Appendixes

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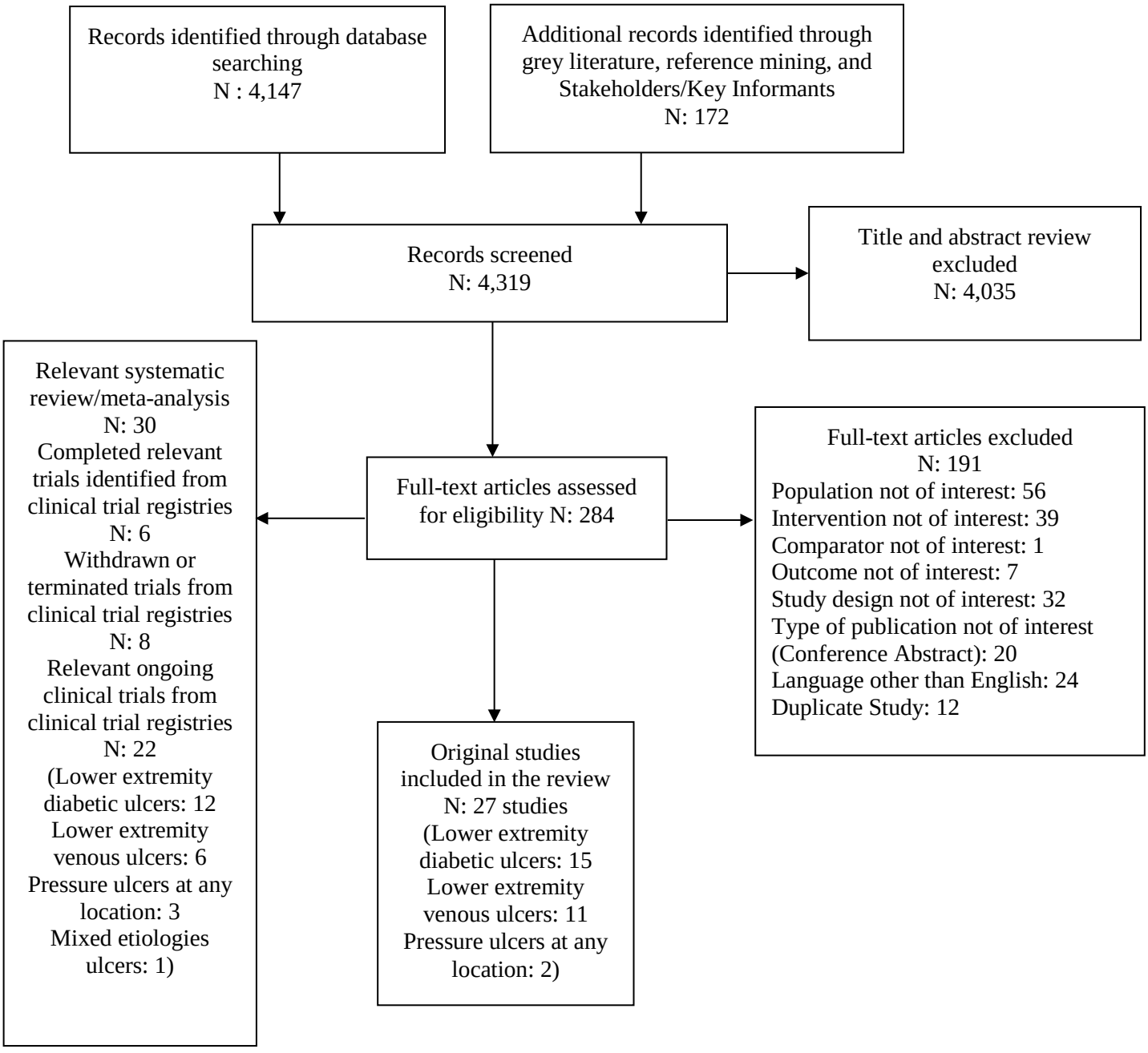
Appendix A Flow Chart

Figure A.1. Flow chart



Appendix B. Search Strategy

Ovid

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials May 2020, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to June 11, 2020, Embase 1974 to 2020 June 11, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to June 11, 2020
Search Strategy:

#	Searches
1	exp Diabetic Foot/
2	exp Pressure Ulcer/
3	exp Varicose Ulcer/
4	(bedsore* or decubiti or decubitus or "diabetic feet" or "diabetic foot" or injur* or sore or sores or trauma* or ulcer* or wound or wounds).ti,ab,hw,kw.
5	1 or 2 or 3 or 4
6	exp Platelet-Rich Plasma/
7	("autologous platelet-rich gel" or "autologous platelet-rich plasma" or becaplermin or "leukocyte-PRF" or "l-prf" or "platelet gel" or "platelet releasate" or "platelet-rich fibrin" or "platelet-rich plasma" or "P-PRF" or PRP or "pure PRF" or "thrombocyte rich plasma" or "thrombocyte-rich fibrin").ti,ab,hw,kw.
8	6 or 7
9	5 and 8
10	exp evidence based medicine/
11	exp meta analysis/
12	exp Meta-Analysis as Topic/
13	exp "systematic review"/
14	exp Guideline/ or exp Practice Guideline/
15	exp controlled study/
16	exp Randomized Controlled Trial/
17	exp triple blind procedure/
18	exp Double-Blind Method/
19	exp Single-Blind Method/
20	exp latin square design/
21	exp Placebos/
22	exp Placebo Effect/
23	exp comparative study/
24	exp intervention studies/
25	exp Cross-Sectional Studies/
26	exp Cross-Over Studies/
27	exp Cohort Studies/
28	exp longitudinal study/
29	exp retrospective study/
30	exp prospective study/
31	exp clinical trial/
32	clinical study/

33 exp case-control studies/
34 exp confidence interval/
35 exp multivariate analysis/
36 ((evidence adj based) or (meta adj analys*) or metaanalys* or (systematic* adj3 review*) or guideline* or (control* adj3 study) or (control* adj3 trial) or (randomized adj3 study) or (randomized adj3 trial) or (randomised adj3 study) or (randomised adj3 trial) or "pragmatic clinical trial" or (random* adj1 allocat*) or (doubl* adj blind*) or (doubl* adj mask*) or (singl* adj blind*) or (singl* adj mask*) or (tripl* adj blind*) or (tripl* adj mask*) or (trebl* adj blind*) or (trebl* adj mask*) or "latin square" or placebo* or nocebo* or multivariate or "comparative study" or "comparative survey" or "comparative analysis" or (intervention* adj2 study) or (intervention* adj2 trial) or "cross-sectional study" or "cross-sectional analysis" or "cross-sectional survey" or "cross-sectional design" or "prevalence study" or "prevalence analysis" or "prevalence survey" or "disease frequency study" or "disease frequency analysis" or "disease frequency survey" or crossover or "cross-over" or cohort* or "longitudinal study" or "longitudinal survey" or "longitudinal analysis" or "longitudinal evaluation" or longitudinal* or ((retrospective or "ex post facto") adj3 (study or survey or analysis or design)) or retrospectiv* or "prospective study" or "prospective survey" or "prospective analysis" or prospectiv* or "concurrent study" or "concurrent survey" or "concurrent analysis" or (("follow-up" or followup) adj (stud* or survey or analysis)) or ((observation or observational) adj (study or survey or analysis)) or "clinical study" or "clinical trial" or (("phase 0" or "phase 1" or "phase I" or "phase 2" or "phase II" or "phase 3" or "phase III" or "phase 4" or "phase IV") adj5 (trial or study)) or "evaluation study" or "evaluation survey" or "evaluation analysis" or "quasi experimental study" or "quasi experimental analysis" or "quasiexperimental study" or "quasiexperimental analysis" or "case control study" or "case base study" or "case referrent study" or "case referent study" or "case referent study" or "case compeer study" or "case comparison study" or "matched case control" or "multicenter study" or "multi-center study" or study or trial or pilot or "odds ratio" or "confidence interval" or "change analysis" or ((study or trial or random* or control*) and compar*)).mp,pt.
37 or/10-36
38 9 and 37
39 limit 38 to ("all adult (19 plus years)" or "young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)") [Limit not valid in CCTR,CDSR,Embase; records were retained]
40 limit 39 to (adult <18 to 64 years> or aged <65+ years>) [Limit not valid in CCTR,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]
41 limit 38 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)" or "newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)") [Limit not valid in CCTR,CDSR,Embase; records were retained]
42 limit 41 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>) [Limit not valid in CCTR,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]
43 42 not 40

44 38 not 43
45 (exp animals/ or exp nonhuman/) not exp humans/
46 ((alpaca or alpacas or amphibian or amphibians or animal or animals or antelope or armadillo or armadillos or avian or baboon or baboons or beagle or beagles or bee or bees or bird or birds or bison or bovine or buffalo or buffaloes or buffalos or "c elegans" or "Caenorhabditis elegans" or camel or camels or canine or canines or carp or cats or cattle or chick or chicken or chickens or chicks or chimp or chimpanze or chimpanzees or chimps or cow or cows or "D melanogaster" or "dairy calf" or "dairy calves" or deer or dog or dogs or donkey or donkeys or drosophila or "Drosophila melanogaster" or duck or duckling or ducklings or ducks or equid or equids or equine or equines or feline or felines or ferret or ferrets or finch or finches or fish or flatworm or flatworms or fox or foxes or frog or frogs or "fruit flies" or "fruit fly" or "G mellonella" or "Galleria mellonella" or geese or gerbil or gerbils or goat or goats or goose or gorilla or gorillas or hamster or hamsters or hare or hares or heifer or heifers or horse or horses or insect or insects or jellyfish or kangaroo or kangaroos or kitten or kittens or lagomorph or lagomorphs or lamb or lambs or llama or llamas or macaque or macaques or macaw or macaws or marmoset or marmosets or mice or minipig or minipigs or mink or minks or monkey or monkeys or mouse or mule or mules or nematode or nematodes or octopus or octopuses or orangutan or "orang-utan" or orangutans or "orang-utans" or oxen or parrot or parrots or pig or pigeon or pigeons or piglet or piglets or pigs or porcine or primate or primates or quail or rabbit or rabbits or rat or rats or reptile or reptiles or rodent or rodents or ruminant or ruminants or salmon or sheep or shrimp or slug or slugs or swine or tamarin or tamarins or toad or toads or trout or urchin or urchins or vole or voles or waxworm or waxworms or worm or worms or xenopus or "zebra fish" or zebrafish) not (human or humans or patient or patients)).ti,ab,hw,kw.
47 44 not (45 or 46)
48 limit 47 to (editorial or erratum or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in CCTR,CDSR,Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]
49 from 48 keep 2-7
50 (47 not 48) or 49
51 remove duplicates from 50

Scopus

1 TITLE-ABS-KEY(bedsore* OR decubiti OR decubitus OR "diabetic feet" OR "diabetic foot" OR injur* OR sore OR sores OR trauma* OR ulcer* OR wound OR wounds)
2 TITLE-ABS-KEY("autologous platelet-rich gel" OR "autologous platelet-rich plasma" OR becaplermin OR "leukocyte-PRF" OR "l-prf" OR "platelet gel" OR "platelet releasate" OR "platelet-rich fibrin" OR "platelet-rich plasma" OR "P-PRF" OR PRP OR "pure PRF" OR "thrombocyte rich plasma" OR "thrombocyte-rich fibrin")
3 TITLE-ABS-KEY((evidence W/1 based) OR (meta W/1 analys*) OR metaanalys* OR (systematic* W/3 review*) OR guideline* OR (control* W/3 study) OR (control* W/3 trial) OR (randomized W/3 study) OR (randomized W/3 trial) OR (randomised W/3 study) OR

(randomised W/3 trial) OR "pragmatic clinical trial" OR (random* W/1 allocat*) OR (doubl* W/1 blind*) OR (doubl* W/1 mask*) OR (singl* W/1 blind*) OR (singl* W/1 mask*) OR (tripl* W/1 blind*) OR (tripl* W/1 mask*) OR (trebl* W/1 blind*) OR (trebl* W/1 mask*) OR "latin square" OR placebo* OR nocebo* OR multivariate OR "comparative study" OR "comparative survey" OR "comparative analysis" OR (intervention* W/2 study) OR (intervention* W/2 trial) OR "cross-sectional study" OR "cross-sectional analysis" OR "cross-sectional survey" OR "cross-sectional design" OR "prevalence study" OR "prevalence analysis" OR "prevalence survey" OR "disease frequency study" OR "disease frequency analysis" OR "disease frequency survey" OR crossover OR "cross-over" OR cohort* OR "longitudinal study" OR "longitudinal survey" OR "longitudinal analysis" OR "longitudinal evaluation" OR longitudinal* OR ((retrospective OR "ex post facto") W/3 (study OR survey OR analysis OR design)) OR retrospectiv* OR "prospective study" OR "prospective survey" OR "prospective analysis" OR prospectiv* OR "concurrent study" OR "concurrent survey" OR "concurrent analysis" OR (("follow-up" or followup) W/1 (stud* or survey or analysis)) OR ((observation or observational) W/1 (study or survey or analysis)) OR "clinical study" OR "clinical trial" OR (("phase 0" or "phase 1" or "phase I" or "phase 2" or "phase II" or "phase 3" or "phase III" or "phase 4" or "phase IV") W/5 (trial or study)) OR "evaluation study" OR "evaluation survey" OR "evaluation analysis" OR "quasi experimental study" OR "quasi experimental analysis" OR "quasiexperimental study" OR "quasiexperimental analysis" OR "case control study" OR "case base study" OR "case referrent study" OR "case referent study" OR "case referent study" OR "case compeer study" OR "case comparison study" OR "matched case control" OR "multicenter study" OR "multi-center study" OR study OR trial OR pilot OR "odds ratio" OR "confidence interval" OR "change analysis" OR ((study OR trial OR random* OR control*) AND compar*))

4 1 and 2 and 3

5 TITLE-ABS-KEY(newborn* or neonat* or infant* or toddler* or child* or adolescent* or paediatric* or pediatric* or girl or girls or boy or boys or teen or teens or teenager* or preschooler* or "pre-schooler*" or preteen or preteens or "pre-teen" or "pre-teens" or youth or youths) AND NOT TITLE-ABS-KEY(adult or adults or "middle age" or "middle aged" OR elderly OR geriatric* OR "old people" OR "old person*" OR "older people" OR "older person*" OR "very old")

6 4 and not 5

7 TITLE-ABS-KEY((alpaca OR alpacas OR amphibian OR amphibians OR animal OR animals OR antelope OR armadillo OR armadillos OR avian OR baboon OR baboons OR beagle OR beagles OR bee OR bees OR bird OR birds OR bison OR bovine OR buffalo OR buffaloes OR buffalos OR "c elegans" OR "Caenorhabditis elegans" OR camel OR camels OR canine OR canines OR carp OR cats OR cattle OR chick OR chicken OR chickens OR chicks OR chimp OR chimpanze OR chimpanzees OR chimps OR cow OR cows OR "D melanogaster" OR "dairy calf" OR "dairy calves" OR deer OR dog OR dogs OR donkey OR donkeys OR drosophila OR "Drosophila melanogaster" OR duck OR duckling OR ducklings OR ducks OR equid OR equids OR equine OR equines OR feline OR felines OR ferret OR ferrets OR finch OR finches OR fish OR flatworm OR flatworms OR fox OR foxes OR frog OR frogs OR "fruit flies" OR "fruit fly" OR "G mellonella" OR "Galleria mellonella" OR geese OR gerbil OR gerbils OR goat OR goats OR goose OR gorilla OR gorillas OR hamster OR hamsters OR hare OR hares OR heifer OR heifers OR horse OR horses OR insect OR insects OR jellyfish OR kangaroo OR kangaroos OR kitten OR kittens OR lagomorph OR lagomorphs OR lamb OR lambs OR llama OR llamas OR macaque OR macaques OR macaw OR macaws OR marmoset OR marmosets OR mice OR

minipig OR minipigs OR mink OR minks OR monkey OR monkeys OR mouse OR mule OR mules OR nematode OR nematodes OR octopus OR octopuses OR orangutan OR "orang-utan" OR orangutans OR "orang-utans" OR oxen OR parrot OR parrots OR pig OR pigeon OR pigeons OR piglet OR piglets OR pigs OR porcine OR primate OR primates OR quail OR rabbit OR rabbits OR rat OR rats OR reptile OR reptiles OR rodent OR rodents OR ruminant OR ruminants OR salmon OR sheep OR shrimp OR slug OR slugs OR swine OR tamarin OR tamarins OR toad OR toads OR trout OR urchin OR urchins OR vole OR voles OR waxworm OR waxworms OR worm OR worms OR xenopus OR "zebra fish" OR zebrafish) AND NOT (human OR humans or patient or patients))
8 6 and not 7
9 DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
10 8 and not 9
11 INDEX(embase) OR INDEX(medline) OR PMID(0* OR 1* OR 2* OR 3* OR 4* OR 5* OR 6* OR 7* OR 8* OR 9*)
12 10 and not 111

ClinicalTrials.gov

Condition or disease
"bed sore" OR "bed sores" OR bedsore OR bedsore* OR bedsores OR decubital OR decubiti OR decubitus OR decubus OR diabetes OR diabetic OR "diabetic feet" OR "diabetic foot" OR feet OR foot OR injur* OR leg OR legs OR pressure OR sore OR sores

Other terms
"autologous platelet-rich gel" OR "autologous platelet-rich plasma" OR becaplermin OR "leukocyte-PRF" OR "l-prf" OR "platelet gel" OR "platelet releasate" OR "platelet-rich fibrin" OR "platelet-rich plasma" OR "P-PRF" OR PRP OR "pure PRF"

Limited to adults

Condition or disease
"bed sore" OR "bed sores" OR bedsore OR bedsore* OR bedsores OR decubital OR decubiti OR decubitus OR decubus OR diabetes OR diabetic OR "diabetic feet" OR "diabetic foot" OR feet OR foot OR injur* OR leg OR legs OR pressure OR sore OR sores

Other terms
"thrombocyte rich plasma" OR "thrombocyte-rich fibrin"

Limited to adults

Condition or disease
stasis OR trauma* OR ulcer* OR varicose OR vein OR veins OR venous OR wound OR wounds

Other terms

"autologous platelet-rich gel" OR "autologous platelet-rich plasma" OR becaplermin OR "leukocyte-PRF" OR "l-prf" OR "platelet gel" OR "platelet releasate" OR "platelet-rich fibrin" OR "platelet-rich plasma" OR "P-PRF" OR PRP OR "pure PRF"

Limited to adults

Condition or disease
stasis OR trauma* OR ulcer* OR varicose OR vein OR veins OR venous OR wound OR wounds

Other terms
"thrombocyte rich plasma" OR "thrombocyte-rich fibrin"

Limited to adults

Appendix C. Excluded Studies

1. 1st Conference of the Lymphological Section of the Polish Phlebological Society. Acta Angiologica Conference: 1st Conference of the Lymphological Section of the Polish Phlebological Society Poland. 2016;22(2). PMID: 614023567.[Type of publication: Conference Abstract]

2. A Randomized Trial on Platelet Rich Plasma Versus Saline Dressing of Diabetic Foot Ulcers. https://clinicaltrialsgov/show/NCT04090008. 2019. PMID: CN-01975733.[Duplicate]

3. Achkasov EE, Ul'ianov AA, Bezuglov EN, et al. [Autoplasma enriched with platelet derived growth factor in surgery and traumatology]. [Russian]. Khirurgiia. 2014(9):48-54. PMID: 603420525.[Foreign language]

4. Acr Biologics LLC. Effectiveness of Autologous Platelet Rich Plasma in the Treatment of Chronic Non-Healing Wounds. 2015 August. PMID: NCT02307448.[Duplicate]

5. Agrawal RP, Jhajharia A, Mohta N, et al. Use of a platelet-derived growth factor gel in chronic diabetic foot ulcers. The Diabetic Foot. 2009;12(2):80-8.[Intervention not of interest]

6. Alfano C, Angelisanti M, Calzoni C, et al. [Treatment of ulcer and difficult wounds of the lower limbs: our experience]. Ann Ital Chir. 2012 Mar-Apr;83(2):135-41. PMID: 22462334.[Foreign language]

7. Amato B, Farina MA, Campisi S, et al. CGF Treatment of Leg Ulcers: a Randomized Controlled Trial. Open Med (Wars). 2019;14:959-67. PMID: 31934641.[Intervention not of interest]

8. Amery CM. Growth factors and the management of the diabetic foot. Diabetic Medicine. 2005 January;22(SUPPL. 1):12-4. PMID: 44933438.[Study design]

9. Aminian B, Shams M, Omrani GR, et al. Topical autologous platelet-derived growth factors in the treatment of chronic diabetic ulcers. 2000.[Population not of interest]

10. Amirzade-Iranaq MH, Masoumi SMR. Autologous platelet rich plasma effect on wound healing: A systematic review and meta-analysis. Iranian Journal of Biotechnology. 2017;ISSUE):124. PMID: 617813646.[Type of publication: Conference Abstract]

11. Anitua E, Aguirre JJ, Algorta J, et al. Effectiveness of autologous preparation rich in growth factors for the treatment of chronic cutaneous ulcers. Journal of biomedical materials research Part B, Applied biomaterials. 2008 Feb;84(2):415-21. doi: 10.1002/jbm.b.30886. PMID: 17595032.[Population not of interest]

12. Assessing the Effect of PRP (Platelet Rich Plasma) Injection in Healing of Diabetic Foot Ulcer. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=IRCT2015021519037N5. 2015. PMID: CN-01844723.[Outcomes not of interest]

13. Assiut U. Perineural Platelet-rich Plasma for Diabetic Neuropathy Pain. 2017 February 1. PMID:

NCT03601494.[Population not of interest]

14. Atri SC, Misra J, Bisht D, et al. Use of homologous platelet factors in achieving total healing of recalcitrant skin ulcers. Surgery. 1990 Sep;108(3):508-12. PMID: 2396195.[Population not of interest]

15. Autologous Platelet-Rich Gel for the Treatment of Diabetic Sinus Tract Wounds: a Clinical Study. J Surg Res. 2019. PMID: CN-02082099 NEW.[Duplicate]

16. Babaei V, Afradi H, Gohardani HZ, et al. Management of chronic diabetic foot ulcers using platelet-rich plasma. J Wound Care. 2017 12 02;26(12):784-7. PMID: 29244965.[Study design]

17. Baloorkar R, Victor M, Patil MB, et al. Study on evaluation of safety and efficacy of local injections of autologous platelet rich plasma in treatment of chronic cutaneous ulcers. Pravara Medical Review. 2019 01 Dec;11(4):37-42. PMID: 631769259.[Population not of interest]

18. Beavers N. New drug helps diabetic patients kick foot ulcers. Drug Topics. 1998 19 Jan;142(2):31. PMID: 28102902.[Study design]

19. Bhansali A, Venkatesh S, Dutta P, et al. Which is the better option: recombinant human PDGF-BB 0.01% gel or standard wound care, in diabetic neuropathic large plantar ulcers off-loaded by a customized contact cast? Diabetes Res Clin Pract. 2009 Jan;83(1):e13-6. PMID: 19081156.[Intervention not of interest]

20. Blood and blood products in treatment of bone healing related to fractures. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=CTRI. 2011;12(002214). PMID: CN-01821151.[Population not of interest]

21. Blume P, Driver VR, Tallis AJ, et al. Formulated collagen gel accelerates healing rate immediately after application in patients with diabetic neuropathic foot ulcers. Wound Repair Regen. 2011 May-Jun;19(3):302-8. PMID: 21371164.[Intervention not of interest]

22. Bogdan VG, Tolstov DA. Prospective randomized clinical trials of efficiency of autologous platelet-derived concentrates to stimulate regeneration of trophic ulcers of venous etiology. Nov Khir. 2014;22(3):344-50.[Foreign language]

23. Buchberger B, Follmann M, Freyer D, et al. The importance of growth factors for the treatment of chronic wounds in the case of diabetic foot ulcers. GMS Health Technol Assess. 2010 Sep 01;6:Doc12. PMID: 21289885.[Intervention not of interest]

24. Burdge JJ, Daffeh M, Hankins T. Treatment of pressure ulcers with autologous bone marrow-derived mononuclear cells, platelet gel, ORC and surgical closure may improve wound healing outcomes in SCI patients. Wound Repair and Regeneration. 2014 March-April;22 (2):A33. PMID: 71687341.[Type of publication: Conference Abstract]

25. Burnouf T, Tzeng YS, Deng SC, et al. Combination of autologous platelet gel and skin graft to treat non-healing

diabetic lower extremity ulcers. Vox Sanguinis. 2013 December;2):27. PMID: 71243715.[Type of publication: Conference Abstract]

26. Carvalho MRd, Silveira IA, Oliveira BGRBd. Treatment of venous ulcers with growth factors: systematic review and meta-analysis. Rev Bras Enferm. 2019 Jan-Feb;72(1):200-10. PMID: 30916287.[Intervention not of interest]

27. Centre Hospitalier Universitaire V. Effect of Platelet Rich Plasma and Keratinocyte Suspensions on Wound Healing. 2005 June. PMID: NCT00856934.[Population not of interest]

28. Cervelli V, De Angelis B, Lucarini L, et al. Tissue regeneration in loss of substance on the lower limbs through use of platelet-rich plasma, stem cells from adipose tissue, and hyaluronic acid. Adv Skin Wound Care. 2010 Jun;23(6):262-72. PMID: 20489388.[Study design]

29. Cervelli V, Gentile P, De Angelis B, et al. Application of enhanced stromal vascular fraction and fat grafting mixed with PRP in post-traumatic lower extremity ulcers. Stem Cell Res. 2011 Mar;6(2):103-11. PMID: 21195687.[Population not of interest]

30. Cervelli V, Gentile P, Grimaldi M. Regenerative surgery: use of fat grafting combined with platelet-rich plasma for chronic lower-extremity ulcers. Aesthetic Plast Surg. 2009 May;33(3):340-5. PMID: 19156458.[Study design]

31. Chantelau E. Becaplermin (Regranex). [German]. Internistische Praxis. 2001;41(4):905-7. PMID: 32953951.[Foreign language]

32. Chen Z. A study on the therapeutic effects of autologous platelet-rich plasma in the treatment of limbsrefractory wound infection. International Journal of Clinical and Experimental Medicine. 2017 30 Nov;10(11):15316-22. PMID: 619429887.[Population not of interest]

33. Chi CO. Study on the application of allograft platelet rich plasma in clinical. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=ChiCTR ONR. 2016;16009374. PMID: CN-01835005.[Population not of interest]

34. Chi CT. A Prospective, Randomized, Controlled Trial of Autologous Platelet-Rich Plasma Gel to treat refractory dermal ulcer. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=ChiCTR TRC. 2009;09000325. PMID: CN-01872756.[Population not of interest]

35. China Medical University H. Treatment of PRP on Diabetes Wound. 2014 January. PMID: NCT02088268.[Study design]

36. Cieslik-Bielecka A, Skowronski R, Jedrusik-Pawlowska M, et al. The application of L-PRP in AIDS patients with crural chronic ulcers: A pilot study. Adv Med Sci. 2018 Mar;63(1):140-6. PMID: 29120855.[Comparator not of interest]

37. Cobos R, Aizpuru F, Parraza N, et al. Effectiveness and efficiency of platelet rich plasma in the treatment of diabetic ulcers. Curr Pharm Biotechnol. 2015;16(7):630-4. PMID: 25934972.[Study design]

38. Cytomedix CTICT. The AutoloGel™ Post-Market Surveillance (TAPS) Program. 2008 September. PMID: NCT00762138.[Population not of interest]

39. De Angelis B, D'Autilio MFLM, Orlandi F, et al. Wound Healing: In Vitro and In Vivo Evaluation of a Bio-Functionalized Scaffold Based on Hyaluronic Acid and Platelet-Rich Plasma in Chronic Ulcers. J. 2019 Sep 18;8(9):18. PMID: 31540446.[Population not of interest]

40. De Brito Belchior A, De Oliveira Lima R, Monique N, et al. Platelet-rich plasma in people with diabetic foot: Experience report. Diabetology and Metabolic Syndrome Conference: 22nd Brazilian Diabetes Society Congress Brazil. 2019;11(Supplement 1). PMID: 629761101.[Outcomes not of interest]

41. De Oliveira BGRB, e Oliveira FP, Teixeira LA, et al. Epidermal growth factor vs platelet-rich plasma: Activity against chronic wound microbiota. Int Wound J. 2019 Dec;16(6):1408-15. PMID: 31571388.[Outcomes not of interest]

