Supplementary Material

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Summary of judgements tables

Recommendation 1 - In a person with diabetes without a foot ulcer, take a relevant history for peripheral artery disease, examine the foot for signs of ischaemia and palpate the foot pulses at least annually, or with any change in clinical status of the feet. (Strong recommendation, low certainty of evidence)

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Large	Diagnosis of disease will affect patient management. Evidence for the diagnostic accuracy of pulse palpation for PAD in people with diabetes without DFU is limited with two studies of low quality demonstrating, there is a small increase in ability to rule disease in where a foot pulse is absent or weak. Other clinical examinations that may be associated with PAD including hair loss, muscle atrophy and reduced peripheral skin temperature. These factors have been shown to be associated with a small increase in the likelihood of PAD
Undesirable Effects	Small	The presence of pulses does not exclude disease. It should be noted that these clinical examinations are highly subjective and such findings may also be associated with neuropathy. PAD may also be asymptomatic or have an atypical presentation in people with diabetes as in other elderly or at risk populations
Certainty of evidence	Low	Included studies were of low quality. Potential for bias was related to the lack of confirmed consecutive recruitment of participants, lack of reporting of participant characteristics, a lack of description of blinding of assessors of the index test to the reference standard and vice versa, partial verification bias from restricting reference testing to those with abnormal index tests, and uncertainty over the interval between the tests. With respect to the index test and reference standard, the primary concerns were a lack of description of methodology to undertake the measurements and threshold values used to classify disease status
Values	No important uncertainty or variability	The Working Group were of the opinion that a person with diabetes will value diagnosis of PAD over undiagnosed disease. Multiple therapies are available to manage disease and effective management will reduce the risk of other cardiovascular events and improve DFU healing outcomes
Balance of effects	Probably favours intervention	Evidence suggests small capacity for tests to rule disease in and out and therefore they are of benefit in diagnosing presence of PAD
Resources required	Negligible costs and savings	Tests are of negligible cost to perform but have limited capacity to rule disease in and out and therefore may generate some savings through early diagnosis
Certainty of evidence of required resources	Low	Limited resources are required to implement these tests, they require no equipment and can be applied by a wide range of practitioners. This judgement is based on expert opinion of the Working Group

Cost effectiveness	Unknown	The Working Group consider there was a lack of direct or indirect evidence to draw conclusions due to variability in health care systems globally
Equity	Probably increased	As there is limited accuracy but these tests can be applied on a broad scale at low cost relative to invasive testing, the Working Group considered it is likely to increase health equity
Acceptability	Yes	It would be acceptable to people with diabetes and practitioners as the testing is non-invasive, quick and can be applied by a range of health practitioners
Feasibility	Yes	It would be feasible to undertake testing on patients with diabetes with DFU. This relates to no equipment being required, the lack of involvement of specialised services in application of the tests and the wide range of practitioners that can apply these tests

Recommendation 2 - In a person with diabetes without a foot ulcer, if peripheral artery disease (PAD) is suspected, consider performing pedal Doppler waveforms in combination with ankle brachial index (ABI) and toe brachial index (TBI). No single modality has been shown to be optimal for diagnosis of PAD and there is no value above which PAD can be excluded. However, PAD is less likely in the presence of ABI 0.9-1.3, TBI ≥ 0.70, and triphasic or biphasic pedal Doppler waveforms. (Conditional, low)

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies			High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Large	Diagnosis of disease will affect patient management. In people with diabetes an ABI of < 0.90 is associated with a moderate to large increase in likelihood of PAD, a value between 0.9-1.3 does not rule out PAD. A TBI < 0.70 and toe pressures are associated with a moderate ability to rule PAD in and out however toe pressure threshold values vary between studies
Undesirable Effects	Small	False positive and false negative rates vary according to test type and capacity of tests to rule disease in and out is moderate. When used in combination this may reduce the likelihood of undetected disease however further research is needed to confirm this
Certainty of evidence	Low	Included studies were of low quality. Potential for bias was related to the lack of confirmed consecutive recruitment of participants, lack of reporting of participant characteristics, a lack of description of blinding of assessors of the index test to the reference standard and vice versa, partial verification bias from restricting reference testing to those with abnormal index tests and uncertainty over the interval between the tests. With respect to the index test and reference standard, the primary concerns were a lack of description of methodology to undertake the measurements and threshold values used to classify disease status
Values	Probably important uncertainty or variability	The Working Group were of the opinion that a person with a DFU will value diagnosis of PAD over undiagnosed disease. Multiple therapies are available to manage disease and effective management will reduce the risk of other cardiovascular events and improve DFU healing outcomes
Balance of effects	Favours intervention	Evidence suggests moderate capacity for tests to rule disease in and out and therefore they are of benefit in diagnosing the presence of PAD
Resources required	Moderate savings	Tests are of low to moderate cost to perform in high and middle income countries (depending on test selection) and have a moderate capacity to rule disease in and out and are therefore likely to generate savings through early diagnosis.
Certainty of evidence of required resources	Low	Limited resources are required to implement these tests, they require relatively low cost equipment and can be applied by a wide range of practitioners. This judgement is based on the expert opinion of the Working Group

Cost effectiveness	Unknown	The Working Group consider there was a lack of direct or indirect evidence to draw conclusions due to variability in health care systems globally
Equity	Probably increased	As there is moderate accuracy and these tests can be applied on a broad scale at low cost relative to invasive testing the Working Group considered it is likely to have a moderate impact on health equity
Acceptability	Yes	It would be acceptable to people with diabetes and practitioners as the testing is non-invasive, quick and can be applied by a range of health practitioners
Feasibility	Yes	It would be feasible to undertake testing on patients with diabetes. This relates to the low cost of equipment, the lack of involvement of specialised services in the application of the tests and the wide range of practitioners that can apply these tests

Recommendation 3 - In a person with diabetes and a foot ulcer or gangrene, take a relevant history for peripheral artery disease, examine the person for signs of ischaemia and palpate the foot pulses. (Strong, low)

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Large	Diagnosis of disease will affect patient management. Evidence for the diagnostic accuracy of pulse palpation for PAD in people with diabetes without DFU is limited with one study of low quality demonstrating, there is a small increase in ability to rule disease in where a foot pulse is absent or weak. Other clinical examinations that may be associated with PAD include hair loss, muscle atrophy and reduced peripheral skin temperature. These factors have been shown to be associated with a small increase in the likelihood of PAD
Undesirable Effects	Small	The presence of pulses does not exclude disease. It should be noted that these clinical examinations are highly subjective and such findings may also be associated with neuropathy. PAD may also be asymptomatic or have an atypical presentation in people with diabetes as in other elderly or at risk populations
Certainty of evidence	Low	Included study was of low quality. Potential for bias was related to the lack of confirmed consecutive recruitment of participants, lack of reporting of participant characteristics, a lack of description of blinding of assessors of the index test to the reference standard and vice versa, partial verification bias from restricting reference testing to those with abnormal index tests, and uncertainty over the interval between the tests. With respect to the index test and reference standard, the primary concerns were a lack of description of methodology to undertake the measurements and threshold values used to classify disease status
Values	No important uncertainty or variability	The Working Group were of the opinion that a person with a DFU will value diagnosis of PAD over undiagnosed disease. Multiple therapies are available to manage disease and effective management will reduce the risk of other cardiovascular events and improve DFU healing outcomes
Balance of effects	Probably favours intervention	Evidence suggests small capacity for tests to rule disease in and out and therefore they are of benefit in diagnosing the presence of PAD
Resources required	Negligible costs and savings	Test is of negligible cost to perform but have limited capacity to rule disease in and out and are therefore unlikely to generate significant savings when used in isolation
Certainty of evidence of required resources	Low	Limited resources are required to implement these tests, they require no equipment and can be applied by a wide range of practitioners. This judgement is based on expert opinion of the Working Group

