ASSESSMENTS AND SUMMARY OF JUDGEMENTS TABLES FOR ALL CLINICAL QUESTIONS IN THE PREVENTION GUIDELINE

CLINICAL QUESTION

In a person with diabetes at risk of foot ulceration, should foot self-care be recommended?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	Foot self-care
COMPARISON:	No foot self-care
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large	This intervention is actually not an intervention for health professionals. As such, it cannot be part of clinical trials. It needs to be studied in observational study designs. We found 2 specific observational studies investigating this. The findings from these 2 studies, together with our clinical reasoning on the effect self-care can have, made us judge this as a moderate effect.	We're not sure if our search was sensitive enough to pick up all observational studies that may have included some self-care factor. In our "future research" section, we should stimulate more observational studies on people without a foot ulcer, and on collecting reliable self-care data in such studies.

○ Varies ○ Don't know		

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	As above, there is almost no evidence. But clinical reasoning on self-care allows us to safely judge the undesirable effects of self-care as trivial.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Very low; based only on non-controlled studies	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Reducing foot ulceration is important to people with diabetes.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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	With moderate effects judged resulting from appropriate self-care, and trivial undesirable effects, the balance of effects probably favours the intervention. However, with the limited evidence, we judged this as probably, as more observational studies are needed to assess this with certainty as favouring the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	People may have to buy equipment for adequate self-care (mirror, emollients), but in all we assess the resources as negligible regarding costs and savings.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	No research available, so very low certainty.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	Despite absence of studies, given the high costs of ulceration and the low/negligible costs of self-care, we judge cost-effectiveness as probably favouring the intervention.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Considering equity in regard to self-care, we noted a number of reasons that may result in reduced equity: · Self-care often requires help or support · People may have to buy equipment for adequate self-care (mirror, emollients) · Some people may already be overburdened, foot self-care only adds to that; these people might struggle harder to perform adequate self-care · Self-care require physical and mental capabilities, not all people at (high)risk may possess these	

	Given these issues, self-care might reduce equity. When implementing self-care improvement programs, these aspects should be considered.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We expect that self-care is generally acceptable, and some qualitative studies are available to support this notion.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We expect that self-care is generally feasible, and some qualitative studies are available to support this notion.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
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
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	**Very low**	Low	Moderate	High			No included studies
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	No included studies
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

CONCLUSIONS

Recommendations

Educate, and after that encourage and remind a person with diabetes who is at risk of foot ulceration (IWGDF risk 1-3) to protect their feet by not walking barefoot, not walking in socks without shoes, or not walking in thin-soled slippers, whether indoors or outdoors. (Strong; Low)

Educate, and after that encourage and remind a person with diabetes who is at risk of foot ulceration (IWGDF risk 1-3) to wash the feet daily (with careful drying, particularly between the toes), use emollients to moisturize dry skin, and cut toenails straight across. (Strong; Low)

Educate, and after that encourage and remind a person with diabetes who is at risk of foot ulceration (IWGDF risk 1-3) to examine the feet daily and with the presence or suspicion of having a (pre-)ulcerative lesion, to rapidly contact an appropriately-trained healthcare professional for further advice. (Strong; Low)

Voting: unanimous for the direction and the strength of the recommendation

Justification

Overall justification
Self-care for ulcer prevention is important, as it can be done on a daily basis, involves the patients in their own care, and is simply a necessity to ensure that a patient gets care when any (pre-)ulcerative lesions are detected via their self-care.
In our recommendations, we are relatively general. This is needed, as details such as regarding the contact of a health professional, very much depend on the setting and organisation.

Detailed justification
Desirable Effects
Despite almost no evidence, this is still a strong recommendation, given its clinical importance and clinical observations of desirable effects when patients perform self-care.
Equity
Special emphasis is put in our descriptions on equity, as self-care might reduce equity. If specific interventions are implemented aiming to increase self-care, this should be carefully considered.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities

More observational studies are needed in people who do not have a foot ulcer. Despite availability of large studies, including meta-analysis of individual data, these observational studies are frequently older, and marred by including only limited self-care variables that are reliably and, where possible, objectively and quantitatively measured. New studies reflective of care at this moment are needed, with the use of sensors and other measuring systems to accurately capture self-care variables and other risk factor

CLINICAL QUESTION

In a person with diabetes at risk of foot ulceration, should structured education be offered or provided?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	Structured education
COMPARISON:	No structured education
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Some studies show an effect on helping prevent ulcers, and on other outcomes, while other studies show no effect, so the effects are small	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	None reported in any of the studies	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Based on the meta-analysis, downgraded from high (5 RCTs) to low for imprecision and inconsistency.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Reducing foot ulceration is most likely important to people with diabetes.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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	With small desirable effects and trivial undesirable, this probably favours the intervention	

Resources required

How large are the resource requirements (costs)?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	To do structured education, we estimate moderate costs, as structured education requires more than just a single leaflet or very quickly telling a patient what self-care is needed. The costs of any approach that is structured requires some time and potentially additional resources (e.g. leaflet, website, video), hence costs are not negligible, but also not large, so judged as moderate.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Structured education can take many forms, and the resources required depend on the choices made, as well as the opportunities to implement it within a healthcare system. Given this large variation, we judge the certainty of the required resources as very low.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	Even though this has not been studied, we judge most structured educational interventions as likely being relatively cheap in comparison to the high costs of the ulcers they aim to prevent. We therefore judge this as probably favouring the intervention.	

