UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
FACULDADE DE MEDICINA

Eusebio Mario Amador Enriquez

Efetividade dos exercícios dos músculos do assoalho pélvico sobre a disfunção muscular e incontinência urinária específica da gestação em mulheres com e sem *diabetes mellitus* gestacional ou hiperglicemia gestacional: Revisão Sistemática e Metanálise de Ensaios Clínicos Randomizados

Effectiveness of pelvic floor muscle exercises on muscle dysfunction and pregnancy-specific urinary incontinence in women with and without gestational diabetes mellitus or gestational hyperglycemia: Systematic Review and Meta-analysis of Randomized Clinical Trials

Defesa de Tese de Doutorado apresentada à Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Campus de Botucatu, como parte dos requisitos para obtenção do título de Doutor em Tocoginecologia.

Orientadora: Prof.ª Emérita Marilza Vieira Cunha Rudge

Coorientadora: Prof.ª Drª. Angélica Mércia Pascon Barbosa

Botucatu

2023

Eusebio Mario Amador Enriquez

Efetividade dos exercícios dos músculos do assoalho pélvico sobre a disfunção muscular e incontinência urinária específica da gestação em mulheres com e sem *diabetes mellitus* gestacional ou hiperglicemia gestacional: Revisão Sistemática e Metanálise de Ensaios Clínicos Randomizados

Defesa de Tese de Doutorado apresentada à Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Campus de Botucatu, como parte dos requisitos para obtenção do título de Doutor em Tocoginecologia.

Orientadora: Prof.ª Emérita Marilza Vieira Cunha Rudge
Coorientadora: Prof.ª Drª. Angélica Mércia Pascon Barbosa

Botucatu
2023

Eusebio Mario Amador Enriquez

Efetividade dos exercícios dos músculos do assoalho pélvico sobre a disfunção muscular e incontinência urinária específica da gestação em mulheres com e sem *diabetes mellitus* gestacional ou hiperglicemia gestacional: Revisão Sistemática e Metanálise de Ensaios Clínicos Randomizados

Defesa de Tese de Doutorado apresentada à Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Campus de Botucatu, como parte dos requisitos para obtenção do título de Doutor em Tocoginecologia

Orientadora: Prof.ª Emérita Marilza Vieira Cunha Rudge
Coorientadora: Prof.ª Drª Angélica Mércia Pascon Barbosa

Comissão Examinadora para Defesa de Tese de Doutorado:

_____
Prof.ª Emérita Dra. Marilza Vieira Cunha Rudge
Faculdade de Medicina de Botucatu – UNESP

_____
Prof.ª Dra. Silvana Andrea Molina Lima
Faculdade de Medicina de Botucatu - UNESP

_____
Prof.ª Dra. Gabriela Marini Prata
Universidade do Sagrado Coração – USC

Botucatu, 10 de março de 2023.

Dedicatórias

À **Deus**, por tudo na minha vida, desde o dia que abri os olhos neste mundo e até o dia que for embora dele.

À minha família maravilhosa, esposa e filhas, por todo o apoio, pela compreensão e pelas forças que me dão para seguir adiante. Gracias por ser parte de mi vida!!!

À minha mãe, **Estrella,** que deu tudo e mais da sua vida para me ver formado, para me educar e ser um melhor homem e profissional cada dia.

A meu pai, **Eusebio,** por tudo, apesar de tudo. Espero que nos podamos ver en el Oriente Eterno y hablar por horas como siempre lo hicimos.

A mi tia **Silvita,** por abrir minha mente, me mostrar que o mundo cabe na palma da mão, por me ensinar como ele funciona e a filosofia de uma boa vida.

Aos meus padrinhos **Hilda e Hugo**, de vocês levo comigo o exemplo do que é uma sagrada família e como cuidar dela. Gracias!!!

Agradecimentos

À **Prof.ª Emérita Marilza Vieira Cunha Rudge**, pelo acolhimento, pela sua sabedoria e profissionalismo ao colaborar com o desenvolvimento da minha pós-graduação desde o primeiro momento.

À **Prof.ª Dra. Angélica Mércia Pascon Barbosa,** que me deu a oportunidade de estar num grupo de pesquisa espetacular, por me ajudar nesta jornada e ser parte de meus sucessos profissionais. Por iluminar meu caminho profissional e me incentivar a ser mais e a querer mais.

Ao meu amigo e colega Dr. David Rafael Abreu Reyes por tudo o apoio incondicional, por me abrir as portas ao mundo acadêmico no Brasil e por me exigir mais esforço no meu trabalho de cada dia.

As professoras Dra. Meline e Dra. Silvana, pela colaboração incondicional, pela ajuda e pelo aprendizado no mundo da revisão sistemática.

Aos funcionários do **Programa de Pós-Graduação da Faculdade de Medicina de Botucatu,** e ao **Departamento de Tocoginecologia**, por toda atenção.

À Fapesp pelo apoio na concessão da bolsa de Doutorado Direto (processo 2020/15629-5), pela qual foi possível financiar esta pesquisa.

Ao Escritório de Apoio à Pesquisa, **Cinthia** e **Cássia,** pelo apoio, pela ajuda, pelas horas trabalhadas em prol do nosso trabalho. A todos do ***Diamater Study Group***, que fazem a diferença nessa trajetória. Obrigado por todos os ensinamentos e pelo trabalho em equipe.

Epígrafe

“Yo soy el Alfa y la Omega, el principio y el fin. Al que tiene sed, yo le daré gratuitamente de la fuente del agua de la vida. El vencedor heredará estas cosas, y yo seré su Dios y él será mi hijo.”

Apocalipsis 21:1-8

Resumo da Tese

A presente Tese de Doutorado visa uma explanação da Efetividade dos Exercicios da Musculatura do Assoalho Pêlvico mediante Revisão Sistemâtica e Metanálise de Ensaios Clínicos Randomizados.

No Primeiro Artigo da Tese apresentamos um Study Protocol com o objetivo de padronizar o trabalho a ser realizado posteriormente, atendendo aos quesitos da metodologia Cochrane de Ensaios Clínicos Randomizados. Neste protocolo de pesquisa visamos o desenvolvimentos de uma estrategia de busca que se adaptase as bases de dados que seria utilizadas posteriormente (Embase, MedLine, Lilacs, Central). Se identificaram os termos MeSH que seria usados assim como os Desfechos Primarios e Secundários, colocando como importante a Incontinência Urinária Específica da Gestação e os Exercícios da Musculatura do Assoalho Pélvico. Descrevemos o Material e Métodos a ser utilizados na Revisão Sistemática. O Artigo como Study Protocol foi publicado na revista Plos One (Qualis A1, MED III – FI: 3,752) e pode ser encontrado no seguinte link: https://impactfactorforjournal.com/plos-one-impact-factor/

No Segundo Artigo demos prioridade a tudo o planejado no Study Protocol com o objetivo de realizar uma Revisão Sistemática sobre a Efetividade dos Exercícios da Musculatura do Assolaho Pêlvico na Disfunção Muscular da Incontinência Urinária Especifica da Gestação em mulheres com e sem Diabetes Mellitus Gestacional. Seguimos o método previsto para a busca nas bases de dados, segundo os nossos desfechos primários e secundários. Nosso resultado foi satisfatorios, conseguindo dados importantes de 5 Ensaios Clínicos Randomizados, com um total de 1697 mulheres grávidas de varias nacionalidades, que nos revelaram que os Exercicios da Musculatura do Assoalho Pélvico foram efetivos para a diminuição da Incontinência Urinaria.

Registro da Revisão Sistemática: PROSPERO CRD42017065281.

Keywords: Pregnancy, Hyperglycemia, Diabetes Mellitus, Gestational diabetes mellitus, Urinary incontinence; Pelvic Floor Disorders, Dysfunctions, Pelvic floor muscle training, Pelvic floor muscle exercises, Involuntary urine loss, Exercise training, Physical activity.

Sumário

Seção 1	**Trajetória acadêmica**	**.....**	**14**
Seção 2	**Contextualização**		**18**
	***Diabetes Mellitus* Gestacional, Treinamento dos MAP e sua relação com IU .....**		**19**
	Referências	**.....**	**24**
Seção 3	**Artigos**	**.....**	**28**
	Artigo 1 - Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol		**29**
	Abstract	**.....**	**30**
	Background	**.....**	**31**
	Methods	**.....**	**32**
	Data Collection	**.....**	**32**
	Quality of evidence	**.....**	**33**
	References	**.....**	**35**
	Artigo 2 - Effectiveness of pelvic floor muscle training for pregnant women with and without gestational diabetes mellitus and pregnancy specific urinary incontinence: Systematic review and meta-analysis of randomized trials		**37**
	Abstract	**.....**	**39**
	Background	**.....**	**40**
	Methods	**.....**	**44**
	Results	**.....**	**46**
	Discussion	**.....**	**60**
	Conclusions	**.....**	**63**
	References	**.....**	**66**
Seção 4	**Perspectivas Acadêmicas e Científicas**	**.....**	**73**
Seção 5	**Diamater Study Group**	**.....**	**75**
Seção 6	**Anexos**	**.....**	**78**

Seção 1

Trajetória Acadêmica

No ano de 2003 dei início a minha formação acadêmica, ingressando no curso de Medicina pela Faculdade de Ciências Médicas de Villa Clara – Cuba, sabendo que ia ter pela frente grandes desafios e muita história para contar. Realizei meu último ano de estudos como parte de um programa de Internado Profissionalizante pela Faculdade de Medicina da Universidade Central de Venezuela, em Caracas, conseguindo ver muito mais de perto as dissimiles condições de saúde pública que afetam nossa América Latina.

Minha vida profissional me levou a vários países do mundo como colaborador de saúde, até chegar no Brasil e por mediação de um grande amigo e colega, Dr. David, conhecer o projeto Diamater e as professoras Angélica e Marilza. Confesso que em um primer momento me senti intrigado em como pode ser possível que um grupo de pesquisa com profissionais de diferentes áreas, tenham um mesmo objetivo, logo depois percebi que não é só pesquisa, é esperança e fé em que pode dar certo, em que podemos ajudar e fazer a diferença. Procurei as respostas e elas vieram com o estudo e a dedicação.

Por um ano formei parte do Diamater como estudante em Treinamento Técnico III, me aprimorando nas técnicas Cochrane para Revisão Sistemática e colaborando em vários estúdios de campo como miografia dos músculos do reto abdominal, e em vários artigos científicos do Grupo Diamater. Participando também em eventos nacionais, e internacionais de maneira virtual.

Em 2019 comecei meus estudos de Mestrado pelo Projeto Temático Fapesp DIAMATER, "*The Diamater Study Group*", sob a orientação da Prof.ª Emérita Drª Marilza Vieira Cunha Rudge e coorientação da Profa. Dra. Angélica Mércia Pascon Barbosa. Ao longo desse ano, começamos um novo projeto de pesquisa titulado "Effectiveness of the pelvic floor muscle training on muscular dysfunction and

pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: Systematic review and meta-analysis of randomized trials", aplicando os conhecimentos obtidos no treinamento técnico prévio, para análise da literatura existente e com o objetivo de avaliar os efeitos dos exercícios dos Músculos do Assoalho Pélvico sobre a Disfunção Muscular do Assoalho Pélvico e a Incontinência Urinaria Específica da Gestação em mulheres com *Diabetes Mellitus* Gestacional ou Hiperglicemia Gestacional.

Foi possível colaborar diretamente em outros 4 artigos publicados em revistas de alto impacto (Anexo 6):

1. "Impact of gestational diabetes on pelvic floor: A prospective cohort study with three-dimensional ultrasound during two-time points in pregnancy. Neurourology and Urodynamics, v. 2020, p. 1-9, 2020."

2. "Pelvic floor muscle dysfunction at 3D transperineal ultrasound in maternal exposure to gestational diabetes mellitus: A prospective cohort study during pregnancy. NEUROUROLOGY AND URODYNAMICS, v. 41, p. 1127-1138, 2022.".

3. "Viability of ex-vivo myography as a diagnostic tool for rectus abdominis muscle electrical activity collected at Cesarean section within a diamater cohort study. BioMedical Engineering OnLine (2022) 21:76".

4. "Pro-angiogenic approach for skeletal muscle regeneration. Biochimica et Biophysica Acta (BBA), v. 1866, p. 1, 2022"

Estes e outros estudos me ajudaram com a possibilidade de obter bolsa de Doutorado Direto pela FAPESP (processo 2020/15629-5) junto ao Programa em Tocoginecologia da FMB Unesp, com projeto vinculado ao Projeto Temático e continuar meus estudos de Revisão Sistemática, Assoalho Pélvico, Exercícios dos MAP e *Diabetes Mellitus* Gestacional.

Meu propósito é concluir o doutorado e continuar me aprimorando e adquirindo conhecimento constante em prol da saúde das nossas mulheres, fazendo a diferença no cenário acadêmico e científico e, por isso, o desejo de dar continuidade aos estudos por meio de Pós-doutorado. Ajudar a comunidade científica com meus conhecimentos de Revisão Sistemática e fazer uso dela como profissional e acadêmico.

Seção 2
Contextualização

Diabetes Mellitus Gestacional, Treinamento dos MAP e sua relação com IU.

Durante a gravidez, o corpo da gestante passa por diversas adaptações fisiológicas. Como consequência ao permitir o crescimento uterino, o assoalho pélvico (AP) também passa por adaptações no período gestacional. Na fáscia endopélvica, responsável pela sustentação dos órgãos acima do assoalho pélvico, ocorrem modificações em seu componente principal, o colágeno (1). A fraqueza nas estruturas do AP é comumente encontrada na gravidez levando à predisposição de disfunção e seus sintomas consequentes (2). A massa corporal materna e o peso uterino geram sobrecarga na musculatura do assoalho pélvico (3). Como forma de compensação a esse aumento na carga, foi observado tônus muscular maior para manter as funções de suporte e continência (4). Além disso, o sobrepeso excessivo pode resultar em aumento na tensão excedente enfraquecendo as estruturas musculares e suscitando disfunções pélvicas (5-7).

A presença de Incontinência Urinária (IU) com primeira ocorrência durante gravidez, denominada Incontinência Urinária Específica da Gestação (IUEG) (8), tem impacto negativo na qualidade de vida (QV) ao longo do tempo (8, 9), com prevalência média de 41% em mulheres grávidas. Mesmo que ainda não inteiramente compreendida a fisiopatologia da IU-EG, a literatura traz como causa as alterações mecânicas e hormonais ocorridas neste período (8). Além disso, IUEG é fator de risco para a IU 2 anos após o parto em que foi observado menor contração dos músculos do assoalho pélvico (MAP) (10) nesse período o que nos remete às suas consequências a longo prazo.

A Incontinência Urinária Específica da Gestação (IUEG), caracterizada pela perda involuntária de urina com primeira ocorrência na gestação, independente do

período gestacional, (11) está associada, entre outros fatores, ao *Diabetes Mellitus* Gestacional (DMG) e Hiperglicemia Gestacional. (12) A relação entre DMG e o aumento da prevalência de IU e disfunção muscular do assoalho pélvico (DMAP) foi claramente demonstrada por Barbosa et al, que concluíram que a prevalência de IUEG e IU dois anos após o parto foi significativamente maior entre as mulheres com DMG quando comparada com as gestantes normoglicêmicas. Com a análise multivariada, foi demonstrado que a DMG foi fator de risco independente para a ocorrência de IUEG e foi demonstrado que mulheres com DMG prévia apresentam fraqueza dos músculos do assoalho pélvico (MAP) dois anos após o nascimento. (13)

O diabete pode lesar o músculo esquelético com atrofia decorrente da neuropatia diabética ou por efeito mais direto sobre o metabolismo das células musculares pelo alto teor de glicose e baixo de insulina. A insulina é fator fundamental na manutenção da proteína do músculo esquelético e a perda de massa muscular no diabete decorre de danos nas vias de sinalização intracelular envolvidos na manutenção e no equilíbrio entre a degradação e a síntese da proteína nova que depende da fosforilação e da expressão de novas proteínas reguladoras específicas (14). Existem alterações no tecido conjuntivo inerentes às alterações hormonais relacionadas ao hormônio relaxina que ainda são pouco conhecidas no DMG (15-17). Paralelamente, também existem alterações musculares (18-20) resultantes, direta e/ou indiretamente dos níveis de CCL7, relaxina, insulina, glicose, paratormônio (PTH), cálcio (Ca), calcitonina e vitamina D (21-23). Estas alterações funcionais, bioquímicas (relaxina, CCL7, insulina, glicose, PTH, Ca, calcitonina e vitamina D) e estruturais no músculo esquelético diminuem a capacidade funcional e acarretam fraqueza muscular; diminuição nas mitocôndrias e transformações nas fibras musculares (24- 27). É consenso na literatura que a atrofia dos MAP tem impacto

negativo na qualidade de vida e na função dos MAP (28).

A literatura científica tem mostrado o impacto negativo da hiperglicemia no músculo: atrofia e desorganização muscular, diminuição da proporção de fibras rápidas, aumento da deposição de colágeno e fibrose severa foram observados em um estudo realizado em ratas grávidas diabéticas (29,30), evidenciando que o DMG altera o músculo esquelético pelo efeito direto da hiperglicemia (31). Sendo assim, surgiu a tríade DMG, miopatia diabética e IU e seus biomarcadores, que é investigada pelo *Diamater Study Group* desde 2006, caracterizando o Projeto Temático (2016/01743-5). O *Conceptual Model* (32), estabelecido da integração entre DMG, IU-EG e miopatia hiperglicêmica tem a funcionalidade dos MAP e MRA como variáveis moderadoras e precisa ser investigado (Figura 1).

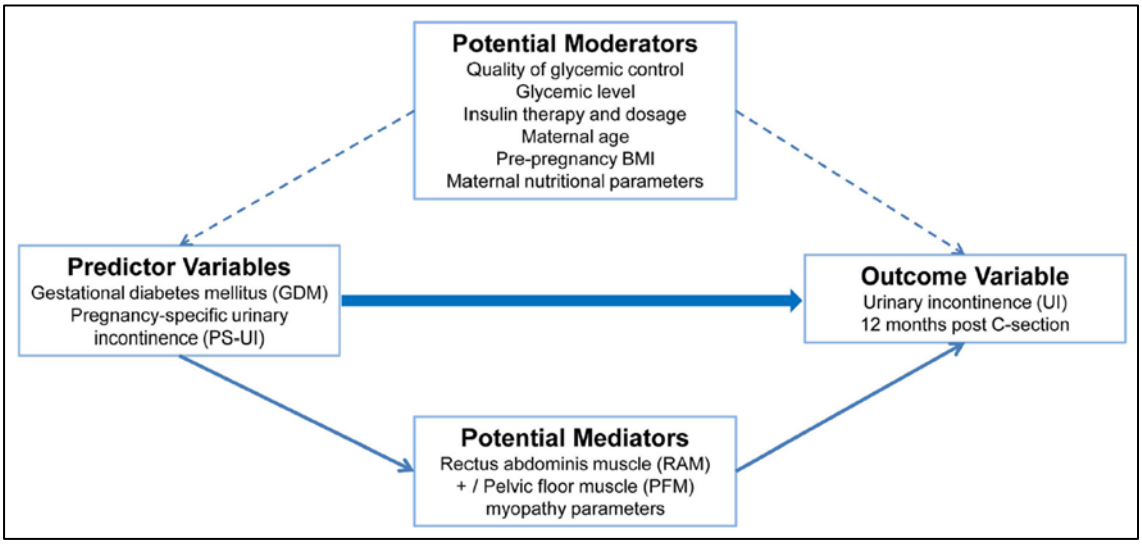


Figura 1: Potenciais confundidores, mediadores e moderadores do Diamater. **Fonte:** Rudge et al., 2020 (37).

O Módulo III do Projeto Temático é realizar Revisão Sistemática com foco no tratamento e prevenção da IUEG em mulheres com DMG. O presente Doutorado Direto se propôs responder os objetivos deste módulo. A proposta se respalda no fato

de que estudos demonstram que exercício incluindo exercícios aeróbicos de resistência e treinamento dos MAP, e boa orientação médica e fisioterapêutica, são eficazes para prevenção, tratamento e redução da IUEG (33,34), contudo, estes resultados não se referem a mulheres com DMG ou hiperglicemia gestacional.

O treinamento e fortalecimento dos MAP (35) durante a gestação complicada pelo DMG fazem-se necessário e destacam-se como eficazes. (36,37) No entanto, não há revisão sistemática que tenha avaliado o programa padronizado de exercícios dos MAP para tratar IUEG e/ou DMAP. Os programas diferiram quanto ao tipo de exercício, intensidade, tipo e duração da aplicação, além da frequência e duração das sessões de tratamento.

O presente estudo será o primeiro a analisar a eficácia dos exercícios dos MAP em gestantes com DMG ou Hiperglicemia com IUEG e/ou DMAP. O estudo primário de intervenção foi o delineamento selecionado para compor esta revisão sistemática, por estudos de ensaios clínicos randomizados (ECR) serem considerados como fonte de melhor evidência científica disponível na literatura. Deste modo, espera-se obter evidências robustas e conclusivas para apoiar a prática clínica, além de promover estudos sobre o tema e contribuir para novos estudos.

A nossa hipótese é que a Revisão Sistemática trará subsídios para terapêutica de exercícios dos MAP efetiva que fundamentem posterior estudo clínico com intervenção por meio de exercícios de forma terapêutica da IUEG e da DMAP em gestantes com DMG e Hiperglicemia Gestacional.

Para defesa desta Tese, estão apresentados no artigo 1 publicado e o artigo 2 em fase de finalização:

Artigo 1 – Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol

Artigo 2 - *Effectiveness of the pelvic floor muscle training for pregnant women with and without gestational diabetes mellitus and pregnancy specific urinary incontinence: Systematic review and meta-analysis of randomized trials*

Referências:

1. Landon CR, Crofts CE, Smith ARB, Trowbridge EA. Mechanical properties of fascia during pregnancy: a possible factor in the development of stress incontinence of urine. Contemp Rev Obstet Gynaecol. 1990;2:40–6.

2. Van Geelen H, Ostergard D, Sand P. A review of the impact of pregnancy and childbirth on pelvic floor function as assessed by objective measurement techniques. Int Urogynecol J [Internet]. 2018 Mar 13;29(3):327–38.

3. Herbert J. Pregnancy and childbirth: the effects on pelvic floor muscles. Nurs Times [Internet]. 105(7):38–41.

4. Moccellin AS, Rett MT, Driusso P. Existe alteração na função dos músculos do assoalho pélvico e abdominais de primigestas no segundo e terceiro trimestre gestacional? Fisioter e Pesqui [Internet].2016Jun;23(2):136–4

5. Kudish BI, Iglesia CB, Sokol RJ, Cochrane B, Richter HE, Larson J, et al. Effect of Weight Change on Natural History of Pelvic Organ Prolapse. Obstet Gynecol [Internet]. 2009 Jan;113(1):818.
6. Greer WJ, Richter HE, Bartolucci AA, Burgio KL. Obesity and Pelvic Floor Disorders. Obstet Gynecol [Internet]. 2008 Aug;112(2, Part 1):341–9.

7. Stothers L, Friedman B. Risk Factors for the Development of Stress Urinary Incontinence in Women. Curr Urol Rep [Internet]. 2011 Oct 22;12(5):363–9.

8. Hvidman L, Foldspang A, Mommsen S, Bugge Nielsen J. Correlates of urinary incontinence in pregnancy. Int Urogynecol J Pelvic Floor Dysfunct. 2002;13(5):278-83.

9. Viktrup L, Lose G. Lower urinary tract symptoms 5 years after the first delivery. Int Urogynecol J Pelvic Floor Dysfunct. 2000 Dec;11(6):336-40.