Cost effectiveness	Unknown	The Working Group consider there was a lack of direct or indirect evidence to draw conclusions due to variability in health care systems globally
Equity	Probably increased	As there is limited accuracy but these tests can be applied on a broad scale at low cost relative to invasive testing the Working Group considered it is likely to increase health equity
Acceptability	Yes	It would be acceptable to people with DFU and practitioners as the testing is non-invasive, quick and can be applied by a range of health practitioners
Feasibility	Yes	It would be feasible to undertake testing on patients with diabetes with DFU. This relates to the fact that no equipment is required, the lack of involvement of specialised services in the application of the tests and the and wide range of practitioners that can apply the tests

Recommendation 4 - In a person with diabetes and a foot ulcer or gangrene, evaluate pedal Doppler waveforms in combination with ankle brachial index (ABI) and toe brachial index (TBI) measurements to identify the presence of peripheral artery disease (PAD). No single modality has been shown to be optimal for the diagnosis of PAD, and there is no value above which PAD can be excluded. However, PAD is less likely in the presence of ABI 0.9-1.3; TBI ≥ 0.70; and triphasic or biphasic pedal Doppler waveforms. (Strong, low)

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies			High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Large	Diagnosis of disease will affect patient management. In people with DFU an ABI of < 0.90 is associated with a moderate to large increase in the likelihood of PAD, a value between 0.9-1.3 does not rule out PAD. A TBI < 0.70 and toe pressures are associated with a moderate ability to rule PAD in and out however toe pressure threshold values vary between studies
Undesirable Effects	Small	Rates of false positive and false negative vary according to test type and capacity of tests to rule disease in and out is moderate. When used in combination this may reduce the likelihood of undetected disease, however further research is needed to confirm this
Certainty of evidence	Low	Included studies were of low quality. Potential for bias was related to the lack of confirmed consecutive recruitment of participants, lack of reporting of participant characteristics, a lack of description of blinding of assessors of the index test to the reference standard and vice versa, partial verification bias from restricting reference testing to those with abnormal index tests and uncertainty over the interval between the tests. With respect to the index test and reference standard, the primary concerns were a lack of description of methodology to undertake the measurements and threshold values used to classify disease status
Values	Probably important uncertainty or variability	The Working Group were of the opinion that a person with a DFU will value diagnosis of PAD over undiagnosed disease. Multiple therapies are available to manage disease and effective management will reduce the risk of other cardiovascular events and improve DFU healing outcomes
Balance of effects	Favours intervention	Evidence suggests moderate capacity for tests to rule disease in and out and therefore they are of benefit in diagnosing presence of PAD
Resources required	Moderate savings	Tests are of low to moderate cost to perform in high and middle income countries (depending on test selection) and have a moderate capacity to rule disease in and out and are therefore likely to generate savings through early diagnosis
Certainty of evidence of required resources	Low	Limited resources are required to implement these tests, they require relatively low cost equipment and can be applied by a wide range of practitioners, This judgement is based on the expert opinion of the Working Group

Cost effectiveness	Unknown	The Working Group consider there was a lack of direct or indirect evidence to draw conclusions due to variability in health care systems globally
Equity	Probably increased	As there is moderate accuracy and these tests can be applied on a broad scale at low cost relative to invasive testing the Working Group considered it is likely to have a moderate impact on health equity
Acceptability	Yes	It would be acceptable to people with DFU and practitioners as the testing is non-invasive, quick, and can be applied by a range of health practitioners
Feasibility	Yes	It would be feasible to undertake testing on patients with diabetes with DFU. This relates to the low cost of equipment, the lack of involvement of specialised services in the application of the tests and the wide range of practitioners that can apply these tests

Recommendation 5- Best Practice Statement: In a person with diabetes without a foot ulcer in whom a non-emergency invasive foot procedure is being considered, peripheral artery disease should be excluded by performing assessment of pedal Doppler waveforms in combination with ankle brachial index and toe brachial index.

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	Diagnosis of PAD will help determine whether non-emergency surgery is suitable for the patient or not, however this is limited by the diagnostic accuracy of individual tests. Bedside testing generally has moderate ability to diagnose PAD or to exclude this disease in people with diabetes mellitus. Any abnormal test result should be considered indicative of PAD. Therefore, it is suggested this recommendation will reduce the risk of undiagnosed severe PAD which would potentially negatively affect post-surgical outcome
Undesirable Effects	Small	False positive and false negative rates vary according to test type and the capacity of tests to rule disease in and out is moderate. When used in combination this may reduce the likelihood of undetected disease however further research is needed to confirm this. Delayed diagnosis or non-healing may occur if surgery is undertaken in a limb with PAD. Therefore, it is suggested this recommendation will reduce the risk of undiagnosed severe PAD which would potentially negatively affect post-surgical outcomes and it is likely that people will value this approach
Certainty of evidence	Low	Based on indirect evidence and expert opinion, no randomised controlled trials (for ethical reasons) or observational studies of sufficient quality have been performed on the added value of performing bedside tests prior to any surgical procedure in the foot
Values	No important uncertainty or variability	Patients will value healing over non-healing therefore diagnosis of PAD prior to non-emergency surgery will potentially avoid negative post-surgical outcomes and it is likely this will be valued by the patient
Balance of effects	Probably favours intervention	Evidence suggests moderate diagnostic accuracy of bedside testing for PAD
Resources required	Moderate savings	Bedside tests are low cost to perform and have moderate effectiveness of identifying those with PAD, and are therefore likely to generate savings identifying individuals for whom surgery is contraindicated based on vascular supply
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Unknown	Unknown
Equity	Probably increased	As there is moderate effectiveness and these tests can be applied on a broad scale at low cost, it is likely to have a moderate impact on health equity

Acceptability	Yes	It would be acceptable as the testing is non-invasive and can be applied by a range of health practitioners
Feasibility	Yes	It would be feasible to undertake testing on patients with diabetes with DFU. This relates to the low cost of equipment, the lack of involvement of specialised services in the application of the tests and the and wide range of practitioners that can apply these tests on patients being considered for non-emergency foot surgery

Recommendation 6 - In a person with diabetes and a foot ulcer or gangrene, consider performing ankle pressures and ankle brachial index (ABI) measurements to assist in the assessment of likelihood of healing and amputation. Ankle pressure and ABI are weak predictors of healing. A low ankle pressure (e.g., < 50 mmHg) or ABI (e.g., < 0.5) may be associated with greater likelihood of impaired healing and greater likelihood of major amputation. (Conditional, low)

CRITERIA	JUDGEMENTS							IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know		High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know		High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies			High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies			High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know		High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know		High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	Increased the pre-test probability of healing by a small amount. One study of low quality indicated that a very low ABI (< 0.4) can increase the pre-test probability of major amputation by a large amount (45%). There are other non-invasive tests that seem to perform better but these tests are not implemented as widely. Thresholds for AP and ABI which were associated with increased probability of healing could not be identified, however a very low ankle pressure (e.g., < 50 mmHg) or ABI (e.g., < 0.5) was associated with a greater likelihood of delayed healing
Undesirable Effects	Small	It was considered that is unlikely an ABI or AP will cause undesirable effects particularly when used in combination with other forms of bedside testing.
Certainty of evidence	Low	We determined this to be low certainty due to high risk of bias and low quality of included studies
Values	No important uncertainty or variability	Patients are likely to value ability to predict healing and to the contribution this makes to preventing delays in referral for revascularisation
Balance of effects	Probably favours comparison	Some evidence suggests limited predicative capacity of both tests for healing outcomes therefore particularly if no other tests are available or if AP or ABI is being used in combination with other tests this may be useful. A low ABI has been shown to result in a large increase in pre-test probability of major amputation however this is based on one study of low quality
Resources required	Negligible costs/savings	AP and ABI are low cost to perform in high and middle income countries but if limited in effectiveness unlikely to generate significant savings, (low cost relative to other tests (invasive) and $TcPO_2$ /SPP for the same outcome)
Certainty of evidence of required resources	Low	Limited resources required, relatively low cost equipment, can be applied by a wide range of practitioners. This judgement is based on the expert opinion of the guideline group
Cost effectiveness	Do not know	No direct or indirect evidence to draw conclusions due to variability in health care systems globally
Equity	Probably increased	Likely to reduce direct costs related to more expensive invasive tests e.g., angiogram. AP and ABI are also less expensive than other forms of bedside testing
Acceptability	yes	It would be acceptable even though of limited use to undertake ABI/AP testing on patients with DFU as the testing is quick and non-invasive
Feasibility	Yes	It would be feasible to undertake ABI/ AP testing on patients with DFU