Equity

What would be the impact on health equity?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	The impact of education on equity may depend on the quality of the structured educational intervention. Only when such an intervention is culturally appropriate, accounts for gender differences, and aligns with a patient's health literacy and personal circumstances, has it the opportunity to increased equity. Given the complexity of developing such an intervention, more general programs might reduce equity, as they are likely better tailored to the majority of patients, thereby disadvantaging individuals with more complex circumstances or with minority needs.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	We judge that any educational intervention will generally be accepted by patients.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Structured education is already considered an essential and integral part of foot ulcer prevention, and is frequently provided in an unstructured way. We therefore judge structured interventions as feasible.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
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
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	**Very low**	Low	Moderate	High			No included studies
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	No included studies
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

CONCLUSIONS

Recommendation

Provide structured education to a person with diabetes who is at risk of foot ulceration (IWGDF risk 1-3) about appropriate foot self-care for preventing a foot ulcer. (Strong; Low)

Voting: unanimous for the direction and the strength of the recommendation

Justification

Overall justification

Despite low evidence, we judge education as very important, and therefore provide a strong recommendation. In many settings, education is the first and sometimes only preventative intervention available. In any setting in the world, education is needed to help patients understand how to self-care, as most preventative interventions require a form of self-care (e.g. monitoring, wearing footwear). Education is also being ingrained in clinical practice all over the world, it is done on a daily basis by healthcare professionals; providing a conditional recommendation would reduce face validity of the guideline and might hinder uptake. Another crucial aspect in our considerations is the education being "structured", as we want to stress how important it is that education should be provided in a structured way.

Detailed justification

Desirable Effects

Despite limited evidence on its effect on ulcer prevention, the desirable effect of increasing knowledge on how to self-care was deemed crucial as minimum knowledge for patients

Undesirable Effects

Education is unlikely to lead to harm

Resources required

Education is done already, so structured education will likely require limited resources

Acceptability

Patients generally value education about how to self-care

Subgroup considerations

Structured education should be culturally appropriate, account for gender differences, and align with a patient's health literacy and personal circumstances.

Implementation considerations

It is not possible to provide globally applicable recommendations on the best form of education, given differences in systems, circumstances, cultures and more. However, we do suggest for implementation that structured foot self-care education should be provided individually or in small groups of patients. It should be provided over several sessions and with periodical reinforcement, to maximize effect.

Monitoring and evaluation

Research priorities

Structured education can have many forms, with different methods, at various intervals, of different lengths, and with different educators. Finding what type of structured education is most beneficial in foot ulcer prevention is needed to investigate in future studies.

CLINICAL QUESTION

In a person with diabetes at risk of foot ulceration should instructions about foot self-management, including home foot temperature monitoring, be given?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	(Instructions about) foot self-management
COMPARISON:	No foot self-management
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large	Based on a relative risk of 0.51 as found in the meta-analysis, which drops to 0.75 based on the two low risk of bias studies, the effect is deemed small.	

○ Varies ○ Don't know		

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	No undesirable effect published. However, an unpublished assessment shows a reduction in quality of life in the intervention group in that study, which means this may have to be reconsidered.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Moderate. Downgraded from high (5 RCTs) to moderate because of imprecision	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability	Reducing foot ulceration important to people with diabetes.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ 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	Desirable effects outweigh undesirable effects.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The intervention requires a temperature measuring device, and additional support from healthcare professionals, which means costs are not negligible. However, costs for these devices are also not large, leading to a judgement of moderate costs.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Costs for devices is available from manufacturers, as well as one study.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ● Favours the intervention ○ Varies ○ No included studies	One abstract of a study that is yet to be published shows a favourable cost-effectiveness.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	This intervention does not appear to promote equity of healthcare. 1. Likely to only be available to those with the ability to pay for the device. 2. Likely to only be available to those who are IT / digitally literate. 3. Likely to be unavailable to those living in geographically disadvantaged locations, e.g. developing countries	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	Experience from RCTs shows that adherence to the intervention is low, and patients experience the intervention as a burden. This suggest that the intervention is probably not acceptable to most.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	In most countries this intervention is probably not feasible to introduce into the healthcare system. Not only do you need availability of the equipment but you would need good support infrastructure ie Maintenance and IT support for the technology plus podiatry of other foot health monitoring system to manage foot emergency. In countries where it might be feasible, it has not yet been widely implemented, which suggests that feasibility is indeed an issue.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
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
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
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	No included studies
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Consider coaching a person with diabetes who is at moderate or high risk of foot ulceration (IWGDF risk 2-3) to self-monitor foot skin temperatures once per day to identify any early signs of foot inflammation and help prevent a first or recurrent plantar foot ulcer. If the temperature difference between corresponding regions of the left and right foot is above a temperature threshold of 2.2 °C on two consecutive days, coach the person to reduce ambulatory activity and consult an adequately trained healthcare professional for further diagnosis and treatment. (Conditional; Moderate)

The decision for a conditional recommendation was not unanimous, with member(s) of the group voting for a strong recommendation. The majority voted for a conditional recommendation.

Justification

Overall justification
The evidence in favour of temperature monitoring leads to a recommendation in favour of this intervention. However, given the doubts regarding equity, acceptability and feasibility, we decided that this is a conditiona recommendation, as the success of this interventions depends on a number of conditions that need to be met.

Detailed justification
Desirable Effects
Clearly demonstrated effect in ulcer prevention from multiple RCTs
Equity
Intervention may benefit patients who already have increased self-care skills
Acceptability
Many patients not adherent to the intervention, showing limited acceptability
Feasibility
Implementation challenging and not widely achieved, despite availability of positive evidence for more than a decade, suggesting limited feasibility.

