APPENDIX A. SEARCH STRATEGIES

MEDLINE

1	Diabetic Foot/ or Foot Ulcer/
2	(diabetic adj1 (foot or feet or ulcer$1)).mp.
3	1 or 2
4	Risk Assessment/
5	(assessment$1 or tool$1 or instrument$1 or (objective clinical measures) or valid* or reliab* or scale$1 or score$1 or predict*).mp.
6	(screen$ or predict$ or sensitive$ or specific$ or risk factor$ or assess$).ti, ab.
7	4 or 5 or 6
8	Orthotic Devices/
9	3 and 7
10	3 and 8
11	9 or 10
12	(systematic review.ti. or meta-analysis.pt. or meta-analysis.ti. or systematic literature review.ti. or this systematic review.tw. or pooling project.tw. or (systematic review.ti,ab. and review.pt.) or meta synthesis.ti. or meta-analy*.ti. or integrative review.tw. or integrative research review.tw. or rapid review.tw. or umbrella review.tw. or consensus development conference.pt. or practice guideline.pt. or drug class reviews.ti. or cochrane database syst rev.jn. or acp journal club.jn. or health technol assess.jn. or evid rep technol assess summ.jn. or jbi database system rev implement rep.jn. or (clinical guideline and management).tw. or ((evidence based.ti. or evidence-based medicine/ or best practice*.ti. or evidence synthesis.ti,ab.) and (((review.pt. or diseases category/ or behavior.mp.) and behavior mechanisms/) or therapeutics/ or evaluation studies.pt. or validation studies.pt. or guideline.pt. or pmcbook.mp.)) or (((systematic or systematically).tw. or critical.ti,ab. or study selection.tw. or ((predetermined or inclusion) and criteri*).tw. or exclusion criteri*.tw. or main outcome measures.tw. or standard of care.tw. or standards of care.tw.) and ((survey or surveys).ti,ab. or overview*.tw. or review.ti,ab. or reviews.ti,ab. or search*.tw. or handsearch.tw. or analysis.ti. or critique.ti,ab. or appraisal.tw. or (reduction.tw. and (risk/ or risk.tw.) and (death or recurrence).mp.)) and ((literature or articles or publications or publication or bibliography or bibliographies or published).ti,ab. or pooled data.tw. or unpublished.tw. or citation.tw. or citations.tw. or database.ti,ab. or internet.ti,ab. or textbooks.ti,ab. or references.tw. or scales.tw. or papers.tw. or datasets.tw. or trials.ti,ab. or meta-analy*.tw. or (clinical and studies).ti,ab. or treatment outcome/ or treatment outcome.tw. or pmcbook.mp.))) not (letter or newspaper article).pt.
13	11 and 12
14	Limit 13 to English language

EMBASE

1	Diabetic Foot/ or Foot Ulcer/
2	(diabetic adj1 (foot or feet or ulcer$1)).mp.
3	1 or 2
4	Risk Assessment/
5	(assessment$1 or tool$1 or instrument$1 or (objective clinical measures) or valid* or reliab* or scale$1 or score$1 or predict*).mp.

6	(screen$ or predict$ or sensitive$ or specific$ or risk factor$ or assess$).ti, ab.
7	4 or 5 or 6
8	Orthotic Devices/
9	3 and 7
10	3 and 8
11	9 or 10
12	(systematic review.ti. or meta-analysis.pt. or meta-analysis.ti. or systematic literature review.ti. or this systematic review.tw. or pooling project.tw. or (systematic review.ti,ab. and review.pt.) or meta synthesis.ti. or meta-analy*.ti. or integrative review.tw. or integrative research review.tw. or rapid review.tw. or umbrella review.tw. or consensus development conference.pt. or practice guideline.pt. or drug class reviews.ti. or cochrane database syst rev.jn. or acp journal club.jn. or health technol assess.jn. or evid rep technol assess summ.jn. or jbi database system rev implement rep.jn. or (clinical guideline and management).tw. or ((evidence based.ti. or evidence-based medicine/ or best practice*.ti. or evidence synthesis.ti,ab.) and (((review.pt. or diseases category/ or behavior.mp.) and behavior mechanisms/) or therapeutics/ or evaluation studies.pt. or validation studies.pt. or guideline.pt. or pmcbook.mp.)) or (((systematic or systematically).tw. or critical.ti,ab. or study selection.tw. or ((predetermined or inclusion) and criteri*).tw. or exclusion criteri*.tw. or main outcome measures.tw. or standard of care.tw. or standards of care.tw.) and ((survey or surveys).ti,ab. or overview*.tw. or review.ti,ab. or reviews.ti,ab. or search*.tw. or handsearch.tw. or analysis.ti. or critique.ti,ab. or appraisal.tw. or (reduction.tw. and (risk/ or risk.tw.) and (death or recurrence).mp.)) and ((literature or articles or publications or publication or bibliography or bibliographies or published).ti,ab. or pooled data.tw. or unpublished.tw. or citation.tw. or citations.tw. or database.ti,ab. or internet.ti,ab. or textbooks.ti,ab. or references.tw. or scales.tw. or papers.tw. or datasets.tw. or trials.ti,ab. or meta-analy*.tw. or (clinical and studies).ti,ab. or treatment outcome/ or treatment outcome.tw. or pmcbook.mp.))) not (letter or newspaper article).pt.
13	11 and 12
14	Limit 13 to English language

APPENDIX B. EXCLUDED STUDIES

1. Adler AI, Erqou S, Lima TAS, Robinson AHN. Association between glycated haemoglobin and the risk of lower extremity amputation in patients with diabetes mellitus-review and meta-analysis. *Diabetologia.* 2010;53(5):840-849. *Ineligible intervention.*

2. Andrews KL, Houdek MT, Kiemele LJ. Wound management of chronic diabetic foot ulcers: from the basics to regenerative medicine. *Prosthetics and orthotics international.* 2015;39(1):29-39. *Ineligible intervention.*

3. Bakker K, Apelqvist J, Lipsky BA, Van Netten JJ, International Working Group on the Diabetic F. The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. *Diabetes/metabolism research and reviews.* 2016;32 Suppl 1:2-6. *Ineligible study design.*

4. Barrera MdP, Sanchez AL, Mejia A, Pinilla AE. Risk factors of diabetes mellitus and diabetic foot: A primary approach to prevention. *Revista Colombiana de Cardiologia.* 2013;20(4):213-222. *Ineligible intervention.*

5. Bergin SM, Gurr JM, Allard BP, et al. Australian Diabetes Foot Network: management of diabetes-related foot ulceration - a clinical update. *The Medical journal of Australia.* 2012;197(4):226-229. *Ineligible study design.*

6. Blanchette V, Brousseau-Foley M, Cloutier L. Evaluation and perspectives of podiatric interventions performed in multidisciplinary context on lower extremity amputations. *Journal of Diabetes Science and Technology.* 2020;14(3):676. *Ineligible study design.*

7. Borkosky SL, Roukis TS. Incidence of re-amputation following partial first ray amputation associated with diabetes mellitus and peripheral sensory neuropathy: A systematic review. *Diabetic Foot and Ankle.* 2012;3. *Ineligible intervention.*

8. Bradley CP, Buckley CM, Perry IJ, Kearney PM. Does contact with a podiatrist prevent the occurrence of a lower extremity amputation in people with diabetes? A systematic review and meta-analysis. *BMJ Open.* 2013;3(5):6. *Ineligible intervention.*

9. Brownrigg JRW, Hinchliffe RJ, Apelqvist J, et al. Performance of prognostic markers in the prediction of wound healing or amputation among patients with foot ulcers in diabetes: a systematic review. *Diabetes/metabolism research and reviews.* 2016;32 Suppl 1:128-135. *Ineligible intervention.*

10. Bus SA, Van Netten JJ, Hinchliffe RJ, et al. Standards for the development and methodology of the 2019 International Working Group on the Diabetic Foot guidelines. *Diabetes/metabolism research and reviews.* 2020;36 Suppl 1:e3267. *Ineligible study design.*

11. Bus SA, van Netten JJ, Monteiro-Soares M, Lipsky BA, Schaper NC. Diabetic foot disease: "The Times They are A Changin' ". *Diabetes/metabolism research and reviews.* 2020;36 Suppl 1:e3249. *Ineligible study design.*

12. Chan KS, Lo ZJ. Wound assessment, imaging and monitoring systems in diabetic foot ulcers: A systematic review. *International Wound Journal.* 2020;17(6):1909-1923. *Ineligible intervention.*

13. Chappell FM, Crawford F, Horne M, et al. Development and validation of a clinical prediction rule for development of diabetic foot ulceration: an analysis of data from five cohort studies. *BMJ open diabetes research & care.* 2021;9(1). *Ineligible intervention.*

14. Chen PY, Elmer S, Callisaya M, Wills K, Greenaway TM, Winzenberg TM. Associations of health literacy with diabetic foot outcomes: a systematic review and meta-analysis. *Diabetic medicine : a journal of the British Diabetic Association.* 2018;35(11):1470-1479. *Ineligible intervention.*

15. Collings R, Glasser S, Freeman J, Latour JM, Paton J. Footwear and insole design features to prevent foot ulceration in people with diabetes: A systematic review protocol. *JBI Database of Systematic Reviews and Implementation Reports.* 2017;15(7):1824-1834. *Ineligible study design.*

16. Crawford F, Anandan C, Chappell FM, et al. Protocol for a systematic review and individual patient data meta-analysis of prognostic factors of foot ulceration in people with diabetes: the international research collaboration for the prediction of diabetic foot ulcerations (PODUS). *BMC medical research methodology.* 2013;13:22. *Ineligible study design.*

17. Crawford F, Cezard G, Chappell FM, Group P. The development and validation of a multivariable prognostic model to predict foot ulceration in diabetes using a systematic review and individual patient data meta-analyses. *Diabetic medicine : a journal of the British Diabetic Association.* 2018;35(11):1480-1493. *Ineligible intervention.*

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20. Dinh TL, Veves A. A review of the mechanisms implicated in the pathogenesis of the diabetic foot. *International Journal of Lower Extremity Wounds.* 2005;4(3):154-159. *Ineligible study design.*

21. Dorresteijn JAN, Kriegsman DMW, Assendelft WJJ, Valk GD. Patient education for preventing diabetic foot ulceration. *The Cochrane database of systematic reviews.* 2014(12):CD001488. *Ineligible intervention.*

