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A Systematic Review of Multidisciplinary Teams to Reduce Major Amputations for Patients with Diabetic Foot Ulcers

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Abstract

Objective: Multiple single-center studies have reported significant reductions in major amputations among patients with diabetic foot ulcers following initiation of multidisciplinary teams. The purpose of this study was to assess the association between multidisciplinary teams (i.e., two or more types of clinicians working together) and the risk of major amputation, and to compile descriptions of these diverse teams.

Methods: We searched PubMed, Scopus, Cumulative Index to Nursing and Allied Health, and Cochrane Central Register of Controlled Trials from inception through May 24, 2019 for studies reporting the association between multidisciplinary teams and major amputation rates for patients with diabetic foot ulcers. We included original studies if: 1) 50% of the patients seen by the multidisciplinary team had diabetes, 2) they included a control group, and 3) they reported the effect of a multidisciplinary team on major amputation rates. Studies were excluded if they were non-English language, abstracts only, or unpublished. We used the 5-domain Systems Engineering Initiative for Patient Safety Model, to describe team composition and function and summarized changes in major amputation rates associated with multidisciplinary team care. A meta-analysis was not performed due to heterogeneity across studies, their observational designs, and the potential for uncontrolled confounding (PROSPERO no. 2017: CRD42017067915).

Results: We included 33 studies, none of which were randomized trials. Multidisciplinary team composition and functions were highly diverse. However, four elements were common across teams: 1) Teams were composed of medical and surgical disciplines. 2) Larger teams benefitted from having a “captain” and a nuclear/ancillary team member structure. 3) Clear referral pathways and care algorithms supported timely, comprehensive care. 4) Multidisciplinary teams addressed four key tasks: glycemic control, local wound management, vascular disease, and infection. Ninety-four percent (31/33) of studies reported a reduction in major amputations following institution of a multidisciplinary team.

Conclusion: Multidisciplinary team composition was variable, but reduced major amputations in 94% of studies. Teams consistently addressed glycemic control, local wound management, vascular disease, and infection in a timely and coordinated manner to reduce major amputation for patients with diabetic foot ulcerations. Care algorithms and referral pathways were key tools to their success.

Keywords

interdisciplinary; patient care team; healthcare team; limb salvage; limb preservation

Nearly 2 million Americans develop a diabetic foot ulcer each year; within 5 years of ulceration, 5% will undergo major amputation and 50–70% will die.^{1–4} Caring for patients with diabetic foot ulcer is complicated by a nexus of comorbidities including diabetes, vascular disease, neuroarthropathy, and peripheral neuropathy that cross the boundaries of usual medical or surgical care. These comorbidities, coupled with secondary infection, stymie ulcer healing, and care gaps further amplify the risk of major amputation.^{3,5} Experts have recommended a multidisciplinary team approach to optimally address these comorbidities in a coordinated manner and reduce major amputations.^{6–8}

Two systematic reviews assessed the impact of multidisciplinary teams on diabetic foot ulcer outcomes.^{9,10} In one, three of three studies reported a decrease in major amputations.⁹ In the other, eight of nine reported reductions in major amputations associated with multidisciplinary team care.¹⁰ Neither of these reviews included systematic descriptions of the multidisciplinary teams.

Given the recent, global surge in multidisciplinary teams to care for patients with diabetic foot ulcers and the lack of understanding how they form and function, we conducted a systematic review using descriptive analysis of teams. In this study, we define a multidisciplinary team as two or more clinicians from different disciplines working together to care for patients with foot ulcers, where the majority of patients have diabetes. We describe consistent elements of multidisciplinary teams that may be instrumental in achieving reductions in major amputations. Descriptions may benefit clinicians who are contemplating starting a multidisciplinary clinic at their institutions, and researchers interested in interventional or comparative-effectiveness studies.

The purpose of this study is two-fold: 1) describe multidisciplinary team composition and function using a systems engineering conceptual model, and 2) summarize the impact of multidisciplinary teams on major amputations. We hypothesize that multidisciplinary teams are associated with a reduced risk of major amputation.

METHODS

We conducted this systematic review in conformity with PRISMA and MOOSE guidelines.^{11,12} We followed a protocol that was registered *a priori* with an international prospective register of systematic reviews (PROSPERO no. 2017: CRD42017067915). Because this systematic review only used results from previously published studies, it was not considered human subjects research and, as such, did not qualify for IRB review.

Search Strategy

Investigators collaborated with a medical reference librarian to develop a comprehensive search strategy using controlled vocabulary and keywords. These included: diabetic foot, foot ulcer, multidisciplinary, interdisciplinary, multispecialty, patient care team, amputation, limb salvage, and limb preservation (full search strategy available in the online Appendix, Supplemental Table I). The librarian searched the following databases from their inceptions through May 24, 2019: PubMed, Scopus, Cumulative Index to Nursing and Allied Health, and Cochrane Central Register of Controlled Trials. We augmented our database search by manually screening reference of all selected articles. We contacted corresponding authors to obtain articles that were unavailable through national and international inter-library loans. Beyond this, we had no contact with authors of identified, screened, or selected studies.

Study Selection Process

We included all original studies which met the following inclusion criteria: 1) 50% of the patients seen by the multidisciplinary team had diabetes, 2) included a control group, 3) reported the effect of a multidisciplinary team, defined as 2 types of clinicians working together, on major (above-ankle) amputation rates for patients with foot ulcers. Studies were excluded if they were written in a language other than English, published as abstracts only, or unpublished. We purposively kept our inclusion and exclusion criteria broad to encompass the experiences of as many different teams as possible and increase the generalizability of our findings. Specifically, if a group of clinicians described themselves as a team, we accepted their self-designation to capture the widest range of teams as possible. We included observational studies because these designs are more frequently used to test interventions at the system-level, rather than individual-level. Two independent reviewers screened all titles and abstracts of the identified studies for inclusion. Discrepancies were resolved by a third, independent reviewer. We repeated this process using full text articles during the second phase of screening. Three articles reported the initial effect of a single multidisciplinary team soon after team formation with more longitudinal data captured in a subsequent publication.^{13–18} When this occurred, we only included the article with the most longitudinal outcome data and excluded the initial article. This allowed us to give equal weights to each unique multidisciplinary team.

