



Meeting 5

Pregnancy

Lead: Ken Powell

Members: Loretta DiPietro

Experts and Consultants



Consultant:

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Previous Work Group Questions

1. What is the relationship between physical activity and the health of the mother during pregnancy?
2. What is the relationship between physical activity and the health of the mother during postpartum (up to one year)?
3. What is the relationship between physical activity during pregnancy and the health of the child at birth?

NEW Work Group Questions



1. What is the relationship between physical activity and weight gain during pregnancy and weight loss during postpartum (up to one year)?
2. What is the relationship between physical activity and the incidence of gestational diabetes mellitus?
3. What is the relationship between physical activity and the incidence of preeclampsia and eclampsia?
4. What is the relationship between physical activity, affect, anxiety, and depression during pregnancy and postpartum (up to one year)?

Source of Search Results

- **Ageing** Q2. What is the relationship between physical activity and physical function?
- **Brain Health** Q2. What is the relationship between physical activity and quality of life?
- **Brain Health** Q3. What is the relationship between physical activity and (1) affect and (2) anxiety?
- **Brain Health** Q4. What is the relationship between physical activity and (1) sleep and (2) circadian rhythms?
- **Weight Management** Q1. What is the relationship between physical activity and prevention of weight gain?
- **Weight Management** Q2. In people with normal blood pressure or pre-hypertension, what is the relationship between physical activity and blood pressure?
 - **Supplementary search: preeclampsia and eclampsia**
- **Weight Management** Q3. In adults without diabetes, what is the relationship between physical activity and type 2 diabetes?
- **High-Quality Existing Reports**

Supplementary Search Terms

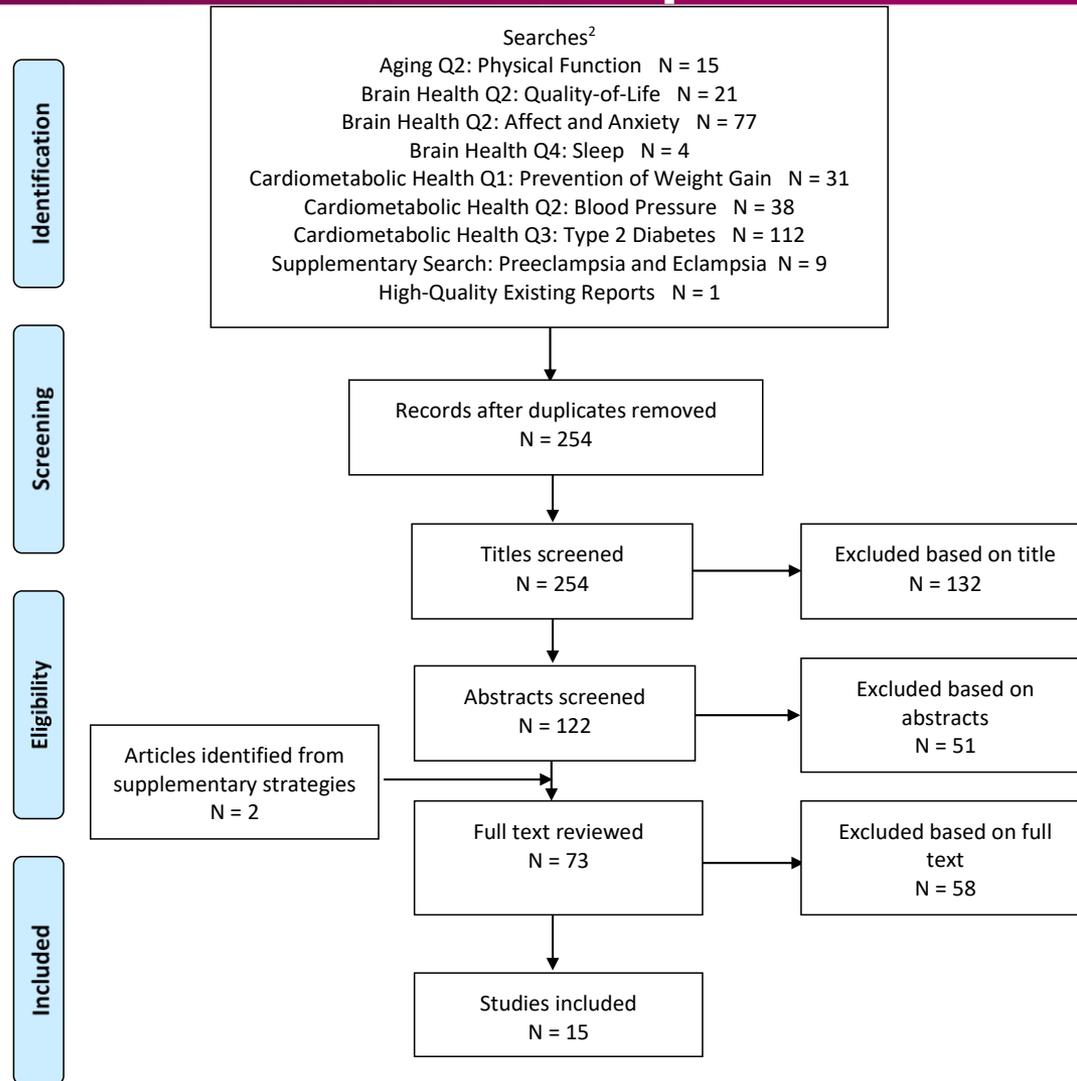
- Outcome Terms
 - Preeclampsia
 - Eclampsia
- Search Results
 - 9 Unique Results

Question 1

1. What is the relationship between physical activity and weight gain during pregnancy and weight loss during postpartum (up to one year)?
 - a) What dose of physical activity is associated with the reported quantitative benefit or risk?
 - b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - c) Does the relationship vary by age, race/ethnicity, socio-economic status, or weight status?

- Source of evidence to answer question:
 - SR and MA

Search Results: High-Quality Reviews¹ and Reports



¹ Reviews include systematic reviews, meta-analyses, and pooled analyses.