22. Dorresteijn JAN, Kriegsman DMW, Valk GD. Complex interventions for preventing diabetic foot ulceration. *The Cochrane database of systematic reviews.* 2010(1):CD007610. *Ineligible intervention.*

23. Droste S, Schuster B, Narres M, et al. Incidence of lower extremity amputations in the diabetic compared with the non-diabetic population: A systematic review. *PLoS ONE.* 2017;12(8):e0182081. *Ineligible intervention.*

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25. Ena J, Carretero-Gomez J, Arevalo-Lorido JC, Sanchez-Ardila C, Zapatero-Gaviria A, Gomez-Huelgas R. The Association Between Elevated Foot Skin Temperature and the Incidence of Diabetic Foot Ulcers: A Meta-Analysis. *International Journal of Lower Extremity Wounds.* 2021;20(2):111-118. *Ineligible intervention.*

26. Feng Y, Schlosser FJ, Sumpio BE. The Semmes Weinstein monofilament examination is a significant predictor of the risk of foot ulceration and amputation in patients with diabetes mellitus. *Journal of vascular surgery.* 2011;53(1):220-225. *Ineligible intervention.*

27. Fernandez-Torres R, Ruiz-Munoz M, Perez-Panero AJ, Garcia-Romero J, Gonzalez-Sanchez M. Instruments of choice for assessment and monitoring diabetic foot: A systematic review. *Journal of Clinical Medicine.* 2020;9(2):602. *Ineligible intervention.*

28. Firdaus MKZH, Jittanoon P. A literature review on intervention programs for diabetic foot care. *Enfermeria clinica.* 2021;31 Suppl 2:S243-S246. *Ineligible intervention.*

29. Formosa C, Gatt A, Chockalingam N. A Critical Evaluation of Existing Diabetic Foot Screening Guidelines. *The review of diabetic studies : RDS.* 2016;13(2-3):158-186. *Ineligible intervention.*

30. Forsythe RO, Apelqvist J, Boyko EJ, et al. Performance of prognostic markers in the prediction of wound healing or amputation among patients with foot ulcers in diabetes: A systematic review. *Diabetes/metabolism research and reviews.* 2020;36 Suppl 1:e3278. *Ineligible intervention.*

31. Freeman J, Paton J, Collings R, Latour JM. Footwear and insole design features for offloading the diabetic at risk foot-A systematic review and meta-analyses. *Endocrinology, Diabetes and Metabolism.* 2021;4(1):e00132. *Ineligible intervention.*

32. Grimmer K, Smith C, Kumar S, Jones S. The clinical effectiveness of podiatric management in the treatment of Charcot foot. *JBI Library of Systematic Reviews.* 2014;3(7 SUPPL.):S59-S73. *Ineligible population.*

33. Hoogeveen RC, Dorresteijn JAN, Kriegsman DMW, Valk GD. Complex interventions for preventing diabetic foot ulceration. *The Cochrane database of systematic reviews.* 2015(8):CD007610. *Ineligible intervention.*

34. Huang Z-H, Li S-Q, Kou Y, Huang L, Yu T, Hu A. Risk factors for the recurrence of diabetic foot ulcers among diabetic patients: a meta-analysis. *International wound journal.* 2019;16(6):1373-1382. *Ineligible intervention.*

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36. Jenkins DA, Mohamed S, Taylor JK, Peek N, van der Veer SN. Potential prognostic factors for delayed healing of common, non-traumatic skin ulcers: A scoping review. *International wound journal.* 2019;16(3):800-812. *Ineligible intervention.*

37. Jones P, Bibb R, Davies M, et al. Prediction of Diabetic Foot Ulceration: The Value of Using Microclimate Sensor Arrays. *Journal of diabetes science and technology.* 2020;14(1):55-64. *Ineligible intervention.*

38. Jones P, Bus SA, Khunti K, Webb D, Davies MJ. Toe gaps and their assessment in footwear for people with diabetes: a narrative review. *Journal of foot and ankle research.* 2020;13(1):70. *Ineligible intervention.*

39. Jones P, Khunti K, Webb D, Davies MJ, Fong DTP. In-shoe pressure thresholds for people with diabetes and neuropathy at risk of ulceration: A systematic review. *Journal of Diabetes and its Complications.* 2021;35(3):107815. *No eligible outcomes.*

40. Kassianos G, Bracknell GP. A summary of the National Institute for Health and Clinical Excellence (NICE) Clinical Guideline 66: The management of type 2 diabetes. *Drugs in Context.* 2008;4(2):185-190. *Ineligible study design.*

41. Kaufman MW, Bowsher JE. Preventing diabetic foot ulcers. *Medsurg nursing : official journal of the Academy of Medical-Surgical Nurses.* 1994;3(3):204-210. *Ineligible study design.*

42. Korada H, Maiya A, Rao SK, Hande M. Effectiveness of customized insoles on maximum plantar pressure in diabetic foot syndrome: A systematic review. *Diabetes & metabolic syndrome.* 2020;14(5):1093-1099. *No eligible outcomes.*

43. Lauri C, Tamminga M, Glaudemans AWJM, et al. Detection of Osteomyelitis in the Diabetic Foot by Imaging Techniques: A Systematic Review and Meta-analysis Comparing MRI, White Blood Cell Scintigraphy, and FDG-PET. *Diabetes care.* 2017;40(8):1111-1120. *Ineligible intervention.*

44. Li D, Yang JY, Wang T, Shen S, Tang H. Risks of diabetic foot syndrome and amputation associated with sodium glucose co-transporter 2 inhibitors: A Meta-analysis of Randomized Controlled Trials. *Diabetes & metabolism.* 2018;44(5):410-414. *Ineligible intervention.*

45. Lin C, Liu J, Sun H. Risk factors for lower extremity amputation in patients with diabetic foot ulcers: A meta-analysis. *PloS one.* 2020;15(9):e0239236. *Ineligible intervention.*

46. Lipsky BA, Peters EJG, Berendt AR, et al. Specific guidelines for the treatment of diabetic foot infections 2011. *Diabetes/metabolism research and reviews.* 2012;28 Suppl 1:234-235. *Ineligible study design.*

47. Margolis DJ, Kantor J, Santanna J, Strom BL, Berlin JA. Risk factors for delayed healing of neuropathic diabetic foot ulcers: a pooled analysis. *Archives of dermatology.* 2000;136(12):1531-1535. *Ineligible intervention.*

48. Mason J, O'Keeffe C, Hutchinson A, McIntosh A, Young R, Booth A. A systematic review of foot ulcer in patients with Type 2 diabetes mellitus. II: treatment. *Diabetic medicine : a journal of the British Diabetic Association.* 1999;16(11):889-909. *Ineligible intervention.*

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50. McGinnis E, Stubbs N. Pressure-relieving devices for treating heel pressure ulcers. *The Cochrane database of systematic reviews.* 2014(2):CD005485. *Ineligible population.*

51. Meneses JCBCd, Viana MCA, Reboucas VdCF, Alencar AMPG, Borges JWP, Silva ARVd. The effects of felted foam in diabetic foot treatment: systematic review with meta-analysis. *Revista da Escola de Enfermagem da U S P.* 2020;54:e03640. *Ineligible intervention.*

52. Meza-Torres B, Carinci F, Heiss C, Joy M, de Lusignan S. Health service organisation impact on lower extremity amputations in people with type 2 diabetes with foot ulcers: systematic review and meta-analysis. *Acta diabetologica.* 2021;58(6):735-747. *Ineligible intervention.*

53. Minc SD, Fogg LF, McCarthy WJ, Shah RC. Racial disparities in primary amputation vs revascularization for critical limb ischemia: A meta-analysis. *Journal of the American College of Surgeons.* 2017;225(4 Supplement 2):e778. *Ineligible intervention.*

54. Mizzi A, Formosa C, Cassar K, Bowen C. A review of the temporal progression of intermittent claudication: Implications for the diabetic foot. *Diabetic Medicine.* 2018;35(Supplement 1):87. *Ineligible study design.*

55. Monteiro-Soares M, Boyko EJ, Ribeiro J, Ribeiro I, Dinis-Ribeiro M. Predictive factors for diabetic foot ulceration: a systematic review. *Diabetes/metabolism research and reviews.* 2012;28(7):574-600. *Ineligible intervention.*

56. Morrison T, Jones S, Causby RS, Thoirs K. Can ultrasound measures of intrinsic foot muscles and plantar soft tissues predict future diabetes-related foot disease? A systematic review. *PloS one.* 2018;13(6):e0199055. *Ineligible intervention.*

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58. Norman G, Cullum N, Westby M, Vedhara K, Game F. Psychosocial and behavioural prognostic factors for diabetic foot ulcer development and healing: a systematic review. *Diabetic Medicine.* 2020;37(8):1244-1255. *Ineligible intervention.*

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60. Ousey K, Chadwick P, Jawien A, et al. Identifying and treating foot ulcers in patients with diabetes: saving feet, legs and lives. *Journal of wound care.* 2018;27(Sup5):S1-S52. *Ineligible study design.*

61. Paton J, Glasser S, Collings R, Kent B. The effects of foot and ankle devices on balance, gait and falls in adults with sensory perception loss: A systematic review protocol. *JBI Database of Systematic Reviews and Implementation Reports.* 2014;12(11):74-91. *No eligible outcomes.*

62. Patry J, Belley R, Cote M, Chateau-Degat M-L. Plantar pressures, plantar forces, and their influence on the pathogenesis of diabetic foot ulcers: a review. *Journal of the American Podiatric Medical Association.* 2013;103(4):322-332. *No eligible outcomes.*

63. Perez-Panero AJ, Ruiz-Munoz M, Cuesta-Vargas AI, Gonzalez-Sanchez M. Prevention, assessment, diagnosis and management of diabetic foot based on clinical practice guidelines: A systematic review. *Medicine.* 2019;98(35):e16877. *Ineligible intervention.*

64. Pinzur MS, Slovenkai MP, Trepman E. Guidelines for diabetic foot care. The Diabetes Committee of the American Orthopaedic Foot and Ankle Society. *Foot & ankle international.* 1999;20(11):695-702. *Ineligible study design.*