Recommendation 7 - In a person with diabetes and a foot ulcer or gangrene consider performing a toe pressure measurement to assess the likelihood of healing and amputation. A toe pressure ≥ 30 mmHg increases the pre-test probability of healing by up to 30% and a value < 30 mmHg increases the pre-test probability of major amputation by approximately 20%. (Conditional, low)

CRITERIA	JUDGEMENTS							IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know		High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know		High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies			High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies			High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know		High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know		High/moderate/low

CRITERIA	Judgement	**Comment**
Desirable Effects	Moderate	In people with DFU and PAD a TP ≥ 30 mmHg may be associated with an increased pre-test probability of DFU and post-minor amputation healing of at least 30% and a TP < 30 mmHg may be associated with a small increase (15%) in pre-test probability of major amputation
Undesirable Effects	Small	It was considered unlikely that TP will cause undesirable effects, particularly considering it significantly increases pre-test probability of healing for DFU and post-minor amputation and that it can be used in combination with other forms of bedside testing
Certainty of evidence	Low	We determined this to be low certainty due to few studies with high risk of bias and of low quality
Values	No important uncertainty or variability	Patients are likely to value the ability to predict healing and the contribution this makes to preventing delays in referral for revascularisation
Balance of effects	Probably favours intervention	Evidence suggests moderate predicative capacity of both tests for healing outcomes (see desirable effects
Resources required	Moderate savings	TP are low cost to perform (although it is acknowledged more expensive than ABI), particularly relative to invasive procedure (e.g., digital subtraction angiography). Given TP has moderate effectiveness of identifying those unlikely to heal, based on expert opinion, it was considered use of this test is likely to generate savings
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Favours the intervention	TP are low cost to perform and have moderate effectiveness
Equity	Probably increased	As there is moderate effectiveness and these tests can be applied on a broad scale at low cost is likely to have a moderate impact on health equity
Acceptability	Yes	It would be acceptable to both patients and health practitioners as the testing is quick and non-invasive
Feasibility	Yes	It would be feasible to undertake TP testing on patients with DFU

Recommendation 8 - In a person with diabetes and a foot ulcer or gangrene, if a toe pressure cannot be performed, consider performing a transcutaneous oxygen pressure (TcPO2) measurement or a skin perfusion pressure (SPP) to assess likelihood of healing. A $TcPO_2 \geq 25$ mmHg increases the pre-test probability of healing by up to 45% and value < 25 mmHg increases the pre-test probability of major amputation by approximately 20%. A SPP ≥ 40 mmHg, increases the pre-test probability of healing by up to 30%. (Conditional, low)

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies / Don't know		High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies / Don't know		High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	Moderate capacity to predict healing. In people with DFU and PAD a $TcPO_2 \geq 25$ mmHg may increase the pre-test probability of DFU healing by up to 45%, $TcPO_2 <$ 20 mmHg may increase the pre-test probability of minor amputation by a small amount but may not increase the pre-test probability of major amputation. This is based on one study of low quality. A SPP of ≥ 40 mmHg may increase the pre-test probability of DFU healing and healing after minor amputation by up to 45% There are other non-invasive tests that perform as well $TcPO_2$ or SPP and these tests are implemented more widely
Undesirable Effects	Trivial	Unlikely an $TcPO_2$ or SPP will cause undesirable effects. False positive rates very low
Certainty of evidence	Low	We determined this to be low certainty due to few studies with high risk of bias and of low quality
Values	No important uncertainty or variability	Patients are likely to value the ability to predict healing and the contribution this makes to preventing delays in referral for revascularisation
Balance of effects	Probably favours intervention	Evidence suggests predicative capacity for healing outcomes, but thresholds used are variable
Resources required	Negligible costs and savings	$TcPO_2$ and SPP significant cost to perform (equipment and consumables) and require specific expertise and have a moderate effectiveness in identifying those unlikely to heal that is similar to less expensive tests, therefore are likely to generate savings
Certainty of evidence of required resources	Moderate	Cost of equipment and expertise is greater than other available non-invasive tests (e.g., ABI)
Cost effectiveness	Do not know	No direct or indirect evidence to draw conclusions due to variability in health care systems globally
Equity	Probably no impact	Not as likely as other bedside tests with similar predictive capacity to reduce out of pocket expenses related to replacing more expensive tests e.g., duplex. Unlikely there will be wide access to these tests particularly in low income countries
Acceptability	yes	It would be acceptable even though of limited use to undertake ABI/AP testing on patients with DFU as the testing is quick and non-invasive
Feasibility	Probably no	It is not as feasible to undertake $TcPO_2$ and SPP testing on patients with DFU on broad scale compared with other bedside tests with similar predictive capacity for healing. $TcPO_2$ and SPP give additional information on healing potential and are useful for measuring perfusion following forefoot amputations when TP are no longer possible. However, in our opinion these are secondary tests of greater

		expense and less equipment availability, and the time and expertise required to apply them

Recommendation 9 - In a person with diabetes and a foot ulcer or gangrene it is suggested the presence of peripheral artery disease and other causes of poor healing should always be assessed. Diabetes related micro-angiopathy should not be considered the primary cause of foot ulceration, gangrene, or poor wound healing without excluding other causes. (Conditional, low)

CRITERIA	JUDGEMENTS							IMPACT
Desirable Effects	Trivial	Small	Moderate	Large		Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial		Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High		No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High		No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	Adequate assessment, identification, and treatment of all causes of delayed wound healing is likely to increase the likelihood of healing
Undesirable Effects	Moderate	Based on the lack of studies showing that diabetes related micro-angiopathy contributes to poor wound healing in DFU there is potential harm if this is assumed. Failure to undertake further evaluation of potential presence of PAD as well as other causes of failure to heal including infection, inadequate offloading, oedema, poor glycaemic control, poor nutritional state and underlying co-morbidities may result in delayed wound healing and or amputation
Certainty of evidence	Low	Based on a limited number of trials of low quality current data do not support the that microvascular angiopathy contributes to impaired wound healing
Values	No important uncertainty or variability	Patient will value DFU healing over non-healing
Balance of effects	Probably favours comparison	Assuming micro-angiopathy is the intervention the balance of effects favours the comparison of assessing for PAD and other causes of poor healing
Resources required	Moderate costs	Assuming presence of microangiopathy is likely to be associated with moderate cost from undiagnosed PAD and or other causes of poor healing
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Unknown	Unknown
Equity	Unknown	Unknown
Acceptability	Probably not	Assuming the presence of microangiopathy at the cost of not diagnosing other causes of poor healing is likely to be unacceptable to the patient and health practitioner
Feasibility	Don’t know	Assumption of micro-angiopathy does not represent an intervention

Recommendation 10 - In a person with diabetes, peripheral artery disease and a foot ulcer or gangrene, consider using the Wound/Ischaemia/foot Infection (WIfI) classification system to estimate healing likelihood and amputation risk. (Conditional, low)

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies / Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies / Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	A high WIfI limb clinical stage is associated with longer time to healing and increased likelihood of non-healing at six and 12 months and high risk of amputation
Undesirable Effects	Small	It was considered unlikely that WIfI will cause undesirable effects
Certainty of evidence	Low	We determined this to be low certainty due to high risk of bias and low quality of included studies
Values	No important uncertainty or variability	Patients are likely to value ability to predict healing and amputation and to value the contribution this makes to preventing delays in referral for revascularisation
Balance of effects	Probably favours the intervention	A high WIfI limb clinical stage is associated with longer time to healing and increased likelihood of non-healing at six and 12 months. Higher WIfI clinical stages are also associated with an increased likelihood of major amputation. Similarly, higher WIfI clinical stages have been linked to high rates of minor amputation and lower rates of amputation free survival at 12 months. For prediction of revascularisation benefit there are few data available and inadequate evidence to determine whether WIfI revascularisation benefit staging predicts healing or amputation outcomes in people undergoing revascularisation
Resources required	Moderate savings	Given WIfI has moderate effectiveness for identifying those unlikely to heal and at risk of amputation, based on expert opinion, it was considered use of this test is likely to generate savings
Certainty of evidence of required resources	Low	Limited resources required, relatively low cost equipment, can be applied by a wide range of practitioners. This judgement is based on the expert opinion of the guideline group
Cost effectiveness	Do not know	No direct or indirect evidence to draw conclusions due to variability in health care systems globally
Equity	Probably increased	Likely to reduce direct costs related to more expensive invasive tests e.g., angiogram
Acceptability	yes	As the WIfI tool has predictive capacity for the key outcomes of wound healing and amputation in people with DFU, has wide availability (also as an online tool), and uses non-invasive bedside testing to determine the

		level of ischaemia, and clinical grading of infection and the wound, facilitating application in clinical practice by a wide range of practitioners
Feasibility	Yes	As a low cost assessment, it is expected to be feasible to apply to people with DFU and acceptable to practitioners as well as being of value to patients. Use of WIfI is likely to increase access to a form of vascular assessment in low income countries where invasive testing may not be a widely available. However further investigation of revascularisation benefit is required