10. Barbosa AM, Dias A, Marini G, Calderon IM, Witkin S, Rudge MV. Urinary incontinence and vaginal squeeze pressure two years post-cesarean delivery in primiparous women with previous gestational diabetes mellitus. Clinics (Sao Paulo). 2011;66(8):1341-6.
11. Rudge MVC, Souza FP, Abbade JF, Hallur RLS, Marcondes JPC, Piculo F, et al. Study protocol to investigate biomolecular muscle profile as predictors of long-term urinary incontinence in women with gestational diabetes mellitus. BMC Pregnancy Childbirth [Internet].2020 Dec 19;20(1):117.
12. Piculo F, Marini G, Barbosa AMP, Damasceno DC, Matheus SM, Felisbino SL, et al. Urethral striated muscle and extracellular matrix morphological characteristics among mildly diabetic pregnant rats: translational approach. Int Urogynecol J Pelvic Floor Dysfunct. 2014;25:403–415. doi: 10.1007/s00192-013-2218-4.

13. Lambertucci AC, Lambertucci RH, Hirabara SM, Curi R, Moriscot AS, Alba-LoureiroTC, et al. Glutamine supplementation stimulates protein-synthetic and inhibits protein- degradative signaling pathways in skeletal muscle of diabetic rats. PLoS One [Internet]. 2012 Jan [cited 2019 Aug6];7(12):e50390.
14. Hvidman, L., Foldspang, A., Mommsen, S., & Nielsen, J.B. (2002). Correlates of Urinary Incontinence in Pregnancy. International Urogynecology Journal, 13, 278-283.

15. Rudge MVC, Girão MJBC, gravidez G acadêmico D e, Grupo acadêmico Aspectos clínicos moleculares e gênicos da incontinência urinária feminina. Diabete gestacional e incontinência urinária: interação entre a Ginecologia e a Obstetrícia TT - Gestational diabetes and urinary incontinence: the interaction of Gynecology and Obstetrics. Rev Bras Ginecol Obs [Internet]. 2011;33(5):207–10. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-72032011000500001

16. Rodrigues, A. M., Girão, M. J. B. C., da Silva, I. D. C. G., Sartori, M. G. F., de Falco Martins, K., & de Aquino Castro, R. (2008). COL1A1 Sp1-binding site polymorphism as a risk factor for genital prolapse. International Urogynecology Journal, 19(11), 1471- 1475.Rudge MVC, Girão MJBC, gravidez G acadêmico D e, Grupo acadêmico Aspectos clínicos moleculares e gênicos da incontinência urinária feminina. Diabete gestacional e incontinência urinária: interação entre a Ginecologia e a Obstetrícia TT - Gestational diabetes and urinary incontinence: the interaction of Gynecology and Obstetrics. Rev Bras Ginecol Obs [Internet]. 2011;33(5):207–10. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0100-72032011000500001
17. Aldabe D, Ribeiro DC, Milosavljevic S, Dawn Bussey M. Pregnancy-related pelvic 15 girdlepain and its relationship with relaxin levels during pregnancy: a systematic review. Eur Spine J. 2012.

18. Wen Y, Zhao Y-Y, Polan ML, Chen B. Effect of relaxin on TGF-betal expression in cultured vaginal fibroblasts from women with stress urinary incontinence. Reprod Sci [Internet]. 2008 Apr [cited 2014 Jul 29];15(3):312-20. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18421026

19. Harvey M-A, Johnston SL, Davies G a L. Mid-trimester serum relaxin concentrations and postpartum pelvic floor dysfunction. Acta Obstet Gynecol Scand [Internet]. 2008 Jan [cited 2014 Jul 28];87(12):1315-21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18951211

20. Zhao J, Brault JJ, Schild A, Cao P, Sandri M, Schiaffino S, Lecker SH, Goldberg AL. FoxO3 coordinately activates protein degradation by the autophagic/lysosomal and proteasomal pathways in atrophying muscle cells. Cell Metab. 2007;6:472-83.

21. Sandri M, Lin J, Handschin C, Yang W, Arany ZP, Lecker SH, Goldberg AL, Spiegelman BM. PGC-1alpha protects skeletal muscle from atrophy by

suppressing FoxO3 action and atrophy-specific gene transcription. Proc Natl Acad Sci U S A. 2006;103:16260-5.

22. D'Souza, Donna M., Dhuha Al-Sajee, and Thomas J. Hawke. Diabetic Myopathy: Impact of Diabetes Mellitus on Skeletal Muscle Progenitor Cells. Frontiers in Physiology 4 (2013): 379. PMC. Web. 5 Nov. 2015.
23. Asemi Z, Karamali M, Esmaillzadeh A. Effects of calcium-vitamin D cosupplementation on glycaemic control, inflammation and oxidative stress in gestational diabetes: a randomised placebocontrolled trial. Diabetologia. 2014 Sep;57(9):1798- 806.

24. Karamali M, Asemi Z, Ahmadi-Dastjerdi M, Esmaillzadeh A. Calcium plus vitamin D 16 supplementation affects pregnancy outcomes in gestational diabetes: randomized, double-blind, placebo-controlled trial. Public Health Nutr. 2015 Mar;20:1-8.

25. Harinarayan CV, Arvind S, Joshi S, Thennarasu K, Vedavyas V, Baindur A. Improvement in Pancreatic P Cell Function with Vitamin D and Calcium Supplementation in Vitamin D Deficient NonDiabetic Subjects. Endocr Pract. 2013 Sep;6:1-33.

26. Zhao J, Brault JJ, Schild A, Cao P, Sandri M, Schiaffino S, Lecker SH, Goldberg AL. FoxO3 coordinately activates protein degradation by the autophagic/lysosomal and proteasomal pathways in atrophying muscle cells. Cell Metab. 2007;6:472-83.

27. Sandri M, Lin J, Handschin C, Yang W, Arany ZP, Lecker SH, Goldberg AL, Spiegelman BM. PGC-1alpha protects skeletal muscle from atrophy by suppressing FoxO3 action and atrophy-specific gene transcription. Proc Natl Acad Sci U S A. 2006;103:16260-5.

28. Jiang LQ,Duque- Guimaraes DE, Machado UF, Zierath JR, Krook A. Altered response of skeletal muscle to IL-6 in type 2 diabetic patients. Diabetes. 2013 Feb;62(2):355-61. doi: 10.2337/db11-1790. Epub 2012 Oct 18..

29. Ramchum N, Mashamba C, Leitch E, Arutchelvam V, Narayanan K, Weaver J, et al. Upper limb musculoskeletal abnormalities and poor metabolic control in diabetes. Eur J Intern Med. 2009 Nov;20(7):718-21.

30. Segedi LM, Ilié KP, Curcié A, Visnjevac N. Quality of life in women with pelvic floor dysfunction. Vojnosanit Pregl. 2011 Nov;68(11):940-7

31. Marini G, Piculo F, Barbosa A, Damasceno D, Matheus S, Rudge M. Importância do modelo animal para testar hipóteses sobre a fisiopatologia do binômio diabetes e incontinência urinária feminina. Scientia Medica. 2011;21 (4): 191-5.
32. Li GY, Cui WS, Zhou F, Gao ZZ, Xin H, Liu T, et al. Pathology of urethral fibromuscular system related to parturition-induced stress urinary incontinence and TGF-beta1/Smad pathway. Molecular and cellular biochemistry. 2012 May;364(1-2):329-35.

33. Kegel AH. Progressive resistance exercise in the functional restoration of the perineal muscles. Am J Obstet Gynecol. 1948;56(2):238-48.

34. Slieker-ten-Hove M, Pool-Goudzwaard A, Eijkemans M, Steegers-Theunissen R, Burger C, Vierhout M. Pelvic floor muscle function in a general population of women with and without pelvic organ prolapse. Int Urogynecol J. 2010;21(3):311 -1.

35. Bo K. Pelvic floor muscle training in treatment of female stress urinary incontinence, pelvic organ prolapses and sexual dysfunction. World J Urol. 2012;30(4):437-43.

36. Mesquita LA, Machado AV, Andrade AV. Fisioterapia para redução da diástase dos músculos retos abdominais no pós-parto. Rev Bras Ginecol e Obs [Internet]. 1999 Jun;21(5):267–72.

37. Bursch SG. Interrater reliability of diastasis recti abdominis measurement. Phys Ther [Internet].1987 Jul [cited 2019 Aug 6];67(7):1077–9.

Seção 3
Artigos

Artigo 1

Artigo Original redigido de acordo com as normas de publicação da revista *Plos One* para a qual foi submetido. Qualis A1 MED III – FI: 3,752 https://impactfactorforjournal.com/plos-one-impact-factor/

PLOS ONE

REGISTERED REPORT PROTOCOL

Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol

Angélica Mércia Pascon Barbosa[1☯‡*], Eusebio Mario Amador Enriquez[2☯‡], Meline Rossetto Kron Rodrigues[3☯], Caroline Baldini Prudencio[2☯], Álvaro Nagib Atallah[4☯], David Rafael Abreu Reyes[2☯], Raghavendra Lakshmana Shetty Hallur[2☯], Sthefanie Kenickel Nunes[2☯], Fabiane Affonso Pinheiro[2☯], Carlos Isaías Sartorão Filho[2☯], Gabriela Lopes Piemonte Andrade[5☯], Bary Berghmans[6☯], Rob de Bie[6☯], Silvana Andréa Molina Lima[7☯‡], Marilza Vieira Cunha Rudge[2☯‡], The Diamater Study Group[¶]

1 Department of Physiotherapy and Occupational Therapy, School of Philosophy and Sciences, São Paulo State University (UNESP), Marilia, São Paulo State, Brazil, **2** Department of Gynecology and Obstetrics, Botucatu Medical School (FMB), São Paulo State University (UNESP), Botucatu, São Paulo State, Brazil, **3** Stricto Sensu Graduate Program in Nursing at UNIVERITAS, Guarulhos University (UNG), Guarulhos, São Paulo, Brazil, **4** Discipline of Evidence-Based Medicine, Paulista School of Medicine-Federal University of São Paulo (EPM-UNIFESP), São Paulo, Brazil, **5** Department of Physiotherapy, Universidade do Oeste Paulista (UNOESTE), Presidente Prudente, São Paulo State, Brazil, **6** Pelvic Care Center Maastricht, Maastricht University Medical Center, Maastricht, The Netherlands, **7** Department of Nursing, Botucatu Medical School (FMB), São Paulo State University (UNESP), Botucatu, São Paulo State, Brazil

☯ These authors contributed equally to this work.
‡ AMPB and EMAE are first authors on this work. SAML and MVCR are last authors on this work.
¶ Membership of The Diamater Study Group is listed in the Acknowledgments.
* angelicapascon@gmail.com

This is a Registered Report and may have an associated publication; please check the article page on the journal site for any related articles.

Citation: Barbosa AMP, Enriquez EMA, Rodrigues MRK, Prudencio CB, Atallah ÁN, Reyes DRA, et al. (2020) Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol. PLoS ONE 15(12): e0241962. https://doi.org/10.1371/journal.pone.0241962

Editor: Frank T. Spradley, University of Mississippi Medical Center, UNITED STATES

Received: April 20, 2020

Accepted: October 9, 2020

Published: December 7, 2020

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0241962

Abstract

Background

There is ample evidence that gestational diabetes mellitus has a direct influence on urinary incontinence and pelvic floor muscles. There are no standardized pelvic floor muscle exercise programs in the literature for the physiotherapy and differ in the type of exercise, intensity, type and duration of application, and the frequency and duration of treatment sessions. The aim of this systematic review will be to investigate that Pelvic Floor Muscle Training can prevent and/or decrease the pregnancy specific urinary incontinence in women with gestational diabetes mellitus or gestational hyperglycemia.

Methods

We will perform a systematic review according to the Cochrane methodology of Randomized Controlled Trials. An overall search strategy will be developed and adapted for Embase, MEDLINE, LILACS, and CENTRAL databases, with the date of consultation until

Data Availability Statement: All relevant data from this study will be made available upon study completion.

Funding: This ongoing (2018-2020) project (FAPESP 2018/17534-1) is funded by the São Paulo Research Foundation-FAPESP, government agency located in São Paulo, Brazil. Linked with the thematic project Fundação de Amparo à Pesquisa do Estado de São Paulo, FAPESP 2016/01743-5. The funders had not and will not have a role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

Abbreviations: UI, Urinary incontinence; SUI, Stress urinary incontinence; GDM, Gestational diabetes mellitus; PFM, Pelvic floor muscles; PFMD, Pelvic floor muscle dysfunction; RCTs, Randomized controlled trials; CI, Confidence interval; PS-UI, Pregnancy specific urinary incontinence.

June 2020. The MeSH terms used will be "Pregnancy", "Hyperglycemia", "Diabetes Mellitus, Type 2", "Diabetes Mellitus, Type 1", "Pregnancy in Diabetics", "Diabetes, Gestational", "Urinary Incontinence", "Pelvic Floor Muscle Strength". *Primary outcomes*: improvement or cure of pregnancy specific urinary incontinence (which can be assessed by questionnaires, and tools such as tampon test, voiding diary, urodynamic study). *Secondary outcomes*: improvement of pelvic floor muscle strength (pelvic floor functional assessment, perineometer, electromyography, functional ultrasonography), improved quality of life (questionnaires), presence or absence of postpartum Urinary Incontinence and adverse effects. Quality assessment by Cochrane instrument. Metanalysis if plausible, will be performed by the software Review Manager 5.3.

Discussion

The present study will be the first to analyze the effectiveness of pelvic floor exercises in pregnant women with Gestational Diabetes Mellitus or Hyperglycemia, who suffer from pregnancy specific urinary incontinence. Randomized Controlled Trials design will be chosen because they present the highest level of evidence. It is expected to obtain robust and conclusive evidence to support clinical practice, in addition to promoting studies on the theme and contributing to new studies.

Trial registration

Systematic review registration: PROSPERO CRD42017065281.

Background

Each day it is more obvious that Urinary Incontinence (UI) in pregnant women is associated, among other factors, with Gestational Diabetes Mellitus (GDM) and Hyperglycemia in Pregnancy. Clinical findings of high prevalence of UI in women with GDM, two years before labor and prior cesarean section, provide evidence of the need to increase knowledge of this association: Prior GDM and UI [1]. The association between GDM and the increased prevalence of UI and pelvic floor muscle dysfunction (PFMD) was clearly demonstrated by Barbosa *et al.* (2011) who concluded that the prevalence of pregnancy specific urinary incontinence (PS-UI) and UI two years postpartum was significantly higher among women with GDM than among normoglycemic pregnant women. Their multivariate analysis demonstrated that GDM is an independent risk factor for the occurrence of PS-UI and they showed that pregnant women with prior GDM have weakness of the pelvic floor muscles (PFM) two years after birth [2].

Santos *et al.* (2006) stated that stress urinary incontinence (SUI) is the most common and prevalent type of UI during the reproductive years [3]. This type of UI is defined as involuntary loss of urine during physical exertion, due to a sudden increase in intra-abdominal pressure in the absence of detrusor contraction or underactivity [4]. The etiology of SUI is not fully understood, but injuries to the pelvic floor during pregnancy and childbirth are suggested as main risk factors [3]. Although the SUI is the most prevalent UI type during pregnancy, women also complain about urgency urinary incontinence and its combination named mixed urinary incontinence [5].

For many years involuntary loss of urine in pregnant women have complaint more often to her doctor or physiotherapist. Although this increase in cases reported by patients was not as

significant as it is today, it was enough for many researchers worldwide to be interested to assess, evaluate, report and look for solutions to prevent or reduce this discomfort in women [6]. A Cochrane review from 2018 considered PFM training as first-line conservative management to SUI and all other types of UI nevertheless they didn't include PS-UI treatment on the revision [7]. Another Cochrane review from 2020 showed that due to the quality and quantity of well designed studies when antenatal or postnatal populations were evaluated the influence of PFM training for treatment and/or prevetion is uncertain or not at all clear [5]. So a little is know about UI during pregnancy, particullary the impact of the diabetes status on the PS-UI [5].

Considering this background, the aim of our study is, using a systematic review of available randomized clinical trials (RCTs), to investigate in GDM pregnant women with gestational hyperglycemia the effect of PFM training for the prevention and/or treatment of PS-UI.

Methods/design

Systematic review

Study inclusion and exclusion criteria. *Inclusion criteria*. RCTs of pregnant women with hyperglycemia (all levels), any type of UI developed during pregnancy, nulliparous, primiparous and multiparous women during pregnancy, receiving PFM training to prevent and/or reduce the symptoms of PS-UI.

Exclusion criteria. All other designs, not being RCT.

Outcomes. *Primary outcomes*. Occurrence, reduction, recurrence, or persistence of PS-UI symptoms.

Secondary outcomes. Improvement of PFM strength (pelvic floor functional assessment, perineometer, electromyography, functional ultrasonography), improved quality of life (questionnaires), presence or absence of postpartum UI and adverse effects.

Literature search strategies. A model strategy will be created and adapted for searching the data bases Embase, Pubmed, Lilacs and CENTRAL to identify studies involving the above-mentioned interventions. RCTs registry sites will be consulted for ongoing studies on the topic (Rebec, Clinicaltrial.gov). Grey literature will be consulted as well as Capes database. Last date of searche will be 30 June 2020. There will be no language restrictions. MeSH terms used for our searches are "Pregnancy", "Hyperglycemia", "Diabetes Mellitus, Type 2", "Diabetes Mellitus, Type 1", "Pregnancy in Diabetics", "Diabetes, Gestational", "Urinary Incontinence" and "Pelvic Floor Muscle Strength".

Data collection and analysis. *Selection of studies*. For each search strategy, two reviewers will independently evaluate the studies retrieved from the databases in the order: title, abstract and full reading. All studies potentially eligible for inclusion in the review will be selected for full reading. In case of disagreement, a third reviewer will be consulted.

Data extraction and management. Data extraction for eligible studies will be performed by two reviewers (EMAE e MRKR) who will independently extract data from articles that meet the inclusion criteria. A standardized form will be used to extract the following information: study characteristics (design, randomization method, blinding, allocation generation and concealment, statistics); participants; interventions (definition of exercises); clinical outcomes (types of outcomes measured: dichotomous or continuous and adverse effects) (Tables 1 and 2).

Table 1. Study characteristics related to the number of participants, inclusion, and exclusion criteria.

Author/ Year	No. of participants	Inclusion criteria	Exclusion criteria

https://doi.org/10.1371/journal.pone.0241962.t001

Table 2. Study characteristics related to the configuration; the number of participants according to the group; gestational age; exercise definition, outcome measures for women; and follow up.

Title, Authors, Years	Location	Number of participants per group	Gestational age (weeks) (baseline)	Definition of exercises (training protocol details)	Outcomes	Follow-up (simplified)	Results	Grade Score

https://doi.org/10.1371/journal.pone.0241962.t002

Studies that do not fully meet the inclusion criteria will be excluded and tabulated with their justification for the exclusion (Table 3).

Methodological quality, risk of bias and statistical report. The risk of bias will be assessed according to the Cochrane Handbook of Interventions Systematic Reviews, which assesses the following domains: allocation generation; concealment of allocation; masking (of participants and researchers); the presence of incomplete data; reporting bias of information and other types of bias. The answers to these domains may be "Yes", "No" or "Uncertain". The final grade of the study will be based on the responses given to the first three domains and will be classified as having high, low or risk of uncertain bias [8]. Dichotomous data will be calculated relative risk, i.e. proportion of events in the treatment group under the relation to the proportion of events in the control group, with a 95% Confidence Interval (CI). Such estimates will be calculated from the intention-to-treat analysis approach. Continuous data will be expressed as means and standard deviation, and the weighted average proportion with 95% CI will be calculated. Publication bias will be evaluated with funnel plots and formally assessed with the Egger test. For variability in results between studies, the I2 statistic and the P-value obtained from the Chi-squared Cochrane test will be used. Review Manager software (RevMan) will be used for all analyses, including meta-analysis if possible [9–11].

Quality of evidence. We intend to use the Evaluation, Development and Evaluation Recommendation Rating (GRADE) to assess the overall strength of evidence assessment. In RCT, the GRADE system evaluates the limitations of the study, inconsistencies, indirect evidence, inaccuracies, and publication bias, classifying the evidence as high, moderate, low, or very low [12].

Discussion

The literature suggest that PFM exercises, accompanied by training of approximately 12 weeks including aerobic and resistance exercises under intense supervised guidance, are effective for prevention, treatment and reduction of PS-UI in women with GDM and/or HG [13–15]. However, there is no systematic review that evaluated the standardized PFM Exercises program for physiotherapy.

In literature there are RCTs, but not summarized. This study design has been chosen because in this way we may assess the highest available level of evidence. The present systematic review will be the first to analyze the effectiveness of PFM exercises in pregnant women with GDM or HD with PSUI.

Table 3. Exclusion table from systematic review and meta-analysis of randomized controlled trials to evaluate the effects of PFM exercise on pregnant women with GDM and gestational urinary incontinence and/or pelvic floor muscle dysfunction.

First author, Years of publication	Title	Reasons for exclusion

https://doi.org/10.1371/journal.pone.0241962.t003

In this way we may obtain robust and conclusive evidence whether or not there is evidence to support clinical practice, in addition to promote high quality studies on the subject.

Supporting information

S1 File. PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: Recommended items to address in a systematic review protocol*.
(DOC)

S2 File. PROSPERO international prospective register of systematic reviews.
(PDF)

Acknowledgments

We thank the Diamater Study Group for making valuable comments.

The Diamater Study Group: Rudge MVC, Barbosa, AMP, Caldeiron IMP, Souza FP, Berghmans B, de Bie R, Thabane L, Junginger B, Graeff CFO, Magalhães CG, Costa RA, Lima SAM, Kron-Rodrigues MR, Felisbino S, Barbosa W, Campos FJ, Bossolan G, Corrente JE, Nunes HRC Abbade J, Rossignoli PS, Pedroni CR, Atallah AN, Di Bella ZIKJ, Uchoa SMM, Hungaro MA, Mareco EA, Sakalem ME, Martinho N, Hallur LSR, Reyes DRA, Alves FCB, Marcondes JPC, Prudencio CB, Pinheiro FA, Sartorão CI, Quiroz SBCV, Pascon T, Nunes SK, Catinelli BB, Reis FVDS, Oliveira RG, Barneze S, Enriquez EMA, Takano L, Carr AM, Magyori ABM, Iamundo LF, Carvalho CNF, Jacomin M, Avramidis RE, Silva AJB, Orlandi MIG, Dangió TD, Bassin HCM, Melo JVF, Takemoto MLS, Menezes MD, Caldeirão TD, Santos NJ, Lourenço IO, Marostica de Sá J, Caruso IP, Rasmussen LT, Garcia GA, Nava GTA, Pascon C, Bussaneli DG, Nogueira VKC, Rudge CVC, Piculo F, Prata GM.

Author Contributions

Conceptualization: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, Álvaro Nagib Atallah, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Data curation: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Formal analysis: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Funding acquisition: Angélica Mércia Pascon Barbosa, Marilza Vieira Cunha Rudge.

Investigation: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, David Rafael Abreu Reyes, Raghavendra Lakshmana Shetty Hallur, Sthefanie Kenickel Nunes, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Methodology: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Project administration: Angélica Mércia Pascon Barbosa, Meline Rossetto Kron Rodrigues, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Resources: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Marilza Vieira Cunha Rudge.

Software: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Supervision: Angélica Mércia Pascon Barbosa, Marilza Vieira Cunha Rudge.

Validation: Angélica Mércia Pascon Barbosa, Marilza Vieira Cunha Rudge.