65. Pinzur MS, Slovenkai MP, Trepman E, Shields NN, Diabetes Committee of American Orthopaedic F, Ankle S. Guidelines for diabetic foot care: recommendations endorsed by the Diabetes Committee of the American Orthopaedic Foot and Ankle Society. *Foot & ankle international.* 2005;26(1):113-119. *Ineligible study design.*

66. Przestrzelski B, Walker K, Stanley S, et al. Novel additive-manufactured foot orthotic achieves comfort equivalent to the traditional standard. *Journal of Orthopaedic Research.* 2016;34(Supplement 1). *Ineligible study design.*

67. Ragnarson Tennvall G, Apelqvist J. Prevention of diabetes-related foot ulcers and amputations: a cost-utility analysis based on Markov model simulations. *Diabetologia.* 2001;44(11):2077-2087. *No eligible outcomes.*

68. Raikou M, McGuire A. The economics of screening and treatment in type 2 diabetes mellitus. *PharmacoEconomics.* 2003;21(8):543-564. *No eligible outcomes.*

69. Raji S, Tariq G. Implementing a lean methodology in diabetic foot care management. *Journal of Wound Care.* 2017;26(SUPPL 6):313-320. *Ineligible study design.*

70. Richard J-L, Lavigne J-P, Sotto A. Diabetes and foot infection: more than double trouble. *Diabetes/metabolism research and reviews.* 2012;28 Suppl 1:46-53. *Ineligible study design.*

71. Rodriguez-Sanchez B, Pena-Longobardo LM, Sinclair AJ. Cost-effectiveness analysis of the Neuropad device as a screening tool for early diabetic peripheral neuropathy. *European Journal of Health Economics.* 2020;21(3):335-349. *Ineligible intervention.*

72. Saliba Thorne C, Gatt A, DeRaffaele C, Bazena A, Formosa C. Digital foot health technology and diabetic foot monitoring: A systematic review. *Diabetes research and clinical practice.* 2021;175:108783. *Ineligible intervention.*

73. Schaper NC, van Netten JJ, Apelqvist J, et al. Practical Guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). *Diabetes/metabolism research and reviews.* 2020;36 Suppl 1:e3266. *Ineligible study design.*

74. Schaper NC, Van Netten JJ, Apelqvist J, Lipsky BA, Bakker K. Prevention and management of foot problems in diabetes: A Summary Guidance for Daily Practice 2015, based on the IWGDF guidance documents. *Diabetes Research and Clinical Practice.* 2017;124:84-92. *Ineligible study design.*

75. Seixas A, Ammer K, Carvalho R, Vilas-Boas JP, Mendes J, Vardasca R. The use of thermal imaging in patients with diabetic foot: Protocol for a systematic review. *Thermology International.* 2018;28(3):133-138. *Ineligible intervention.*

76. Sen P, Demirdal T, Emir B. Meta-analysis of risk factors for amputation in diabetic foot infections. *Diabetes/metabolism research and reviews.* 2019;35(7):e3165. *Ineligible intervention.*

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78. Sharma S, Gupta R, Compay A, et al. Identification of diagnostic and prognostic biomarkers to improve the management of diabetes-related ulcers. *Asian Pacific Journal of Tropical Disease.* 2014;4(3):228. *Ineligible study design.*

79. Shin JY, Roh S-G, Lee N-H, Yang K-M. Influence of Epidemiologic and Patient Behavior-Related Predictors on Amputation Rates in Diabetic Patients: Systematic Review and Meta-Analysis. *The international journal of lower extremity wounds.* 2017;16(1):14-22. *Ineligible intervention.*

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83. Tan LS. The clinical use of the 10g monofilament and its limitations: a review. *Diabetes research and clinical practice.* 2010;90(1):1-7. *Ineligible intervention.*

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88. Tu HA, Costa V, Xie X, et al. Cost-effectiveness of fiberglass total contact casting, irremovable cast walkers and removable cast walkers in the treatment of patients with diabetic foot ulcers in Ontario, Canada. *Value in Health.* 2017;20(5):A242. *Ineligible intervention.*

89. van Netten JJ, Sacco ICN, Lavery LA, et al. Treatment of modifiable risk factors for foot ulceration in persons with diabetes: a systematic review. *Diabetes/metabolism research and reviews.* 2020;36 Suppl 1:e3271. *Ineligible intervention.*

90. van Reijen NS, Ponchant K, Ubbink DT, Koelemay MJW. Editor's Choice - The Prognostic Value of the WIfI Classification in Patients with Chronic Limb Threatening Ischaemia: A Systematic Review and Meta-Analysis. *European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery.* 2019;58(3):362-371. *Ineligible population.*

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92. Wang N, Yang B-H, Wang G, et al. A meta-analysis of the relationship between foot local characteristics and major lower extremity amputation in diabetic foot patients. *Journal of cellular biochemistry.* 2019;120(6):9091-9096. *Ineligible intervention.*

93. Wang Z, Hasan R, Firwana B, et al. A systematic review and meta-analysis of tests to predict wound healing in diabetic foot. *Journal of vascular surgery.* 2016;63(2 Suppl):29S-22. *Ineligible intervention.*

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diabetes related foot complications. *Diabetic medicine : a journal of the British Diabetic Association.* 2005;22(2):127-136. *Ineligible intervention.*

96. Wu X-J, Fan L. Sex difference for the risk of amputation in diabetic patients: A systematic review and meta-analysis. *PLoS ONE.* 2021;16(3 March):e0243797. *Ineligible intervention.*

97. Yammine K, Assi C. Surgery Versus Nonsurgical Methods in Treating Neuropathic Plantar Forefoot Ulcers: A Meta-Analysis of Comparative Studies. *International Journal of Lower Extremity Wounds.* 2020. *Ineligible study design.*

98. Zhang Y, Cramb S, van Netten JJ, et al. Diabetes-related foot disease in Australia: a systematic review of the prevalence and incidence of risk factors, disease and amputation in Australian populations. *Journal of foot and ankle research.* 2021;14(1):8. *Ineligible intervention.*

APPENDIX C. QUALITY ASSESSMENT

CRITERIA USED IN ASSESSING RISK OF BIAS (ROBIS TOOL)

DOMAIN 1: STUDY ELIGIBILITY CRITERIA	
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:	
1.1 Did the review adhere to pre-defined objectives and eligibility criteria?	Y/PY/PN/N/NI
1.2 Were the eligibility criteria appropriate for the review question?	Y/PY/PN/N/NI
1.3 Were eligibility criteria unambiguous?	Y/PY/PN/N/NI
1.4 Were any restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)?	Y/PY/PN/N/NI
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)?	Y/PY/PN/N/NI
Concerns regarding specification of study eligibility criteria	LOW/HIGH/UNCLEAR
Rationale for concern:	

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES	
Describe methods of study identification and selection (e.g. number of reviewers involved):	
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports?	Y/PY/PN/N/NI
2.2 Were methods additional to database searching used to identify relevant reports?	Y/PY/PN/N/NI
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible?	Y/PY/PN/N/NI
2.4 Were restrictions based on date, publication format, or language appropriate?	Y/PY/PN/N/NI
2.5 Were efforts made to minimise error in selection of studies?	Y/PY/PN/N/NI
Concerns regarding methods used to identify and/or select studies	LOW/HIGH/UNCLEAR
Rationale for concern:	

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL	
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:	
3.1 Were efforts made to minimise error in data collection?	Y/PY/PN/N/NI
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results?	Y/PY/PN/N/NI
3.3 Were all relevant study results collected for use in the synthesis?	Y/PY/PN/N/NI
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria?	Y/PY/PN/N/NI
3.5 Were efforts made to minimise error in risk of bias assessment?	Y/PY/PN/N/NI
Concerns regarding methods used to collect data and appraise studies	LOW/HIGH/UNCLEAR
Rationale for concern:	

DOMAIN 4: SYNTHESIS AND FINDINGS	
Describe synthesis methods:	
4.1 Did the synthesis include all studies that it should?	Y/PY/PN/N/NI
4.2 Were all pre-defined analyses reported or departures explained?	Y/PY/PN/N/NI
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies?	Y/PY/PN/N/NI
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis?	Y/PY/PN/N/NI
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses?	Y/PY/PN/N/NI
4.6 Were biases in primary studies minimal or addressed in the synthesis?	Y/PY/PN/N/NI
Concerns regarding the synthesis and findings Rationale for concern:	LOW/HIGH/UNCLEAR

Y=YES, PY=PROBABLY YES, PN=PROBABLY NO, N=NO, NI=NO INFORMATION

RISK OF BIAS RATINGS FOR ALL ELIGIBLE SYSTEMATIC REVIEWS

Author, Year	Domain 1 Summary: Concerns regarding specification of study eligibility criteria	Domain 2 Summary: Concerns regarding methods used to identify and/or select studies	Domain 3 Summary: Concerns regarding methods used to collect data and appraise studies	Domain 4 Summary: Concerns regarding the synthesis and findings	Overall risk of bias in the review
Arad, 2011[30]	Low	Unclear	Unclear	Low	Moderate
Beulens, 2021[16]	Low	Low	Low	Low	Low
Bus, 2016[12]	Low	Low	Low	Unclear	Low
Bus, 2008[14]	Low	Low	Low	Low	Low
Crawford, 2020[23]	Low	Low	Low	Low	Low
Elraiyah, 2016[37]	Low	Low	Low	Low	Low
Fernandez-Torres, 2020[19]	Low	Unclear	Unclear	Unclear	Moderate
Healy, 2018[38]	Low	Low	Low	Low	Low
Healy, 2014[36]	Low	Low	Low	Low	Low
Healy, 2013[25]	Low	Low	Low	Low	Low
Heuch, 2016[29]	Low	Unclear	Unclear	Low	Moderate
Hingorani, 2016[31]	High	High	High	High	High
Hunt, 2011[13]	Low	Unclear	High	Unclear	High
Health Quality Ontario, 2017[39]	Low	Unclear	High	Low	Moderate
Jarl, 2016[32]	High	High	High	Unclear	High
Karthikesalingam, 2010[21]	Low	Unclear	High	Low	High
Lazzarini, 2020[35]	Low	Low	Low	Low	Low
Singh, 2005[33]	Low	Unclear	High	Low	High
Mason, 1999[34]	Low	Low	High	High	High
Alahakoon, 2020[28]	Low	Unclear	Unclear	Low	Moderate
Monteiro-Soares, 2021[18]	Low	Low	Low	Unclear	Moderate
Monteiro-Soares, 2014[20]	Low	Low	Unclear	Low	Moderate