42. Deng W, He M, Chen B, et al. Efficacy and safety of allogeneic platelet rich plasma in treatment of diabetic patients with lower limb ulcers: A pilot study. Diabetes Conference: 79th Scientific Sessions of the American Diabetes Association, ADA. 2019;68(Supplement 1). PMID: 629615815.[Type of publication: Abstract conference]

43. Dhua S, Suhas TR, Tilak BG. The Effectiveness of Autologous Platelet Rich Plasma Application in the Wound Bed Prior to Resurfacing with Split Thickness Skin Graft vs. Conventional Mechanical Fixation Using Sutures and Staples. World j. 2019 May;8(2):185-94. PMID: 31309055.[Population not of interest]

44. Di Domenico G, Leonardi GM, Mottola M, et al. Analysis of the impact of alloimmunization in patients treated with homologous platelet gel. Vox Sanguinis. 2010 July;1):383. PMID: 70237737.[Study design]

45. Di Domenico G, Leonardi GM, Mottola M, et al. Platelet gel and wound care: The weight of the platelets concentration in the cliniciantherapeutic practice. Vox Sanguinis. 2009 April;1):249. PMID: 70097809.[Type of publication: Conference Abstract]

46. Dionyssiou D, Demiri E, Foroglou P, et al. The effectiveness of intralesional injection of platelet-rich plasma in accelerating the healing of chronic ulcers: an experimental and clinical study. International Wound Journal. 2013 Aug;10(4):397-406. PMID: 22672105.[Population not of interest]

47. Dougherty EJ. An evidence-based model comparing the cost-effectiveness of platelet-rich plasma gel to alternative therapies for patients with nonhealing diabetic foot ulcers. Adv Skin Wound Care. 2008 Dec;21(12):568-75. PMID: 19065083.[Study design]

48. Dreizler T, Born F, Lipps C, et al. PRP and APG - Overview and own results. [German]. Kardiotechnik. 2008 December;17(4):102-5. PMID: 352826439.[Foreign language]

49. Driver VR. A prospective, randomized, controlled, blinded, multicenter pivotal trial of a platelet rich

plasma gel[Type of publication: Conference Abstract]

50. D'Souza MS, D'Souza J, Karkada SN. Foot care education and platelet derived growth factor on wound healing in foot ulcers among adults. International Journal of Nutrition, Pharmacology, Neurological Diseases. 2016 July-September;6(3):111-8. PMID: 611175348.[Intervention not of interest]

51. Duan W, Zhao S, Mao H, et al. One-stop treatment of severe lower limb ischemic diabetic foot ulcers by endocrinology. Diabetes/Metabolism Research and Reviews. 2018 October;34 (Supplement 1):42-3. PMID: 625228224.[Intervention not of interest]

52. Effect of platelet dressing on wound healing in diabetic foot. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=IRCT2014060415574N3. 2014. PMID: CN-01856492.[Outcomes not of interest]

53. Effective treatment of diabetic foot ulcers still centers on wound care basic. Geriatrics. 2002 01 Aug;57(8):36. PMID: 35252393.[Study design]

54. Elsaid A, El-Said M, Emile S, et al. Randomized Controlled Trial on Autologous Platelet-Rich Plasma Versus Saline Dressing in Treatment of Non-healing Diabetic Foot Ulcers. World journal of surgery. 2019. PMID: CN-02051589 NEW.[Duplicate]

55. Escamilla Cardenosa M, Dominguez-Maldonado G, Cordoba-Fernandez A. Efficacy and safety of the use of platelet-rich plasma to manage venous ulcers. Journal of tissue viability. 2016;24. PMID: CN-01302509.[Duplicate]

56. Euctr ES. Check if fatible and can be effective if the use of PRP in vascular ulcers in the field of primary care. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=EUCTR2012. 2012. PMID: CN-01851073.[Type of publication: Conference Abstract]

57. Evaluate the Safety and Efficacy of RegenKit Autologous PRP Gel for the Treatment of Diabetic Foot Ulcer. https://clinicaltrialsgov/show/nct02402374. 2015. PMID: CN-01505354.[Duplicate]

58. Evaluation of the Effect of Vivostat Platelet Rich Fibrin(PRF) in the Treatment of Diabetic Foot Ulcers. 2008 July. PMID: NCT00770939.[Study design]

59. Fang Z, Yang X, Wu G, et al. The use of autologous platelet-rich plasma gel increases wound healing and reduces scar development in split-thickness skin graft donor sites. J Plast Surg Hand Surg. 2019 Jul 03:1-5. PMID: 31268389.[Population not of interest]

60. Fernandez-Montequin JI, Infante-Cristia E, Valenzuela-Silva C, et al. Intralesional injections of Citoprot-P (recombinant human epidermal growth factor) in advanced diabetic foot ulcers with risk of amputation. International wound journal. 2007 Dec;4(4):333-43. doi: 10.1111/j.1742-481X.2007.00344.x. Epub 2007 Oct 22. PMID: 17953679.[Intervention not of interest]

61. Fernandez-Montequin JI, Valenzuela-Silva CM, Diaz OG, et al. Intra-lesional injections of recombinant human epidermal growth factor promote granulation and healing in advanced diabetic foot ulcers: multicenter, randomised, placebo-controlled, double-

blind study. International wound journal. 2009 Dec;6(6):432-43. doi: 10.1111/j.1742-481X.2009.00641.x. PMID: 20051095.[Intervention not of interest]

62. Friese G, Herten M, Scherbaum WA. The use of autologous platelet concentrate activated by autologous thrombin (APC+) is effective and safe in the treatment of chronic diabetic foot ulcers: a randomized controlled trial[Type of publication: Conference Abstract]

63. Frykberg RG, Driver VR, Carman D, et al. Chronic wounds treated with a physiologically relevant concentration of platelet-rich plasma gel: a prospective case series. Ostomy Wound Manage. 2010 Jun;56(6):36-44. PMID: 20567053.[Study design]

64. Game F, Jeffcoate W, Tarnow L, et al. The LeucoPatch system in the management of hard-to-heal diabetic foot ulcers: study protocol for a randomised controlled trial. Trials. 2017 Oct 10;18(1):469. PMID: 29017535.[Study design]

65. Ganio C, Tenewitz FE, Wilson RC, et al. The treatment of chronic nonhealing wounds using autologous platelet-derived growth factors. The Journal of foot and ankle surgery : official publication of the American College of Foot and Ankle Surgeons. 1993 May-Jun;32(3):263-8. PMID: 8339079.[Study design]

66. Gomez-Villa R, Aguilar-Rebolledo F, Lozano-Platonoff A, et al. Efficacy of intralesional recombinant human epidermal growth factor in diabetic foot ulcers in Mexican patients: a randomized double-blinded controlled trial. Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society. 2014 Jul-Aug;22(4):497-503. doi: 10.1111/wrr.12187. PMID: 25041620.[Intervention not of interest]

67. Hanan J, University of J. The Use of Allogenic Platelet Rich Plasma for the Treatment of Diabetic Foot Ulcer. 2018 February 3. PMID: NCT02972528.[Intervention not of interest]

68. Hanft JR, Pollak RA, Barbul A, et al. Phase I trial on the safety of topical rhVEGF on chronic neuropathic diabetic foot ulcers. Journal of wound care. 2008 Jan;17(1):30-2, 4-7. doi: 10.12968/jowc.2008.17.1.27917. PMID: 18210954.[Intervention not of interest]

69. Hardikar JV, Reddy YC, Bung DD, et al. Efficacy of recombinant human Platelet-Derived Growth Factor (rhPDGF) based gel in diabetic foot ulcers: A randomized, multicenter, double-blind, placebo-controlled study in India. 2005 06/01;17:141-52.[Intervention not of interest]

70. He JD, Xiao-bo O, Zhang L, et al. Autologous platelet-rich gel for diabetic foot ulcer: A systematic review of randomized controlled trials. [Chinese]. Chinese Journal of Evidence-Based Medicine. 2010;10(7):838-41. PMID: 359728064.[Foreign language]

71. He L, Ran X, Wang Y, et al. Dynamic changes of MMP-1, MMP-9 and TIMP-1 in the refractory diabetic dermal ulcers treated with autologous platelet-rich gel. Diabetes Conference: 70th Scientific Sessions of the American Diabetes Association Orlando, FL United States Conference Publication:.

2010. PMID: 71602301.[Foreign language]

72. He L-P, Wang C, Chen D-W, et al. [Dynamic changes of MMP-1, MMP-9 and TIMP-1 in the refractory diabetic dermal ulcers treated by autologous Platelet-rich gel]. Sichuan Da Xue Xue Bao Yi Xue Ban. 2012 Sep;43(5):757-61. PMID: 23230755.[Foreign language]

73. Hersant B, SidAhmed-Mezi M, Bosc R, et al. Autologous Platelet-Rich Plasma/Thrombin Gel Combined with Split-Thickness Skin Graft to Manage Postinfectious Skin Defects: A Randomized Controlled Study. Adv Skin Wound Care. 2017 Nov;30(11):502-8. PMID: 29049258.[Population not of interest]

74. Holloway GA. A randomized, controlled, multicenter, dose response trial of activated platelet supernatent, topical CT-102 in chronic, nonhealing, diabetic wounds. Wounds. 1993;5:198-206.[Intervention not of interest]

75. Hosseini ES, Goodarzi A, Molavi B, et al. Randomized double blind clinical trial: Utilization of umbilical cord blood-derived platelet gel for treatment of diabetic foot ulcers. Cell Journal. 2014 Summer;1):46-7. PMID: 71942666.[Type of publication: Conference Abstract]

76. Hosseini SE, Molavi B, Goodarzi A, et al. The efficacy of platelet gel derived from umbilical cord blood on diabetic foot ulcers: A double-blind randomized clinical trial. Wound Medicine. 2020 March;28 (no pagination)(100178). PMID: 2004656584.[Intervention not of interest]

77. Jagati A, Chaudhary RG, Rathod SP, et al. Preparation of Platelet-rich Fibrin Membrane over Scaffold of Collagen Sheet, its Advantages over Compression Method: A Novel and Simple Technique. J. 2019 Jul-Sep;12(3):174-8. PMID: 31619889.[Population not of interest]

78. Jaiswal SS, Gambhir RPS, Agrawal A, et al. Efficacy of topical recombinant human platelet derived growth factor on wound healing in patients with chronic diabetic lower limb ulcers. Indian J Surg. 2010;72(1):27-31. PMID: 23133200.[Intervention not of interest]

79. Jeong E, Yoo IK, Cakir OO, et al. Effectiveness of Autologous Platelet-Rich Plasma for the Healing of Ulcers after Endoscopic Submucosal Dissection. Clin. 2019 May 17;17:17. PMID: 31096727.[Population not of interest]

80. Jeong S-H, Han S-K, Kim W-K. Treatment of diabetic foot ulcers using a blood bank platelet concentrate. Plast Reconstr Surg. 2010 Mar;125(3):944-52. PMID: 20195121.[Intervention not of interest]

81. Joshi S. Role of platelet-rich plasma in healing diabetic and leprosy foot ulcers in resource poor setting. Research and Practice in Thrombosis and Haemostasis. 2019 July;3 (Supplement 1):564. PMID: 628814387.[Type of publication: Conference Abstract]

82. Jprn U. An exploratory clinical trial using platelet-rich plasma in patients with chronic skin ulcers. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=JPRN UMIN000015689. 2014. PMID: CN-01865498.[Study design]

83. Jprn U. Clinical study for the treatment of chronic wounds using Platelet-rich Plasma. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=JPRN UMIN000004840. 2011. PMID: CN-01797950.[Population not of interest]

84. Jprn U. clinical trial of platelet rich plasma for the treatment of chronic cutaneous ulcers. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=JPRN UMIN000022258. 2016. PMID: CN-01839232.[Population not of interest]

85. Katzman P, Fagher K, Lundquist R, et al. Treatment of hard-to-heal diabetic foot ulcers probing to bone with leucopatchTM, a leukocytes and platelet rich fibrin patch. Diabetes. 2014 June;1):A581. PMID: 71560640.[Type of publication: Conference Abstract]

86. Keyser JE. Diabetic wound healing and limb salvage in an outpatient wound care program. Southern medical journal. 1993 Mar;86(3):311-7. doi: 10.1097/00007611-199303000-00013. PMID: 8451671.[Study design]

87. Khorvash F, Pourahmad M, Khoshchingol N, et al. Comparing the effects of the platelet-rich plasma gel with wound therapeutic methods on the treatment of diabetic foot. [Persian]. Journal of Isfahan Medical School. 2017 01 Dec;35(450):1389-95. PMID: 2001511711.[Foreign language]

88. Knighton DR, Ciresi K, Fiegel VD, et al. Stimulation of repair in chronic, nonhealing, cutaneous ulcers using platelet-derived wound healing formula. Surgery, gynecology & obstetrics. 1990 Jan;170(1):56-60. PMID: 2403699.[Population not of interest]

89. Knighton DR, Ciresi KF, Fiegel VD, et al. Classification and treatment of chronic nonhealing wounds. Successful treatment with autologous platelet-derived wound healing factors (PDWHF). Annals of surgery. 1986 Sep;204(3):322-30. doi: 10.1097/00000658-198609000-00011. PMID: 3753059.[Population not of interest]

90. Kok YO, Loh C, Tan SSY, et al. Wound healing topical growth factors: A meta-analysis. Proceedings of Singapore Healthcare. 2012 March;1):S56. PMID: 72034980.[Intervention not of interest]

91. Krupski WC, Reilly LM, Perez S, et al. A prospective randomized trial of autologous platelet-derived wound healing factors for treatment of chronic nonhealing wounds: a preliminary report. Journal of vascular surgery. 1991 Oct;14(4):526-32; discussion 32-6. PMID: 1920650.[Population not of interest]

92. Li L, Wang C, Wang Y, et al. [Impact of topical application of autologous platelet-rich gel on medical expenditure and length of stay in hospitals in diabetic patients with refractory cutaneous ulcers]. Sichuan Da Xue Xue Bao Yi Xue Ban. 2012 Sep;43(5):762-5. PMID: 23230756.[Foreign language]

93. Li Y, Lv X, Gao Y, et al. Autologous platelet-rich gel treatment for diabetic chronic cutaneous ulcers: A meta-analysis of randomized controlled trials. Diabetes/Metabolism Research and Reviews Conference: 21st Scientific Meeting of the Chinese Diabetes Society China. 2017;33(Supplement 1). PMID: 619417974.[Type of publication: Conference Abstract]

94. Liao X, Liang J-X, Li S-H, et al. Allogeneic Platelet-Rich Plasma Therapy as an Effective and Safe Adjuvant Method for Chronic Wounds. J Surg Res. 2020 02;246:284-91. PMID: 31622885.[Intervention not of interest]

95. Links TP. New treatments for diabetic foot ulcers. [Dutch]. Pharmaceutisch Weekblad. 2001 03 Aug;136(31):1143-5. PMID: 32708020.[Foreign language]

96. Linyi People's H. Effectiveness of Platelet Rich Plasma in Wound Healing. 2015 October. PMID: NCT02831374.[Population not of interest]

97. Liu GY, Deng XL, Sun Y, et al. Effect of autologous platelet-rich gel on the treatment of diabetic foot ulcers. [Chinese]. Journal of Xi'an Jiaotong University (Medical Sciences). 2016 05 Mar;37(2):264-7. PMID: 609608732.[Foreign language]

98. Ma C, Hernandez MA, Kirkpatrick VE, et al. Topical platelet-derived growth factor vs placebo therapy of diabetic foot ulcers offloaded with windowed casts: a randomized, controlled trial. Wounds. 2015 Apr;27(4):83-91. PMID: 25855851.[Intervention not of interest]

99. Madhumitha M, Srinivasan S. A study of efficacy of autologous platelet rich plasma in the treatment of chronic diabetic foot ulcers. International Journal of Pharmaceutical Research. 2019 October-December;11(Supplementry 1):190-6. PMID: 2003563369.[Type of publication: Abstract conference]

100. Mansoura U. PRP IN Planter Fascitis. 2017 October 1. PMID: NCT03938896.[Population not of interest]

101. Margolis DJ, Bartus C, Hoffstad O, et al. Effectiveness of recombinant human platelet-derived growth factor for the treatment of diabetic neuropathic foot ulcers. Wound Repair and Regeneration. 2005 November;13(6):531-6. PMID: 43934520.[Intervention not of interest]

102. Margolis DJ, Kantor J, Santanna J, et al. Effectiveness of platelet releasate for the treatment of diabetic neuropathic foot ulcers. Diabetes Care. 2001 Mar;24(3):483-8. PMID: 11289472.[Intervention not of interest]

103. Marinacci M. Treatment of diabetic ulcers, using autologous platelet and fibrinic gel. Experience the FIBRINET device. Transfusion and Apheresis Science. 2010 October;43(2):171-2. PMID: 51097009.[Study design]

104. Massara M, Barilla D, De Caridi G, et al. Application of autologous platelet-rich plasma to enhance wound healing after lower limb revascularization: A case series and literature review. Semin Vasc Surg. 2015 Sep-Dec;28(3-4):195-200. PMID: 27113287.[Study design]

105. McAleer JP, Kaplan E, Persich G. Efficacy of concentrated autologous platelet-derived growth factors in chronic lower-extremity wounds. Journal of the American Podiatric Medical Association. 2006 Nov-Dec;96(6):482-8. doi: 10.7547/0960482. PMID: 17114601.[Population not of interest]

106. Medical University of V. PRF With Topical Antibiotics or Antiseptics in Chronical Wounds Version 1.4. 2014 June. PMID:

NCT02652169.[Intervention not of interest]

107. Miyake Y, Fukuda S, Iguchi Y, et al. Treatment streategy for refractory ulcers by critical limb ischemia (CLI). Jpn J Plast Surg. 2009;52(6):711-9.[Foreign language]

108. Moghazy AM, Ellabban MA, Adly OA, et al. Evaluation of the use of vacuum-assisted closure (VAC) and platelet-rich plasma gel (PRP) in management of complex wounds. European Journal of Plastic Surgery. 2015 01 Dec;38(6):463-70. PMID: 606536250.[Population not of interest]

109. Mohammadi MH, Molavi B, Mohammadi S, et al. Evaluation of wound healing in diabetic foot ulcer using platelet-rich plasma gel: A single-arm clinical trial. Transfus Apheresis Sci. 2017 Apr;56(2):160-4. PMID: 27839965.[Study design]

110. Mohammadi MH, Molavi B, Mohammadi S, et al. Evaluation of wound healing in diabetic foot ulcer using platelet-rich plasma gel: a single-arm clinical trial. Transfusion and apheresis science. 2016;24. PMID: CN-01287620 NEW.[Study design]

111. Monami M, Mirabella C, Scatena A, et al. CO2 laser for the treatment of diabetic foot ulcers with exposed bone. A consecutive series of type 2 diabetic patients. J Endocrinol Invest. 2017 Aug;40(8):819-22. PMID: 28260184.[Study design]

112. Moraes VY, Lenza M, Tamaoki MJ, et al. Platelet-rich therapies for musculoskeletal soft tissue injuries. Cochrane Database Syst Rev. 2013 Dec 23(12):CD010071. PMID: 24363098.[Population not of interest]

113. Morimoto N, Kakudo N, Matsui M, et al. Exploratory clinical trial of combination wound therapy with a gelatin sheet and platelet-rich plasma in patients with chronic skin ulcers: study protocol. BMJ Open. 2015 May 11;5(5):e007733. PMID: 25968005.[Study design]

114. Mustoe TA, Cutler NR, Allman RM, et al. A phase II study to evaluate recombinant platelet-derived growth factor-BB in the treatment of stage 3 and 4 pressure ulcers. Arch Surg. 1994 Feb;129(2):213-9. PMID: 8304833.[Intervention not of interest]

115. Na J-I, Choi J-W, Choi H-R, et al. Rapid healing and reduced erythema after ablative fractional carbon dioxide laser resurfacing combined with the application of autologous platelet-rich plasma. Dermatol Surg. 2011 Apr;37(4):463-8. PMID: 21481064.[Population not of interest]

116. Noha Mohsen O, Menoufia U. Role of Platelet Rich Plasma in Enhancing Graft Take in Chronic Venous Ulcers. 2016 February 1. PMID: NCT03526913.[Population not of interest]

117. Obolenskiy VN, Ermolova DA, Laberko LA. Clinical and economic effectiveness of the use of platelet-rich plasma in the treatment of chronic wounds. Wound Medicine. 2017 December;19:27-32. PMID: 618495668.[Intervention not of interest]

118. Obolensky VN, Ermolova DA, Makarov MS, et al. Clinical and experimental study: Stimulation of

regenerative processes in chronic wounds using platelets rich autoplasma. Clin Exp Surg. 2016;4(1):38-43.[Foreign language]

119. Oliveira MGd, Abbade LPF, Miot HA, et al. Pilot study of homologous platelet gel in venous ulcers. An Bras Dermatol. 2017 Jul-Aug;92(4):499-504. PMID: 28954098.[Intervention not of interest]

120. Oregon H, Science U, Oregon C, et al. Diabetes PRP and OCT. 2013 August. PMID: NCT01928550.[Population not of interest]

121. Otero GE, Sujanov A, Falco S, et al. Cell therapy with autologous platelet rich plasma in the treatment of chronic venous leg ulcers. Preliminary results of a prospective randomised phase 2 trial. Cytotherapy. 2018 May;20 (5 Supplement 1):S117. PMID: 622628018.[Type of publication: Conference Abstract]

122. P Waiker V, Shivalingappa S. Comparison between Conventional Mechanical Fixation and Use of Autologous Platelet Rich Plasma (PRP) in Wound Beds Prior to Resurfacing with Split Thickness Skin Graft. World j. 2015 Jan;4(1):50-9. PMID: 25606477.[Population not of interest]

123. Padilla S, Sanchez M, Orive G, et al. Towards a correct timing and dosage in PRP applications. Injury. 2015 Aug;46(8):1697-8. PMID: 25920374.[Study design]

124. Park KY, Kim IS, Yeo IK, et al. Treatment of refractory venous stasis ulcers with autologous platelet-rich plasma and light-emitting diodes: a pilot study. J Dermatolog Treat. 2013 Oct;24(5):332-5. PMID: 23738854.[Study design]

125. Perrero L, Persico D, Bellora A, et al. Pressure ulcers in the elderly: Advanced treatments and use of Platelet Gel (PRP/gel). [Italian]. Giornale di Gerontologia. 2003 February;51(1):12-7. PMID: 36869560.[Foreign language]

126. Pietramaggiori G, Scherer SS, Mathews JC, et al. Quiescent platelets stimulate angiogenesis and diabetic wound repair. J Surg Res. 2010 May 01;160(1):169-77. PMID: 19482315.[Population not of interest]

127. Platelet-derived growth factor for diabetic ulcers. Medical Letter on Drugs and Therapeutics. 1998 17 Jul;40(1031):73-4. PMID: 28350996.[Type of publication: Conference Abstract]

128. Platelet Rich Plasma (PRP) Bio Stimulant Gel Dressing in Treating Chronic Non Healing Leg and Foot Ulcers: cost and Effectiveness. https://clinicaltrialsgov/show/NCT04065594. 2019. PMID: CN-01983675.[Duplicate]

129. Pravin AJS, Sridhar V, Srinivasan BN. Autologous platelet rich plasma (PRP) versus leucocyte-platelet rich fibrin (L-PRF) in chronic non-healing leg ulcers—A randomised, open labelled, comparative study. J Evol Med Dent Sci. 2016;5:7460.[Population not of interest]

130. Project RAPID: restorative Autologous Platelet biotherapies for Injuries & Delayed wound healing. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=ISRCTN84928077. 2013.

PMID: CN-01869529.[Population not of interest]

131. Prp Concepts LLC. A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Pressure Ulcers. 2019 April. PMID: NCT02312570.[Duplicate]

132. Prp Concepts LLC. A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Venous Leg Ulcers. 2019 April. PMID: NCT02312518.[Duplicate]

133. Prp Concepts LLC. A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Non-Healing Diabetic Foot Ulcers. 2019 April. PMID: NCT02312596.[Duplicate]

134. Pu D, Lei X, Leng W, et al. Lower limb arterial intervention or autologous platelet-rich gel treatment of diabetic lower extremity arterial disease patients with foot ulcers. Annals of Translational Medicine. 2019 01 Sep;7 (18) (no pagination)(87). PMID: 629529450.[Population not of interest]

135. Qi K, Chen T, Piao J, et al. Application of autologous platelet gels in the treatment of diabetic foot ulcer. Chin J Diab. 2014;22:1102-5.[Foreign language]

136. Qin X, Wang J. [Clinical study of local injection of autologous platelet-rich plasma in treatment of diabetic foot ulcer]. Chung Kuo Hsiu Fu Chung Chien Wai Ko Tsa Chih. 2019 Dec 15;33(12):1547-51. PMID: 31823556.[Foreign language]

137. Qinan W. Lower limb arterial intervention or autologous platelet-rich gel treatment of diabetic lower extremity arterial disease with foot ulcer. Diabetes Technology and Therapeutics. 2020 February;22 (Supplement 1):A-202. PMID: 631246813.[Type of publication: Abstract conference]

138. Raeissadat SA, Babaee M, Rayegani SM, et al. An overview of platelet products (PRP, PRGF, PRF, etc.) in the Iranian studies. Future Sci OA. 2017 11;3(4):FSO231. PMID: 29134118.[Population not of interest]

139. Rainys D, Cepas A, Dambrauskaite K, et al. Effectiveness of autologous platelet-rich plasma gel in the treatment of hard-to-heal leg ulcers: a randomised control trial. J Wound Care. 2019 Oct 02;28(10):658-67. PMID: 31600109.[Population not of interest]

140. Ramos-Torrecillas J, Garcia-Martinez O, De Luna-Bertos E, et al. Effectiveness of platelet-rich plasma and hyaluronic acid for the treatment and care of pressure ulcers. Biol Res Nurs. 2015 Mar;17(2):152-8. PMID: 24848975.[Outcomes not of interest]

141. Raposio E, Bertozzi N, Bonomini S, et al. Adipose-derived Stem Cells Added to Platelet-rich Plasma for Chronic Skin Ulcer Therapy. Wounds. 2016 Apr;28(4):126-31. PMID: 27071140.[Population not of interest]

142. Raposio E, Bertozzi N, Trevisan M, et al. Transcutaneous oximetry and laser Doppler flowmetry values in patients with chronic skin ulcers treated with platelet rich plasma and stromal vascular fraction cells: a pilot study. European Journal of Plastic Surgery. 2018 01 Oct;41(5):577-82. PMID: 620681824.[Study design]

143. Redler LH, Thompson SA, Hsu SH, et al. Platelet-rich plasma therapy: a systematic literature review and evidence for clinical use. Phys Sportsmed. 2011 Feb;39(1):42-51. PMID: 21378486.[Population not of interest]

144. Regen Lab SA, RegenLab UL. Evaluate the Safety and Efficacy of RegenKit Autologous PRP Gel for the Treatment of Diabetic Foot Ulcer. 2018 April 12. PMID: NCT02402374. [Duplicate]

145. Rees RS, Robson MC, Smiell JM, et al. Becaplermin gel in the treatment of pressure ulcers: a phase II randomized, double-blind, placebo-controlled study. Wound Repair Regen. 1999 May-Jun;7(3):141-7. PMID: 10417749.[Intervention not of interest]

146. Reutter H, Bort S, Jung M, et al. Questionable efficacy of autologous platelet growth factors (PDHWF) in the treatment of venous leg ulcers. Der Hautarzt; Zeitschrift für Dermatologie, Venerologie, und verwandte Gebiete. 2000 01/01;50:859-65.[Foreign language]

147. Richard JL, Parer-Richard C, Daures JP, et al. Effect of topical basic fibroblast growth factor on the healing of chronic diabetic neuropathic ulcer of the foot. A pilot, randomized, double-blind, placebo-controlled study. Diabetes Care. 1995 Jan;18(1):64-9. doi: 10.2337/diacare.18.1.64. PMID: 7698050.[Intervention not of interest]

148. Robson MC, Phillips LG, Thomason A, et al. Platelet-derived growth factor BB for the treatment of chronic pressure ulcers. Lancet. 1992 Jan 04;339(8784):23-5. PMID: 1345953.[Type of publication: Conference Abstract]

149. Role of Platelet Rich Plasma in Enhancing Graft Take in Chronic Venous Ulcers. Https://clinicaltrialsgov/show/nct03526913. 2018. PMID: CN-01659587 NEW.[Population not of interest]