Visualization: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, David Rafael Abreu Reyes, Raghavendra Lakshmana Shetty Hallur, Sthefanie Kenickel Nunes, Fabiane Affonso Pinheiro, Carlos Isaías Sartorão Filho, Gabriela Lopes Piemonte Andrade, Bary Berghmans, Rob de Bie, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Writing – original draft: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, David Rafael Abreu Reyes, Raghavendra Lakshmana Shetty Hallur, Sthefanie Kenickel Nunes, Fabiane Affonso Pinheiro, Carlos Isaías Sartorão Filho, Gabriela Lopes Piemonte Andrade, Bary Berghmans, Rob de Bie, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

Writing – review & editing: Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, Caroline Baldini Prudencio, Raghavendra Lakshmana Shetty Hallur, Fabiane Affonso Pinheiro, Carlos Isaías Sartorão Filho, Gabriela Lopes Piemonte Andrade, Bary Berghmans, Rob de Bie, Silvana Andréa Molina Lima, Marilza Vieira Cunha Rudge.

References

1. Rudge MVC, Girão MJBC, gravidez G acadêmico D e, Grupo acadêmico Aspectos clínicos moleculares e gênicos da incontinência urinária feminina. Diabete gestacional e incontinência urinária: interação entre a Ginecologia e a Obstetrícia TT—Gestational diabetes and urinary incontinence: the interaction of Gynecology and Obstetrics. Rev Bras Ginecol Obs. 2011; 33(5):207–10.
2. Barbosa AMP, Adriano Dias GM, Calderon IMP, Rudgel MVC, Witkin S. Urinary incontinence and vaginal squeeze pressure two years post-cesarean delivery in primiparous women with previous gestational diabetes mellitus. Clinics. 2011; 66(8):1341–5. https://doi.org/10.1590/s1807-59322011000800006 PMID: 21915481
3. Santos PC, Mendonça D, Alves O, Barbosa AM. [Prevalence and impact of stress urinary incontinence before and during pregnancy]. Acta Med Port. 2006; 19(5):349–56. PMID: 17376320
4. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology. 2003 Jan; 61(1):37–49. https://doi.org/10.1016/s0090-4295(02)02243-4 PMID: 12559262
5. Woodley SJ, Lawrenson P, Boyle R, Cody JD, Mørkved S, Kernohan A, et al. Pelvic floor muscle training for preventing and treating urinary and faecal incontinence in antenatal and postnatal women. Cochrane Database Syst Rev [Internet]. 2020 May 6; Available from: http://doi.wiley.com/10.1002/14651858.CD007471.pub4 PMID: 32378735
6. Davenport MH, Nagpal TS, Mottola MF, Skow RJ, Riske L, Poitras VJ, et al. Prenatal exercise (including but not limited to pelvic floor muscle training) and urinary incontinence during and following pregnancy: a systematic review and meta-analysis. Br J Sports Med. 2018 Nov; 52(21):1397–404. https://doi.org/10.1136/bjsports-2018-099780 PMID: 30337466
7. Dumoulin C, Cacciari LP, Hay-Smith EJC. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. Cochrane Database Syst Rev [Internet]. 2018 Oct 4; Available from: http://doi.wiley.com/10.1002/14651858.CD005654.pub4 PMID: 30288727
8. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015 Dec; 4(1):1. https://doi.org/10.1186/2046-4053-4-1 PMID: 25554246
9. Higgins JP, Savović J, Page MJ, Elbers RG, Sterne JA. Assessing risk of bias in a randomized trial. In: Cochrane Handbook for Systematic Reviews of Interventions. Wiley; 2019. p. 205–28.

10. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. PLoS Med. 2009 Jul; 6(7):e1000100.
11. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014
12. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008 Apr; 336 (7650):924–6. https://doi.org/10.1136/bmj.39489.470347.AD PMID: 18436948
13. Van Kampen M, Devoogdt N, De Groef A, Gielen A, Geraerts I. The efficacy of physiotherapy for the prevention and treatment of prenatal symptoms: a systematic review. Int Urogynecol J. 2015 Nov; 26 (11):1575–86. https://doi.org/10.1007/s00192-015-2684-y PMID: 25822028
14. Stafne S, Salvesen K, Romundstad P, Torjusen I, Mørkved S. Does regular exercise including pelvic floor muscle training prevent urinary and anal incontinence during pregnancy? A randomised controlled trial. BJOG An Int J Obstet Gynaecol. 2012 Sep; 119(10):1270–80. https://doi.org/10.1111/j.1471-0528.2012.03426.x PMID: 22804796
15. Perales M, Santos-Lozano A, Ruiz JR, Lucia A, Barakat R. Benefits of aerobic or resistance training during pregnancy on maternal health and perinatal outcomes: A systematic review. Early Hum Dev. 2016 Mar; 94:43–8. https://doi.org/10.1016/j.earlhumdev.2016.01.004 PMID: 26850782

Artigo 2

Artigo Original redigido de acordo com as normas de publicação da revista *Plos One* para a qual será submetido. Qualis A1 MED III – FI: 3,752 https://impactfactorforjournal.com/plos-one-impact-factor/

Effectiveness of pelvic floor muscle training for pregnant women with and without gestational diabetes mellitus and pregnancy specific urinary incontinence: Systematic review and meta-analysis of randomized trials

Eusebio Mario Amador Enriquez[1ab] Angélica Mércia Pascon Barbosa[1,2ab], Meline Rossetto Kron-Rodrigues [3b], Caroline Baldini Prudencio[1b], Carolina Neiva Frota de Carvalho[1b], Álvaro Nagib Atallah[4c], David Rafael Abreu Reyes[1c], Raghavendra Hallur Lakshmana Shetty[1c], Sthefanie Kenickel Nunes[1c], Fabiane Affonso Pinheiro[1c], Carlos Isaías Sartorão Filho[1c], Gabriela Lopes Piemonte Andrade[5c], Bary Berghmans[6c], Rob de Bie[6c], Silvana Andréa Molina Lima[7bd], Marilza Vieira Cunha Rudge[1bd*] and The Diamater Study Group[#]

a AMPB and EMAE are first authors on this work

b,c These authors contributed equally to this work

d SAML and MVCR are last authors on this work

1 São Paulo State University (UNESP) Postgraduate Program on Tocogynecology Botucatu Medical School (FMB) Botucatu CEP 18618-687 São Paulo State Brazil.

2 Department of Physiotherapy and Occupational Therapy São Paulo State University (UNESP) School of Philosophy and Sciences Marília São Paulo Brazil.

3 PhD Professor at the Stricto Sensu Graduate Program in Nursing at UNIVERITAS, Guarulhos University (UNG), Guarulhos, São Paulo, Brazil.

4 Discipline of Evidence-Based Medicine, Paulista School of Medicine-Federal University of São Paulo (EPM-UNIFESP), São Paulo-SP 04024-002, Brazil.

5 Department of Physiotherapy, Universidade do Oeste Paulista (UNOESTE), Presidente Prudente, São Paulo State, Brazil.

6 Pelvic care Center Maastricht, Maastricht University Medical Center, Maastricht, The Netherlands

7 Department of Nursing, Botucatu Medical School (FMB), São Paulo State University (UNESP), Botucatu, São Paulo State, Brazil.

The Diamater Study Group: Rudge MVC, Barbosa AMP, Calderon IMP, Souza FP, Lehana T, Graeff CFO, Rodrigues MRK, Felisbino SL, Barbosa WF, Bossolan G, Corrente JE, Nunes HRC, Abbade JF, Rossignoli PS, Pedroni CR, Jármy-Di Bella ZI, Uchôa SMM, Duarte MAH, Mareco EA, Sakalem ME, Martinho NM, Bussaneli DG, Orlandi MIG, Pascon C, Dangió TD, Rudge CVC, Piculo F, Prata GM, Avramidis RE, Carvalho CNF, Magyori ABM, Nava GTA, Caldeirão TCD, Shetty RHL, Reyes DRA, Alves FCB, Marcondes JPC, Takemoto MLS, Prudencio CB, Pinheiro FA, Sartorao Filho CI, Quiroz SBCV, Pascon T, Nunes SK, Catinelli BB, Reis FVDS, Oliveira RG, Costa SMB, Menezes MO, Santos NJ, Enriquez EMA, Takano L, Carr AM, Garcia GA, Iamundo LF, Bassin HCM, Barbosa VP, Jacomin M, Silva AJB, Lourenço IO, Marostica de Sá J, Caruso IP, Rasmussen LT, Nogueira VKC, Ribeiro-Paes JT, França DCH, Bastos HVM, Heliodoro MLA, Kuroda MN, Carvalho, H.L., Mosele, FC

* Corresponding author:
Prof. Marilza Vieira Cunha Rudge, MD, PhD
Postgraduate Program on Tocogynecology
Botucatu Medical School
São Paulo State University (Unesp)
Botucatu, São Paulo State Brazil
e-mail: marilzarudge@gmail.com

Abstract

Background: There is a broad evidence that Gestational Diabetes Mellitus (GDM) has a direct influence on urinary incontinence and pelvic floor muscles.

Targeted PFMT is effective in Pelvic floor muscle training (PFMT) is effective in the prevention and treatment of UI during pregnancy and after birth either for preventing or treating incontinence.

Our aims were to investigate the systematic review of the effectiveness of Pelvic Floor Muscle Training(PFMT) on muscular dysfuntion of Pregnancy-Specific Urinary Incontinence (PSUI) in GDM and non-GDM women) **Methods:** A systematic review with meta-analysis according to the Cochrane methodology of Randomized Controlled Trials was conducted to measure the effects of exercise on all relevant exercise-based interventions for the treatment of muscular dysfunction in pregnancy specific urinary incontinence in GDM and non-GDM women pregnant women. Relevant articles were retrieved through the electronic databases and adapted for Embase, MEDLINE, LILACS, and CENTRAL databases, from the date of index inception to June 2020. This study adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The MeSH terms used was "Pregnancy", "Hyperglycemia", "Diabetes Mellitus, Type 2", "Diabetes Mellitus, Type 1", "Pregnancy in Diabetics", "Diabetes, Gestational", "Urinary Incontinence". *Primary outcomes:* improvement or cure of PSUI that were evaluated by questionnaires and tools such as tampon test, voiding diary, urodynamic study). *Secondary outcomes:* improvement of pelvic floor muscle strength (pelvic floor functional assessment, perineometer, electromyography, functional ultrasonography), quality of life improvement (questionnaires), presence or absence of postpartum urinary incontinence and adverse effects. Quality assessment by Cochrane instrument. Metanalysis was performed by the software Review Manager 5.3.

Results: The present systematic review and meta-analysis comprising data from 5 RCTs studies, including 1697 pregnant women of different nationalities reveals that PFMT was relatively effective in decreasing long-UI in GDM pregnant women unlike in the controls. **Conclusion:** The results confirm that PFMT applied in pregnancy is effective in the treatment and prevention of UI specially in non-GDM population, but confidence in the effect is limited (low). Concerning the effects of PFMT on special population as GDM pregnant we detected a gap on knowledge about its effect.

Systematic review registration: PROSPERO CRD42017065281.
Keywords: Pregnancy, Hyperglycemia, Diabetes Mellitus, Gestational diabetes mellitus, Urinary incontinence; Pelvic Floor Disorders, Dysfunctions, Pelvic floor muscle training, Pelvic floor muscle exercises, Involuntary urine loss, Exercise training, Physical activity.

Background

Pregnancy and delivery are considered important risk factors for developing Pregnancy-Specific Urinary Incontinence (PSUI) (1), a urinary incontinence (UI) that starts during pregnancy. The increased burden of pregnancy on the pelvic floor and hormonal changes may reduce strength and function of the pelvic floor muscles (PFMs).(1) Incidence and severity of PSUI increases throughout pregnancy and often continues into the postpartum period. (2)

Not only non-GDM women but also GDM women showed either high prevalence of PSUI during pregnancy (50.8% vs. 31.6%) or high long-UI after C-section compared to non-GDM (44.8% vs. 18.4%). In a multivariate analysis, GDM was an independent risk factor for the occurrence of PSUI and pregnant women with prior GDM have weakness of the pelvic floor muscles (PFM) two years after birth.(3)

The pelvic floor plays an important part in maintaining continence.(4) Contraction of the pelvic floor muscles (PFMs) causes an inward lift and squeeze around the urethra, vagina and rectum,(5) resulting in closure, stabilization and resistance to downward movement.(6)

Pelvic floor muscle training (PFMT) has the potential to strengthen PFM and enhance function and may be able to prevent weakening of the periurethral muscles.(7) Targeted PFMT is effective in prevention and treatment of UI among pregnant (8) and non-pregnant women.(9) A Cochrane review from 2017 considered PFMT as first-line conservative management to SUI and all other types of UI ,nevertheless they didn't include PSUI treatment on the revision [7]. Another Cochrane review from 2020 showed that due to the quality and quantity of well-designed studies when antenatal or postnatal populations were evaluated the influence of PFMT for treatment and/or prevention is uncertain or not at all clear.(8) So a little is known about PSUI prevention or treatment, particularly the impact of Hyperglycemic status on the

PSUI. (8)

While all of these studies have focused on UI, a recurrent issue raised whether PSUI associated or not with GDM will benefit of PFMT**.** Efforts to develop specific therapies for this binomial have been mostly unsuccessfull, likely reflecting the poor understanding of PSUI either in GDM or non-GDM pregnant women.

Gestational diabetes mellitus (GDM) is a global health problem and considered the most common metabolic disorder during pregnancy.(10) According to the report of the International Diabetes Federation, the global prevalence of GDM in 2017 has reached 14.0%, affecting nearly 21.3 million live births.(11) Urinary incontinence (UI) is defined as “any complaint of involuntary loss of urine”.(12) The highly prevalent nature of UI (13) in prenatal and postpartum period is striking: 18–75% of patients in late gestation and one-third of women after childbirth. (14)

UI may reduce quality of life, and many women withdraw from social settings and physical activities because of fear of leakage and an unpleasant odor.(15) GDM and Urinary Incontinence (UI) are two clinical entities with substantial social and economic burden, associated with significant direct and indirect public health costs.(16) PSUI in GDM women worsen the occurrence and severity of UI, and the impact of UI on QoL over the first year postpartum. These results emphasize the interaction between PSUI, GDM and long-term maternal UI.(17) This current and undervalued finding provides evidence of the requirement to increase knowledge of appropriate treatment for this binomial: prior GDM and long-UI Pelvic floor muscle training (PFMT)exerts the potential to strengthen pelvic floor muscles and therefore may be able to prevent weakening of the periurethral muscles.(14)

It is important to highlight that a systematic review by Cochrane (2020) provides evidence that early, structured PFMT in early pregnancy for continent women may prevent the onset of UI in late pregnancy and postpartum. Population approaches (recruiting antenatal women regardless of continence status) may have a smaller effect on UI, although the reasons for this are unclear. A population-based approach for delivering postnatal PFMT is not likely to reduce UI. Uncertainty surrounds the effects of PFMT as a treatment for UI in antenatal and postnatal women, which contrasts with the more established effectiveness in mid-life women and for GDM women.

Several meta-analysis (18–25), two systematic reviews (26,27) and one RCT (28) evidenced that exercise during pregnancy had a beneficial effect on GDM,

reporting a risk reduction between 28% (RR = 0.72, 95% CI = 0.58 to 0.91) (24)and 59% (RR = 0.41, 95% CI = 0.24 to 0.68).(25) This benefit was found across different populations - obese and overweight women (RR = 0.71, 95% CI = 0.57 to 0.89) (19) and previously healthy women (18–25). Although, none of these studies are involved with the treatment or prevention of muscular dysfunction of PFM in PSUI of non-GDM and GDM pregnant women.

The mechanism of the interrelationship between GDM and PSUI is under development. Previously, we demonstrated in translational and clinical studies that a Gestational Diabetic induced Myopathy (GDiM) appears to be the pathophysiological basis of the mutual connection between PSUI and GDM.(29–35) This GDiM of the skeletal muscles linked into the UI mechanism as Pelvic Floor Muscle (PFM) and Rectus Abdominis Muscle (RAM) has been described as an atrophic and stiff muscle caused by collagen I/III ratio alteration.(35,36) These atrophic and stiff muscle characteristics was detected too on PFM 3D US and on electromyography (33,34).

Skeletal muscle atrophy is a pathological condition so far without effective treatment and poorly understood at a molecular level.(37) However, skeletal muscle is an unmatched regenerative tissue with the ability to undergoes extensive adaptation by changing its fiber type composition and cross-sectional area (CSA) upon external stimuli.(38,39)

Skeletal muscle has been considered an organ highly adaptable largely depending on the microcirculation homeostasis.(40) During muscle regeneration both myogenesis and angiogenesis occur, and endothelial cells (ECs) and myogenic precursor cells interact to expand and differentiate.(41) Skeletal muscle regeneration process in response to injury requires an intricate coordination among different populations of cells to develop a new muscle fiber.(42)

An imbalance of M1 and M2 macrophages seems to lead to impaired satellite cell activation, and these are the main cells that function during skeletal muscle regeneration, after muscle damage. This imbalance leads to the accumulation of Fibro-adipogenic progenitors (FAPs) in skeletal muscle, increasing the production of pro-fibrotic factors (e.g., extracellular matrix components), impairing the niche for proper satellite cell activation and differentiation. Strategies to revert chronic inflammation into a pro-regenerative pattern are required. There is a potential role of chronic physical activity and exercise in restoring the M1 and M2 macrophage balance and

consequently, the satellite cell niche to improve skeletal muscle regeneration after injury.(43)

Angiogenesis is another fundamental step for regeneration and recovery of skeletal muscle function. In recent review, we concluded that scientific and technological advances to engineering methodologies are fundamental in the development of more effective and safer proangiogenic therapies, even when enormous advances have been made in this area in the recent years.(44) Since angiogenesis is required for muscle regeneration and proangiogenic therapies, i.e., therapeutic angiogenesis, is considered as a key phenomenon in clinical and preclinical studies. Ang1 effect on fiber regeneration, myogenesis, and angiogenesis has been assessed in a mice model of injured tibialis muscle.(45) Although, only preclinical trials are under development.

Physical exercise (PE), defined as a planned, structured physical activity performed to improve one or more components of physical fitness is a key element of a healthy lifestyle, contributing to the prevention and treatment of several diseases.(46)

The terms “PE” or just “exercise,” refers to physical activity-any movement requiring energy, such as walking, manual labor, or housework—will induce similar benefits as PE— movement intended to maintain or increase physical health or performance—provided that the load is comparable. The load of PE is quantified by providing information on the type, duration, and intensity of the exercise; the number of series and repetitions; as well as the duration of rest in between repetitions and in between series. Exercise induces several physiological adaptive processes by modulating cellular and molecular regulatory mechanisms. Modification of molecular pathways including intracellular and extracellular signaling may be attributed to alteration of gene/protein expressions leading to cellular/tissue phenotypic changes. In addition, the role of immune and satellite cells in muscle regeneration and restoration as well as hereditary genetic differences are the most important factors affecting exercise-induced physiological adaptive processes.(47)

PE has presented interesting findings to improve the niche for skeletal muscle regeneration. Although, exercise intensity should be interpreted with caution depending on the level of inflammation in the skeletal muscle. Further studies are required to determine the cause–effect relationship between adaptations observed by physical exercise in the role of main cells required for a proper skeletal muscle

regeneration.(43)

Skeletal muscle is an adaptive tissue with the ability to regenerate in response to exercise training. In contrast, exercise training is an incomparable physiological-hypertrophy stimulus with the skill to lead muscle regeneration throw increasing myofiber CSA.(48) Exercise therapy can slow down or even reverse muscle atrophy, one of the main findings of the GDiM.(49)

A pre-clinical study carried out by the same authors of the present review aimed to determine whether swimming exercise (SE) has a therapeutic effect in diabetic pregnant rats. The findings showed that SE during pregnancy reversed long-term rectus abdominis myopathy in diabetic pregnant rats. These findings may be considered in pregnant women with rectus abdominis muscle myopathy damage caused by GDM.(50)

Hence, in this study, we decided to gather more comprehensive scientific evidence to enhance our understanding about the effectiveness of PFMT for the treatment of muscular dysfunction of PFM in PSUI of GDM and non-GDM pregnant women. The overall goal of the proposed systematic review and meta-analysis is to perform evidence from randomized controlled trials (RCTs) and meta-analysis on related studies aiming, ultimately, at establishing a more convincing conclusion.

Materials and methods

Protocol and registration

The present systematic review and meta-analysis was performed following Cochrane methodology (51) and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.(52) The study protocol was discussed and agreed upon in advance by all authors and published.(53) Its protocol was registered in the International Prospective Register of Systematic Reviews database, accessible under the protocol number CRD4201706528. The protocol was also published in manuscript format in this same scientific journal.

Study inclusion and exclusion criteria

Inclusion criteria: RCTs of pregnant women non-GDM or with hyperglycemia (all levels), nulliparous, primiparous and multiparous women during pregnancy, receiving PFM training to prevent and/or reduce the symptoms of PSUI.

Exclusion criteria: all other designs, not being RCT.

Outcomes

Primary outcomes: Occurrence, reduction, recurrence, or persistence of PSUI symptoms.

Secondary outcomes: Improvement of PFM strength (pelvic floor functional assessment, perineometer, electromyography,functional ultrasonography), quality of life improvement (questionnaires), presence or absence of postpartum UI and adverse effects.

Literature search strategies

A model strategy was created and adapted for searching the data bases Embase, Pubmed, Lilacs and CENTRAL to identify studies involving the above-mentioned interventions. RCTs registry sites were consulted for ongoing studies on the topic (Rebec, Clinicaltrial.gov). Grey literature was consulted as well as Capes database. There was no language restrictions. MeSH terms used for our searches are "Pregnancy", "Hyperglycemia", "Diabetes Mellitus, Type 2", "Diabetes Mellitus, Type 1", "Pregnancy in Diabetics", "Diabetes, Gestational", "Urinary Incontinence".The searches were carried out in the month of March 2021. Information on ongoing RCTs was consulted through the Clinical Trials website of the National Institute of Health (54) and through the Brazilian Registry of Clinical Trials-ReBEC.(55)

Data collection and analysis: Selection of studies: For each search strategy, two reviewers (EMAE e MRKR) were independently evaluate the studies retrieved from the databases in the order: title, abstract and full reading. In case of overlapping study populations, only the larger study was included. All studies potentially eligible for inclusion in the review were selected for full reading. In case of disagreement, a third reviewer were consulted.