Monteiro-Soares, 2011[17]	Low	Low	Low	Low	Low
Crawford, 2020[11]	Low	Low	Low	Low	Low
O'Meara, 2000[27]	Low	Low	Low	Low	Low
Paton, 2011[26]	Low	Low	Low	Low	Low
Snyder, 2014[40]	High	High	High	High	High
Steed, 2006[15]	High	Unclear	High	High	High
van Netten, 2020[22]	Low	Low	Low	Low	Low
van Netten, 2016[24]	Low	Low	Low	Low	Low

APPENDIX D. PEER REVIEW DISPOSITION

Comment #	Reviewer #	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?			
1	1	Yes	Thank you.
2	4	Yes	Thank you.
3	5	Yes	Thank you.
4	6	Yes	Thank you.
5	7	Yes	Thank you.
6	8	Yes	Thank you.
Is there any indication of bias in our synthesis of the evidence?			
7	1	No	Thank you.
8	4	No	Thank you.
9	5	No	Thank you.
10	6	No	Thank you.
11	7	No	Thank you.
12	8	No	Thank you.
Are there any published or unpublished studies that we may have overlooked?			
13	1	No	Thank you.
14	4	No	Thank you.
15	5	No	Thank you.
16	6	No	Thank you.
17	7	No	Thank you.
18	8	No	Thank you.
Additional suggestions or comments can be provided below.			
19	1	In discussion of PODUS 2020 clinical applicability (pg.45, Line 55-60) I would have liked to have seen some mention of provider inconsistency in reliable use of monofilament, monofilament calibration, and provider interpretation. However, the evidence review, methodology, and description were well done.	Thank you. We have added the below statement to Discussion Sections in Executive Summary (page 15) and Full Report (page 46): "The prognostic performance of PODUS 2020 depends on the ability of clinicians to accurately assess for neuropathy using a 10 g monofilament, and

Comment #	Reviewer #	Comment	Author Response
			palpable pedal pulses. Although our evidence review did not formally conduct a primary literature review of the performance characteristics of these clinically assessed variables included in PODUS 2020, one study showed sub-optimal validity and reliability (inter- and intra-rater).[44] Performance characteristics for these variables (neuropathy and arterial disease) likely also varies based on clinicians' specialty and experience. Future research could systematically examine the literature for studies describing the performance characteristics of these clinically assessed variables or conduct such studies if not done." Also, entered an abbreviated version on this in Future research page 49
20	4	Non-content related issues observed: 1. P23 Table 1 – error; reference not found comment	Thank you, we have updated the formatting and the issue was resolved.
21	4	2. In a few instances, the acronyms DFU were interchanged with DUF. Perhaps these were references to a source article who used the acronym this way??	Thank you, this was an error. We have corrected this to use the acronym DFU throughout.
22	4	3. The organization and layout of the document flows nicely.	Thank you.
23	4	Content related observations: The authors distill the content into conclusions. Further, in the discussion, authors layout 'key findings' which helps readers grab the takeaway points. A few suggestions on this: Consider re-naming the 'key findings' into 'evidence (or empirical) evidence statements. In doing so, it seems one speaks in first person ('we did not'). Consider not having any first person language in this section. Then also consider referencing the evidence that supports each key finding. Then finally, based on the strength of the evidence supporting each key finding (empirical evidence statement), consider adding either a strength of evidentiary support or a confidence in the evidence (ie low, moderate, high) just to add a bit more emphasis and objectivity so that the policy office or researchers who may pick this up, have a sense of	Thank you for the thoughtful and supportive observations. The current framework for evaluating the certainty of evidence that is commonly used is GRADE. For this report, the certainty (or strength) of evidence was not assessed because there are not well-established methods for using GRADE in "umbrella reviews" (review of reviews). Furthermore, most of the individual reviews that informed our key questions did not formally use GRADE or other methods to assess certainty of findings and provided only a narrative or qualitative summary of findings. For the reviews that did assess certainty of evidence we captured those findings in the review characteristics table. We did perform and reported on the Risk of Bias using the ROBIS tool to assess the quality of the systematic reviews which provides some

Comment #	Reviewer #	Comment	Author Response
		how strong the statement is and what may be acted upon as stated compared with what may need further study before implementing.	information about the confidence in the results of specific reviews. Therefore, as GRADE was not performed, we believe the term "Key Findings" ais more appropriate and is also more consistent with most VA-ESP report formats. We removed the first person language in the key findings.
24	5	The review of reviews is very good. I really don't have any significant comments regarding the content of the review. The only comment that I have is in the Executive Summary section in the paragraph below. "Although PODUS 2020 predicts risk of DFU at 2 years, no data exist to inform how risks change over time and appropriate re-screening intervals for any tool. Thus, it is uncertain how often patients with DM should be screened for risk of DFU or amputation. Frequent screening intervals of 1 year are unlikely to yield better risk stratification." Comment – may want to clarify the last sentence; "Frequent screening intervals of 1 year are unlikely to yield better risk stratification."	We have deleted this sentence from the executive summary. We do however, comment further in the Discussion Sections in Executive Summary (page 15) and Full Report (page 47): Lastly, all studies of the identified tools, including PODUS 2020, assessed one-time use of the tool to predict DFU development or amputation at subsequent time horizons ranging from 1 to 5 years (2 years for PODUS 2020). There were no studies of sequential use of the tools at defined time intervals to identify how risks for DFU development change over time. Although VA guidelines recommend rescreening annually for DFU risk using PAVE, the benefit of re-screening or the appropriate re-screening interval (if done) for DFU risk with any tool is unknown. Also, entered an abbreviated version on this in Future research page 49
25	6	The results are not surprising considering the variability of the inclusion and exclusion criteria of the studies reviewed as well as the quality of protoplasm individual patients present. I think the conclusions are accurate and indicate that the tool works, in most circumstances, that proper footwear works in many circumstances and that off-loading devices, especially TCC are effective in many circumstances.	Thank you. As stated in the key findings and discussion we caution that the evidence is limited regarding the effectiveness and comparative effectiveness of offloading and therapeutic footwear prevents the development of primary and recurrent DFU. There is some evidence that total contact casts and other devices may improve DFU healing, however the issue of adherence with these other devices confounds the association between the devices and treatment of DFU and must be considered. Future research should consider investigating and addressing patient adherence of these devices in the prevention and treatment of DFU. We modified this paragraph to highlight these points

Comment #	Reviewer #	Comment	Author Response
26	7	Outstanding report with clear and concise conclusions. My only concern is the definition of offloading. I recognize that it is inconsistent in the literature and not a reflection of the reviewers language selection. However, in bullet 5 of the key findings and in response to KQ2 "offloading" appears to be reporting on accommodative insoles being used with therapeutic footwear. This may lead to confusion by readers. Total contact casts, removable devices that cross the ankle are offloading by design, but the accommodative insoles that are described with therapeutic footwear are not offloading. Therefore, in bullet 6 of the key findings, saying "While methodological limitations exist in the primary literature and systematic reviews of offloading footwear, total contact casts (TCC) and available removable devices may improve DFU healing," may also lead to confusion because a TCC is by definition offloading footwear. If it is appropriate, may benefit the report to modify the term offloading to accommodative insoles when referring to prescribed inserts that are placed within therapeutic footwear with the goal to prevent development of primary and recurrent DFU.	Thank you for this clarification, we have updated.
27	8	In multiple places the report says "predict risks" or "risk prediction tools." That language is unclear to me. A prediction is a probability and risk can be a probability too. It would be similar to saying "we are going to predict what the weather forecast will be" when the aim is to predict what the actual weather will be. You could just say "predict DFUs" or "predict ulcers." I assume the writers are thinking of risk as an absolute risk or relative risk which is an event but makes the meaning less clear since the meaning of risk in that research-based situation is different from the meaning in everyday language. There are at least a couple of "its'". The possessive form of "it" is just "its"; no apostrophe. Unless a usage manual for research says differently. On page ii, line 5 it says "Minneapolis VA Portland Health Care System." Sounds like "Portland" got added accidentally or an "and" got left out.	Thank you. We agree, we have clarified throughout the manuscript that the tools predict DFU development or amputation. The Minneapolis VA error has also been corrected.

APPENDIX E. SUPPLEMENTAL TABLES

Supplemental Table 1. Description of Prognostic Tools or Models that Predict Diabetic Foot Ulcer (DFU) or Amputation with a Time Horizon For Prediction

Tool	Tool Characteristics	
Boyko et al (2006)[42]	Variables:	HbA1C, vision poorer than 20/40, history of foot ulcer, history of amputation, monofilament insensitivity, tinea pedis, onychomycosis
	Model:	A1C x 0.0975 + 0.7101 (neuropathy present) + 0.3888 (poor vision) - 0.3206 (tinea pedis present) + 0.4579 (onychomycosis present) + 0.7784 (past history of foot ulcer) + 0.943 (past history of lower limb amputation)
	Outcome Predicted:	DFU
	Time Horizon:	1 and 5 years
	Risk Categories:	Quantified by risk score quartiles as below: Lowest quartile: 0.61-1.47 Second lowest: 1.48-1.99 Second highest: 2.00-2.61 Highest: 2.62-5.07
Martins-Mendes et al [original] (2014)[43]	Variables:	Physical impairment, PAD complication history, complications count (retinopathy, nephropathy, neuropathy, cerebrovascular, cardiovascular, peripheral arterial disease and metabolic (ketoacidosis, hyperosmolar coma or other coma)), prior DFU
	Model:	-3.29 + 0.55 x Physical impairment + 0.93 x PAD complication history presence + 0.27 x number of complications count + 1.51 x Previous DFU
	Outcome Predicted:	DFU or amputation
	Time Horizon:	3 years
	Risk Categories:	unclear
Martins-Mendes et al [simplified] (2014)[43]	Variables:	Complications count (retinopathy, nephropathy, neuropathy, cerebrovascular, cardiovascular, peripheral arterial disease and metabolic (ketoacidosis, hyperosmolar coma or other coma))
	Model:	Simplified model for predicting DFU -2.86 + 0.46 x number of complications* count + 1.84 x previous DFU Simplified model for predicting amputation -5.35 + 0.61 x number of complications count + 1.91 x previous DFU
	Outcome Predicted:	DFU or amputation
	Time Horizon:	3 years

