Immunomodulatory Protein Hydrolysates and Their Application
Review

Attenuating Pregnancy Weight Gain—What Works and Why: A Systematic Review and Meta-Analysis

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Abstract: Excessive maternal gestational weight gain (GWG) contributes to generational obesity. Our aim was to explore efficacy and intervention characteristics (trimester, duration, frequency, intensity, and delivery method) of interventions to prevent excessive GWG. CINAHL, Cochrane, EMBASE, LILACS, MEDLINE, PsycINFO, and Scopus were searched up to May 2018 (no date or language restrictions). Keywords and MeSH terms for diet, GWG, intervention, lifestyle, maternal, physical activity, and pregnancy were used to locate randomized-controlled trials (RCTs). The Cochrane Collaboration tool for assessing risk of bias was applied. Eighty-nine RCTs were included. Meta-analysis (60 trials) estimated that women in diet only (WMD: −3.27; 95% CI: −4.96, −1.58, p < 0.01), physical activity (PA) (WMD: −1.02; 95% CI: −1.56, −0.49, p < 0.01), and lifestyle interventions (combining diet and PA) (WMD: −0.84; 95% CI: −1.29, −0.39, p < 0.01) gained significantly less weight than controls. The three eHealth interventions favored neither intervention nor control (WMD: −1.06; 95% CI: −2.00, 0.94, p = 0.50). Meta-regression demonstrated no optimal duration, frequency, intensity, setting, or diet type. Traditional face to face delivery of weight management interventions during pregnancy can be successful. Delivery via eHealth has potential to extend its reach to younger women but needs further evaluation of its success.

Keywords: interventions; gestational weight gain; pregnancy; maternal; lifestyle; physical activity; diet

1. Introduction

Excessive maternal gestational weight gain (GWG) contributes to the global obesity epidemic and is a serious public health concern [1,2]. Criteria set by the United States’ Institute of Medicine (IOM) in 2009 [3], which are based on maternal pre-conception body mass index (BMI), have been adopted to define optimal GWG, with recommended GWG being lower for those of a higher BMI than for their thinner counterparts. Approximately 40–70% of women gain in excess of the IOM recommendations [2,4–6] with those most at-risk being already overweight or obese at conception [5]. The generational impact of obesity continues as those who experience excessive GWG are more likely to retain weight post-partum, enter subsequent pregnancies in a higher weight category [7,8], and their
offspring are more likely to become overweight or obese [8–11]. Excessive GWG increases the risk of pregnancy complications such as gestational diabetes mellitus (GDM) [12] and hypertension [13] and infants are at a greater risk of being large for gestational age (LGA) (weight > 90th percentile), delivered by caesarean section [10,14,15], or experience birth trauma [10,16]. Additionally, a mother’s nutrition, lifestyle, and weight-gain during pregnancy impacts on fetal gene expression in utero and creates a ‘health blue-print’ that determines a child’s predisposition to chronic disease later in life [1,17].

There is no doubt that innovative and cost-effective interventions that prevent excessive GWG are required at the community level [15], particularly for women who are already overweight or obese [18,19]. Previous systematic reviews have proved effectiveness of lifestyle interventions based on altering diet and/or physical activity (PA) in clinical and community settings [19–25], but the heterogeneity of interventions, small sample sizes, and inconsistent results between women of different weight categories has made it impossible to define what makes an “ideal” intervention [20,26]. Interventions that are proven effective in clinical trials generally fail to be translated effectively into the real world [27]. Emerging use of innovative eHealth models that deliver information through the Internet or related technology [28] may assist in the engagement of younger women [29,30], but it is unknown whether addressing other lifestyle factors such as sleep may be helpful additive strategies. To date, there is no systematic review of all randomized-controlled trials (RCTs) aimed at preventing GWG that include all potentially modifiable lifestyle behaviors (including sleep) and medical interventions or using eHealth. Furthermore, individual components of interventions, such as duration and frequency, have not been evaluated in order to provide insight into specific characteristics that are more likely to result in success [26,31]. The aims of this systematic review and meta-analyses were to address these gaps by comparing the efficacy of all approaches that have been used to prevent excessive GWG (e.g., diet, PA, lifestyle, sleep, eHealth, and medical) and to further describe and explore characteristics that can be analyzed across intervention types such as, when they commenced (trimester), duration (weeks), frequency (occasions of contact with those delivering the intervention), intensity (hours), and delivery method (individual, group, or mixed). This knowledge would enable practitioners to have a tool box of ‘best bets’ in terms of what works that they can apply directly into practice settings.

2. Materials and Methods

The review protocol was developed using the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines and registered on 29 February 2016 on the PROSPERO database for systematic reviews (PROSPERO 2016:CRD42016035907). This review reports on the primary outcomes only. The secondary outcomes are reported elsewhere [32].