² The initial articles were identified by searching the titles and abstracts of each of the relevant searches' results for topics related to the Pregnancy Work Group using the terms "gestation," "pregn," "postp," "natal," and "maternal."

Description of the Evidence: Post-partum weight loss

- A total of 5 systematic reviews and/or meta-analyses (Adegboye, 2013; Berger, 2014; Elliott-Sale, 2017; Nascimento, 2014; Van der Pligt 2013) that included only 6 original research articles and a total of 287 study subjects have addressed the relationship between physical activity and *weight loss during post-partum*;
- None of the meta-analyses reported significant findings in either direction.

Draft Conclusion Statement: Post-partum Weight Loss

- Insufficient evidence is available to determine if there is a relationship between physical activity and weight loss during the post-partum period. **PAGAC Grade: Grade not assignable.**
- Insufficient evidence is available to determine what dose of physical activity is effective for weight loss during post-partum. **PAGAC Grade: Grade not assignable.**
- Insufficient evidence is available to determine whether there is a dose-response relationship between physical activity and weight loss during post-partum. **PAGAC Grade: Grade not assignable.**
- Insufficient evidence is available to determine whether the relationship between physical activity and weight loss during post-partum varies by age, race/ethnicity, socio-economic status, or weight status. **PAGAC Grade: Grade not assignable.**

Committee Discussion

1. What is the relationship between physical activity and weight gain during pregnancy and weight loss during postpartum (up to one year)?
 - a) What dose of physical activity is associated with the reported quantitative benefit or risk?
 - b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - c) Does the relationship vary by age, race/ethnicity, socio-economic status, or weight status?

Question 2

2. What is the relationship between physical activity and the incidence of gestational diabetes mellitus?
 - a) What dose of physical activity is associated with the reported quantitative benefit or risk?
 - b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - c) Does the relationship vary by age, race/ethnicity, socio-economic status, or weight status?
- Source of evidence to answer question:
 - SR and MA

Analytical Framework

Systematic Review Question

What is the relationship between physical activity and the incidence of gestational diabetes mellitus?

Target Population

Pregnant adolescents and women and post-partum mothers

Comparison

Pregnant adolescents and women and post-partum mothers who participate in varying levels of physical activity, including no reported physical activity

Intervention/Exposure

All types and intensities of physical activity including lifestyle activities, leisure activities, and sedentary behavior