Tool	Tool Characteristics	
	Risk Categories:	unclear
PODUS 2020[46]	Variables:	Neuropathy, PAD, history of DFU or lower-extremity amputation
	Model:	Quantifies risk with total potential scores 0 to 4 using the sum of: Score 1 if insensitive to a 10 g monofilament. Score 1 if any pedal pulse is absent (dorsalis pedis and posterior tibial pulses on both feet) Score 2 if there is history of previous ulcer or amputation.
	Outcome Predicted:	DFU
	Time Horizon:	2 years
	Risk Categories:	Score 0—average risk is 2.4% (95% CI 1.4% to 3.9%) at 2 years Score 1—average risk is 6.0% (95% CI 3.5% to 9.5%) at 2 years Score 2—average risk is 14% (95% CI 8.5% to 21%) at 2 years Score 3—average risk is 29% (95% CI 19% to 41%) at 2 years Score 4—average risk is 51% (95% CI 38% to 64%) at 2 years

DFU: diabetic foot ulcer

Supplemental Table 2. Description of Risk Classification Tools or Models that Predict Diabetic Foot Ulcer (DFU) Development or Amputation without a Time Horizon

Tool	Tool Characteristics	
PODUS 2015	Variables:	Neuropathy, PAD, history of DFU or lower extremity amputation
	Model:	--
	Outcome Predicted:	DFU
	Time Horizon:	Unclear
	Risk Categories:	Moderate risk: neuropathy or PAD High risk: patient's history of DFU or amputation
Queensland High Risk Foot Form (QHRFF) tool	Variables:	Foot deformity, neuropathy, PAD, previous ulcer or amputation
	Model:	--
	Outcome Predicted:	DFU
	Time Horizon:	Unclear
	Risk Categories:	Low risk: No neuropathy or PAD At risk: Neuropathy or PAD High risk: foot deformity with neuropathy and/or PAD or previous ulcer or amputation or critical PAD
Prevention of Amputation in Veterans Everywhere (PAVE)	Variables:	Neuropathy, PAD, specified deformity (bunion, hammertoe, claw toe, mallet toe, metatarsal head deformity, etc), prior DFU/osteomyelitis/amputation, intermittent claudication/rest pain, gangrene/peripheral bypass surgery/angiography, ESRD
	Model:	--
	Outcome Predicted:	Unclear
	Time Horizon:	Unclear
	Risk Categories:	0 Normal risk: Diabetes with no other problems 1 Low risk: Diabetes with minor deformity 2 Moderate risk: Diabetes with diminished circulation (but not diagnosed PAD) and/or sensory neuropathy with or without deformity 3 Highest risk: Diabetes with diagnosed PAD, with or without sensory neuropathy and any patient who has end stage renal disease, diagnosed PAD, Charcot foot, past history of gangrene, foot ulceration or amputation

DFU: Diabetic foot ulcer; PAVE: Prevention of Amputation in Veterans Everywhere

Supplemental Table 3. Description of Risk Classification Tools that Predict Outcome of DFU without a Time Horizon

Tool	Tool Characteristics	
Perfusion, Extent, Depth, Infection, and Sensation (PEDIS)	Variables:	Perfusion (palpation of pedal pulses and non-invasive vascular studies), extent (ulcer area), depth, infection (evaluation for symptoms and signs of inflammation), sensation (loss of sensation to monofilament and/or vibration)
	Model:	--
	Outcome Predicted:	Healed, unhealed, amputation, or death
	Time Horizon:	Unclear (ranged from 6 to 82 months)
	Risk Categories:	See Chuan et al
Site, Ischemia, Neuropathy, Bacterial Infection, Area, and Depth score (SINBAD)	Variables:	Site of DFU (forefoot or midfoot/hindfoot), ischemia (palpation of pedal pulses), neuropathy (loss of sensation to monofilament), bacterial infection, area (<1cm^2 or ≥1cm^2), depth of ulcer
	Model:	--
	Outcome Predicted:	Time to healing
	Time Horizon:	Unclear
	Risk Categories:	See Ince et al

DFU: diabetic foot ulcer; PEDIS: Perfusion, Extent, Depth, Infection, and Sensation; SINBAD: Site, Ischemia, Neuropathy, Bacterial Infection, Area, and Depth score (SINBAD)

Supplemental Table 4. Characteristics and Results for Systematic Reviews Relevant to KQ2

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I (Intervention)/C (*Comparators)*	Outcomes Assessed	Review Author Conclusions
Review of Reviews					
Crawford (2020a)[11]; Inception – February 2019; (Medline, Embase, Cochrane); **LOW**	Adults with a diagnosis of diabetes mellitus, either type 1 or type 2	Qualitative; RCT and observational; 20 systematic reviews	I: Simple interventions (*eg*, pressure-distributing insoles or bespoke footwear or education packages in relation to foot care or other aspects of self-management aimed at patients or health-care professionals) or complex interventions (*eg*, care from a specialist multidisciplinary team in which several interacting interventions were evident) were considered for inclusion in the review. *C: standard care or active comparators, including simple and complex interventions*	Absolute number of incident ulcers; absolute number of recurrent ulcers; time to ulceration; quality of life	Although no robust pooled estimates of effect were identified, the majority of SRs by researchers globally to identify preventative interventions for DFUs reflects the high degree of clinical uncertainty among those delivering care and a clear desire to establish an evidence-based approach for the prevention of foot ulcers. The authors concluded conducting a new systematic review of interventions to prevent ulcer and re-ulcer was warranted.
Systematic Reviews					
van Netten (2020)[22]; Inception – July 24, 2018	Adults at risk for foot ulceration, defined	Qualitative; RCT and observational: 35 controlled, 46 non-controlled	I:1. Foot self-care 2. Structured education about foot self-care	Primary: first ever diabetic foot ulcer and recurrent	Evidence Statement: Orthotic interventions: "In people with diabetes with moderately

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I (Intervention)/C (*Comparators)*	Outcomes Assessed	Review Author Conclusions
(PubMed, Embase, CINAHL, Cochrane); **LOW**	according to the IWFDF risk stratification as "people with diabetes mellitus and peripheral neuropathy."		3. Foot self-management 4. Treatment of risk factors or pre-ulcerative signs on the foot 5. Orthotic interventions 6. Surgical interventions 7. Foot-related exercises 8. Integrated foot care *C: any*	diabetic foot ulcer Secondary: lower-extremity amputation, ulcer severity, ulcer-free survival days, heal-related quality of life, and financial costs	increased risk for foot ulceration (IWGDF risk 2), therapeutic footwear, including shoes, insoles or orthoses, may reduce the risk of a first-ever foot ulcer." LOW* quality of evidence "In people with diabetes at high risk for foot ulceration (IWGDF risk 3), therapeutic footwear, including custom-made shoes or insoles with a demonstrated plantar pressure-reducing effect on the plantar surface of the foot during walking, and that the patient actually wears, reduces the risk of a recurrent plantar diabetic foot ulcer." MODERATE* quality of evidence (this was reduced from high to moderate as the findings between RCTs were inconsistent (CIs cross the 0 line), and there were large confidence intervals around the effect found (imprecision).) *GRADE certainty of evidence statements
Crawford (2020b)[23]; Inception – February 2019; OVID MEDLINE and OVID EMBASE, and Cochrane Central Register of Controlled Trials; **LOW**	Adults with a diagnosis of type 1 or type 2 diabetes, with or without a history of ulceration, but free from foot ulceration at trial entry	Quantitative and qualitative; RCT only; 22	I: Digital silicone devices-further defined as bespoke silicone digital orthotics, custom made footwear and offloading insoles (not defined) including cork insoles, and elastic compression stockings *C: a control group not receiving the intervention under study*	Presence of incident, primary or recurrent foot ulcers, absolute numbers of incident primary ulcers and of incident recurrent ulcers	Twenty-two RCTs of 8 interventions were eligible for analysis. One trial of digital silicone devices (RR 0.07 [95% CI 0.01, 0.55]) and meta-analyses of dermal infrared thermometry (RR 0.41 [95% CI 0.19, 0.86]), complex interventions (RR 0.59 [95% CI 0.38, 0.90], and custom-made footwear and offloading insoles (RR 0.53 [95% CI 0.33, 0.85]; 6 RCTs) showed beneficial effects for these interventions. Conclusion: Four interventions were identified as being effective in preventing foot ulcers in people with diabetes, but uncertainty remains about what works and who is most likely to benefit.

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I (Intervention)/C (*Comparators)*	Outcomes Assessed	Review Author Conclusions
Alahakoon (2020)[28]; Inception – October 11, 2019; Medline, PubMed, CINAHL, Scopus, and Cochrane; **MODERATE**	Participants had diabetes and were all at risk of developing a diabetic foot ulcer (IWGDF risk category 2 or 3)	Quantitative; RCT only; 17 RCTs	I: Home foot temperature monitoring, education of the person with diabetes, or offloading footwear *C: a control group not receiving the intervention under study*	Development of foot ulcer	The main meta-analysis suggested that offloading footwear reduced the incidence of diabetes-related foot ulcers (OR 0.48, 95% CI 0.29 to 0.80; p= 0.0005). Heterogeneity among studies was moderate (I^2 = 72%). A subgroup meta-analysis was also eligible and suggested that custom-made orthoses/footwear reduced diabetes-related foot ulcer incidence (OR 0.47, 95% CI 0.27 to 0.82; p =0.0008) despite moderate heterogeneity (I^2 = 70%). The meta-analysis suggests that offloading footwear is effective at reducing the incidence of diabetes-related foot ulcers.
Heuch (2016)[29]; Inception – November, 2013; (PubMed, Cochrane, CINAHL, EMBASE, SCOPUS, and Google Scholar); **MODERATE**	Adults with diabetes mellitus, regardless of age, gender, ethnicity, duration or type of diabetes, with no history of DFUs and in any clinical setting	Qualitative; RCT and observational; 3	I: All offloading methods, including, but not limited to padding (in-shoe and attached directly to the foot), customized insoles, customized orthotic devices, and customized footwear *C: any*	Foot ulceration (primary)	There is limited and low-quality evidence that in a population of adults with diabetes with no history of DFU, the use of footwear with customized or prefabricated orthotic devices may provide some reduction in plantar pressure and therefore help to prevent a primary DFU. There is a lack of evidence on the relative effectiveness of different offloading options.
van Netten (2016)[24];	Persons with type 1 or 2	Qualitative; RCTs and observational;	I: 1. Care 2. Self-management 3. Medical	First and recurrent	Studies on the specific role of therapeutic footwear in preventing a first foot ulcer in at-risk individuals with diabetes are lacking and are