Recommendation 11 - Best Practice Statement: In a person with diabetes, peripheral artery disease and a foot ulcer or gangrene who is being considered for revascularisation, evaluate the entire lower extremity arterial circulation (from aorta to foot) with detailed visualisation of the below knee and pedal arteries

CRITERIA	JUDGEMENTS							IMPACT
Desirable Effects	Trivial	Small	Moderate	Large		Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial		Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High		No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High		No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Large	Anatomical imaging will help determine the most appropriate revascularisation strategy and is therefore likely to contribute to better surgical outcomes and help identify those unsuitable for revascularisation
Undesirable Effects	Small	Potential complications of each imaging modality and lack of diagnostic certainty in some situations e.g., medial arterial calcification
Certainty of evidence	Low	Based on indirect evidence and expert opinion
Values	No important uncertainty or variability	Patient will value additional information for planning of vascular intervention over no information. When a revascularisation is being considered, further anatomical information on the arteries of the lower limb should be obtained to assess the presence, severity, and distribution of arterial stenoses or occlusions. In this process, adequate imaging of the tibial and pedal vessels is of critical importance, particularly in planning intervention in people with diabetes and a foot ulcer
Balance of effects	Favours intervention	Based on expert opinion, surgery is successful when preceded by anatomical imaging to guide the choice of revascularisation technique
Resources required	Moderate costs	Anatomical imaging requires specialist equipment and training
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Unknown	Unknown. Each of the imaging techniques have their advantages and disadvantages and their use will depend heavily on the availability of equipment and local expertise, preferences of the individual, and associated costs
Equity	Probably no impact	Will depend on the site and whether there is the available expertise and equipment
Acceptability	Probably yes	Likely to be acceptable to the patient and health practitioner due to the improved surgical outcomes (this is based on expert opinion)
Feasibility	Probably yes	Likely to be feasible in middle to high income countries. The cost of the equipment and requirement for expertise to conduct the testing will limit the feasibility

Recommendation 12 - Best Practice Statement: In a person with diabetes, peripheral artery disease, a foot ulcer and clinical findings of ischaemia, a revascularisation procedure should be considered. Findings of ischaemia include absent pulses, monophasic or absent pedal doppler waveforms, ankle pressure < 100 mm Hg or toe pressure < 60 mm Hg. Consult a vascular specialist unless major amputation is considered medically urgent.

CRITERIA	JUDGEMENTS							IMPACT
Desirable Effects	Trivial	Small	Moderate	Large		Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial		Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High		No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High		No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Large	Analysis of the evidence for revascularisation suggests that revascularisation in appropriately selected people with diabetes and haemodynamically significant PAD, can improve perfusion, expedite wound healing and reduce major limb amputations. Therefore, consultation with a vascular specialist is likely to be of benefit
Undesirable Effects	Small	Low likelihood of undesirable effects from a consultation, small possibility of inadequate or inaccurate assessment
Certainty of evidence	Low	Based on indirect evidence and expert opinion, it was judged in our systematic review that the certainty of the evidence on the effects of revascularisation on wound healing and amputation risk is low, as many important factors that can affect outcomes were not reported such as the availability of vein conduit, wound care, offloading and sufficient anatomical details about the extent and severity of lesions treated
Values	No important uncertainty or variability	People will value a consultation with a vascular specialist over no consultation. People with signs of ischaemia, e.g., as defined by WIfI and the Global Vascular Guidelines: absent pulses and monophasic or absent pedal Doppler waveforms, ankle pressure < 100 mm Hg or toe pressure < 60 mm Hg, are very likely to have significant PAD that could impact wound healing potential and amputation risk
Balance of effects	Favours intervention	Based on expert opinion consultation with a vascular specialist is likely to improve patient outcomes e.g., through timely revascularisation
Resources required	Moderate costs	Requires specialist training
Certainty of evidence of required resources	No included studies	Not assessed.
Cost effectiveness	Unknown	Based on expert opinion consultation with a vascular specialist is likely to improve patient outcomes e.g. through timely revascularisation
Equity	Probably no impact	Will depend on the site and whether there is the available expertise. More likely to have vascular consultation with specialist in middle to high income countries
Acceptability	Probably yes	Will be acceptable to the patient and health practitioner due to the improved surgical outcomes (this is based on expert opinion)
Feasibility	Probably yes	Likely to be feasible in middle to high income countries

Recommendation 13 - Best Practice Statement: In a person with diabetes, peripheral artery disease, a foot ulcer, and severe ischaemia i.e., an ankle brachial index < 0.4, ankle pressure < 50 mmHg, toe pressure < 30 mmHg or transcutaneous oxygen pressure < 30 mmHg or monophasic or absent pedal Doppler waveforms, urgently consult a vascular specialist regarding possible revascularisation.

CRITERIA	JUDGEMENTS							IMPACT
Desirable Effects	Trivial	Small	Moderate	Large		Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial		Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High		No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High		No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

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CRITERIA	Judgement	Comment
Desirable Effects	Large	Consultation with vascular specialist will have a large desirable effect (assist with determination of need for revascularisation). Severe ischaemia is defined in the Global Vascular Guidelines (GVG) as an ABI < 0.4, AP pressure < 50 mmHg, TP < 30 mmHg or $TcPO_2$ < 30 mmHg or monophasic or absent pedal Doppler waveforms. Such perfusion deficits are, as also stated in the GVG, an indication for revascularisation, unless contraindicated or technically not possible
Undesirable Effects	Small	Low likelihood of undesirable effects from a consultation, small possibility of inadequate or inaccurate assessment
Certainty of evidence	Low	Based on indirect evidence and expert opinion
Values	No important uncertainty or variability	People will value consultation with specialist over no consultation.
Balance of effects	Favours intervention	Based on expert opinion consultation with vascular specialist is likely to improve patient outcomes e.g., through timely revascularisation. There is retrospective evidence demonstrating that a delay in revascularisation of more than two weeks in people with diabetes results in increased risk of limb loss
Resources required	Moderate costs	Requires specialist training
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Favours intervention	Based on expert opinion consultation with a vascular specialist is likely to improve patient outcomes e.g., through timely revascularisation
Equity	Probably no impact	Will depend on the site and whether there is the available expertise. More likely to have vascular consultation with specialist in middle to high income countries
Acceptability	Yes	Will be acceptable to the patient and health practitioner due to the improved surgical outcomes (this is based on expert opinion)
Feasibility	Probably yes	Likely to be feasible in middle to high income countries

Recommendation 14 - Best Practice Statement: In a person with diabetes, peripheral artery disease and a foot ulcer with infection or gangrene involving any portion of the foot, urgently consult a vascular specialist in order to determine the timing of a drainage procedure and a revascularisation procedure.