Theoretical Model

Prior systematic reviews did not provide descriptions of the heterogeneous teams or their functions, which we thought would be useful in understanding *how* multidisciplinary teams might reduce major amputation rates for patients with diabetic foot ulcers.^{9,10} We used the Systems Engineering Initiative for Patient Safety (SEIPS) model to systematically compile team descriptions. The SEIPS model focuses on five work system domains — people, tasks, tools and technologies, physical environment, and organizational conditions. The model describes how elements of multidisciplinary teams interact to influence processes (managing diabetic foot ulcers) and outcomes (major amputation, Figure 1).¹⁹

Data Abstraction

The primary outcome of this review was the change in major amputation rates. We abstracted the following study attributes: publication year, design, location, sample size, length of enrollment, and whether team composition and function were reported. We abstracted the following patient attributes impacting the risk of major amputation and potentially confounding results: age, sex, race, whether a majority or all of the patients managed by the multidisciplinary team had diabetes, mean hemoglobin A1C levels, the proportion with peripheral vascular disease, the proportion with peripheral neuropathy, and whether the ulcer required hospitalization. We abstracted the following multidisciplinary team attributes, corresponding to the work system components of the SEIPS model: team composition by discipline (people); practice setting of inpatient or outpatient, and whether teams functioned in a universal healthcare system (environment); aspects of clinical care addressed (tasks); what tools and technology were used (tools and technology); and organizational changes to implement the multidisciplinary care teams (organization, Figure 1). Two reviewers independently abstracted all data using standardized, web-based forms. Reviewers met to resolve differences and clean data.

Risk of Bias Assessment

Two independent reviewers assessed the methodological quality and risk of bias for each included study using a modified Downs and Black checklist for randomized and non-randomized studies of healthcare interventions.²⁰ Higher scores indicated higher quality studies, with a maximum modified score of 25. Scores within 3 points of each other were averaged. Otherwise, reviewers discussed discrepancies and agreed upon a final score. Studies were also assigned descriptors of study quality (excellent, good, fair, or poor) based upon the final score and previously reported ranges.²¹

Analysis

We created descriptions of the multidisciplinary teams using the SEIPS model; we focused on commonalities that might be necessary, core components to reduce major amputations. We constructed a summarizing Forest plot of all studies reporting odds ratios, or raw data from which odds ratios could be calculated. We also tabulated studies reporting population-based incidence rates and reported results from papers reporting high-to-low amputation ratios. A meta-analysis was not performed due to heterogeneity across studies, their observational designs, and the potential for uncontrolled confounding that might significantly bias the resulting summary statistic.

RESULTS

Our search identified 1047 distinct articles, of which 605 were excluded during title and abstract screening. The remaining 442 full-text articles were reviewed, and 33 met inclusion criteria (Figure 2).

Study Characteristics

All 33 studies were observational, with global center representation (Table I). No randomized trials met our inclusion criteria. Twenty-six (73%) included at least 50 patients

treated by their respective multidisciplinary teams.^{14,24–46} Length of enrollment varied greatly among the 21 studies (64%) that reported it, in terms of calendar time or time to clinical endpoints.^{14,17,24–32,34,36–38,40,43,44,47–49} Some studies, often those using a historically controlled (pre-post design) had unclear follow-up (Table II, with brief case and control descriptions available in the online Appendix, Supplemental Table II). The mean bias score was 15.3 (SD 1.9), and most studies (82%) ranked fair. Lack of randomization and blinding— at the level of patients, providers, and researchers—commonly detracted from study quality.

Patient Characteristics

All but two multidisciplinary teams exclusively treated those with diabetes.^{16,47} Most studies (22/33, or 67%) limited their recruitment to patients with ulcers severe enough to warrant hospitalization.^{14,24–28,30,32–34,36,38–41,43–45,47,49–51} Six studies further restricted to those requiring either revascularization, major or minor amputation, or plastic surgery reconstruction.^{26,32,36,38,47,50}

When reported, patient characteristics were generally well balanced between those who received multidisciplinary care and those who did not. The mean patient age ranged from 56 to 76 years.^{14,17,24–34,38,39,41,43–47,49–51} Men composed 34–100% of patients.^{14,17,24–27,29–34,38–41,43–47,49,50} Five studies reported patient race; four included predominantly (>80%) white patients, and one included 100% Asian patients.^{14,16,29,31,51} The proportion of patients with peripheral vascular disease ranged from 42–100%.^{14,27,28,31–33,38,43,45–47,49,50} Three studies were entirely comprised of patients with peripheral vascular disease.^{27,38,47} The proportion of patients with peripheral neuropathy ranged from 64–100%.^{14,28,30,38,43,45,46,49,50} In the eleven studies reporting mean hemoglobin A1C values, two were less than 8%.^{25,28,32,33,43,45–47,49–51}

Multidisciplinary Team Characteristics

People: Team composition was highly heterogeneous, with 36 different disciplines represented on the 27 teams reporting their members.^{14,16,17,28–48,50–52} The average team included physicians from 5 distinct disciplines (range 3–9 physician disciplines/team). Typically, larger teams were divided into a nuclear team led by two or three physicians and ancillary team members called upon as needed. Some studies stressed that it was important to identify a team “captain” to coordinate efforts.^{16,32,36} Another large team reported a “learning curve,” as teamwork improved and major amputation rates fell over time.³⁸

All but one team included physicians from medical and surgical disciplines (Table III). Endocrinology was the most common medical specialty (82%). To a lesser extent, infectious disease (37%), general medicine (30%), and physical medicine and rehabilitation (22%) specialists were involved. Most teams (85%) included two or more surgical specialties.^{14,16,17,29–33,35–44,47,48,50–52} Peripheral vascular surgery was the most common surgical specialty (74%), although orthopedic surgery (67%), podiatry (52%), and plastic surgery (44%) were involved frequently.