Subgroup considerations

Implementation considerations

When implementing temperature monitoring, considerations on systems used and patients for whom this applies are important. However, these factors are unknown currently, see research priorities below.

Monitoring and evaluation

Research priorities

This intervention has only been investigated in RCTs that used one specific device. However, other systems are available on the market. While these systems may have improved acceptability and feasibility, their effect have never been studied, nor their costs (with these systems being more expensive) or cost-effectiveness. Given doubts about the working mechanism of the intervention, not all feet heat up before they break down, these other systems need to be investigated in RCTs before judgements can be made. As these other systems measure temperature, but do not involve the necessity of looking at the foot at the same time, which migh be an important part of the intervention with the device currently investigated. Investigating these other systems in RCTs is a key research priority.
Another research priority is investigating for which patients this intervention is acceptable and feasible, to better personalise the condition under which this recommendation can be implemented.

CLINICAL QUESTION

In a person with diabetes at risk of foot ulceration, what orthotic interventions, including therapeutic footwear, should be used?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	Orthotic intervention(s), including therapeutic footwear
COMPARISON:	No or another orthotic intervention(s)
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	2 meta-analyses were conducted, one on the comparison of therapeutic footwear to own footwear and one on the comparison of pressure-optimized footwear to non-optimized footwear. Both show large but non-significant effects with relative risk ratios of 0.53 and 0.62, respectively. Heterogeneity was large for both. Other meta-analyses were not possible, due to the heterogeneity of the conditions compared (i.e. type of footwear studied) and control groups	

	(no footwear, any type of footwear, custom-made footwear, etc.). Based on these outcomes, we judge the desirable effects as moderate, as appropriate footwear can prevent foot ulcers. Effects will be larger if the risk of ulceration is larger. But even in those at low risk (IWGDF risk 1), we judge the effect of appropriate footwear on desirable outcomes as moderate, as footwear may prevent foot ulcers, pre-ulcers, also in this population.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	In those studies that did report adverse events, undesirable effects directly related to appropriate footwear were small. If footwear causes blisters or other pre-ulcers, it is because the footwear was not appropriate for the fit of the person's foot shape.	We do acknowledge the undesirable effect of having to wear footwear in situations where that can be uncommon or unwanted for people (e.g. inside the home, inside places of religion), for people who are not used to wearing footwear (e.g. in populations where walking barefoot is the norm), and for in warm climates. For these sub populations, undesirable effects may be considered moderate.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ● Moderate ○ High ○ No included studies	Moderate for those with a healed plantar foot ulcer. Low for all other populations. See systematic review for details.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Reducing foot ulceration important to people with diabetes.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ 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	With footwear preventing foot ulcers, we judge that the balance of effects probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Appropriate footwear is not cheap. To provide a person with appropriate footwear, moderate costs are required. For specific populations (e.g. those with a healed plantar foot ulcer), costs may even be large (custom-made footwear is even more expensive; pressure measurements for optimization requires expensive equipment).	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Based on assessment of footwear costs in multiple countries.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	Based on one unpublished cost-effectiveness analysis of pressure-optimized custom-made footwear, as well as on the costs of foot ulceration, we judge that the cost-effectiveness will probably favour the intervention.	

Equity

What would be the impact on health equity?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	On balance, we judge that this recommendation probably has no impact on health equity. Footwear is generally worn globally, and in when appropriate footwear is available, in a setting, people at risk of foot ulceration can access it. However, for specific populations, this may reduce equity. See additional considerations at undesirable effects for populations where this may play a role. Also, if only expensive appropriate footwear is available, while not reimbursed by the healthcare system, financial situation plays a role and may reduce equity.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	With the exception of earlier-mentioned subpopulation, appropriate footwear is generally acceptable, especially if people are aware of its importance.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Providing appropriate footwear is feasible in most settings. However, in resource-poor settings, this may be challenging. Also, measuring pressure distribution requires equipment that is not yet widely available, which may impact feasibility.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
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
RESOURCES REQUIRED	**Large costs**	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
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	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

CONCLUSIONS

Recommendation

In a person with diabetes who is at risk of foot ulceration

a. and with no or limited foot deformity, no pre-ulcerative sign and no plantar ulcer history (IWGDF risk 1-3), educate to wear footwear that accommodates the shape of the feet and that fits properly. (Strong; Low)
b. and with a foot deformity that significantly increases pressure or a pre-ulcerative sign (IWGDF risk 2 or 3), consider prescribing extra-depth shoes, custom-made footwear, custom-made insoles, and/or toe orthoses. (Strong; Low)
c. and with a healed plantar foot ulcer (IWGDF risk 3), prescribe therapeutic footwear that has a demonstrated plantar pressure relieving effect during walking, to help prevent a recurrent plantar foot ulcer; furthermore, encourage the person to consistently wear this prescribed footwear, both indoors and outdoors. (Strong; Moderate)

Voting: unanimous for the direction and the strength of the recommendation

Justification

Appropriate footwear is of crucial importance to protect the feet from damage. With the severe consequences of foot ulceration, this is very important. As such, footwear is the primary protective intervention in people with diabetes, hence our strong recommendations.

Subgroup considerations

Implementation considerations

Two key items are important to consider for implementation:
- Development of footwear for low resource settings. Various working groups globally are busy working on this.
- Availability of reliable pressure measurement equipment. At this moment, such equipment has limited availability, as systems are either expensive, or lacking reliability. Development of more affordable systems that can be implemented more widely globally is an important area of development.