Data extraction and management: Data extraction for eligible studies was performed by two reviewers who were independently extract data from articles that meet the inclusion criteria. A standardized form was used to extract the following information: study characteristics (design, randomization method, blinding, allocation

generation and concealment, statistics); participants; interventions; clinical outcomes (types of outcomes measured: dichotomous or continuous and adverse effects) (Table 1 and 2)

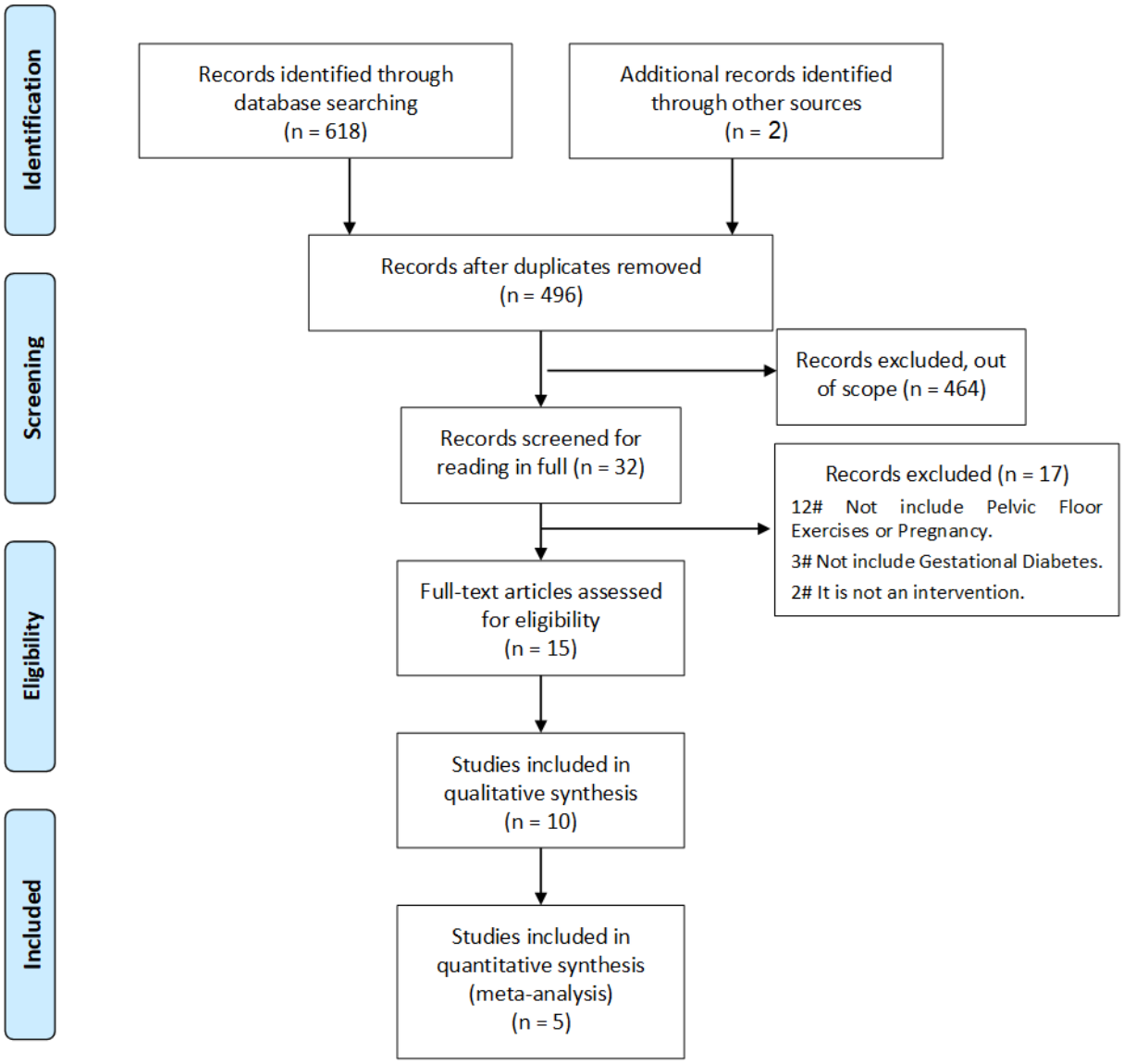
Methodological quality, risk of bias and statistical report. The risk of bias was assessed according to the Cochrane Handbook of Interventions Systematic Reviews, which assesses the following domains: allocation generation; concealment of allocation; masking (of participants and researchers); the presence of incomplete data; reporting bias of information and other types of bias. The answers to these domains may be “Yes”, “No” or “Uncertain”. The final grade of the study was based on the responses given to the first three domains and was classified as having high, low or risk of uncertain bias.(51) Dichotomous data was calculated relative risk, i.e., proportion of events in the treatment group under the relation to the proportion of events in the control group, with a 95% Confidence Interval (CI). Such estimates was calculated from the intention-to-treat analysis approach. Continuous data was expressed as means and standard deviation, and the weighted average proportion with 95% CI was calculated. Publication bias was evaluated with funnel plots and formally assessed with the Egger test. For variability in results between studies, the I2 statistic and the P-value obtained from the Chi-squared Cochrane test was used. Review Manager software (RevMan) was used for all analyses, including meta-analysis if possible.(56)

Quality of evidence. We use the Evaluation, Development and Evaluation Recommendation Rating (GRADE) to assess the overall strength of evidence assessment. In RCT, the GRADE system evaluates the limitations of the study, inconsistencies, indirect evidence, inaccuracies, and publication bias, classifying the evidence as high, moderate, low, or very low.(57)

Results

After reading the articles resulting from the nT in their entirety, only 4 of them fall within the parameters of the scope of our (Types of intervention (I): studies whose intervention was the exercise of the pelvic floor muscles as a treatment for UI during the gestational period) and 2 of these articles were duplicated in the Cochrane and

Embase databases. Articles that did not include intervention or that did not meet the inclusion criteria were excluded. (Flowchart 1) Of the excluded articles, 6 of them was used to write the discussion of our systematic review.



Flowchart 1. Exclusion flowchart in a systematic review and meta-analysis of randomized controlled trials to assess the effects of PFMT in pregnant women women non-GDM or GDM.

Description of the studies

5 RCT`s were included with non-GDM pregnant women, as no RCTs were identified with pregnant women with mild hyperglycemia or diabetes during pregnancy,(58–62) totaling 1697 pregnant women of different nationalities, aged

between 18 to 45 years old and with pregnancies between 18 to 35 weeks. In all the studies there were two research groups (intervention and control) where these women performed different types of exercises (aerobic, light strength, calisthenics) for the prevention of urinary incontinence or the so-called vaginal squeeze, which they had complained about previously.

These trials demonstrates that pregnant women who followed a 12-week course of regular exercise including PFMT were less likely to report UI and SUI in late pregnancy than women given standard care, including written instructions for PFMT. Studies that do not fully meet the inclusion criteria was excluded and tabulated with their justification for the exclusion.

Table 1. Study characteristics related to the number of participants, inclusion, and exclusion criteria.

Author/ Year	No. of participants	Inclusion criteria	Exclusion criteria
Gorbea, Viridiana et al (2005)	72 women. 52.7% performed pelvic floor exercises and 47.2% did not.	The study was conducted in nulliparous women between 15 and 35 years of age and in pregnant women at 20 weeks of gestation who did not have stress urinary incontinence, according to the definition of the International Continence Society, at the time of inclusion in the study. and willing to do pelvic floor exercises.	Women with multiple pregnancies, with two or more caesarean sections, with pregnancies with oligohydramnios or polyhydramnios, or with complications, such as isthmic-cervical incompetence, maternal-fetal isoimmunization, serious conditions, such as severe pregnancy-induced hypertensive disease, were not included or chronic degenerative conditions that affect the function of the pelvic floor, such as multiple sclerosis.
M. Pelaez et al (2014)	169 women were randomized by a central computer system.	Being healthy and primiparous pregnant with singleton fetus, being in gestational week 10–14, not suffering from UI, able to communicate in Spanish and able to give informed written consent.	Planning not to give birth in Fuenlabrada University Hospital and any contraindication according to the American College of Obstetricians and Gynecologists Guidelines.
Morkved et al (2003)	301 women were randomly allocated. Training (n= 148) or a control group (n= 153). Randomization was done in blocks of a maxi- mum of 32 with the use of opaque, sealed envelopes.	Women were eligible for the trial if they were nulliparous and 18 years or older, with a single live fetus at the routine ultrasound scan.	Pregnancy complications, high risk for preterm labor, pain during pelvic floor muscle contractions, ongoing urinary tract infection, or diseases that could interfere with participation. In addition, women who lived too far from Trondheim to be able to attend weekly training groups were excluded.
P. Ko et al (2011)	300 women were randomly assigned to the PFME group and control group.	Women over 18 years of age, between 16 and 24 gestational weeks with involuntary urine loss.	Exclusion criteria included multiparity, multiple gestations, severe pregnancy complications, high risk for preterm labor, pain during PFME, diseases that could interfere with participation, or would be unavailable for follow-up
S. Stafne et al (2012)	A total of 855 women were included in this trial.	Inclusion criteria were age ‡18 years and a singleton live fetus.	Exclusion criteria were high-risk pregnancies and/or diseases that could interfere with participation. For practical reasons we also excluded women who lived too far from the hospitals to attend weekly training groups (judged as more than 30-minutes' drive)

Table 2. Study characteristics related to the configuration; the number of participants according to the group; gestational age; exercise definition, outcome measures for women; and follow up.

Authors, Year, location	Number of participants per group	Gestational age (weeks) (baseline)	Definition of exercises	Outcomes	Follow-up (simplified)	Results
Gorbea, Viridiana et al (2005) México, DF	37 in the control group and 38 in the intervention group.	From 20 weeks of pregnancy until delivery.	In the pelvic floor physiotherapy group: 10 exercises per day consisting of fast and slow contractions; each exercise consisted of performing a slow contraction for eight seconds, followed by three fast contractions for one second each, and six seconds of rest between each exercise. The exercises were performed in supine position, with the legs slightly bent. When the patient mastered the exercise, it was done standing or sitting. The control group was not asked to do pelvic floor exercises during pregnancy.	The outcome variable was the presence of stress urinary incontinence. Variables were controlled, such as the number of pelvic floor exercises performed, gestational age at which the pregnancy resolved, route of resolution of the pregnancy, delivery instrumentation, perianal tears, duration of the second phase of labor (expulsive period), weight of the newborn, age of the patient, weight at 20, 28 and 35 weeks of gestation, weight gain from 20 to 35 weeks of gestation, adverse and beneficial effects of pelvic floor physiotherapy (referred by the patient), number of consultations with the physical therapist and urinary tract infection.	Using the electromyograph, the activity of the pelvic floor muscles was recorded during the maximum contraction (by stimulating the patient to contract as hard as possible and hold the contraction for eight seconds) at 20, 28 and 35 weeks of gestation, as well as six weeks after the resolution of the pregnancy. Weight was recorded at 20, 28 and 35 weeks of gestation. The clinical file was reviewed to complete the data collection sheet.	75 patients who met the selection criteria, there were two losses: one due to death not related to pregnancy and another due to change of address, one more was eliminated due to immature delivery at 23 weeks of gestation. 72 women participated, 34 (47.2%) did not perform pelvic floor exercises, while 38 (52.7%) did. The frequency of stress urinary incontinence at 28 weeks of gestation, in the group that did not exercise, was 17.6%, while at 35 weeks it was 41.2% ($p < 0.0001$). A protective effect was found for stress urinary incontinence at 35 weeks of gestation in women who performed pelvic floor exercises during pregnancy, with a relative risk of 0.031 and a 95% confidence interval, (95% CI) 0.002, 0.5 and 0.66 (95% CI) 0.241, 0.852, respectively. At 28 weeks of gestation, six women in the control group had urinary incontinence, of which only two had a positive cough test; at 35 weeks, 14 patients in the same group had urinary incontinence and only six had a positive cough test. Electromyography was conducted only in 26 women, since when the first cut was made and the results were analyzed, it was significant from 28 weeks of gestation, with $p = 0.08$, at 35

						weeks of gestation, with p = 0.000, and at six weeks after the resolution of the pregnancy, with p = 0.000; For this reason and because it is an invasive maneuver, it was not performed in the rest of the women. The exercise group had greater pelvic floor muscle strength at 35 weeks' gestation.
M. Pelaez et al (2014) Madrid, Spain.	Exercise group (EG) (exercise class including PFMT) (n = 73) and a control group (CG) (n = 96)	14–36 weeks of gestation	The program consisted of 70–78 group sessions (8–12 women). The sessions were held three times per week and were 55–60 min in duration. Each session consisted of 8 min of warm-up; 30 min of low impact aerobics (performing different choreographies) including 10 min of general strength training (e.g., core muscles, pectoralis, gluteus, quadriceps, calves, biceps); 10 min of PFMT and 7 min of cool down, which included stretching, relaxation, or massage. Women in the control group (CG) received usual care (which included follow up by midwifes including information about PFMT) and were not asked to train their pelvic floor muscles.	The primary outcomes were (i) the reported frequency, (ii) amount, and (iii) impact on daily life of UI.	The PFMT followed a progression, starting with one set of eight contractions and increasing the number of total contractions to one hundred, divided in different sets of slow (6 sec) and fast contractions (five contractions as fast as possible). To increase motivation and abilities, we used different exercises, positions and sometimes music to follow the beat. Women were encouraged to perform 100 contractions distributed in different sets every day.	Data from 152 women were analyzed (10.1% loss to follow-up: 10 from the EG and 7 from the CG). At the end of intervention (week 36 of pregnancy) there were statistically significant differences in favor of the EG as shown in Table II). 95.2% of women in the EG reported no leakage versus a 60.7% of women in the CG. Only women of CG had a frequency of leakage more than of once a week (17/19.1%). The amount of leakage reported by incontinent women in the EG is referred as a "a small amount" (3/4.8%) but in the CG, women reported "a small amount" (27/30.6%), "a moderate amount" (5/5.6%), and even "a large amount" (3/3.4%). Regarding how much leaking affects their daily lives, the mean in the CG was higher than in the EG (0.9 (SD 1.8) vs. 0.1 (SD 0.6), respectively. Finally, ICIQ-UI SF Score shows statistically significant differences between the groups and the estimated effect size was 0.8.
Morkved et al (2003) Oslo, Norway.	301 women were randomly allocated to a training (n = 148) or a control group (n= 153). Randomization was done in blocks of a maxi- mum of 32 with the use of opaque, sealed	At 18 weeks' pregnancy were invited to participate in the study	All women in both groups were individually instructed in pelvic floor anatomy and how to contract the pelvic floor muscles correctly by a physiotherapist before randomization. The training group followed a specially designed exercise	The primary outcome measure was self-reported symptoms of urinary incontinence. The secondary outcome measure was pelvic floor muscle strength.	Women were examined at 20- and 36-weeks' gestation. Vaginal palpation and observation during con- traction were used to assess the women's ability to perform pelvic floor muscle contraction. Pelvic floor muscle strength (vaginal squeeze pressure) was	At follow-up, significantly fewer women in the training group than in the control group reported urinary incontinence: 48 of 148 (32%) versus 74 of 153 (48%) at 36 weeks' pregnancy. Potential effects of differences between groups according to baseline characteristics (age, body mass

	envelopes.		course including pelvic floor muscle and general exercises. They trained with a physiotherapist for 60 minutes once a week for a period of 12 weeks (between 20 and 36 pregnancy weeks). The physiotherapist encouraged the women to perform near maximal pelvic floor muscle contractions, and to hold the contraction 6–8 seconds. At the end of each contraction the women were asked to add three to four fast contractions. The resting period was about 6 seconds. Group training was performed in lying, sitting, kneeling, and standing positions with legs apart to emphasize specific strength training of the pelvic floor muscles and relaxation of other muscles. Body awareness, breathing, and relaxation exercises and strength training for the abdominal, back, and thigh muscles were performed to music between positions. In addition, the women were encouraged to use their preferred position and perform eight to 12 equally intensive pelvic floor muscle contractions twice per day at home. Women in the control group were not discouraged from doing pelvic floor muscle exercise on their own.		measured by a vaginal balloon catheter connected to a pressure transducer. The method was found to be dependable and valid in a previous study.	index, pelvic floor muscle strength, physical activity, urinary incontinence at baseline) were analyzed by logistic regression for odds ratio and did not change the results of the relative risk estimates. The number of episodes of involuntary leakage during the 3 days directly after the first assessment did not significantly differ between the two groups. At follow-up at 36 weeks' pregnancy the number of leakage episodes was significantly lower in the training group (25 of 148 versus 44 of 144, P⁄⁄ .014). The pelvic floor muscle strength was significantly higher in the training group at 36 weeks' pregnancy (P⁄⁄ .008). No negative side effects of the training were reported.
P. Ko et al (2011) Taiwan, Republic of China	300 women were randomly assigned to the PFME group (n=150) or the control group (n=150). Randomization was achieved by selection of sealed envelopes, which	Nulliparous women at 16 to 24 gestational weeks to 36 gestational weeks.	The exercise group followed a specially designed pelvic floor muscle training course, as published previously by Reilly et al. [10]. However, we did not ask pregnant women to increase the number of contractions per repetition from eight to 12 at the third trimester as Reilly et al. did. The	Evaluate the effect of antenatal pelvic floor muscle exercise (PFME) in the prevention and treatment of urinary incontinence during pregnancy.	Compliance in the PFME group was monitored using diaries to record the number of daily exercises performed from the first examination to 36 gestational weeks. We considered women in the exercise group who reported practice PFME at least 75% as adherent.	The incidence of self-reported urinary incontinence was analyzed by the generalized estimating equations with results produced as follows: There is a significantly lower incidence of self-reported urinary incontinence in the PFME group than the control group (odds ratio=1.63, 95% confidence

	were opened at entry.		exercises comprised three repetitions of eight contractions each held for 6 s, with 2-min rest between repetitions. These were repeated twice daily at home with additional training in groups once a week for 45 min by a physical therapist and lasted throughout a 12-weeks' period. Each training group included around 10 women. Group training was performed in sitting and standing positions with legs apart to emphasize specific strength training of the pelvic floor muscles and relaxation of other muscles. Women of the control group also received regular prenatal care and received the customary written instructions that did not include PFME.		All women were interviewed by a research nurse and administered the questionnaires via face-to-face method at 36 gestational weeks	interval between 1.52 and 1.74, P<0.05) during late pregnancy (36 pregnancy weeks). During late pregnancy, the PFME group had significantly lower total UDI-6 and IIQ-7 scores as well as lower scores for questions 2, 3, and 4 of the UDI-6 Questionnaire (Table 2). Question 2 concerns urine leakage related to the feeling of urgency; question 3 investigates urine leakage related to activity, coughing, or sneezing; question 4 investigates small amounts of urine leakage. Total IIQ-7 scores show that quality of life related to incontinence is significantly better in the PFME group compared with the control group at 36 pregnancy weeks. The incidence of self-reported urinary incontinence was analyzed by the generalized estimating equations with results produced as follows: There is a significantly lower incidence of self-reported urinary incontinence in the PFME group than the control group (odds ratio=1.63, 95% confidence interval between 1.52 and 1.74, P<0.05) during late pregnancy (36 pregnancy weeks)
S. Kocaoz et al (2012) Ankara, Turkey.	A total of 102 women was included in the study. N = 52 intervention group. N = 50 control group.	Both groups were evaluated in terms of SUI at the 14th–20th, 28th and 32nd weeks of gestation.	The pregnant women in the control group were not instructed to do PFME. The exercise sessions consisted of three applications. Each application contained exercises for the contraction and relaxation of the pelvic floor muscles repeated 10 times. The pregnant women were asked to contract their pelvic floor muscles maximally and to hold for 10 s. The women were asked to record the number of times they did their exercises,	The primary outcome measure was the presence of SUI based on a negative 1-hour pad test (<2g in weight). Secondary outcome measures included urinary diary and verbal statements.	Subjects in both the intervention and control groups were followed-up at the 28th and 32nd weeks of gestation. The participants were asked questions such as 'Do you experience incontinence when you laugh, sneeze, cough, lift heavy objects, walk, or exercise?' for verbal assessment of SUI. Data concerning SUI frequency was obtained from the participants' urinary diaries and verbal statements.	When the distribution of SUI was evaluated according to follow-up week, 5.8% of the women in the intervention group developed SUI at the 28th gestational week, 17.3% at the 32nd gestational week. The relative percentages were 30, 48 and 18% for the pregnant women in the control group. A statistically significant difference was found between the intervention and control groups in terms of SUI presence at the 28th and 32nd gestational weeks

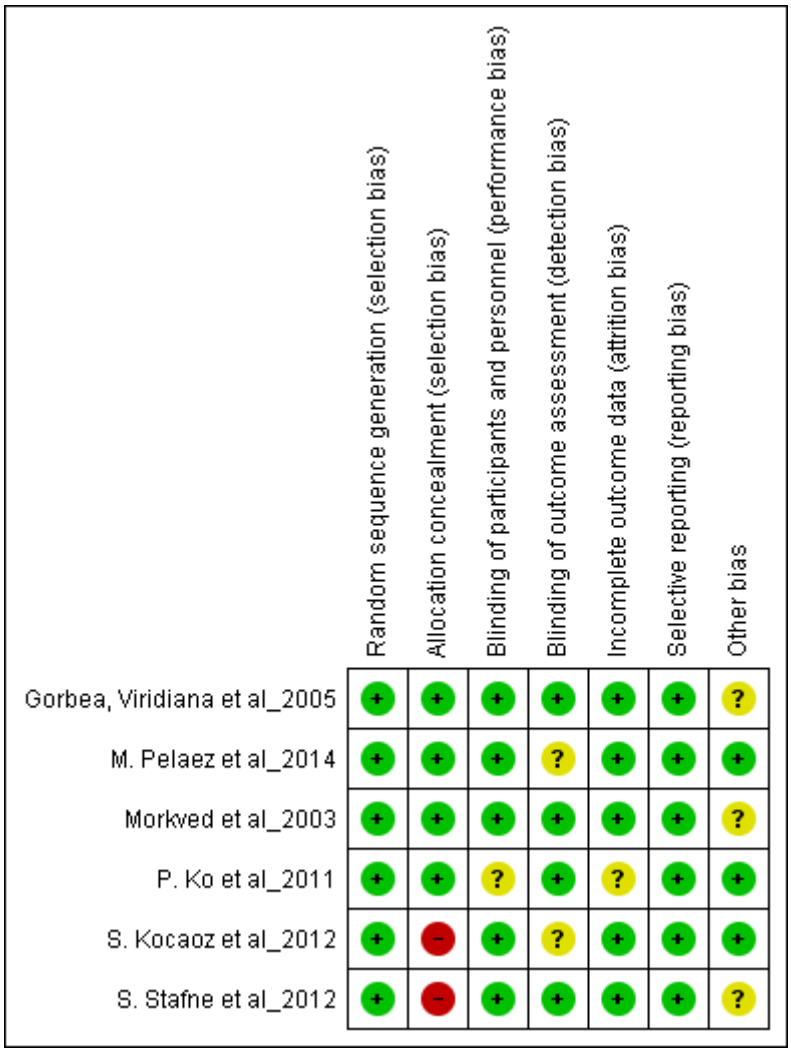
			the previous values, and any progress. The PFME protocol presented in table 1 was used in the protocol, and all women in the intervention group were asked to perform level 3 exercises during pregnancy. To evaluate whether the pelvic floor muscles had contracted correctly, direct observation of the perineum to see its introversion during the contraction and/or digital vaginal palpation (DVP) were used. All women in the PFME group were taught the exercises and asked to observe the inward movement of the perineum during the contraction.			(p < 0.05). At the 28th week of pregnancy, 1 of the 3 women with SUI in the intervention group and 14 of the 15 women with SUI in the control group reported experiencing SUI at least several times a week. An analysis of the frequency of SUI episodes at the 32nd gestational week revealed that four out of the nine women with incontinence in the intervention group experienced incontinence once a week or less, while only 3 of the 24 incontinent women in the control group stated the same level of incontinence.
S. Stafne et al (2012) Trondheim, Norway	855 women were randomly allocated to an intervention group or a control group. However, 32 women in the intervention group and 61 in the control group were lost to follow-up. Data from 397 women in the intervention group and 365 women in the control group were included in a complete case analysis.	20 and 36 weeks of gestation.	Women in the intervention group received a standardized exercise programme, including aerobic activity, strength training (including specific PFM exercises) and balance exercises. Training sessions of 60 minutes, in groups of between eight and 15 women, instructed by a physiotherapist were offered once a week over a period of 12 weeks (between 20 and 36 weeks of gestation). Each group session consisted of three parts: 1 30–35 minutes of low-impact aerobics (no running or jumping). Step length and body rotations were reduced to a minimum and crossing legs and sharp and sudden changes of position were avoided. The aerobic dance programme was performed at moderate intensity, defined as 13 and 14 on Borg's rating scale of perceived exertion.18 2 20–25 minutes of strength	The main outcomes were urinary incontinence, as measured by self-report. The outcome measures of UI were further divided into two severity categories with respect to frequency: 'urinary leak- age < once per week' or 'urinary leakage >= once per week (severe UI).'	All participants answered a questionnaire, including questions related to urinary incontinence (Sandvik's severity index) and anal incontinence (St. Marks score), at both the start (18–22 weeks of gestation) and the end (32–36 weeks of gestation) of the intervention period. Women were asked to report their urinary leakage for the following situations with a 'yes' or 'no': (A) when coughing, sneezing, or laughing; (B) while being physically active (running or jumping); (C) when making sudden changes in position or lifting; or (D) any leakage accompanied by a strong urgency to void. Urinary leakage was subclassified according to the definitions given in the standardized terminology of lower urinary tract symptoms.3 Women confirming any type of urinary leakage (A, B, C or D) were referred to as having urinary incontinence (UI).	The groups were similar in baseline characteristics except for severe UI and SUI, which were more frequent in the control group (P = 0.05 and 0.01, respectively; Table 1). After the intervention period, significantly less women in the intervention group reported UI and SUI, irrespective of severity (Table 2). The findings were consistent when adjusting for baseline values. Subgroup analyses were performed for nulliparous and multiparous women. At baseline, the prevalence of severe UI and SUI were lower in the intervention group among nulliparous women. After the intervention (at 32–36 weeks of gestation) the prevalence of UI among nulliparous women was 35 versus 47% in the intervention and control groups, respectively (OR 0.6, adjusted for baseline values; 95% CI 0.4–0.9; P = 0.03), and the prevalence of severe UI was 6 versus 14% (OR

			exercises, using body weight as resistance, including exercises for the upper and lower limbs, back extensors, deep abdominal muscles, and PFMs. Three sets of ten repetitions of each exercise were performed. 3 5–10 minutes of light stretching, body awareness, breathing and relaxation exercises. In addition, women were encouraged to follow a written 45-minute home exercise programme, including PFMT, at least twice a week (30 minutes of endurance training and 15 minutes of strength and balance exercises). Women were encouraged to perform three sets of eight to twelve close to maximum contractions of the PFMs and were encouraged to hold the contraction for 6–8 seconds and, if possible, to add three fast contractions at the end of the contraction. Women in the control group received standard antenatal care and the customary information given by their midwife or general practitioner. They were not discouraged from exercising on their own.		Women confirming loss of urine in association with A, B or C were defined as having stress urinary incontinence (SUI), whereas women confirming loss of urine in association with D were defined as having urge urinary incontinence (UUI). Frequency, intensity, and type of physical activity, including PFMT, were recorded for both groups at inclusion and at follow-up by self-report in a questionnaire. In addition, women in the intervention group registered PFMT in a training diary.	0.4, adjusted for baseline values; 95% CI 0.2–0.9; P = 0.02). The subgroup analyses showed that in women who were continent for urine at inclusion, the proportions of women reporting SUI ‡ once per week and UUI were significantly lower (P = 0.03 and 0.006, respectively) in the intervention group after the intervention period. In the intervention group, 95% reported weekly PFMT at follow-up, compared with 79% in the control group (P < 0.001). The proportion of women in the intervention group performing PFMT three times per week or more was 67%, compared to 40% in the control group (P < 0.01). UI were not more frequent among women in the intervention group who adhered to the protocol (n = 217), compared with the total control group at the end of the intervention. No serious adverse events related to physical exercise were seen.