In general, the roles of nurses and allied health professionals were less well documented. Team tasks, such as use of negative pressure wound therapy and casting, suggest these disciplines were under reported. The involvement of nurses was explicitly stated in 15 studies (56%), including general nursing, wound care nursing, and nurse case management.^{14,16,31,35,37–39,42–44,46,48,50–52} The contributions of allied health professionals were cited in 14 studies (52%), with even broader discipline involvement: casting, diabetes education, medical quality, nutrition, occupational therapy, orthotics, pharmacy, physical therapy, prosthetics, and social work.^{29–31,34,36–38,40,43,44,47,48,51,52} Of these, orthotics was the allied health professional discipline most commonly included on teams (8/28, or 30%).

Tasks: Despite varied compositions, teams consistently addressed four key clinical tasks: glycemic control, local wound management, vascular disease, and infection (Table IV). Twenty-six teams (79%) addressed three or more of these key factors. Regarding local wound management, most (29/32, 91%) were able to surgically debride and perform minor amputations, in addition to non-surgical interventions such as bedside debridement and off-loading.^{14,16,17,25,27–48,50–52} When addressing vascular disease, most teams (24/32, 75%) were able to revascularize patients as needed, in addition to performing diagnostic testing and medical management.^{14,16,17,26–28,31,32,35–41,43–48,51–53} Tasks associated with medical management of vascular disease, such as diagnosis and treatment of dyslipidemias, anti-platelet therapy, and smoking cessation were not well described in the majority of the articles. Only one mentioned smoking cessation as an explicit task.⁴⁰ Eleven teams directly addressed patient education.^{24,29,35–37,39,40,44,48,51,52} One study commented that team members would reinforce each other's recommendations, sending a consistent message and increasing patient adherence.⁵⁰

Studies stressed that individual tasks performed by multidisciplinary teams could, and often did, happen in standard practice. However, performing all tasks for all patients, especially in a coordinated and expedited manner, was not facilitated using the standard practice model. Multidisciplinary teams credited their improved outcomes to the combination of 1) consistently and synchronously addressing all contributing factors, and 2) providing timely care.^{16,27,32,35,39,41,48,50}

Teams held standing meetings or rounded together to coordinate and expedite care. Typically, meetings were held weekly.^{27,33,41,43,47} Some larger teams met weekly with the nuclear team and convened the whole team less frequently.^{33,41} One team stressed “Continuous Multidisciplinary Activity,” or daily interactions between team members to improve multidisciplinary work beyond meetings.¹⁶ In addition to focusing on individual patient care, meetings were used to address access and resource allocation.³⁹ One team dedicated a portion of these meetings to review the care plans of high-utilization patients.¹⁶

Tools and Technology: Teams used basic tools to assist with communication and coordination, not advanced technology. The most common tool was a care algorithm.^{24–28,30–32,34,39,43,45,46,48} This tool helped ensure teams were providing comprehensive care in an agreed upon order, by designated disciplines. Usually, care algorithms were constructed with input from team members prior to initiating multidisciplinary team care.^{31,34,39,46,48} Algorithms varied greatly in the amount of detail and complexity they

contained, with more detailed and complex algorithms tending to be more prescriptive^{24–28,30–32,34,39,43,45,46,48} One team used existing guidelines as a general framework, tailoring details to their specific team and system.¹⁷ Another stressed innovation when designing their algorithm, an approach which resulted in a combined group- and home-based patient educational program they thought was much more effective than their previous standard lectures and pamphlets.³⁹ Another used the algorithm to not only address physiological factors but facilitate inpatient-to-outpatient transitions.²⁸ One team designated a nurse to implement the algorithm and track patients' care through them.³⁹ Another used patient-tailored care algorithms as a metric of accountability among team members.³³ Tools utilized less frequently included: standardized documentation templates and order sets, antibiotic algorithms, and patient pamphlets.^{39,43,44,52}

Within individual disciplines, advanced technologies were employed. These included endovascular revascularization protocols, advanced plastic surgery closures, and wound vacuums.^{26,30,32,38}

Environment: Teams functioned in inpatient (9, 27%),^{14,24–26,33,37,41,44,45} outpatient (6, 18%),^{29,31,35,46,49,52} or both settings (18, 55%).^{16,17,27,28,30,32,34,36,38–40,42,43,47,48,50,51,53} Some described starting in either the inpatient or outpatient setting and then expanding to encompass both as their teams became more established. This facilitated continuity of care, which the multidisciplinary teams highly valued.⁴³ When caring for inpatients, co-locating patients on the same ward facilitated team rounding.^{33,43} Most studies (28/33, 85%) took place within universal healthcare systems.^{14,16,17,25,27–30,32,34,35,37–44,48–53}

Organization: Teams worked with existing resources and focused on changing system organization to improve patient outcomes.^{39,41,46} Before initiating multidisciplinary team care, organizational changes focused on two areas: within-team organization, and the interface between the team and other healthcare providers. Within-team organizational change included developing care algorithms and rules of conduct between team members, including: who would “captain” the team, which discipline would serve as the primary admitting service, and how consults would be called.^{16,32,34,36,39,44,48} Two outpatient teams grouped patients who required surgical consultation on the same day, increasing the efficient consultation of ancillary, surgical team members.^{40,42} Two teams incorporated *a priori* systems for improvement, either through annual audit-and-feedback or a patient registry.^{34,48}

Prior to initiating care, multidisciplinary teams met with specialists and primary care providers within their healthcare systems to establish clear referral pathways.^{16,17,27,28,35,42,50,52,53} Consensus among specialists was needed so that patients referred to specialists who were not part of the multidisciplinary team would be redirected to the team.^{42,52} Meetings with primary care providers focused on advertising the multidisciplinary teams and introducing referral pathways.^{16,28,35,42,52} Rapid triage was emphasized. One team guaranteed new patient evaluation within 24 hours.³⁵ Others developed telephone triage lines for referring providers so that new patients could be seen in an appropriate timeframe and setting (e.g. outpatient clinic or hospital admission).^{16,27} Recognizing that the specialists involved in these multidisciplinary teams were a limited resource, some teams focused on educating primary care providers on how to care for less complicated diabetic

foot ulcers so that the multidisciplinary teams could focus on patients with severe ulcerations.^{35,53} These efforts included clear parameters to refer to specialty care and pre-referral work-ups.³⁵ Two teams noted a steady increase in referrals over time, which expanded outside initial catchment areas.^{16,52}