Monitoring and evaluation

Research priorities

Footwear interventions for people at moderate risk of ulceration (IWGDF 2) or those with a healed non-plantar ulcer (IWGDF risk 3) have received little attention in research. More studies are needed in these populations.
Footwear interventions for populations and settings where it is challenging to wear footwear are needed. Recent developments have seen custom-made indoor footwear being developed. The effects of such indoor footwear should be investigated in controlled studies, and similar new interventions (e.g. for warm climates) should be developed.
Cost-effectiveness remains important to be studied, especially with footwear requiring moderate costs at delivery, and savings primarily found in costs not made later on.

CLINICAL QUESTION

In a person with diabetes at risk of foot ulceration, how should pre-ulcerative signs and symptoms be treated?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	Callus removal
COMPARISON:	No callus removal
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	In all studies PP was reduced by a significant amount but effect size was not reported. No RCTs. Long term change in PP was not reported. Reduction in clinical pre-ulcerative signs (less callus) or ulceration incidence was either not achieved or not reported.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	No undesirable effects reported in the literature. Although this assumes that those delivering the intervention are appropriately trained.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	Based on statement of evidence. Two non-controlled studies with high risk of bias.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability	Reducing foot ulceration is important to people with diabetes. Reducing peak pressures and pre ulcerative signs is important to clinicians.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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	Despite desirable effects being small, they likely outweigh the undesirable effects (trivial). There are no adverse effects reported	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ○ Negligible costs and savings ● Moderate savings ○ Large savings ○ Varies ○ Don't know	Estimated cost of resources for callus removal (Cost of Podiatry) comparatively low and likely to be cost effective when compared to cost high-cost burden of foot ulceration / amputation (Kerr 2018). NOTE: This decision has been reduced to moderate from Large Savings to take into account those LIC without existing staff on the front line to deliver the service and the cost of setting up such a service.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Cost of intervention moderately low. Cost of savings could be substantial, but this is unproven.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	In the absence of any cost effectiveness data, given the massive cost saving of preventing one foot ulceration and subsequent ulceration and based upon the clinical opinion that it is highly likely that some ulcerations could be prevented, we anticipate that cost effectiveness probably favours the intervention	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ● Probably increased ○ Increased ○ Varies ○ Don't know	Treatment of pre ulcerative signs and symptoms using podiatry and callus removal is standard practice in most High-Income Countries with a foot care service and is available to all at risk of foot ulceration in those counties with a free health service or health insurance coverage. The introduction of this service in Low Income Countries is likely to increase health equity.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Regular removal of callus is highly acceptable to patients. One of the few preventative interventions for foot ulcer that has an immediate tangible benefit for patients (reduction of pain, increase in comfort). Also low undesirable consequences.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Feasible to implement in High Income Countries. Probably feasible to implement globally. Barriers to implementation of (callus reduction) include training of clinicians, limited availability / access to clinics. Comparison made to 'education about foot protection' which is highly feasible given comparatively low cost and training requirements.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	**No important uncertainty or variability**			
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
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	**Moderate savings**	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
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	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	○	●

CONCLUSIONS

Recommendation

Provide appropriate treatment for any pre-ulcerative sign or abundant callus on the foot, for ingrown toe nails, and for fungal infections on the foot, to help prevent a foot ulcer in a person with diabetes who is at risk of foot ulceration (IWGDF risk 1-3). (Strong; Very low).

Voting: unanimous for the direction and the strength of the recommendation

Justification

Our recommendations reflect the belief that most people with diabetes threatened with foot ulceration will place a high value on receiving treatment for pre-ulcerative signs such as callus even if the size of the reduction in ulceration risk is small or uncertain. Callus removal is effective in reducing peak plantar pressure immediately following treatment. This is evidence of benefit based two non-controlled studies. Despite a lack of evidence, we consider this standard practice and therefore in favor of this recommendation

DETAIL
Reducing foot ulceration is important to people with diabetes and reducing peak pressures and pre ulcerative signs is a key treatment aim for clinicians managing foot ulcer prevention. No undesirable effects reported in the literature. Although this assumes that those delivering the intervention are appropriately trained.

Subgroup considerations

Implementation considerations

Treatment of pre ulcerative signs and symptoms using podiatry and callus removal is standard practice in most High-Income Countries with a foot care service and is available to all at risk of foot ulceration in those counties with a free health service or health insurance coverage. The introduction of this service in Low Income Countries is likely to increase health equity

Feasible to implement in High Income Countries. Probably feasible to implement globally. Barriers to implementation of (callus reduction) include training of clinicians, limited availability / access to clinics.

Comparison made to 'education about foot protection' which is highly feasible given comparatively low cost and training requirements.

Research priorities

Further research is needed using to assess the benefit of callus reduction in people living at risk of foot ulceration.

The traditional RCT design of these studies may be challenged by the wide spread acceptance of callus removal as standard care making it difficult to create a meaningful comparator group.

More information is also needed regarding frequency of treatment.

CLINICAL QUESTION

Should flexor tenotomy be used in a person with diabetes at risk of foot ulceration?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	flexor tenotomy
COMPARISON:	toe orthoses or other usual care
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know	Based on 1 RCT and multiple non-controlled studies showing a beneficial effect of flexor tenotomy over usual care to prevent a foot ulcer on the toe	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	Based on few adverse events reported in all these studies.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Low; downgraded from moderate (1 RCT) to low because of risk of bias (incomplete reporting))	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Reducing foot ulceration is important to people with diabetes.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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	Following judgements above, we assess that the desirable effects probably outweigh the undesirable effects.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	While a surgeon is required to perform the tenotomy, doing so saves the requirement of making a toe orthosis. As such, we judge that the costs and savings balance out, and resources required are therefore considered negligible.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Detailed cost breakdown is not available.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	Given the costs of treating a foot ulcer, the cost-effectiveness probably favours the intervention.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Assessed based on a system where a surgeon to perform the tenotomy is available, we judge this as probably not having an impact, as it can be done on any person, and surgeons are generally available and reimbursed within the system. However, the working group does note that on a global scale, this may reduce equity, as surgeons (or other adequately trained professionals) to perform the tenotomy are not available in all settings.	