150. Rucigaj TP, Lunder T. Stimulation of venous leg ulcers with thrombocytic growth factors: A randomized study[Type of publication: Conference Abstract]

151. Safety And Efficacy Of Topical Platelet Rich Plasma And Thrombin Coagulum. Https://clinicaltrialsgov/show/nct02802995. 2016. PMID: CN-01559094.[Population not of interest]

152. Saha S, Patra AC, Gowda SP, et al. Effectiveness and safety of autologous platelet-rich plasma therapy with total contact casting versus total contact casting alone in treatment of trophic ulcer in leprosy: An observer-blind, randomized controlled trial. Indian J Dermatol Venereol Leprol. 2020 May-Jun;86(3):262-71. PMID: 31997794.[Population not of interest]

153. Sakata J, Sasaki S, Handa K, et al. A retrospective, longitudinal study to evaluate healing lower extremity wounds in patients with diabetes mellitus and ischemia using standard protocols of care and platelet-rich plasma gel in a Japanese wound care program. Ostomy Wound Manage. 2012 Apr;58(4):36-49. PMID: 22466132.[Study design]

154. Salazar-Alvarez AE, Riera-del-Moral LF, Garcia-Arranz M, et al. Use of platelet-rich plasma in the healing of

chronic ulcers of the lower extremity. Actas Dermosifiliogr. 2014 Jul-Aug;105(6):597-604. PMID: 24630241.[Foreign language]

155. Saldalamacchia G, Lapice E, Cuomo V, et al. Use of autologous platelet gel for the treatment of diabetic foot ulcers. [Italian]. Giornale Italiano di Diabetologia e Metabolismo. 2004 September;24(3):103-5. PMID: 39490673.[Foreign language]

156. San Sebastian KM, Lobato I, Hernandez I, et al. Efficacy and safety of autologous platelet rich plasma for the treatment of vascular ulcers in primary care: Phase III study. BMC Fam Pract. 2014 Dec 30;15:211. PMID: 25547983.[Study design]

157. Semenic D, Cirman T, Rozman P, et al. Regeneration of Chronic Wounds with Allogeneic Platelet Gel Versus Hydrogel Treatment: A Prospective Study. Acta Clin. 2018 Sep;57(3):434-42. PMID: 31168175.[Population not of interest]

158. Singh R, Dhayal RK, Sehgal PK, et al. To evaluate antimicrobial properties of platelet rich plasma and source of colonization in pressure ulcers in spinal injury patients. Ulcers. 2015 28 Jan;2015 (no pagination)(749585). PMID: 604162128.[Outcomes not of interest]

159. Singla S, Garg R, Kumar A, et al. Efficacy of topical application of beta urogastrone (recombinant human epidermal growth factor) in Wagner's Grade 1 and 2 diabetic foot ulcers: Comparative analysis of 50 patients. Journal of natural science, biology, and medicine. 2014 Jul;5(2):273-7. doi: 10.4103/0976-9668.136160. PMID: 25097397.[Intervention not of interest]

160. Slaninka I, Klein L, Cap R, et al. [Optimizing the treatment procedure in crural ulcers - a pilot study of the surgical method]. Rozhl Chir. 2015 Feb;94(2):69-73. PMID: 25659256.[Foreign language]

161. Smagin MA, Demura AI, Shumkov OA, et al. Platelet-rich plasma in treatment of non-healing ulcers. Int Conf Bioinform Genome Regul Struct\Syst Biol, BGRS\SB - Proc. 2018:62-5.[Population not of interest]

162. Smith OJ, Kanapathy M, Khajuria A, et al. Systematic review of the efficacy of fat grafting and platelet-rich plasma for wound healing. International Wound Journal. 2018;15(4):519-26. PMID: 622088208.[Intervention not of interest]

163. So TI, Lee YJ, Choi JH, et al. Endoscopic application of autologous platelet rich plasma on gastric ulcer after endoscopic submucosal dissection: A pilot study. United European Gastroenterology Journal. 2018 October;6 (8 Supplement):A379-A80. PMID: 625972966.[Population not of interest]

164. Sokolov T, Manukova A, Karakoleva S, et al. Analysis of the results of applying the method platelet-rich plasma (PRP) for the treatment of problematic skin wounds. Journal of IMAB - Annual Proceeding (Scientific Papers). 2017 01 Jan;23(1):1460-5. PMID: 614494212.[Population not of interest]

165. Sokolov T, Valentinov B, Andonov J, et al. Contaminated problematic skin wounds in diabetic patients treated with autologous platelet - Rich plasma (PRP): A case series study. Journal of IMAB -

Annual Proceeding (Scientific Papers). 2016 January-March;22(1):1067-71. PMID: 610112659.[Study design]

166. Solsys Medical LLC. TheraGauze™ Alone and Regranex®Gel 0.01% Plus TheraGauze™ in the Treatment of Wagner Stage I Diabetic Foot Ulcers. 2006 September. PMID: NCT00389636.[Intervention not of interest]

167. Sridharan K, Sivaramakrishnan G. Growth factors for the management of diabetic foot ulcers: Mixed treatment comparisons of randomized controlled trials. Value in Health. 2017 OctoberNovember;20 (9):A919. PMID: 619025019.[Intervention not of interest]

168. Sriram S, Kavitha MM, Tamilselvam TN, et al. Role and efficacy of platelet rich plasma (PRP) in chronic non healing resistant vasculitic ulcers. Indian Journal of Rheumatology. 2014 July;9 (5 Supplement):S1-S2. PMID: 619194931.[Type of publication: Conference Abstract]

169. Sriram S. Role and efficacy of autologous platelet rich plasma in chronic resistant non healing vasculitic ulcers. Annals of the Rheumatic Diseases. 2015 June;2):1120. PMID: 72154072.[Population not of interest]

170. St. Antonius H. The Influence of Growth Factors (PDGF), Applied as Autologous Thrombocyte Concentrate, on Functional Recovery. 2010 July. PMID: NCT01510639.[Population not of interest]

171. Steed DL, Donohoe D, Webster MW, et al. Effect of extensive debridement and treatment on the healing of diabetic foot ulcers. Diabetic Ulcer Study Group. J Am Coll Surg. 1996 Jul;183(1):61-4. PMID: 8673309.[Intervention not of interest]

172. Steed DL, Edington HD, Webster MW. Recurrence rate of diabetic neurotrophic foot ulcers healed using topical application of growth factors released from platelets. Wound repair and regeneration : official publication of the Wound Healing Society [and] the European Tissue Repair Society. 1996 Apr-Jun;4(2):230-3. doi: 10.1046/j.1524-475X.1996.40210.x. PMID: 17177818.[Intervention not of interest]

173. Steed DL, Goslen JB, Holloway GA, et al. Randomized Prospective Double-Blind Trial in Healing Chronic Diabetic Foot Ulcers: CT-102 activated platelet supernatant, topical versus placebo. 1992;15(11):1598-604.[Intervention not of interest]

174. Steed DL. Platelet-Derived Growth Factor in the Treatment of Diabetic Foot Ulcers. Wounds. 2000;12(6 SUPPL. B):95B-8B.[Study design]

175. The Effect of Platelet-Rich Plasma-Fibrin Glue in Combination With Vitamin E and C for Treatment of Non-healing Diabetic Foot Ulcers. https://clinicaltrialsgov/show/NCT04315909. 2020. PMID: CN-02089241 NEW.[Duplicate]

176. Tinsley BA, Ferreira JV, Dukas AG, et al. Platelet-Rich Plasma Nonoperative Injection Therapy-A Review of Indications and Evidence. Operative Techniques in Sports Medicine. 2012 June;20(2):192-200. PMID: 364985215.[Study design]

177. Tsachiridi M, Galyfos G, Andreou A, et al. Autologous Platelet-Rich Plasma for Nonhealing Ulcers: A Comparative Study. Vasc. 2019 Mar;35(1):22-7. PMID: 30993104.[Population not of interest]

178. Tsai H-C, Lehman CW, Chen C-M. Use of platelet-rich plasma and platelet-derived patches to treat chronic wounds. J Wound Care. 2019 01 02;28(1):15-21. PMID: 30625042.[Population not of interest]

179. Uchi H, Igarashi A, Urabe K, et al. Clinical efficacy of basic fibroblast growth factor (bFGF) for diabetic ulcer. European journal of dermatology : EJD. 2009 Sep-Oct;19(5):461-8. doi: 10.1684/ejd.2009.0750. Epub 2009 Jul 29. PMID: 19638336.[Intervention not of interest]

180. University of M. A Prospective Comparison of Ultrasound-Guided Percutaneous Platelet-Rich Plasma Injection. 2010 July. PMID: NCT01600326.[Population not of interest]

181. University of Pennsylvania NIoA, Musculoskeletal SD. Preliminary Testing of New Treatment for Chronic Leg Wounds. 2005 January. PMID: NCT00000431.[Intervention not of interest]

182. Velier M, Magalon J, Daumas A, et al. Production of platelet-rich plasma gel from elderly patients under antithrombotic drugs: Perspectives in chronic wounds care. Platelets. 2018 Jul;29(5):496-503. PMID: 28805478.[Outcomes not of interest]

183. Victor M, Baloorkar R, Patil MB, et al. Study on evaluation of safety and efficacy of local injections of autologous platelet rich plasma in treatment of chronic cutaneous ulcers. Pravara Medical Review. 2020 01 Mar;12(1):30-3. PMID: 631886354.[Population not of interest]

184. Viswanathan V, Pendsey S, Sekar N, et al. A phase III study to evaluate the safety and efficacy of recombinant human epidermal growth factor (REGEN-D™ 150) in healing diabetic foot ulcers. Wounds. 2006 07/01;18:186-96.[Intervention not of interest]

185. Volakakis E, Papadakis M, Manios A, et al. Platelet-rich Plasma Improves Healing of Pressure Ulcers as Objectively Assessed by Digital Planimetry. Wounds. 2019 Jul 31;31:31. PMID: 31461402.[Study design]

186. Volpe P, Marcuccio D, Stilo G, et al. Efficacy of cord blood platelet gel application for enhancing diabetic foot ulcer healing after lower limb revascularization. Semin Vasc Surg. 2017 Dec;30(4):106-12. PMID: 29793677.[Population not of interest]

187. Wang L, Gu Z, Gao C. [Platelet-rich plasma for treating acute wounds: a meta-analysis]. Chung Hua I Hsueh Tsa Chih. 2014 Jul 22;94(28):2169-74. PMID: 25331465.[Foreign language]

188. Wang Y, Wang C, Liping HE, et al. A prospective randomized controlled study on topical autologous platelet-rich plasma gel for the treatment of diabetic non-healing dermal ulcers. Chinese Journal of Diabetes. 2009;17(11):822-5.[Foreign language]

189. Weed B, Davis MDP, Felty CL, et al. Autologous platelet lysate product versus placebo in patients with chronic

leg ulcerations: a pilot study using a randomized, double-blind, placebo-controlled trial. Wounds. 2004;16(9):273-82.[Population not of interest]
190. Xu J, Wang Q-Y, Li W. Autologous platelet-rich gel and continuous vacuum sealing drainage for the treatment of patients with diabetic foot ulcer: Study Protocol. Medicine (Baltimore). 2019 Nov;98(46):e17928. PMID: 31725645.[Study design]
191. Zhou X, Yang Z, Wang W, et al. Efficacy of autologous platelet rich gel in the treatment of dabetic foot uclers. Diab New World. 2015;35:82-4.[Foreign language]

Appendix D. Characteristics of Included Studies

Table D.1. Characteristics of included studies for lower extremity diabetic ulcers

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Ahmed, 2017 [1]	RCT in Egypt, 2012 to 2014, out-patient	PRP	Debridement of any necrotic tissue, if present	28 patients aged 43.2±18.2 years, female 28.6%, smokers 61%, hypertension 92%, ischemic heart disease 21%, hyperlipidemia 46%, hemoglobinA_{1c} (HbA_{1c}) 7±0.5 mmol/mol, ankle brachial index 0.83±0.01	Duration of ulcer 12.5±1 weeks, length*width 2.6±0.7 cm*2.4±1.1 cm, heel 25%, metatarsal 57.1%, toe 17.9%, University of Texas diabetic wound classification grade IA 3.6%, grade IIA 17.9%, grade IC 10.7%, grade IIC 67.9%	N/A	None	None
		Antiseptic ointment dressing		28 patients aged 49.8±15.4 years, female 35.7%, smokers 46%, hypertension 89%, ischemic heart disease 29%, hyperlipidemia 57%, HbA_{1c} 6.9±0.6 mmol/mol, ankle brachial index 0.85±0.04	Duration of ulcer 11.5±2.8 weeks, length*width 2.2±1.2 cm*2.6±0.4 cm, heel 28.5%, metatarsal 50%, toe 21.4%, University of Texas diabetic wound classification grade IA 7.1%, grade IIA 14.3%, grade IC 17.9%, grade IIC 60.7%			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Driver, 2006[2]	RCT in United States, out-patient	PRP	1-week run-in period with excision/ debridement	40 patients aged 56.4±10.2 years, female 20%, Caucasian 65%, Hispanic 20%, African American 12.5%, HbA_{1c} 8.1±1.8%	Area 4.0±5.3 cm^2, volume 1.7±4.1 cm^3, heel 45%, toe 32.5%, University of Texas treatment-based diabetic foot classification system grade 1A 100%	N/A	12 weeks	12 weeks
		Saline gel (proprietary, contains an antimicrobial silver compound, NormlGel, Mölnlycke Health Care, Norcross, Ga)		32 patients aged 57.5±9.1 years, female 15.63%, Caucasian 56.25%, Hispanic 28.13%, African American 9.38%, 8.0±1.8% HbA_{1c}	Area 3.2±3.5 cm^2, volume 0.9±1.2 cm^3, heel 31.25%, toe 43.75% University of Texas treatment-based diabetic foot classification system grade 1A 100%			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Elsaid, 2020, RCT[3]	RCT in Egypt, 08/2017 to 02/2019, out-patient	PRP gel	Surgical debridement	12 patients aged 54.7±6.6 years, female 33%, BMI 30±5.4, obesity 33.3%, ischemic heart disease 0, HbA1c 7.62±1%, hypertension 41.6%, serum albumin 4.15±0.26 gm/dl, platelet count 212.9 ± 52	Duration of ulcer 5.25±3.4 months, dorsum and forefoot 67%, heal and sole 33%, neuropathic 50%, non-neuropathic 50%, maximum longitudinal diameter 4.56±2.47 cm, maximum horizontal diameter 5.39±3.37 cm	N/A	Unclear	None
		Normal saline dressing		12 patients aged 55.6±6.5 years, female 50%, BMI 30.7±4.2, obesity 33.3%, ischemic heart disease 8%, HbA1c 8.14±0.89%, hypertension 33.3%, ischemic heart disease 8.3%, serum albumin 4.21±0.42 gm/dl, platelet count 207.4 ± 46	Duration of ulcer 5.58±2.7 months, dorsum and forefoot 75%, heal and sole 25%, neuropathic 66.66%, non-neuropathic 33.33%, maximum longitudinal diameter 4±1.5 cm, maximum horizontal diameter 3.79±1.4 cm	Antibiotics if clinically indicated		

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Game, 2018[4]	RCT in the UK, Denmark and Sweden, 08/30/2013 to 05/03/2017, out-patient	PRP plus standard care	4-week run-in period using the best available standard care per International Working Group of the Diabetic Foot guidelines	132 patients aged 61.9±11.4 years, female 19%, patients with diabetes 85%, HbA_{1c} median(IQR) 8.3%(7·2-9·2:66mmol/mol), GFR (20–30 mL/min per 1.73m^2) 7%, GFR (31–45 mL/min per 1.73m^2) 14%, GFR (46–60 mL/min per 1.73m^2) 27%, GFR (>60 mL/min per 1.73m^2), ankle brachial index (0.5-0.79) 11%, ankle brachial index (0.8-0.99) 23%, ankle brachial index (1.0-1.4) 49%, and ankle brachial index (>1.4) 17%, nephropathy 36%, cardiovascular 42%, cerebrovascular 10% and retinopathy 66% as diabetes-related complications unspecified stage	Area 228.8±207.43 mm^2 Depth of ulcer: superficial 83%, down to tendon 12%, down to bone 5%	N/A	At least 6 weeks	6 weeks

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Usual care (according to International Working Group of the Diabetic Foot guidelines)		137 patients aged 62±11.9 years, female 18%, patients with diabetes 82%, HbA_{1c} median (IQR) 8.2%(7.1-9.0: 67mmol/mol), GFR (20–30 mL/min per 1.73m^2) 2%, GFR (31–45 mL/min per 1.73m^2) 11%, GFR (46–60 mL/min per 1.73m^2) 25%, GFR (>60 mL/min per 1.73m^2) 61%, ankle brachial index (0.5-0.79) 12%, ankle brachial index (0.8-0.99) 17%, ankle brachial index (1.0-1.4) 55%, and ankle brachial index(>1.4) 16%, nephropathy 31%, cardiovascular 43%, cerebrovascular 13% and retinopathy 65% as diabetes-related complications unspecified stage	Area 252.7±226.5 mm^2, Depth of ulcer: superficial 90%, down to tendon 8%, down to bone 2%			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Gude, 2019[5]	RCT in United States, out-patient	PRP with usual care	Usual care for at least 2 weeks. Investigators were instructed to follow the Standard of Care Considerations for Chronic Cutaneous Ulcers as described in 2006 FDA guidance.	66 patients aged 64.7 years, female 22.7%, White 90.5%, African American 6.3%, smokers 57.6%, chronic kidney disease unspecified stage 12.1%, peripheral arterial disease 39.4%, arthritis 3%, transplant recipients 7.6%, immuno-suppression 6.1%	Duration of ulcer 1 month, area 4.1 cm^2, Wagner grade classification grade 1: 4.54%, grade 2: 48.48%, grade 3: 40.91%, grade 4: 6.06%	Antibiotic therapy was administered if clinically indicated.	2 weeks	1 week
		Usual care		63 patients aged 66.9 years, female 22.2%, White 81.8%, African American 7.6%, Asian 3%, smokers 46%, chronic kidney disease unspecified stage 11.1%, peripheral arterial disease 47.6%, arthritis 4.8%, transplant recipients 3.2%, immuno-suppression 6.3%	Duration of ulcer 1 month, area 5.6 cm^2, Wagner grade classification grade 1: 11.11%, grade 2: 30.16%, grade 3: 49.21%, grade 4: 9.52%	Usual care only group could also receive the following: hyperbaric oxygen, negative pressure therapy, and/or cellular/ tissue-based products. Antibiotic therapy was administered if clinically indicated.		

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Kakagia, 2007[6]	RCT in Greece, 12/2004 to 12/2006, out-patient	Oxidized regenerated cellulose/ collagen biomaterial	Debridement of the ulcer followed by standard moist gauze for at least 4 weeks	17 patients aged 58±10 years, female 56.8%, HbA_{1c} 8.9±3.1 mmol/mol, creatinine 1.6±0.9 mg/dl, albumin level 3.7±0.7 g/dl	Duration of ulcer 4.2±2.7 months, area 25.8±15.2 cm^2, foot 100%	N/A	Unclear	Unclear
		PRP		17 patients aged 57±12 years, female 56.8%, HbA_{1c} 8.1±2.8 mmol/mol, creatinine 1.3± 0.7 mg/dl, albumin level 3.6±0.9 g/dl	Duration of ulcer 5±1.5 months, area 28.4±13.6 cm^2, foot 100%			
		Combination of Oxidized regenerated cellulose/collagen biomaterial plus PRP		17 patients aged 61±9 years, female 56.8%, 8.5±4 mmol/mol HbA_{1c}, creatinine 2±1.1 mg/dl, albumin level 3.7±0.6 g/dl	Duration of ulcer 4.7±2 months, area 27.6±17.5 cm^2, foot 100%			
Karimi, 2016[7]	RCT in Iran, 07/2014 to 04/2015, out-patient	PRP-impregnated sterile dressing applied after debridement	Surgical debridement	30 patients, female 20%, smokers 8%, BMI >25: 60%, HbA_{1c} 8.38±1.03 mmol/mol	Area 12.79±14.86 mm^2 depth 19.08±14.01 mm, foot 100%, Wagner grade classification grades 1 or 2 100%	Insulin injection or oral agents for blood sugar control	Unclear	Unclear
		Sterile dressing irrigated with normal saline applied after debridement		30 patients, female 28%, smokers 0%, BMI >25: 48%, HbA_{1c} 7.86±0.88 mmol/mol	Area 14.17±8.52 mm^2, depth 15.08±10.43 mm, Foot 100%, Wagner grade classification grades 1 or 2 100%			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Li, 2015[8]	RCT in China, 01/01/2007 to 12/31/2009, inpatient	PRP plus standard care	"Systemic therapies" including intensive insulin therapy, treatment of any infection, nutritional support, symptomatic management, optimized medications for patients with hypertension and/or dyslipidemia, wound debridement if indicated, and if indicated amputation or vascular reconstruction.	55 patients aged 61.4±13.1 years, female 37.3%, HbA_{1c} 9.8±3.1 mmol/mol, creatinine 88.6±38.2 umol/L, ankle brachial index ≥0.6	Duration of ulcer median (IQR) 30 days (15-90), area median (IQR) 4.1 cm^2 (1.4-11.4), foot 94.8%, Wagner's grade classification grade 2-3 100%	All "systemic therapies" were continued concurrently through the treatment period in all subjects.	0-11 weeks	Unclear
		Standard care		48 patients aged 64.1±9.4 years, female 34.5%, HbA_{1c} 9.8±3 mmol/mol, creatinine 91.1±57.2 umol/L, ankle brachial index ≥0.6	Duration of ulcer median (IQR) 23 days (14-60), area median (IQR) 2.9 (1.0-10.5 cm^2), foot 81.4%, Wagner's grade classification grade 2-3 100%			
Milek, 2017[9]	Comparative observational study, Poland, inpatient and out-patient	PRP covered by hydrocolloid gel dressing	All patients underwent surgical debridement of the wound to remove nonviable tissue to decrease bacterial load and stimulate epithelialization	50 patients aged 70.24±9.15 years, female 32%, smokers 38%, arterial hypertension 52%, coronary heart disease 10%, history of myocardial infarction 4%, chronic kidney disease unspecified stage 30%, creatinine <1mg/dl, atherosclerotic disease of the arteries of the lower extremities 48%	Duration of ulcer 7.3 months, area 1.9 mm^2, lower leg and foot ulcers 100%, University of San Antonio scale; degree I stage C 74%, degree II stage C 26%	N/A	At least 5 months	5 months

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Hydrocolloid gel dressing		50 patients aged 66.32±6.54 years, female 22%, smokers 34%, arterial hypertension 42%, coronary heart disease 14%, history of myocardial infarction 2%, chronic kidney disease unspecified stage 34%, creatinine <1mg/dl, atherosclerotic disease of the arteries of the lower extremities 78%	Duration of ulcer 7.3 months, area 1.9 mm^2, lower leg and foot ulcers 100%, University of San Antonio scale; degree I stage C 68%, degree II stage C 32%			
Saad Setta, 2011[10]	Comparative observational study in Egypt	PRP	Debridement to remove any necrotic tissue if present.	24 patients aged 40-60 years, hypertension 70%, obese 45.8%, smokers 33.3%, pre-albumin level <2.5 g/dl reported for the entire study population	Area mean (range): 10.25 cm^2 (5-21)	N/A	None	None
		Platelet-poor plasma			Area mean (range): 8.5 cm^2 (4-20)			
Saldala-macchia, 2004[11]	RCT in Italy	PRP plus standard care	N/A	7 patients aged 61.1±9.4 years, female 42.9%, duration of diabetes 16.3±7.9 years, HbA_{1c} 9.5±1.7%, ankle brachial index 0.95±0.18	Duration of ulcer 2 months, area , 273±156 mm^2 , foot 100%, Wagner grade classification grade 2/3 ulcers 100%	N/A	Unclear	Unclear
		Standard care		7 patients aged 58.14±7.8 years, female 71.4%, Duration of diabetes 19.7±9.9 years, HbA_{1c} 8.8±1.7%, ankle brachial index 1.02±0.10	Duration of ulcer 2 months, area 170±89 mm^2, foot 100% Wagner grade classification grade 2/3 ulcers 100%			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Serra, 2014[12]	RCT in Italy, 12/2010 to 12/2013, out-patient	Standard treatment, PRP and skin graft	Patients with chronic venous ulcers were treated with usual care and skin graft. Patients with arterial ulcers underwent revascularization for restoration of blood flow after failing 5 months' usual care. Patients with mixed arterial and venous ulcers underwent surgical treatment according to level of Vein incompetence. Patients with diabetic foot ulcers were treated with debridement, antibiotics, and revascularization if necessary as well as skin graft.	8 patients aged 67.8±4.5 years, female 25%, smoker 25%, arterial hypertension 37.5%, heart failure 25%, dyslipidemia 75%, coronary heart disease 12.5%, cerebral vascular disease 25%, chronic obstructive pulmonary disease 25%, chronic kidney disease unspecified stage 12.5%, osteomyelitis 25%, ankle brachial index ≤0.9	Duration of ulcer 1.5 month, area 3.6 cm^2 Rutherford class 5 75%, Class 6 25%	N/A	At least 11 months	11 months
		Standard treatment plus skin grafting only		5 patients aged 68.4±5.5 years, female 60%, smoker 20%, arterial hypertension 40%, dyslipidemia 80%, coronary heart disease 40%, chronic obstructive pulmonary disease 20%, ankle brachial index ≤0.9	Duration of ulcer 1.5 month, area 4.1 cm^2 Rutherford class 5 80%, Class 6 20%			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Singh, 2018[13]	RCT in India, 10/2013 to 07/2015	PRP	N/A	29 patients aged 53.76±10.38 years, female 34.5%, duration of diabetes 10.34±3.71 years	Duration of ulcer at least 1 month, at or below the ankle 100%	N/A	Unclear	None
		Standard therapy		26 patients aged 55.69±10.35 years, female 42.3%, duration of diabetes 11.19±2.3 years				
Xie, 2020, RCT[14]	RCT in China, 2018 to 2019, inpatient and out-patient	Autologous platelet-rich gel	Optimization of glucose control, antibiotic therapy in culture-demonstrated infection	25 patients aged 60.50±8.27 years, female 44%, HbA1c 7.77±1.88%, duration of diabetes 9.12±5.02 years, bacterial infection 84%	Duration of ulcer 21.60±18.50 days, pelma 20%, acrotarsium 16%, toe 40%, crus 24%, wound size 11.80±9.67 cm^2, wound depth 2.12±0.94 cm, classification: I: 6 (24%) II: 10 (40%) III: 7 (24%) IV: 2 (12%)	Strict glucose monitoring and treatment	Unclear	Unclear

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Saline dressings		25 patients aged 61.10±7.90 years, female 43.4%, HbA1c 7.79±2.10%, duration of diabetes 9.78±5.51 years, bacterial infection 86.9%	Duration of ulcer 24.3±16.96 days, pelma 13.04%, acrotarsium 17.39%, toe 39.13%, crus 30.43%, wound size 11.70±7.78 cm^2, wound depth 2.20±0.88 cm, classification: I: 4 (17.39%) II: 9 (39.13%) III: 8 (34.78%) IV: 2 (8.70%)			
Yang, 2017[15]	RCT in China, 01/2016 to 03/2017, inpatient and out-patient	PRP plus usual care	All subjects underwent IV antibiotic treatment (treatment duration dependent on clinical appearance of ulcer), debridement, and strict glucose and blood pressure control.	38 patients aged 40.1±10.2 years, female 55%, history of hypertension 47.40%, history of hyperlipidemia 28.90%, HbA_{1c} 6.8±0.4%, ankle brachial index ≥0.6	Foot 96% and leg 4%, Wagner grade classification grade 3-4 100%	N/A	1 month	1 month
		Usual care only (including topical dressing changes)		38 patients aged 43.7±9.8 years, female 50%, history of hypertension 44.70%, history of hyperlipidemia 31.60%, HbA_{1c} 6.6±0.6%, ankle brachial index ≥0.6				

BMI = body mass index; cm = centimeter; cm^2 = square centime; g/dl = gram/deciliter; GFR = glomerular filtration rate; HbA_{1c} = hemoglobin A_{1c}; HBO = hyperbaric oxygen; IQR = interquartile range; ml/min = milliliter/minute; mmol/mol = millimoles/mole; mL = milliliter; mg/dl = milligram/deciliter; N/A = not available; PRP = platelet-rich plasma; RCT= randomized controlled trial; UCC = usual and customary care; umol/L = micromoles/liter