Endpoint Health Outcomes

Gestational diabetes mellitus

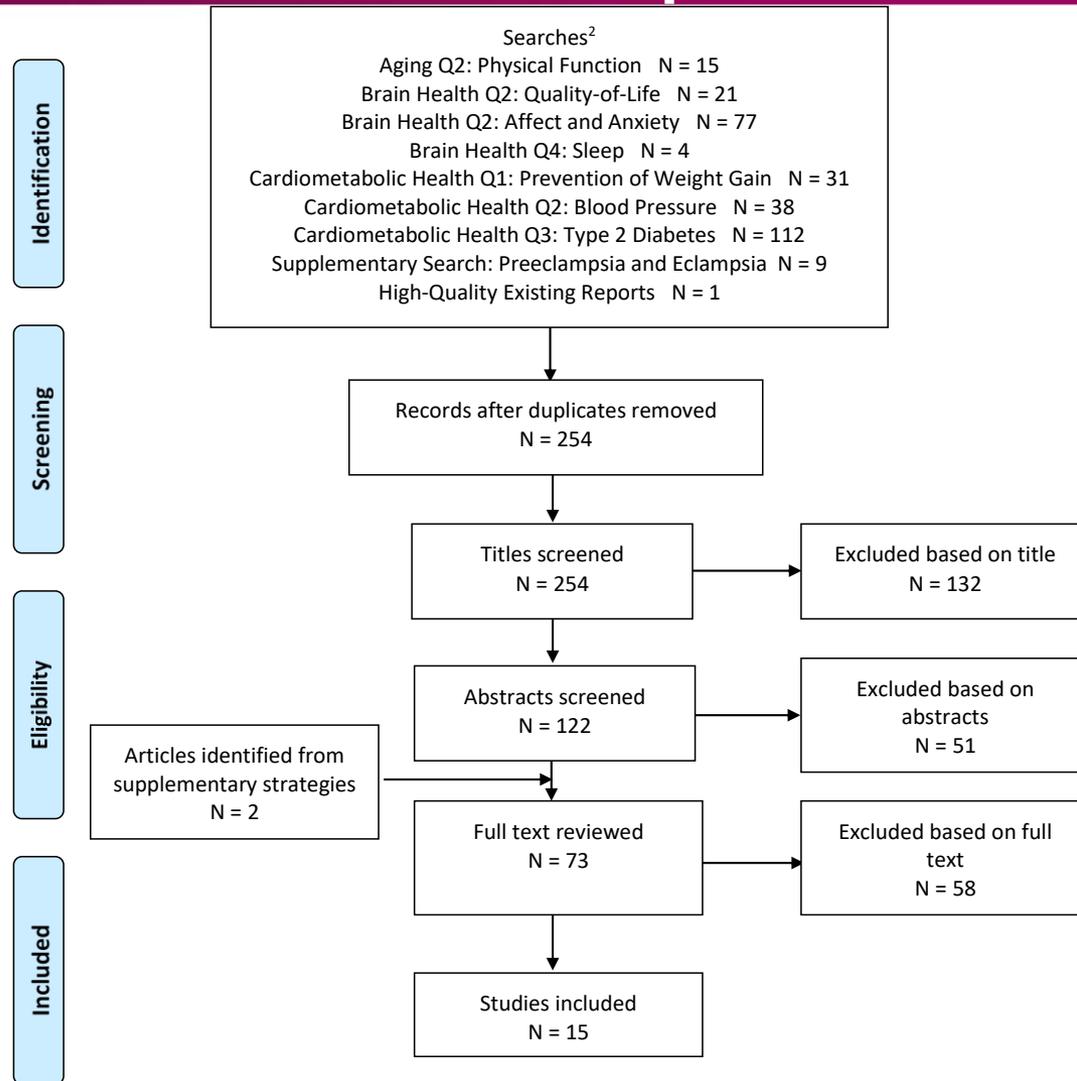
Key Definitions

Postpartum period: Date of birth through one year after birth

Inclusion/Exclusion Criteria

- Date of Publication
 - Original Research: Not included
 - Existing Sources: Include 2011 - Present
- Study Subjects
 - Include: Pregnant women, Postpartum mothers, and Children at birth
- Study Design
 - Include: Systematic reviews, Meta-analyses, Pooled analyses, PAGAC-Approved reports
 - Exclude: Original research, Narrative reviews, Commentaries, Editorials
- Exposure/Intervention
 - Include: All types and intensities of physical activity
 - Exclude: Missing physical activity, Therapeutic exercise, Single-acute sessions of physical activity, Physical fitness as the exposure, Physical activity only used as confounding variable
- Outcome
 - Include: **Gestational diabetes mellitus**

Search Results: High-Quality Reviews¹ and Reports



¹ Reviews include systematic reviews, meta-analyses, and pooled analyses.

² The initial articles were identified by searching the titles and abstracts of each of the relevant searches' results for topics related to the Pregnancy Work Group using the terms "gestation," "pregn," "postp," "natal," and "maternal."

Description of the Evidence: GDM

- A total of 15 systematic reviews and meta-analyses have addressed the relationship between physical activity and GDM.
- The number of studies included in each of the reviews ranged from 3 (Han 2012) to 41 (de Oliveira Dode, 2009) and comprised a mixture of randomized controlled trials (RCTs) and observational cohort studies.

Draft Key Findings- GDM

- 11 of the 15 systematic reviews/meta-analyses report a beneficial effect of physical activity performed before and/or during pregnancy on GDM, with risk reduction ranging between 20% and 55%;
- The median RR or OR from these 11 studies is 0.72;

Draft Key Findings- GDM: Meta-analyses

Author, year	Study Design	Effect (95% CI)
PRE-PREGNANCY PHYSICAL ACTIVITY		
Aune, 2016	Cohort (n=8)	sRR=0.78 (0.61, 1.00)
Tobias, 2011	Cohort/Cc (n=7)	pOR 0.45 (0.28, 0.75)
EARLY PREGNANCY PHYSICAL ACTIVITY		
Aune, 2016	Cohort (n=5) RCT (n=12) Combined (n=17)	sRR=0.97 (0.73, 1.28) sRR=0.69 (0.50, 0.96) sRR=0.80 (0.64, 1.00)
DaSilva, 2017	Cohort (n=6) RCT (n=10)	sOR=0.75 (0.55, 1.01) sOR=0.67 (0.49, 0.92)
DiMascio, 2016	RCT (n=4)	sRR=0.51 (0.31, 0.82)
Russo, 2015	RCT (n=10)	sRR=0.72 (0.58, 0.91)
Sanabria-M, 2015	RCT (n=8)	sRR=0.69 (0.52, 0.91)
Song, 2016	RCT (n=10)	sRR=0.77 (0.54, 1.09)
Tobias, 2011	Cohort/Cc (n=5)	pOR=0.76 (0.70, 0.83)
Yu, 2017/Zheng, 2017	RCT (n=5/n=4)	SMD=0.59 (0.39, 0.88)

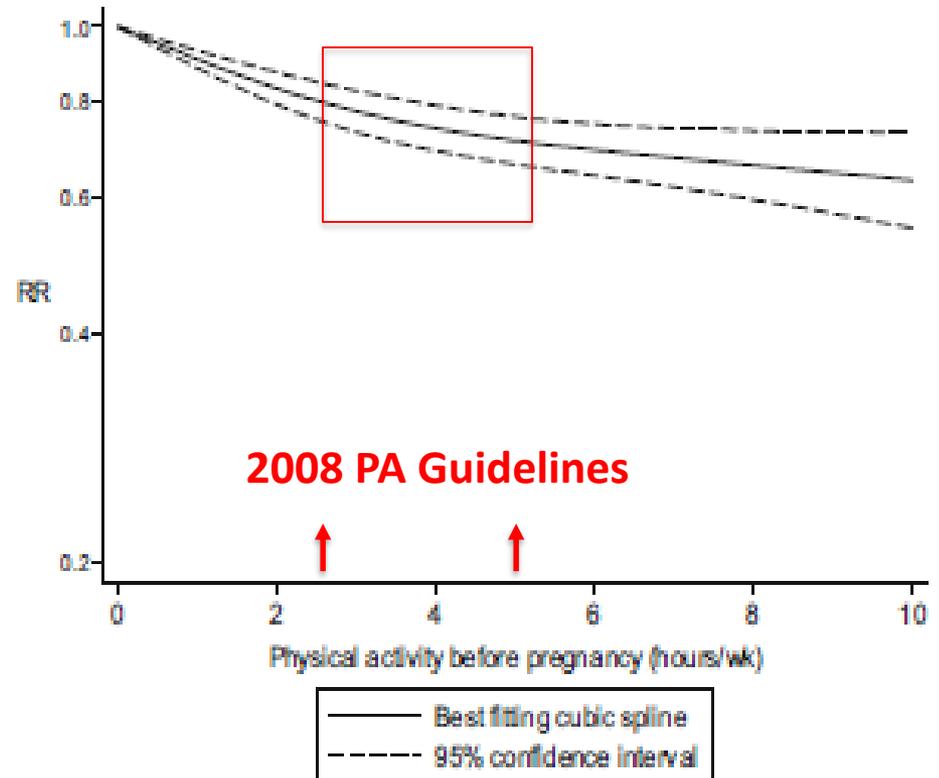
Draft Key Findings: GDM

Dose

- The dose of physical activity of physical activity prescribed in the RCTs varied among the studies. Similarly, the assessment and categorization of reported LTPA from observational studies was not detailed nor consistent;
- It appears, however, that most RCT interventions used an exercise regimen involving primarily aerobic activity of at least moderate-intensity (walking, cycling, swimming, aerobic dance), occurring at least 3 times per week for a duration of 30-60 min per bout;