Acceptability

Is the intervention acceptable to key stakeholders?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	The procedure is simple with limited side effects, and most patients in all studies showed acceptance. However, some patients refuse any type of surgery, and as such we assess this as probably yes.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Provided a surgeon is available, the procedure is feasible, as it is simple to perform, and can be done in an outpatient clinic.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
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
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	**Low**	Moderate	High			No included studies
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	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

In a person with diabetes at risk of foot ulceration (IWGDF risk 1-3) and a non-rigid hammertoe with nail changes, abundant callus or a pre-ulcerative lesion on the apex or distal part of this toe:

a. consider digital flexor tendon tenotomy for treating these outcomes and for preventing a first or recurrent foot ulcer. (Conditional; Moderate), or
b. consider prescribing orthotic interventions, such as toe silicone or (semi-)rigid orthotic devices, to help reduce abundant callus on the toe. (Conditional; Low)

Voting: unanimous for the direction and the strength of the recommendation

Justification

Flexor tenotomy is a simple procedure with limited side effects or adverse events, and effective in changing the structure of the toe to prevent foot ulcers from occurring. Silicon toe orthoses are also simple devices that can be made relatively easily. However, these require a person to consistently wear it, and these require creating new ones when worn out. Also, the evidence base for orthoses is lower. However, given no clear superiority of tenotomy over toe orthoses, given the inherent risk of surgery, and the requirement of having a surgeon available, we provide a conditional recommendation for both options.

Subgroup considerations

Monitoring and evaluation

Research priorities

Flexor tenotomy has now been investigated in 1 RCT. More RCTs remain needed, to confirm findings in other settings. Also, the comparison condition of 'usual care' may be changed to a direct comparison with toe orthoses. Cost-effectiveness studies of both tenotomy and toe orthoses also remain needed.

CLINICAL QUESTION

Should nerve decompression be used in a person with diabetes at risk of foot ulceration?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	Nerve decompression
COMPARISON:	No nerve decompression
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	While studies have been performed, their designs are not appropriate to investigate foot ulceration as an outcome (i.e. using a contralateral leg for comparison). While RCTs are ongoing, results still have not been published. Because in clinical practice none of the working group members has any experience with or knowledge of centers where this surgery is being performed, we also have no clinical judgements to assess desirable effects. As such, we judge this as "don't know", to further stress that this is an intervention with a risk, but the desirable effects on ulcer prevention are unknown.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	Any surgery comes with risk, but the adverse events reported in the studies suggest these undesirable effects are small.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies	There is no adequate evidence.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Reducing foot ulceration important to people with diabetes.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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	With no known desirable effects, and with undesirable effects present, the balance probably favours the comparison.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Requires surgery on the leg in an operating room.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Surgery in an operating room always comes with costs, irrespective of the setting.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	While one Markov-analysis suggests otherwise, we decided this study could not be included given the modelling is based on flawed studies with wrong designs. Because we do not know the desirable effects (see above), we cannot assess cost-effectiveness.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	If it was to be considered, it would probably have reduced equity, as the surgery is not straightforward and may not be available to any person that meets the criteria for surgery.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	With no known benefits and risks involved, it is probably not acceptable.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	While feasible to perform for a trained surgeon, with limited clinical experience globally with this type of surgery, we assess that it is probably not feasible to perform if it were to be considered for recommendation.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
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
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
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	**No included studies**
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	**Conditional recommendation against the intervention**	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	●	○	○	○

CONCLUSIONS

Recommendation

In a person with diabetes who is at risk of foot ulceration (IWGDF risk 1-3), we suggest not to use a nerve decompression procedure to help prevent a foot ulcer. (Conditional; Very low)

Voting: unanimous for the direction and the strength of the recommendation

Justification

With no known benefits, and the inherent risk of surgery, we suggest this procedure should not be performed to prevent foot ulcers.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities

We suggest not to undertake any new research initiatives, until the results from 2 ongoing RCTs on this topic are being published. Given the risks and our recommendation against this intervention, obtaining the outcomes from the ongoing trials first is imperative before further research is to be considered.