2.1. Sources

A systematic search was conducted in April 2016 and updated in May 2018 by two independent reviewers. Electronic databases were MEDLINE, EMBASE, Cochrane Library, PsycINFO, CINAHL, Scopus, and LILACS. The search strategy (Table S1) of keywords and MeSH terms was adapted to each database. Keywords were searched as free text in title, heading, and subheading with no date or language limits. Additional publications were identified from searching reference lists of included trials and systematic reviews.

2.2. Study Selection

The search located RCTs of all interventions designed to prevent excessive GWG. Interventions that had GWG as a secondary outcome were also included. Comparators were standard care, an alternate intervention, or placebo. Participants were women of all ages, ethnicities, and pre-pregnancy weight status with singleton pregnancies. Studies specifically designed for women with pre-existing diabetes (type 1 or type 2) or GDM were not included due to the variation in their nutritional and medication requirements.
Following the removal of duplicates, two reviewers independently assessed each study for eligibility based on title and abstract. Eligible studies were reviewed in full text and subjected to a second assessment for inclusion by two reviewers. Discrepancies were resolved by a third independent reviewer. If there were multiple reports of a single study, the publication that reported GWG as a primary outcome was included.

Mean GWG (kg) with standard deviation for intervention and control groups, characteristics of participants and the interventions (when they commenced, duration, frequency, intensity, and setting) were extracted from each study. Missing information was sought from primary authors.

2.3. Assessment of Risk of Bias in Included Studies

The Cochrane Collaboration tool for assessing risk of bias [33] was used to evaluate seven domains: random sequence allocation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; selective reporting; other bias. Bias was classified as being “low risk”, “high risk”, or “unclear” according to predetermined criteria set by the Cochrane Collaboration [33]. Two reviewers per paper independently assessed the risk of bias with discrepancies resolved through discussion or the input of a third reviewer. All studies were included in the initial analyses; however studies identified as being “high risk” were removed from the sensitivity analyses.

2.4. Statistical Analyses

Studies were categorized into one of five groups: (i) diet, (ii) PA, (iii) lifestyle (a combination of PA and diet), (iv) eHealth, and (v) other (interventions specifically targeting adolescents, drug-based interventions, and interventions that could not be classified into any of the groups). Consistent with previous systematic reviews where interventions aimed at preventing excessive GWG types were classified into groups [20,22]. Despite eHealth interventions incorporating aspects of diet and PA, they were treated as a separate group because of their unique delivery characteristics and in an effort to keep heterogeneity within groups to a minimum. Meta-analyses were only possible for certain groups and were conducted for diet, PA, lifestyle, and eHealth interventions. Meta-analysis was not possible for studies classified as ‘other’ because of the vast differences between their designs. Studies were excluded from the meta-analyses for no true control [34–44] or insufficient data [45–52]. Due to different definitions and measurements for GWG, GWG was classified into sub groups (i) >24 weeks, (ii) 12–24 weeks, and (iii) <12 weeks.

High degrees of heterogeneity were expected among studies so the DerSimonian and Laird [53] approach for random-effects models was used to compute weighted mean differences (WMD) (the pooled average difference based on the size/weight of each trial) and 95% confidence intervals (CI). Heterogeneity was evaluated using the I² statistic. Funnel plots with Egger’s test were used as a visual aid to detect publication bias [33,53,54]. Sensitivity analyses were conducted to investigate the influence of a single study on the overall analyses.

Meta-regressions used six study characteristics as covariates to explain the heterogeneity between studies and explore whether study characteristics had a relationship with the effect sizes [55]. Study characteristics were based on a previous review [56] and included (i) the trimester in which the intervention commenced, (ii) duration (weeks—if a range the longest duration was used), (iii) frequency (one to three, four to eight, and >eight occasions of contact), (iv) intensity (<four, four to eight, and >eight hours of contact over the intervention), (v) delivery method (individual, group, and combination), (iv) diet (healthy eating advice, low-glycemic index (GI), calorie restricted, and pro-biotic).

In order to further compare the characteristics of interventions, studies were classified as being either effective or ineffective. This assessment was made by a relatively crude assessment of GWG results. Studies were classified as being effective if the intervention group had significantly less overall or weekly GWG than the control (p < 0.05). While this is not an ideal measure, this method has been used in previous systematic reviews [56–58]. The Chi-square test for independence was used to
compare the characteristics of effective and ineffective studies with a statistically significant difference defined as \( p < 0.05 \). All meta-analyses and meta-regression were carried out using Stata 12 statistical software [59].

3. Results

Data were extracted from 89 published RCTs that included 25,345 women (Figure 1). Studies reported on singleton pregnancies in women of all BMIs \((n = 51)\), healthy weight only \((n = 3)\), healthy weight and overweight \((n = 1)\), overweight and obese only \((n = 21)\), or obese only \((n = 13)\). Studies were carried out in samples of women from 24 countries the United States \((n = 22)\), Australia \((n = 11)\), Spain \((n = 10)\), and Italy \((n = 5)\) being most highly represented. Studies did not consistently report exclusion criteria for age, but those that did tended to exclude women >45 years, nor did they consistently report on baseline characteristics for SES or ethnicity. No study focused on optimizing sleep quality or duration in order to prevent excessive GWG.