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies			High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know		High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know		High/moderate/low

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CRITERIA	Judgement	Comment
Desirable Effects	Large	Consultation with a vascular specialist will have a large desirable effect (assist with determination of need for revascularisation). Severe ischaemia is defined in the Global Vascular Guidelines (GVG) as an ABI < 0.4, AP pressure < 50 mmHg, TP < 30 mmHg or $TcPO_2$ < 30 mmHg or monophasic or absent pedal Doppler waveforms. Such perfusion deficits are, as also stated in the GVG, an indication for revascularisation, unless contraindicated or technically not possible
Undesirable Effects	Small	Low likelihood of undesirable effects from a consultation, small possibility of inadequate or inaccurate assessment
Certainty of evidence	Low	Based on indirect evidence and expert opinion
Values	No important uncertainty or variability	People will value consultation with specialist over no consultation
Balance of effects	Favours intervention	Based on expert opinion consultation with a vascular specialist is likely to improve patient outcomes e.g., through timely revascularisation. There is retrospective evidence demonstrating that a delay in revascularisation of more than two weeks in people with diabetes results in increased risk of limb loss
Resources required	Moderate costs	Requires specialist training
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Favours intervention	Based on expert opinion consultation with a vascular specialist is likely to improve patient outcomes e.g., through timely revascularisation
Equity	Probably no impact	Will depend on the site and whether there is the available expertise. More likely to have vascular consultation with specialist in middle to high income countries
Acceptability	Yes	Will be acceptable to the patient and health practitioner due to the improved surgical outcomes (this is based on expert opinion)
Feasibility	Probably yes	Likely to be feasible in middle to high income countries

Recommendation 15 - Best Practice Statement: In a person with diabetes and a foot ulcer, when the wound deteriorates or fails to significantly improve (e.g., a less than 50% reduction in wound area within four weeks) despite appropriate infection and glucose control, wound care, and offloading, reassess the vascular status and consult with a vascular specialist regarding possible revascularisation.

CRITERIA	JUDGEMENTS							IMPACT
Desirable Effects	Trivial	Small	Moderate	Large		Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial		Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High		No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability				High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High		No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes		Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Large	Reassessment of vascular status and consultation with vascular specialist will have a large desirable effect (assist with determination of need for revascularisation)
Undesirable Effects	Small	Low likelihood of undesirable effects from a consultation, small possibility of inadequate or inaccurate assessment.
Certainty of evidence	Low	Based on indirect evidence and expert opinion
Values	No important uncertainty or variability	People will value re-assessment and consultation with specialist over no further assessment or consultation
Balance of effects	Favours intervention	Based on expert opinion, re-assessment of vascular status and consultation with a vascular specialist is likely to improve patient outcomes e.g., through timely revascularisation
Resources required	Moderate costs	Requires specialist training. Bedside tests are of low cost however additional vascular assessment e.g., CDUS and DSA have greater costs
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Favours intervention	Based on expert opinion re-assessment and consultation with vascular specialist is likely to improve patient outcomes e.g., through timely revascularisation
Equity	Probably no impact	Will depend on the site and whether there is the available expertise. More likely to have vascular consultation with specialist in middle to high income countries
Acceptability	Yes	Will be acceptable to the patient and health practitioner due to the improved surgical outcomes (this is based on expert opinion)
Feasibility	Probably yes	Likely to be feasible in middle to high income countries

Recommendation 16 - Best Practice Statement: In a person with diabetes, peripheral artery disease and a foot ulcer or gangrene, avoid revascularisation when the risk–benefit ratio for the probability of success of the intervention is clearly unfavourable.

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low

This table is based on the Grade Summary of Judgements Table as provided in the GradePRO software.

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	Will reduce the risk of futile revascularisation and undertaking ineffective procedures in patients at high surgical risk. Any revascularisation procedure is unlikely to be of benefit to the person and may cause harm. Many affected individuals pose high peri-procedural risk because of comorbidities. In particular, the following people may not be suitable for revascularisation: those who are very frail, have short life expectancy, have poor functional status, are bed bound, and or have a large area of tissue destruction that renders the foot functionally unsalvageable, and those who cannot realistically be expected to mobilise following revascularisation
Undesirable Effects	Small	It was considered that there is only a small possibility of avoidable amputation.
Certainty of evidence	Low	There is evidence from several observational studies of a 50% healing rate for ischaemic DFU in people with diabetes unsuitable for revascularisation and this should also be considered in determining choice of care. This judgement is therefore based on indirect evidence and expert opinion
Values	Possibly important uncertainty or variability	Some patients may value any likelihood of limb salvage over other outcomes
Balance of effects	Favours intervention	Based on expert opinion of the benefit of no intervention where the risk benefit ratio is unacceptable e.g., high risk of peri-operative death or low likelihood of surgical success
Resources required	Moderate costs	Requires specialist assessment
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Favours intervention	Based on expert opinion re-assessment and consultation with a vascular specialist is likely to improve patient outcomes.
Equity	Probably no impact	Will depend on the site and whether there is the available expertise. More likely to have vascular consultation with specialist in middle to high income countries
Acceptability	Probably yes	Some people may not accept the surgical risk benefit analysis
Feasibility	Probably yes	Likely to be feasible in middle to high income countries

Recommendation 17 - In a person with diabetes, peripheral artery disease and a foot ulcer or gangrene who has an adequate single segment saphenous vein in whom infra-inguinal revascularisation is indicated and who is suitable for either approach, consider bypass in preference to endovascular therapy. (Conditional, moderate)

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	People will value a favourable outcome (reduced risk of death or adverse limb event or amputation)
Undesirable Effects	Small	More invasive procedure requires longer recovery time however is associated with fewer repeat procedures
Certainty of evidence	Moderate	Based on subanalysis of data from one randomised controlled trial with low risk of bias
Values	Possibly no important uncertainty or variability	Patients are likely to value reduced mortality and risk of amputation
Balance of effects	Probably favours the intervention	Bypass more invasive but less likely to be associated with death and adverse limb events
Resources required	Moderate costs	Both endovascular and open approaches require specialist expertise. Open surgery is more invasive, however endovascular approach is more likely to need re-intervention
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Favours intervention	Reduced likelihood of adverse limb event will increase cost effectiveness of open surgery compared with endovascular intervention. Considering costs there are probably no major differences except the length of hospital stay however this is yet to be determined and may be an additional outcome of the BEST-CLI study. Subsequent analyses are also awaited to shed more light on the anatomical patterns and extent of disease treated, as well as which patterns of disease were not well represented or excluded.
Equity	Probably reduced	Will depend on the site and whether there is the available expertise. More likely to have endovascular expertise available. Open surgery may not be an option in some centres
Acceptability	Probably yes	Patients likely to find successful outcome of open surgery more acceptable than less invasive procedure (i.e., endovascular surgery)
Feasibility	Probably yes	Likely to be feasible in middle to high income countries. The recommendation may not be feasible in the short term in all countries due to the lack of equipment and expertise

Recommendation 18 - Best Practice Statement: A person with diabetes, peripheral artery disease (PAD) and a foot ulcer or gangrene, should be treated in centres with expertise in, or rapid access to, endovascular and surgical bypass revascularisation. In this setting, consider making treatment decisions based on the risk to and preference of the individual, limb threat severity, anatomical distribution of PAD, and the availability of autogenous vein.

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	Patients will value a favourable outcome from rapid access to treatment and availability of the most effective treatment options. As there is no one size fits all approach to treatment for people with diabetes, PAD, and foot ulceration or gangrene, it is important that a treating centre has the expertise and facilities to provide a range of treatment options with availability of both endovascular and open techniques
Undesirable Effects	Trivial	Few undesirable effects of access to appropriate treatment
Certainty of evidence	Moderate	Based on indirect evidence (low quality observational studies for time to revascularisation) and expert opinion
Values	Possibly no important uncertainty or variability	Patients likely to value adequate care access over no access
Balance of effects	Favours the intervention	Based on evidence of delayed revascularisation having worse outcomes for healing, evidence of reduced mortality and adverse limb events in specific circumstances with open surgery and expert opinion
Resources required	Moderate costs	Both endovascular and open approaches require specialist expertise
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Probably favours intervention	Reduced likelihood of adverse limb events with rapid referral and availability of open procedures will increase cost effectiveness
Equity	Probably reduced	Will depend on the site and whether there is the available expertise. More likely to have endovascular expertise available. Open surgery may not be an option in some centres
Acceptability	Yes	Patients and health practitioners likely to value rapid access to specialist care and find this acceptable.
Feasibility	Probably yes	Likely to be feasible in middle to high income countries however this will depend on local factors which may impact care delivery e.g., geographical remoteness

Recommendation 19 - Best Practice Statement: In a person with diabetes, peripheral artery disease and a foot ulcer or gangrene, revascularisation procedures should aim to restore in line blood flow to at least one of the foot arteries.

