].

Combined counselling

Similarly, the overall and differential effects of combined diet and physical activity during pregnancy varied by the pattern, timing and prevalence of exercise or diet.

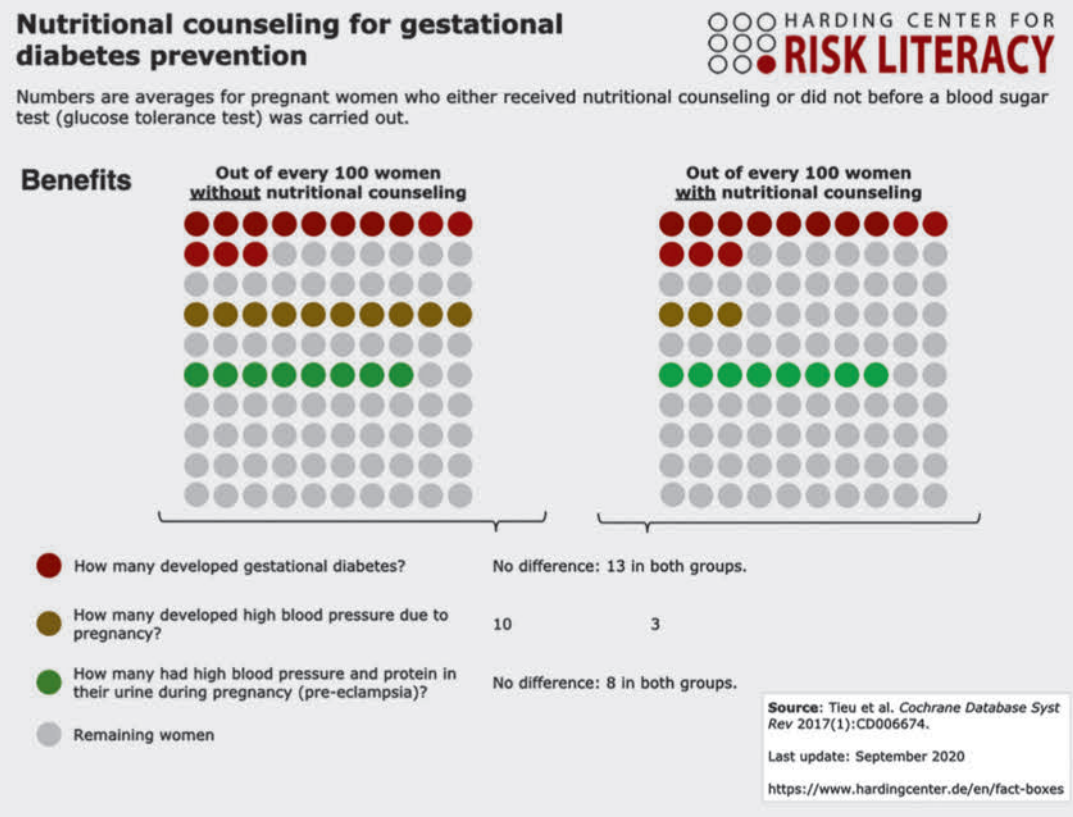
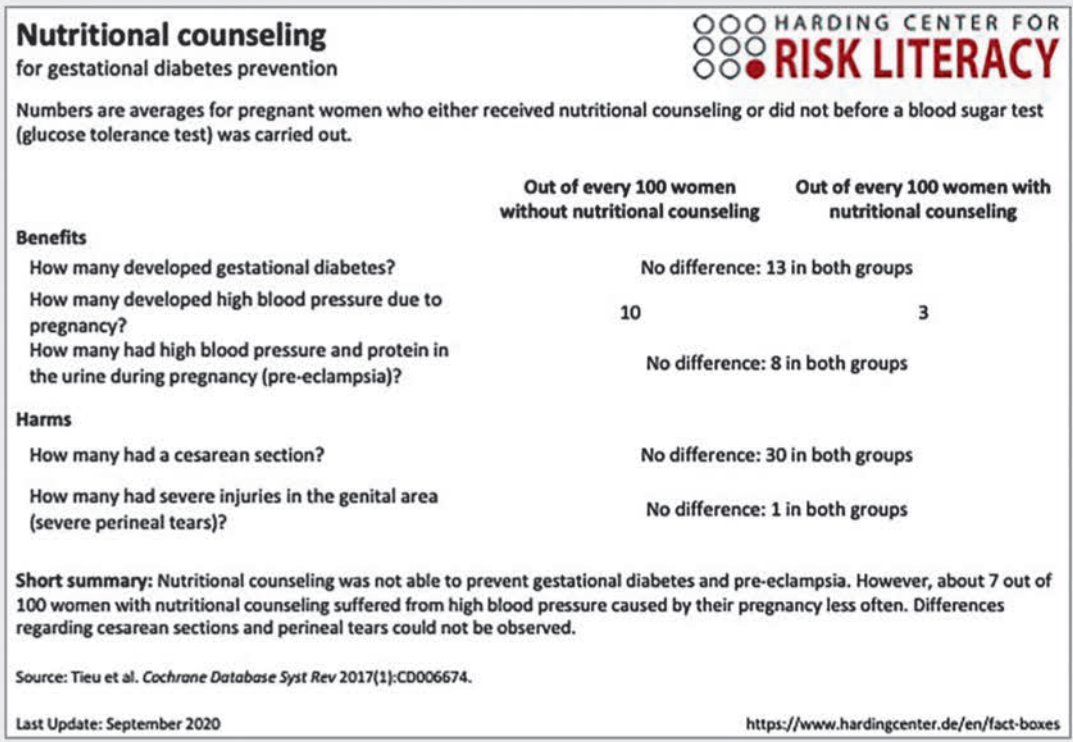
Pharmacological interventions