Draft Key Findings: GDM Dose-Response

- Aune, et al., (2016) performed a dose-response analysis and reported that each 5 h/week increment in pre-pregnancy physical activity lowered the risk of GDM by about 30% (RR=0.70; 95 % CI: 0.49, 1.01; n=3);
- A similar relationship was not observed for physical activity performed during early pregnancy (RR=0.98; 95% CI: 0.87, 1.09; n=3);

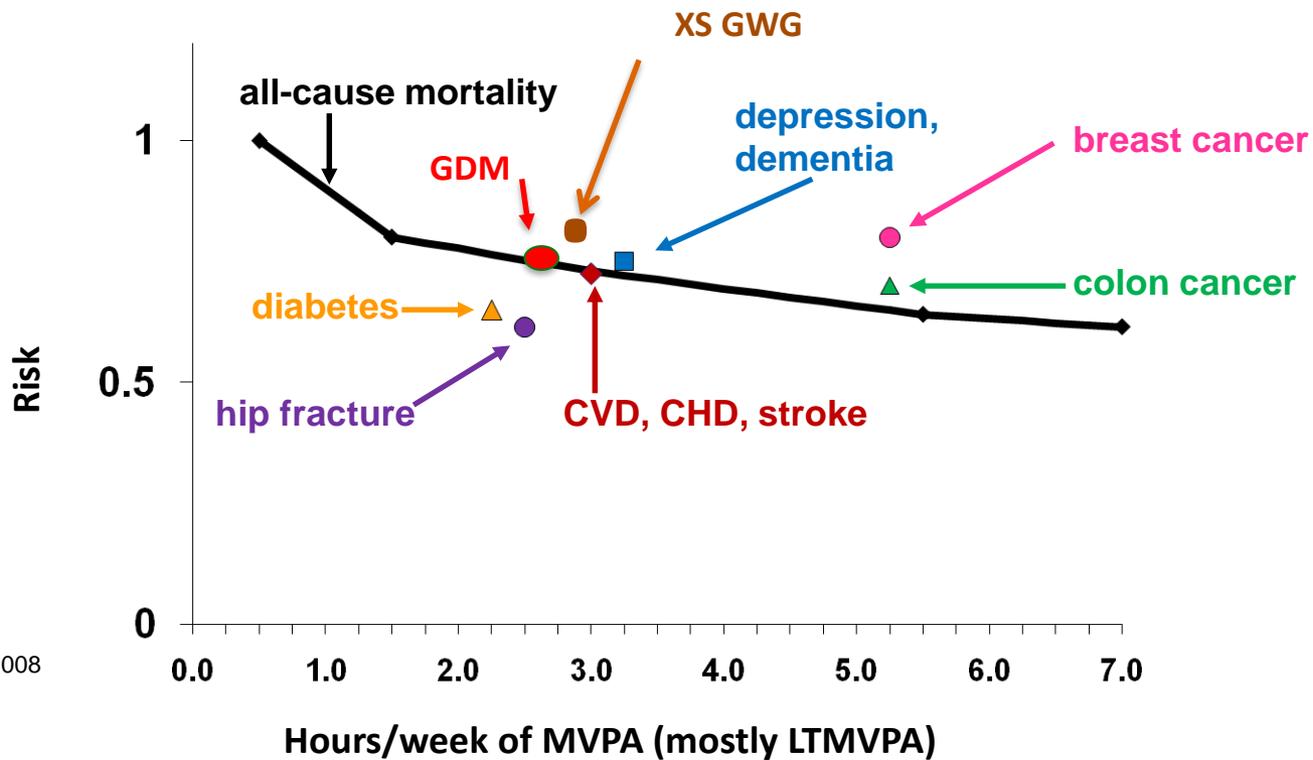


Aune D, et al., *Eur J Epidemiol.* 2016; 31:967-697.

Draft Key Findings: GDM Effect Modification

- Almost none of the systematic reviews or meta-analyses assessed whether the relationship between physical activity and GDM varied by age, race/ethnicity, or socio-economic status;
- The review by Song, et al., (2016) reported that physical activity during pregnancy had a significant impact on GDM risk in women ≥ 30 years, but not in women < 30 years old.

Dose and dose-response curves



Data from PAGAC Report 2008
Figure published in
Ann Rev Public Health
2011;32:349-365

Draft Conclusion Statements

- Strong evidence demonstrates a significant inverse relationship between LTPA and risk of GDM. **PAGAC Grade: Strong**
- Limited evidence suggests that a dose of physical activity similar to the 2008 U.S. Physical Activity Guidelines (150-180 min/week of moderate-intensity activity) is associated with a lower risk of GDM. **PAGAC Grade: Limited**
- Limited evidence suggests that there is a dose-response relationship between physical activity and GDM. **PAGAC Grade: Limited.**
- Insufficient evidence is available to determine whether the relationship between physical activity and GDM varies by age, race/ethnicity, socio-economic status, or weight status. **PAGAC Grade: Grade not assignable.**

Committee Discussion

2. What is the relationship between physical activity and the incidence of gestational diabetes mellitus?
 - a. What dose of physical activity is associated with the reported quantitative benefit or risk?
 - b. Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - c. Does the relationship vary by age, race/ethnicity, socio-economic status, or weight status?

Question 3

3. What is the relationship between physical activity and the incidence of preeclampsia and eclampsia?
 - a) What dose of physical activity is associated with the reported quantitative benefit or risk?
 - b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - c) Does the relationship vary by age, race/ethnicity, socio-economic status, or weight status?

- Source of evidence to answer question:
 - SR, MA, and Existing Report

Analytical Framework

Systematic Review Question

What is the relationship between physical activity and the incidence of preeclampsia and eclampsia?