CLINICAL QUESTION

In a person with diabetes at risk of foot ulceration, should foot-related exercises be done?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	Foot-related exercises
COMPARISON:	No foot-related exercises
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	Our meta-analysis found positive effects on most outcomes, but these effects reached statistical significance only for range of motion. As such, we judge the desirable effects as small. For details please see the meta-analysis.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	Undesirable effects directly resulting from the foot-ankle exercises were trivial, as found in our meta-analysis.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	The certainty of the evidence of effects is low, primarily given imprecision and indirectness as described in our meta-analyses.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Reducing foot ulceration is important to people with diabetes. Improving foot and ankle strength and function is probably also important, as patients will directly profit from these improvements, and the process evaluations of some RCTs show positive experiences from participants.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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	For the outcomes that we ranked as "critically important for decision-making" (e.g. ulcer occurrence/recurrence, ulcer severity - see further our systematic review), the intervention does not favour the comparison. The intervention shows no effect on these outcomes. For outcomes that we ranked lower (e.g. range of motion, neuropathy signs/symptoms), the intervention favours the comparison according to our meta-analysis. As such, our overall judgement is "probably favours the intervention".	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Programs that require an appropriately trained healthcare professional for 8-12 weeks involve moderate costs, being the human capital costs involved in such a program. Some small additional costs may be required, such as elastic belts for the exercises. Because programs that do involve a healthcare professional show better results on some outcomes, and because we value the importance of involving a professional during the course of a program to support patients, we assess the costs as moderate.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	Costs for healthcare professionals are known in almost all settings, and we therefore asses this as being of moderate certainty.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● Probably favours the intervention ○ Favours the intervention ○ Varies ○ No included studies	An ongoing RCT with cost-effective analysis shows that this probably favours the intervention (personal communication from the researchers).	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Foot-ankle exercises are easy to perform, and with support of a healthcare professional, we judge that this is likely the situation for all, and therefore assess this as probably not having an impact on equity.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	The process evaluations of some RCTs on this topic show that the intervention is acceptable for patients, with high adherence.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	The process evaluation of some RCTs shows that this intervention is generally feasible to implement. While it is frequently performed by physical therapists, other healthcare professionals can be trained to support patients in performing these exercises. As such professionals can even be trained from a distance, we judge that this is probably feasible.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
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
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
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	No included studies
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Consider advising and referring a person with diabetes who is at low or moderate risk for foot ulceration (IWGDF risk 1 or 2) to participate in an 8-12-weeks foot-ankle exercise program, preferably under the supervision of an appropriately trained healthcare professional, and to continue performing foot-ankle exercises afterwards, with the aim of reducing risk factors of ulceration. (Conditional; Low)

The decision for a conditional recommendation was not unanimous, with member(s) of the group voting for a strong recommendation. The majority voted for a conditional recommendation.

Justification

Overall justification
Primary reason for a recommendation in favour is that there is a decent body of evidence showing effect, feasibility and acceptability of the intervention. The intervention also has the benefit that it requires limited resources outside the human capital. This means it is possible to train healthcare professionals globally, and provide this intervention. That's different from, for example, footwear. However, by providing a conditional recommendation (not a strong one) we aim to emphasize that – if investments in ulcer prevention programs are considered – one should first investigate the opportunities for footwear and other strong recommendations, before conditional recommendations are implemented.
Primary reason for a conditional recommendation concerns the effect. There is an effect of the intervention on outcomes such as range of motion and neuropathy. This may, in the end, have positive effects on ulcer outcomes. However, it will require quite an effort to get there, and the direct link between improving ROM/neuropathy and reducing ulcers has not yet been proven, also not in the RCTs on the effect of foot-ankle exercises.

Detailed justification
Desirable Effects
See justification above.
Undesirable Effects
Foot-ankle exercises can be done with almost no undesirable effects, hence our reason to recommend in favour of this intervention.
Acceptability
Foot-ankle exercises have shown to be acceptable to patients, with high adherence to the 8-12 weeks programs. However, we also stress that adherence to continuing the exercises after the program is unknown, and might be much lower.
Feasibility
8-12 weeks foot-ankle exercises are feasible in many different settings, as they require limited resources beyond the human capital. As lifelong continued support is not feasible, we recommend that patients continue after the program. Feasibility of this part of our recommendation has not been studied, and it is unknown how patients assess this.In addition, regarding feasibility, the working group thought it important to recognize the following: by providing a conditional recommendation (not a strong one) we aim to emphasize that – if investments in ulcer prevention programs are considered – one should first investigate the opportunities for footwear and other strong recommendations, before conditional recommendations are implemented.

Subgroup considerations

Implementation considerations

When implementing foot-ankle exercises are considered as part of ulcer prevention programs, we stress the importance of first focusing on strong recommendations, such as the availability of adequate footwear.

Monitoring and evaluation

Research priorities

In RCTs, longer follow-up beyond the program is required. With such follow-up, acceptability and feasibility of continuing with foot-ankle exercises at home can be investigated, and outcomes can be monitored over longer periods.
In addition, with inconsistency in some outcomes as found in various RCTs, more studies remain needed to better investigate the effect of foot-ankle exercises on the numerous outcomes important for ulcer prevention and foot/ankle characteristics, primarily on ulcer prevention itself, which has not been proven to date
Finally, for mechanical stress, focus lies on reducing peak plantar pressure. This is logical, as evidence is available showing peak pressure is related to the development of ulceration. However, other aspects of pressure might also play a role in gait and in patient experiences, such as changes in roll-over or an improved pressure distribution. Both the impact of such changes on ulcer and gait outcomes, as well as the changes foot-ankle exercises may have on these various parameters, should be investigated in future research.