Table D.2. Characteristics of included studies for lower extremity venous ulcers

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Burgos-Alonso, 2018[16]	RCT in Spain, 08/2014 to 12/2015, out-patient	PRP	Usual care	5 patients aged 76.6±8.7 years, female 60%, patients with diabetes 20%, ankle brachial index ≥0.8-≤1.5, previous injuries 80%	Duration of ulcer at least 6 months, area 7.1±9.1 cm2, leg 100%	Compression therapy (10-40 mm Hg), antibiotic if indicated	0-4 weeks	None
		Usual care – defined by the Basque Health Service as 2-3 times weekly application of waterproof polyurethane dressing		3 patients aged 69.7±11.1 years, female 0%, patients with diabetes 33.3%, ankle brachial index ≥0.8-≤1.5, previous injuries 100%	Duration of ulcer at least 6 months, area 8.9±6.8 cm2, leg 100%			
Elbar-bary, 2020[17]	RCT in Egypt, 07/2018 to 12/2019, out-patient	PRP dressings plus compression	Ulcer debridement and systemic antibiotics were offered in case of gross infection, necrotic tissue, or positive cultures before starting treatment	30 patients aged 45.4±9.35 years, female 13.4%, BMI 25.3±7.3, smokers 46.7%, diabetes 6.7%, previous deep venous thrombosis 40%, previous great venous stripping 26.7%	Duration of current ulcer 6.2±3.1 years, duration of previous ulcer duration 11.2±3.5 years, recurrent ulcers 40%, medial ulcers 73.3%, single ulcer 80.0%, ulcer size: 15.7 ± 7.4 cm^2	Great saphenous vein stripping 26.7%, sclerotherapy 6.7%	1 year	10 months

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Local PRP injections plus compression		30 patients aged 43.4±13 years, female 26.3%, BMI 26.8±4.1, smokers 33.3%, diabetes 3.3%, previous deep venous thrombosis 46.7%, previous great venous stripping 20%	Duration of current ulcer 5.4±2.6 years, duration of previous ulcer duration 9.7±4.6 years, recurrent ulcers 46.7%, medial ulcers 80%, single ulcer 86.7%, ulcer size: 16.5 ± 8.2 cm^2	Great saphenous vein stripping 33.3%, sclerotherapy 13.3%		
		Compression therapy alone		30 patients aged 41.80±13.3 years, female 20%, BMI 27.8±5.6, smokers 40.0%, diabetes 3.3%, previous deep venous thrombosis 36.7%, previous great venous stripping 20%	Duration of current ulcer 6.4±2.8 years, duration of previous ulcer duration 10.5±4.8 years, recurrent ulcers 33.3%, medial ulcers 73.3%, single ulcer 93.3%, ulcer size: 17.8 ± 5.4 cm^2	Great saphenous vein stripping 20%, sclerotherapy 6.7%		
Esca-milla Car-denosa, 2017[18]	RCT in Spain, 09/2009 to 03/2014, out-patient	PRP	6-week standard care and a 2-week run-in period with washing with debridement and compressive bandage.	31 patients aged 65±13.7 years, female 72.7%, ankle brachial index 0.8-1.2	Duration of ulcer 1.5 month, area 13.69±30 cm^2, primary venous insufficiency 4.26%, secondary insufficiency 95.74%	In case of infection systemic antibiotic was allowed	Unclear	None

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Standard care		30 patients aged 69±16.3 years, female 65.9%, ankle brachial index 0.8-1.2	Duration of ulcer 1.5 month, area 16.67±23.87 cm2, primary venous insufficiency 1.82%, secondary insufficiency 98.18%			
Etugov, 2018[19]	Compara-tive obser-vational study in Bulgaria Each patient served as own control (one ulcer treated with PRP, the other with UC)	PRP	N/A	23 patients (46 venous leg ulcers) age range 55-78 years, female 60.8%	Area: 13.68±11.85 cm^2	N/A	Unclear	1 month
		Usual care – treated according to their clinical stage with debridement, antiseptics and "epithelotonic agents" (first cleaned with Octelinin solution, then with Dermazin cream)			Area: 8.83±5.41 cm^2			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Gluk-hov, 2017[20]	RCT in Russia, out-patient	PRP plus collagen	N/A	26 patients aged 63.2±9.4 years, female 84.6%	Duration of ulcer 8.5±6.4 years, area 16.2±4.8 cm2, front surface of lower third leg 15.38%, medial surface of lower third of leg 50%, lateral surface of lower third of leg 15.38%, prednimustine surface of middle third of leg 19.23%, 6th stage chronic venous insufficiency according to international classification of CEAP	N/A	0-1 month	None

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Modern dressings only		19 patients aged 65.3±7.2 years, female 68.4%	Duration of ulcer 5.5±6.3 years, area 10.3±5.8 cm^2, front surface of lower third leg 21.05%, medial surface of lower third of leg 42.11%, prednimustine surface of middle third of leg 36.84%, 6th stage chronic venous insufficiency according to international classification of CEAP			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Collagen		22 patients aged 76.8±8.4 years, female 86.3%	Duration of ulcer 6.5±6.1 years, area 18.1±1.8 cm^2, front surface of lower third leg 45.45%, medial surface of lower third of leg 18.18%, lateral surface of lower third of leg 4.54%, prednimustine surface of middle third of leg 31.82%, 6th stage chronic venous insufficiency according to international classification of CEAP			
		PRP		18 patients aged 51.5±6.2 years, female 100%	Duration of ulcer 7.5±6.3 years, area 17.2±2.8 cm^2, front surface of lower third leg 27%, medial surface of lower third of leg 55%, lateral surface of lower third of leg 16.66%			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Milek, 2019[21]	Compara-tive obser-vational study in Poland	PRP	Successful revascularization	50 patients age range 53-89 years, female 32%, BMI 20.97±2.96, smoker 38%, arterial hypertension 52%, coronary heart disease 10%, history of myocardial infarction 4%, chronic kidney disease 30%, creatinine <1.0 mg/dl, atherosclerosis of lower extremities 48%	Duration of ulcer an average of 7.3 months, area 3.7±1.0 cm^2	N/A	0 to 10 days	None
		Hydrocolloid dressings (AQUACEL Ag Surgical dressing; ConvaTec Inc., Greensboro, NC)		50 patients age range 54-79 years, female 22%, BMI 20.97±2.96, arterial hypertension 42%, coronary heart disease 14%, history of myocardial infarction 2%, smoker 34%, chronic kidney disease 34%, creatinine <1.0 mg/dl, atherosclerosis of lower extremities 78%	Duration of ulcer an average of 7.3 months, area 3.7±1.1 cm^2			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Moneib, 2018 [22]	Compara-tive obser-vational study in Egypt	PRP	N/A	20 patients aged 36.4±10.2 years, female 5%, patients with diabetes 10%, smokers 85%, long standing jobs 70%, ankle brachial index >0.80, primary ulcers 90%, secondary ulcers 10%, incompetent perforators above knee 55%, incompetent perforators below knee 35%, no perforators 2%	Duration of ulcer 6 months, length*width*area 3.28±2.81 cm, 1.99±1.43 cm, and 7.97±16.88 cm^2	N/A	Unclear	Unclear
		Compression using graduated elastic stockings below the knee and dressing using saline and Vaseline gauze		20 patients aged 32.5±7.5 years, patients with diabetes 0%, smokers 85%, ankle brachial index >0.80, primary ulcers 85%, secondary ulcers 15%, incompetent perforators above knee 50%, incompetent perforators below knee 35%, no perforators 15%	Duration of ulcer 6 months, length*width*area 2.3±0.21 cm, 1.65±0.65 cm, 2.94±1.22 cm^2			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Senet, 2003[23]	RCT in France, 01/1998 to 12/2000, out-patient	PRP with hydrocolloid dressing	All patients received "standardized conservative treatment" prior to enrollment	8 patients aged 72.3±10.75 years, female 42.8%, BMI 29.1±6.07, patients with diabetes 14.3%	Duration of ulcer 50.6 months, area 13.7cm^2, CEAP classification C6 100%, deep venous insufficiency 57% , superficial venous insufficiency 57%, popliteal reflux 42.8%, postthrombotic syndrome 42.8%, or homolateral venous stripping 28.5%	Medications for other illnesses were allowed.	4 weeks	Unclear
		Placebo (normal saline solution) with hydrocolloid dressing		7 patients aged 72.3±8.25 years, female 50%, BMI 29±2.9, patients with diabetes 16.7%	Duration of ulcer 70 months, area 10.85 cm^2, CEAP classification C6 100%, deep venous insufficiency 66.6%, superficial venous insufficiency 50%, popliteal reflux 66.6%, postthrombotic syndrome 33.3% or homolateral venous stripping 66.6%			

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Serra, 2014[12]	RCT in Italy, 12/2010 to 12/2013, out-patient	Standard treatment, PRP and skin graft	N/A	54 patients aged 68.3±6.25 years, female 68.5%, ankle brachial index >0.9	Duration of ulcer 1.5 month, area 11.4 cm^2, superficial vein incompetence 44.44%, perforating vein competence 24.07%, superficial and perforating vein incompetence 50%, class 6 of CEAP classification 100%	N/A	At least 11 months	11 months
		Standard treatment plus skin grafting only		51 patients aged 69.1±5.5 years, female 54.9%, ankle brachial index >0.9	Duration of ulcer 1.5 month, area 10.7 cm^2, superficial vein incompetence 31.37%, perforating vein competence 13.73%, superficial and perforating vein incompetence 35.29%, class 6 of CEAP classification 100%			
Yuvasri, 2020[24]	RCT in India, out-patient	PRP dressing	N/A	N/A	Ulcer area 5.1cm^2, lower extremity 100%	Compression stockings	1 week	None

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Zinc oxide (Unna's) paste dressing			Ulcer area 8.37cm^2, lower extremity 100%			

BMI = body mass index; CEAP = Clinical-Etiology-Anatomy-Pathophysiology; cm = centimeter; mg/dl = milligram/deciliter; N/A = not available; PRP = platelet-rich plasma; RCT = randomized controlled trial

Table D.3. Characteristics of included studies for pressure ulcers at any location

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
Singh, 2014 [25]	Comparative observational study in India, 05/2009 to 03/2012, inpatient	PRP	Conventional treatment	25 patients aged 36.84±12.67 years, female 24%, BMI 20.97±2.96, anemia 36%, muscle atrophy 40%, spasticity 4%, contractures 12%	Duration of ulcer 2.42±0.75 months, area 77.7 cm^2, sacrum 64%, trochanter 20%, ischial tuberosity 12%, malleolus 4%, EPUAP grade IV 100%	N/A	Unclear	At least 6 months (6 to 18.5 months)
		Normal saline dressing			Duration of ulcer 2.42±0.75 months, area 22.84 cm^2, sacrum 4%, trochanter 72%, ischial tuberosity 8%, malleolus 4%, heel 8%, medial epicondyle of humerus 4%, EPUAP grade II 44%, grade III 16%, grade IV 40%			
Ucar, 2020[26]	RCT in Turkey, 01/01/2018 to 12/31/2018, inpatient	Dressing with PRP gel	Debridement performed "if necessary"	30 patients aged 68.30±6.37 years, female 47.60%, BMI 25.83±0.99, obesity 33.3%, smoking 57.9%	PUSH total score 8.43±2.34, exudate amount 1.93±0.74, length per width 4.7± 1.78 cm^2, coccyx 100%, EPUAP grade II 100%	N/A	Unclear	None

Author, Year	Country, Study Design, Study Period, Setting	Intervention(s) and comparison	Pretreatment	Baseline patient characteristics	Baseline wound characteristics	Concurrent treatments	Length of followup after complete wound healing	Length of followup after the intervention period
		Normal saline dressing		30 patients aged 67.80±5.86 years, female 52.4%, BMI 25.87±1.04, obesity 30%, smoking 42.1%	PUSH total score 9.53±2.21, exudate amount 2.17±0.70, length x width 4.83± 1.34 cm^2, coccyx 100%, EPUAP grade II 100%			

BMI = body mass index; cm = centimeter; EPUAP = European Pressure Ulcer Advisory Panel; N/A = not available; PRP = platelet-rich plasma; PUSH = Pressure ulcer scale for healing; RCT = randomized controlled trial

Appendix E. Inclusion and Exclusion Criteria and Study Design of Included Studies

Table E.1. Inclusion and exclusion criteria and study design of included studies for lower extremity diabetic ulcers

Author, Year, study design	Methods of patient enrollment	Inclusion criteria	Exclusion criteria	Run-in period
Ahmed, 2017, RCT[1]	NR	Aged 18-80 years; non-healed foot ulcer for more than 6 weeks; Grade I-II stage A or C according to University of Texas diabetic wound classification system.	Ulcer size< 2 cm; the presence of symptoms or signs suggesting infection; ankle brachial pressure index <0.8; pregnant and lactating patients; ejection fraction <30; hemoglobin <10 g/dL; platelet count <150,000/dL; associated lymphedema	NR
Driver, 2006, RCT[2]	NR	Type 1 or type 2 diabetes patients; ages between 18 and 95; ulcer of at least 4-weeks duration.	Ulcer decreased ≥50% in area during 7-day screening period; non-diabetic etiology; blood vessels non-compressible for ankle brachial index testing; evidence of gangrene in ulcer or on any part of the foot; radiographic evidence consistent with diagnosis of acute Charcot foot; radiation or chemotherapy within 3 months of randomization; topical, oral, or IV antibiotic/antimicrobial agents or medications within 48 hours of randomization; growth factor therapy within 7 days of randomization; screening serum albumin level <2.5 g/dL; screening hemoglobin <10.5 mg/dL; screening platelet count < 100 x 109/L; undergoing renal dialysis; known immune insufficiency; known abnormal platelet activation disorders —i.e., gray platelet syndrome; liver disease; active cancer (except remote basal cell of the skin);eating/ nutritional, hematologic, collagen vascular disease, rheumatic disease, or bleeding disorders; history of peripheral vascular repair within the 30 days of randomization; known or suspected osteomyelitis; surgical correction (other than debridement) required for ulcer to heal; index ulcer has exposed tendons, ligaments, muscle, or bone; psychological, developmental, physical, emotional, or social disorder, or any other situation that may interfere with compliance with study requirements and/or healing of the ulcer; history of alcohol or drug abuse within the last year prior to randomization; inadequate venous access for blood draw; religious or cultural conflict with the use of platelet gel treatment; pregnant or lactating women; infected index ulcer.	1 week

Author, Year, study design	Methods of patient enrollment	Inclusion criteria	Exclusion criteria	Run-in period
Elsaid, 2020, RCT[3]	NR	Adult patients, both sexes, non-infected chronic foot ulcer confined to one anatomical site, ulcer non-healing for ≥ 12 weeks.	Chronic limb ischemia, evidence of osteomyelitis in the affected foot, exposed tendons, ligaments, or bones at the base of ulcer, received radiotherapy or chemotherapy at the time of study or within 3 months of its beginning and patients having low platelet count (<150,000/mm^3), low serum albumin level (<2.5 gm/dL), or low hemoglobin level (<10 g/dL).	NR
Game, 2018, RCT[4]	Enrollment continued until the targeted number of patients (269) was randomized.	Age ≥ 18 years; diabetes (as defined by WHO criteria) complicated by one or more foot ulcers, and a baseline HbA_{1c} of no more than 12% (108 mmol/mol); ulcers below the level of the malleoli; hard to heal ulcers, meaning that the cross-sectional area decreased by less than 50%, and the cross-sectional area of the index ulcer was 50–1000 mm2, at the end of the 4-week run-in period.	Cross-sectional area of the index ulcer had increased by at least 25% or had decreased by less than 50% during the 4-week run-in period, or was either smaller than 50 mm^2 or larger than 1000 mm^2 at the end of the 4-week run-in period; clinical signs of infection of the index ulcer or other reason to suspect an infection at randomization; if a revascularization procedure in the affected limb was planned or had been undertaken within the 4 weeks before the baseline visit; foot ulcer had been treated with growth factors, stem cells, or an equivalent preparation within the 8 weeks before the baseline visit or there was a need for continued use of negative pressure wound therapy; hemoglobin < 105 g/L at screening; diagnosis of sickle-cell anemia, hemophilia, thrombocytopenia (<100 × 109/L), or any other clinically significant blood dyscrasia; known potential infectivity of blood products, including known HIV and hepatitis; receipt of renal dialysis or an estimated glomerular filtration rate < 20 mL/min per 1.73 m2; current treatment with cytotoxic drugs or with systemically administered glucocorticoids or other immunosuppressants; unlikely to comply with the need for weekly visits; involvement in another interventional clinical foot ulcer healing trial within the 4 weeks before the baseline visit; ulcers were confined solely to the interdigital clefts.	Four weeks

Author, Year, study design	Methods of patient enrollment	Inclusion criteria	Exclusion criteria	Run-in period
Gude, 2019, RCT[5]	NR	18 years or older, Medicare as their primary insurance coverage, type 1 or type 2 diabetes, Wagner grade 1 through 5 diabetic foot ulcer located on the foot or heel at least 1 month old; debrided ulcer size between 0.5 and 50 cm^2 (not stratified); have a demonstrated offloading regimen have demonstrated inadequate progress toward healing (as determined by the provider) following active treatment at the investigative site for a minimum of 2 weeks immediately prior to screening; and have adequate venous access for periodic blood draws.	Chemotherapeutic agents; malignancy in the wound area; serum albumin < 2.5 g/dL; platelet count < 100 x 109/L; and/or hemoglobin <10.5 g/dL; presence of another wound that could interfere with treatment of the index ulcer.	NR
Kakagia, 2007, RCT[6]	NR	Diabetic patients with significant soft tissue defects of the foot, for at least 3 months; all target ulcers >=2.5 cm in any one dimension after debridement.	Previous treatment with vacuum, hyperbaric oxygen, corticosteroid, immunosuppressive agents, radiation, and growth factors; anemia; presence of cellulitis; venous stasis; inadequate perfusion determined by toe pulses of <40; osteomyelitis; malignancy in the wound	NR
Karimi, 2016, RCT[7]	Eligible patients referred to the institution.	Diabetic foot ulcers grades 1 or 2 (Wagner classification); hemoglobin > 10 gr/dL; platelets > 100000 mm3	Immunosuppressive and contraceptive medications; known coagulopathy, immune deficiency; cancer; signs of ischemia around the ulcer, sepsis, osteomyelitis, deep vein thrombosis, limb paralysis; chemotherapy; history of spinal cord injury and stroke	NR
Li, 2015, RCT[8]	Enrollment stopped after the targeted numbed of patients finished treatment.	Diabetic patients over 18 years of age; at least one cutaneous ulcer, which did not improve significantly after at least 2-week standard treatments; 2-3 Wagner's grade for the diabetic foot ulcers; ankle brachial index value 0.6; platelet count ≥ 100,000 /mm3; no history of various drug or dressing allergies.	Nondiabetic, diabetic acute complications; uncontrolled systemic or local infection; severe cardiovascular, lung, liver or kidney diseases; systemic treatment medications like corticosteroids, immunosuppressive agents, as well as radiation or chemotherapy at the target sites within 3 weeks before this study; broken behavioral competence and compliance.	NR
Milek, 2017, Comparative observational study [9]	NR	Patients with ischemic diabetic foot syndrome complicated ulcer < 5 cm; lower limb ischemia clinically and radiologically proven by CT angiography; creatinine < 1.0 mg/dl.	< 18 years of age; ulceration > 5 cm; venous ulcer and ulcer without ischemia.	NR
Saad Setta, 2011, Comparative observational study[10]	NR	Age between 40 and 60; type I or type II diabetes – and in a controlled status; normal peripheral platelet count (>150 000/mm^3).	Radiation or chemotherapy within 3 months of study; serum albumin level <2.5 g/dl or hemoglobin <10.5 mg/dl or platelet count <100 × (10)/1; peripheral vascular disease; biopsy was taken from each ulcer and if the bacterial count exceeded 105 organisms per gram of tissue patient; ulcers that had exposed tendons, ligaments or bone.	NR

Author, Year, study design	Methods of patient enrollment	Inclusion criteria	Exclusion criteria	Run-in period
Saldalamacchia, 2004, RCT[11]	NR	Grade II/III ulcers according to Wagner; lasting for at least 8 weeks; no signs of infection at recruitment.	None	NR
Serra, 2014, RCT[12]	NR	Clinical and instrumental diagnosis of vascular lower limbs ulcer; duration > 6 weeks; indication for skin graft. For chronic venous ulcers: older than 20 years with a clinical and instrumental diagnosis of venous ulcer (class 6 of CEAP classification); presence of venous reflux flow; ankle brachial pressure index >0.9; size 2.5-10 cm2 and >50% granulation tissue on the wound bed. For diabetic foot ulcers: patients with peripheral arterial disease; intermittent claudication and diagnosis of type II diabetes confirmed by either a resting ankle brachial index of ≤0.90 and a ≥10 mmHg decrease in ankle pressure measured 1 minute after walking to maximal distance and a positive ultrasound evaluation of lower limb arteries with the evidence of atherosclerotic occlusive or stenotic lesions in the peripheral circulation, and a baseline pain-free walking distance of at least 50 m.	None	NR
Singh, 2018, RCT[13]	NR	Patients with diabetic foot ulcer of area >l cm2, at or below the ankle, for at least 4 weeks; in the case of more than one ulcer or bilateral ulcers, one index ulcer, typically the largest one, was selected for intervention (the remaining ulcers received the standard care and were not included in the study); type 1 or type 2 diabetes; no gross necrotic material present.	Patients with clear indication for surgery such as vascular reconstruction or gangrene; ulcer with exposed bone or bone involvement; platelet count <140,000/µl; co-existing medical conditions such as renal failure, blood dyscrasia and communicable diseases.	NR
Xie, 2020, RCT[14]	NR	Diabetic ulcer wounds combined with sinus tract, inflammatory exudation without pus, wounds not healed for more than 1 week without any granulation tissue growth, wound depth ≥ 0.5 cm, controlled random blood sugar level in the range of 100-160 mg/d.	Blood system diseases, hemoglobin <110 g/L, platelet count <100 x 10^9/L, hypertension, heart disease, mental illness, diabetic stage IV patients with multiple terminal complications of diabetes and refusal to donate blood for the procedure.	NR

Author, Year, study design	Methods of patient enrollment	Inclusion criteria	Exclusion criteria	Run-in period
Yang, 2017, RCT[15]	NR	Lower-extremity ischemic ulcers; good blood supply in the region adjacent to the ischemic ulcers lesions; lower extremity segmental blood pressure (ankle brachial index ≥ 0.6)	Significant dysfunctions in heart, brain, lung, kidney and other organs; serious complications associated with diabetes and systemic infection; poor general conditions or allergies to the study drugs; use of immunosuppressive agents; autologous platelet-rich gel allergies.	NR

CEAP = Clinical-Etiology-Anatomy-Pathophysiology; cm = centimeters; cm^2 = square centimeters; CT = computed tomography; g/Dl = grams/deciliter; g/L = grams/liter; HbA_{1c} = hemoglobin A_{1c}; L = liter; m = meter; mg/dL = milligrams/deciliter; mL = milliliter; mm = millimeter; mm^2 = square millimeter; mm^3 = cubic millimeter; mmHg = millimeter of mercury; mmol/mol = milimole/moles; NR = not reported; RCT = randomized controlled trial; WHO = World Health Organization

Table E.2. Inclusion and exclusion criteria and study design of included studies for lower extremity venous ulcers

Author, Year, study design	Methods of patient enrollment	Inclusion criteria	Exclusion criteria	Run-in period
Burgos-Alonso, 2018, RCT[16]	NR	Age ≥ 40 years old; either sex; having a venous leg ulcer > 8 weeks without response to conventional treatment; having normal cell counts and hematocrit values; a venous leg ulcer of <7.7 cm in diameter; ankle brachial index ≥0.8 and <1.5	Pregnancy; breastfeeding; fertile age and not using contraceptive methods; chronic use of immunosuppressants or anti-retroviral drugs; clotting disorders, chronic infectious diseases; treatment with radiotherapy or chemotherapy; active infection or fever at the beginning of the study.	NR
Elbarbary, 2020, RCT[17]	NR	Adult patients with chronic venous leg ulcers (class C6 of CEAP classification), without adequate healing tendency (<50% healing) for at least the last 6 weeks, ankle brachial index ≥ 0.9, and a platelet count of 150,000 to 450,000/mm^3.	Renal, hepatic or cardiac failure, uncontrolled diabetes mellitus, malignancy, connective tissue disorder, pregnancy, lactation, local active infection, ulcers with bone or tendon exposure, or anti-platelets, steroids, or immunosuppressive drug administration, a history of poor compliance to compression therapy.	NR
Escamilla Cardenosa, 2017, RCT[18]	NR	Patients with venous ulcers of >6 weeks; clinical course with ankle-arm index 0.8-1.2 who had not been operated for their venous insufficiency; normal blood count and platelet count > 150,000 platelets/mL; patients without long-standing treatment with non-steroidal anti-inflammatories, corticosteroids, anti-aggregates or anticoagulants	Patients suffering from cancer-related, liver or kidney disease in addition to poorly controlled diabetic patients (HbA_{1c} > 7.5%).	Two weeks
Etugov, 2018, Comparative observational study[19]	NR	2 venous leg ulcers with similar localization and clinical stage.	None	NR
Glukhov, 2017, RCT[20]	NR	Chronic venous insufficiency of the 6th international stage (CEAP classification); small and medium sized trophic ulcers with area of the wounds < 20 cm2.	None	NR
Milek, 2019, Comparative observational study[21]	NR	Ulcer size <= 5 cm2; lower limb ischemia clinically and radiologically evidenced with CT angiography; recent successful revascularization; and blood creatinine <1.0 mg/dL.	Ischemic ulcers	NR
Moneib, 2018, Comparative observational study[22]	NR	Patients with chronic venous leg ulcers for more than 6 months of duration who have not received any previous treatment; wound size <10 cm2; ankle brachial index of >0.80.	Saphenofemoral incompetency; uncontrolled diabetes; active infection; ischemic heart disease; compromised immune function; coagulation disorders; radiation or chemotherapy within 3 months of the study; history of cancer; and pregnant or lactating females.	NR

Author, Year, study design	Methods of patient enrollment	Inclusion criteria	Exclusion criteria	Run-in period
Senet, 2003, RCT[23]	NR	Patients with one or more venous leg ulcers; >18 years; ulcer duration at least 2 months reference ulcer surface 3 to 50 cm2; no tendency for healing in the past 2 months; clinical findings consistent with venous disease and confirmed at venous duplex ultrasound scanning during the preceding 6 months; no arterial insufficiency; platelet count > 150,000/mm3; hemoglobin >11 g/dL, and albumin concentration >35 g/L; diabetes included if glucose concentration < 2 g/L.	Pregnancy; allergy to hydrocolloid dressings; uncontrolled systemic disease; serum creatinine > 180 mol/L; corticosteroid or cytotoxic medications; limited physical capacity; ulcers with exposed tendons or bones; infected ulcer; history of poor compliance with compression therapy; positive HIV, hepatitis C, or human T lymphocyte virus I or II; presence of antibodies against hepatitis B surface antigen or hepatitis B core antigen; serologic test results positive for syphilis; abnormal LFTs.	NR
Serra, 2014, RCT[12]	NR	Clinical and instrumental diagnosis of vascular lower limbs ulcer; duration > 6 weeks; indication for skin graft. For chronic venous ulcers: older than 20 years with a clinical and instrumental diagnosis of venous ulcer (class 6 of CEAP classification); presence of venous reflux flow; ankle brachial pressure index >0.9; size 2.5-10 cm2 and >50% granulation tissue on the wound bed. For diabetic foot ulcers: patients with peripheral arterial disease; intermittent claudication and diagnosis of type II diabetes confirmed by either a resting ankle brachial index of ≤0.90 and a ≥10 mmHg decrease in ankle pressure measured 1 minute after walking to maximal distance and a positive ultrasound evaluation of lower limb arteries with the evidence of atherosclerotic occlusive or stenotic lesions in the peripheral circulation, and a baseline pain-free walking distance of at least 50 m.	None	NR
Stacey, 2000, RCT[27]	All patients attending the leg ulcer clinic	Patients with proven venous ulceration, with no other possible cause for the poor healing in their leg ulcer, venous refilling time was less than 25 seconds.	None	NR
Yuvasri, 2020, RCT[24]	NR	Chronic venous ulcers of the lower extremity for more than 6 months, and having an ulcer area of 1 cm × 1 cm to 5 cm × 5 cm.	Ulcers of less than 6 months duration and of other etiology such as arterial ulcer, diabetic ulcer, neuropathic and vasculitic ulcers, osteomyelitis affecting the area of the ulcer, exposed tendons or bones, infection, and patients receiving anticoagulants, antiplatelet drugs or bleeding diathesis.	NR

CEAP = Clinical-Etiology-Anatomy-Pathophysiology; cm = centimeter; cm^2 = square centimeters; CT = computed tomography; g/dL = grams/deciliter; g/L = grams/Liter; HbA_{1c} = hemoglobin A_{1c}; m = meter; mg/dL = milligrams/deciliter; mm^3 = cubic millimeter; mmHg = millimeter of mercury mol/L = moles/liter; NR = Not reported; RCT = randomized controlled trial.