Target Population

Pregnant adolescents and women and post-partum mothers

Comparison

Pregnant adolescents and women and post-partum mothers who participate in varying levels of physical activity, including no reported physical activity

Intervention/Exposure

All types and intensities of physical activity including lifestyle activities, leisure activities, and sedentary behavior

Endpoint Health Outcomes

Eclampsia
Preeclampsia

Key Definitions

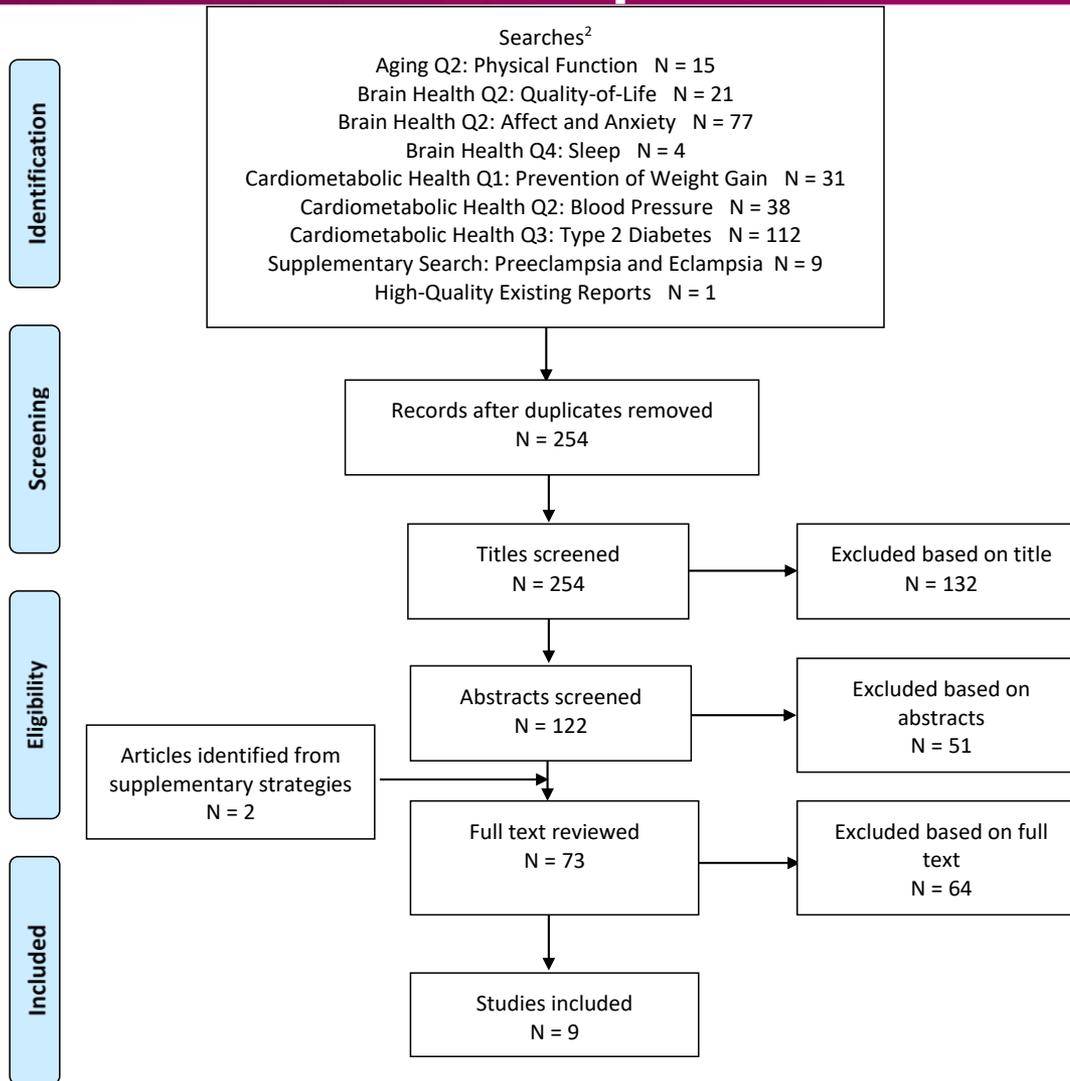
Postpartum period: Date of birth through one year after birth

Inclusion/Exclusion Criteria



- Date of Publication
 - Original Research: Not included
 - Existing Sources: Include 2011 - Present
- Study Subjects
 - Include: Pregnant women, Postpartum mothers, and Children at birth
- Study Design
 - Include: Systematic reviews, Meta-analyses, Pooled analyses, PAGAC-Approved reports
 - Exclude: Original research, Narrative reviews, Commentaries, Editorials
- Exposure/Intervention
 - Include: All types and intensities of physical activity
 - Exclude: Missing physical activity, Therapeutic exercise, Single-acute sessions of physical activity, Physical fitness as the exposure, Physical activity only used as confounding variable
- Outcome
 - Include: **Eclampsia, Preeclampsia**

Search Results: High-Quality Reviews¹ and Reports



¹ Reviews include systematic reviews, meta-analyses, and pooled analyses.

² The initial articles were identified by searching the titles and abstracts of each of the relevant searches' results for topics related to the Pregnancy Work Group using the terms "gestation," "pregn," "postp," "natal," and "maternal."