Risk of bias

The risk of bias assessment is shown in Fig 2. Regarding the randomization process, all trials used a random numerical list generated by a computerized system and were therefore classified as low risk. Regarding allocation concealment, in the studies by Gorbea, Viridiana et al (2005) (58), M. Pelaez et al (2014) (59), Morkved et al (2003) (63) and P. Ko et al (2011) (61) the allocations were hidden from the researcher and of participants until the main analyzes were completed (low risk of bias). The studies by S. Kocaoz et al (2012) (64) and S. Stafne et al. (2012) (65) were classified as at high risk of bias due to the nature of the study, it was not blinded. In all included trials, participants and staff were blinded, except for P. Ko et al (2011) (61), in which there was no clarification of this information. To blind the evaluation of results, M. Pelaez et al. (2014) (59) did an open-label study, but that did not compromise the research outcome, and in the remaining trials the results were analyzed blindly. Regarding incomplete outcome data, M. Pelaez et al. (2014) (59) to improve the quality of the measures, the three interviewers were trained and informed on how to make women comfortable talking about their UI. S. Kocaoz et al. (2012) (64) did not clarify how it was performed. The remaining studies reported that all participants completed treatment (low risk).

Fig 2. Assessment of bias risk of randomized clinical trials included



In the judgment of P. Ko et al. (2011) (61), less than 15% of patients were lost to follow-up and were not included in the final analysis, although the number of patients who were lost was not significantly different between the groups, we consider the risk of bias uncertain. In all trials the protocol was available, all results were reported as intended, and we considered a low risk of bias for selective reporting. In the studies by M. Pelaez et al. (2014) (59), P. Ko et al. (2011) (61), S. Kocaoz et al. (2012) (64) all are free from other sources of apparent bias, whereas in the remaining studies this issue was uncertain or not stated.

Meta-analysis

For the primary outcomes (postpartum urinary incontinence, postpartum urine loss and Frequency of loss of urine during pregnancy) a meta-analysis was performed and for the secondary outcomes there was no analysis because the studies did not report them.

Postpartum urinary incontinence (long-UI) was reported in three (12–14) studies and was shown to be favorable to the group of women who performed pelvic floor muscle exercises (RR 0.49, 95% CI 0.31 to 0.78) with low heterogeneity (I^2 =35%) between the studies (Figure 3).

Observation on this figure: were favorable, but the results must be interpreted with caution, because the force of evidence is moderate according to GRADE. The outcomes (postpartum-UI) were measured at different times. Gorbea and P. Ko (58,61) measured this loss with 6 weeks postpartum and Morkved (63) analyzed the postpartum loss of urine only 3 months after delivery.

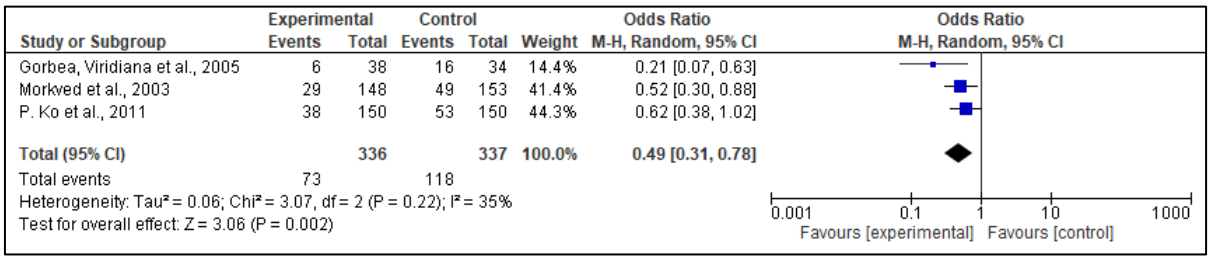


Figure 3- Meta-analysis of postpartum urine loss

The loss of urine during pregnancy was reported in three studies (58,61,63) and was shown to be favorable to the group of women who performed pelvic floor muscle exercises (RR 0.44, 95% CI 0.22 to 0.85) with median heterogeneity (I^2 =63%) between the studies (Figure 4).

Observation on this figure: The loss of urine during pregnancy was measured between 35s (58) and 36s (61,63).

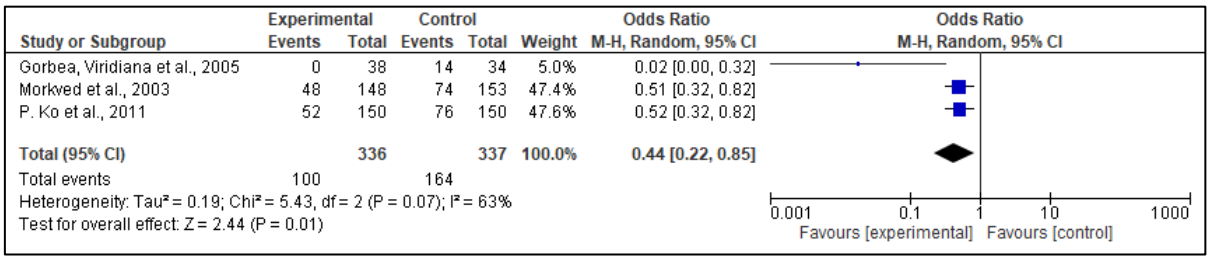


Figure 4- Meta-analysis of urine loss during pregnancy (PSUI).

The loss of urine during pregnancy was reported in two (59,64) studies and was shown to be lower in the group of women who performed pelvic floor muscle exercises (RR 0.31, 95% CI 0.11 to 0.87) with low heterogeneity (I^2 =46%) between the studies (Figure 5).

Observation on this figure: Frequency of urine loss during pregnancy at 36s (59) and at 32s (64).

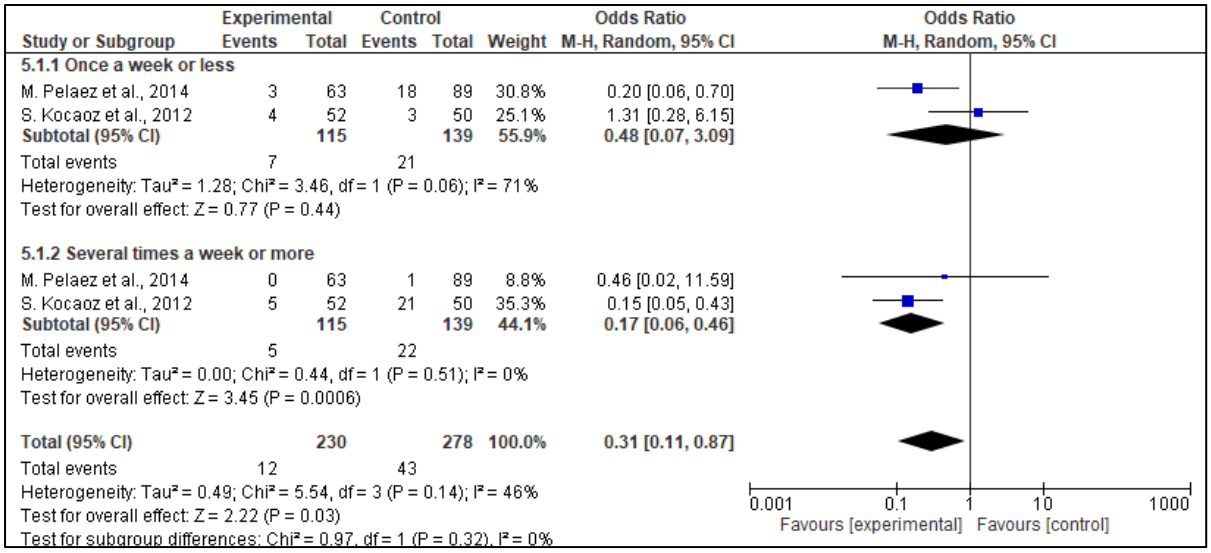


Figure 5- Frequency of loss of urine during pregnancy (PSUI)

Evaluation of the quality of evidence according to GRADE (Table 3)

Assessment of the quality of evidence was performed for the primary outcomes. The quality of evidence was considered low for sepsis, number of venipunctures and mortality. As fewer than ten RCTs were included in this review, it was not possible to analyze the presence of publication bias (Table 3).

Table 3-Summary of Evidence Quality Assessment according to GRADE

Outcomes	Patients (no.)	Risk of bias	Inconsistency	Indirect evidence	Vagueness	Risk of publication bias	Quality of evidence
Postpartum urinary incontinence (Long-UI)	673 (3 RCTs)	don't record	don't record	don't record	wide confidence interval [a](-one) *	probably not	⊕⊕⊕ ○ moderate
UI during pregnancy (PSUI)	673 (3 RCTs)	don't record	severe inconsistency (-1)	don't record	wide confidence interval [a](-one) *	probably not	⊕⊕ ○○ low
Frequency of urine loss during pregnancy	254 (2 RCTs)	don't record	severe inconsistency (-1)	don't record	wide confidence interval [a](-one) *	probably not	⊕⊕ ○○ low

[an] Amplitude at 95% confidence interval.

Note: To determine a GRADE quality of evidence, the GRADE approach starts by assigning findings to one of two initial levels of quality, depending on the study design. Randomized clinical trials are of high quality, while observational studies are of low quality.

Evidence can be considered at four levels: High, Moderate, Low and Very Low.

Studies may be updated or downgraded based on certain factors:

a) Risk of bias (-1 if severe risk of bias, -2 if very serious risk of bias).

b) Inconsistency or heterogeneity of evidence (-1 if severe inconsistency, -2 if very severe inconsistency)
c) Indirect evidence (-1 if severe, -2 if very severe)
d) Inaccuracy of results (-1 if wide confidence interval, -2 if very wide confidence interval)
e) Publication bias (-1 if likely, -2 if very likely) * Small events and large confidence interval. Poor quality of evidence: the authors do not trust the effect estimate and the actual value may differ substantially from this.

Discussion

Summary of evidence

One of the objectives of the present review was to identify the effectiveness of the PFMT in the muscular dysfunction of PSUI in GDM women. In a REGISTERED REPORT PROTOCOL published in 2020 our research group proposed a systematic review analysis to investigate PFMT to prevent and/or decrease the PSUI in GDM women.(53)

Unexpected results were a lack of RCTs reported in this population. This result was somewhat astonished as the GDiM has been considered the underline cause of PSUI in GDM women and predictor of long-UI. (17,29–31,33,66–68). In addition, myopathies are commonly treated by exercise (50) in preclinical study, we demonstrated that Swimming Exercise (SE) intervention training in diabetic pregnant rats during whole pregnancy imposes a positive influence on DiM being capable of reversing this muscle atrophy and transforming a stiff into a soft healthy skeletal muscle. Therefore, these findings of reversal DM suggest that SE training during the whole pregnancy may play a therapeutic role in regulating the damages caused by the maternal hyperglycemic environment and may be considered as a potential treatment for RAM damage caused by GDM. (50)

Faced with this gap identified in the literature, the authors started a feasibility randomized prospective study (RCT) in order to produce evidence with a robust design and a gold standard in the literature to finally answer the question about the effectiveness of PFMT in the muscle dysfunction of PSUI in GDM women (process: Fapesp 2021/10665-6).

The feasibility of conducting a future definitive RCT investigating the effectiveness and cost-effectiveness of PFMT in GDM women with PSUI as an intervention to improve health-related quality of life amongst people with and without GDM and PSUI, recruiting through primary care allow us for a definitive trial. We hope this study supported by PFMT will demonstrate significant feasibility issues with the conduct of not only a trial but also a prospective cohort study either in GDM and non-GDM women. This approach would currently be

feasible with the major barrier being the lack of a whole systems approach to long maternal health.

Urinary incontinence is a chronic health complaint that severely reduces quality of life and has many sufferers reporting effects on their social, domestic, physical, occupational, and leisure activities.(8,63,69)

It is well stablished in the literature that PFMT course during normal pregnancy period is an effective method for the prevention of postpartum urinary incontinence. (8,63,69) As the MeSH terms used included **"Pregnancy",** "Hyperglycemia", "Diabetes Mellitus, Type 2", "Diabetes Mellitus, Type 1", "Pregnancy in Diabetics", "Diabetes, Gestational", "Urinary Incontinence", "Pelvic Floor Muscle Strength", our decision was to consider Non-GDM women included as “pregnancy” and made this first systematic review with methodological rigor evaluating the effectiveness of the PFMT in the muscle dysfunction of PSUI in non-GDM women having postpartum urinary incontinence, loss of urine during and frequency of urine loss during pregnancy as outcomes. However, our results, unsurprisingly, suggest that for the postpartum urine loss outcome, the findings suggest that they are favorable for performing pelvic floor exercises. Nevertheless, they should be interpreted with caution, since the strength of evidence reported by the studies is moderate. This means that the impact of PFMT on UI and PSUI needs to be examined further, as it may change the confidence in the effect estimate and may even modify the estimate.

For the outcomes loss of urine during pregnancy and frequency of urine loss during pregnancy, the findings were also favorable to PFMT. Once again, caution should be exercised, as the strength of evidence is low, that means, limited. Future work is likely to have an important impact on confidence in the effect estimated.

It is estimated that the assessment of the quality of evidence was downgraded due to clinical heterogeneity between studies, which is caused by differences in the characteristics of the studies included in the review, such as study design, number of patients withdrawn from the study, differences in patients included (e.g., mean age, disease stage, etc.) and differences in intervention such as dose or duration of treatment or its effect on different subgroups of patients. In the present review, the outcome regarding postpartum urine loss was measured at different times. Gorbea, Viridiana et al (2005) (58) and P. Ko et al.

(2011) (61) measured this outcome at 6 weeks postpartum and Morkved et al (2003) (63) analyzed postpartum urine loss only 3 months after delivery. Urine loss during pregnancy was measured between 35s Gorbea, Viridiana et al (2005) (58) and 36s (P. Ko et al. (2011) (61) and Morkved et al (2003) (63). For the outcome frequency of urine loss during pregnancy, measurements refer to 36 weeks M. Pelaez et al. (2014) (33) and 32 weeks in the study by S. Kocaoz et al. (2012) (38). Despite differences in gestational age, all these studies treated pregnant women in the third trimester.

Limitations and strengths

This current research needs to be considered alongside its limitations and strengths. The questions in this systematic review were designed based on the strong findings from a preclinical study (50) and on the published systematic review protocol (53). This systematic review protocol had a well-defined objective to analyze the effectiveness of PFMT in GDM women with PSUI. Robust conclusions were expected to support clinical application.

During the preparation of this SR, we were surprised by the lack of trials relating GDM and PSUI. In order to avoid other fails, we decided to start a pilot feasibility TRIAL in order to identify the real condition of its implementation. Pregnant women are being prioritized recruited through prenatal primary care in the first trimester of pregnancy. Publishing protocols of trials including protocols of pilot and feasibility trials-designed to inform the designs of main trials—has been advocated as an important strategy towards improving transparency in the conduct and reporting of main trials and pilot/feasibility trials. (71)

Sadly, however, this systematic review has limitations. The main one related to the small number of clinical trials and women included in the analysis. The option to insert only RCT can also be a limiting factor for the analyses, but the choice was based on the search for studies that reported the best design to obtain the best available evidence. The small number of clinical trials included resulted in a small population analyzed and this factor contributed to the large confidence interval between studies.

CONCLUSION

Implications for practice

There is a lot of RCT related to PFMT to prevent and treat UI. The results confirm that PFMT applied in pregnancy is effective in the treatment and prevention of UI. Although, it can be estimated that PFMT intervention is a protective factor for postpartum urinary incontinence with moderate confidence in its applicability. As for urine loss during pregnancy and decrease in the frequency of urine loss during pregnancy, confidence in the effect is limited (low). Thus, our findings suggest caution in its practical application in non-GDM pregnant women and lack of subsidy for analysis in GDM women.

Implications for future research

It is recommended the elaboration of RCTs after the results of our *in - progress* pilot feasibility trial with the inclusion of large and rigorous populations so that the effectiveness of PFMT in the muscle dysfunction of PSUI in non-GDM and GDM women are identified.

Abbreviations:

UI: Urinary incontinence;
SUI: Stress urinary incontinence;
GDM: Gestational diabetes mellitus;
PFM: Pelvic floor muscles;
PFMD: Pelvic floor muscle dysfunction;
RCTs: Randomized controlled trials;
CI: Confidence interval;
PSUI: Specific Pregnancy - urinary incontinence;
GDiM: Gestational Diabetic induced Myopathy

Declarations

Ethics approval and consent to participate:

Not applicable.

Consent for publication:

Not applicable.

Availability of data and equipment:

Not applicable (this is a systematic review protocol. There are no data available).

Competing interests:

The authors declare that they have no competing interests.

Funding:

This systematic review, is part of a PhD degree project. Funding is provided by the Fapesp 2018/17534-1, Linked Process: Fapesp 2016/01743-5.

Authors Contributions

Conceptualization: Angélica M. P. Barbosa, Àlvaro N. Atallah, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge.

Data curation: Angélica M. P. Barbosa, Eusebio M. A. Enriquez, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge.

Formal analysis: Angélica M. P. Barbosa, Eusebio M. A. Enriquez, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge.

Funding acquisition: Angélica M. P. Barbosa, Marilza V. C. Rudge.

Investigation: Eusebio M. A. Enriquez, Angélica M. P. Barbosa, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge, David R. A. Reyes.

Methodology: Angélica M. P. Barbosa, Eusebio M. A. Enriquez, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge. **Bary Berghmans[6, b], Rob de Bie[6]**

Project administration: Angélica M. P. Barbosa, Marilza V. C. Rudge.

Supervision: M.V.C.R., A.M.P.B. and Alvaro Attalah.

Resources: Angélica M. P. Barbosa, Marilza V. C. Rudge.

Software: Eusebio M. A. Enriquez, Angélica M. P. Barbosa, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge.

Supervision: Angélica M. P. Barbosa, Marilza V. C. Rudge.

Validation: Eusebio M. A. Enriquez, Angélica M. P. Barbosa.
Visualization: Eusebio M. A. Enriquez, Angélica M. P. Barbosa, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge, David R. A. Reyes, Raghavendra Hallur Lakshmana Shetty.
Writing – original draft: Eusebio M. A. Enriquez, Angélica M. P. Barbosa, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge, Carolina Neiva Frota de Carvalho, David R. A. Reyes, Raghavendra Hallur Lakshmana Shetty
Writing – review & editing: Angélica M. P. Barbosa, Caroline B. Prudencio, Eusebio M. A. Enriquez, Meline R. Kron, Silvana A. M. Lima, Marilza V. C. Rudge, Raghavendra Hallur Lakshmana Shetty, Bary Berghmans, Rob de Bie. Alvaro Attalah

The Diamater Study Group designated as authors qualify for authorship as a fundamental part of this study. All authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Acknowledgments

The authors thank the support from researchers of Diamater Study Group for making valuable comments.

This study was supported by FAPESP—Fundação de Amparo à Pesquisa do Estado de São Paulo (Grant number 2016/01743-5), CNPq—Conselho Nacional de Desenvolvimento Científco e Tecnológico to MVC Rudge (305116/2018-5). Eusebio Mario Amador Enriquez received a PhD scholarship from FAPESP—Fundação de Amparo à Pesquisa do Estado de São Paulo (2020/15629-5), RLS Hallur received Posdoctoral fellowships from FAPESP (Grant numbers 2017/21783-4 and 2018/02979-8). David Rafael Abreu Reyes[2] received Posdoctoral fellowship from FAPESP (Grant number 2018/10661-8); Caroline Baldini Prudencio (received Posdoctoral fellowships from FAPESP (Grant number: 2021/10665-6).