### 3.1. Diet Interventions

Sixteen diet only studies reported a total of 3681 participants (Table S2). Four interventions delivered basic healthy eating advice [46,47,60,61], four were based on a low-GI diet [36,38,44,62], and six involved calorie-restriction [37,63–67]. Ilmonen et al. [68] delivered dietary advice with a probiotic and Bosauxes et al. [51] advised women to increase their fish intake in addition to general dietary advice. All studies commenced in the first or second trimester, had varying degrees of intensity and frequency and were delivered to women individually except for Walsh et al. [62] who delivered their intervention to both individuals and groups (Table S3). Nine diet interventions [60–68] were included in the meta-analyses (Table 1) (Figure S1). McCarthy et al. [61] did not report overall GWG for the entire intervention and control groups, therefore the GWG for sub-groups and their controls were used instead. The meta-analysis showed that dietary interventions were more effective than the control groups (WMD: \(-3.27\); 95% CI: \(-4.96, -1.58\), \(p < 0.01\); \(I^2 = 92.8\%\)). Meta-regression revealed none of the study characteristics significantly influenced the pooled effect size (Table 2).
Table 1. Random-effects meta-analyses for diet, physical activity, lifestyle, and eHealth interventions (WMD and 95% CI). (Figures of meta-analyses are Supplementary Figures S1–S4).

<table>
<thead>
<tr>
<th>Sub-Group and Overall</th>
<th>Studies a</th>
<th>Participants</th>
<th>Overall Effect Size WMD (95% CI)</th>
<th>p Value</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet</td>
<td>Overall: Measurement GWG &gt; 24 weeks</td>
<td>9</td>
<td>2049</td>
<td>−3.27 (−4.96, −1.58)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Measurement GWG 12–24 weeks</td>
<td>3</td>
<td>250</td>
<td>−0.83 (−3.55, 1.90)</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>Measurement GWG &gt; 24 weeks</td>
<td>21</td>
<td>4651</td>
<td>−1.02 (−1.56, −0.47)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td></td>
<td>Overall</td>
<td>24</td>
<td>4901</td>
<td>−1.02 (−1.56, −0.49)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>Measurement GWG 12–24 weeks</td>
<td>5</td>
<td>2908</td>
<td>−0.67 (−1.58, 0.23)</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>Measurement GWG &gt; 24 weeks</td>
<td>19</td>
<td>4471</td>
<td>−0.92 (−1.48, −0.36)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td></td>
<td>Overall</td>
<td>24</td>
<td>7379</td>
<td>−0.84 (−1.29, −0.39)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>eHealth</td>
<td>Overall: Measurement GWG &gt; 24 weeks</td>
<td>3</td>
<td>192</td>
<td>−1.06 (−4.13, 2.00)</td>
<td>0.50</td>
</tr>
</tbody>
</table>

* Some studies included sub-groups as no overall GWG was reported.

Table 2. Meta-regression of characteristics of diet and lifestyle interventions designed to prevent excessive GWG.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Diet (10 Observations)</th>
<th>PA (25 Observations) I² = 82.0%</th>
<th>Lifestyle (27 Observations) I² = 71.0%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=</td>
<td>β</td>
<td>95% CI</td>
</tr>
<tr>
<td>Trimester</td>
<td>9</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td></td>
<td>Ref</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>−4.61, 5.32</td>
<td>0.87</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Intensity</td>
<td>10</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td>1–4 h</td>
<td>5</td>
<td>−1.08</td>
<td>−7.43, 5.28</td>
</tr>
<tr>
<td>&gt;4–8 h</td>
<td>2</td>
<td>−0.71</td>
<td>−5.04, 6.46</td>
</tr>
<tr>
<td>≥8 times</td>
<td>4</td>
<td></td>
<td>Ref</td>
</tr>
<tr>
<td>Frequency</td>
<td>10</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>1–3 times</td>
<td>5</td>
<td>−1.92</td>
<td>−10.18, 6.33</td>
</tr>
<tr>
<td>4–7 times</td>
<td>1</td>
<td></td>
<td>Ref</td>
</tr>
<tr>
<td>≥8 times</td>
<td>4</td>
<td>−0.46</td>
<td>−4.73, 5.65</td>
</tr>
</tbody>
</table>
Table 2. Cont.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Diet (10 Observations)</th>
<th>PA (25 Observations) $I^2 = 82.0%$</th>
<th>Lifestyle (27 Observations) $I^2 = 71.0%$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n=\beta$ 95% CI $p$</td>
<td>$n=\beta$ 95% CI $p$</td>
<td>$n=\beta$ 95% CI $p$</td>
</tr>
<tr>
<td>Setting</td>
<td>10 20</td>
<td>20 20</td>
<td>27</td>
</tr>
<tr>
<td>Individual</td>
<td>9 20</td>
<td>7 20</td>
<td>19</td>
</tr>
<tr>
<td>Group</td>
<td>0 NA NA NA 11</td>
<td>11 −0.62 −1.56, 0.31 0.18</td>
<td>8 −1.09 −2.28, 0.09 0.07</td>
</tr>
<tr>
<td>Mixed</td>
<td>1 2.01 −5.17, 9.20 0.54</td>
<td>2 −1.99 −3.45, −0.52 0.01</td>
<td>0 NA NA NA NA</td>
</tr>
<tr>
<td>Duration</td>
<td>9 25</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>Reference</td>
<td>9 Ref</td>
<td>9 Ref</td>
<td>27 Ref</td>
</tr>
<tr>
<td>Type</td>
<td>10</td>
<td>3 Ref</td>
<td>5 Ref</td>
</tr>
<tr>
<td>General</td>
<td>3 Ref</td>
<td>3 Ref</td>
<td>3 Ref</td>
</tr>
<tr>
<td>Low-GI</td>
<td>1 −0.06 −8.59, 8.48 0.99</td>
<td>1 −0.06 −8.59, 8.48 0.99</td>
<td>1 −0.06 −8.59, 8.48 0.99</td>
</tr>
<tr>
<td>KJ restriction</td>
<td>5 −3.20 −8.81, 2.42 0.21</td>
<td>5 −3.20 −8.81, 2.42 0.21</td>
<td>5 −3.20 −8.81, 2.42 0.21</td>
</tr>
<tr>
<td>Probiotic</td>
<td>1 −2.56 −11.32, 6.21 0.50</td>
<td>1 −2.56 −11.32, 6.21 0.50</td>
<td>1 −2.56 −11.32, 6.21 0.50</td>
</tr>
</tbody>
</table>