Description of the Evidence: Pre-eclampsia



Source of evidence included 9 systematic reviews and meta-analyses

Supplementary materials included:

1. the relevant original research articles cited by the systematic reviews and meta-analyses;
2. the 2008 PAGAC Scientific Report; and
3. the 2015 The American College of Obstetricians and Gynecologists Statement on Physical Activity and Exercise During Pregnancy and the Postpartum Period

Description of the Evidence: Pre-eclampsia

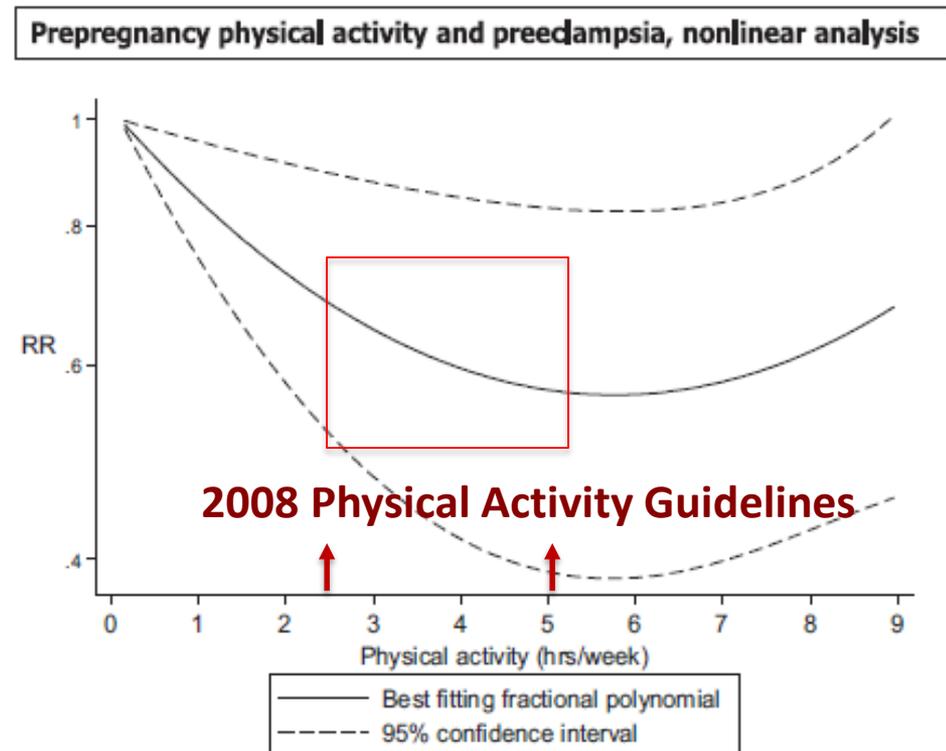


Author, year	Study Design	Effect (95% CI)
PRE-PREGNANCY PHYSICAL ACTIVITY		
Aune, 2014	Cohort (n=4) + C-c (n=1)	sRR=0.65 (0.47, 0.89)
DaSilva, 2017	Cohort (n=8)	sOR=0.88 (0.73, 1.06)
Kasawara, 2012	Cohort (n=3)	sOR=0.85 (0.67, 1.09)
	Case-control (n=2)	sOR=0.56 (0.41, 0.76)
EARLY PREGNANCY PHYSICAL ACTIVITY		
Aune, 2014	Cohort (n=7) + C-c (n=4)	sRR=0.79 (0.70, 0.91)
DaSilva, 2017	RCT (n=3)	sOR=0.93 (0.55, 1.57)
Kasawara, 2012	Cohort (n=10)	OR=0.99 (0.93, 1.05)
	Case-control (n=6)	OR=0.77 (0.64, 0.91)
Muktabhant 2015	RCTs (n=4)	avgRR: 0.99 (0.58, 1.66)
Zheng, 2017	RCTs (n=2)	pOR=1.05 (0.53, 2.07)

sRR=Standardized risk ratio; sOR=standardized odds ratio; OR=odds ratio; avgRR=average risk ratio; pOR=pooled odds ratio.

Draft Key Findings: Pre-eclampsia

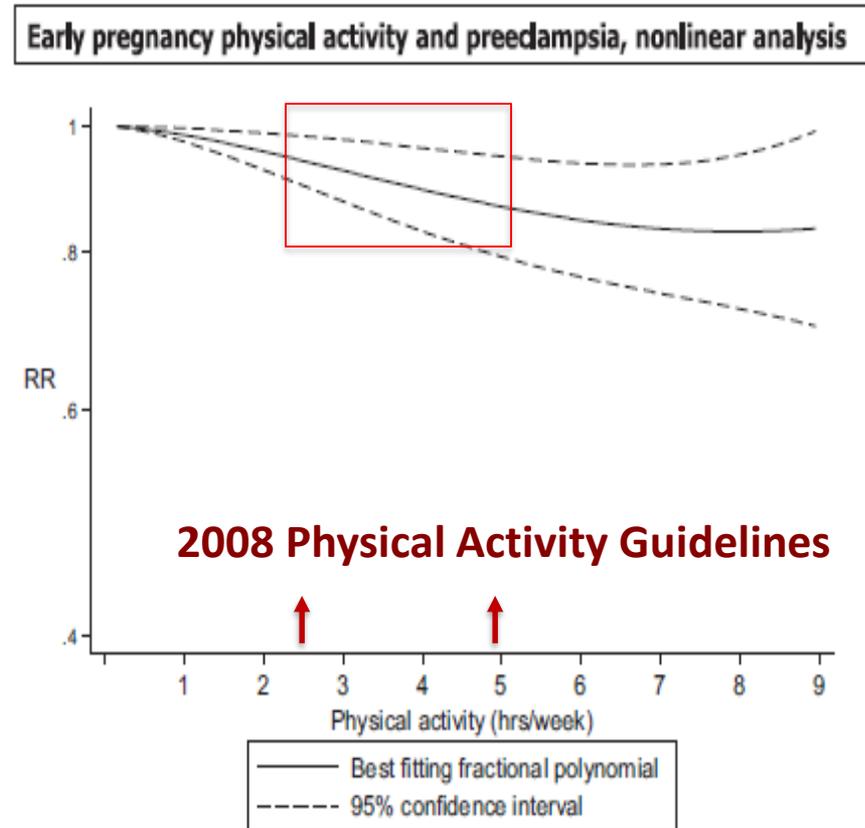
- Aune, (2014) performed a MA on 11 cohort and 4 case-control studies and reported a summary RR for high vs. low pre-pregnancy PA of 0.65 (95% CI: 0.47–0.89, n = 5 studies).
- In the dose–response analysis, the summary RR was 0.72 (95% CI: 0.53–0.99; n = 3 studies) per 1 h/day and 0.78 (95% CI: 0.63–0.96; n = 2 studies) per 20 MET-h/week.
- This relationship appeared non-linear with a flattening of the curve at higher levels of activity, with a 40% reduction in risk up to 5–6 hours per week but no further reductions at higher activity levels.