CLINICAL QUESTION

In a person with diabetes at risk of foot ulceration, can the level of weight-bearing physical activity be increased?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	An increase in the level of weight-bearing activity
COMPARISON:	No increase in the level of weight-bearing activity
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know	An increase in weight-bearing activity has no effect on ulcer incidence (see meta-analysis), but we expect that it has an effect on general health, and it also improves some other outcomes such as range of motion (see meta-analysis). As such, we judge the desirable effects as small.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	An increase in weight-bearing activity has no effect on ulcer incidence (see meta-analysis), and no other undesirable effects were reported in the RCTs, or were present based on our clinical judgement. As such, we judge this as small.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Low certainty of evidence, as elaborated in the meta-analysis.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	Reducing foot ulceration is important to people with diabetes. We also subjectively assess from our clinical experiences that improving weight-bearing activity is also an important value for patients.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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	With a gain in weight-bearing activity, and no difference in ulcer outcomes, we assess that this probably favours the intervention.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	While some professional support or equipment to monitor weight-bearing activity may be useful, it is not essential, and as such we judge this as negligible.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies	It is with moderate certainty that we judge the resources required as described above, based on our clinical reasoning.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies	Has never been investigated, and is not under study at this moment either.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ● Increased ○ Varies ○ Don't know	Increasing weight-bearing activity is feasible for basically any patient, as patient are already weight-bearing. Increasing this can be done via short walks, or in multiple other ways. With this wide availability and the positive health outcomes that may follow from being active, we judge that this has the potential to increase equity.	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Based on clinical reasoning, we assess that this is acceptable to patients. Moreover, patients frequently indicate in clinical practice that they would like to be more active.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Increasing weight-bearing activity does not require resources, it only requires some opportunities in one's living surroundings to be active. We therefore judge this as probably feasible.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
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
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	**Moderate**	High			No included studies
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	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	**Increased**	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Consider communicating to a person with diabetes who is at low or moderate risk for foot ulceration (IWGDF risk 1 or 2) that an increase in the level of walking-related weight-bearing daily activity by an extra 1000 steps/day is likely to be safe regarding risk of foot ulceration. Advise this person to wear appropriate footwear when undertaking weight-bearing activities, and to frequently monitor the skin for (pre-)ulcerative lesions. (Conditional; Low)

Voting: unanimous for the direction and the strength of the recommendation

Justification

Overall justification

Increasing weight-bearing activity is important for patients. It improves health and well-being, supports independence, and is frequently an important goal for patients. As the evidence suggests this can be done safely, without increasing the risk for ulceration, the recommendation is in favour.

However, it is a conditional recommendation. First, the recommendation is given on the condition that a patient possess adequate footwear when undertaking weight-bearing activity. Second, some patients who increase their activity do ulcerate, so it remains important to carefully monitor the skin for (pre-)ulcerative lesions.

Detailed justification

Equity

Increasing weight-bearing activity is feasible for basically anyone. If done so, it increases health benefits. As this may therefore increase equity, we judge this as an important recommendation.

Subgroup considerations

Implementation considerations

Monitoring and evaluation

Research priorities

More studies remain needed on this topic. The 3 RCTs that include this component all show no effect, but ulcer outcomes were small and these studies were not powered to detect such an effect. Larger trials remain needed. In addition, more observational studies are required investigating the effect of weight-bearing activity on ulcer outcomes. The available studies show that higher activity might have an association with ulceration, but large variations are seen within the study. Larger studies are therefore needed. Also, these studies should have longitudinal designs, with multiple measures of weight-bearing activity, rather than the cross-sectional design of existing studies. Such studies should also investigate outcomes beyond the number of steps. These may include variability in weight-bearing activity (for which different directions of effect are seen in the 2 studies to date), bouts and durations of weight-bearing activity, and sedentary activity.

CLINICAL QUESTION

In a person with diabetes at risk of foot ulceration, should integrated care be provided?	
POPULATION:	People with diabetes at risk of foot ulceration
INTERVENTION:	Integrated foot care
COMPARISON:	No integrated foot care
MAIN OUTCOMES:	Diabetic foot ulcer; ulcer severity, pre-ulcerative lesion; ulcer-free survival days; health-related quality of life; costs; mortality; foot-related mechanical stress; weight-bearing daily activity; foot and ankle muscle strength / function; self-efficacy; knowledge; adherence; well-being; adverse events;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	A priori decided for all clinical questions given the burden of diabetes-related foot ulcers.	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ● **Small** ○ Moderate ○ Large ○ Varies ○ Don't know	RCT and cohort studies: Some inconsistency in results for primary outcome measure possibly dependent on population. In the studies recruiting patients with previous ulceration (1 cohort, 1 RCT) ulcer incidence was significantly reduced. In studies (RCT) recruiting patients with no history of foot ulcer severity but not incidence was reduced. One other study recruiting participants from all three risk categories no sig effect was found.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● **Trivial** ○ Varies ○ Don't know	No undesirable effects anticipated	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	Low; downgraded from high (3 RCTs) to low because of imprecision and publication bias (1 unpublished study).	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability	Reducing foot ulceration important to people with diabetes.	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ 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	Desirable effects favours the intervention in those patient's at high risk of foot ulcer and probably favourable in those at moderate risk but loss to follow up is higher in lower risk groups.	

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ● **Large savings** ○ Varies ○ Don't know	In those at high-risk high cost and high savings i.e. foot ulcers prevented.	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ● High ○ No included studies	Most integrated care packages include a multidisciplinary team plus ongoing frequent patient contact over weeks or years.	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ● **Probably favours the intervention** ○ Favours the intervention ○ Varies ○c No included studies	Unclear but in the absence of any cost effectiveness data, PROBABLY FAVOURS THE INTEVENTION: In patients at high risk of foot ulceration the cost of delivering the intervention per patient is likely to be less than the benefit both in terms of QoL and cost savings for every foot ulcer prevented.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● **Probably reduced** ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	Likely to be only available to those with the ability to pay or those with a high level of health literacy (clear understanding of which health services to use and when to use them)	

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ No ○ Probably no ● **Probably yes** ○ Yes ○ Varies ○ Don't know	Probably yes based on personal experience pt acceptability/preference for multidisciplinary diabetic foot clinics that offer a one stop shop. But mindful that some budget holders are unlikely to accept the costs of setting up an integrated provision when the health benefits and cost savings are in the future.	