Note: Observations, not studies (some studies were analyzed as sub-groups). Characteristics unknown for some studies. Abbreviations: NA = none of the studies in that intervention type displayed this characteristic. Ref: Reference group.
3.2. Physical Activity

Twenty-seven PA only studies reported on 5725 participants (Table S4). The PA prescriptions included light to moderate aerobic, muscle strength, toning, and flexibility exercises, or dancing, walking, or aquatics. Nine studies had relatively long durations (≥30 weeks), 24 had high levels of frequency and intensity in comparison with diet and lifestyle interventions, and most described interventions with an opportunity for women to have 80–85 occasions of contact (Table S3). Twenty-four PA interventions [69–92] were included in the meta-analyses (Table 1) (Figure S2). Meta-analysis showed that women in PA interventions gained significantly less weight than those in the control groups (WMD: −1.02; 95% CI: −1.56, −0.49, p < 0.01; I² = 81.9%). Intervention effectiveness was significantly higher in studies that combined individual and group-delivery of interventions, compared with studies that were delivered to individuals only or groups only (Table 2).

3.3. Lifestyle Interventions (Combining Both Diet and PA), Delivered Face-to-Face

Thirty-three lifestyle studies reported on 9201 participants (Table S5). Key aspects of interventions were general healthy eating advice, 30–60 min of PA on most days, and self-monitoring. Most lifestyle interventions had a duration of 13–29 weeks with varying frequencies and intensities (Table S3). Twenty-four lifestyle interventions [93–116] were included in the meta-analyses (Table 1) (Figure S3). Four studies [94,95,102] did not report overall GWG for the entire intervention and control groups, therefore the GWG for weight sub-categories based on BMI were used. Bogaerts et al. [104] and Guelinckx et al. [99] included two intervention groups with one control group. For these studies, the more intensive intervention (lifestyle advice and a brochure) was chosen for meta-analysis. Results from the meta-analysis favored LS interventions over comparators (WMD: −0.84; 95% CI: −1.29, −0.39, p < 0.01; I² = 71.0%). Meta-regression revealed no significant differences across studies observed by any study characteristic (Table 2).

3.4. eHealth Interventions

Five studies reporting on 2168 women incorporated aspects of information technology, eHealth or mHealth (use of mobile device) (Table S6). Herring et al. [117] and Willcox et al. [118] provided regular health coaching regarding lifestyle, physical activity, and GWG to women via Facebook, text-messaging and/or a website, booklets, and phone-calls. Olsen et al. [119] and Smith et al. [120] based their interventions on websites and Jackson et al. [121] described an intervention that added ‘Video Doctor’ counseling in addition to their routine antenatal care (Table S3). Three eHealth interventions [117,118,120] were included in a meta-analysis which favored neither intervention nor control (WMD: −1.06; 95% CI: −4.13, 2.00, p = 0.50; I² = 73.6%) (Table 1) (Figure S4).