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I (Intervention)/C (*Comparators)*	Outcomes Assessed	Review Author Conclusions
Inception – July 24, 2014; (PubMed, Embase, CINAHL, and Cochrane); **LOW**	diabetes mellitus who are at risk for foot ulceration	30 RCTs, 44 uncontrolled	*C: any*	diabetic foot ulcer	therefore urgently needed. Several recently published high-quality RCTs indicate that specific modalities of therapeutic footwear can be effective in the prevention of a recurrent plantar foot ulcer compared with more standard of care therapeutic footwear. This systematic review of the literature shows that the evidence base to support the use of interventions that aim to prevent a first foot ulcer in the at-risk patient with diabetes is practically nonexistent. More data are available on the prevention of a recurrent foot ulcer, with strong evidence supporting the home monitoring of foot skin temperatures with subsequent preventative actions and the use of therapeutic footwear with demonstrated pressure-relieving effect that is consistently worn by the patient.
Jarl (2016)[32]; Inception – June, 2016; (Pubmed, CINAHL, and PsychINFO); **HIGH**	Patients with diabetes with a healed ulcer	Qualitative; observational only; 6 studies	I: Therapeutic footwear *C: any*	Adherence	There are too few studies to draw any definitive conclusions about factors associated with adherence to wearing therapeutic shoes.
Bus (2015)[12]; May 1, 2006 – July 29, 2014 (PubMed, EMBASE, CINAHL, Cochrane, Database of Abstracts of Review of Effect,	Patients with diabetes mellitus type 1 or 2, and clinical problem addressed was a foot ulcer	Qualitative; RCT and observational; 2 systematic reviews, 20 RCTs, 4 other controlled studies, 54 non-controlled studies	I: 1. Casting 2. Footwear 3. Surgical offloading 4. Other offloading techniques *C: any offloading technique or standard or care*	Ulcer prevention and the reduction of mechanical pressure	The evidence base to support the use of interventions that prevent a first foot ulcer and prevent or heal non-plantar foot ulcers or ischemic or infected ulcers is practically non-existent.

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I (Intervention)/C (*Comparators)*	Outcomes Assessed	Review Author Conclusions
Central Register of Controlled Trials, National Health Service Economic Evaluation Database, Health Technology Assessment Database); **LOW**					
Healy (2013)[25]; Inception – December 2012; (CINAHL, Medline and Cochrane); **LOW**	Participants had diabetes (type 1 or 2)	Qualitative; RCT and observational; 14 studies	I: Footwear *C: standard care or a control group*	Ulceration or reulceration	No research to date has examined the effectiveness of footwear in preventing ulceration and the effectiveness of footwear interventions to prevent reulceration is conflicting. Results from cross-sectional studies support the use of rocker sole footwear and custom orthoses in plantar pressure reduction; however, the effect of orthoses in ulceration prevention needs to be verified through longitudinal studies. Additionally, generic recommendations on these features are not possible as the optimal design will be patient specific. Conflicting results on the effectiveness of footwear in preventing ulcer relapse are present in the literature. In addition to providing information on ulceration rates, it would be beneficial if future studies provided information on the location of the ulcers. This would allow researchers to assess the relationship between the footwear intervention and the development of the ulcer.
Hunt (2011)[13]; Inception – September 2010;	People with diabetes, with and	Qualitative; RCT and observational; 50 SRs and RCTs	I: Interventions to prevent or treat foot	Ulcer development rates,	We don't know whether therapeutic footwear is more effective at reducing the incidence of foot

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I (Intervention)/C (*Comparators)*	Outcomes Assessed	Review Author Conclusions
(Medline, Embase and Cochrane); **HIGH**	without an ulcer	– 2 studies (1 RCT and 1 observational relevant to KQ2)	ulcers and amputations *C: usual footwear*	amputation rates, ulcer healing rate, infection rates, and adverse effects	ulcers after 1 to 2 years in people without severe foot deformity (low-quality evidence). Individuals with significant foot deformities (such as hammer toes or Charcot foot) should be considered for referral for assessment for customized shoes that can accommodate the altered foot anatomy. In the absence of significant deformities, high-quality well-fitting non-prescription footwear seems to be a reasonable option.
Paton (2011)[26]; Inception – 2008; (Medline and CINAHL); **LOW**	People with diabetes (type 1 or 2) with neuropathy	Qualitative; RCT and observational; 5 studies	I: footwear *C: standard of care or usual footwear*	Ulceration and time to ulceration	Insoles designed to prevent ulceration in the diabetic neuropathic foot appear to be of some value and should be considered within the prevention strategy for the diabetic neuropathic foot. Recommendation cannot be made at this time regarding the type and specification of insoles best suited for purpose. There is a need for further research investigating the following: 1) comparison of a range of insoles with differing mode of action 2) comparison of pre-fabricated and custom-made insoles 3) longevity of devices 4) economic evaluation of insoles 5) effectiveness of insoles specific to (neuropathic) foot pathology 6) patient perception of changes in foot health and quality of life. Within the limitations of the current evidence, insoles are effective in reducing ulceration rate and peak pressure in people with diabetes and neuropathy.

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I (Intervention)/C (*Comparators)*	Outcomes Assessed	Review Author Conclusions
Aard (2011)[30]; January 1, 1960 – April 30, 2010; (Medline and PubMed); **MODERATE**	Subjects deemed at risk of diabetic foot ulcers	Qualitative; RCTs and observational; 12 RCTs	I: Therapeutic shoes; insole inserts; shear-reducing insole *C: any*	Ulceration and recurrent ulceration	On the basis of our review, the evidence for most of the interventions to prevent a foot ulcer falls short. Although the data do not support the use of therapeutic shoes or vertical stress-reducing insoles, shear stress-reducing insoles seem more promising.
Bus (2008)[14]; Inception – May 1, 2006; (Medline, Embase, CINAHL, Cochrane, DARE, EED, and HTA); **LOW**	Patients with type 1 or 2 diabetes, with or without a foot ulcer	Qualitative; RCT and observational; 21 controlled, 108 uncontrolled/cross-sectional	I: 1. Casting techniques 2. Footwear-related techniques 3. Surgical offloading techniques 4. Other offloading techniques *C: any*	Ulcer prevention	No experimental studies exist on the role of footwear and offloading in primary ulcer prevention. There are indications that therapeutic shoes may be effective in secondary prevention compared to standard footwear, although one RCT has found no effect.
Singh (2005)[33]; January 1980 – April 2004; (EBSCO, MEDLINE, and National Guideline Clearinghouse); **HIGH**	Patients at risk for diabetic foot ulcer	Qualitative; RCT and observational; 165, 22 RCTs (4 studies related to KQ2)	I: Educational, clinical, custom footwear and orthotics, debridement, foot specialist and multidisciplinary team care, prophylactic foot surgeries *C: any*	Ulcer recurrence	The value of prescription footwear for ulcer prevention is unclear.
O'Meara (2000)[27]; Inception – December 1998; (19 databases including MEDLINE,	Patients with foot ulcers resulting from	Qualitative; RCT and observational; 39 trials, 2 economic evaluations	I: 1. Footwear 2. Hosiery 3. Education 4. Screening and foot protection program 5. Podiatry	The development and incidence of ulceration; ulcer	A second small trial showed a significant reduction in ulcer recurrence in patients wearing special shoes. There is weak evidence, from one trial of 69 patients, that molded footwear may influence ulcer

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I (Intervention)/C (*Comparators)*	Outcomes Assessed	Review Author Conclusions
CINAHL, British Diabetic Foot Association); **LOW**	diabetes mellitus		*C: any*	recurrence rate	recurrence at 12 months. …the research in the area of prevention and treatment of diabetic foot ulcers is extremely poor quality and relatively uninformative.
Mason (1999)[34]; 1983 – NR; (Cochrane, Medline, Embase, CINAHL, Psyclit, HealthStar, Science Citation Index, and Social Science Citation Index); **HIGH**	People with type 1 or 2 diabetes	Qualitative; RCT and observational; 2 RCTs	I: Screening, management, prevention or education relating to foot care of people with diabetes *C: any*	Ulceration, relapse	This remains a research issue where 'optimized' normal shoes could be usefully compared with special therapeutic footwear. Without consideration of this pragmatic alternative and confirmatory studies on larger patient numbers, the relative effectiveness and cost effectiveness of providing therapeutic shoes remains uncertain.
Steed (2006)[15]; NR; ((Previous guidelines, PubMed, Medline, Embase, Cochrane); **HIGH**	Patients with diabetes	Qualitative; RCT and observational; guideline 2.1 – 7 studies	I: Diagnosis, offloading, infection control, wound bed preparation, dressings, surgery, adjuvant agents (topical, device, systemic), and prevention recurrence *C: any*	Ulcer development	Guideline 2.1: Protective footwear should be prescribed in any patient at risk for amputation (significant arterial insufficiency, significant neuropathy, previous amputation, previous ulcer formation, preulcerative callus, foot deformity, evidence of callus formation). (Level II) Principle: The incidence of ulceration in diabetic patients at risk for ulceration can be reduced by using protective footwear *Level II: Less than Level I, but at least 1 RCT and at least 2 significant clinical series or expert opinion papers with literature reviews supporting the intervention.