Major Amputation Rates

All but two studies (31/33, or 94%) reported a decrease in major amputations associated with multidisciplinary teams. Twenty-five studies reported odds ratios, or raw data from which odds ratios could be calculated.^{14,24–34,38–49,51} Of these, the absolute percent change in major amputations associated with multidisciplinary teams ranged from a 2% increase⁴⁵ (OR 1.14, 95% CI 0.59–2.20) to a 51% absolute or 89% relative reduction (OR 0.11, 95% CI 0.05–0.25; Figure 3).²⁵ Six studies reported changes in incidence rates;^{16,17,35,37,52,53} all of these took place within national healthcare systems, involved stable populations, and reported decreases in major amputation rates associated with multidisciplinary teams (Table V). Two studies used the high-to-low (major-to-minor) amputation ratio.^{36,50} One of these reported a decrease from 0.35 to 0.27 following introduction of a multidisciplinary care team.³⁶ The other reported an increase from 0.46 to 0.55.⁵⁰

DISCUSSION

Despite heterogeneous team composition and function, multidisciplinary teams are associated with significant reductions in major amputations for patients with diabetic foot ulcers. Although we were unable to perform a meta-analysis, the direction of the association between multidisciplinary teams and major amputation is clear. Thirty-one of 33 studies found multidisciplinary teams were associated with fewer major amputations for patients with diabetic foot ulcers. Consistent reductions in major amputations across studies and diverse teams also contribute to the robustness of the finding. Multidisciplinary teams embedded in a variety of healthcare systems and composed of different provider combinations were able to reduce major amputations by collaboratively and efficiently addressing underlying factors.

Multidisciplinary team care is an effective strategy for the highest risk patients, especially those with 1) ulcers severe enough to warrant hospitalization, and 2) underlying peripheral vascular disease (i.e. the majority of patients served by multidisciplinary teams included in this review). It is consistent with expert opinion guidelines suggesting a tiered approach to care based on ulcer severity.^{7,54,55} In this model, primary care is responsible for preventing foot ulcers. Relatively straightforward ulcers can be managed locally with collaboration between primary care and populous specialties with wide geographic distributions, such as podiatry. Large multidisciplinary teams, like those included in this review, are in tertiary care centers and reserved for patients with severe ulcers. This model depends on effective triage so that patients receive the appropriate level of care.⁵⁶

Our review includes descriptions of how multidisciplinary teams integrate into their broader healthcare organizations and provides evidence to support aspects of this tiered model. Teams educated primary care providers and other local healthcare professionals to screen and care for patients with minimally complex ulcers. They also focused on streamlined

trriage into their highly-specialized multidisciplinary teams for patients with severe ulcers. These results support health services research within the U.S. and England demonstrating decreased major amputation rates in systems with effective referral pathways.^{57,58} What is lacking is an understanding of how best to leverage these resource-intensive, multidisciplinary teams. Subsequent investigations should focus on identifying the severity threshold for initiating multidisciplinary team care, which is likely to fluctuate based on available resources.

We were able to identify common elements of successful multidisciplinary teams using a health systems engineering conceptual model. Commonalities between these successful teams are important to identify because they may represent core elements, or facets of multidisciplinary team care that are necessary to reduce major amputations.⁵⁹ Clinicians starting a multidisciplinary team may want to incorporate these elements, and researchers may opt to investigate which common elements are necessary, core elements, for success. With this in mind, we noted the following. 1) Teams were composed of medical and surgical disciplines. 2) Larger teams benefitted from having a “captain” and a nuclear/ancillary team member structure. 3) Clear referral pathways and care algorithms supported timely, comprehensive care. Each of the preceding elements addressed work system conditions that enabled the multidisciplinary teams to perform their tasks consistently, collaboratively, and rapidly. 4) Multidisciplinary teams addressed four key tasks: glycemic control; local wound management, including surgical debridement and minor amputation; diagnosis and management of vascular disease, including revascularization; and diagnosis and management of infection. Prior studies also suggested coordination facilitated by referral pathways and care algorithms (consistent element 3), as well as comprehensively addressing all comorbidities contributing to ulceration (consistent element 4), are tactics used by teams to reduce major amputation rates.^{57,60}

The most notable limitation of our study is the quality of included studies, with the majority being ranked fair. This precluded our ability to perform a meta-analysis. It also introduced potential bias favoring multidisciplinary teams. Most studies used a historically controlled (pre-post) design, with controls receiving care before cases. In some studies, this difference was substantial and may have biased results; the formation of a multidisciplinary team may have occurred soon after increased utilization of endoscopic revascularizations or other advanced technologies. These technologies may have partially accounted for reductions in major amputations that were attributed solely to the multidisciplinary team. However, we do not think that this could entirely account for our findings as some studies utilized more robust designs, and some historically controlled (pre-post) studies took place over relatively brief periods where secular trends would be less influential. Another concern is that, as teams’ reputations and capacities increased, they cared for patients with less severe ulcers than controls. This may bias results towards multidisciplinary care, depending on how controls were selected. However, this potential bias should not exist in the six population-based studies, all of which reported a decreased incidence of major amputation following institution of multidisciplinary teams (Table V). We understand that studies of major shifts in care delivery, such as new multidisciplinary teams, are difficult to design. Treatment diffusion and lack of blinding make controlled study designs difficult. A step-wise wedge approach may offer a viable and ethically appropriate option.⁶¹ Pre/post study design using

historical controls can improve rigor using interrupted time series analysis.⁶² We would welcome future studies incorporating these methods. In addition to improving study design, adjusting for confounders with multivariate statistical modeling would have improved study quality. All reported odds ratios were unadjusted, raising the potential that differences in comorbidities between treatment and control groups could confound results. This concern is somewhat assuaged by generally well balanced treatment and control groups, among those studies reporting comorbidities. Another limitation was the exclusion of non-English language articles, although our intent was to perform a systematic review that would best inform efforts to improve the care of patients with diabetic foot ulcers in the United States. The global representation of English-language articles speaks to the widespread uptake of multidisciplinary team care for patients with diabetic foot ulcers. Our search identified 115 non-English language studies, some of which may have met the remaining inclusion criteria and reported a negative association between multidisciplinary teams and major amputation. Our results should be applied cautiously to settings outside of Europe and North America, where the excluded, non-English speaking articles may be more relevant. Finally, publication bias may have resulted in an overly favorable conclusion that multidisciplinary teams reduce the risk of major amputation for patients with diabetic foot ulcer.