3.5. ‘Other’ Interventions

Eight studies reporting on 1906 women were classified as “other” (Table S7). Four interventions were based on regular weighing [30,122–124] however, only Quinlivan et al. [124], incorporating continuity of care and dietary counseling reported a significant difference between intervention and control. Syngelaki et al. [29] compared metformin with placebo in pregnant women without GDM, Bechtel-Blackwell et al. [30] described an intervention designed for 46 African-American pregnant adolescents and Santamaria et al. [125] explored whether myo-inositol supplementation could decrease the incidence of GDM in women who were overweight. Herrera-Perdigon et al. [126] conducted a secondary analysis of an RCT in high-risk pregnancies where every second visit in usual physician-led care was substituted with home-based visits from advanced practice nurses. The characteristics of ‘other’ studies varied with only four [29,117,118,124] reporting significantly less GWG in the intervention groups (Table S3).
3.6. Effectiveness of Interventions According to Their Characteristics

Of the 89 studies included, 73 could be classified as being either effective (32 studies) or ineffective (41 studies) (Table 3). Studies could not be classified because of no overall p value to classify them as effective or ineffective [47,94,95,102,127] or not having a true control [34–44]. Interventions delivered to women individually were significantly more likely to be ineffective (ineffective 66.7%, effective 33.3%; χ² 4.43 p = 0.04). In contrast, when combining interventions delivered to groups and those delivered to individuals with a group component involved, a significantly larger proportion were effective (effective 62.5%, ineffective 37.35%; χ² 5.06 p = 0.02).

Table 3. Summary of the effectiveness of interventions according to characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Effective, p &lt; 0.05 (n = 32)</th>
<th>Ineffective, p &gt; 0.05 (n = 41)</th>
<th>Total a (n = 73)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Commenced (Trimester)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>12 (41.4)</td>
<td>17 (58.6)</td>
<td>29 0.73</td>
</tr>
<tr>
<td>2</td>
<td>18 (45.0)</td>
<td>22 (55.0)</td>
<td>40 0.83</td>
</tr>
<tr>
<td>3</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 -</td>
</tr>
<tr>
<td>Unsure</td>
<td>2 (50.0)</td>
<td>2 (50.0)</td>
<td>4 0.80</td>
</tr>
<tr>
<td>Duration (Weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>2 (66.7)</td>
<td>1 (33.3)</td>
<td>3 0.42</td>
</tr>
<tr>
<td>12–29</td>
<td>21 (40.4)</td>
<td>31 (59.6)</td>
<td>52 0.35</td>
</tr>
<tr>
<td>≥30</td>
<td>7 (50.0)</td>
<td>7 (50.0)</td>
<td>14 0.61</td>
</tr>
<tr>
<td>Unsure</td>
<td>2 (50.0)</td>
<td>2 (50.0)</td>
<td>4 0.80</td>
</tr>
<tr>
<td>Intensity (Hours)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>&lt;4</td>
<td>6 (33.3)</td>
<td>12 (66.7)</td>
<td>18 0.30</td>
</tr>
<tr>
<td>4–8</td>
<td>3 (37.5)</td>
<td>5 (62.5)</td>
<td>8 0.70</td>
</tr>
<tr>
<td>&gt;8</td>
<td>14 (43.8)</td>
<td>18 (56.3)</td>
<td>32 0.99</td>
</tr>
<tr>
<td>Unsure</td>
<td>9 (60.0)</td>
<td>6 (40.0)</td>
<td>15 0.16</td>
</tr>
<tr>
<td>Frequency (Contact)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3</td>
<td>4 (33.3)</td>
<td>8 (66.7)</td>
<td>12 0.42</td>
</tr>
<tr>
<td>4–7</td>
<td>4 (30.8)</td>
<td>9 (69.2)</td>
<td>13 0.30</td>
</tr>
<tr>
<td>≥8</td>
<td>19 (47.5)</td>
<td>21 (52.5)</td>
<td>40 0.49</td>
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<tr>
<td>Unsure</td>
<td>5 (62.5)</td>
<td>3 (37.5)</td>
<td>8 0.26</td>
</tr>
<tr>
<td>Delivery method</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Individual</td>
<td>14 (33.3)</td>
<td>28 (66.7)</td>
<td>42 0.04</td>
</tr>
<tr>
<td>Group b</td>
<td>15 (62.5)</td>
<td>9 (37.5)</td>
<td>24 0.02</td>
</tr>
<tr>
<td>Unsure</td>
<td>3 (42.9)</td>
<td>4 (51.7)</td>
<td>7 0.96</td>
</tr>
</tbody>
</table>

a No overall p value (or differing significance for sub-groups) and no control. b Combining interventions that involve group delivery and a combination of individual and group delivery.

3.7. Risk of Bias

A high risk of bias was allocated across domains and overall, 24% (n = 21) of interventions had a high risk of bias (Figure 2). Most studies had an unclear risk of bias for blinding participants, personnel, and outcomes as it was not possible to definitively assess whether minimal blinding inherent in dietary and lifestyle interventions impacted on outcomes. Studies were allocated either unclear or high for selective reporting as they did not have a published protocol, or they did not report on all outcomes. This was particularly true for older publications.
To explore whether the high level of asymmetry displayed in the funnel plots (Figures S5–S8) was due to publication bias, selective outcome reporting, and/or inadequate analysis in individual studies [128], studies with a high risk of bias were removed. There was slightly less asymmetry in the GDM and eHealth funnel plots only, a potential explanation being the considerable differences in characteristics (i.e., intensity) of studies included in each meta-analysis [128]. There were too few studies in the GDM and eHealth meta-analyses to differentiate between chance and true asymmetry [128].