Aune, D, et al., *Epidemiology* 2014; 25: 331-343.

Draft Key Findings: Pre-eclampsia

- Summary RR for high versus low physical activity in early pregnancy was 0.79 (95% CI: 0.70–0.91; n = 11 studies).
- In the dose–response analysis, the summary RR per 1 h/day was 0.83 (95% CI: 0.72–0.95; n = 7 studies) and 0.85 (95% CI: 0.68–1.07; n = 3 studies) per 20 Met-h/ week.
- This dose-response relationship appeared to be linear.



Aune, D, et al., *Epidemiology* 2014; 25: 331-343.

Draft Conclusion Statement

- Limited evidence suggests that physical activity performed pre-pregnancy or during early pregnancy lowers the risk of pre-eclampsia. **PAGAC Grade: Limited.**
- Limited evidence suggests that 3-4 h/week of MVPA performed before or in early pregnancy is associated with a lower risk of pre-eclampsia. **PAGAC Grade: Limited**
- Limited evidence suggests that there is an inverse dose-response relationship between physical activity and risk of pre-eclampsia. **PAGAC Grade: Limited.**
- Insufficient evidence is available to determine whether the relationship between physical activity and pre-eclampsia varies by age, race/ethnicity, socio-economic status, or weight status. **PAGAC Grade: Grade not assignable**

Committee Discussion

3. What is the relationship between physical activity and the incidence of preeclampsia and eclampsia?
 - a) What dose of physical activity is associated with the reported quantitative benefit or risk?
 - b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - c) Does the relationship vary by age, race/ethnicity, socio-economic status, or weight status?

Question 4

4. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depression during pregnancy and postpartum (up to one year)?
 - a) What dose of physical activity is associated with the reported quantitative benefit or risk?
 - b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - c) Does the relationship vary by age, race/ethnicity, socio-economic status, or weight status?

- Source of evidence to answer question:
 - SR and MA

Analytical Framework

Systematic Review Question

What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depression during pregnancy and postpartum (up to one year)?

Target Population

Pregnant adolescents and women and postpartum mothers

Endpoint Health Outcomes

Affect
Anxiety
Depression

Comparison

Pregnant adolescents and women and postpartum mothers who participate in varying levels of physical activity, including no reported physical activity

Intervention/Exposure

All types and intensities of physical activity including lifestyle activities, leisure activities, and sedentary behavior

Key Definitions

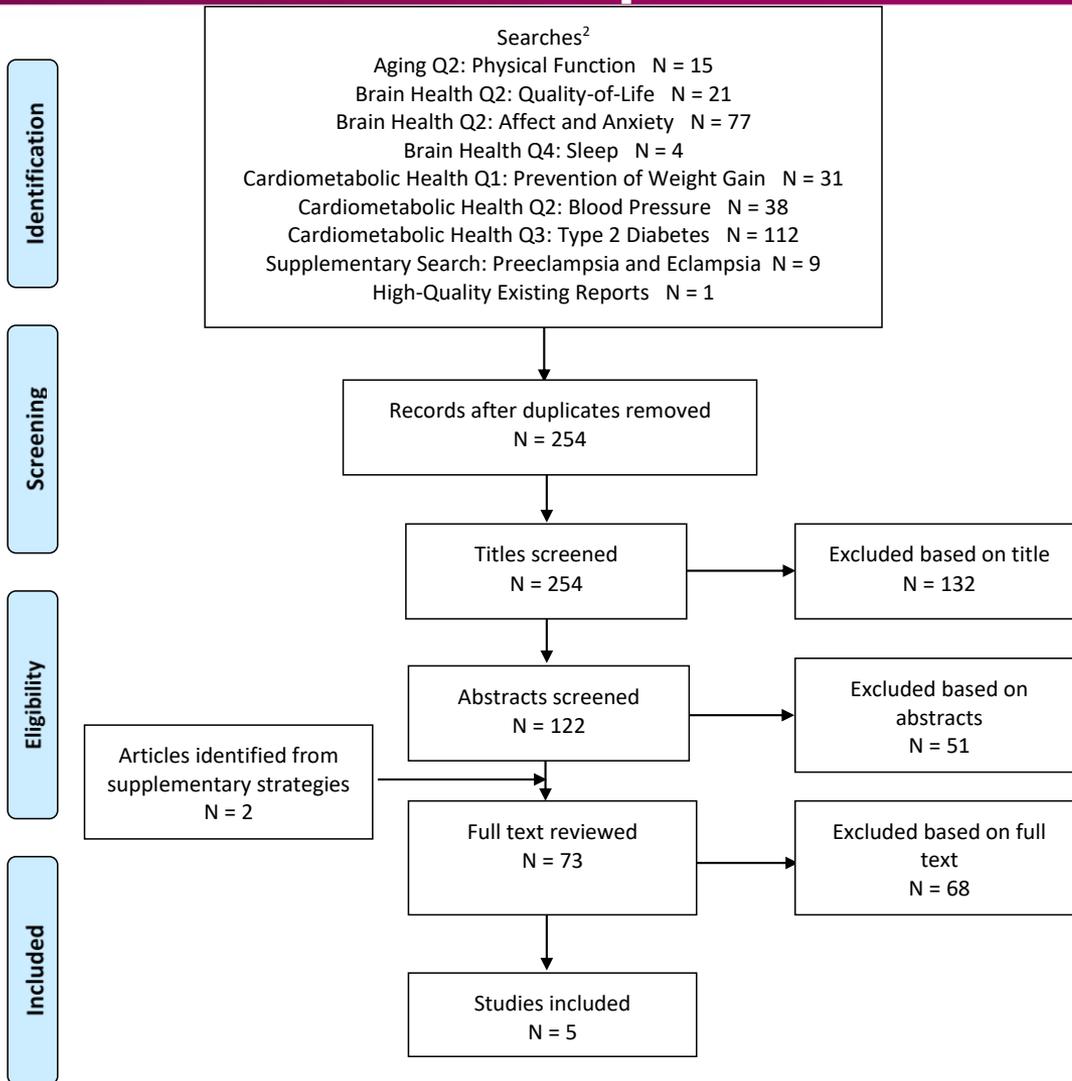
Postpartum period: Date of birth through one year after birth