CONCLUSION

Multidisciplinary teams— especially those able to address glycemic control, local wound management, vascular disease, and infection— are associated with a reduce the risk of major amputation for patients with severe diabetic foot ulcerations. Further studies⁶² are needed to clarify core elements of these teams and the thresholds of patient severity served by these resource- intense, highly effective teams.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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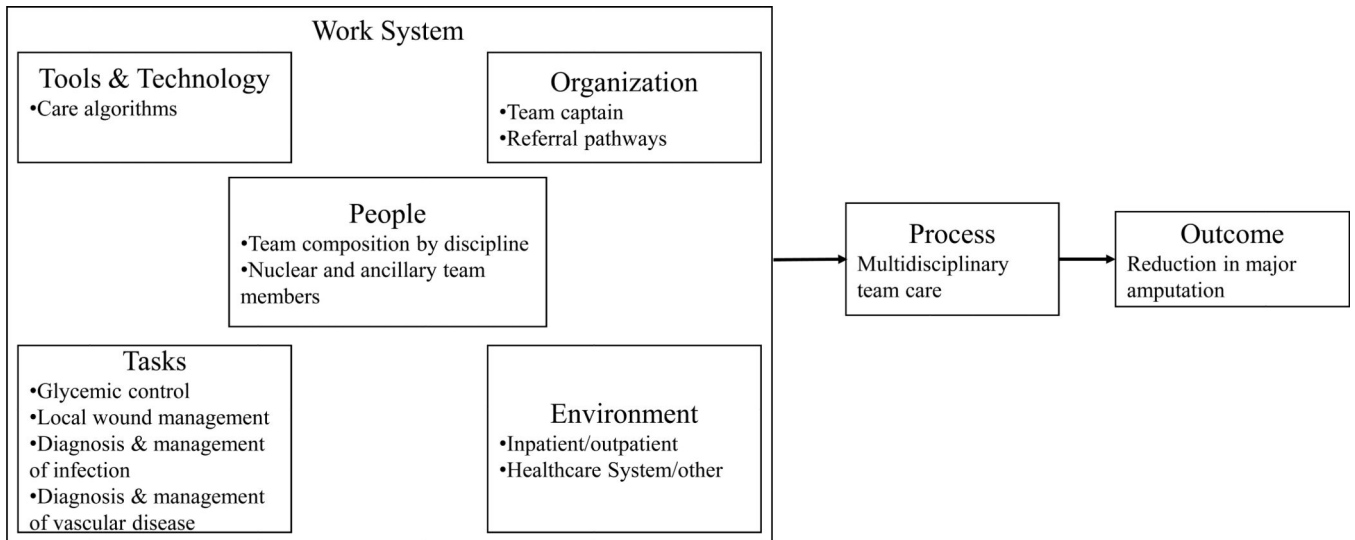


Figure 1. Systems Engineering Initiative for Patient Safety (SEIPS) model, adapted to the context of multidisciplinary care teams for diabetic foot ulcers.¹⁹