Table E.3. Inclusion and exclusion criteria and study design of included studies for pressure ulcers at any location

Author, Year, study design	Methods of patient enrollment	Inclusion criteria	Exclusion criteria	Run-in period
Singh, 2014, Comparative observational study[25]	NR	Traumatic spinal cord injury with injury below C4 with at least two pressure ulcers, pressure ulcers that had not shown any improvement, a minimum regular followup of 6 months, older than 18 years.	Only a single pressure ulcer; associated malignant disorder; non-traumatic spinal cord lesion.	NR
Ucar, 2020, RCT[26]	NR	Aged 18 years old or older, normal signs of renal function, albumin, platelets, blood glucose, normal mobility is semi or fully limited, presented to the palliative department due to surgical intervention, coccyx stage II pressure ulcer with no immunodeficiency diagnosis.	NR	NR

NR = not reported; RCT = randomized controlled trial

Appendix F. Description of Management Without PRP of the Included Studies

Table F.1. Description of management without PRP for lower extremity diabetic ulcers

Author, Year	Comparison intervention	Frequency	Duration
Ahmed, 2017[1]	Conventional treatment: Daily dressing which involves cleaning the wound with normal saline, and then povidone iodine 10% ointment was applied and covered by sterile dressing.	Daily	3 months
Driver, 2006[2]	Standard care: Normal saline gel applied to the wound following wound bed preparation. A contact layer dressing was applied over the saline gel, followed by the non-absorbent side of a foam dressing, and covered with the absorbent side of a foam dressing before being secured.	Twice a week	12 weeks
Elsaid, 2020[3]	Regular saline dressing: Wounds prepared by surgical debridement, then, irrigated with normal saline. Daily dressing with normal saline only.	Daily	20 weeks
Game, 2018[4]	Standard care: As per International Working Group of the Diabetic Foot guidelines, including formal assessment of ulcer and surrounding skin, provision of any necessary offloading, debridement, appropriate dressing products, appropriate antibiotic therapy, nutrition and self-care, optimal glycemic control, revascularization if deemed clinically necessary, and continued close observation	Once a week	20 weeks
Gude, 2019[5]	Usual and Customary Care: Any treatment modality or combination of available treatment modalities so long as the treating clinician and patient considered it to be in the best interest to heal the chronic ulcer.	Once weekly	12 weeks
Kakagia, 2007[6]	Oxidized regenerated cellulose with collagen biomaterial: Debridement of the ulcer followed by standard moist gauze treatment. Oxidized regenerated cellulose and collagen biomaterial (Promogran, Johnson & Johnson).	Once a week	8 weeks
Karimi, 2016[7]	Simple Dressing: After debridement, the wounds were irrigated with normal saline and dressed with sterile gauzes.	Every other day	3 weeks
Li, 2015[8]	Standard treatment: Topical washing, cleaning, draining, and debridement of callous and necrotic tissue, as well as dressing changes with Suile Wound Dressing (Hedonist Biochemical Technologies Co. Ltd., Taipei,Taiwan) which contained Vaseline mostly and was occlusive, and then bandages.	Once every 3 days	12 weeks
Milek, 2017[9]	Conventional treatment: Surgical debridement. Wounds were covered with hydrocolloid AQUACEL dressings.	Once every 10 days	3 months
Saad Setta, 2011[10]	Platelet-poor plasma (PPP): After applying the PPP, Vaseline gauze was applied followed by a dressing.	Twice a week	20 weeks
Saldalamacchia, 2004[11]	Standard care. No other information provided.	Once a week	5 weeks
Serra, 2014[12]	Standard treatment and skin graft: Debridement, antibiotics, revascularization (if it is necessary), and skin graft. Through debridement, the wound margins were extended approximately 2-3 mm into healthy, bleeding, soft non-hyperkeratotic skin. The tie-over dressing was removed after 3 to 5 days, immobilization was stopped after 7 to 10 days; a compressive bandage was not applied. Treated area was sealed with an occlusive protective dressing.	Once	1 month
Singh, 2018[13]	Standard therapy: Debridement, antibiotics, and aseptic wound dressing were used after cleaning with normal saline solution on alternate days.	Every other day	4 weeks
Xie, 2020[14]	Conventional wound dressing: Wounds disinfected, debrided by removing the inactive and necrotic tissue. The debridement process was carried out carefully, moving from the shallow to the deep areas. Cleaning the wound with normal saline and scratching the wound lightly until it bled. Then 0.1% rivanor (2-ethoxy-6, 9-aminoacridine lactate) gauze was applied, and the wound was covered with a sterile dressing.	Twice a week	8 weeks

Author, Year	Comparison intervention	Frequency	Duration
Yang, 2017[15]	Standard treatment: Subcutaneous injection of low-molecular-weight heparin calcium at 0.1 ml/10 kg for anticoagulation once every 12 hours for 7 days; daily IV antibiotic infusion, with the treatment time depending on the picture of wound healing and bacterial culture, as well as intravenous infusion of compound vitamin solution along with nutritional support. And complete debridement was performed to remove the erosions and necrotic tissues to expose healthy tissues. The normal saline containing metronidazole solution and gentamicin was used to repeatedly rinse the ulcers/wounds, and a drainage catheter was inserted into the site for decompression. The ulcers/wounds were covered with sterile dressing, which was replaced every other day until healing.	Every other day.	30 days

IV = intravenous; mm = millimeter, PPP = platelet-poor plasma

Table F.2. Description of management without PRP for lower extremity venous ulcers

Author, Year	Comparison intervention	Frequency	Duration
Burgos-Alonso, 2018[16]	Standard care: The usual care that was applied two to three times a week to maintain a moist healing environment. Waterproof polyurethane dressing (Mepilex) was used to control exudate. Compression therapy with a tubular bandage (Tubilast SC) that was specially designed for vascular problems to facilitate return circulation through a gradual and decreasing compression from the foot to the compression stockings, with the ability to apply 10-40 mmHg of pressure.	2.5 times per week	9 weeks
Elbarbary, 2020[17]	Standard treatment: Standard compression with class II elastic stockings, treatment of the underlying venous pathology.	NR	NR
Escamilla Cardenosa, 2017[18]	Standard treatment: Dressing with gauze soaked in saline with a second cover of dry gauze and single layer pressure bandage (Wet to dry).	Once a week	24 weeks
Etugov, 2018[19]	Conventional treatment: Debridement, antiseptics and epithelotonic agents. The ulcer was first cleaned with Octenilin (Aqua valde purificata, Glycerol, Ethylhexylglycerin, Octenidine. HCl) with subsequent dressing with Dermazin cream (1%silver sulfadiazine).	Not reported	30 days
Glukhov, 2017[20]	Modern dressings: Polyurethane foam dressings, hydrogels, alginates were used as well as, water-solubility hydrocolloids-kolloidnye bandage, a change of which occurred every 2-4 days, in some cases every 7 days. Compression therapy was also used which included wearing the elastic knit of the second degree of compression.	Once every 2 4 days	2 months
	Collagen: Collagen membrane soaked in 0.9% NaCl solution and cut in the shape of the wound. The prepared membrane was laid on the wound surface and stitched.	Once every 5-7 days	2 months
Milek, 2019[21]	Conventional treatment: Surgical debridement. The wound was covered with a hydrocolloid AQUACEL dressing.	Once every 10 days	1 month
Moneib, 2018[22]	Conventional treatment: Compression using graduated elastic stockings below the knee and dressing using saline and Vaseline gauze.	Once a week	6 weeks
Senet, 2003[23]	Standard topical treatment and compression with placebo (normal saline solution): After the wound was cleansed with normal saline solution, the appropriate volume of placebo was applied to the wound surface with a syringe. Standardized dressing and compression bandages were replaced after each application. Dressings used were hydrocolloid (Comfeel Plus Opaque; Coloplast, Fontenay-Sous-Bois, France). Standard graded compression, with cotton bandages (Nylex; Laboratoires URGO, Chenove, France) and elastic bandages (Biflex Plus Forte; Laboratoires Thuasne, Levallois-Perret, France).	Three times per week	12 weeks
Serra, 2014[12]	Venous ulcer group: Standard treatment and skin graft: Skin grafting and elastic bandaging. Postoperative immobilization for 2 to 5 days in the position of maximal skin graft stretching.	Once	1 month
Stacey, 2000[27]	Conventional therapy: A piece of plain unbleached gauze placed over the surface of the ulcer, this was then soaked with placebo. The gauze was cut to the exact size of the ulcer and it had been predetermined that this would deliver a volume of 150 uL of the solution per cm^2 of ulcer. The dressing was then covered with a Viscopaste bandage (Smith & Nephew) from the base of the toes to just below the knee, followed by two Comprilan bandages (Beiersdorf) from the base of the toes to just below the knee. A Tubigrip stockingette (Seton) was placed over the bandages to keep them in position.	Twice weekly	9 months
Yuvasri, 2020[24]	Unna’s paste dressing: Ulcers covered with gauze impregnated with Unna’s paste which was in turn covered with a sterile gauze-pad followed by a sterile roller bandage. This dressing was left in place for 1 week. Compression stockings used.	Once a week	4 weeks

cm^2 = square centimeter; HCl = hydrochloride acid; uL = microliter; mmHg = millimeter of mercury; NaCL = sodium chloride

Table F.3. Description of management without PRP for pressure ulcers at any location

Author, Year	Comparison intervention	Frequency	Duration
Singh, 2014[25]	Conventional therapy: Debridement and saline dressing.	Twice a week	Minimal 5 weeks
Ucar, 2020[26]	Serum physiologic gas dressing: Ulcers washed and cleaned with serum physiologic. Wound debridement before dressing if necessary. Ulcers closed with sterile gauze and fixed with cotton tapes.	Once daily	2 months

Appendix G. Risk of Bias

Table G.1. Risk of bias (Cochrane Risk of Bias tool for randomized trials [RoB 2.0]) for included randomized controlled trials studies

Author, Year	ROB from randomization process	ROB due to deviations from intended interventions	ROB due to missing outcome data	ROB in measurement of outcomes	ROB in selection of the reported results	Overall ROB
Ahmed, 2017[1]	Moderate risk	Moderate risk	Low risk	Low risk	Moderate risk	Moderate risk
Burgos-Alonso, 2018[16]	High risk	Moderate risk	Low risk	Moderate risk	Low risk	High risk
Driver, 2006[2]	Low risk	Low risk	High risk	Low risk	Low risk	High risk
Elbarbary, 2020[17]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Elsaid, 2020[3]	Low risk	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk
Escamilla Cardenosa, 2017[18]	Moderate risk	Moderate risk	Low risk	Moderate risk	Low risk	Moderate risk
Game, 2018[4]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Glukhov, 2017[20]	Moderate risk	High risk	High risk	Moderate risk	Moderate risk	High risk
Gude, 2019[5]	Low risk	Moderate risk	High risk	Moderate risk	Moderate risk	High risk
Kakagia, 2007[6]	Low risk	High risk	High risk	Low risk	Low risk	High risk
Karimi, 2016[7]	Moderate risk	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk
Li, 2015[8]	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Saad Setta, 2011[10]	High risk	High risk	Low risk	Moderate risk	Moderate risk	High risk
Saldalamacchia, 2004[11]	Moderate risk	High risk	High risk	Moderate risk	Moderate risk	High risk
Senet, 2003[23]	Moderate risk	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk
Serra, 2014[12]	Moderate risk	High risk	High risk	Moderate risk	Moderate risk	High risk
Singh, 2018[13]	Moderate risk	High risk	High risk	Moderate risk	Low risk	High risk
Stacey, 2000[27]	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk
Ucar, 2020[26]	Moderate risk	Moderate risk	Low risk	Moderate risk	Moderate risk	Moderate risk
Xie, 2020[14]	Moderate risk	Moderate risk	Low risk	Moderate risk	Moderate risk	Moderate risk
Yang, 2017[15]	Moderate risk	High risk	High risk	Moderate risk	Moderate risk	High risk
Yuvasri, 2020[24]	Moderate risk	Low risk	High risk	Moderate risk	Moderate risk	High risk

ROB = risk of bias

Table G.2. Risk of bias (Newcastle-Ottawa Scale) for included comparative observational studies

Author, Year	Representativeness of study cohort	Ascertainment of exposure	Outcome not present before the exposure	Comparability between groups	Outcome data source	Independent blind assessment of outcome	Loss during followup	Overall ROB
Etugov, 2018[19]	Moderate risk	Moderate risk	Low risk	High risk	Moderate risk	Moderate risk	Moderate risk	High risk
Milek, 2017[9]	Low risk	Moderate risk	Low risk	High risk	Moderate risk	High risk	Moderate risk	High risk
Milek, 2019[21]	Moderate risk	Low risk	Low risk	High risk	Low risk	High risk	Moderate risk	High risk
Moneib, 2018[22]	Low risk	Low risk	Low risk	High risk	Moderate risk	High risk	Moderate risk	High risk
Singh, 2014[25]	Low risk	Low risk	Low risk	High risk	Low risk	High risk	Moderate risk	High risk

ROB = risk of bias

Appendix H. Description of PRP Formulation and Application

Table H.1. Description of PRP formulation and application for lower extremity diabetic ulcers

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Ahmed, 2017[1]	Surgical and Clinical Pathology department	NR, gel, PRP pellet after centrifugation diluted in 3 ml of plasma and autologous thrombin and 10% calcium gluconate , incubation at 37°C for 15-30 minutes, 10% $CaCl_2$ added, became gelatinous during 10-15 minutes incubation in Petri dish	NR, 1500rpm, 3500 rpm, N/A, NR, 5 min, 5 min, N/A, NR, gel	PRP gel, secondary non-absorbing dressing and elastic compression band (Surepress®), activated, external	20 ml, 1-1.2 million/µL, pellet from 20 ml of blood, with 3 ml of plasma, bi-weekly, until closure or occurrence of infection or 3 months	NR	NR, NR, NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Driver, 2006[2]	Wound care clinic	NR, NR, AutoloGel™, reagents added to PRP to form the gel within 15-30 seconds	NR, NR, N/A, N/A, patients in treatment group had an average hematocrit 40.6% at baseline; 40.1% at endpoint; control patients had 39.2% at baseline, 38.5% at endpoint, 1.5 min, N/A, N/A, NR, gel	PRP, contact dressing and foam dressing (non-absorbent side and also absorbent side), barrier cream on area surrounding the wound, activated, external	Up to 20 ml, NR, NR, bi-weekly at 3-4 days intervals, bi-weekly for 12 weeks (at least 24 times) or until healing occurred	Fixed ankle foot orthoses that could be removed for the dressing change and at night. Crutches or a walker used for added safety	Exclusion criteria: chemotherapy within 3 months of randomization, topical oral or intravenous antibiotic /antimicrobial agents or medications have been used within 2 days (48 hours) of randomization, patient has received growth factor therapy (e.g., autologous platelet-rich plasma gel, becaplermin, bilayered cell therapy, dermal substitute, extracellular matrix) within 7 days of randomization., NR, NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Elsaid, 2020[3]	General surgery	NR, NR, at the time of application, 20% calcium chloride was added to the PRP to form platelet gel ready for application	NR, 3600 rpm, 2400 rpm, N/A, NR, NR, N/A, NR, gel	PRP gel was applied, covered with Vaseline gauze, few layers of sterile gauze, and non-compressible bandage, activated, external	20ml, NR, NR, 2/week, 20 weeks or until complete healing occurred	NR	Excluded if chemotherapy or radiotherapy at the time of study or within 3 months from the beginning

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Game, 2018[4]	Diabetic foot clinics	Three-layered gel, WBC included, venous blood into a LeucoPatch device, then transferred to a LeucoPatch Centrifuge, spun according to an automatic and prespecified program. The final three-layered LeucoPatch was then removed from the device, cut and put onto the ulcer with the leucocyte side adjacent to the surface of the ulcer.	LeucoPatch Centrifuge (Reapplix ApS; Birkerød, Denmark), NR, N/A, N/A, NR, 20 min, N/A, N/A, NR, gel	LeucoPatch was covered by a low adherent, knitted viscose rayon primary dressing (Tricotex, Smith & Nephew, London) UK) and a protective secondary dressing, non-activated, external	18 ml, NR, NR, weekly, 20 weeks	Offloading (classified into 9 types: bedbound or immobile, normal footwear, normal footwear plus fitted insoles or inserts, fitted footwear or orthoses, padded slipper or shoe, removable device or cast for foot, removable cast or device for lower leg)	Exclusion: Current treatment with cytotoxic drugs or with systemically administered glucocorticoids or other immunosuppressants, NR, NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Gude, 2019[5]	NR	NR, NR, Aurix System – pharmaceutical grade reagents, PRP added to mixing chamber, inverted for 15-30 seconds to produce gel	Aurix System, NR, N/A, N/A, NR, approximately 1 min, N/A, N/A,NR, gel	Aurix gel, nonadherent contact dressing, absorbent layer, activated, external use	5-20ml, NR, NR, weekly or bi-weekly (first two weeks biweekly, then weekly and at clinician's discretion), 12-14 treatments, if not healed completely but at least 50% reduction was achieved after 12 weeks, treatment could continue for up to 20 weeks	Offloading as recommended per standard of care considerations for chronic cutaneous ulcers as described in the 2006 FDA Guidance	Exclusion: chemotherapeutics, during study use of materials containing any active ingredient in was prohibited (e.g. methylene blue, gentian violet, zinc oxide, silver, hydrogen peroxide, acetic acid, or iodine) in the PRP plus standard care group, NR, following off-loading regimen
Kakagia, 2007[6]	NR	Growth factors delivered with Gravitational Platelet Separation System, NR, N/A	Gravitational Platelet Separation System, (GPS, Biomet) NR, NR, NR, NR, NR, NR, NR, NR, NR	Vapor permeable film on PRP layer; NR, external	At least 55 ml, NR, NR, weekly, 8 weeks	NR	Exclusion: steroid use, immunosuppressive agents, growth factors, NR, NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Karimi, 2016[7]	NR	NR, NR, N/A	Digital full-R5702 model (Eppendorf, Germany), 200 rpm, N/A, N/A, NR, 10 min, N/A, N/A, NR, dressing	Sterile gauze impregnated with PRP, dry sterile gauzes and fixed using cotton bands, non-activated, external	30 ml, 100 000/ml, 5 ml, one dressing with PRP only, followed by ordinary dressing and saline every other day, 3 weeks	NR	Exclusion criteria: no immunosuppressive and contraceptive medications, no chemotherapy, patients instructed not to use any other material on the ulcer and to avoid dressing change without informing the researcher, whole treatment period
Li, 2015[8]	Department of Endocrinology and Metabolism, Diabetic Foot Care Center	NR, NR, PRP mixed with thrombin and calcium gluconate (10:1) at the bed site and trickled onto the wound bed through a three-way pipe	NR, 313g, 1252g, N/A, NR, 4 min, 6 min, N/A, NR, gel	PRP trickled on the wound bed, Suile dressing, bandages, activated, external	20-100 ml, NR, NR, every 3 days, if the wound area reduction did not reach 80% or higher, or ulcers were larger than $1cm^2$ at 2 weeks after the application, treatments were repeated, 12 weeks	NR	Exclusion: systemic treatment medications like corticosteroids, immunosuppressive agents, as well as radiation or chemotherapy at the target sites within 3 weeks before this study, NR, NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Milek, 2017[9]	NR	NR, WBC poor, N/A	NR, NR, NR, NR, NR, NR, NR, NR, NR, dressing	PRP dressing was covered with hydrocolloid dressing, activated, external	18 ml, NR, NR, 4 times repeated after 10, 20 and 30 days of treatment, 4 treatments total	NR	NR, NR, NR
Saad Setta, 2011[10]	Department of Plastic Surgery	NR,NR, PRP mixed with bovine thrombin (0.2 ml for every 1ml PRP) and $CaCl_2$ 10% (0.1ml) added to PRP in Petri dish	NR, 1007 g, 447.5 g, N/A, NR, NR, NR, N/A, NR, gel	PRP, Vaseline gauze, dressing, activated, external	10 ml, NR, NR, bi-weekly(3-4 days apart), up to 20 weeks	Patients were recommended to avoid pressure on ulcer area and provided with special shoes with moulded insoles, elevation of feet recommended during sitting or lying down	Exclusion: no chemotherapy within 3 months of study, NR, NR
Saldalamacchia, 2004[11]	NR	NR, NR, NR	NR, NR, NR, NR, NR, NR, NR, NR, NR, gel	NR, activated, external	NR, NR, NR, weekly, 5 times	NR	NR, NR, NR
Serra, 2014[12]	NR	NR, PRP centrifuged to separate platelet concentrate and platelet-poor	NR, 399 g, 959 g, N/A, NR, 11 min, 11 min, N/A, NR, gel	Gauze impregnated with PRP was placed on the ulcer surface (skin	15 ml, 1-1.5 million/uL, NR, weekly, first after surgery and then weekly for a	NR	NR, in diabetic and arterial ulcers postoperative immobilization for 5 to 10 days in the

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
		plasma. Platelet concentrate was placed in a mixer, whereas PPP immediately frozen at -80 °C (stored in refrigerator at 4 °C overnight to slowly thaw and produce cryoprecipitate). The next morning the thawed PPP centrifuged (704 g for 11 minutes); PPP and cryoprecipitate were separated, the latter was transferred into the bag with platelet concentrate. average fibrinogen concentration in the		graft) and supported by two pieces of dry sterile gauzes and fixed using cotton Bands, no compression in diabetic ulcers, in other compression bandage applied, activated, external	month		position of maximal skin stretching, the tie-over dressing removed after 3 to 5 days, immobilization stopped after 7 to 10 days, treated area sealed with an occlusive protective dressing; in chronic venous ulcers: elastic bandaging at the end of surgical procedure, postoperative immobilization for 2 to 5 days in the position of maximal skin stretching, in mixed ulcers - patients had application of a multicomponent, multilayer, compression bandage with pressure of 20-30 mmHg

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
		cryoprecipitate must be equal to : 642·7 (mg/U) – factor VIII (>70 IU/L)					
Singh, 2018[13]	Surgery and Pathology Department	NR, NR, N/A	REMI P-24 microprocessor controlled centrifuge (REMI Lab Instruments, India), 2000-3200rpm, N/A, N/A, NR, 10-15 min, N/A, N/A, NR, injectate	PRP injectate, dressing used but not described in further detail, activated (calcium chloride or thrombin, (0.2ml $CaCl_2$:1ml PRP); intralesional injection	Up to 20ml, NR, 3-4ml of PRP on 5x10cm ulcer, weekly	NR	NR, NR, NR
Xie, 2020[14]	Department of Plastic and Reconstructive Surgery	NR, NR, PRP and thrombin+$CaCl_2$ mixture were combined at a ratio of 10:1 to obtain the gel	KYZ-2 medical centrifuge, 2000 rpm, 4000 rpm, N/A, 4mins, 6mins, N/A, NR, gel	Gel was placed into the wound tract and on the ulcer to cover the wound and covered with a layer of Vaseline Petrolatum Gauze and a pressure bandage was applied, activated, external	20 ml, NR, 3ml, every 3 days, 8 weeks	NR	NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, third centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, third centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Yang, 2017[15]	Orthopedic Surgery Department	NR, NR, PRP mixed with 1 ml $CaCl_2$ + 1000U of thrombin at a ratio of 1 ml:200U	NR, 1500 bpm, 3600 bpm, N/A, NR, 10 min, 10 min, N/A, NR, gel	PRP gel and sterile dressing, activated, external	10 ml, NR, NR, every other week, until healing - 30 days maximum	NR	Exclusion: immunosuppressants, NR, NR

bpm = beats per minute; $CaCl_2$ = calcium chloride; °C = centigrade; cm = centimeter; g = grams; µL = microliter; mg/U = milligram/Unit; mL = milliliter; mmHg = millimeter of mercury; min = minute; NR = not reported; PC = platelet concentrate; PPP = platelet-poor plasma; PRP = platelet-rich plasma; rpm = revolutions per minute; U = unit; WBC = white blood cell.