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies			High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know		High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know		High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	People will value a favourable outcome for healing and avoidance of amputation from successful revascularisation. In people with diabetes and a foot ulcer or gangrene in whom revascularisation is required, optimising blood flow to the foot is important to optimise the chance of healing the foot and avoiding amputation
Undesirable Effects	Small	Some risks related to revascularisation failure and peri-operative morbidity and death
Certainty of evidence	Low	Based on indirect evidence and low quality studies. Pedal arch patency also seems to be associated with improved wound healing and reduced risk of major amputation
Values	No important uncertainty or variability	Patient likely to value healing and avoidance of amputation
Balance of effects	Probably favours the intervention	Incomplete revascularisation (including treating inflow disease when distal disease is present or bypassing into blind segment arteries with no runoff), can result in delayed or non-wound healing and significant risk of amputation
Resources required	Moderatee saving	Increased likelihood of intervention success and avoidance of amputation with restoration of direct inline flow suggest this approach would generate moderate saving. This is based on expert opinion
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Probably favours intervention	Likely to be more cost effective due to increased limb salvage and wound healing associated with restoration of direct inline flow
Equity	Probably not impact	Unlikely to change the access to care and expertise
Acceptability	Yes	Patients and health practitioners likely to value the most effective intervention being used
Feasibility	Probably yes	Likely to be feasible in middle to high income countries

Recommendation 20- In a person with diabetes, peripheral artery disease and a foot ulcer or gangrene undergoing an endovascular procedure, consider targeting the artery on angiography that supplies the anatomical region of the ulcer, when possible or practical. (Conditional, very low)

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies / Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies / Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies / Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies / Don't know		High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies / Don't know		High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Moderate	Patients will value a favourable outcome for healing and avoidance of amputation
Undesirable Effects	Small	Some risks related to revascularisation failure and peri-operative morbidity and death but similar to indirect revascularisation (IR)
Certainty of evidence	Very low	Very low quality of included studies. These studies had a high risk of bias, lacked randomisation (and it is unlikely that this will ever be possible) and were mostly retrospective. Baseline variables such as wound/foot staging (e.g., by WIfI) and extent of tissue loss were reported infrequently. Heterogeneity of the included studies was found to be high preventing meta-analysis. This is likely to be due to high variability in participants and wound stage (extent of tissue loss, severity of ischaemia, presence of infection). Comparison of primary outcomes (healing and amputation) or adverse events is therefore problematic
Values	No important uncertainty or variability	Patient likely to value healing and avoidance of amputation
Balance of effects	Probably favours the intervention	Based on evidence it is possible that DR has better outcomes than IR for wound healing and amputation. For endovascular interventions healing and amputation outcomes for endovascular DR and IR shows that if DR is possible, DFU healing time and major amputation may be reduced compared with indirect revascularisation. There is inadequate evidence to determine if DR is superior to IR to prevent minor amputation
Resources required	Negligible costs and savings	Little difference in costs associated with IR and DR - based on expert opinion of the group.
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Probably favours intervention	Likely to be more cost effective due to increased limb salvage and wound healing associated with DR approach
Equity	Probably not impact	Unlikely to change the access to care and expertise for both methods are standard
Acceptability	Yes	Patients and health practitioners likely to value the most effective intervention being used
Feasibility	Probably yes	Likely to be feasible in middle to high income countries

Recommendation 21 - Best Practice Statement: In a person with diabetes and either a foot ulcer or gangrene who has undergone revascularisation, objectively assess adequacy of perfusion e.g., using non-invasive bedside testing.

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low

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CRITERIA	Judgement	Comment
Desirable Effects	Large	Vascular assessment will help determine whether revascularisation has been successful and healing is going to be achieved.
Undesirable Effects	Trivial	Unlikely to be undesirable effects of bedside testing
Certainty of evidence	Low	Based on indirect evidence and expert opinion. Frequently long term patency is not achieved in endovascular treatment of tibial lesions Regular assessment of perfusion post-revascularisation should therefore be undertaken due to the risk of occlusion or re-stenosis after intervention. This should be conducted in combination with regular assessment of the foot lesion to determine whether healing is indeed taking place
Values	No important uncertainty or variability	People will value timely identification of failed procedures
Balance of effects	Probably favours intervention	Favours assessment over no assessment to monitor surgical outcomes, procedural success, and wound healing capacity. Limited by variable predictive capacity of bedside tests for wound healing
Resources required	Moderate savings	More likely to prevent amputation if revascularisation failure is identified promptly
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Unknown	Unknown
Equity	Probably no impact	Will depend on the site and whether there is the available expertise and equipment.
Acceptability	Yes	Bedside tests are non-invasive and are likely to be acceptable to the patient for this purpose
Feasibility	Yes	Bedside tests are largely low cost and easily applied. This relates to the low cost of equipment, the lack of involvement of specialised services in application of the tests, and the and wide range of practitioners that can apply these tests.

Recommendation 22 - Best Practice Statement: A person with diabetes, peripheral artery disease and either a foot ulcer or gangrene should be treated by a multidisciplinary team as part of a comprehensive care plan.

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies		High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low

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CRITERIA	Judgement	Comment
Desirable Effects	Large	Multidisciplinary team (MDT) care is associated with improved outcomes for wound healing and avoidance of amputation.
Undesirable Effects	Trivial	Unlikely to be undesirable effects of multidisciplinary care
Certainty of evidence	Low	Based on indirect evidence and expert opinion. Wound healing and avoidance of amputation more likely with MDT care
Values	No important uncertainty or variability	Patient will value wound healing and avoidance of amputation and will value a comprehensive care plan that addresses other important issues including: prompt treatment of concurrent infection, regular wound debridement, biomechanical offloading, control of blood glucose, cardiovascular risk reduction, and treatment of co-morbidities as well as prevention of ulcer recurrence
Balance of effects	Favours intervention	Based on indirect evidence and expert opinion. Wound healing and avoidance of amputation more likely with MDT care
Resources required	Moderate savings	There is likely to be an immediate increase in costs with the provision of MDT care however prevention of amputation is likely to generate savings. This is more likely to be achieved with MDT care.
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Unknown	Unknown. Likely to favour the intervention, based on expert opinion
Equity	Probably no impact	Will depend on the site and whether there is the available expertise and equipment
Acceptability	Yes	Multidisciplinary treatment likely to be acceptable to patients and health practitioners
Feasibility	Probably yes	Likely to be feasible in middle to high income countries however this will depend on local factors which may impact care delivery e.g., geographical remoteness. In rural and remote locations and areas where specialist access is challenging referral pathways that address care access (e.g., through virtual referral pathways) are essential to establish, to provide multidisciplinary care

Recommendation 23 - Best Practice Statement

In a person with diabetes and peripheral artery disease the following target levels should be:

- HbA1c < 8% (< 64 mmol/mol), but higher target HbA1c value can be necessary depending on the risk of severe hypoglycaemia.
- Blood pressure < 140/ 90 mmHg but higher target levels can be necessary depending on the risk of orthostatic hypotension and other side effects.
- Low density lipoprotein target of < 1.8 mmol/l (< 70 mg/dl) and reduced by at least 50% of baseline. If high intensity statin therapy (with or without ezetimibe) is tolerated, target levels < 1.4 mmol/l (55 mg/dl) are recommended.

Recommendation 24 - Best Practice Statement

A person with diabetes and symptomatic peripheral artery disease:

- should be treated with single antiplatelet therapy.
- treatment with clopidogrel should be considered as first choice in preference to aspirin.
- combination therapy with aspirin (75 mg to 100 mg once daily) plus low dose rivaroxaban (2.5 mg twice daily) should be considered for people without a high bleeding risk.