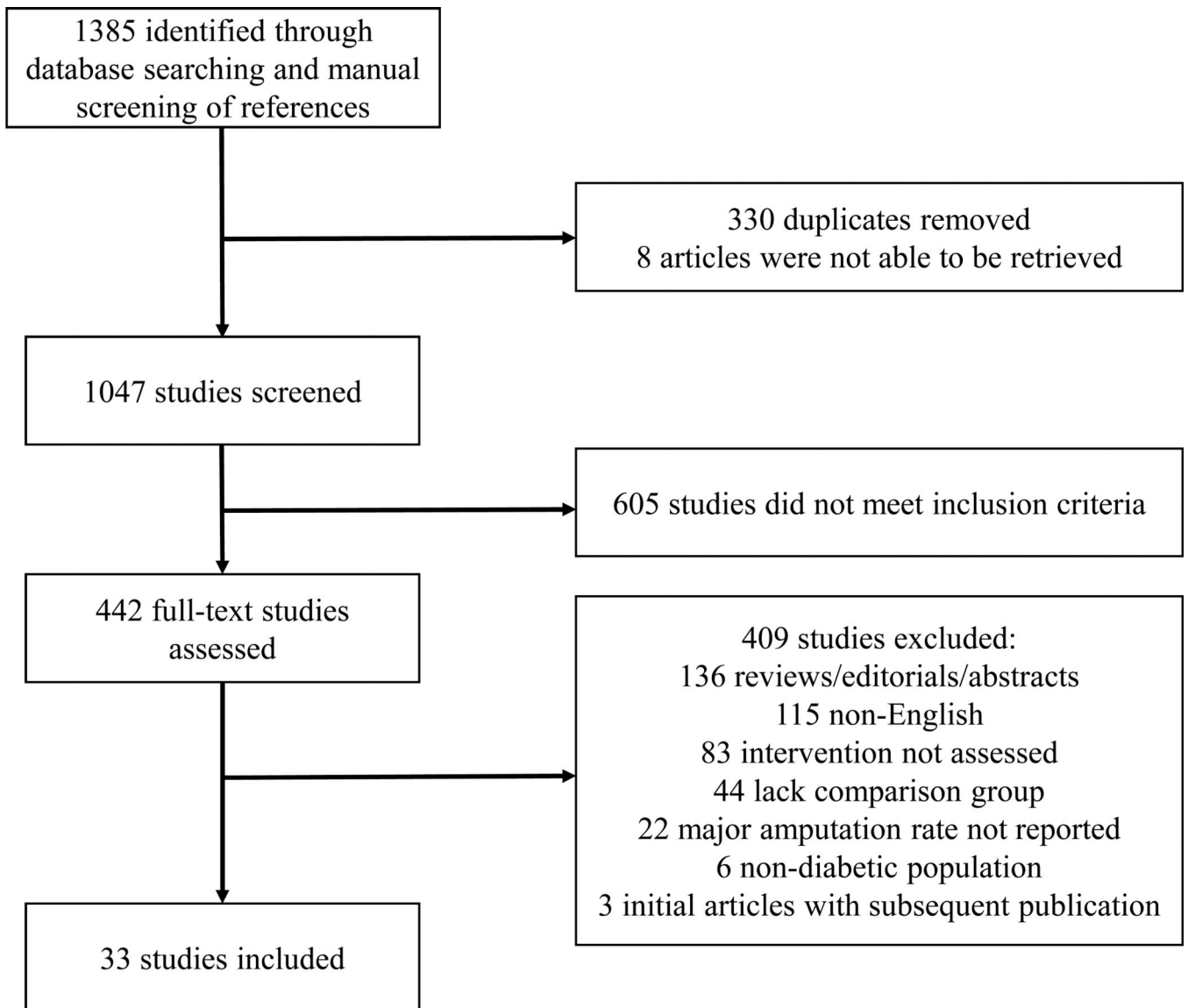


Figure 2.
PRISMA diagram for inclusion and exclusion of studies

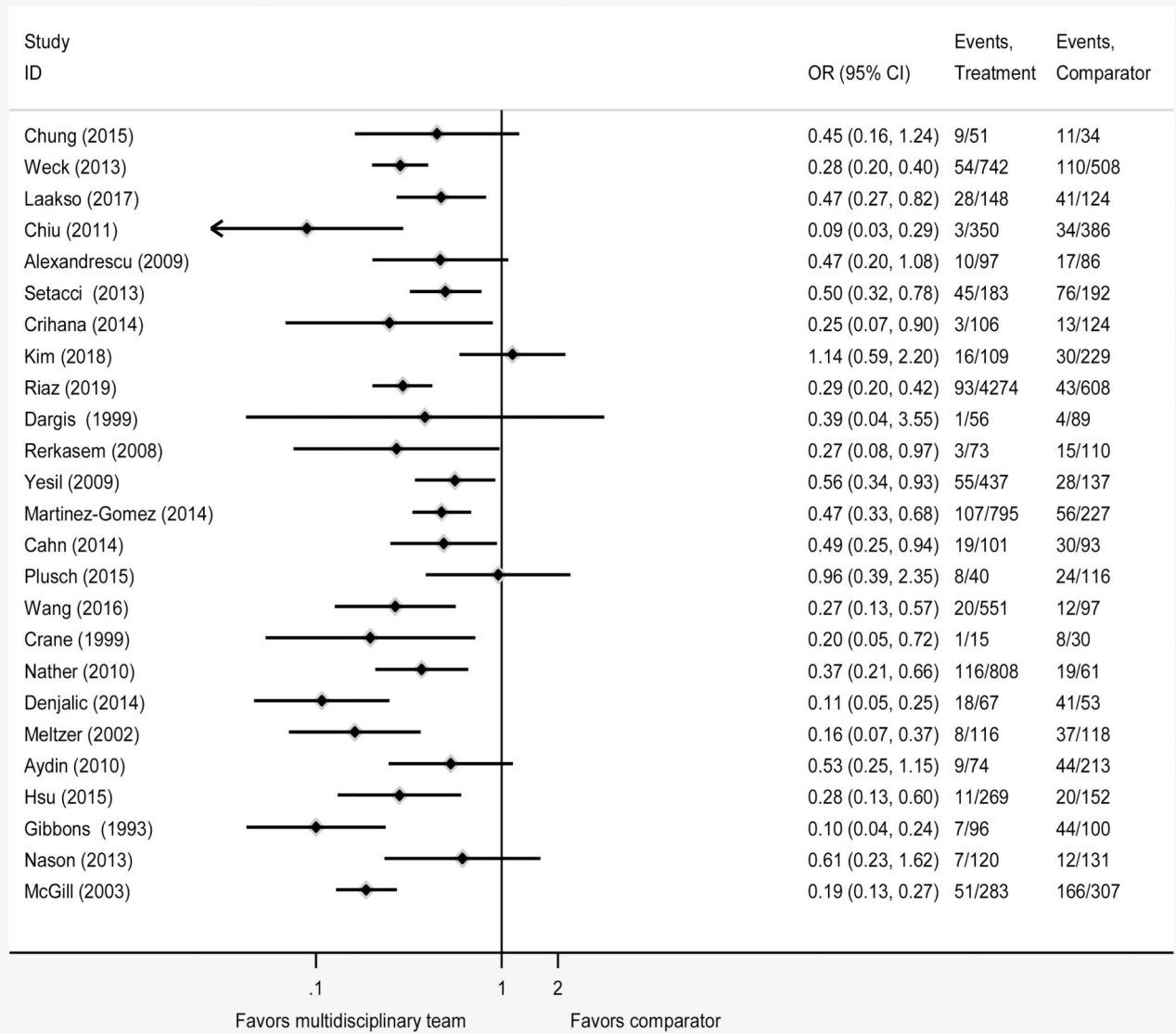


Figure 3. Forest plot of the estimated odds ratios for the change in major amputation rates following initiation of multidisciplinary care compared to standard care for 25 of the 33 included studies for which odds ratios could be calculated.

Table I.

Characteristics of the 33 included studies

Study Characteristic	N (%)	
Publication Date	Before 1990	0
	1990 – 1999	3 (9)
	2000 – 2009	8 (24)
	2010 - February 2019	22 (67)
Design *	Historically controlled (pre-post)	26 (76)
	Retrospective cohort	4 (12)
	Prospective cohort	2 (6)
	Case-controlled	2 (6)
	Randomized controlled	0
Location	Europe	18 (55)
	South America, Asia, or Africa	8 (24)
	North America	5 (15)
	Australia	2 (6)
Number of patients (multidisciplinary care)	0 – 24	0 (0)
	25 – 49	2 (6)
	50 – 74	6 (18)
	75 – 100	2 (6)
	>100	18 (55)
	Unknown	5 (15)
Length of enrollment	Unknown	12 (36)
	Until hospital discharge	7 (21)
	Until ulcer healed/major amputation	5 (15)
	Other	9 (27)
Bias score	22 – 25 (excellent)	0 (0)
	17 – 21 (good)	4 (12)
	12 – 16 (fair)	27 (82)
	<12 (poor)	2 (6)

* The n for Study Design totals 34, rather than 33, because one study used both a case-control design and a retrospective cohort design. We counted it in both categories.²⁴

Table II.