References

1. Hvidman L, Hvidman L, Foldspang A, Mommsen S, Bugge Nielsen J. Correlates of Urinary Incontinence in Pregnancy. Int Urogynecol J. 2002 Oct 1;13(5):278–83.
2. Yount SM, Fay RA, Kissler KJ. Prenatal and Postpartum Experience, Knowledge and Engagement with Kegels: A Longitudinal, Prospective, Multisite Study. J Womens Health. 2021 Jun 1;30(6):891–901.
3. Barbosa AMP, Adriano Dias GM, Calderon IMP, RudgeI MVC, Witkin S. Urinary incontinence and vaginal squeeze pressure two years post-cesarean delivery in primiparous women with previous gestational diabetes mellitus. Clinics. 2011;66(8):1341–5.
4. ASHTON-MILLER JA, DELANCEY JOL. Functional Anatomy of the Female Pelvic Floor. Ann N Y Acad Sci [Internet]. 2007 Feb 15;1101(1):266–96. Available from: http://doi.wiley.com/10.1196/annals.1389.034
5. Bo K, Lilles F, Talseth T, Hedland H. Dynamic MRI of the pelvic floor muscles in an upright sitting position. Neurourol Urodyn. 2001;20(2):167–74.
6. Bo K. Pelvic floor muscle training is effective in treatment of female stress urinary incontinence, but how does it work? Int Urogynecol J Pelvic Floor Dysfunct. 2004 Apr 1;15(2):76–84.
7. Bo K, Frawley HC, Haylen BT, Abramov Y, Almeida FG, Berghmans B, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for the conservative and nonpharmacological management of female pelvic floor dysfunction. Int Urogynecol J. 2017 Feb 5;28(2):191–213.
8. Woodley SJ, Lawrenson P, Boyle R, Cody JD, Mørkved S, Kernohan A, et al. Pelvic floor muscle training for preventing and treating urinary and faecal incontinence in antenatal and postnatal women. Cochrane Database of Systematic Reviews. 2020 May 7;2021(3).
9. Dumoulin C, Cacciari LP, Hay-Smith EJC. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women [Internet]. Vol. 2018, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2018 [cited 2020 Jul 9]. Available from: https://pubmed.ncbi.nlm.nih.gov/30288727/

10. ACOG Practice Bulletin No. 190: Gestational Diabetes Mellitus. Obstetrics & Gynecology. 2018 Feb;131(2):e49–64.
11. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract. 2018 Apr;138:271–81.
12. Haylen B, Ridder D, Freeman R, Swift S, Berghmans B, Lee J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. International braz j urol. 2010 Feb;36(1):116–116.
13. Sangsawang B, Sangsawang N. Stress urinary incontinence in pregnant women: A review of prevalence, pathophysiology, and treatment. Int Urogynecol J. 2013;24(6):901–12.
14. Boyle R, Hay-Smith EJC, Cody JD, Mørkved S. Pelvic floor muscle training for prevention and treatment of urinary and faecal incontinence in antenatal and postnatal women. Cochrane Database of Systematic Reviews [Internet]. 2012 Oct 17; Available from: http://doi.wiley.com/10.1002/14651858.CD007471.pub2
15. Bø K. Physiotherapy management of urinary incontinence in females. J Physiother. 2020 Jul;66(3):147–54.
16. Ajala O, Jensen LA, Ryan E, Chik C. Women with a history of gestational diabetes on long-term follow up have normal vascular function despite more dysglycemia, dyslipidemia and adiposity. Diabetes Res Clin Pract. 2015 Dec;110(3):309–14.
17. Piculo F, Marini G, Vesentini G, Morceli G, Damasceno DC, Sobrevia L, et al. Pregnancy-specific urinary incontinence in women with gestational hyperglycaemia worsens the occurrence and severity of urinary incontinence and quality of life over the first year post partum. European Journal of Obstetrics & Gynecology and Reproductive Biology [Internet]. 2020 Sep;252:336–43. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0301211520304036
18. Davenport MH, Ruchat SM, Poitras VJ, Jaramillo Garcia A, Gray CE, Barrowman N, et al. Prenatal exercise for the prevention of gestational diabetes mellitus and hypertensive disorders of pregnancy: a systematic review and meta-analysis. Br J Sports Med. 2018 Nov;52(21):1367–75.
19. Du M, Ouyang Y, Nie X, Huang Y, Redding SR. Effects of physical exercise during pregnancy on maternal and infant outcomes in overweight and obese pregnant women: A meta-analysis. Birth. 2019 Jun 21;46(2):211–21.

20. Sanabria-Martínez G, García-Hermoso A, Poyatos-León R, Álvarez-Bueno C, Sánchez-López M, Martínez-Vizcaíno V. Effectiveness of physical activity interventions on preventing gestational diabetes mellitus and excessive maternal weight gain: a meta-analysis. BJOG. 2015 Aug;122(9):1167–74.
21. Ming WK, Ding W, Zhang CJP, Zhong L, Long Y, Li Z, et al. The effect of exercise during pregnancy on gestational diabetes mellitus in normal-weight women: a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2018 Dec 12;18(1):440.
22. Yu Y, Xie R, Shen C, Shu L. Effect of exercise during pregnancy to prevent gestational diabetes mellitus: a systematic review and meta-analysis. The Journal of Maternal-Fetal & Neonatal Medicine. 2018 Jun 18;31(12):1632–7.
23. Mijatovic-Vukas J, Capling L, Cheng S, Stamatakis E, Louie J, Cheung NW, et al. Associations of Diet and Physical Activity with Risk for Gestational Diabetes Mellitus: A Systematic Review and Meta-Analysis. Nutrients. 2018 May;10(6).
24. Russo LM, Nobles C, Ertel KA, Chasan-Taber L, Whitcomb BW. Physical Activity Interventions in Pregnancy and Risk of Gestational Diabetes Mellitus. Obstetrics & Gynecology. 2015 Mar;125(3):576–82.
25. di Mascio D, Magro-Malosso ER, Saccone G, Marhefka GD, Berghella V. Exercise during pregnancy in normal-weight women and risk of preterm birth: a systematic review and meta-analysis of randomized controlled trials. Am J Obstet Gynecol. 2016 Nov;215(5):561–71.
26. da Silva SG, Ricardo LI, Evenson KR, Hallal PC. Leisure-Time Physical Activity in Pregnancy and Maternal-Child Health: A Systematic Review and Meta-Analysis of Randomized Controlled Trials and Cohort Studies. Sports Med. 2017 Feb;47(2):295–317.
27. Schlüssel MM, Souza EB de, Reichenheim ME, Kac G. Physical activity during pregnancy and maternal-child health outcomes: a systematic literature review. Cad Saude Publica. 2008;24(suppl 4):s531–44.
28. CORDERO Y, MOTTOLA MF, VARGAS J, BLANCO M, BARAKAT R. Exercise Is Associated with a Reduction in Gestational Diabetes Mellitus. Med Sci Sports Exerc. 2015 Jul;47(7):1328–33.
29. Piculo F, Marini G, Barbosa AMP, Damasceno DC, Matheus SMM, Felisbino SL, et al. Urethral striated muscle and extracellular matrix morphological characteristics among mildly diabetic pregnant rats: translational approach. Int

Urogynecol J. 2014 Mar;25(3):403–15.

30. Marini G, Piculo F, Vesentini G, Barbosa AMP, Damasceno DC, Matheus SMM, et al. Effects of short-term severe and long-term mild STZ-induced diabetes in urethral tissue of female rats. Neurourol Urodyn. 2017 Mar;36(3):574–9.
31. Vesentini G, Marini G, Piculo F, Damasceno DC, Matheus SMM, Felisbino SL, et al. Morphological changes in rat rectus abdominis muscle induced by diabetes and pregnancy. Brazilian Journal of Medical and Biological Research. 2018 Mar;51(4).
32. Vesentini G, Barbosa AMP, Floriano JF, Felisbino SL, Costa SMB, Piculo F, et al. Deleterious effects of gestational diabetes mellitus on the characteristics of the rectus abdominis muscle associated with pregnancy-specific urinary incontinence. Diabetes Res Clin Pract. 2020 Aug;166:108315.
33. Sartorão Filho CI, Pinheiro FA, Prudencio CB, Nunes SK, Takano L, Enriquez EMA, et al. Impact of gestational diabetes on pelvic floor: A prospective cohort study with three-dimensional ultrasound during two-time points in pregnancy. Neurourol Urodyn [Internet]. 2020 Aug 28;nau.24491. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/nau.24491
34. Prudencio CB, Rudge MVC, Pinheiro FA, Sartorão Filho CI, Nunes SK, Pedroni CR, et al. Negative impact of gestational diabetes mellitus on progress of pelvic floor muscle electromyography activity: Cohort study. Palatnik A, editor. PLoS One. 2019 Nov 7;14(11):e0223261.
35. Marini G, Piculo F, Vesentini G, Damasceno DC, Delella FK, Calderon IMP, et al. The influence of hyperglycemia on the remodeling of urethral connective tissue in pregnant rats. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2018 Feb;221:81–8.
36. Vesentini G, Barbosa AMP, Damasceno DC, Marini G, Piculo F, Matheus SMM, et al. Alterations in the structural characteristics of rectus abdominis muscles caused by diabetes and pregnancy: A comparative study of the rat model and women. Li L, editor. PLoS One. 2020 Apr 3;15(4):e0231096.
37. Reinoso-Sánchez JF, Baroli G, Duranti G, Scaricamazza S, Sabatini S, Valle C, et al. Emerging Role for Linear and Circular Spermine Oxidase RNAs in Skeletal Muscle Physiopathology. Int J Mol Sci. 2020 Nov 3;21(21):8227.
38. Massenet J, Gardner E, Chazaud B, Dilworth FJ. Epigenetic regulation of satellite cell fate during skeletal muscle regeneration. Skelet Muscle. 2021 Dec

11;11(1):4.

39. Fry CS, Lee JD, Mula J, Kirby TJ, Jackson JR, Liu F, et al. Inducible depletion of satellite cells in adult, sedentary mice impairs muscle regenerative capacity without affecting sarcopenia. Nat Med. 2015 Jan 15;21(1):76–80.
40. Hendrickse P, Degens H. The role of the microcirculation in muscle function and plasticity. J Muscle Res Cell Motil. 2019 Jun 5;40(2):127–40.
41. Latroche C, Weiss-Gayet M, Chazaud B. Investigating the Vascular Niche: Three-Dimensional Co-culture of Human Skeletal Muscle Stem Cells and Endothelial Cells. In 2018. p. 121–8.
42. Relaix F, Zammit PS. Satellite cells are essential for skeletal muscle regeneration: the cell on the edge returns centre stage. Development. 2012 Aug 15;139(16):2845–56.
43. Perandini LA, Chimin P, Lutkemeyer D da S, Câmara NOS. Chronic inflammation in skeletal muscle impairs satellite cells function during regeneration: can physical exercise restore the satellite cell niche? FEBS J. 2018 Jun 8;285(11):1973–84.
44. Floriano JF, Emanueli C, Vega S, Barbosa AMP, Oliveira RG de, Floriano EAF, et al. Pro-angiogenic approach for skeletal muscle regeneration. Biochimica et Biophysica Acta (BBA) - General Subjects. 2022 Feb;1866(2):130059.
45. Mofarrahi M, McClung JM, Kontos CD, Davis EC, Tappuni B, Moroz N, et al. Angiopoietin-1 enhances skeletal muscle regeneration in mice. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2015 Apr 1;308(7):R576–89.
46. Guidelines Review Committee. Global recommendations on physical activity for health. WHO. 2010;1(1):1–58.
47. Gholamnezhad Z, Mégarbane B, Rezaee R. Molecular Mechanisms Mediating Adaptation to Exercise. In 2020. p. 45–61.
48. Rahmati M, Rashno A. Automated image segmentation method to analyse skeletal muscle cross section in exercise-induced regenerating myofibers. Sci Rep. 2021 Dec 29;11(1):21327.
49. He N, Ye H. Exercise and Muscle Atrophy. In 2020. p. 255–67.
50. Catinelli BB, Rossignoli PS, Floriano JF, Carr AM, de Oliveira RG, dos Santos NJ, et al. Reversal of diabetic-induced myopathy by swimming exercise in pregnant rats: a translational intervention study. Sci Rep. 2022 May 5;12(1):7375.

51. Higgins JP, Savović J, Page MJ, Elbers RG, Sterne JA. Assessing risk of bias in a randomized trial. In: Cochrane Handbook for Systematic Reviews of Interventions. Wiley; 2019. p. 205–28.
52. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. PLoS Med. 2009 Jul;6(7):e1000100.
53. Barbosa AMP, Enriquez EMA, Rodrigues MRK, Prudencio CB, Atallah ÁN, Reyes DRA, et al. Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol. Spradley FT, editor. PLoS One [Internet]. 2020 Dec 7;15(12):e0241962. Available from: https://dx.plos.org/10.1371/journal.pone.0241962
54. National Institutes of Heatlh. Finding a Clinical Trial [Internet]. Available from: https://www.nih.gov/health-information/nih-clinical-research-trials-you/finding-clinical-trial
55. The Brazilian Registry of Clinical Trials [Internet]. Available from: https://ensaiosclinicos.gov.br/
56. RevMan 5.3 User Guide.
57. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008 Apr;336(7650):924–6.
58. Gorbea Chávez V, Velázquez Sánchez M del P, Kunhardt Rasch JR. [Effect of pelvic floor exercise during pregnancy and puerperium on prevention of urinary stress incontinence]. Ginecol Obstet Mex. 2004 Dec;72:628–36.
59. Pelaez M, Gonzalez-Cerron S, Montejo R, Barakat R. Pelvic floor muscle training included in a pregnancy exercise program is effective in primary prevention of urinary incontinence: A randomized controlled trial. Neurourol Urodyn. 2014 Jan;33(1):67–71.
60. Mørkved S, Bø K, Schei B, Salvesen KÅ. Pelvic floor muscle training during pregnancy to prevent urinary incontinence: A single-blind randomized controlled trial. Obstetrics and Gynecology. 2003;
61. Ko PC, Liang CC, Chang SD, Lee JT, Chao AS, Cheng PJ. A randomized controlled trial of antenatal pelvic floor exercises to prevent and treat urinary

incontinence. Int Urogynecol J. 2011 Jan 25;22(1):17–22.

62. Stafne S, Salvesen K, Romundstad P, Torjusen I, Mørkved S. Does regular exercise including pelvic floor muscle training prevent urinary and anal incontinence during pregnancy? A randomised controlled trial. BJOG. 2012 Sep;119(10):1270–80.
63. Mørkved S. Pelvic floor muscle training during pregnancy to prevent urinary incontinence: a single-blind randomized controlled trial. Obstetrics & Gynecology [Internet]. 2003 Feb;101(2):313–9. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0029784402027114
64. Kocaöz S, Eroglu K, Sivaslioglu AA. Role of Pelvic Floor Muscle Exercises in the Prevention of Stress Urinary Incontinence during Pregnancy and the Postpartum Period. Gynecol Obstet Invest. 2013;75(1):34–40.
65. Marini G, Piculo F, Vesentini G, Barbosa AMP, Damasceno DC, Matheus SMM, et al. Effects of short-term severe and long-term mild STZ-induced diabetes in urethral tissue of female rats. Neurourol Urodyn. 2017 Mar;36:574–579.
66. Marini G, Barbosa AMP, Matheus SMaM, Rudge MVC. Alterações morfológicas das fibras tipos I e II do músculo estriado uretral de ratas prenhes diabéticas. 2010.
67. Prudencio CB, Rudge MVC, Pinheiro FA, Sartorão Filho CI, Nunes SK, Pedroni CR, et al. Negative impact of gestational diabetes mellitus on progress of pelvic floor muscle electromyography activity: Cohort study. Palatnik A, editor. PLoS One [Internet]. 2019 Nov 7;14(11):e0223261. Available from: https://dx.plos.org/10.1371/journal.pone.0223261
70. Davenport MH, Nagpal TS, Mottola MF, Skow RJ, Riske L, Poitras VJ, et al. Prenatal exercise (including but not limited to pelvic floor muscle training) and urinary incontinence during and following pregnancy: a systematic review and meta-analysis. Br J Sports Med. 2018 Nov;52(21):1397–404.
71. Thabane L, Lancaster G. A guide to the reporting of protocols of pilot and feasibility trials. Pilot Feasibility Stud. 2019 Dec 28;5(1):37.

Seção 4

Perspectivas Acadêmicas e Científicas

Nesta fase da minha vida profissional penso muito em como aplicar os conhecimentos obtidos até aqui, em como posso passar esses conhecimentos para a classe médica que muitas vezes não está a par dos novos acontecimentos, e que como eu, em certos momentos pensamos que condições médicas da mulher formam parte de um ciclo vital, como é a gravidez, sem saber que tem muito mais por trás do desconforto da perda de urina involuntária. A meu ver, a falta de conhecimentos muitas vezes é por falta de guia profissional, de alguém que ajude a enxergar melhor o que está acontecendo. Como médico, trabalhar com pesquisa na área de Tocoginecologia tem sido muito importante, pois se abriram portas do conhecimento que não sabia que existiam.

Para a continuidade da busca do conhecimento e na colaboração para melhorar a assistência a mulher, a proposta é permanecer como aluno de Pós-doutorado, na mesma linha de pesquisa desta trajetória, de uma forma mais ativa, levando os conhecimentos adquiridos aos meus colegas, aos meus futuros alunos, e continuar colaborando com o Diamater na Revisão Sistemática, na produção de artigos científicos relevantes, e na busca de novos conhecimentos que possam ajudar a diminuir, prevenir ou curar a Incontinência Urinaria causada pela Disfunção da Musculatura do Assoalho Pélvico em mulheres com Diabetes Mellitus Gestacional ou Hiperglicemia Gestacional.

Sinto-me honrado em ser parte do *Diamater Study Group* e espero continuar contribuindo ativamente com ele no futuro!

Seção 5

Diamater Study Group

Abaixo segue nominalmente o grupo Diamater

Pesquisadores Nacionais

Profa. Emérita Marilza Vieira Cunha Rudge
Profa. Titular Iracema de Mattos Paranhos Calderon
Profa. Dra. Angélica Mérica Pascon Barbosa
Profa. Dra. Fátima Pereira de Souza
Prof. Titular Carlos Frederico de Oliveira Graeff
Prof. Titular Manoel João Batista Castello Girão
Profa. Dra. Cláudia Garcia Magalhães
Prof. Dr. Roberto Antonio de Araujo Costa
Profa. Adjunto Silvana Andréa Molina Lima
Profa. Dra. Meline Rossetto Kron Rodrigues
Prof. Adjunto Sérgio Luis Felisbino
Prof. Dr. Walnei Fernandes Barbosa
Profa. Dra. Grasiela Bossolan
Prof. Dr. José Eduardo Corrente
Prof. Dr. Hélio Rubens de Carvalho Nunes
Prof. Dr. Joelcio Francisco Abbade
Profa. Dra Patrícia de Souza Rossignoli
Profa. Dra. Cristiane Rodrigues Pedroni
Prof. Titular Álvaro Nagib Atallah
Profa. Dra. Zsuzsanna Ilona K. de Jarmy Di Bella
Profa. Silvana Maria de Macêdo Uchôa
Prof. Titular Marco Antonio Hungaro Duarte
Prof. Dr. Edson Assunção Mareco
Profa. Adjunta Marna Eliana Sakalem
Profa. Dra. Natalia Miguel Martinho Fogaça
Prof. Dr. Diego Girotto Bussaneli
Profa. Titular Maeli Dal Pai
Profa. Dra. Selma Maria Michelin Matheus
Profa. Dra. Ana Karina Cristiuma De Luca
Profa. Dra. Daisy Maria Fávero Salvadori
Prof. Dr. Rondinelli Donizetti Herculano
Prof. Dr. Spencer Luiz Marques Payao

Pesquisadores Associados

PhD Raghavendra Hallur Lakshmana Shetty
PhD David Rafael Abreu Reyes
Dra Fernanda Cristina Bérgamo Alves
Dr João Paulo de Castro Marcondes
Dra Maíra Libertad Soligo Takemoto
Dra Juliana Ferreira Floriano
Dra. Fernanda Piculo
Dra. Gabriela Marini Prata
Dra Cibele Vieria Cunha Rudge
Dr. Fabio Joly Campos
Dr. Ícaro Putinhon Caruso
Dr. Lucas Trevizani Rasmussen
Dr Vinícius Krieger Costa Nogueira
Ms. Caroline Baldini Prudencio
Ms. Fabiane Affonso Pinheiro
Ms. Carlos Izaias Sartorão Filho
Ms. Sofia Beatriz Carolina Vega Quiroz
Ms. Tawana Pascon
Ms. Sthefanie Kenickel Nunes
Ms. Bruna Bologna Catinelli
Ms. Fabiana Vieira Duarte de Souza Reis
Ms. Rafael Guilen de Oliveira
Ms. Sarah Maria Barneze Costa
Ms. Mariane de Oliveira Menezes
Ms. Nilton José dos Santo
Ms. Isabella Otenio de Lourenço
Ms. Jéssica Maróstica de Sá
Ms. Raissa Escandiusi Avramidis
Ms Guilherme Thomaz de Aquino Nava
Ms Talita Costa Domingues
Eusebio Mario Amador Enriquez
Jose Vitor Freitas Melo (*in memoriam)*
Luiz Takano
Aline Medolago Carr
Gabriela Azevedo Garcia
Adriely Bittencourt Morgenstern Magyori
Carolina Neiva Frota de Carvalho
Luana Fávaro Iamundo
Henrique Caetano Mingoranci Bassin
Carolina Neiva Frota de Carvalho
Carolina Pascon Marques
Michele Jacomin
Ana Julia Bimbatti Silva
Maiara Isabele Gonçalves Orlandi
Tatiana Daniele Dangió

Pesquisadores Internacionais

PhD Adonis Hijas
PhD Luis Sobrevia Luarte
PhD Bary Berghmans
PhD Rob de Bie
PhD Costanza Emanueli
PhD Baerbel Junginger
PhD Antonio Musàro
PhD Lehana Thabane

Apoio à Pesquisa

Rita de Cássia Athanázio
Cinthia Scolástico Cecilio


USAR UM PROGRAMA BASEADO
EM EVIDÊNCIAS

Seção 6
Anexos

Anexo 1 – Fichas de Extração de Dados

Apêndice 2- Formulário para extração de dados

Sobrenome Primeiro Autor	Ano
Gorbea, Viridiana et al	2005

Elegibilidade

Ensaio Clínico Randomizado	Participantes relevantes	Intervenção relevante	Desfecho relevante
Sim	Sim	Sim	Sim

Participantes	
Tamanho da amostra	72 mulheres. 52,7% realizaram exercícios para assoalho pélvico e 47,2% não.
Idade(media, DP e faixa)	15 a 35 años de edad
P (participantes)	72 mulheres
I (intervenção)	38 no grupo de intervenção.
C (comparador)	37 no grupo controle
O (outcomes)	presença de incontinência urinária de esforço, número de exercícios para assoalho pélvico realizados, idade gestacional, peso às 20, 28 e 35 semanas de gestação, ganho de peso de 20 a 35 semanas de gestação, efeitos adversos e benéficos da fisioterapia do assoalho pélvico (referido pela paciente)
Características do estudo	
	Detalhes
Multicentrinco / centro único	centro único
Países	México
Critérios de inclusão de participantes e exclusão	O estudo foi realizado em mulheres nulíparas entre 15 e 35 anos e em gestantes com 20 semanas de gestação que não apresentavam incontinência urinária de esforço, conforme definição da International Continence Society, no momento de inclusão no estudar e desejar realizar exercícios para o assoalho pélvico. Não foram incluídas mulheres com gestações múltiplas, com duas ou mais cesarianas, com gestações

	com oligoidrâmnio ou polidrâmnio ou com complicações, como incompetência ítmica cervical, isoimunização materno-fetal, condições graves, como doença hipertensiva grave induzida pela gravidez ou doenças degenerativas crônicas que afetam a função do assoalho pélvico, como a esclerose múltipla.
Número participantes randomizados	**75 pacientes que atenderam aos critérios de seleção**
Perdas	**Ocorreram duas perdas: uma por óbito não relacionado à gravidez e outra por mudança de endereço, mais uma foi eliminada por manifestar parto imaturo com 23 semanas de gestação.**
Número participantes analisados	**72 mulheres participaram**
Tempo de seguimento	**A partir das 20 sem de gestação até 6 sem pós-parto.**
Desfechos Primários	
Materno:	**Presente no artigo**
Ocorrência, redução, recorrência ou persistência dos sintomas de PS-UI.	**Sim**
Desfechos secundários	
Melhora da força dos MAP (avaliação funcional do assoalho pélvico, perineômetro, eletromiografia, ultrassonografia funcional), melhora da qualidade de vida (questionários), presença ou ausência de IU pós-parto e efeitos adversos.	**Sim**

Extração de dados contínuos

Desfecho	Intervenção		Controle		Observação
	n	Média (DP)	n	Média (DP)	

Extração de dados dicotômicos

Incontinecia Urinaria de Esforço as 28 e 35 sem de gestação e 6 sem posteriores a resolução da gravidez nos grupos com e sem exercícios.					
Incontinencia Urinaria	Sim N= 38	Não N=34	Fisher	p	Risco Relativo (IC 95%)
Ocorrência 28s	0	6 (17,6%)	4,57	0,032	0,069
35 semanas	0	14 (41,2%)	15,99	< 0,0001	0,031
6 semanas após parto	6 (15,7%)	16 (47%)	6,86	0,009	0,336

Apêndice 2- Formulário para extração de dados

Sobrenome Primeiro Autor	Ano
M. Pelaez et al	2014

Elegibilidade

Ensaio Clínico Randomizado	Participantes relevantes	Intervenção relevante	Desfecho relevante
Sim	Sim	Sim	Sim

Participantes	
Tamanho da amostra	**169 women were randomized by a central computer system.**
Idade(media, DP e faixa)	**primiparous pregnant with singleton fetus**
P (participantes)	**Data from 152 women were analyzed (10.1% loss to follow-up: 10 from the EG and 7 from the CG)**
I (intervenção)	**(exercise class including PFMT) (n = 73)**
C (comparador)	**a control group (CG) (n = 96)**
O (outcomes)	**The primary outcomes were (i) the reported frequency, (ii) amount, and (iii) impact on daily life of UI**
Características do estudo	
	Detalhes
Multicentrinco / centro único	**Centro unico**
Países	**Espanha**
Critérios de inclusão de participantes e exclusão	**being healthy and primiparous pregnant with singleton fetus, being in gestational week 10–14, not suffering from UI, able to communicate in Spanish and able to give informed written consent.** **planning not to give birth in Fuenlabrada University Hospital and any contraindication according to the American College of Obstetricians and Gynecologists Guidelines.**
Número participantes randomizados	**169 women**
Perdas	**(10.1% loss to follow-up: 10 from the EG and 7 from the CG)**
Número participantes analisados	**152 women**
Tempo de seguimento	**14–36 weeks of gestation**

Desfechos Primários	
Materno:	**Presente no artigo**
Ocorrência, redução, recorrência ou persistência dos sintomas de PS-UI.	**Sim**
Desfechos secundários	
Melhora da força dos MAP (avaliação funcional do assoalho	**Sim**

pélvico, perineômetro, eletromiografia, ultrassonografia funcional), melhora da qualidade de vida (questionários), presença ou ausência de IU pós-parto e efeitos adversos.	