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ● Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	Most low income countries are unlikely to have the health infrastructure, trained staff, or resources to support integrated care. In more developed countries the cost of implementation over time would prohibit the scale up of this intervention beyond providing targeted care for those at high risk of foot ulceration.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	**No important uncertainty or variability**			
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
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	**Large savings**	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	**High**			No included studies
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	No included studies
EQUITY	Reduced	Probably reduced	Probably no impact	**Probably increased**	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	**Probably no**	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Provide integrated foot care for a person with diabetes who is at moderate or high risk of foot ulceration (IWGDF risk 2 and 3) to help prevent a first or recurrent foot ulcer. This integrated foot care should include at least professional foot care, adequate footwear and structured education about self-care. Repeat this foot care or re-evaluate the need for it once every one to three months for high risk, and once every three to six months for moderate risk, as necessary. (Strong; Low)

Voting: unanimous for the direction and the strength of the recommendation

Justification

Overall justification
The evidence consistently shows that in people at HIGH risk of ulceration integrated care reduces the risk of diabetic foot ulceration, although these results are based on studies with small numbers of patients. However, the evidence to support the use of integrated care for those at moderate risk is less convincing. In studies (RCT) recruiting patients with no history of foot ulcer severity but not incidence was reduced. The recommendation is in favour, and this is a strong recommentdation
However, it should be noted that loss to follow up was high for people at moderate risk. Integrated care may not suit all patients at moderate risk. Therefore, the added treatment burden and resource cost may need to be offset by reducing frequency of repeat visits or targeting certain people at moderate risk.

Detailed justification
There are no undesirable effects arising from this intervention. Foot ulceration is an important concern for people with diabetes. Desirable effects favour the intervention in those patient's at high risk of foot ulcer and is probably favourable for those at moderate risk despite higher loss to follow up.

The cost of delivering the intervention per patient is likely to be less than the benefit both in terms of QoL and cost savings for every foot ulcer prevented.

Subgroup considerations

Implementation considerations

Most low-income countries are unlikely to have the health infrastructure, trained staff, or resources to support integrated care. In more developed countries the cost of implementation over time would prohibit the scale up of this intervention beyond providing targeted care for those at high risk of foot ulceration.

Monitoring and evaluation

Research priorities

More large scale RCTs with longer follow up are needed on this topic, and should include more contemporary (state-pf-the-art) intervention protocols for the different aspects of integrated foot care (i.e. footwear, education, self-management) . Research is particularly required to investigate the specific population that this intervention might benefit and consider impact on related but important outcome measures such as severity of ulceration, time to ulceration or number of ulcer free days.

Future RCTs should also evaluate integrated care in the framework of a complex intervention and thus also consider the interaction between the integrated care intervention and its delivery in a given context or setting.

Finally future work is needed to ascertain if the effects of the intervention justify the cost, particularly in those at moderate risk.

Definitions for the items (criteria) used in these Summary of Judgement tables (obtained from: https://gdt.gradepro.org/app/handbook/handbook.html#h.xr5ac2p2khuq)

Criteria	Questions	Explanations
How substantial are the desirable anticipated effects?	How substantial (large)are the desirable anticipated effects (including health and other benefits) of the option (taking into account the severity or importance of the desirable consequences and the number of people affected)?	The larger the benefit, the more likely it is that an option should be recommended.
How substantial are the undesirable anticipated effects?	How substantial (large) are the undesirable anticipated effects (including harms to health and other harms) of the option (taking into account the severity or importance of the adverse effects and the number of people affected)?	The greater the harm, the less likely it is that an option should be recommended.
Do the desirable effects outweigh the undesirable effects?	Are the desirable effects large relative to the undesirable effects?	The larger the desirable effects in relation to the undesirable effects, taking into account the values of those affected (i.e. the relative value they attach to the desirable and undesirable outcomes) the more likely it is that an option should be recommended.
How large are the resource requirements?	How large an investment of resources would the option require or save?	The greater the cost, the less likely it is that an option should be a priority. Conversely, the greater the savings, the more likely it is that an option should be a priority.
How large is the incremental cost relative to the net benefit?	Is the cost small relative to the net benefits (benefits minus harms)?	The greater the cost per unit of benefit, the less likely it is that an option should be a priority.
What would be the impact on health inequities?	Would the option reduce or increase health inequities?	Policies or programmes that reduce inequities are more likely to be a priority than ones that do not (or ones that increase inequities).
Is the option acceptable to key stakeholders?	Are key stakeholders likely to find the option acceptable (given the relative importance they attach to the desirable and undesirable consequences of the option; the timing of the benefits, harms and costs; and their moral values)?	The less acceptable an option is to key stakeholders, the less likely it is that it should be recommended, or if it is recommended, the more likely it is that the recommendation should include an implementation strategy to address concerns about acceptability. Acceptability might reflect who benefits (or is harmed) and who pays (or saves); and when the benefits, adverse effects, and costs occur (and the discount rates of key stakeholders; e.g. politicians may have a high discount rate for anything that occurs beyond the next election). Unacceptability may be due to some stakeholders: • Not accepting the distribution of the benefits, harms and costs • Not accepting costs or undesirable effects in the short term for desirable effects (benefits) in the future • Attaching more value (relative importance) to the undesirable consequences than to the desirable consequences or costs of an option (because of how they might be affected personally or because of their perceptions of the relative importance of consequences for others) • Morally disapproving (i.e. in relationship to ethical principles such as autonomy, nonmaleficence, beneficence or justice)
Is the option feasible to implement?	Can the option be accomplished or brought about?	The less feasible (capable of being accomplished or brought about) an option is, the less likely it is that it should be recommended (i.e. the more barriers there are that would be difficult to overcome).