Inclusion/Exclusion Criteria



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- Study Subjects
 - Include: Pregnant women, Postpartum mothers, and Children at birth
- Study Design
 - Include: Systematic reviews, Meta-analyses, Pooled analyses, PAGAC-Approved reports
 - Exclude: Original research, Narrative reviews, Commentaries, Editorials
- Exposure/Intervention
 - Include: All types and intensities of physical activity
 - Exclude: Missing physical activity, Therapeutic exercise, Single-acute sessions of physical activity, Physical fitness as the exposure, Physical activity only used as confounding variable
- Outcome
 - Include: **Affect, Anxiety, Depression**

Search Results: High-Quality Reviews¹ and Reports



¹ Reviews include systematic reviews, meta-analyses, and pooled analyses.

² The initial articles were identified by searching the titles and abstracts of each of the relevant searches' results for topics related to the Pregnancy Work Group using the terms "gestation," "pregn," "postp," "natal," and "maternal."

Description of the Evidence & *Draft Conclusion: Affect*

Affect

- No systematic reviews or meta-analyses on Affect
- Insufficient evidence is available to determine the relationship between physical activity and affect during pregnancy and the post-partum period.
PAGAC Grade not assignable.

Description of the Evidence & *Draft* Conclusion Statements: Anxiety

Antenatal Anxiety

- 2 systematic reviews (Sheffield 2016; Shivakumar 2011)
 - 5/5 studies of yoga reported decreased anxiety (Sheffield)
 - 1/1 study of “exercise” reported decreased anxiety (Shivakumar);
- Limited evidence suggests the physical activity decreases symptoms of anxiety during pregnancy. **PAGAC Grade: Limited.**
- Insufficient evidence is available to evaluate any of the sub-questions. **PAGAC Grade: Grade not assignable.**

Description of the Evidence: Affect, Anxiety, and Depression

Postpartum Anxiety

- No systematic reviews or meta-analyses on post-partum anxiety
- Insufficient evidence is available to determine the relationship between physical activity and post-partum anxiety. **PAGAC Grade: Grade not assignable.**

Description of the Evidence & *Draft* Conclusion Statements: Depression

Antenatal Depression

- 2 systematic reviews (Sheffield, 2016; Shivakumar, 2011);
 - 6/7 studies of yoga reported reduced depressive symptoms;
 - 1/1 study reported reduced depressive symptoms
- Limited evidence suggests that physical activity reduces symptoms of depression during pregnancy. **PAGAC Grade: Limited.**
- Insufficient evidence is available to evaluate the sub-questions. **PAGAC GRADE: Grade not assignable.**

Description of the Evidence: Depression

Post-partum Depression

- 2 SR/MA (McCurdy, 2017; Poyatos-Leon 2017)
- 1 SR (Teychenne, 2013)

Draft Key Findings: Post-partum Depression

Post-partum Depression

- Among the *prevention* trials (both indicating improvement):
 - 6 RCTs (McCurdy) Standardized Mean Difference = -0.22 (-0.08 to -0.36);
 - 7 RCTs, (Poyatos-Leon) Effect size = 0.29 (0.14 to 0.45);
- Among the *treatment* trials (both indicating improvement):
 - 10 RCTs (McCurdy) SMD= -0.48 (-0.73 to -0.22);
 - Exercising women with depression increased the odds of resolving depression post-intervention by 54% (OR=0.46; 95% CI: 0.25–0.84) compared with the control group (McCurdy);
 - 6 RCTs (Poyatos-Leon) Effect size = 0.67 (0.44, 0.90);
- Systematic review:
 - 7/7 RCTs report benefit of PA;
 - 4/6 longitudinal observational studies report benefit of PA;



Post-partum Depression

- Strong evidence demonstrates an inverse relationship between physical activity and risk of postpartum depression. **PAGAC Grade: Strong.**
- Insufficient evidence is available to evaluate the sub-questions. **PAGAC Grade: Grade not assignable**

Research Recommendations



Conduct large exposure-related RCTs and observational studies of:

1. The *dose-response relationship* between PA and the previously mentioned outcomes: weight status, gestational diabetes, preeclampsia, anxiety, depression, quality of life, or quality of sleep
2. The effects of exercise *timing* (pre-pregnancy, during pregnancy, or both) on the aforementioned outcomes;
3. The impact of high intensity aerobic or strength training on maternal and fetal outcomes;
4. The role of *occupational* physical activity on maternal and fetal outcomes.
5. The effect of age, race/ethnicity, SES, or weight status on these relationships.

Research Recommendations: Affect, Anxiety, and Depression

Conduct large outcomes-related RCTs and observational studies examining:

1. The relationship between physical activity and anxiety during pregnancy and postpartum.
2. The relationship between physical activity and QOL during pregnancy and postpartum.
3. The relationship between physical activity and quality of sleep during pregnancy and postpartum.
4. The effect of age, race/ethnicity, SES, or weight status on these relationships.

Committee Discussion

4. What is the relationship between physical activity and (1) affect, (2) anxiety, and (3) depression during pregnancy and postpartum (up to one year)?
 - a) What dose of physical activity is associated with the reported quantitative benefit or risk?
 - b) Is there a dose-response relationship? If yes, what is the shape of the relationship?
 - c) Does the relationship vary by age, race/ethnicity, socio-economic status, or weight status?