![Risk of bias assessed using the Cochrane collaboration tool for assessing risk of bias.](image)

### 3.8. Sensitivity Analyses

The sensitivity analyses revealed that no single study introduced a large degree of bias to any of the meta-analyses. To explore whether the quality of studies, as rated by risk of bias, impacted on the meta-analyses, all studies with a high risk of bias were removed. This resulted in slight reductions in the heterogeneity of all meta-analyses except for diet and PA (Table S8). Results for LS interventions (WMD: $−0.73; 95\%\ CI: −1.17, −0.29, p < 0.01; I^2 = 65.7\%$) were tempered. In contrast, the WMD of eHealth interventions shifted to favor intervention (WMD: $−2.26; 95\%\ CI: −3.84, −0.69, p < 0.01; I^2 = 0.00\%$).

### 4. Discussion

This systematic review demonstrated that women exposed to interventions with a primary or secondary outcome of GWG gained less weight than control groups. This reaffirms that interventions aimed at preventing excessive GWG can be effective across a range of settings and population groups [19,20,22,24]. The evidence base regarding interventions that incorporate eHealth and information technology is small, however our findings highlight their potential to support women throughout pregnancy. Unique to this review is meta-regression that found there is no optimal duration, frequency, intensity, delivery method, or diet for interventions aiming to prevent excessive GWG, making it impossible to definitively describe a tool box of ‘best bets’ that can be applied directly into practice settings. Despite this, our synthesis of international literature provides valuable insights to guide clinical practice and the planning and implementation of future interventions that are tailored to meet the needs and expectations of women from a diverse range of cultures and social contexts.
Rogozinska et al. [31] used individual patient level data from 33 trials to report that women who undertook any type of intervention involving diet and/or PA during pregnancy could gain 0.7 kg less than those not exposed to an intervention. Their analysis consisted of mainly white (80%), high income participants of whom 40% were obese at the time of conception and/or reported no exercise at baseline. Shifting energy balance to favor weight-loss or weight maintenance by dietary restriction is far simpler than it is by expending energy via activity [129], especially in those who are not used to undertaking planned exercise, which requires substantial shifts in behavior. Knight and Foster [130], commenting on Rogozinska’s review, suggest that it supports the safety of current diet and PA recommendations but state that it provides little evidence of the benefit of ‘lifestyle’ interventions per se. This unidirectional outlook misses the long term impact that small shifts in dietary patterns towards those with greater nutrient density can have on future generations [17], especially in those who are already obese and have very sedentary lifestyles.

4.1. Dietary Interventions

The meta-analyses revealed the largest WMD in diet interventions, upholding that a diet-based approach is more effective than PA or lifestyle interventions [22]. Meta-regression suggested that the type of diet, whether it be low-GI, calorie restriction, or simple healthy eating advice was not a factor that influences the outcome, however, the small data-set included in this component of the analyses should be taken into consideration. The hypothesis that any type of healthy diet can be effective in preventing excessive GWG is supported by individual studies included in this review. Moses et al. [44] and Rhodes et al. [38] found no difference in GWG when comparing to different diet-types. It seems that any dietary improvement is better than doing nothing for the prevention of excessive GWG and simple dietary advice may be just as effective as time-consuming and labor-intensive personalized dietary regimens. Healthy eating should not be overlooked as a key pillar of antenatal care for all women, particularly when for the first time in history there are more people in the world who are overweight than underweight [131], and more than half of women enter pregnancy already overweight or obese [31,132].

4.2. Individual, Group or Mixed Delivery?

Meta-regression did not consistently distinguish between individual and group delivery of interventions with a combined approach appearing to be more effective in PA interventions only. Intervention groups in the two eHealth studies that used Facebook as part of a multifaceted approach [117,118] had significantly less GWG than controls. In contrast, intervention groups in eHealth interventions using websites or information technology with no opportunity for women to interact with each other did not gain significantly less weight than control groups. Comparison of intervention effectiveness according to characteristics (Table 3) found a significantly larger proportion of interventions that had a group element were effective than ineffective. This has important implications for future interventions and their translation in real-world settings. Interventions delivered to groups of women have the potential to reach a wider audience in communities at a lower cost [133,134]. There are also aspects of group-based interventions upon which value cannot be placed or measured. These include emotional and social support, peer-contribution to learning, affirmation, and a sense of ‘togetherness’ that increases women’s motivation to achieve their health goals [134]. It should be emphasized that interventions are likely to have a greater impact on population incidence of overweight and obesity if sub-groups most at-risk for excessive GWG, such as women who are already overweight and obese, low socioeconomic status (SES), and certain ethnic minorities are targeted [133].