Recommendation 25 - Best Practice Statement

In a person with type 2 diabetes and peripheral artery disease:

- with an eGFR > 30 ml/min/1.73m^2, a sodium–glucose cotransporter 2 (SGLT-2) inhibitor or a glucagon like peptide 1 receptor agonist with demonstrated cardiovascular disease benefit should be considered, irrespective of the blood glucose level.
- SGLT-2 inhibitors should not be started in drug naïve people with a diabetes related foot ulcer or gangrene and temporary discontinuation should be considered in people already using these drugs, until the affected foot is healed.

CRITERIA	JUDGEMENTS						IMPACT
Desirable Effects	Trivial	Small	Moderate	Large	Varies	Don't know	High/moderate/low
Undesirable Effects	Large	Moderate	Small	Trivial	Varies	Don't know	High/moderate/low
Certainty of evidence	Very low	Low	Moderate	High	No included studies		High/moderate/low
Values	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			High/moderate/low
Balance of effects	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Resources required	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know	High/moderate/low
Certainty of evidence of required resources	Very low	Low	Moderate	High	No included studies			High/moderate/low
Cost effectiveness	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know	High/moderate/low
Equity	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know	High/moderate/low
Acceptability	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low
Feasibility	No	Probably no	Probably yes	Yes	Varies	Don't know	High/moderate/low

CRITERIA	Judgement	Comment
Desirable Effects	Large	Large desirable effect reducing risk of MACE and MALE. People with an ischaemic diabetes related foot ulcer have an overall five year cardiovascular mortality around 50% therefore these individuals have a very high cardiovascular risk
Undesirable Effects	Small	Undesirable effects likely to be related to adverse drug reactions. Many people with an ischaemic foot ulcer usually have other diabetes related complications as well as several co-morbidities, resulting in a high burden of diseases and multiple medications.
Certainty of evidence	Moderate	Based on available international guidelines this was judged as moderate
Values	No important uncertainty or variability	It was judged that people will value avoidance of MACE and MALE however, people with a ischaemic DFU are also likely to be elderly, frail and living in vulnerable socio-economic circumstances with a low quality of life. It is therefore essential that cardiovascular risk factor management in these people should be individualised
Balance of effects	Favours intervention	Based on available evidence significant reduction in MACE and MALE
Resources required	Moderate costs	Direct cost of medications. Some of these may be significant and will vary from country to country
Certainty of evidence of required resources	No included studies	Not assessed
Cost effectiveness	Unknown	Unknown, but likely to favour the intervention based on expert opinion
Equity	Probably no impact	Will depend on the site and whether there is the availability and subsidy of medication
Acceptability	Yes	Multidisciplinary treatment likely to be acceptable to patients and health practitioners. However, acceptability may be affected by individual circumstances. Treatment should be part of a shared decision making process, taking life expectancy, diabetes related complications and

		comorbidities, expected benefit, treatment burden, drug interactions and undesirable treatment effects into account
Feasibility	Probably yes	Feasible in middle to high income countries. Access to and costs of medications and lack of health professional access may impact feasibility

Evidence Tables - The prognostic capacity of microvascular measures for DFU healing and amputation

Evidence Table - Study characteristics: the prognostic capacity of microvascular measures for DFU healing and amputation

Author	Age (years, SD)	Sex (M/F)	Total Participants	Type 1/2	Participants w/ Diabetes (%)	Diabetes Duration	Participants w/ PAD (%)	PAD Diagnosis	Intervention
Arora, 2002	62 ± 3	11/2	13	1/12	100	20 ± 3	100	$TcPO_2$: 40 ± 6	Lower extremity arterial revascularisation
Chang, 2016	63.4 ± 13.7	16/14	30	Not reported	100	13.6 ± 8.2	Severe - 11% (5) Moderate - 30% (14) Borderline-Normal - 15% (7) Normal - 43% (20) Total - 46 Ulcer only total - 34	Mean SPP (mmHg) Severe - <30 Moderate - 30-49 Borderline-Normal - 50-59 Normal - >60	Buerger Exercise

Author	Age (years, SD)	Sex (M/F)	Total Participants	Type 1/2	Participants w/ Diabetes (%)	Diabetes Duration	Participants w/ PAD (%)	PAD Diagnosis	Intervention
Dwars, 1988	68 (range: 50-85)	15/11	26	N/A	100 Separate control group (?) 4	N/A	100	N/A	Amputation at individually specified site
Faris, 1985	Range: 38-86 Median: 72	37/24	61	N/A	100	6 months - 40 years Median: 10 years	N/A	N/A	Conservative treatment (25), toe amputation or abscess drainage (14), transmetatarsal amputation (2) Femoropopliteal bypass (10), Femorotibial bypass (7). BTK amputation (6)

Author	Age (years, SD)	Sex (M/F)	Total Participants	Type 1/2	Participants w/ Diabetes (%)	Diabetes Duration	Participants w/ PAD (%)	PAD Diagnosis	Intervention
Faris, 1988	69 (35-90)	102/103	205	N/A	100	<1-50 years (median: 10)		<40 mmHg 40-60 mmHg >60 mmHg	Conservative treatment, amputation or vascular reconstruction
Fiordaliso, 2016	72 ± 10.0	26/4	Total - 70 Neuro-ischaemic - 30 Neuropathic - 30 Control - 10	0/30	100	17.9 ± 13.2	100	$TcPO_2$: <30mmHg Ankle pressure: <70mmHg	Biopsies taken from healthy skin adjacent to existing wound during amputation of 1st ray
Galanakis, 2020	Median 68 (58-79	6/4	10	N/A	80	N/A	100	Rutherford's Classification of PAD	Percutaneous Angioplasty. Follow up amputation if indicated
Jorneskog, 1993	63 (range 47-80)	N/A	10	N/A	100	23 (range 4-53)	100	TBI ≤0.8	Low molecular weight Heparin Dalteparin (Fragmin)

Author	Age (years, SD)	Sex (M/F)	Total Participants	Type 1/2	Participants w/ Diabetes (%)	Diabetes Duration	Participants w/ PAD (%)	PAD Diagnosis	Intervention
Kalani, 2007	Case: 73 ± 8 Control: 72 ± 11	Case: 29/14 Control: 31/11	85	Case: 5/38 Control: 7/35	100	Case: 20 ± 13 Control: 21 ± 14	100	≤0.6mmHg TBI	Low molecular weight heparin Dalteparin (Fragmin)
Lee, 2021	68.9 ± 11.9	185 males (78.4%)	172 (236 limbs)		80.5% (190 limbs)		100	Rutherford 5 or 6	N/A
Mennes , 2021	66.7 ± 12.8	42/11	53	3/50	100	≤10: 20 >10: 26 Unknown: 7	Ischaemic: 28 Critical Ischaemic: 18	Critically ischaemic-ABI:≤0.39 Ankle pressure: <50mmHg Toe Pressure or TcPO2: ≤30mmHg Ischaemic-ABI: 0.4-0.79 Ankle pressure: 50-100mmHg Toe	Offloading, debridement, wound dressings, antibiotic treatment

Author	Age (years, SD)	Sex (M/F)	Total Participants	Type 1/2	Participants w/ Diabetes (%)	Diabetes Duration	Participants w/ PAD (%)	PAD Diagnosis	Intervention
								pressure or $TcPO_2$: 30-59mmHg	
Yotsu, 2014	35-87 (65.2 ± 12.1)	Ischaemic: 16/20 (80.0) Neuro-ischaemic: 11/14 (78.6)	Ischaemic: 20 Neuro-ischaemic: 14 Neuro: 39 Total: 73	0/73	100	Ischaemic: 24.2 ± 14.1 Neuro-ischaemic: 18.2 ± 7.2	62% (45)	ABI:≤ 0.9 SPP: <40mmHg TcPO2: <40mmHg	N/A

ABI = ankle brachial index, SD = standard deviation, SPP = skin perfusion pressure, $TcPO_2$ = transcutaneous oxygen pressure

Evidence Table - Study outcomes: the prognostic capacity of microvascular measures for DFU healing and amputation