DFU: diabetic foot ulcer; RCT: randomized controlled trial; TCC: total contact cast; RCW: removable cast walker

Supplemental Table 5. KQ2 Citation Matrix

Included Studies*	Crawford[51]	van Netten[22]	Alahakoon[28]
Bus SA, Waarjman R, Arts M et al (2013) Effect of custom-made footwear on foot ulcer recurrence in diabetes: a multicenter randomized controlled trial. Diabetes Care 36 (12): 4109-4116	X	X	X
Busche K, Chantelau E. Effectiveness of a brand of stock 'diabetic' shoes to protect against diabetic foot ulcer relapse. A prospective cohort study. Diabet Med. 2003 Aug; 20(8):665-669.		X	
Lavery LA, Lafontaine J, Higgins KR, Lanctot DR, Constantinides G (2012) Shear-reducing insoles to prevent foot ulceration in high-risk diabetic patients. Adv Skin Wound Care 25 (11): 519-524	X	X	X
Reiber GE, Smith DG, Wallace C et al (2002) Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. JAMA 287(19): 2552-2558	X	X	X
Reike H, Bruning A, Rischbieter E, Vogler F, Angelkort B. Recurrence of foot lesions in patients with diabetic foot syndrome: influence of custom-molded orthotic device. Diabetes Stoffwechsel. 1997;6: 107-113		X	
Rizzo L, Tedeshi A, Fallani E et al (2012) Custom-made orthosis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. Int J Low Extrem Wounds 11(1):59-64	X	X	X
Scire V, Leporati E, Teobaldi I, Nobili LA, Rizzo L, Piagessi A. Effectiveness and safety of using Podikon digital silicone padding in the primary prevention of neuropathic lesions in the forefoot of diabetic patients. J Am Podiatr Med Assoc. 2009 Jan – Feb; 99(1): 28-34.	X	X	
Uccioli L, Faglia E, Monticone G et al (1995) Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes Care 18 (10): 1376-1378	X	X	X
Ulbrecht JS, Hurley T, Mauger DT, Cavanagh PR (2014) Prevention of recurrent foot ulcers with plantar pressure-based in-shoe orthoses: the CareFUL prevention multicenter randomized controlled trial. Diabetes Care 37(7): 1982-1989.	X	X	X
Viswanathan V, Madhavan S, Gnanasundaram S, et al Effectiveness of different types of footwear insoles for the diabetic neuropathic foot: a follow-up study. Diabetes Care 2004 Feb; 27(2):474-477		X	
Lopez-Moral M, Lazaro-Martinez JL, Garcia-Morales E, Garcia-Alvarez Y, Alvaro-Afonso FJ, Molines-Barroso RJ. Clinical efficacy of therapeutic footwear with a rigid rocker sole in the prevention of recurrence in patients with diabetes mellitus and diabetic polyneuropathy: a randomized clinical trial. PLoS One 2019; 14:e0219537			X

*Studies grouped under therapeutic or offloading footwear by review authors

Supplemental Table 6. Characteristics and Results for Systematic Reviews Relevant to KQ3

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I/C	Outcomes Assessed	Overall Conclusions
Lazzarini (2020)[35]; July 29, 2014 - August 13, 2018; (PubMed, EMBASE, Cochrane Library); **LOW**	Patients with a DFU, defined as any full thickness lesion below the malleoli associated with peripheral neuropathy and/or peripheral artery disease in people with diabetes.	Qualitative; RCT and observational; 126 studies	I: any intervention undertaken with the intention of relieving mechanical stress from a specific region of the foot. *C: any*	Healed DFU	Nonremovable knee-high offloading devices are more effective than removable offloading devices to heal the DFU – HIGH* Removable knee-high offloading devices and removable ankle-high offloading devices are equally effective to heal the DFU – MODERATE* Therapeutic footwear is less effective than non-removable knee-high offloading devices to health the DFU – MODERATE* Removable knee-high walkers seem to be more cost-effective than therapeutic footwear in healing the DFU. -Low* Custom-made light-weight fiberglass heel cast in addition to usual care seems to be equally cost effective as using usual care alone in patients with a neuropathic rearfoot DFU. – Low* * Use of GRADE to determine low, moderate, or high certainty.
Healy (2018)[38]; Inception - September 27, 2015; (Web of Science, Medline, Pubmed, CINAHL Plus, EMBASE,	Adults with physical impairments, limb loss, functional limitations or deformities in limb or spine	Qualitative; RCT only; 346 (15 related to DFU)	I: Prosthesis: externally applied device used to replace wholly, or in part, an absent limb or deficient limb segment *C: non-provision of prosthetics or orthotics, provision of*	Disability adjusted life years (DALY)/quality-adjusted life years (QALY); better health outcomes (functioning	When it comes to treating active ulceration, total contact casts showed superior results in most of the RCTs. Our findings are in line with previous research in this area.

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I/C	Outcomes Assessed	Overall Conclusions
SCOPUS, Rehabdata, PsycInfo, ERIC, Education Research Complete, Business Source Complete, IEEE, NIHR, and CEA registry); **LOW**			*prosthetic or orthotic, provision of a non-prosthetic or non-orthotic*	and quality of life);	
Health Quality Ontario_Costa (2017)[39]; Inception - August 17, 2016 (Medline, embase, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Health Technology Assessment, National Health Service Economic Evaluation Database, and Database of Abstracts of Reviews of	Patients with type 1 or 2 diabetes who had neuropathic infected or noninfected foot ulcers	Quantitative; RCTs only; 13 studies	I: Fiberglass total contact casting *C: other offloading devices: total contact casting prepared using materials other than fiberglass, therapeutic shoes, custom braces, or ankle and foot orthoses non-offloading ulcer treatments (ulcer dressings)*	Ulcer healing time to ulcer healing	Total contact casting versus therapeutic shoes, percentage of healed ulcers Risk difference Mantel Haenszel fix effects [95%CI] 0.25 [0.04, 0.46] Risk Ratio Mantel Haenszel Random [95%CI] 1.62 [1.11, 2.38] Our meta-analysis showed a statistically significant improvement in ulcer healing with total contact casting compared with therapeutic shoes within 1 to 4 months of follow-up. GRADE for evidence profile for total contact casting versus therapeutic shoes: Moderate for percentage of patients with a healed ulcer Moderate for time to healing Removable cast walkers versus therapeutic shoes, percentage of healed ulcers

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I/C	Outcomes Assessed	Overall Conclusions
Effects, CINAHL); **MODERATE**					Risk difference Mantel Haenszel fix effects [95%CI] -0.13 [-0.31, 0.06] Risk Ratio Mantel Haenszel Random [95%CI] 0.75 [0.48, 1.16] At 3 months of follow-up, the percentage of patients with a healed ulcer in each study was 22% and 52% with removable cast walkers, and 44% and 56% with therapeutic shoes. GRADE evidence profile for cast walkers versus therapeutic shoes Very low for percentage patients with a healed ulcer Very low for time to healing
Elraiyah (2016)[37]; Inception – October 2011; (Medline, Embase, Cochrane, and Scopus); **LOW**	Patients with diabetic foot ulcers	Quantitative; RCT and observational; 19 studies	I: Off loading methods *C: any other offloading method*	Rate of complete wound healing, time to complete wound healing, amputation	Although based on low-quality evidence (*ie*, evidence warranting lower certainty), benefits are demonstrated for use of total contact casting and irremovable cast walkers in the treatment of diabetic foot ulcers. Reduced relapse rate is demonstrated with various therapeutic shoes and insoles in comparison with regular footwear. Therapeutic shoes and insoles versus regular footwear, relapse. Risk ratio = .34 [0.15, 0.79] p = 0.012
Bus (2015)[12]; May 1, 2006 – July 29, 2014 (PubMed, EMBASE,	Patients with diabetes mellitus type 1 or 2, and clinical	Qualitative; RCT and observational; 2 systematic reviews, 20	I: 1. Casting 2. Footwear 3. Surgical offloading 4. Other offloading techniques	Ulcer prevention and the reduction of	The evidence base to support the use of interventions that prevent a first foot ulcer and prevent or heal nonplantar foot ulcers or ischemic or infected ulcers is practically non-existent.

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I/C	Outcomes Assessed	Overall Conclusions
CINAHL, Cochrane, Database of Abstracts of Review of Effect, Central Register of Controlled Trials, National Health Service Economic Evaluation Database, Health Technology Assessment Database); **LOW**	problem addressed was a foot ulcer.	RCTs, 4 other controlled studies, 54 non-controlled studies	*C: any offloading technique or standard or care*	mechanical pressure	
Healy (2014)[36]; Inception – January 13, 2014; (CINAHL, Medline, and Cochrane); **LOW**	Participants had diabetes (type 1 or 2) and a current foot ulcer	Qualitative; RCT and observational; 17 studies	I: Footwear or a removable offloading device *C: another treatment, irremovable device, or repeated measure of a minimum 2 types of footwear or removable offloading device*	Clinical assessment (ulcer healing rates/times or ulcer size)	From research to date in this area it is not possible to make strong conclusions on which footwear or removable offloading device is most effective for ulcer treatment; this is due to the lack of RCT studies conducted in this area. While further structured research with appropriately designed RCTs is needed, it appears that with regards to the use of footwear alone in the treatment of diabetic neuropathic ulcerations, currently available therapeutic shoes are the least effective intervention. This was followed by half or heel relief shoes with removable cast walkers found to be the most effective of the removable offloading devices.
Snyder (2014)[40]; NR; (PubMed); **HIGH**	Patients with diabetes	Qualitative; RCT and observational; consensus	I: Offloading device or technique *C: other offloading device or technique*	DFU healing	Consensus statement 2: Adequate offloading increases the likelihood of DFU healing (moderate/strong)

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I/C	Outcomes Assessed	Overall Conclusions
		statement 2: 26 (4 SRs, 8 RCTs, 14 observational)			Evidence is clear that adequate offloading increases the likelihood of DFU healing and that increased clinician use of effective offloading is necessary. Consensus statement 6: The likelihood of DFU healing is increased with offloading adherence (moderate/strong). The likelihood of DFU healing is increased with offloading adherence, and current evidence favors the use of nonremovable casts or fixed ankle walking braces as optimum offloading modalities.
Hunt (2011)[13]; Inception to September 2010 (Medline, Embase, Cochrane Library); **HIGH**	Adults with diabetes, with and without an ulcer	Qualitative; RCT and observational; 50 SRs and RCTs (2 studies (1 RCT and 1 observational related to KQ2))	I: Interventions to prevent or treat foot ulcers and amputations *C: any*	Ulcer healing rate	Felted foam padding applied to the skin compared with being inserted into footwear - felted foam padding applied to the skin and padding inserted into footwear seem equally effective at promoting ulcer healing.
Bus (2008)[14]; Inception to May 2006 (Medline, Embase, CINAHL, Cochrane, DARE, EED, and HTA); **LOW**	Adults with type 1 or 2 diabetes, with or without a foot ulcer	Qualitative; RCT and observational; 21 controlled, 108 uncontrolled/ cross-sectional	I: 1. Casting techniques 2. Footwear-related techniques 3.Surgical offloading techniques 4. Other offloading techniques *C: any*	Ulcer healing	There is a fairly strong evidence base showing that total contact casts heal a higher proportion of neuropathic plantar ulcers at a faster rate than other, mainly removable, offloading modalities. On the basis of the available evidence, therapeutic footwear does not appear suitable for ulcer treatment since other offloading modalities such as total contact casts are more effective.
Steed (2006)[15]; NR; (Previous guidelines,	Patients with diabetes	Qualitative; RCT and observational;	I: Diagnosis, offloading, infection control, wound bed	Healing, re-ulceration	Guideline 2.2: Acceptable methods of offloading include crutches, walkers, wheelchairs, custom shoes, depth shoes, shoe modifications, custom

Author (year); Search Dates (sources); ROBIS Rating	Population	Synthesis Method; Included Study Design; Number of Studies	I/C	Outcomes Assessed	Overall Conclusions
PubMed, Medline, Embase, Cochrane); **HIGH**		guideline 2.2 – 8 studies	preparation, dressings, surgery, adjuvant agents (topical, device, systemic), and prevention recurrence *C: any*		inserts, custom relief orthotic walkers (CROW), diabetic boots, forefoot and heel relief shoes, and total contact casts. (LEVEL I*) Principle: relieving pressure on the diabetic wound is necessary to maximize healing potential. *Level I: Meta-analysis of multiple RCTs or at least two RCTs supporting the intervention of the guideline.