4.3. Intensity and Frequency of Interventions

Neither the frequency nor intensity of interventions aimed at preventing excessive GWG had a consistent influence on the overall effect size of interventions. There is accumulating evidence
from individual trials suggesting that interventions with low levels of intensity and frequency can be successful. The HeLP-her cluster RCT [135] found that weight gain could be prevented in women living in metropolitan Australia, with a low intensity and frequency intervention. These findings were replicated when carried out in rural settings in Australia [136]. When the HeLP-her methodology was applied in a pregnant population at risk of GDM, it resulted in significantly less weight gain in the intervention group compared with the control [105]. This synthesis is important as it suggests that intensive and costly interventions are not essential in order to prevent excessive GWG. In the future, well-designed interventions aimed at preventing excessive GWG should include a standardized cost-effectiveness analysis so that this theory can be investigated further.

4.4. Trimester and Duration of Interventions

Excessive GWG in the first trimester (in excess of 0.5–2 kg) [3] is predictive of excessive GWG throughout pregnancy [137], maternal hyperglycemia [138], and the development of GDM [18]. Therefore, preventing excessive GWG in early pregnancy is important for preventing pregnancy complications and excessive GWG overall [18,137]. This is problematic, considering that a woman’s first antenatal check-up may not occur until well into the first trimester and half of pregnancies are unplanned [139]. Therefore, public health campaigns regarding optimal nutrition and lifestyle targeted to all women of childbearing age plans are required [140]. When considering that women tend to gain approximately 500 g–1 kg per year from their early 20s until middle-age [141], such campaigns would be of benefit to all women and not just those planning pregnancy.

4.5. Future Directions

Increased prevalence of being overweight or obese at conception and excessive GWG have ignited the debate regarding routine weighing by health professionals [142]. One side of the debate argues that there is ‘no point assessing weight gain if there is no way of influencing it’, [142], and that routine weighing may be a cause of unnecessary stress for women [143]. The other side argues that rates of excessive GWG are increasing and routine weighing by a health professional is a low-cost intervention that can be applied in established antenatal care settings [142,144]. Routine weighing by a health professional was a key component of four studies in this systematic review [30,122–124]. Interestingly, only one of these studies that also involved regular dietary counseling and continuity of care resulted in a significant difference in GWG between intervention and control [124]. An important aspect of antenatal care in relation to this issue is that pregnant women require appropriate information and advice and continuity of care in order to fully support weight management [124]. This is supported by recent qualitative research that has found that women want clear, consistent advice regarding weight management during pregnancy [145]. Barriers that hinder health professionals from providing this advice could be addressed, at least in part, by providing them with further training in how to initiate a conversation regarding GWG and then equipping them to provide consistent and patient-centered advice [139,146,147].

Potential assets for the prevention of excessive GWG that have been overlooked in many RCTs are established antenatal care models within the local context of intervention settings. Even simple conversations regarding weight management initiated by a health professional and integrated into routine antenatal care may be highly effective in preventing excessive GWG [26,148], not to mention adverse pregnancy outcomes associated with excessive GWG that were outside the scope of this study such as GDM [32], large for gestational age, macrosomia, and cesarean delivery [15]. Rather than developing expensive and intensive interventions as an adjunct to antenatal care, perhaps the focus should be supporting and refining pre-existing antenatal services that already receive government funding [26]. Incorporating aspects of eHealth (including mHealth) may facilitate health messages with a broader reach [149]. What makes interventions successful (or not) is rarely elucidated in RCTs, suggesting that alternate intervention designs that incorporate qualitative evaluation may be of value.
In terms of implications for practice, the earlier dietary or lifestyle changes are adopted for pregnancy, the better. We have confirmed that dietary improvement can be effective in attenuating GWG, however, we cannot describe the optimal ‘pregnancy diet’ based on our results. This is an important reminder that dietary advice should consider an individual’s preferences, budget, lifestyle, and food preparation skills [150,151]. The value of small “nudges” towards achievable dietary and lifestyle changes from trusted health professionals [139], and the potential benefits of offering advice in a group context where women may receive encouragement and support from peers [134] should not be underestimated. Put simply, doing something is better than doing nothing.

4.6. Strengths and Limitations

A strength of this review is its broad general applicability across populations and population sub-groups. This is because of a robust study design that included RCTs only, with no language or date limits, from seven international databases. It is also the first review of interventions aimed at preventing excessive GWG to analyze and report on which characteristics of interventions may be more likely to influence their success.

The high levels of heterogeneity ($I^2 > 75\%$) [152] in three of the five meta-analyses is a limiting factor, an issue associated with earlier reviews on the same topic [19,22,23]. Proactive steps were taken to address this in the design of this research, such as dividing interventions into five different meta-analyses and not including ‘other’ studies. A random-effects model for meta-analysis was deemed appropriate from the outset [53] and meta-regression was embedded into the design to determine the degree to which statistical heterogeneity can be attributed to covariates (study characteristics) [53]. There were very few studies within sub-groups for each meta-regression and therefore, caution should be taken when interpreting these data. Despite high levels of heterogeneity, our conclusion that interventions designed to prevent excessive GWG can be effective, and diet interventions are most effective, is consistent with previous research [22].