Study Descriptions

Study	Bias Score	Study Design				Follow up
		Prospective cohort	Retrospective cohort	Case-control	Historically controlled (pre-post)	
Chung 2015	20		X			Median 539 days (IQR 314 +/- 679)
Weck 2013	18.5	X				730 days
Laakso 2016	17.5				X	Unclear
Chiu 2011	17			X		Until wound healing or amputation
Riaz 2019	16.5				X	Unclear
Kim 2018	16.5				X	Unclear
Crihana 2014	16.5				X	Duration of admission
Seiaci 2013	16.5				X	182 days
Alexandrescu 2009	16.5				X	Mean: 700 days (range 30 – 2040 days)
Martinez-	16				X	Inpatient followed until discharge; outpatient and
Gómez 2014						inpatient followed for 730 days after admission
Yesil 2009	16				X	300 days after discharge
Hedetoft 2009	16			X		Unclear
Rerkasem 2008	16				X	Unclear
Dargis 1999	16	X				730 days
Jiménez 2017	15.5				X	Until ulcer healing, sometimes longer on case-by-case basis
Wang 2016	15.5				X	Duration of hospitalization
Plusch 2015	15.5		X			Duration of hospitalization
Cahn 2014	15.5				X	Duration of hospitalization
Denjalic 2014	15				X	Followed until ulcer healing (did not follow for recurrence)
Nather 2010	15				X	Duration of admission and follow up care for surgical intervention (length of stay average 10.81–20.36 days)
Crane 1999*	15				X	Duration of admission
Hsu 2015	14.5				X	Until wound healed

Study	Bias Score	Study Design				Historically controlled (pre-post)	Follow up
		Prospective cohort	Retrospective cohort	Case-control			
Armstrong 2012	14.5				X	Through wound healing, surgical post-operative care, metabolic control, and others. Timing was not reported.	
Witsø 2010	14.5				X	Unclear	
Aydin 2010	14.5				X	Duration of hospitalization (mean length of stay 26.9 days)	
Meltzer 2002	14.5				X	Between 1 day and 1095 days, but poorly defined	
Anchini 2007	14				X	Unclear	
Nason 2013	13.5				X	Unclear, LOS reported for those who were hospitalized	
Holstein 2000	2000				X	Until 1996	
Gibbons 1993					X	365 days	
Troisi 2016	11.5				X	Unclear	
McGill 2003			X			Unclear	

Table III.

Multidisciplinary team compositions.

Study	Bias Score(1)	OR for change in major amputation rate following multidisciplinary care	Physician Disciplines										Nursing (3) & Allied Health Professionals						
			Medical					Surgical					Other (2)						
			Endocrinology	General Medicine	Infectious Disease	PM&R	General Surgery	Orthopedics	Vascular Surgery	Plastic Surgery	Podiatry	Other	Nursing	Orthotics	Other (4)				
Chung 2015	20	0.45 (0.16, 1.24)		X	X							X	X						X
Szek 2013	18.5	0.28 (0.20, 0.40)	X									X							X
Lukso 2017	17.5	0.47 (0.27, 0.82)		X	X					X		X							X
Caru 2011	17	0.09 (0.03, 0.29)	X									X							
Alexandrescu 2009	16.5	0.47 (0.20, 1.08)	X	X	X					X		X	X					X	
Chiana 2014	16.5	0.25 (0.07, 0.90)	X					X				X						X	
Ken 2018	16.5	1.14(0.59, 2.20)	X							X		X							
Raj 2019	16.5	0.29 (0.20, 0.42)	X							X		X						X	
Dagis 1999	16	0.39(0.04, 3.55)	X						X					X					
Helletoft 2009	16	*	X							X				X					
Martinez-Camacho 2014	16	0.47 (0.33, 0.68)	X	X	X				X									X	
Raksem 2008	16	0.27 (0.08, 0.97)	X	X					X			X						X	
Williams 2018	16	-368/100,000								X		X						X	
Yesil 2009	16	0.56 (0.34, 0.93)	X		X				X			X						X	X
Cahn 2014	15.5	0.49 (0.25, 0.94)	X		X					X		X							
Wang 2016	15.5	0.27 (0.13, 0.57)	X							X		X						X	
Jiménez 2017	15.5	-1.6/100,000/year	X	X	X				X	X				X					
Nather 2010	15	0.37 (0.21, 0.66)	X		X					X		X		X				X	X

Study	Bias Score(1)	OR for change in major amputation rate following multidisciplinary care	Physician Disciplines						Nursing (3) & Allied Health Professionals					
			Medical			Surgical			Other (2)					
			Endocrinology	General Medicine	Infectious Disease	PM&R	General Surgery	Orthopedics	Vascular Surgery	Plastic Surgery	Podiatry	Nursing	Orthotics	Other (4)
Armstrong 2012	14.5	***		X	X				X		X			X
Aydin 2010	14.5	0.53 (0.25, 1.15)	X		X			X		X		X		
Hsu 2015	14.5	0.28 (0.13, 0.60)	X			X	X	X	X	X		X		X
Muller 2002	14.5	0.16 (0.07, 0.37)							X	X	X	X		X
Wang 2010	14.5	-160/100,000/year	X					X	X		X	X	X	X
Agichini 2007	14	-3.2/100,000	X				X	X	X		X	X		
Hirstein 2010	13.5	-20.3/100,000	X					X	X		X	X	X	
Nelson 2013	13.5	0.61 (0.23, 1.62)	X					X	X		X		X	
McGill 2003	9.5	0.19 (0.13, 0.27)	X	X			X				X	X		
Total (%)			22 (82)	8 (30)	10 (37)	6 (22)	6 (22)	18 (67)	20 (74)	12 (44)	14 (52)	15 (56)	8 (30)	8 (30)

(1) Studies are ordered based on bias scores, with higher quality studies listed first.