Table H.2. Description of PRP formulation and application for lower extremity venous ulcers

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, radius of rotor, autologous or allogenic, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any peri-procedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Burgos-Alonso, 2018[16]	NR	NR, NR, gel formed by adding 50ul of $CaCl_2$/ml of PRP (final conc.22mM)	NR, 580g, N/A, N/A, normal blood hematocrit at collection, 8 min, N/A, N/A, NR, gel	PRP gel, foam polyurethan or hydrofiber as secondary dressing, compression stockings 10-40 mmHg, activated, external	9-30ml, NR, NR, weekly, up to 9 weeks	NR	Exclusion: OCP use, chronic use of immunosupressants, anti-retrovirals, chemotherapy, NR, NR
Elbarbary, 2020[17]	Department of Vascular Surgery	NR, NR, NR, NR	80-2 Electronic Laboratory Medical Centrifuge, Shanghai, China, 2500 rpm, 3500 rpm, N/A, NR, 10 minutes, 5 minutes, N/A, N/A, NR	Nonabsorbent dressing (Vaseline gauze), single layer of elastic bandage from the toes to just below the knee, class II elastic stockings, activated, group 1-dressing, group 2 injection	20-45 mL, NR (but 30 ml concentrated to 3-5ml), NR, every 2 weeks, up to 8 weeks	NR	Excluded if using antiplatelet drugs, steroids or immunosuppressant

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, radius of rotor, autologous or allogenic, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any peri-procedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Escamilla Cardenosa, 2017[18]	NR	NR,WBC poor , PRGF Endoret method	PRGF Endoret BTI system, NR, none, none, NR, , none, none, NR, gel	Platelet gel, selective micro-adherence dressing =elastic network of silicon-covered polyamide, secondary dressing of gauze and single layer pressure bandage, activated with 10% calcium chloride, external	NR, NR, NR, weekly, 24 weeks	NR	Patients without long-standing treatment with non-steroidal anti-inflammatories, corticosteroids, anti-aggregates or anticoagulants, NR, NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, radius of rotor, autologous or allogenic, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any peri-procedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Etugov, 2018[19]	Department of Dermatology and Venerology	NR, NR, NR	RegenLab 80-2C, 3100/min, N/A, N/A, NR, 4 min, N/A, N/A, NR, injectable	Occlusive dressing with sterile gauze for 5 days, followed by silver sulfadiazine 1% cream every second day, non-activated, injection intralesional	10 ml, NR, 0.2 ml PRP per cm^2, single application, NR	NR	NR, NR, NR
Glukhov, 2017[20]	Surgery	NR, NR, NR	NR, NR, NR, NR, NR, NR, NR, NR, NR, NR	Two PRP groups: 1: PRP only 2:collagen drugs and PRP - first dressing infiltrated with PRP, covered with collagen membrane, gauze with saline, non-activated, external	NR, NR, NR, every 5-7 days until the complete healing or max 60 days	NR	NR, NR, NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, radius of rotor, autologous or allogenic, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any peri-procedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Milek, 2019[21]	NR	NR, NR, NR	NR, NR, NR, NR, NR, NR, NR, NR, gel	Dressing fortified with PRP (PRP Regeneris Medical; North Attleboro) covered with hydrocolloid Aquacel dressing MA and hydrocolloid , activated, external	18 ml, NR, NR, repeated after 20 and 30 days of treatment, 3 times in 30 days	NR	NR, NR, NR
Moneib, 2018[22]	Vascular surgery, dermatology outpatient clinics	NR, NR, PRP mixed with Ca gluconate (0.1ml per ml PRP) and kept in incubator at 37°C to form the gel	Beckman J-6M Induction Drive Centrifuge, 277g, 277 g, N/A, NR, 10 min, 5 min, N/A, NR, gel	PRP gel and nonabsorbent dressing (Vaseline gauze) for 3 days, elastic stockings, activated (0.1 ml Calcium gluconate at each 1 ml PRP), external	10 ml, NR, 1 ml/dose, 1ml/weekly 6 weeks (6 doses total)	Elevation of affected limb	Exclusion: chemotherapeutics use in the past 3 months, NR, NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, radius of rotor, autologous or allogenic, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any peri-procedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Senet, 2003[23]	NR	NR, NR, NR	NR, 5000g, 300g, 1500g NR, 7 min, 5 min, 10 min, NR, dressing	PRP and hydrocolloid and compression cotton bandages, elastic bandages, non-activated, external	Max 7ml/kg, $5x10^8$/ml, 10 mil platelets/cm^2 of wound surface, 3 times a week, 3 times/week for up to 12 weeks	NR	Exclusion: systemic treatment with corticosteroid agents or cytotoxic drugs, NR; NR

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, radius of rotor, autologous or allogenic, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any peri-procedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Serra, 2014[12]	NR	NR, PRP centrifuged to separate platelet concentrate and platelet-poor plasma. Platelet concentrate was placed in a mixer, whereas PPP immediately frozen at -80 °C (stored in refrigerator at 4 °C overnight to slowly thaw and produce cryoprecipitate). The next morning the thawed PPP centrifuged (704g for 11 minutes), PPP and cryoprecipitate were separated, the latter was transferred into the bag with platelet concentrate. average fibrinogen concentration in the cryoprecipitate must be equal to: 642.7 (mg/U) – factor VIII (>70 IU/L)	NR, 399g, 959g, N/A, NR, 11 min, 11 min, N/A, NR, gel	Gauze impregnated with PRP was placed on the ulcer surface (skin graft) and supported by two pieces of dry sterile gauzes and fixed using cotton Bands, no compression in diabetic ulcers, in other compression bandage applied, activated, external	15 ml, 1-1.5 million/uL, NR, weekly, first after surgery and then weekly for a month	NR	NR, in diabetic and arterial ulcers postoperative immobilization for 5 to 10 days in the position of maximal skin stretching, the tie-over dressing removed after 3 to 5 days, immobilization stopped after 7 to 10 days, treated area sealed with an occlusive protective dressing, in chronic venous ulcers: elastic bandaging at the end of surgical procedure, postoperative immobilization for 2 to 5 days in the position of maximal skin stretching, in mixed ulcers - patients had application of a multicomponent, multilayer, compression bandage with pressure of 20-30 mmHg

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, radius of rotor, autologous or allogenic, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any peri-procedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Yuvasri, 2020[24]	Department of Dermatology	After centrifugation, PRP gel appeared in the center of the vacutainer tube and was transferred with forceps to the wound after separation of adhered RBC	NR, 3000 rpm, N/A, N/A, NR, 15mins, N/A, N/A, NR, gel	Gel was covered with sterile gauze and sterile gauze pad, held in place with a roller bandage, non-activated, external	10ml, NR, 2.5ml, weekly, 4 weeks	NR	Patients receiving anticoagulation of antiplatelet drugs were excluded

Ca = calcium; Cl = chloride; $CaCl_2$ = calcium chloride; °C = centigrade; cm^2 = square centimeter; g = grams; mg/U = milligram/Unit; min = minute; mL = milliliter; mmHg = millimeter of mercury; N/A = not applicable; NR = not reported; OCP = oral contraceptive; PDGF = platelet-derived growth factor; PC = platelet concentrate; PPP = platelet-poor plasma; PRP = platelet-rich plasma; rpm = revolutions per minute; WBC = white blood cell

Table H.3. Description of PRP formulation and application for pressure ulcers at any location

Author, Year	PRP provider	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, first centrifuge speed, second centrifuge speed, hematocrit %, first centrifuge time, second centrifuge time, radius of rotor, formulation)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration)	PRP offloading procedures	Any periprocedural restrictions regarding medications, any activity restrictions after procedure, duration activity restrictions after procedure
Singh, 2014[25]	NR	NR, NR, PRP agitated in a vacutainer tube, mixed 6:1 with $CaCl_2$ (10%) for 5-10s	Cryfuge 6000i, 2000 rpm, 2000 rpm, N/A, NR, 10 min, 10 min, N/A, NR, gel	PRP gel, non-absorbent Vaseline gauze, dry cotton gauze and cotton pad, transparent drape, activated (PRP: $CaCl_2$ 10% (6:1), external	30 ml, NR, NR, bi-weekly, minimum 10 times	Patients were mobile and were actively participating in routine recreational and rehabilitation activities	NR, NR, NR
Ucar, 2020[26]	Department of Nursing	NR, NR, after blood centrifugation, PRP gel was separated from the tube with sterile forceps and placed on sterile gauze.	NR, 2000 rpm, N/A, N/A, 5 minutes, N/A, N/A, gel	Gauze impregnated with PRP placed on the wound, fixed with cotton tapes	10 ml, NR, NR, every 3 days, 2 months	NR	NR

Ca = calcium; Cl = chloride; $CaCl_2$ = calcium chloride; ml = milliliter; NR = not reported; N/A = not applicable; PRP = platelet-rich plasma; rpm = revolution per minute; s = seconds; WBC = white blood cell

Appendix I. Wound Measurement and Assessment Methods

Table I.1. Wound measurement and assessment methods for lower extremity diabetic ulcers

Author, Year	Method of wound assessment	Inter- or intra-rater checks of wound measurements.	Frequency and time points for assessment	Blinding of assessors	Definition of "failure to heal" and "completely healed" wound
Ahmed, 2017[1]	NR	NR	Twice weekly for 12 weeks	Yes	
Driver, 2006[2]	Wounds were assessed and measured (length, width, and depth) using a metric tape measure.	NR	Twice a week for 12 weeks; then Week 1, 3, 7, and 11 after the 12-week treatment..	Yes	Completely healed wound: 100% epithelialization
Elsaid, 2020[3]	The wound was measured with tape in terms of length and width and pictures were taken for documentation.	NR	Weekly for 20 weeks	NR	
Game, 2018[4]	Wound area was assessed from digital images of acetate tracings using software, Image J.	NR	At Week 4, 12, 16, 20, and 26 of the 26-week study period.	Yes	Completely healed wound: 100% epithelialization in the absence of discharge for 4 weeks
Gude, 2019[5]	Imaged the wound with digital photography; measured length, width, depth; established a "clock face" over the wound bed in which 12:00 was oriented toward the patient's head. The length and width of the wound were to be always considered from 12:00 to 6:00 and from 3:00 to 9:00, to reduce subjectivity.	NR	Weekly for 13 weeks	NR	Completely healed wound: 100% epithelialization in the absence of drainage without need for wound dressings
Kakagia, 2007[6]	Ulcer wounds were photographed digitally with a reference marker of scale in three dimensions. Computerized planimetry was used to compare the progression of wound healing in the three groups.	NR	Weekly for 8 weeks	Yes	
Karimi, 2016[7]	Ulcer depth and surface area were measured using a digital camera. All photos were taken from a distance of 30 cm while a transparent, millimeter scaled ruler was placed near the ulcers.	NR	Weekly for three weeks	NR	
Li, 2015[8]	Ulcers were examined and photographed with the picture-processing software ImageJ.	NR	Once every three days for 12 weeks.	Yes	Completely healed wound: Complete epithelial cover in the absence of discharge

Author, Year	Method of wound assessment	Inter- or intra-rater checks of wound measurements.	Frequency and time points for assessment	Blinding of assessors	Definition of "failure to heal" and "completely healed" wound
Milek, 2017[9]	Appearance, size and depth of ulcer wounds were examined with a 50 MHz ultrasound probe. The formation of granulation tissue was examined histologically.	NR	Every 10 days for one month, then at 3-month and 6-month followup	NR	
Saad Setta, 2011[10]	Wound evaluation was carried out by measuring the ulcer's dimensions (length and width) using metric tapes.	NR	Weekly for 20 weeks	NR	
Saldalamacchia, 2004[11]	Wound area was estimated by measuring the largest and shortest dimensions of the wound.	NR	Weekly for 5 weeks	Yes	
Serra, 2014[12]	Wound healing was assessed by means of direct ulcer tracing onto clear plastic sheet and subsequent computerized planimetry.	NR	At baseline and 2nd, 6th, and 12th month of the 1-year study period.	NR	
Singh, 2018[13]	Wound assessment was done according to the Bates Jensen Wound Assessment Tool.	NR	Weekly for 4 weeks	NR	Completely healed wound: full skin coverage of the wound
Xie, 2020[14]	A camera was used to record the wound changes over time. The ulcer area was calculated according to the formula for the most appropriate shape (triangle, square, rectangle, or ellipse). Histologic evaluation was performed using a microscopy with hematoxylin and eosin staining.	NR	Weekly for 8 weeks	NR	Cured wounds: sinus closure and wound healing.
Yang, 2017[15]	Wound area was calculated by the online image recognition system.	NR	At 1 month after treatment.	NR	Completely healed wound: 100% epithelialization

cm = centimeter; MHz = megahertz; NR = not reported

Table I.2. Wound measurement and assessment methods for lower extremity venous ulcers

Author, Year	Method of wound assessment	Inter- or intra-rater checks of wound measurements.	Frequency and time points for assessment	Blinding of assessors	Definition of "failure to heal" and "completely healed" wound
Burgos-Alonso, 2018[16]	The surface area of the venous leg ulcer was measured using ImageJ software to analyze photographs of the wounds. Two blinded measures were performed for each venous leg ulcer, and a mean of both areas was used.	Inter- or intra-rater checks	Weekly for 9 weeks, or as required	NR	
Elbarbary, 2020[17]	Wound area was measured using "ulcer tracing technique" by applying a sterile transparent cellophane paper on the ulcer and delineating the edge by an indelible pen, a graph paper divided into 1 cm^2 squares was used to count the delineated area.	NR	Once monthly for 12 months	Yes	
Escamilla Cardenosa, 2017[18]	The ulcer area was measured using the Kundin method formula: Area = Length x Width x 0.785.	NR	Baseline and the end of 24- week treatment	NR	
Etugov, 2018[19]	NR	NR	Every 15 days for one month.	NR	
Glukhov, 2017[20]	The ulcer area was measured using vector-raster redactron Spotlight Pro 10, after photographing wounds.	NR	At Day 7, 14, 30, and 60 of the 60-day study period..	NR	
Milek, 2019[21]	Appearance, size and depth of ulcer wounds were examined with a 50 MHz ultrasound probe. The formation of granulation tissue was examined histologically.	NR	Every 10 days for one month.	NR	
Moneib, 2018[22]	The ulcer area was calculated and photographs were taken using a digital camera. The ulcer area was calculated using the formula: Area = length x width x 0.785.	NR	Weekly for 6 weeks.	NR	Completely healed wound: 100% epithelialization

Author, Year	Method of wound assessment	Inter- or intra-rater checks of wound measurements.	Frequency and time points for assessment	Blinding of assessors	Definition of "failure to heal" and "completely healed" wound
Senet, 2003[23]	Surface evaluation was assessed by measuring wound width and length and with four successive numerical pictures at each visit. Pictures were obtained with a camera. Focal distance was set at 30 cm throughout the study. A standardized semi-rigid frame with colorimetric (white and black) and metric scales were used. Once the standardized frame was placed on the wound, it entirely framed the picture when the camera was placed at 90 degrees and 30 cm from the ulcer. The camera was turned so that the optical axis remained the same. Reflections were eliminated, because light came from the left for the first two pictures and from the right for the last two pictures. The metric scale of the frame was used to resize the picture on the computer. Reflections were eliminated by superimposition of the resized pictures on the computer. Wound outlines were manually determined on the computer on the resized and recorded pictures Each picture was subsequently computer-processed, and the final wound area and perimeter were taken as the mean of the measurements calculated from the four pictures.	Intra-rater checks	Once every 4 weeks for 16 weeks	NR	Completely healed wound: 100% epithelialization.
Serra, 2014[12]	Wound healing was assessed by means of direct ulcer tracing onto clear plastic sheet and subsequent computerized planimetry.	NR	At baseline and 2nd, 6th, and 12th month of the 1-year study period.	NR	
Stacey, 2000[27]	Ulcers were photographed, traced and the size assessed by planimetry.	NR	Weekly for 9 months	NR	
Yuvasri, 2020[24]	The greatest length and the greatest breadth were measured using a thread and a scale (the clock face method). Digital photographs were taken before the start and at the end of treatment.	NR	Weekly for 4 weeks	NR	Completely healed wound: complete closure of the ulcer.

cm^2 = square centimeter; MHz = megahertz; NR = not reported

Table I.3. Wound measurement and assessment methods for pressure ulcers at any location

Author, Year	Method of wound assessment	Inter- or intra-rater checks of wound measurements.	Frequency and time points for assessment	Blinding of assessors	Definition of "failure to heal" and "completely healed" wound
Singh, 2014[25]	Wound evaluation was done clinically by wound measurement and photographs. The wound surface area was calculated by linear measurement of length and width with a measuring tape. Wound healing was assessed by Pressure Ulcer Scale for Healing (PUSH). A punch biopsy was taken to monitor histopathological signs of healing in the entire grade III and IV pressure ulcers.	NR	Weekly for 5 weeks, then monthly for 6 months	NR	
Ucar, 2020[26]	Ulcers were observed and visualized with a mobile phone camera and measured with a disposable wound ruler.	NR	Once every three days for two months	NR	

NR = not reported, PUSH = Pressure Ulcer Scale for Healing

Appendix J. Summary of Findings of Included Studies

Table J.1. Summary of findings by included studies for lower extremity diabetic ulcers

Author, Year, study design*	Intervention(s) and comparator	Summary of findings
Ahmed, 2017, RCT[1]	PRP vs. Antiseptic ointment dressing	PRP was associated with significantly higher complete healing rate and lower wound infection than antiseptic ointment dressing.
Driver, 2006, RCT[2]	PRP vs. Saline gel	PRP was not statistically different with saline gel dressing on number of patients with completed closure, wound recurrence, and adverse events. There were 6 serious adverse events in the PRP group and 17 in the saline gel group.
Elsaid, 2020, RCT[3]	PRP gel vs. Normal saline dressing	Compared with saline dressing, PRP was associated with significantly more percentage reduction in the longitudinal and horizontal dimensions of the ulcers, though there was no significant difference on complete wound healing and maximal longitudinal and horizontal dimensions of the ulcers. No adverse event was reported.
Game, 2018, RCT[4]	PRP plus standard care vs. Usual care	PRP was associated with significantly increased number of complete healing, reduced wound area, and time to wound healing, compared with standard care. There was no significant difference on pain reduction, minor or major amputations, adverse events, or serious adverse events. The most common serious adverse events were diabetic foot infection.
Gude, 2019, RCT[5]	PRP with usual care vs. Usual care	Significantly more patients treated by PRP achieved completed healed wounds than those treated by standard of care. There was no significant difference on adverse events. 7 cases of serious adverse events were reported (3 in the PRP group and 4 in the standard care group).
Kakagia, 2007, RCT[6]	Oxidized regenerated cellulose/collagen biomaterial vs. PRP vs. Combination of Oxidized regenerated cellulose/collagen biomaterial plus PRP	The combination of PRP and oxidized regenerated cellulose/collagen biomaterial was associated with significant more reduction of wound area and depth, compared with PRP only or oxidized regenerated cellulose/collagen biomaterial only. The changes of wound area and depth were not significantly different between PRP and oxidized regenerated cellulose/collagen biomaterial. There was no statistical difference on complete wound healing. No adverse events were reported in any of the three groups.
Karimi, 2016, RCT[7]	PRP impregnated sterile dressing applied after debridement vs. Sterile dressing irrigated with normal saline applied after debridement	PRP was associated with significant more reduction of wound area and depth, compared with simple dressing. There was no statistical difference on complete wound healing. No adverse events were reported in the PRP group.
Li, 2015, RCT[8]	PRP plus standard vs. Standard care	PRP was associated with significantly more complete wound healing than standard care. No death was reported in the PRP group.
Milek, 2017, Comparative observational study[9]	PRP covered by hydrocolloid gel dressing vs. Hydrocolloid gel dressing	All wounds in the PRP group were healed after 6-month post-treatment; while only small wounds in the standard care group were healed.

Author, Year, study design*	Intervention(s) and comparator	Summary of findings
Saad Setta, 2011, RCT[10]	PRP vs. Platelet-poor plasma	The healing time for PRP was significantly shorter than platelet-poor plasma. There was no statistical difference on number patients with healed wounds.
Saldalamacchia, 2004, RCT[11]	PRP plus standard care vs. Standard care	Compared with standard care, PRP significantly reduce wound area after 5 weeks of treatment. There was no significant difference on number of patients with complete healing. No adverse effects were reported in the PRP group.
Serra, 2014, RCT[12]	Standard treatment, PRP and skin graft vs. Standard treatment plus skin grafting only	There was no significant difference on number of complete healing between PRP and standard care.
Singh, 2018, RCT[13]	PRP vs. Standard therapy	PRP was associated with significant reduction of wounds and time to complete wound closure, compared with standard care. No adverse events were reported in the PRP group
Xie, 2020, RCT[14]	Autologous platelet-rich gel vs. Saline dressings	Compared with saline dressing, PRP significantly reduced length of hospitalization. There was no significant difference in complete wound healing between the two groups. No adverse events was reported.
Yang, 2017, RCT[15]	PRP plus usual care vs. Usual care only (including topical dressing changes)	PRP was associated with significant shorter wound healing time, better pain reduction, compared with standard care. There was no difference on adverse events.

PRP = platelet-rich plasma; RCT = randomized controlled trial

Table J.2. Summary of findings by included studies for lower extremity venous ulcers

Author, Year, study design*	Intervention(s) and comparator	Conclusion
Burgos-Alonso, 2018, RCT[16]	PRP vs. Usual care	There was no significant reduction of wound area, number of healed wounds, and pain reduction. No significant difference on adverse events was reported.
Elbarbary, 2020, RCT[17]	PRP dressing plus compression vs. Local PRP injection plus compression vs. Compression therapy	Compared with compression therapy, PRP dressings and PRP injection were associated with significantly more wound area reduction, complete wound healing. Compared with PRP dressing, PRP injections significantly improved complete wound healing rate. There was no significant difference on wound recurrence or adverse events.
Escamilla Cardenosa, 2017, RCT[18]	PRP vs. Standard care	Compared with standard care, PRP led to significant reduction of wound area and paint. No adverse events were reported.
Etugov, 2018, Comparative observational study[19]	PRP vs. Usual care – treated according to their clinical stage with debridement, antiseptics and "epithelotonic agents" (first cleaned with Octelinin solution, then with Dermazin cream)	Compared with standard care, PRP was associated with significantly more reduction of wound surface area.
Glukhov, 2017, RCT[20]	PRP plus collagen vs. Modern Dressings only vs. Collagen vs. PRP	The combination of PRP and collagen was associated with significantly more patients with completely healing than PRP alone or dressing only. There was no significant difference on wound healing between PRP only and dressing only, or between PRP plus collagen and collagen only.
Milek, 2019, Comparative observational study[21]	PRP vs. Hydrocolloid dressings (AQUACEL Ag Surgical dressing; ConvaTec Inc., Greensboro, NC)	PRP was associated with significant reduction of wound area, compared with hydrocolloid AQUACEL dressing. No observable complications were reported in the PRP group.
Moneib, 2018, Comparative observational study[22]	PRP vs. Compression using graduated elastic stockings below the knee and dressing using saline and Vaseline gauze	Compared with conventional treatment, PRP was associated with significant reduction of wound area and significant more patients with complete wound healing. No adverse events were reported in the PRP group.
Senet, 2003, RCT[23]	PRP with hydrocolloid dressing vs. Placebo (normal saline solution) with hydrocolloid dressing	There was no statistical difference between the two groups on number of complete wound healing, wound recurrence, reduction of wound area, or adverse events.
Serra, 2014, RCT[12]	Standard treatment, PRP and skin graft vs. Standard treatment plus skin grafting only	There was no significant difference on number of complete healing between PRP and standard care.
Stacey, 2000, RCT[27]	Autologous platelet lysate vs. Placebo buffer solution	Compared with placebo buffer solution, platelet lysate was not associated with significant difference on healed wounds, and time to complete wound closure. There was no adverse event related to platelet lysate. The number of withdrawals were similar between the two group.

Author, Year, study design*	Intervention(s) and comparator	Conclusion
Yuvasri, 2020, RCT[24]	PRP dressing vs. Zinc oxide (Unna's) paste dressing	There was no significant difference on complete wound healing and wound area reduction.

PRP = platelet-rich plasma; RCT = randomized controlled trial

Table J.3. Summary of findings by included studies for pressure ulcers at any location

Author, Year, study design*	Intervention(s) and comparator	Conclusion
Singh, 2014, Comparative observational study[25]	PRP vs. Normal saline dressings	PRP was associated with significantly more reduction of wound surface area than saline dressing. There was no significant difference between the two groups on decrease of PUSH (Pressure Ulcer Scale for Healing) scores.
Ucar, 2020, RCT[26]	Dressing with PRP gel vs. Normal saline dressings	Compared with serum physiologic dressing, PRP significantly reduced more wound area.

PRP = platelet-rich plasma; PUSH = Pressure Ulcer Scale for Healing; RCT = randomized controlled trial

Appendix K. Adverse Events

Table K.1. Adverse events: PRP vs. management without PRP for lower extremity diabetic ulcers

Comparison	Outcomes	Findings	Study Design
PRP vs. Management without PRP	Dermatological AE	Rate Ratio: 1.32; 95% CI: 0.21 to 8.07; I^2 =0.00%	2 RCTs[2, 5]
	Hematologic AE	Rate Ratio: 1.23; 95% CI: 0.55 to 2.74; I^2 =N/A	1 RCT[4]
	Other AE	Rate Ratio: 1.00; 95% CI: 0.14 to 7.10; I^2 =N/A	1 RCT[15]
	Neurological AE	Rate Ratio: 0.88; 95% CI: 0.32 to 2.41; I^2 =N/A	1 RCT[15]
	Rheumatology AE	Rate Ratio: 1.25; 95% CI: 0.34 to 4.65; I^2 =N/A	1 RCT[15]
	Serious AE	Rate Ratio: 0.93; 95% CI: 0.63 to 1.37; I^2 =86.90%	2 RCTs[2, 4]
	Death	Rate Ratio: 0.66; 95% CI: 0.19 to 2.29; I^2 =0.00%	2 RCTs[2]
	Total AE	Rate Ratio: 1.09; 95% CI: 0.92 to 1.31; I^2 =0.00%	9 RCTs[1-6, 13-15]
	Withdrawal	RR: 0.94; 95% CI: 0.61 to 1.45; I^2 =0.00%	7 RCTs,[2-5, 7, 13, 14] 1 Comparative observational study[9]
	Withdrawal due to AE	RR: 0.94; 95% CI: 0.12 to 7.51; I^2 =0.00%	5 RCTs,[2, 3, 5, 13, 14] 1 Comparative observational study[9]

AE = adverse event; CI = confidence interval; N/A = not applicable; RCT = randomized controlled trial; RR = relative risk

Table K.2. Adverse events: PRP vs. management without PRP for lower extremity venous ulcers

Comparison	Outcome	Findings	Study Design
PRP vs. Management without PRP	Dermatological AE	Rate Ratio: 0.89; 95% CI: 0.30 to 2.66; I^2 =0.00%	4 RCTs[16, 17, 20, 23]
	Hematological AE	Rate Ratio: 1.75; 95% CI: 0.06 to 52.16; I^2 =N/A	1 RCT[23]
	Total AE	Rate Ratio: 1.36; 95% CI: 0.44 to 4.21; I^2 =0.00%	5 RCTs[16-18, 20, 23] 2 Comparative observational studies[21, 22]
	Withdrawal	RR: 1.07; 95% CI: 0.28 to 4.02; I^2 =0.00%	5 RCTs[16-18, 23, 24]
	Withdrawal due to AE	RR: 0.78; 95% CI: 0.14 to 4.22; I^2 =0.00%	5 RCTs[16-18, 23, 24]

AE = adverse event; CI = confidence interval; N/A = not applicable; RCT = randomized controlled trial; RR = risk ratio

Table K.3. Adverse events: autologous platelet lysate for lower extremity venous ulcers

Comparison	Outcome	Findings	Study Design
Autologous platelet lysate vs. placebo buffer solution	Any AE	0 related to lysate	1 RCT[27]

AE = adverse events

Appendix L. Patient Characteristics Commonly Considered for the Initiation and Continuation/Discontinuation of PRP

Table L.1. Patient characteristics commonly considered for the initiation and continuation/discontinuation of PRP for lower extremity diabetic ulcers

Author, Year	ABI	Platelet count	Hemoglobin A_{1c} (HbA_{1c})	Wound grade	Ulcer size	Chronicity	Study Treatment Duration	Definition of wound closure
Ahmed, 2017[1]	>0.8	>150,000/µL					12 weeks	
Driver, 2006[2]	"Adequate perfusion" on ABI (not defined)	>100,000/µL	<12.0%	Grade 1A	0.5-20 cm^2	4 weeks	Up to 12 weeks	Completely healed wound: 100% epithelialization
Elsaid 2020[3]		<150,000/µL		Patients with exposed tendons, ligaments, or bones at the base of ulcer were excluded		12 or more weeks	Up to 20 weeks	Not defined
Game, 2018[4]	0.5-1.4 OR the dorsalis pedis or tibialis posterior pulse was palpable	>100,000/µL	<12.0%		0.5-10 cm^2	4 week run-in period prior to treatment, however chronicity not defined	20 weeks	Completely healed wound: 100% epithelialization in the absence of discharge for 4 weeks
Gude, 2019[5]		>100,000/µL		Wagner grade 1-5 diabetic food ulcer	0.5-50 cm^2	2 weeks of failed conservative care	12 weeks	Completely healed wound: 100% epithelialization in the absence of drainage without need for wound dressings
Kakagia, 2007[6]					>2.5 cm in diameter	Failure of 4 weeks of debridement followed by standard moist gauze treatment	8 weeks	

Author, Year	ABI	Platelet count	Hemoglobin A_{1c} (HbA_{1c})	Wound grade	Ulcer size	Chronicity	Study Treatment Duration	Definition of wound closure
Karimi, 2016[7]		>100,000/µL		1-2				
Li, 2015[8]	>0.6	>100,000/µL		Grade 2-3		Failure of 2 weeks of standard care	12 weeks	Completely healed wound: Complete epithelial cover in the absence of discharge
Milek, 2017[9]					<5 cm^2	No minimum defined, however chronicity of wounds in the study ranged from 6 to 16 months	30 days	
Saad Setta, 2011[10]	Patients with PVD were excluded	>150,000/µL			Not pre-defined, but average surface area ranged from 4-21 cm^2	12 weeks	Up to 20 weeks	
Saldalamacchia, 2004[11]				Grade 2-3		8 weeks	5 weeks	
Serra, 2014[12]	>0.9 (venous) 0.30-0.40 (arterial) 0.5-0.8 (mixed)						Single treatment – application was done at time of skin graft surgery	
Singh, 2018[13]		>140,000/µL			>1 cm^2	4 weeks	28 days	Completely healed wound: full skin coverage of the wound
Xie, 2020[14]		>100,000/µL			Wound depth no less than 0.5 cm	1 week	Dressing applied weekly until healed	Cured wounds: sinus closure and wound healing.