Author	Microvascular measurements	Revascularisations	Measurement	Baseline	Follow ups	Follow up time	*p* value	Healing outcomes
Arora, 2002	Laser Doppler (LSH- 44 degrees; Iontophoresis - 1% ACh and 1% SNP)	100%	% in increase over baseline measured in volts	LSH: 289% ± 90% ACh: 6% ± 4% SNP: 10% ± 4%	LSH: 427% ± 61% ACh: 26% ± 8% SNP: 29% ± 9%		LSH: < .05 ACh: < .05 SNP: < .05	Tissue Loss: 8 non-healing that healed 4-6 weeks post-op: 4 Clean and healing: 2 Amputations post op: 2
Chang, 2016	SPP - Laser Doppler	0%	Mean SPP (SD)	Severe - 22.1 (4.4) Moderate - 42.2 (4.3) Borderline-Normal - 52.9 (2.7) Normal - 80.6 (17.5) Total - 58.3 (24.3) Ulcer only total - 58.3 (26.9)	Severe - 37.3 (16.4) Moderate - 64.4 (19.9) Borderline-Normal - 65.4 (9.1) Normal - 83.8 (20.5) Total - 70.0 (23.3) Ulcer only total - 71.5 (26.5)	3 months	.043 .001 .028 .239 <.001 <.001	Healed - 9 (29%) Improving - 14 (41%) Static - 6 (18%) Progressing - 3 (9%) Amputation - 2 (6%)
Dwars, 1988	Modified Scintigraphic Technique SPP SBF		Mean SBF ml/min per 100g tissue for each SPP (mmHg)	SBF range: 0.88-40.0	SPP <20: 5.58 (3.86) SPP =25: 13.29 (10.92) SPP =35: 17.06 (8.72)		SPP < 20 mmHg and SPP= 25mmHg (p < .05) SPP	Healed Amputation: 10.88 (range 2.78-40.0) Failed Minor Amp: 4.33

Author	Microvascular measurements	Revascularisations	Measurement	Baseline	Follow ups	Follow up time	*p* value	Healing outcomes
				SPP median: 35mmHg	SPP =45: 13.90 (7.37) SPP >50: 11.38 (6.71)		<20mmHg and SPP = 35mmHg (p <.01) SPP <20mmHg and SPP > 50mmHg (p < .01)	Failed Major Amp: 0.88 SPP>20mmHg: 26 healed SPP<20mmHg: 1 healed 2 failed
Faris, 1985	SPP - Intradermal injections and 99mTc-pertechnetate.	28	SPP (mmHg)		Healed SPP: 59 ± 16mmHg) Unhealed SPP: 35 ± 11mmHg)		<.001	Healing with conservative treatment: 25 Local Surgery (toe amp or local drainage of abscess: 14 Transmetatarsal amp: 2 Femoropopliteal bypass: 10 Femorotibial bypass: 7 Below Knee Amp: 6
Faris, 1988	SPP					6-42 (median: 22 months)	SPP < .0016	Conservative treatment: 97 (69% healed) Local Amputation: 43 (75% healed) Arterial

Author	Microvascular measurements	Revascularisations	Measurement	Baseline	Follow ups	Follow up time	*p* value	Healing outcomes
								Reconstruction: 48 BTK Amputation: 14
Fiordaliso, 2016						7,14 and 30 days post-surgery and then until healing		Healing: 58? Major Amputation (above ankle): 2 Death: 1
Galanakis, 2020	LDF PORH 3 min arterial occlusion at 250mmHg Skin temperature continuously recorded	0	Resting LDF Peak LDF			1-2 Before treatment 4-7 weeks of treatment 2 weeks post treatment		Nil improvement seen during or after treatment of LFD with Fragmin
Jorneskog, 1993	LDF PORH 4 min arterial occlusion at the ankle at cuff pressure of 250mmHg. Probes then heated to 44 degrees celsius during six mins		Coefficient of Variation for peak LDF Resting LDF (PU) Peak LDF% Time to peak LDF Follow up -	65 ± 48 78 ± 85 151 ± 97	-0.8 (45.0) 0.00 (96.0) -12.8 (55.0)	Until healing or six months of Dalteparin	.264	Healed with intact skin: Increased ulcer area: 5 Improved (</= 50% reduction of ulcer area: Amputation

Author	Microvascular measurements	Revascularisations	Measurement	Baseline	Follow ups	Follow up time	*p* value	Healing outcomes
			comparison of changes					above or below ankle: 2
Lee, 2021	SPP		mmHg	overall: 40.0 ± 21.8; healed: 44.1 ± 21.0; unhealed: 33.5 ± 21.7	Overall: 52.4 ± 22.5; Healed: 61.8 ± 18.5; unhealed 37.4 ± 19.9	3-6 months	<.001 pre- and post-	
Mennes , 2021	Laser speckle contrast imaging - POHR	Nil - Pts who underwent revascularisation were excluded	Mean ± SD	Foot: Baseline:50.3 ± 14.6 Post-occlusion Peak: 77.3 ± 26.6 Ulcer: Baseline:104.8 ± 34.6 Post-occlusion Peak:104.0± 33.4 Ulcer Edge: Baseline:92.2 ±30.7 Post-occlusion Peak:102.0 ± 32.9	Healed Foot-12 Weeks Baseline:49.3± 15.1 Post-occlusion Peak:76.7± 24.4 26 Weeks Baseline:49.4 ± 13.9 Post-occlusion Peak: 52.3± 16.3 Ulcer- 12 Weeks Baseline: 108.8± 33 Post-occlusion Peak:107± 32.6 26 Weeks Baseline:109.1± 35.7	12 and 26 weeks	Foot-12 Weeks Baseline: .654 Post occlusion Peak: .889 26 Weeks Baseline: .508 Post occlusion Peak: .983 Ulcer- 12 Weeks Baseline: .467 Post occlusion Peak: .473 26 Weeks Baseline: .197 Post occlusion Peak: .190 Ulcer Edge-	N/A

Author	Microvascular measurements	Revascularisations	Measurement	Baseline	Follow ups	Follow up time	*p* value	Healing outcomes
					Post-occlusion Peak: 108.2± 35.2 Ulcer Edge- 12 Weeks Baseline: 96.3± 33.4 Post-occlusion Peak:108.1± 33.9 26 Weeks Baseline:94.2± 33.8 Post-occlusion Peak: 104.8± 35.3 Non-healed Foot- 12 Weeks Baseline:51.1± 14.5 Post-occlusion Peak:77.8± 28.6 26 Weeks Baseline:52.3± 16.3 Post occlusion Peak:77.2± 33.6		12 Weeks Baseline: .402 Post occlusion Peak:0.239 26 Weeks Baseline: .509 Post occlusion Peak: .373	

Author	Microvascular measurements	Revascularisations	Measurement	Baseline	Follow ups	Follow up time	*p* value	Healing outcomes
					Ulcer-12 Weeks Baseline:101.8± 36.1 Post-occlusion Peak: 101.1± 34.3 26 Weeks Baseline:95.8± 31.2 Post-occlusion Peak:95.2± 28.2 Ulcer Edge-12 Weeks Baseline: 89.1± 28.6 Post-occlusion Peak: 97.3± 31.9 26 Weeks: Baseline: 88.1± 23 Post-occlusion Peak: 96± 27.4			
Yotsu, 2014	SPP (mmHg)		**Mean SPP (SD)**	Ischaemic: 27.0 ± 14.1 Neuro-	Ischaemic-Median (25%, 75%) Healed:37	4.5 year period	.341	Healing: Ischaemic: 9 Neuro-ischaemic: 9

Author	Microvascular measurements	Revascularisations	Measurement	Baseline	Follow ups	Follow up time	*p* value	Healing outcomes
				ischaemic: 34.6 ± 23.2	(17;43) Non-healed: 20 (15;37) Neuro-ischaemic Healed: 38(22;51) Non-healed: 17(16;32)		.141	Non healed: isch:4 neuro-ischaemic:1 Amputation: Ischaemic: 4 Neuro-ischaemic: 2 Death: Ischaemic: 3 Neuro-ischaemic: 1

ABI = ankle brachial index, Ach = acetylcholine, LDF = Laser Doppler Fluxmetry, LSH = Local skin heating, PORH = post-occlusive reactive hyperaemia, SD = standard deviation, SBF = skin blood flow, SNP = sodium nitroprusside, SPP = skin perfusion pressure, $TcPO_2$ = transcutaneous oxygen pressure