(2) Other physician-based disciplines included: anesthesiology & pain services, cardiology, cardiovascular surgery, dermatology, emergency medicine, interventional angiography, microbiology, neurology, psychology, and radiology

(3) Nursing disciplines spanned: general nursing, nurse case management, diabetic foot nursing, vascular nursing, and wound care nursing

(4) Other allied health professions included: diabetes educators, medical quality, nutrition, occupational therapy, pharmacy, physical therapy, plaster technicians, prosthetics, and social work

* Hedetoft and colleagues reported an increase in the high-to-low (major-to-minor) amputation ratio from 0.46 to 0.55 following introduction of a multidisciplinary team.

** Armstrong and colleagues reported a reduction in the high-to-low (major-to-minor) amputation ratio from 0.35 to 0.27 following introduction of a multidisciplinary team.

Table IV.

Four key clinical tasks addressed by multidisciplinary teams

Study	Bias score (I)	OR for major amputation	Key clinical task						# tasks addressed
			Glycemic control	Wound care		Infection	Vascular Disease		
				Surgical	Non-surgical		Revascularization	Diagnostic/ Medically managed	
Chung 2015	20	0.45 (0.16, 1.24)	X	X	X	X	X	X	4
Weck 2013	18.5	0.28 (0.20, 0.40)	X		X	X	X	X	4
Laakso 2017	17.5	0.47 (0.27, 0.82)	X	X	X	X	X	X	4
Chiu 2011	17	0.09 (0.03, 0.29)	X	X	X		X	X	3
Alexandrescu 2009	16.5	0.47 (0.20, 1.08)	X	X	X	X	X	X	4
Crihana 2014	16.5	0.25 (0.07, 0.90)	X	X	X	X		X	4
Setacci 2013	16.5	0.70 (0.50, 0.96)		X	X	X	X	X	3
Kim 2018	16.5	1.14 (0.59, 2.20)	X	X	X		X	X	3
Riaz 2019	16.5	0.29 (0.20, 0.42)	X	X	X		X	X	3
Dargis 1999	16	0.39 (0.04, 3.55)	X	X	X			X	3
Hedetoft 2009	16	*	X	X	X				2
Martinez-Gómez 2014	16	0.47 (0.33, 0.68)	X	X	X	X		X	4
Rerkasem 2008	16	0.27 (0.08, 0.97)	X	X	X		X	X	3
Williams 2018	16	-368/100,000		X	X		X	X	2
Yesil 2009	16	0.56 (0.34, 0.93)	X	X	X	X	X	X	4
Cahn 2014	15.5	0.49 (0.25, 0.94)	X	X	X	X			3
Wang 2016	15.5	0.27 (0.13, 0.57)	X	X	X		X	X	3
Jiménez 2017	15.5	-1.6/100,000/yr	X	X	X	X	X	X	4
Crane 1999	15	0.30 (0.10, 0.92)	X			X			2
Denjalic 2014	15	0.49 (0.30, 0.78)	X	X	X				3
Nather 2010	15	0.37 (0.21, 0.66)	X	X	X		X	X	4
Armstrong 2012	14.5	**		X	X	X	X	X	3

Study	Bias score (I)	OR for major amputation	Key clinical task						# tasks addressed
			Glycemic control	Wound care		Infection	Vascular Disease		
				Surgical	Non-surgical		Revascularization	Diagnostic/Medically managed	
Aydin 2010	14.5	0.53 (0.25, 1.15)	X	X	X	X	X	X	4
Hsu 2015	14.5	0.28 (0.13, 0.60)	X	X			X	X	3
Meltzer 2002	14.5	0.16 (0.07, 0.37)	X	X	X	X	X	X	4
Witsø 2010	14.5	-160/100,000/yr	X	X	X	X	X	X	4
Anichini 2007	14	-3.2/100,000	X	X			X	X	3
Gibbons 1993	13.5	0.22 (0.10, 0.47)			X	X	X	X	2
Holstein 2000	13.5	-20.3/100,000	X	X	X	X	X	X	4
Nason 2013	13.5	0.61 (0.23, 1.62)	X	X	X	X	X	X	4
Troisi 2016	11.5	-8.8/100,000					X	X	1
McGill 2003	9.5	0.19 (0.13, 0.27)	X	X					2
Total (%)			27 (84)	28 (88)	29 (91)	20 (63)	24 (75)	27 (84)	Mean= 3.22

(1) Studies are ordered based on bias scores, with higher quality studies listed first.

* Hedetoft and colleagues reported a reduction in the high:low (major:minor) amputation ratio from 0.56 to 0.46 following introduction of a multidisciplinary team.

** Armstrong and colleagues reported a reduction in the high:low (major:minor) amputation ratio from 0.35 to 0.27 following introduction of a multidisciplinary team.

Table V.

Decrease in incidence rates of major amputations associated with multidisciplinary teams for patients with diabetic foot ulcers

Study, Country	Bias score (1)	Incidence of major amputation /100,000 inhabitants with diabetes Controls	Incidence of major amputation/100,000 inhabitants with diabetes Multidisciplinary Teams	Decrease in incidence with multidisciplinary teams
Williams 2018, United Kingdom	16	412 *	44 *	368 *
Jiménez 2017, Spain	15.5	6.1 **	4.5 **	1.6 **
Witsø 2010, Norway	14.5	400 ***	240 ***	160 ***
Anichini 2007, Italy	14	6.3	3.1	3.2
Holstein 2000, Denmark	13.5	27.2	6.9	20.3
Troisi 2016, Italy	11.5	37.5	28.7	8.8

(1) Studies are ordered based on bias scores, with higher quality studies listed first.

* Williams and colleagues expressed the incidence of major amputation based on 100,000 inhabitants with diabetes, adjusted for age and sex.

** Jiménez and colleagues expressed the incidence of major amputation based on 100,000 general inhabitants per year.

*** Witsø and colleagues expressed the incidence of major amputation based on 100,000 inhabitants with diabetes per year.