DFU: diabetic foot ulcer; RCT: randomized controlled trial; TCC: total contact cast; RCW: removable cast walker

Supplemental Table 7. KQ3 Citation Matrix

Included Studies*	Lazzarini[51]	Healy[22]
Armstrong DG, van Schie CHM, Nguyen HC, Boulton AJM, Lavery LA, Harkless LB. Off-loading the diabetic foot wound – a randomized clinical trial. Diabetes Care. 2001; 24(6):1019-1022	X	X
Armstrong DG, Lavery LA, Wu S, Boulton AJM. Evaluation of removable and irremovable cast walkers in the healing of diabetic foot wounds – a randomized controlled trial. Diabetes Care. 2005;28(3):551-554	X	X
Armstrong DG, Lavery LA, Wrobel JS, Vileikyte L. Quality of life in healing diabetic wounds: does the end justify the means? Journal of Foot & Ankle Surgery. 2008;47(4):278-82		X
Burns J, Wegener C, Begg L, Vicaretti M, Fletcher J. Randomized trial of custom orthoses and footwear on foot pain and plantar pressure in diabetic peripheral arterial disease. Diabetic Medicine. 2009; 26(9):893-9		X
Bus SA, Waaijman R, Arts M, de Haart M, Busch-Westbroek T, van Baal J, et al. Effect of custom-made footwear on foot ulcer recurrence in diabetes: a multicenter randomized controlled trial. Diabetes Care. 2013; 36(12):4109-16.		X
Bus SA, JJv N, Kottink AIR, et al. The efficacy of removable devices to offload and heal neuropathic plantar forefoot ulcers in people with diabetes: a single-blinded multicentre randomized controlled trial. Int Wound J. 2018; 15(1): 65-74	X	
Caravaggi C, Faglia E, DeGiglio R, et al. Effectiveness and safety of a non-removable fiberglass off-bearing cast versus a therapeutic shoe in the treatment of neuropathic foot ulcers: a randomized study. Diabetes Care. 2000;23(12):1746-1751	X	X
Caravaggi C, Sgnazaroli A, Fabbi M, et al. Nonwindowed non-removable fiberglass off-loading cast versus removable pneumatic cast (AircastXP diabetic walker) in the treatment of neuropathic noninfected plantar ulcers. Diabetes Care. 2007;30(10):2577-2578	X	
Chakraborty PP, Ray S, Biswas D, et al. A comparative study between total contact cast and pressure-relieving ankle foot orthosis in diabetic neuropathic foot ulcers. J Diabetes Sci Technol. 2015; 9(2):302-308.	X	
Dallimore SM, Kaminski MR. Tendon lengthening and fascia release for healing and preventing diabetic foot ulcers: a systematic review and meta-analysis. J Foot Ankle Res. 2015;8:33.	X	
Elraiyah T, Prutsky G, Domecq JP, et al. A systematic review and meta-analysis of off-loading methods for diabetic foot ulcers. J Vasc Surg. 2016;63(2):59S-68S e1-2.	X	
Faglia E, Caravaggi C, Clerici G, et al. Effectiveness of removable cast versus non-removable fiberglass off-bearing cast in the healing of diabetic plantar foot ulcer a randomized controlled trial. Diabetes Care. 2010; 33(7):1419-1423	X	X
Ganguly S, Chakraborty K, Mandal PK, et al. A comparative study between total contact casting and conventional dressings in the non-surgical management of diabetic plantar foot ulcers. J Indian Med Assoc 2008; 106(4):237-239, 244.	X	

Included Studies*	Lazzarini[51]	Healy[22]
Gutekunst DJ, Hastings MK, Bohnert KL, Strube MJ, Sinacore DR. Removable cast walker boots yield greater forefoot off-loading than total contact casts. Clin Biomech (Bristol, Avon). 2011;26(6):649-654	X	
Health Quality Ontario. Fibreglass total contact casting, removable cast walkers, and irremovable cast walkers to treat diabetic neuropathic foot ulcers: a health technology assessment. Ont Health Technol Assess Ser. 2017; 17(12):1-124	x	
Jeffcoate W, Game F, Turtle-Savage V, et al. Evaluation of the effectiveness and cost-effectiveness of lightweight fiberglass heel casts in the management of ulcers of the heel in diabetes: a randomize controlled trial. Health Technol Assess. 2017; 21(34): 1-92	X	
Johnson DJ, Saar BJ, Shevitz AJ, et al. A Total offloading foot brace for the treatment of diabetic foot ulcers: results from a halted randomized controlled trial. Wounds 2018;30(7):182-185	X	
Katz IA, Harlan A, Miranda-Palma B, et al. A randomized trial of two irremovable off-loading devices in the management of plantar neuropathic diabetic foot ulcers. Diabetes Care. 2005;28(3):555-559	X	
Lavery LA, Higgins KR, La Fontaine J, Zamorano RG, Constantinides GP, Kim PJ. Randomised clinical trial to compare total contact casts, healing sandals and a shear-reducing removable boot to heal diabetic foot ulcers. Int Wound J. 2015; 12(6):710-715	X	
Lewis J, Lipp A. Pressure-relieving interventions for treating diabetic foot ulcers. Cochrane Database Syst Rev. 2013;1:CD002302	X	
Martins de Oliveira AL, Moore Z. Treatment of the diabetic foot by offloading: a systematic review. J Wound Care 2015; 24(12):560, 562-570	X	
Miyan Z, Ahmed J, Zaidi SI, Ahmedani MY, Fawwad A, Basit A. Use of locally made off-loading techniques for diabetic plantar foot ulcer in Karachi, Pakistan. Int Wound J. 2014; 11(6):691-695	X	X
Morona JK, Buckley ES, Jones S, Reddin EA, Merlin TL. Comparison of the clinical effectiveness of different off-loading devices for the treatment of neuropathic foot ulcers in patients with diabetes: a systematic review and meta-analysis. Diabetes Metab Res Rev. 2013; 39(3):183-193.	X	
Mueller MJ, Diamond JE, Sinacore DR, et al. Total contact casting in treatment of diabetic plantar ulcers. Controlled clinical trial. Diabetes Care. 1989; 12(6):384-388.	X	
Najafi B, Grewal GS, Bharara M, Menzies R, Talal TK, Armstrong DG. Can't stand the pressure: the association between unprotected standing, walking, and wound healing in people with diabetes. J Diabetes Sci Technol. 2017; 11(4):657-667.	X	
Nube VL, Molyneaux L, Bolton T, Clingan T, Palmer E, Yue DK. The use of felt deflective padding in the management of plantar hallux and forefoot ulcers in patients with diabetes. The foot. 2006;16(1):38-43	X	
Paton JS, Stenhouse EA, Bruce G, Zahra D, Jones RB. A comparison of customized and prefabricated insoles to reduce risk factors for neuropathic diabetic foot ulceration: a participant-blinded randomized controlled trial. J. 2012;5(1):31		X

Included Studies*	Lazzarini[51]	Healy[22]
Piaggesi A, Macchiarini S, Rizzo L, et al. An off-the-shelf instant contact casting device for the management of diabetic foot ulcers – a randomized prospective trial versus traditional fiberglass cast. Diabetes Care. 2007;30(3):586-590	X	
Piaggesi A, Goretti C, Iacopi E, et al. Comparison of removable and irremovable walking boot to total contact casting in offloading the neuropathic diabetic foot ulceration. Foot Ankle Int 2016;37(8):855-861	X	
Reiber GE, Smith DG, Wallace C, Sullivan K, Hayes S, Vath C, et al. Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. JAMA: Journal of the American Medical Association. 2002;287(19):2552.		X
Rizzo L, Tedeshchi A, Fallani E, Coppelli A, Vallini V, Iacopi E, et al. Custom-made orthesis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. Int. 2012; 11(1)59-64.		X
Scire V, Leporati E, Teobaldi I, Nobili LA, Rizzo L, Piaggesi A. Effectiveness and safety of using podikon digital silicone padding in the primary prevention of neuropathic lesions in the forefoot of diabetic patients. Journal of the American Podiatric Medical Association. 2009; 99(1):28-34.		X
Uccioli L, Faglia E, Monticone G, Favales F, Durola L, Aldeghi A, et al. Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes Care. 1995; 18(10):1376-8.		X
Ulbrecht JS, Hurley T, Mauger DT, Cavanagh PR. Prevention of recurrent foot ulcers with plantar pressure-based in-shoe orthoses: the CareFUL prevention multicenter randomized controlled trial. Diabetes Care. 2014; 37(7):1982-9.		X
Van de Weg FB, Van Der Windt DA, Vahl AC. Wound healing: total contact cast vs. custom-made temporary footwear for patients with diabetic foot ulceration. Prosthet Orthot Int. 2008;32(1):3-11.	X	X
Zimny S, Schatz H, Pfohl U. The effects of applied felted foam on wound healing and healing times in the therapy of neuropathic diabetic foot ulcers. Diabet Med. 2003;20(8):622-625.	X	