Author, Year	ABI	Platelet count	Hemoglobin A_{1c} (HbA_{1c})	Wound grade	Ulcer size	Chronicity	Study Treatment Duration	Definition of wound closure
Yang, 2017[15]	>0.6			Grade 3-4			30 days	Completely healed wound: 100% epithelialization

ABI = ankle brachial index; cm = centimeter; cm^2 = square centimeter; HbA_{1c} = hemoglobin $A_{1c;}$ uL=microliter; PVD = peripheral venous disease

Table L.2. Patient characteristics commonly considered for the initiation and continuation/discontinuation of PRP for lower extremity venous ulcers

Author, Year	ABI	Platelet count	Hemoglobin A_{1c} (HbA_{1c})	Wound grade	Ulcer size	Chronicity	Study Treatment Duration	Definition of "completely healed wound"
Burgos-Alonso, 2018[16]	>0.8, <1.5				<7.7 cm diameter	6 months; 8 weeks of failed conservative care	9 weeks	
Elbarbary, 2020[17]	≥0.9	150,000-450,000/µL	"Uncontrolled" diabetes mellitus was excluded	Ulcers with bone or tissue exposure were excluded	N/A	At least 6 weeks of failed conservative care for chronic venous ulcer	Up to 8 weeks	
Escamilla Cardenosa, 2017[18]	0.8-1.2	>150,000/µL	<7.5%			Failure of 6 weeks of standard care	24 weeks	
Etugov, 2018[19]							Single application	
Glukhov, 2017[20]					<20 cm^2			
Milek, 2019[21]					<5 cm^2	No minimum defined, however chronicity of wounds in the study ranged from 6 to 16 months	30 days	
Moneib, 2018[22]	>0.8	>150,000/µL	Diabetes mellitus if present had to be "controlled" (no limit defined)		<10 cm^2		6 weeks	Completely healed wound: 100% epithelialization
Senet, 2003 [23]	>0.8 OR presence of peripheral pulses	>150,000/µL			3-50 cm^2	2 months	12 weeks	Completely healed wound: 100% epithelialization.
Serra, 2014[12]	>0.9 (venous) 0.30-0.40 (arterial) 0.5-0.8 (mixed)			>50% granulation on the wound bed (venous, mixed)	2.5-10 cm^2 (venous, mixed)	6 weeks	Single treatment – application was done at time of skin graft surgery	
Stacey, 2000[27]							9 months	

Author, Year	ABI	Platelet count	Hemoglobin A_{1c} (HbA_{1c})	Wound grade	Ulcer size	Chronicity	Study Treatment Duration	Definition of "completely healed wound"
Yuvasri, 2020[24]	N/A; patients with diagnosis of arterial ulcer were excluded (not further specified)	Patients receiving antiplatelet drugs were excluded; not further specified	N/A	Patients with exposed tendon or bone were excluded, not further specified	Between 1 cm x 1 cm and 5 cm x 5 cm	>6 months	4 weeks	Completely healed wound: complete closure of the ulcer.

ABI = ankle brachial index; cm = centimeter; cm^2 = square centimeter; HbA_{1c} = hemoglobin $A_{1c;}$ Ul =microliter; OR = odds ratio

Table L.3. Patient characteristics commonly considered for the initiation and continuation/discontinuation of PRP for pressure ulcers at any location

Author, Year	ABI	Platelet count	Hemoglobin A_{1c} (HbA_{1c})	Wound grade	Ulcer size	Chronicity	Study Treatment Duration	Definition of wound closure
Singh, 2014[25]				Not pre-defined, but 25 (100%) subjects treated by PRP had wounds Grade 4			Twice weekly dressings done for minimum of 10 sessions; patients whose wound had still not healed continued therapy	
Ucar, 2020[26]		"Normal"	"Normal blood glucose"	Coccyx stage II pressure ulcer			20 weeks	

ABI = ankle brachial index; HbA_{1c} = hemoglobin A_{1c}

Appendix M. FDA Cleared Device for Autologous PRP Preparation

Table M.1. FDA cleared device for autologous PRP preparation

Device Model	Manufacturer
BioCUE	Zimmer Biomet
GPS III	Zimmer Biomet
Pure PRP II (Genesis CS)	EmCyte Co.
Arthrex ACP System	Arthrex
Arthrex Angel System for BMC	Arthex
Magellan Autologous Platelet Separator System	Medtronic Sofamor Danek
SmartPrep	Harvest
Res-Q 60 BMC	Thermogenesis
Aurix System	Nuo Therapeutics
Reapplix 3C patch	Reapplix Inc

FDA = Food and Drug Administration

Appendix N. Description of PRP Being Investigated in Ongoing Trials

Table N.1. Description of PRP being investigated in ongoing trials for lower extremity diabetic ulcers

Sponsor, registration number	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, centrifuge speed, centrifuge time, radius of rotor, formulation type)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration, followup time)	PRP offloading procedures (e.g., total contact casting, removable CAM WalkerTM, irremovable offloading devices)	Other wound care treatments
All India Institute of Medical Sciences CTRI/2018/11/016470[28]	NR, NR, NR	NR, NR, NR, NR, gel and injectable	Daily saline dressing and "proper debridement", NR, external and injection	NR, NR, NR, NR, NR, every week for a month, every 2 weeks for 2 months then monthly until complete closure	NR	No
Cytonics Corporation NCT02209662[29]	NR, NR, NR	NR, NR, NR, NR, NR, NR	Saline plus standard care, NR, NR	NR, NR, NR, NR, NR, 12 weeks	NR	NR
Dr G RAY, Indira Gandhi Medical College and research Institute, CTRI/2019/08/020959[30]	NR, NR, NR	NR, NR, NR, NR, NR, NR	Injection into the edge of the ulcer	Once weekly for three weeks, total duration including followup of four weeks	NR	No
Hanaa Mohammed Riad, Assiut University NCT03890172[31]	NR, NR, NR	NR, NR, NR, NR, PRP is all that is specified	NR, NR, external	20-100mL, NR, NR, 2x/week, NR, 16 weeks	NR	NR
Mashhad University of Medical Sciences, NCT04315909[32]	PRP-fibrin glue, NR, NR	NR, NR, NR, NR, NR	NR, NR, NR	NR, NR, NR, NR, 8 weeks, 8 weeks	NR	Vitamin C (250mg/2days) and E (200 IU/2days) supplements
Nuo Therapeutics NCT02352480[33]	NR, NR, NR	NR, NR, NR, NR, gel	NR, NR, external	NR, NR, NR, 2x/week for 2 weeks then weekly for "treatment period", NR, 12 weeks	NR	NR
PRP Concepts, LLC NCT02312596[34]	NR, NR, NR	NR, NR, NR, NR, "PRP concepts fibrin Bio Matrix"	NR, NR, NR	NR, NR, NR, NR, NR, 12 weeks	NR	NR

Sponsor, registration number	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, centrifuge speed, centrifuge time, radius of rotor, formulation type)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration, followup time)	PRP offloading procedures (e.g., total contact casting, removable CAM WalkerTM, irremovable offloading devices)	Other wound care treatments
Regen Lab SA NCT02402374[35]	NR, NR, NR	NR, NR, NR, NR, gel	NR, NR, external	NR, NR, NR, NR, NR, 16 weeks	NR	NR
Royan Institute NCT02134132[36]	NR, NR, NR	NR, NR, NR, NR, NR,	NR, NR, NR	NR, NR, NR, NR, NR, NR	NR	NR
Shahid Beheshti University of Medical Sciences, IRCT20160803029181N8[37]	NR, NR, NR	NR, NR, NR, NR, NR	NR, activated, external (dressing)	NR, NR, NR, q3 days, until 90% healed, until 90% healed	NR	No
University College, London NCT03085550[38]	NR, NR, NR	Angel device, NR, NR, NR, PRP mixed with fat	"Conventional dressings", NR, NR	NR, NR, NR, NR, NR, 12 weeks	NR	Yes, PRP is injected with fat harvested per the Coleman technique. PRP is mixed with fat and infiltrated into the wounds
Universidad de Guanajuato, NCT04145154[39]	NR, NR, NR	NR, NR, NR, NR, NR	NR, NR, “intradermal”	NR, NR, NR, weekly, 4 weeks, 4 weeks	NR	No

NR = not reported; PRP = platelet-rich plasma; WBC = white blood cell

Table N.2. Description of PRP being investigated in ongoing trials for lower extremity venous ulcers

Sponsor, registration number	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, centrifuge speed, centrifuge time, radius of rotor, formulation type)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration, followup time)	PRP offloading procedures (e.g., total contact casting, removable CAM WalkerTM, irremovable offloading devices)	Other wound care treatments
Comarca Ezkerraldea-Enkarterri (OSAKIDETZA) EUCTR2014-001514-26-ES[40]	NR, NR, NR	NR, NR, NR, NR , cutaneous patch	NR, NR, external	NR, 150-400 IU, NR, NR, 1 month, 5th week and 9th week after initiating therapy	NR	No
Fakultni remocnice Ostrava EUCTR2013-003104-39-CZ[41]	NR, NR, NR	NR, NR, NR, NR, cutaneous spray, emulsion	NR, NR, External	NR, NR, NR, NR, NR, 12 weeks	NR	Yes, extracellular Matrix
Hospital Universitario La Paz EUCTR2017-000314-29-ES[42]	PRGF, NR, NR	NR, NR, NR, NR, concentrate for cutaneous solution	NR, NR, external	NR, 150.000-300000 per microliter (Typo, very large range), NR, NR, NR, weekly until 52 weeks	NR	No
Kepa M. San Sebastián Moreno, Basque Health Service NCT01817218[43]	NR, NR, NR	NR, NR, NR, NR, NR	"Moist wound care", activated, NR	9-30 mL, NR, NR, NR, NR, 9 weeks	NR	No
PRP Concepts, LLC NCT02312518[44]	NR, NR, NR	NR, NR, NR, NR, "PRP concepts fibrin Bio Matrix"	NR, NR, NR	NR, NR, NR, NR, NR, 12 weeks	NR	NR
Universidade Estadual de Campinas - Campinas, SP, British Indian Ocean Territory, RBR-7zhgb3[45]	NR, WBC poor, NR	NR, NR, NR, NR, NR	NR, NR, external (dressing)	NR, NR, NR, weekly, 12 months, 12 months	NR	Compression stockings

IU = International units; mL = milliliter; NR = not reported; PRGF = plasma rich in growth factors; PRP = platelet-rich plasma; WBC = white blood cell

Table N.3. Description of PRP being investigated in ongoing trials for pressure ulcers at any location

Sponsor, registration number	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, centrifuge speed, centrifuge time, radius of rotor, formulation type)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration, followup time)	PRP offloading procedures (e.g., total contact casting, removable CAM WalkerTM, irremovable offloading devices)	Other wound care treatments
Cytomedix NCT01819142[46]	NR, NR, NR	NR, NR, NR, NR, NR	NR, NR, NR	NR, NR, NR, NR, NR, NR	NR	NR
Nuo Therapeutics NCT02352467[47]	NR, NR, NR	NR, NR, NR, NR, gel	NR, NR, external	NR, NR, NR, 2x/week for 2 weeks then weekly for "treatment period", NR, 16 weeks	NR	NR
PRP Concepts, LLC NCT02312570[48]	NR, NR, NR	NR, NR, NR, NR, "PRP concepts fibrin Bio Matrix"	NR, NR, NR	NR, NR, NR, NR, NR, 12 weeks	NR	NR

NR = not reported; PRP = platelet-rich plasma; WBC = white blood cell

Table N.4. Description of PRP being investigated in ongoing trials for mixed etiologies

Sponsor, registration number	Formulation (PRP components, WBC rich/poor, gel method and component)	Formulation techniques (centrifuge type, centrifuge speed, centrifuge time, radius of rotor, formulation type)	Application techniques (dressing type, activated/non-activated PRP, injection/external use)	Dosage (volume of blood, concentration, total PRP volume used, PRP frequency, PRP duration, followup time)	PRP offloading procedures (e.g., total contact casting, removable CAM WalkerTM, irremovable offloading devices)	Other wound care treatments
ACR Biologics, LLC NCT02307448[49]	NR, NR, NR	NR, NR, NR, NR, NR	NR, NR, NR	NR, NR, NR, Weekly, 20 weeks, 20 weeks	NR	NR

NR = not reported; PRP = platelet-rich plasma; WBC = white blood cell

Appendix O. Sensitivity Analysis

Table O.1. Sensitivity analysis by excluding studies with high risk of bias for lower extremity diabetic ulcers

Comparison	Outcome	Subgroup	Findings
PRP vs. Management without PRP	Complete wound healing	Moderate ROB	RR: 1.28; 95% CI: 1.09 to 1.51; I^2=0.00%
		Overall	RR: 1.20; 95% CI: 1.09 to 1.32; I^2=0.00%
	Wound area (cm^2)	Moderate ROB	WMD: -0.10; 95% CI:-0.15 to -0.06 ; I^2=0.00%
		Overall	WMD: -0.11; 95% CI: -0.15 to -0.06; I^2=77.40%
	Amputation	Moderate ROB	RR: 0.96; 95% CI: 0.46 to 1.97; I^2 =0.00%
		Overall	RR: 0.89; 95% CI: 0.43 to 1.84; I^2=0.00%
	Infection	Moderate ROB	RR: 0.80; 95% CI: 0.61 to 1.06; I^2=0.00%
		Overall	RR: 0.77; 95% CI: 0.54 to 1.11; I^2=3.00%
	Amputation	Excluding Milek, 2017	RR: 0.81; 95% CI: 0.27 to 2.45; I^2=0.00%
		Overall	RR: 0.89; 95% CI: 0.43 to 1.84; I^2=0.00%
	Complete wound healing	Excluding Karimi, 2016[$]	RR: 1.21; 95% CI: 1.10 to 1.33; I^2=0.00%
		Overall	RR: 1.20; 95% CI: 1.09 to 1.32; I^2=0.00%
	Amputation	Excluding Karimi, 2016[$]	RR: 0.87; 95% CI: 0.36 to 2.12; I^2=0.00%
		Overall	RR: 0.89; 95% CI: 0.43 to 1.84; I^2=0.00%
	Infection	Excluding Karimi, 2016[$]	RR: 0.72; 95% CI: 0.41 to 1.27; I^2=17.80%
		Overall	RR: 0.77; 95% CI: 0.54 to 1.11; I^2=3.00%
	Wound area (cm^2)	Excluding Karimi, 2016[$]	WMD: -0.13; 95% CI: -0.20 to -0.06; I^2=87.80%
		Overall	WMD: -0.11; 95% CI: -0.15 to -0.06; I^2=77.40%

CI = confidence interval; N/A = not applicable; PRP = platelet-rich plasma; ROB = risk of bias; RR = relative risk; WMD = weighted mean deviation

* Milek, 2017 and Milek 2019 reported very similar methods (patient, intervention, comparison, and outcome) with different etiologies (diabetic food ulcer vs. venous ulcer).

[$] Karimi, 2016 reported conflicting numbers in different sections of the paper.

Table O.2. Sensitivity analysis by excluding studies with high risk of bias for lower extremity venous ulcers

Comparison	Outcome	Subgroup	Findings
PRP vs. Management without PRP	Complete wound healing	Moderate ROB	RR: 1.53; 95% CI: 1.02 to 2.31; I^2=0.00%
		Overall	RR: 1.49; 95% CI: 0.72 to 3.06; I^2=29.40%
	Infection	Moderate ROB	RR: 0.86; 95% CI: 0.19 to 3.88; I^2=0.00%
		Overall	RR: 0.79; 95% CI: 0.22 to 2.81; I^2=0.00%
	Wound area (cm^2)	Moderate ROB	WMD: -2.65; 95% CI: -3.21 to -2.09; I^2=0.00%
		Overall	WMD: -1.17; 95% CI: -4.09 to 1.75; I^2=92.30%
	Wound area (cm^2)	Excluding Milek, 2019*	WMD: -0.73; 95% CI: -3.08 to 1.62; I^2=95.20%
		Overall	WMD: -1.17; 95% CI: -4.09 to 1.75; I^2=92.30%

CI = confidence interval; N/A = not applicable; PRP = platelet-rich plasma; ROB = risk of bias; RR = relative risk; cm^2 = square centimeter; WMD = weighted mean deviation

* Milek, 2017 and Milek 2019 reported very similar methods (patient, intervention, comparison, and outcome) with different etiologies (diabetic food ulcer vs. venous ulcer)

Appendix P. Subgroup Analysis

Table P.1. Subgroup analysis for lower extremity diabetic ulcers

Comparison	Outcome	Subgroup category	Subgroup	Findings
PRP vs. Management without PRP	Amputation	Administration route	External	RR: 0.93; 95% CI: 0.40 to 2.17; I^2 =0.00%
			Injection	RR: 0.18; 95% CI: 0.01 to 3.58; I^2 =N/A
		Length of followup	Less than 6 weeks	RR: 0.19; 95% CI: 0.01 to 3.90; I^2 =0.00%
			6 weeks or more	RR: 0.97; 95% CI: 0.55 to 1.71; I^2 =0.00%
		Leukocyte counts	Poor	RR: 1.00; 95% CI: 0.46 to 2.19; I^2 =N/A
			Rich	RR: 0.94; 95% CI: 0.41 to 2.15; I^2 =N/A
		PRP activation	Activated	RR: 0.72; 95% CI: 0.35 to 1.47; I^2 =10.60%
			Non-activated	RR: 0.96; 95% CI: 0.46 to 1.97; I^2 =0.00%
		PRP formulation	Dressing	RR: 1.00; 95% CI: 0.50 to 2.01; I^2=0.00%
			Gel	RR: 0.80; 95% CI: 0.37 to 1.74; I^2=2.00%
			Injectate	RR: 0.18; 95% CI: 0.01 to 3.58; I^2=N/A
	Complete wound healing	Antibiotics	Antibiotics	RR: 2.31; 95% CI: 0.74 to 7.23; I^2=N/A
			No antibiotics	RR: 1.55; 95% CI: 0.95 to 2.51; I^2=N/A
		Length of followup	Less than 6 weeks	RR: 1.32; 95% CI: 1.09 to 1.60; I^2 =0.00%
			6 weeks or more	RR: 1.49; 95% CI: 1.05 to 2.11; I^2 =0.00%
		Management without PRP	Standard care	RR: 1.18; 95% CI: 1.06 to 1.31; I^2=0.00%
			Non-standard care	RR: 1.32; 95% CI: 0.93 to 1.86; I^2=N/A
		Peripheral arterial disease	Peripheral arterial disease	RR: 2.15; 95% CI: 1.10 to 4.20; I^2=N/A
			No peripheral arterial disease	RR: 1.49; 95% CI: 0.80 to 2.76; I^2=N/A
		PRP activation	Activated	RR: 1.19; 95% CI: 1.07 to 1.32; I^2=0.00%
			Non-activated	RR: 1.43; 95% CI: 1.00 to 2.02; I^2=45.10%
		PRP formulation	Dressing	RR: 1.19; 95% CI: 0.59 to 2.40; I^2=50.30%
			Gel	RR: 1.31; 95% CI: 1.14 to 1.50; I^2=0.00%
		Setting	Inpatient	RR: 1.27; 95% CI: 1.02 to 1.58; I^2=0.00%
			Outpatient	RR: 1.19; 95% CI: 1.07 to 1.32; I^2=0.00%
		Smoking	Smoker	RR: 1.91; 95% CI: 1.10 to 3.31; I^2=N/A
			Non smoker	RR: 0.94; 95% CI: 0.40 to 2.21; I^2=N/A
	Hospitalization	Length of followup	Less than 6 weeks	RR: 0.48; 95% CI: 0.09 to 2.51; I^2 =0.00%
			6 weeks or more	RR: 0.53; 95% CI: 0.16 to 1.31; I^2 =0.00%
	Infection	Administration route	External	RR: 0.78; 95% CI: 0.53 to 1.16; I^2=4.70%
			Injection	RR: 0.18; 95% CI: 0.01 to 3.58; I^2=0.00%
		Length of followup	Less than 6 weeks	RR: 0.69; 95% CI: 0.06 to 7.91; I^2 =40.50%
			6 weeks or more	RR: 0.81; 95% CI: 0.61 to 1.07; I^2 =14.90%
		PRP activation	Activated	RR: 0.56; 95% CI: 0.19 to 1.69; I^2=15.30%
			Non-activated	RR: 0.85; 95% CI: 0.64 to 1.12; I^2=0.00%
		PRP formulation	Dressing	RR: 1.00; 95% CI: 0.22 to 4.56; I^2=N/A
			Gel	RR: 1.00; 95% CI: 0.22 to 4.56; I^2=0.00%
			Injectate	RR: 0.18; 95% CI: 0.01 to 3.58; I^2=N/A

Comparison	Outcome	Subgroup category	Subgroup	Findings
		Management without PRP	Standard care	RR: 0.80; 95% CI: 0.55 to 1.17; I^2=0.00%
			Non-standard care	RR: 0.60; 95% CI: 0.30 to 1.20; I^2=N/A
	Recurrence	Length of followup	Less than 6 weeks	RR: 1.91; 95% CI: 0.18 to 20.53; I^2 =0.00%
			6 weeks or more	RR: 2.41; 95% CI: 0.10 to 57.35; I^2 =0.00%
	Wound area cm^2	Length of followup	Less than 6 weeks	WMD: -0.10; 95% CI:-0.15 to -0.04; I^2=88.30%
			6 weeks or more	WMD: -0.12; 95% CI:-0.19 to -0.05; I^2=N/A
		PRP activation	Activated	WMD: -1.85; 95% CI:-3.03 to -0.67; I^2=N/A
			Non-activated	WMD: -0.10; 95% CI:-0.15 to -0.06; I^2=0.00%
		PRP formulation	Dressing	WMD: -0.09; 95% CI:-0.15 to -0.04; I^2=N/A
			Gel	WMD: -0.13; 95% CI:-0.20 to -0.06; I^2=87.80%

CI = confidence interval; N/A = not applicable; PRP = platelet-rich plasma; RR = risk ratio; cm^2 = square centimeter; WMD = weigh mean deviation

Table P.2. Subgroup analysis for lower extremity venous ulcers

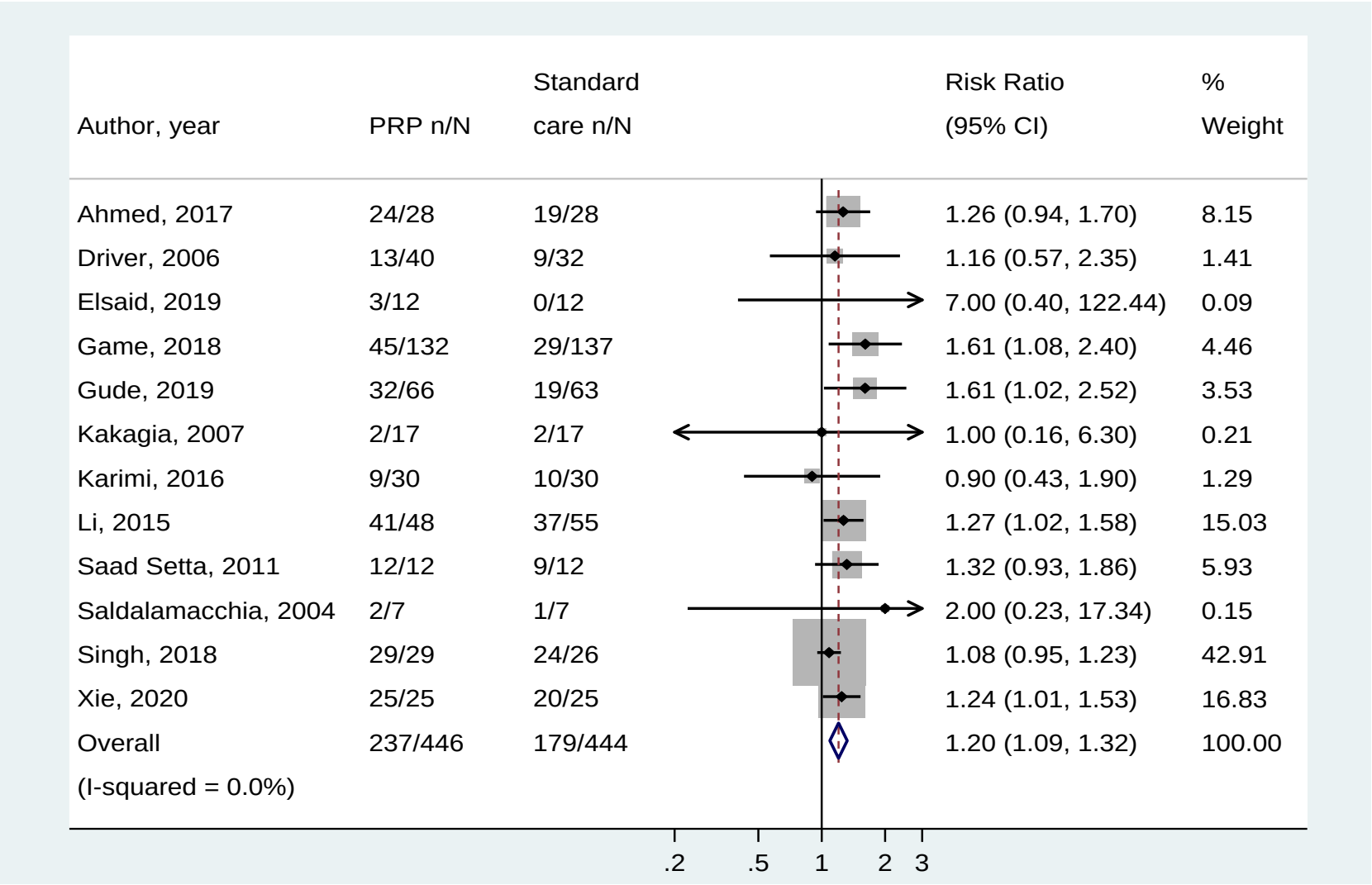
Comparison	Outcome	Subgroup category	Subgroup	Findings
PRP vs. Management without PRP	Complete wound healing	Length of followup	Less than 6 weeks	RR: 1.32; 95% CI: 0.85 to 2.06; I^2=13.30%
			6 weeks or more	RR: 1.57; 95% CI: 1.04 to 2.37; I^2=N/A
		Management without PRP	Standard care	RR=1.44; 95% CI: 0.69 to 2.87; I^2=24.60%
			Non-standard care	RR: 9.00; 95% CI: 0.55 to 147.95; I^2=N/A
		PRP activation	Activated	RR: 1.92; 95% CI: 1.27 to 2.91; I^2=66.50%
			Non-activated	RR: 1.32; 95% CI: 0.85 to 2.06; I^2=13.30%
		PRP formulation	Dressing	RR: 1.39; 95% CI: 0.88 to 2.19; I^2=0.00%
			Injectate	RR: 1.71; 95 CI; 1.12 to 2.62; I^2=N/A
			Gel	RR: 12.00; 95% CI: 1.66 to 86.82; I^2=0.00%
		PRP injection	External	RR: 1.41; 95% CI: 0.70 to 2.87; I^2=24.70%
			Injection	RR: 1.71; 95% CI: 1.12 to 2.62, I^2=N/A
	Infection	Length of followup	Less than 6 weeks	RR: 1.21; 95% CI: 0.20 to 7.24; I^2=0.00%
			6 weeks or more	RR: 0.50; 95% CI: 0.07 to 3.38; I^2=N/A
		PRP activation	Activated	RR: 0.53; 95% CI: 0.12 to 2.37; I^2=0.00%
			Non-activated	RR: 2.67; 95% CI: 0.13 to 56.63; I^2=N/A
		PRP formulation	Dressing	RR: 0.63; 95% CI: 0.11 to 3.71; I^2=29.60%
			Injectate	RR: 1.00; 95% CI: 0.15 to 6.64; I^2=N/A
			Gel	RR: 0.60; 95% CI: 0.06 to 6.44; I^2=N/A
		PRP injection	External	RR: 0.62; 95% CI: 0.15 to 2.61; I^2=0.00%
			Injection	RR: 1.00: 95% CI: 0.15 to 6.64; I^2=N/A
	Wound area cm^2	Length of followup	Less than 6 weeks	WMD: -0.90; 95% CI; -1.07 to -0.72; I^2=0.00%
			6 weeks or more	WMD: -2.65; 95% CI: -3.21 to -2.09; I^2=N/A
		Management without PRP	Standard care	WMD: -1.05; 95% CI: -1.22 to -0.88; I^2=94.80%
			Non-standard care	WMD: -0.87; 95% CI: -1.84 to 0.10; I^2=N/A
		PRP activation	Activated	WMD: -1.05; 95% CI: -1.22 to -0.88, I^2=94.80%
			Non-activated	WMD: -0.87; 95% CI: -1.84 to 0.10; I^2=N/A
		PRP formulation	Dressing	WMD: -2.60; 95% CI: -3.17 to 2.03; I^2=N/A
			Injectate	WMD: -2.70; 95% CI: -3.26 to -2.14; I^2=N/A
			Gel	WMD: -0.89; 95% CI: -1.07 to -0.72, I^2=55.90%
		PRP injection	External	WMD: -1.17; 95% CI: -4.02 to 1.69: I^2=91.80%
			Injection	WMD: -2.70; 95% CI: -3.26 to -2.14; I^2=N/A
	Wound recurrence	PRP formulation	Dressing	RR: 0.50 95% CI: 0.10 to 2.53, I^2=N/A
			Injectate	RR: 0.25; 95% CI: 0.03 to 2.11: I^2=N/A
PRP dressing vs. PRP injection	Complete wound healing	PRP formulation	Dressing vs. Injectate	RR: 0.83; 95% CI: 0.61 to 1.14, I^2=N/A
	Infection	PRP formulation	Dressing vs. Injectate	RR: 0.20; 95% CI: 0.01 to 4.00; I^2=N/A
	Wound area cm^2	PRP formulation	Dressing vs. Injectate	WMD: 0.10; 95% CI: -0.13 to 0.33; I^2=N/A
	Wound recurrence	PRP formulation	Dressing vs. Injectate	RR: 2.00, 95% CI: 0.19 to 20.90; I^2=N/A
PRP external vs. PRP injection	Complete wound healing	PRP injection	External vs. Injection	RR: 0.83; 95% CI: 0.61 to 1.14, I^2=N/A
	Infection	PRP injection	External vs. Injection	RR: 0.20; 95% CI: 0.01 to 4.00; I^2=N/A