Although we did not systematically include pharmacological SRs, some SRs about lifestyle compared the interventions with patients where medication was administered. In general, metformin in obese women was involved [80], myo-inositol [64, 81] and probiotics [64, 82]. Pregnant women should not use metformin to prevent GDM or poor pregnancy outcomes in obese non-diabetic women. In contrast, in women who are already diagnosed with GDM, metformin reduces PIH as compared with other treatments or placebo [83]. Four RCTs on antenatal supplementation with myo-inositol during pregnancy showed a potential benefit to reduce GDM, whereas a network meta-analysis summarized that inositol supplementation did not significantly alter GDM risk. There were no differences in PIH, macrosomia or perinatal mortality when compared with controls. Up to now, only one RCT within our investigated SRs showed a decrease in GDM when women used probiotics [82].

Discussion and Conclusion

Several RCTs have shown that fact boxes and icon arrays are effective tools for informing laypeople. They can improve the understanding of statistical data and of benefits and harms. Although we already suggested the use of fact boxes, albeit not in combination with icon arrays [84, 85], unfortunately, these tools have not yet been integrated into maternal-fetal medicine. Fact boxes and icon arrays could supplement the state-of-the-art within guidelines for parents who must make decisions for or against screening tools, invasive procedures, medical treatments or the place of birth and support women in their decisions not biased by false incentives [86].

The strength of this umbrella review is to evoke awareness towards the increasing number and various quality of retrospective SRs and meta-analyses. Shennan et al. indirectly criticized a lack of consistent primary evidence and the heterogeneity in so-called network meta-analyses in different populations and healthcare systems [87]. Similarly, Prior characterized meta-analyses with a selection bias due to absent or delayed registration of the protocol or non-consistent outcome as "p-hacking" [88]. Another potential error is to apply Cochrane tools for RCTs which contain an item of *blinding participants and health care providers*. This item is of limited



► Fig. 2 Fact box combined with an icon array designed to communicate the main benefits and harms of nutritional counselling for pregnant women to prevent gestational diabetes based on the Cochrane Review by Tieu et al. [38] (Source: Creation by C. Ellermann on behalf of Harding Center for Risk Literacy based on data by Tieu et al. 2017 [38]).

value for lifestyle interventions since neither counselling of health care specialists nor women following lifestyle interventions can be blinded [89].

Limitations of this umbrella review are that among all retrospective SRs, only 2/36 were designed as an individual participant data meta-analysis [36, 63]. Not all studies applied a sensitivity analysis. In addition, it has not yet been shown that fact boxes improve the understanding of parents-to-be and the dialogue between pregnant patients and their healthcare providers as demonstrated for other fields [90, 91]. Therefore, we are currently examining the acceptance in different social and patient groups.

We consciously concentrated on lifestyle interventions because, during pregnancy, women play an active part in the health outcomes of themselves and their offspring. Pregnant women are more sensitive to advice and particularly often in contact with the medical system.

In the future, *prospective* meta-analyses and Delphi procedures as already performed for GDM [92] may avoid weaknesses of retrospective SRs and improve the sources for counselling.

Ideally, interventions should be continued after birth and similarly, long-term outcomes of mothers and their children should be evaluated. As preconceptional BMI is associated with an increase in pregnancy complications, it is recommended to control and possibly reduce body weight before pregnancy [93]. An inter-generational approach to address childhood adiposity should start preconceptionally and continue until early childhood or even puberty [94]. Improved health literacy obtained during pregnancy may help mothers maintain a healthier lifestyle and improve the health of their offspring. Increased awareness and compliance towards evidence-based counselling may hopefully improve compliance and outcomes of mothers and their offspring.

In the meantime, editorial boards should critically analyze the “tsunamis” of SRs and meta-analyses, so that only the best evidence is translated into patient counselling. It is often difficult to retrospectively determine how the interventions were integrated into the daily routine. To motivate patients intellectual models may be helpful, but possibly it is even more important that health care providers show empathy with their patients which cannot be analyzed from studies.

Specified practices to increase health literacy of pregnant women in low and high-income countries and different socioeconomic populations should become part of medical education and would possibly reduce costs and increase satisfaction and the health of societies as in the “Triple Aim” model [95]. Our proposals may be a small step to interrupt vicious circles of the obesity epidemic.

Contributors' Statement

SB performed the literature search, analyzed the quality of the systematic reviews applying ROBIS and AMSTAR criteria and wrote the manuscript. BA designed the manuscript and essentially contributed to the writing. All authors have studied and revised the manuscript.

Acknowledgement

We thank Christin Ellermann and Mirjam Jenny for designing the fact box and icon array. Furthermore, we thank Prof. Gerd Gigerenzer and Dr. Jens Stupin for their inspiration and support.

Conflict of Interest

The authors declare that they have no conflict of interest.

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