Extração de dados contínuos

Desfecho	**Intervenção**		**Controle**		**Observação**
	n	**Média (DP)**	**n**	**Média (DP)**	

Extração de dados dicotômicos

Results From ICIQ-UI SF Questionnaire After Intervention in Exercise and Control Groups					
Reported frequency of UI					
	Exercise (n = 63)	**Control (n = 89)**	**P -value**		
Never	**60/95,2**	**54/60,7**	**0,0001**		
Once a week	**3/4,8**	**18/20,2**			
2-3 times per week	**0/0,0**	**9/10,1**			
Once a day	**0/0,0**	**7/7,9**			
Several times per day	**0/0,0**	**1/1,1**			
Amount of leakage					
	Exercise (n = 63)	**Control (n = 89)**	**P -value**		
None	**60/95,2**	**54/60,7**	**0,0001**		
A small amount	**3/4,8**	**27/30,3**			
A moderate amount	**0**	**5/5,6**			
A large amount	**0**	**3/3,4**			
How much does leaking affect daily life	**0,10(0,64)**	**0,97(1,8)**	**0,001**		
ICIQ-Score	**0,24(1,2)**	**2,66(4,1)**	**0,001**		

Apêndice 2- Formulário para extração de dados

Sobrenome Primeiro Autor	Ano
Morkved et al	2003

Elegibilidade

Ensaio Clínico Randomizado	Participantes relevantes	Intervenção relevante	Desfecho relevante
Sim	Sim	Sim	Sim

Participantes	
Tamanho da amostra	342 women
Idade(media, DP e faixa)	Women over 18 years of age
P (participantes)	301 women
I (intervenção)	148 no grupo de intervenção.
C (comparador)	153 no grupo controle
O (outcomes)	The primary outcome measure was self-reports of urinary incontinence. Women reporting urinary incontinence once per week or more during the last month were categorized as incontinent. Secondary outcomes were recordings, in a home voiding diary, of episodes of involuntary leakage during the 3 days directly after the first assessment (20 weeks' pregnancy) and immediately before the second (36 weeks' pregnancy) and third (3 months postpartum) assessments.
Características do estudo	
	Detalhes
Multicentrinco / centro único	centro único
Países	Norway
Critérios de inclusão de participantes e exclusão	Women were eligible for the trial if they were nulliparous and 18 years or older, with a single live fetus at the routine ultrasound scan. Women were pregnancy complications, high risk for preterm labor, pain during pelvic floor muscle contractions, ongoing urinary tract infection, or diseases that could interfere with

	participation. In addition, women who lived too far to be able to attend weekly training groups were excluded.
Número participantes randomizados	**301 women**
Perdas	**41 women were excluded or withdrew before the first examination: 17 lived too far away to be able to attend the training groups, eight had pregnancy complications, four were not nulliparous, two had twin pregnancies, five were not able to meet for the first assessment, and five withdrew for unknown reasons**
Número participantes analisados	**289 women (143/ 146)**
Tempo de seguimento	**Women were examined at 20- and 36-weeks' gestation and 3 months after childbirth.**
Desfechos Primários	
Materno:	**Presente no artigo**
Ocorrência, redução, recorrência ou persistência dos sintomas de PS-UI.	**Sim**
Desfechos secundários	
Melhora da força dos MAP (avaliação funcional do assoalho pélvico, perineômetro, eletromiografia, ultrassonografia funcional), melhora da qualidade de vida (questionários), presença ou ausência de IU pós-parto e efeitos adversos.	**Sim**

Extração de dados contínuos

Desfecho	**Intervenção**		**Controle**		**Observação**
	n	**Média (DP)**	**n**	**Média (DP)**	

Extração de dados dicotômicos

Women with Self-Reported Urinary Incontinence at 36 Weeks' Pregnancy and 3 Months After Delivery.	**Women With Self-Reported**

					Urinary Incontinence at 36 Weeks' Pregnancy and 3 Months After Delivery
Desfecho	**Intervenção: N=148**	**Controle: N=153**			
Incontinencia Urinaria	**PFMT n/ %**	**Control n/ %**	**Significance**	**Rekative Risk (95% CI)**	
36 semanas gestação	**48 (32)**	**74 (48)**	**X^2=7,9; p=0,007**	**0,67(0,50; 0,89)**	
3 mo after delivery	**29 (20)**	**49 (32)**	**X^2=6,1; p=0,018**	**0,61(0,40; 0,90)**	
Pelvic Floor Muscle Strength (Mean and 95% Confidence Interval) at 36 Weeks' Pregnancy and 3 Months After Delivery, Measured by Vaginal Squeeze Pressure (cm H2O)					
PFMT	**Training Group**	**Control Group**	**P***		
36 semanas gestação	**39,9 (37,1; 42,7)**	**34,4 (31,6; 37,1)**	**0,008**		
3 mo after delivery	**29,5 (26,8; 32,2)**	**25,6 (23,2; 27,9)**	**0,048**		

Apêndice 2- Formulário para extração de dados

Sobrenome Primeiro Autor	**Ano**
P. Ko et al	**2011**

Elegibilidade

Ensaio Clínico Randomizado	**Participantes relevantes**	**Intervenção relevante**	**Desfecho relevante**
Sim	**Sim**	**Sim**	**Sim**

Participantes	
Tamanho da amostra	**300 women were randomly assigned to the PFME group and control group.**
Idade (média, DP e faixa)	**Women over 18 years of age**
P (participantes)	**300 women**
I (intervenção)	**150 no grupo de intervenção.**
C (comparador)	**150 no grupo controle**
O (outcomes)	**Evaluate the effect of antenatal pelvic floor muscle exercise (PFME) in the prevention and treatment of urinary incontinence during pregnancy.**
Características do estudo	
	Detalhes
Multicentrinco / centro único	**centro único**
Países	**China**
Critérios de inclusão de participantes e exclusão	**Women over 18 years of age, between 16 and 24 gestational weeks with involuntary urine loss. Exclusion criteria included multiparity, multiple gestations, severe pregnancy complications, high risk for preterm labor, pain during PFME, diseases that could interfere with participation, or would be unavailable for follow-up**
Número participantes randomizados	**315 women gave their signed consent to participate in this trial.**
Perdas	**15 women were excluded or withdrew before the first examination: Five had pregnancy complications, four had twin pregnancies, and six withdrew for unknown reasons.**
Número participantes analisados	**300 women**
Tempo de seguimento	**16 to 24 gestational weeks to 36 gestational weeks, and via telephone 6 weeks and 6 months postpartum.**

Desfechos Primários	
Materno:	**Presente no artigo**
Ocorrência, redução, recorrência ou persistência dos sintomas de	**Sim**

PS-UI.	
Desfechos secundários	
Melhora da força dos MAP (avaliação funcional do assoalho pélvico, perineômetro, eletromiografia, ultrassonografia funcional), melhora da qualidade de vida (questionários), presença ou ausência de IU pós-parto e efeitos adversos.	**Sim**

Extração de dados contínuos

Desfecho	**Intervenção**		**Controle**		**Observação**
	n	**Média (DP)**	**n**	**Média (DP)**	

Extração de dados dicotômicos

Self-reported urinary incontinence during pregnancy and after birth					
Desfecho	**Intervenção: N=150**	**Controle: N=150**			
Incontinencia Urinaria	**PFME**	**Control**	**P value**		
16 – 24 sem	**41 (27)**	**45 (30)**	**0,61**		
36 semanas gestação	**52 (34)**	**76 (51)**	**<0,01**		
3 days after delivery	**46 (30)**	**62 (41)**	**0,07**		
6 weeks after delivery	**38 (25)**	**53 (35)**	**0,06**		
24 weeks after delivery	**25 (16)**	**42 (27)**	**0,04**		
Comparisons of UDI-6 and IIQ-7 between PFME group and control group					
Questionario	**Training Group**	**Control Group**	**P***		
UDI – 6a	**1,27+-1,54**	**1,36+-1,55**	**0,49**		
UDI – 6b	**3,44+-3,26**	**4,66+-3,32**	**<0,01**		
UDI – 6c	**1,42+-2,04**	**2,31+-2,16**	**<0,01**		
UDI – 6d	**0,81+-1,36**	**1,54+-1,59**	**<0,01**		
UDI – 6e	**0,35+-0,84**	**0,86+-1,14**	**<0,01**		
IIQ – 7a	**1,11+-2,47**	**1,21+-**	**0,18**		

		2,44			
IIQ – 7b	3,77+-6,01	5,28+-5,61	<0,01		
IIQ – 7d	1,73+-3,57	2,86+-3,52	<0,01		
IIQ – 7e	0,77+-2,07	1,56+-2,20	<0,01		
Data are presented as mean ± standard deviation and calculated with Mann–Whitney U test a Pregnancy at 16 to 24 weeks b Pregnancy at 36 weeks c Three days after delivery d Six weeks after delivery e Six months after delivery					

Apêndice 2- Formulário para extração de dados

Sobrenome Primeiro Autor	Ano
S. Kocaoz et al	2012

Elegibilidade

Ensaio Clínico Randomizado	Participantes relevantes	Intervenção relevante	Desfecho relevante
Sim	Sim	Sim	Sim

Participantes	
Tamanho da amostra	n = 157
Idade (média, DP e faixa)	being between 20 and 35 years of age
P (participantes)	A total of 102 women was included in the study.
I (intervenção)	52 no grupo de intervenção.
C (comparador)	50 no grupo controle
O (outcomes)	The primary outcome measure was the presence of SUI based on a negative 1-hour pad test (< 2 g in weight). Secondary outcome measures included urinary diary and verbal statements.
Características do estudo	
	Detalhes
Multicentrinco / centro único	centro único
Países	Turkey
Critérios de inclusão de participantes e exclusão	The inclusion criteria were (1) being able to attend pregnancy outpa- tient visits regularly, (2)

	being in the 14th–20th gestational week during the first attendance, (3) being between 20 and 35 years of age, (4) having completed at least elementary school, (5) having no UI complaints or urinary tract infection (UTI), (6) having a BMI below 40, and (7) having no chronic disease (such as asthma) or genitourinary pathology (such as pelvic organ prolapse) requiring treatment. **All pregnant women were trained to use a 'urinary diary' and were asked to bring their diary to the next follow-up a week later. The pregnant women were then asked to fill out the 'urinary diary' for the 3 days prior to each follow-up visit. Women who did not meet the inclusion criteria during these procedures were excluded from the study.**
Número participantes randomizados	**136 pregnant women**
Perdas	**34 women dropped out of the study due to family-relat- ed, financial or medical reasons**
Número participantes analisados	**102 women**
Tempo de seguimento	**Subjects in both the intervention and control groups were followed-up at the 28th and 32nd weeks of gestation and at the post- partum 12th week.**

Desfechos Primários	
Materno:	**Presente no artigo**
Ocorrência, redução, recorrência ou persistência dos sintomas de PS-UI.	**Sim**
Desfechos secundários	
Melhora da força dos MAP (avaliação funcional do assoalho pélvico, perineômetro, eletromiografia, ultrassonografia funcional), melhora da qualidade de	**Sim**

vida (questionários), presença ou ausência de IU pós-parto e efeitos adversos.	

Extração de dados contínuos

Desfecho	**Intervenção**		**Controle**		**Observação**
	n	**Média (DP)**	**n**	**Média (DP)**	

Extração de dados dicotômicos

Distribution of SUI presence according to the pad test results by follow-up week Follow-up					
Desfecho	**Intervenção: N=52**	**Controle: N=50**			
SUI	**Sim/ Não**	**Sim/ Não**	**X²**	**P value**	
28 sem gest	**3(5,8%)/ 49(94,2%)**	**15(30,0%)/ 35(70,0%)**	**-**	**0,002[2]**	
32 sem gest	**9(17,3%)/ 43(82,7%)**	**24(48,0%)/ 26(52,0%)**	**9,614[3]**	**0,002**	
12 sem pós parto	**1(1,9%)/ 51(98,1%)**	**9(18,0%)/ 41(82,0%)**	**-**	**0,007[2]**	
[1] Results of 2 g and above according to the pad test were evaluated as the presence of SUI. [2] Fisher's exact test was used. [3] The Yates's correction for continuity was used.					
Distribution of incontinence frequency by follow-up week					
Follow-up	**Intervention**	**Control**	**Total**		
Gestational week 28 Frequency of incontinence:					
Once a week or less	**2 (66,7%)**	**1 (6,7%)**	**3 (16,7%)**		
Several times a week or more	**1 (33,3%)**	**14 (93,3%)**	**15 (83,3%)**		
Gestational week 32 Frequency of incontinence:					

Once a week or less	**4 (44,4%)**	**3 (12,5%)**	**7 (21,2%)**		
Several times a week or more	**5 (55,6%)**	**21 (87,5%)**	**26 (78,8%)**		
12 weeks postpartum Frequency of incontinence:					
Once a week or less	**1 (100,0%)**	**2 (22,2%)**	**3 (30,0%)**		
Several times a week or more	**-**	**7 (77,8%)**	**7 (70,0%)**		

Apêndice 2- Formulário para extração de dados

Sobrenome Primeiro Autor	**Ano**
S. Stafne et al	**2012**

Elegibilidade

Ensaio Clínico Randomizado	**Participantes relevantes**	**Intervenção relevante**	**Desfecho relevante**
Sim	**Sim**	**Sim**	**Sim**

Participantes	
Tamanho da amostra	**In all, 875 women consented to participate in the trial.**
Idade (média, DP e faixa)	**Over 18 yo.**
P (participantes)	**855 women**
I (intervenção)	**397 no grupo de intervenção.**
C (comparador)	**365 no grupo controle**
O (outcomes)	**The main outcomes were urinary incontinence, as measured by self-report. The outcome measures of UI were further divided into two severity categories with respect to**

	frequency: 'urinary leak- age < once per week' or 'urinary leakage >= once per week (severe UI)'.
Características do estudo	
	Detalhes
Multicentrinco / centro único	**Multicentrico**
Países	**Norway**
Critérios de inclusão de participantes e exclusão	**Inclusion criteria were age ‡18 years and a singleton live fetus. Exclusion criteria were high-risk pregnancies and/or diseases that could interfere with participation. For practical reasons we also excluded women who lived too far from the hospitals to attend weekly training groups (judged as more than 30-minutes' drive)**
Número participantes randomizados	**A total of 855 women were randomly allocated to an intervention group or a control group**
Perdas	**20 women were excluded or withdrew before the first examination: 13 did not meet the inclusion criteria, 5 miscarried and 2 had twin pregnancies. However, 32 women in the intervention group and 61 in the control group were lost to follow-up.**
Número participantes analisados	**Data from 397 women in the intervention group and 365 women in the control group were included in a complete case analysis.**
Tempo de seguimento	**Between 20 and 36 weeks of gestation.**

Desfechos Primários	
Materno:	**Presente no artigo**
Ocorrência, redução, recorrência ou persistência dos sintomas de PS-UI.	**Sim**
Desfechos secundários	
Melhora da força dos MAP (avaliação funcional do assoalho pélvico, perineômetro, eletromiografia, ultrassonografia funcional), melhora da qualidade de vida (questionários), presença ou	**Sim**

ausência de IU pós-parto e efeitos adversos.	

Extração de dados contínuos

Desfecho	**Intervenção**		**Controle**		**Observação**
	n	**Média (DP)**	**n**	**Média (DP)**	

Extração de dados dicotômicos

Urinary incontinence (UI) at 32–36 weeks of gestation in the intervention group and control group, including women who did or did not report urinary leakage at inclusion.					
Desfecho	**Intervenção: N=397**	**Controle: N=365**	**Adjusted for baseline**		
IU(Variações)	**n/ %**	**n/ %**	**OR**	**95% CI**	**P value**
UI*	**166/ 42**	**192/ 53**	**0,6**	**0,4; 0,9**	**0,004**
UI >= 1 PW*	**44/ 11**	**68/ 19**	**0,5**	**0,3; 0,8**	**0,006**
SUI**	**102/ 28**	**128/ 37**	**0,7**	**0,5; 0,9**	**0,02**
SUI >= 1 PW**	**25/ 7**	**45/ 13**	**0,5**	**0,3; 0,9**	**0,03**
UUI***	**11/ 3**	**20/ 6**	**0,4**	**0,2; 0,9**	**0,04**
UUI >= 1 PW***	**0/ 0**	**3/ 1**	**-**	**-**	**-**
***Data missing in 0.7% of cases. **Data missing in 6.0% of cases. ***Data missing in 1.0% of cases.**					

Anexo 2 – Estratégia de busca utilizada

#1 - "Pregnancy"[Mesh] OR Pregnancies OR Gestation OR Pregnant

#2 - "Hyperglycemia"[Mesh] OR Hyperglycemias OR Hyperglycemia, Postprandial OR Hyperglycemias, Postprandial OR Postprandial Hyperglycemias OR Postprandial Hyperglycemia

#3 - "Diabetes Mellitus, Type 2"[Mesh] OR Diabetes Mellitus, Noninsulin-Dependent OR Diabetes Mellitus, Ketosis-Resistant OR Diabetes Mellitus, Ketosis Resistant OR Ketosis-Resistant Diabetes Mellitus OR Diabetes Mellitus, Non-Insulin Dependent OR Diabetes Mellitus, Non-Insulin-Dependent OR Non-Insulin-Dependent Diabetes Mellitus OR Diabetes Mellitus, Stable OR Stable Diabetes Mellitus OR Diabetes Mellitus, Type II OR NIDDM OR Diabetes Mellitus, Noninsulin Dependent OR Diabetes Mellitus, Maturity-Onset OR Diabetes Mellitus, Maturity Onset OR Maturity-Onset Diabetes Mellitus OR Maturity Onset Diabetes Mellitus OR MODY OR Diabetes Mellitus, Slow-Onset OR Diabetes Mellitus, Slow Onset OR Slow-Onset Diabetes Mellitus OR Type 2 Diabetes Mellitus OR Noninsulin-Dependent Diabetes Mellitus OR Noninsulin Dependent Diabetes Mellitus OR Maturity-Onset Diabetes OR Diabetes, Maturity-Onset OR Maturity Onset Diabetes OR Type 2 Diabetes OR Diabetes, Type 2 OR Diabetes Mellitus, Adult-Onset OR Adult-Onset Diabetes Mellitus OR Diabetes Mellitus, Adult Onset

#4 - "Diabetes Mellitus, Type 1"[Mesh] OR Diabetes Mellitus, Brittle OR Brittle Diabetes Mellitus OR Diabetes Mellitus, Insulin-Dependent OR Diabetes Mellitus, Insulin Dependent OR Insulin-Dependent Diabetes Mellitus OR Diabetes Mellitus, Juvenile-Onset OR Diabetes Mellitus, Juvenile Onset OR Juvenile-Onset Diabetes Mellitus OR Diabetes Mellitus, Ketosis-Prone OR Diabetes Mellitus, Ketosis Prone OR Ketosis-Prone Diabetes Mellitus OR Juvenile-Onset Diabetes OR Diabetes, Juvenile-Onset OR Juvenile Onset Diabetes OR Diabetes Mellitus, Type I OR Diabetes Mellitus, Sudden-Onset OR Diabetes Mellitus, Sudden Onset OR Mellitus, Sudden-Onset Diabetes OR Sudden-Onset Diabetes Mellitus OR Type 1 Diabetes Mellitus OR Diabetes Mellitus, Insulin-Dependent, 1 OR Insulin-Dependent Diabetes Mellitus 1 OR Insulin Dependent Diabetes Mellitus 1 OR Type 1 Diabetes OR Diabetes, Type 1 OR IDDM OR Diabetes, Autoimmune OR Autoimmune Diabetes

#5 - "Pregnancy in Diabetics"[Mesh] OR Pregnancy in Diabetic OR Pregnancy in Diabetes OR Pregnancy in Diabetes

#6 - "Diabetes, Gestational"[Mesh] OR Diabetes, Pregnancy-Induced OR Diabetes, Pregnancy Induced OR Pregnancy-Induced Diabetes OR Gestational Diabetes OR Diabetes Mellitus, Gestational OR Gestational Diabetes Mellitus

#7 - "Urinary Incontinence"[Mesh] OR Incontinence, Urinary

Formula de pesquisa: (#1 AND #2 OR #3 OR #4) OR #5 OR #6 AND #7.

Para BVS /LILACS:

#1 - Gestação OR Gravidez

#2 - Hiperglicemia OR Hiperglucemia OR Hiperglicemia Pós-Prandial OR Hiperglucemia Pós-Prandial

#3 - Diabetes Mellitus Tipo 2 OR Diabetes Mellitus de Início no Adulto OR Diabetes Mellitus Resistente a Cetose OR Diabetes Mellitus não Insulinodependente OR Diabetes Mellitus não Insulino-Dependente OR Diabetes Mellitus não Dependente de Insulina OR Diabetes Mellitus Estável OR DMNID OR Diabetes Mellitus de Início na Maturidade OR MODY OR Diabetes Mellitus de Início Gradativo

#4 - Diabetes Mellitus Tipo 1 OR Diabetes Mellitus Instável OR Diabetes Mellitus Insulinodependente OR Diabetes Mellitus Insulino-Dependente OR Diabetes Mellitus Dependente de Insulina OR Diabetes Mellitus de Início na Juventude OR Diabetes Mellitus com Tendência à Cetose OR Dmid OR Diabetes Autoimune OR Diabetes Mellitus de Início Súbito

#5 - Diabetes Gestacional OR Diabetes Mellitus Gestacional OR Diabetes Induzida pela Gravidez OR Diabetes Induzida por Gravidez

#6 - Incontinência Urinária

Formula de pesquisa: (#1 AND #2 OR #3 OR #4) OR #5 AND #6.

Anexo 3 – Participação em eventos internacionais e nacionais

July, 2022

MMD

To Whom It May Concern

This letter certifies that **EUSEBIO AMADOR** (Brazil) has completed (in full) the activities of the postgraduate international course Mechanisms of Metabolic Disorders (MMD) 2022 (April 4 until July 8, 2022).