The analysis and interpretation of these data is further limited by the inconsistent outcome measures used for GWG. Using broad categories that cluster different measurements of GWG is not ideal, however, recent research has found using an early pregnancy weight (4–10 weeks gestation) is a reasonably accurate surrogate measure for pre-pregnancy BMI [153]. While this justifies the decision to cluster pre-pregnancy and early pregnancy measurements of GWG together, it does not justify clustering together interventions of a similar duration that began at different points of pregnancy where IOM recommendations for weekly GWG are different. Some studies did not specify how they calculated GWG, requiring reviewers to make assumptions based on baseline characteristics and overall GWG. In the future, these limitations could be mitigated if interventions clearly report a standard measure for GWG and other maternal and fetal outcomes [31]. The quality of studies must also be considered in the interpretation of results. Future studies should report measures taken to ensure blinding and all outcomes outlined in registered protocols which would allow greater detail to be provided of the actual content of the intervention.

This review highlights several key areas where future research is required regarding weight management in pregnancy. Interventions should adopt universal definitions and measurements for key outcomes such as GWG and GDM, as well as standardized cost-effectiveness analyses. In order to improve the quality of studies, measures should be taken to ensure blinding and that all outcomes are outlined in registered protocols.

Other methods of assessing intervention success may need to be explored, given the high levels of heterogeneity found within ‘like’ studies that have been frequently clustered together in meta-analyses [19,22]. There may be benefit in focusing on population sub-groups most at risk of excessive GWG, and apply findings by making specific recommendations for sub-groups rather than a ‘one size fits all’ approach. Attention should also be given to reporting change in diet quality to provide more insight into micronutrient status and also metabolic outcomes pertinent to PA interventions such as strength or aerobic fitness. Qualitative methods may be required to truly understand the context,
barriers, and enablers of interventions. Despite the lack of a universally accepted approach to weight management in pregnancy, it is clear that doing something is better than doing nothing. The timely translation of research into practice is crucial when considering that excessive GWG has emerged as a significant health issue for all women in low, middle, and high income countries [1,10,154].

5. Conclusions

This review found that interventions aimed at preventing excessive GWG can be successful, however, characteristics of interventions such as when they commence, their intensity, frequency, duration, or delivery methods are not predictors of success. This has important implications for designing future interventions that may reach more women with less expense. Refining pre-existing antenatal care models and/or incorporating some dietary aspects of all interventions could be cost-effective approaches. Some women may experience only a slight reduction in GWG as a result of the advice they receive during pregnancy. Despite this, healthy lifestyle behaviors, adopted at a time when women are highly motivated to make lifestyle changes and with the ongoing support of a health professional, have the potential to positively impact on families and households even after a child is born.

Supplementary Materials: The following are available online at http://www.mdpi.com/2072-6643/10/7/944/s1, Table S1: MEDLINE search strategy for interventions aimed at preventing excessive gestational weight gain (modified to suit other databases when necessary), Table S2: Description of diet interventions aimed at preventing excessive gestational weight gain, Table S3: The frequency of characteristics of all interventions aimed at preventing excessive gestational weight gain, Table S4: Description of physical activity interventions aimed at preventing excessive gestational weight gain, Table S5: Description of lifestyle interventions aimed at preventing excessive gestational weight gain, Table S6: Description of eHealth interventions aimed at preventing excessive gestational weight gain, Table S7: Description of “other” interventions aimed at preventing excessive gestational weight gain. Table S8: Meta-analyses (random-effect) of diet, physical activity, lifestyle and eHealth interventions. Studies with a high risk of bias removed. Figure S1: Meta-analysis (random-effect) of diet interventions aimed at preventing excessive gestational weight gain, Figure S2: Meta-analysis (random-effect) of physical activity interventions aimed at preventing excessive gestational weight gain, Figure S3: Meta-analysis (random-effect) of lifestyle interventions aimed at preventing excessive gestational weight gain, Figure S4: Meta-analysis (random-effect) of eHealth interventions aimed at preventing excessive gestational weight gain, Figure S5: Funnel-plot of meta-analysis (random-effect) of diet interventions aimed at preventing excessive gestational weight gain, Figure S6: Funnel-plot of meta-analysis (random-effect) of physical activity interventions aimed at preventing excessive gestational weight gain, Figure S7: Funnel-plot of meta-analysis (random-effect) of lifestyle interventions aimed at preventing excessive gestational weight gain, Figure S8: Funnel-plot of meta-analysis (random-effect) of eHealth interventions aimed at preventing excessive gestational weight gain.


Conflicts of Interest: The authors declare no conflicts of interest.

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