Comparison	Outcome	Subgroup category	Subgroup	Findings
	Wound area cm^2	PRP injection	External vs. Injection	WMD: 0.10; 95% CI: -0.13 to 0.33; I^2=N/A
	Wound recurrence	PRP injection	External vs. Injection	RR: 2.00; 95% CI: 0.19 to 20.90; I^2=N/A

CI = confidence interval; N/A = not applicable; PRP = platelet-rich plasma RR = risk ratio; WMD = weigh mean deviation

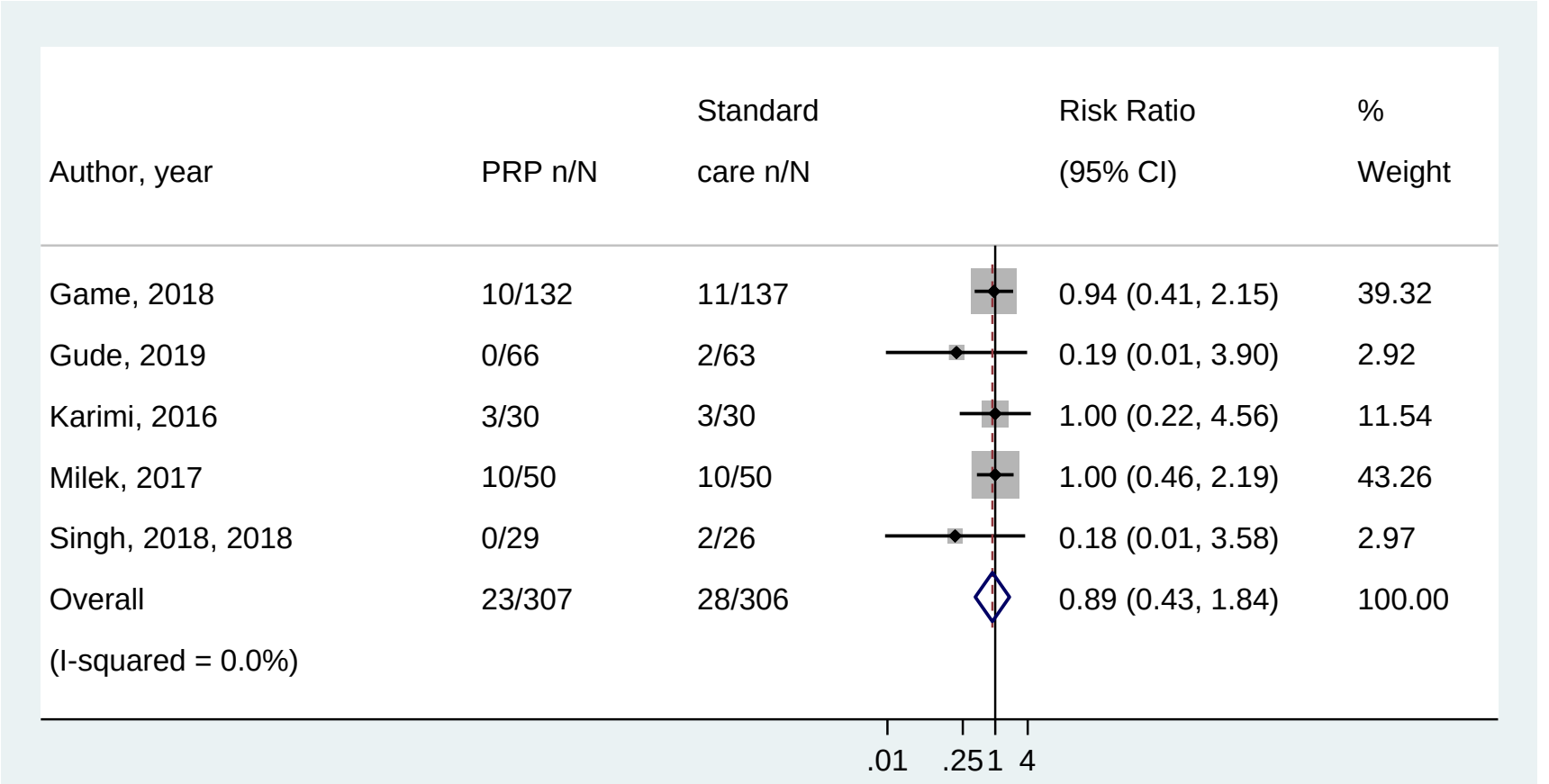
Appendix Q. Forest Plot

Figure Q.1.1. Forest plot: PRP vs. management without PRP for complete healed wounds for lower extremity diabetic ulcers



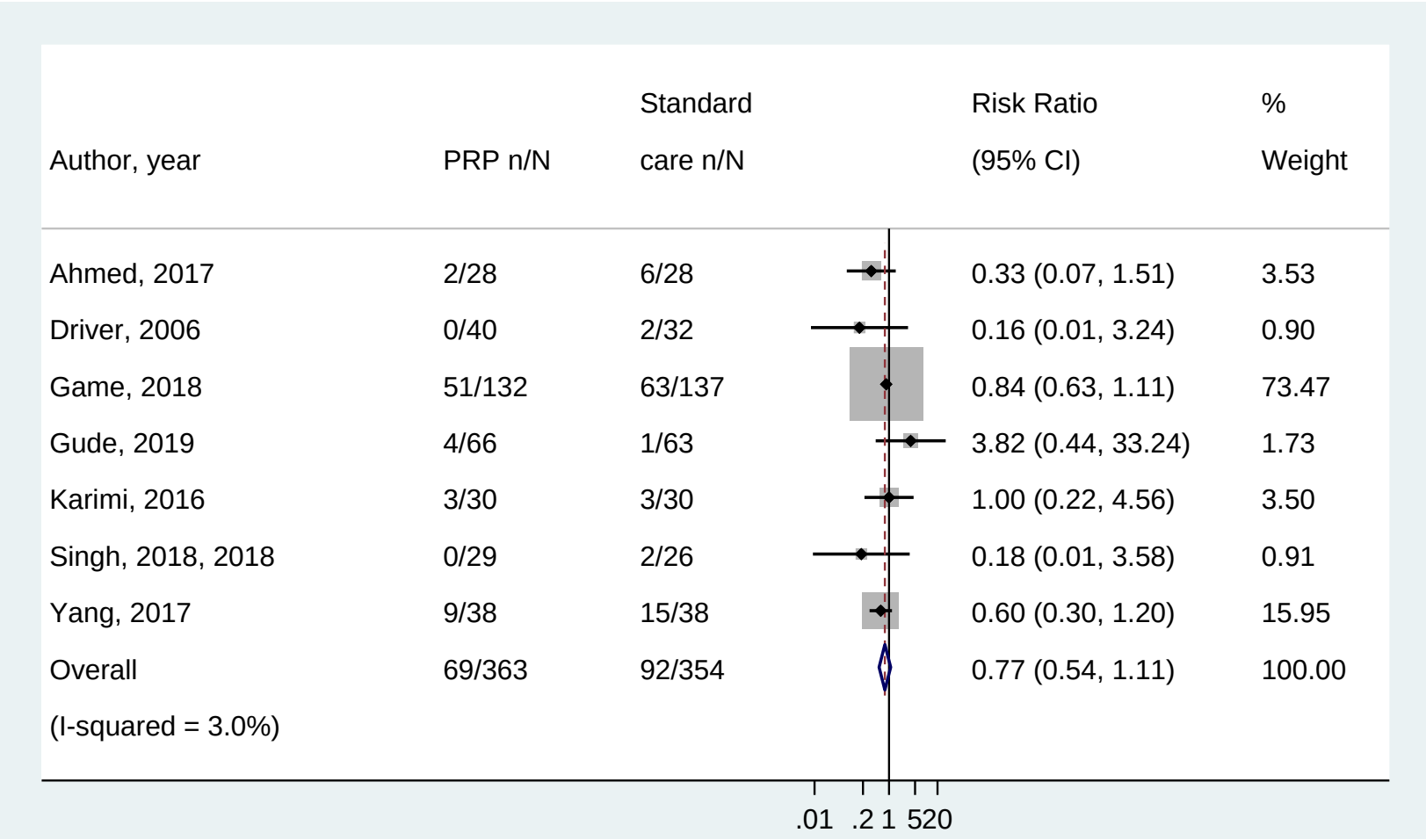
CI = confidence interval; n = number of events; N = numbers of patients; PRP = platelet-rich plasma

Figure Q.1.2. Forest plot: PRP vs. management without PRP for amputation for lower extremity diabetic ulcers



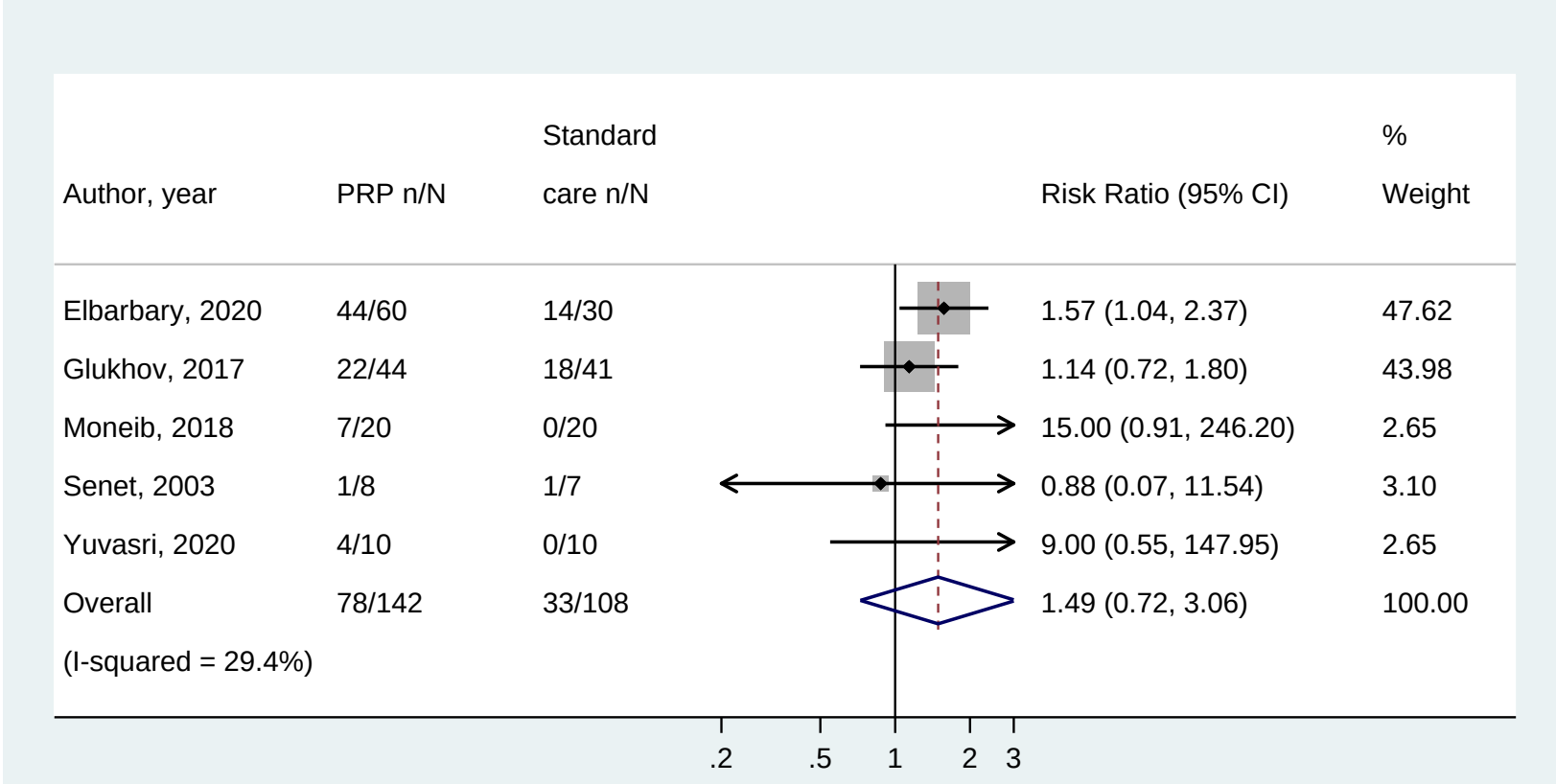
CI = confidence interval; n = number of events; N = numbers of patients; PRP = platelet-rich plasma

Figure Q.1.3. Forest plot: PRP vs. management without PRP for wound infection for lower extremity diabetic ulcers



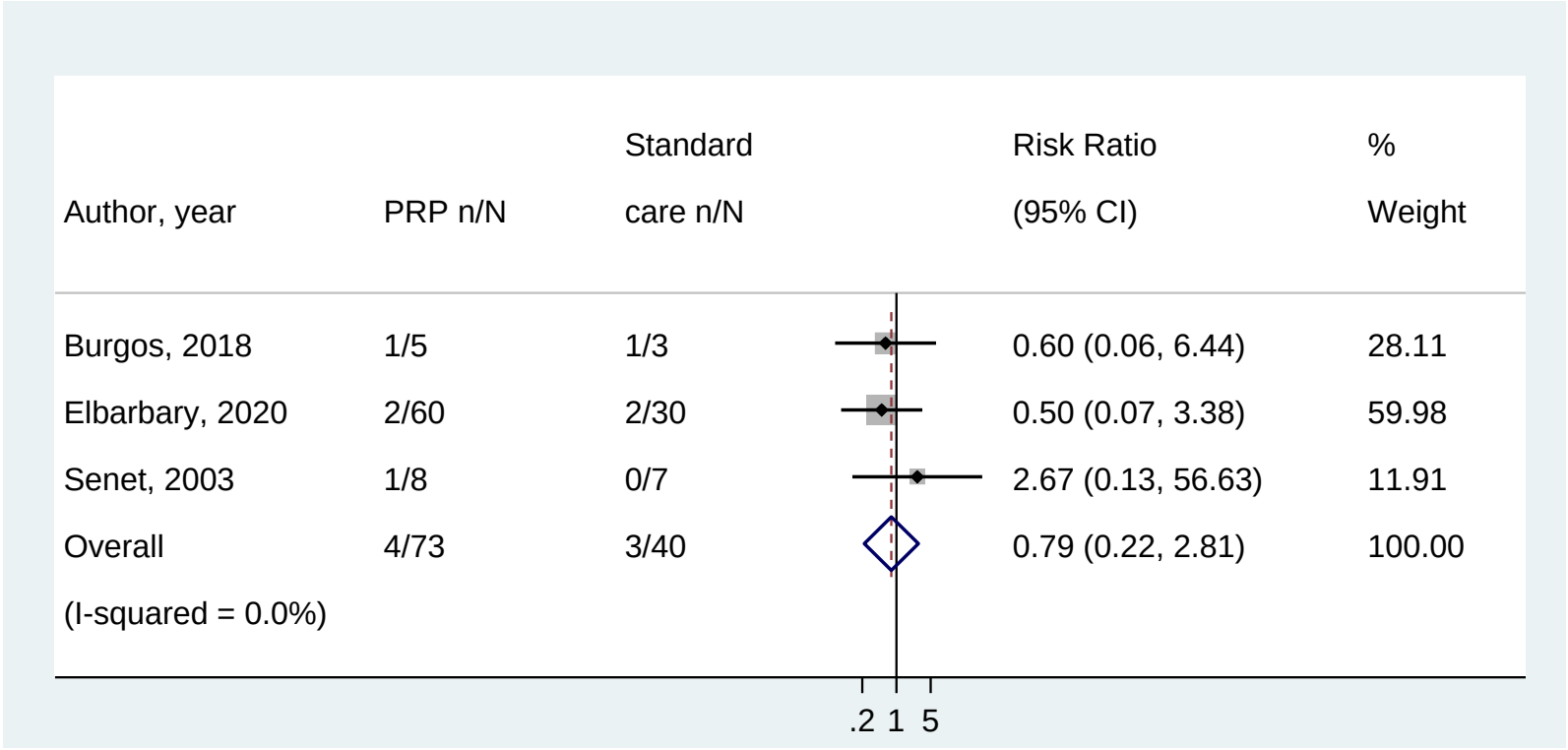
CI = confidence interval; n = number of events; N = numbers of patients; PRP = platelet-rich plasma

Figure Q.2.1. Forest plot: PRP vs. management without PRP for complete healed wounds for lower extremity venous ulcers



CI = confidence interval; n = number of events; N = numbers of patients; PRP = platelet-rich plasma

Figure Q.2.2. Forest plot: PRP vs. management without PRP for wound infection for lower extremity venous ulcers



CI = confidence interval; n = number of events; N = numbers of patients; PRP = platelet-rich plasma

Appendix R. Appendix References

1. Ahmed M, Reffat SA, Hassan A, et al. Platelet-Rich Plasma for the Treatment of Clean Diabetic Foot Ulcers. Annals of Vascular Surgery. 2017 Jan;38:206-11. PMID: 27522981.
2. Driver VR, Hanft J, Fylling CP, et al. A prospective, randomized, controlled trial of autologous platelet-rich plasma gel for the treatment of diabetic foot ulcers. Ostomy Wound Management. 2006 Jun;52(6):68-70, 2, 4 passim. PMID: 16799184.
3. Elsaid A, El-Said M, Emile S, et al. Randomized Controlled Trial on Autologous Platelet-Rich Plasma Versus Saline Dressing in Treatment of Non-healing Diabetic Foot Ulcers. World J Surg. 2020 Apr;44(4):1294-301. PMID: 31811339.
4. Game F, Jeffcoate W, Tarnow L, et al. LeucoPatch system for the management of hard-to-heal diabetic foot ulcers in the UK, Denmark, and Sweden: an observer-masked, randomised controlled trial. Lancet Diabetes Endocrinol. 2018 Nov;6(11):870-8. doi: 10.1016/s2213-8587(18)30240-7. PMID: 30243803.
5. Gude W, Hagan D, Abood F, et al. Aurix Gel Is an Effective Intervention for Chronic Diabetic Foot Ulcers: A Pragmatic Randomized Controlled Trial. Advances in Skin & Wound Care. 2019 Sep;32(9):416-26. PMID: 31436621.
6. Kakagia DD, Kazakos KJ, Xarchas KC, et al. Synergistic action of protease-modulating matrix and autologous growth factors in healing of diabetic foot ulcers. A prospective randomized trial. J Diabetes Complications. 2007 Nov-Dec;21(6):387-91. doi: 10.1016/j.jdiacomp.2007.03.006. PMID: 17967712.
7. Karimi R, Afshar M, Salimian M, et al. The effect of platelet rich plasma dressing on healing diabetic foot ulcers. Nurs Midwifery Stud. 2016;5(3):e30314.
8. Li L, Chen D, Wang C, et al. Autologous platelet-rich gel for treatment of diabetic chronic refractory cutaneous ulcers: A prospective, randomized clinical trial. Wound Repair & Regeneration. 2015 Jul-Aug;23(4):495-505. PMID: 25847503.
9. Milek T, Baranowski K, Zydlewski P, et al. Role of plasma growth factor in the healing of chronic ulcers of the lower legs and foot due to ischaemia in diabetic patients. Postepy Dermatologii I Alergologii. 2017 Dec;34(6):601-6. PMID: 29422826.
10. Saad Setta H, Elshahat A, Elsherbiny K, et al. Platelet-rich plasma versus platelet-poor plasma in the management of chronic diabetic foot ulcers: a comparative study. Int Wound J. 2011 Jun;8(3):307-12. PMID: 21470370.
11. Saldalamacchia G, Lapice E, Cuomo V, et al. A controlled study of the use of autologous platelet gel for the treatment of diabetic foot ulcers. Nutrition Metabolism & Cardiovascular Diseases. 2004 Dec;14(6):395-6. PMID: 15853123.
12. Serra R, Grande R, Butrico L, et al. Skin grafting and topical application of platelet gel in the treatment of vascular lower extremity ulcers. Acta Phlebologica. 2014 01 Dec;15(3):129-36. PMID: 602984677.
13. Singh SP, Kumar V, Pandey A, et al. Role of platelet-rich plasma in healing diabetic foot ulcers: a prospective study. Journal of Wound Care. 2018 09 02;27(9):550-6. PMID: 30204574.
14. Xie J, Fang Y, Zhao Y, et al. Autologous Platelet-Rich Gel for the Treatment of Diabetic Sinus Tract Wounds: A Clinical Study. J Surg Res. 2020 Mar;247:271-9. PMID: 31706541.
15. Yang L, Gao L, Lv Y, et al. Autologous platelet-rich gel for lower-extremity ischemic ulcers in patients with type 2 diabetes. International Journal of Clinical and Experimental Medicine. 2017 30 Sep;10(9):13796-801. PMID: 618515574.
16. Burgos-Alonso N, Lobato I, Hernandez I, et al. Autologous platelet-rich plasma in the treatment of venous leg ulcers in primary care: a randomised controlled, pilot study. Journal of Wound Care. 2018 Jun 01;27(Sup6):S20-S4. PMID: 29883294.

17. Elbarbary AH, Hassan HA, Elbendak EA. Autologous platelet-rich plasma injection enhances healing of chronic venous leg ulcer: A prospective randomised study. Int Wound J. 2020 Apr 13;13:13. PMID: 32285617.

18. Escamilla Cardenosa M, Dominguez-Maldonado G, Cordoba-Fernandez A. Efficacy and safety of the use of platelet-rich plasma to manage venous ulcers. J Tissue Viability. 2017 May;26(2):138-43. PMID: 27955807.

19. Etugov D, Mateeva V, Mateev G. Autologous platelet-rich plasma for treatment of venous leg ulcers: A prospective controlled study. Journal of Biological Regulators and Homeostatic Agents. 2018 01 May;32(3):593-7. PMID: 622715514.

20. Glukhov AA, Aralova MV. The study of the effectiveness of the drug combination of collagen and platelet-rich plasma for the regional treatment of venous ulcers. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2017;8(2):2258-63. PMID: 616066685.

21. Milek T, Nagraba L, Mitek T, et al. Autologous Platelet-Rich Plasma Reduces Healing Time of Chronic Venous Leg Ulcers: A Prospective Observational Study. Advances in Experimental Medicine & Biology. 2019;1176:109-17. PMID: 31134552.

22. Moneib HA, Youssef SS, Aly DG, et al. Autologous platelet-rich plasma versus conventional therapy for the treatment of chronic venous leg ulcers: A comparative study. Journal of Cosmetic Dermatology. 2018 Jun;17(3):495-501. PMID: 28834103.

23. Senet P, Bon FX, Benbunan M, et al. Randomized trial and local biological effect of autologous platelets used as adjuvant therapy for chronic venous leg ulcers. J Vasc Surg. 2003 Dec;38(6):1342-8. doi: 10.1016/s0741-5214(03)00908-x. PMID: 14681639.

24. Yuvasri G, Rai R. Comparison of Efficacy of Autologous Platelet-Rich Fibrin versus Unna's Paste Dressing in Chronic Venous Leg Ulcers: A Comparative Study. Indian dermatol. 2020 Jan-Feb;11(1):58-61. PMID: 32055510.

25. Singh R, Rohilla RK, Dhayal RK, et al. Role of local application of autologous platelet-rich plasma in the management of pressure ulcers in spinal cord injury patients. Spinal Cord. 2014 Nov;52(11):809-16. PMID: 25179658.

26. Ucar O, Celik S. Comparison of platelet-rich plasma gel in the care of the pressure ulcers with the dressing with serum physiology in terms of healing process and dressing costs. Int Wound J. 2020 Mar 24;24:24. PMID: 32212258.

27. Stacey MC, Mata SD, Trengove NJ, et al. Randomised double-blind placebo controlled trial of topical autologous platelet lysate in venous ulcer healing. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery. 2000 Sep;20(3):296-301. doi: 10.1053/ejvs.2000.1134. PMID: 10986030.

28. Care of wounds due to healing foot wound with your own blood product and daily care. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=CTRI. 2018;11(016470). PMID: CN-01947733.

29. Safety and Efficacy Study of APIC-PRP in Non-healing Diabetic Foot Ulcers. Https://clinicaltrialsgov/show/nct02209662. 2014. PMID: CN-01547795.

30. Use of blood products in healing of diabetic leg wound. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=CTRI. 2019;08(020959). PMID: CN-02066339 NEW.

31. Assiut U. Efficacy of Platelets Rich Plasma as a Therapeutic Tool in Diabetic Foot Ulcers. 2019 July 30. PMID: NCT03890172.

32. Mashhad University of Medical S. The Effect of Platelet-Rich Plasma-Fibrin Glue in Combination With Vitamin E and C for Treatment of Non-healing Diabetic Foot Ulcers. 2019 August 28. PMID: NCT04315909.

33. Effectiveness of Aurix Therapy in Diabetic Foot Ulcers. Https://clinicaltrialsgov/show/nct02352480. 2015. PMID: CN-01551872.

34. A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Non-Healing Diabetic Foot Ulcers. Https://clinicaltrialsgov/show/nct02312596. 2014. PMID: CN-01550793.

35. Efficacy of AutoloGel Therapy to Usual and Customary Care in Wagner gd 1 and 2 Diabetic Foot Ulcers. Https://clinicaltrialsgov/show/nct01816672. 2013. PMID: CN-01541185.

36. Utilization of Platelet Gel for Treatment of Diabetic Foot Ulcers. Https://clinicaltrialsgov/show/nct02134132. 2014. PMID: CN-01545598.

37. Evaluation of the efficacy of platelet-rich plasma in non-infectious diabetic wound healing. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=IRCT20160803029181N8. 2019. PMID: CN-02069143 NEW.

38. Platelet Rich Plasma and Autologous Fat Graft for Diabetic Ulcer. Https://clinicaltrialsgov/show/nct03085550. 2017. PMID: CN-01562747.

39. Universidad de G. Plasma and Scarring of Diabetic Ulcers. 2020 June 5. PMID: NCT04145154.

40. Euctr ES. Check the efficacy of PRP in vascular ulcers in primary care. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=EUCTR2014. 2014. PMID: CN-01886180.

41. Euctr CZ. Randomised Clinical Study of Safety of Efficacy of Extracelular Matrix (SIS-Biodesign layer) in combination with growth factors released from Autologous Platelet Rich Plasma Concentrate separated in the same time procedure with SmartPReP2 separator for Wound Healing. Ischemic and venous leg Ulcers will be treated with Biodesign+autologous PRP concentrate in randomised study. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=EUCTR2013. 2013. PMID: CN-01870178.

42. Euctr ES. Clinical trial to evaluate the effectiveness in the healing of chronic venous leg ulcers of rich in platelets plasma treatment. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=EUCTR2017. 2017. PMID: CN-01885238.

43. Feasibility and Safety and Evaluation of the Potential Efficacy of Autologous Platelet-rich Plasma in the Treatment of Vascular Venous Ulcers. Https://clinicaltrialsgov/show/nct01817218. 2013. PMID: CN-01541202.

44. A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Venous Leg Ulcers. Https://clinicaltrialsgov/show/nct02312518. 2014. PMID: CN-01550789.

45. RBR. Comparison of treatment of platelet-rich plasma non-healing wounds in patients with venous abnormalities. http://wwwwhoint/trialsearch/Trial2aspx?TrialID=RBR 7zhgb3. 2019. PMID: CN-02071550 NEW.

46. AutoloGel Therapy to Usual and Customary Care in Pressure Ulcers. Https://clinicaltrialsgov/show/nct01819142. 2013. PMID: CN-01541255.

47. Effectiveness of Aurix Therapy in Pressure Ulcers. Https://clinicaltrialsgov/show/nct02352467. 2015. PMID: CN-01551871.

48. A Prospective, Randomized Clinical Trial of PRP Concepts Fibrin Bio-Matrix in Chronic Non-Healing Pressure Ulcers. Https://clinicaltrialsgov/show/nct02312570. 2014. PMID: CN-01550792.

49. Effectiveness of Autologous Platelet Rich Plasma in the Treatment of Chronic Non-Healing Wounds. Https://clinicaltrialsgov/show/nct02307448. 2014. PMID: CN-01550667.