The MMD course was organized by the Cellular and Molecular Physiology Laboratory (CMPL) from the Faculty of Medicine, Pontificia Universidad Católica de Chile, and the University Medical Centre Groningen (UMCG), University of Groningen, The Netherlands.

The MMD course consisted of 49 lectures delivered by international experts, 21 seminars from MMD students, four conferences from journal Editors-in-Chief, six Rector and Vice-Rectors and three Ambassadors messages.

In-full attendance consisted of synchronic activities (online) in 28.5 chronological hours, equivalent to 57 academic hours (45 min per educational hour).

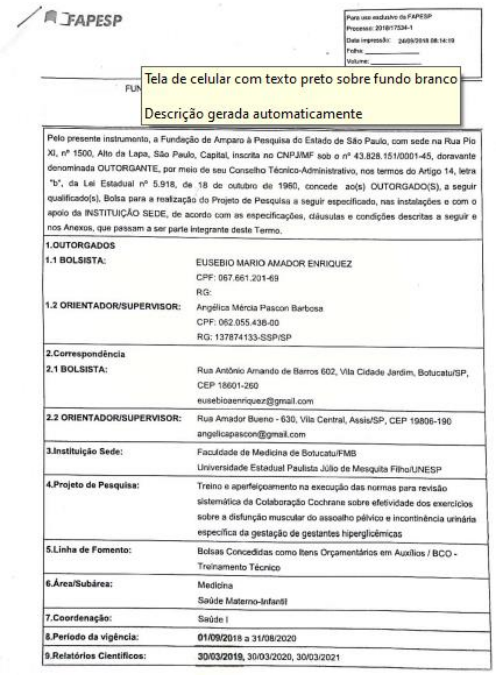
Having completed the requirement of in-full attendance and having delivered a seminar at the symposia part of the course programme, **EUSEBIO AMADOR** is granted five (5) academic credits by the MMD course.

Sponsors: The International Union of Physiological Sciences (IUPS), Latin American Association of Physiological Sciences (ALACF), The Physiological Society (TPS), Sociedad Española de Ciencias Fisiológicas (SECF), Sociedad Chilena de Ciencias Fisiológicas (SCHCF), Bentham Science Publishers (BSP), SERNATUR (Chile), FONDECYT 1190316 (Chile), The Institute for Obesity Research, Tecnologico de Monterrey (Mexico).

Luis Sobrevia
MMD course coordinator
CMPL, Chile

Harry van Goor
MMD course coordinator
UMCG, The Netherlands

Anexo 4 – Concessão Bolsa Treinamento Técnico



FAPESP

Para uso exclusivo da FAPESP
Processo: 2018/17534-1
Data impressão: 24/09/2018 08:14:19
Folha: _____
Volume: _____

Tela de celular com texto preto sobre fundo branco

Descrição gerada automaticamente

Pelo presente instrumento, a Fundação de Amparo à Pesquisa do Estado de São Paulo, com sede na Rua Pio XI, nº 1500, Alto da Lapa, São Paulo, Capital, inscrita no CNPJ/MF sob o nº 43.828.151/0001-45, doravante denominada OUTORGANTE, por meio de seu Conselho Técnico-Administrativo, nos termos do Artigo 14, letra "b", da Lei Estadual nº 5.918, de 18 de outubro de 1960, concede ao(s) OUTORGADO(S), a seguir qualificado(s), Bolsa para a realização do Projeto de Pesquisa a seguir especificado, nas instalações e com o apoio da INSTITUIÇÃO SEDE, de acordo com as especificações, cláusulas e condições descritas a seguir e nos Anexos, que passam a ser parte integrante deste Termo.

1.OUTORGADOS	
1.1 BOLSISTA:	EUSEBIO MARIO AMADOR ENRIQUEZ CPF: 067.661.201-69 RG:
1.2 ORIENTADOR/SUPERVISOR:	Angélica Mércia Pascon Barbosa CPF: 062.055.438-00 RG: 137874133-SSP/SP
2.Correspondência	
2.1 BOLSISTA:	Rua Antônio Amando de Barros 602, Vila Cidade Jardim, Botucatu/SP, CEP 18601-260 eusebioenriquez@gmail.com
2.2 ORIENTADOR/SUPERVISOR:	Rua Amador Bueno - 630, Vila Central, Assis/SP, CEP 19806-190 angelicapascon@gmail.com
3.Instituição Sede:	Faculdade de Medicina de Botucatu/FMB Universidade Estadual Paulista Júlio de Mesquita Filho/UNESP
4.Projeto de Pesquisa:	Treino e aperfeiçoamento na execução das normas para revisão sistemática da Colaboração Cochrane sobre efetividade dos exercícios sobre a disfunção muscular do assoalho pélvico e incontinência urinária específica da gestação de gestantes hiperglicêmicas
5.Linha de Fomento:	Bolsas Concedidas como Itens Orçamentários em Auxílios / BCO - Treinamento Técnico
6.Área/Subárea:	Medicina Saúde Materno-Infantil
7.Coordenação:	Saúde I
8.Período da vigência:	**01/09/2018** a 31/08/2020
9.Relatórios Científicos:	**30/03/2019**, 30/03/2020, 30/03/2021

Anexo 5 – Concessão de Mestrado Académico

unesp UNIVERSIDADE ESTADUAL PAULISTA
Câmpus de Botucatu

FMB

ATESTADO

Atestamos, para os devidos fins, que EUSEBIO MARIO AMADOR ENRIQUEZ, RA nº TOC190373, RNE nº G010796-L, é discente regularmente matriculado, no Programa de Pós-Graduação em Tocoginecologia, área: Saúde Materna e Infantil, Curso de Mestrado Acadêmico, reconhecido pela Portaria MEC número 609/2019 de 14/03/2019.

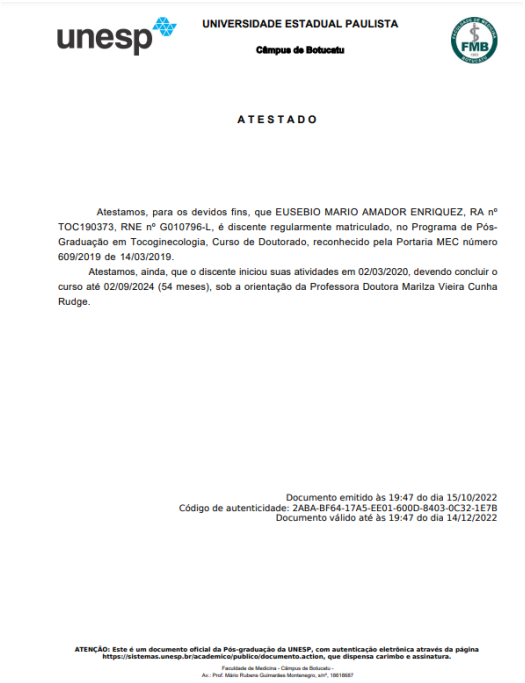
Atestamos, ainda, que o discente iniciará suas atividades em 02/03/2020, devendo concluir o curso até 02/03/2022 (24 meses), sob a orientação da Professora Doutora Marilza Vieira Cunha Rudge.

Botucatu, 06 de dezembro de 2019.

UNIVERSIDADE ESTADUAL PAULISTA FACULDADE DE MEDICINA SEÇÃO TÉCNICA DE PÓS-GRADUAÇÃO CAMPUS DE BOTUCATU

Solange Sako Cagliari
Secretária

Anexo 6 – Concessão de Doutorado Direto e Bolsa DD



unesp

UNIVERSIDADE ESTADUAL PAULISTA

Câmpus de Botucatu

FMB

ATESTADO

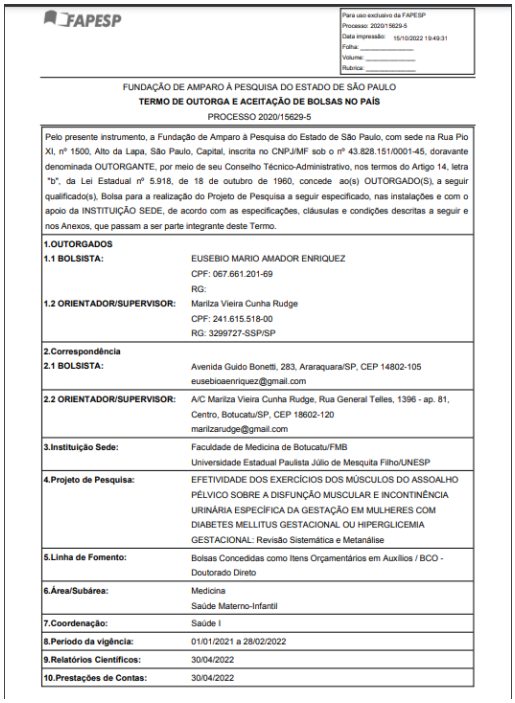
Atestamos, para os devidos fins, que EUSEBIO MARIO AMADOR ENRIQUEZ, RA nº TOC190373, RNE nº G010796-L, é discente regularmente matriculado, no Programa de Pós-Graduação em Tocoginecologia, Curso de Doutorado, reconhecido pela Portaria MEC número 609/2019 de 14/03/2019.

Atestamos, ainda, que o discente iniciou suas atividades em 02/03/2020, devendo concluir o curso até 02/09/2024 (54 meses), sob a orientação da Professora Doutora Marilza Vieira Cunha Rudge.

Documento emitido às 19:47 do dia 15/10/2022
Código de autenticidade: 2ABA-BF64-17A5-EE01-600D-8403-0C32-1E7B
Documento válido até às 19:47 do dia 14/12/2022

ATENÇÃO: Este é um documento oficial da Pós-graduação da UNESP, com autenticação eletrônica através da página https://sistemas.unesp.br/academico/publico/documento.action, que dispensa carimbo e assinatura.

Faculdade de Medicina - Câmpus de Botucatu -
Av.: Prof. Mário Rubens Guimarães Montenegro, s/nº, 18618687



FAPESP

Para uso exclusivo da FAPESP
Processo: 2020/15629-5
Data impressão: 15/10/2022 19:49:31
Folha: _____
Volume: _____
Rubrica: _____

FUNDAÇÃO DE AMPARO À PESQUISA DO ESTADO DE SÃO PAULO

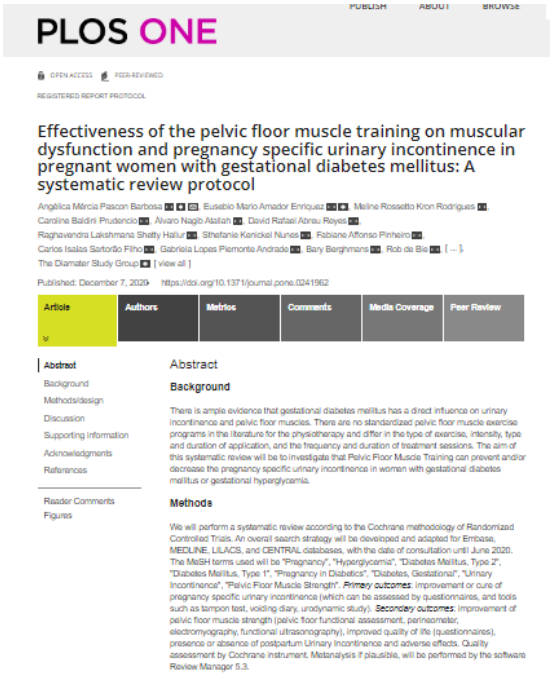
TERMO DE OUTORGA E ACEITAÇÃO DE BOLSAS NO PAÍS

PROCESSO 2020/15629-5

Pelo presente instrumento, a Fundação de Amparo à Pesquisa do Estado de São Paulo, com sede na Rua Pio XI, nº 1500, Alto da Lapa, São Paulo, Capital, inscrita no CNPJ/MF sob o nº 43.828.151/0001-45, doravante denominada OUTORGANTE, por meio de seu Conselho Técnico-Administrativo, nos termos do Artigo 14, letra "b", da Lei Estadual nº 5.918, de 18 de outubro de 1960, concede ao(s) OUTORGADO(S), a seguir qualificado(s), Bolsa para a realização do Projeto de Pesquisa a seguir especificado, nas instalações e com o apoio da INSTITUIÇÃO SEDE, de acordo com as especificações, cláusulas e condições descritas a seguir e nos Anexos, que passam a ser parte integrante deste Termo.

1.OUTORGADOS	
1.1 BOLSISTA:	EUSEBIO MARIO AMADOR ENRIQUEZ CPF: 067.661.201-69 RG:
1.2 ORIENTADOR/SUPERVISOR:	Marilza Vieira Cunha Rudge CPF: 241.615.518-00 RG: 3299727-SSP/SP
2.Correspondência	
2.1 BOLSISTA:	Avenida Guido Bonetti, 283, Araraquara/SP, CEP 14802-105 eusebioaenriquez@gmail.com
2.2 ORIENTADOR/SUPERVISOR:	A/C Marilza Vieira Cunha Rudge, Rua General Telles, 1396 - ap. 81, Centro, Botucatu/SP, CEP 18602-120 marilzarudge@gmail.com
3.Instituição Sede:	Faculdade de Medicina de Botucatu/FMB Universidade Estadual Paulista Júlio de Mesquita Filho/UNESP
4.Projeto de Pesquisa:	EFETIVIDADE DOS EXERCÍCIOS DOS MÚSCULOS DO ASSOALHO PÉLVICO SOBRE A DISFUNÇÃO MUSCULAR E INCONTINÊNCIA URINÁRIA ESPECÍFICA DA GESTAÇÃO EM MULHERES COM DIABETES MELLITUS GESTACIONAL OU HIPERGLICEMIA GESTACIONAL: Revisão Sistemática e Metanálise
5.Linha de Fomento:	Bolsas Concedidas como Itens Orçamentários em Auxílios / BCO - Doutorado Direto
6.Área/Subárea:	Medicina Saúde Materno-Infantil
7.Coordenação:	Saúde I
8.Período da vigência:	01/01/2021 a 28/02/2022
9.Relatórios Científicos:	30/04/2022
10.Prestações de Contas:	30/04/2022

Anexo 7 – Artigo publicado em periódico



PLOS ONE

OPEN ACCESS PEER-REVIEWED

REGISTERED REPORT PROTOCOL

Effectiveness of the pelvic floor muscle training on muscular dysfunction and pregnancy specific urinary incontinence in pregnant women with gestational diabetes mellitus: A systematic review protocol

Angélica Mércia Pascon Barbosa, Eusebio Mario Amador Enriquez, Meline Rossetto Kron Rodrigues, Caroline Baldini Prudencio, Álvaro Nagib Atallah, David Rafael Abreu Reyes, Raghavendra Lakshmana Shetty Hallur, Sthefanie Kenickel Nunes, Fabiane Affonso Pinheiro, Carlos Isaias Sartorão Filho, Gabriela Lopes Piemonte Andrade, Bary Berghmans, Rob de Bie, [...], The Diamater Study Group [view all]

Published: December 7, 2020 https://doi.org/10.1371/journal.pone.0241962

Article | Authors | Metrics | Comments | Media Coverage | Peer Review

Abstract
Background
Methods/design
Discussion
Supporting information
Acknowledgments
References
Reader Comments
Figures

Abstract

Background

There is ample evidence that gestational diabetes mellitus has a direct influence on urinary incontinence and pelvic floor muscles. There are no standardized pelvic floor muscle exercise programs in the literature for the physiotherapy and differ in the type of exercise, intensity, type and duration of application, and the frequency and duration of treatment sessions. The aim of this systematic review will be to investigate that Pelvic Floor Muscle Training can prevent and/or decrease the pregnancy specific urinary incontinence in women with gestational diabetes mellitus or gestational hyperglycaemia.

Methods

We will perform a systematic review according to the Cochrane methodology of Randomized Controlled Trials. An overall search strategy will be developed and adapted for Embase, MEDLINE, LILACS, and CENTRAL databases, with the date of consultation until June 2020. The MeSH terms used will be "Pregnancy", "Hyperglycemia", "Diabetes Mellitus, Type 2", "Diabetes Mellitus, Type 1", "Pregnancy in Diabetics", "Diabetes, Gestational", "Urinary Incontinence", "Pelvic Floor Muscle Strength". *Primary outcomes*: improvement or cure of pregnancy specific urinary incontinence (which can be assessed by questionnaires, and tools such as tampon test, voiding diary, urodynamic study). *Secondary outcomes*: improvement of pelvic floor muscle strength (pelvic floor functional assessment, perineometer, electromyography, functional ultrasonography), improved quality of life (questionnaires), presence or absence of postpartum Urinary Incontinence and adverse effects. Quality assessment by Cochrane instrument. Metanalysis if plausible, will be performed by the software Review Manager 5.3.

SpringerLink

Original Article | Published: 03 June 2022

Relaxin-2 during pregnancy according to glycemia, continence status, and pelvic floor muscle function

Caroline Baldini Prudencio, Sthefanie Kenickel Nunes, Fabiane Affonso Pinheiro, Carlos Isaias Sartorão Filho, Flávia Ignácio Antônio, Guilherme Thomaz de Aquino Nava, Marilza Vieira Cunha Rudge, Angélica Mércia Pascon Barbosa & Diamater Study Group

International Urogynecology Journal **33**, 3203–3211 (2022) | Cite this article

231 Accesses | Metrics

Abstract

Introduction and hypothesis

To investigate relaxin-2 concentration comparing gestational diabetes mellitus (GDM) and non-GDM patients during pregnancy according to urinary incontinence (UI) and pelvic function status.

Methods

This is a cross-sectional study evaluating 282 pregnant women from 24 weeks of gestation. The participants were divided into two groups, non-GDM and GDM, according to American Diabetes Association's diabetes mellitus gestational threshold. In addition, according to subanalysis, both groups were subdivided according to the presence of pregnancy-specific urinary incontinence: non-GDM continent, non-GDM incontinent, GDM continent, and GDM incontinent. All participants filled in questionnaires on clinical, obstetric, and urinary continence status (International Consultation on Incontinence Questionnaire-Short Form, ICIQ-SF, and Incontinence Severity Index, ISI), followed by pelvic floor muscle evaluation by the PERFECT scheme in which strength, endurance, and speed of contractions were evaluated.

Neurourology Urodynamics

CLINICAL ARTICLE

Pelvic floor muscle dysfunction at 3D transperineal ultrasound in maternal exposure to gestational diabetes mellitus: A prospective cohort study during pregnancy

Fabiane A. Pinheiro, Carlos I. Sartorão Filho, Caroline B. Prudencio, Sthefanie K. Nunes, Tawana Pascon, Ragavendra L. S. Hallur, Luis Takano, Eusébio M. A. Enriquez, Bruna B. Catinelli ... See all authors

First published: 14 April 2022 | https://doi.org/10.1002/nau.24927

Fabiane A. Pinheiro, Carlos I. Sartorão Filho, Marilza V. C. Rudge, and Angélica M. P. Barbosa contributed equally to this study.
Fabiane A. Pinheiro and Carlos I. Sartorão Filho are co-first authors.
Marilza V. C. Rudge and Angélica M. P. Barbosa are last authors of this study.

Read the full text > PDF TOOLS SHARE

Abstract

Aim

This study aimed to assess, for the first time, the dynamic morphometry of pelvic floor muscles (PFM) using three-dimensional transperineal ultrasound (3D-TPUS) and its progression at two-time points of gestation between women with and without gestational diabetes mellitus (GDM), and whether the PFM dysfunction is connected to GDM.

Methods

The study comprised 83 consecutive pregnant women with (n = 38) and without (n = 45) GDM screened at 24–30 and 38–40 weeks of gestation. 3D-TPUS and a mobility test were used to quantify PFM dynamic morphometry during maximum contraction and the Valsalva maneuver.

Reyes et al. BioMedical Engineering OnLine (2022) 21:76
https://doi.org/10.1186/s12938-022-01042-2

BioMedical Engineering OnLine

RESEARCH Open Access

Viability of ex-vivo myography as a diagnostic tool for rectus abdominis muscle electrical activity collected at Cesarean section within a diamater cohort study

David R. A. Reyes[1†], Angelica M. P. Barbosa[1,2†], Floriano F. Juliana[1], Quiroz B. C. V. Sofia[1], Sarah M. B. Costa[1], Raghavendra L. S. Hallur[1,3], Eusebio M. A. Enriquez[1], Rafael G. Oliveira[1], Patrícia de Souza Rossignolli[2], Cristiane Rodrigues Pedroni[2], Fernanda C. B. Alves[1], Gabriela A. Garcia[1], Joelcio F. Abbade[1], Carolina N. F. Carvalho[1], Luis Sobrevia[1,4,5,6,7], Marilza V. C. Rudge[1*†], Iracema I. M. P. Calderon[1†] and The Diamater Study Group

[1]David R. A. Reyes and Angelica M. P. Barbosa are the first authors
[1]Marilza V. C. Rudge and Iracema I. M. P. Calderon are the last authors
*Correspondence: marilzarudge@gmail.com
† Department of Gynecology and Obstetrics, Botucatu Medical School (FMB), São Paulo State University (UNESP), Botucatu, São Paulo CEP 18618-687, Brazil
Full list of author information is available at the end of the article

Abstract

Background: *Ex-vivo* myography enables the assessment of muscle electrical activity response. This study explored the viability of determining the physiological responses in muscles without tendon, as rectus abdominis muscle (RAM), through *ex-vivo* myography to assess its potential as a diagnostic tool.

Results: All tested RAM samples (five different samples) show patterns of electrical activity. A positive response was observed in 100% of the programmed stimulation. RAM 3 showed greater weight (0.47 g), length (1.66 cm), and width (0.77 cm) compared to RAM 1, RAM 2, RAM 4 and RAM 5 with more sustained electrical activity over time, a higher percentage of fatigue was analyzed at half the time of the electrical activity. The order of electrical activity (Mn) was RAM 3 > RAM 5 > RAM 1 > RAM 4 > RAM 2. No electrical activity was recorded in the Sham group.

Conclusions: This study shows that it is feasible to assess the physiological responses of striated muscle without tendon as RAM, obtained at C-section, under *ex vivo* myography. These results could be recorded, properly analyzed, and demonstrated its potential as a diagnostic tool for rectus abdominis muscle electrical activity.

Keywords: Contractility, Rectus abdominis muscle, C-section, Myography, Skeletal muscle

Background

The Rectus Abdominis Muscle (RAM), a striated muscle without tendon, extending along the abdomen to the pubic symphysis, undergoes physiological adaptations during pregnancy [1–5]. As a striated muscle, the main focus of research has been on contractile muscle cells [6]. RAM has synergistic contractile activity with the pelvic floor

Neurourology Urodynamics

ORIGINAL CLINICAL ARTICLE

Impact of gestational diabetes on pelvic floor: A prospective cohort study with three-dimensional ultrasound during two-time points in pregnancy

Carlos I. Sartorão Filho, Fabiane A. Pinheiro, Caroline B. Prudencio, Sthefanie K. Nunes, Luiz Takano, Eusebio M. A. Enriquez, Maiara I. G. Orlandi, Baerbel Junginger ... See all authors

First published: 28 August 2020 | https://doi.org/10.1002/nau.24491 | Citations: 3

Carlos I. Sartorão Filho, Fabiane A. Pinheiro, Caroline B. Prudencio, Sthefanie K. Nunes, Luiz Takano, Eusebio M.A. Enriquez, Maiara I. Orlandi, Baerbel Junginger, Marilza V. C. Rudge, and Angélica M.P. Barbosa contributed equally to this work.
Carlos I. Sartorão Filho and Fabiane A. Pinheiro are the first authors on this work.
Angélica M.P. Barbosa and Marilza V. C. Rudge are the last authors on this work.

Read the full text > PDF TOOLS SHARE

Abstract

Aim

To evaluate the pelvic floor (PF) biometry using three-dimensional ultrasound (US) at two-time points of gestational in pregnant women with gestational diabetes mellitus (GDM).