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LETTER

Assessing data on the incidence of lower limb amputation in diabetes

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Abbreviations
LEA Lower extremity amputation
PAD Peripheral arterial disease

To the Editor: Ulceration of the foot is a major complication of diabetes and is the cause of considerable suffering worldwide [1–5], as well as a very considerable cost to both healthcare services [6, 7] and the patient [8]. But much of the detail on the assessment of the disease burden has centred on the number of amputations performed, despite the fact that amputation is a relatively uncommon outcome, with only 1.8% of 24,200 ulcer episodes documented in the National Diabetes Foot Care Audit of England and Wales resulting in major amputation within 6 months [9]. On the other hand, data on the numbers of amputations performed are fairly reliably documented in hospitals throughout the world and it is, therefore, relatively easy to assess amputation incidence. Nevertheless, a large number of factors need to be considered before such assessments can be compared and before the significance of any differences can be interpreted. Many of these are inherent in the analysis of any electronic health records in diabetes, as has recently been reviewed [10], but the focus of the present commentary is on those factors that require particular consideration when interpreting data on the incidence of amputation of all or part of the lower limb in people with diabetes [3]. Details of population selection (and associated ethnic, socio-demographic and clinical details), assessment of amputation incidence and interpretation of the findings are considered in turn.

Study population

The study population (the denominator) should be the number of people in the chosen area of study who are 'at risk' (all people with diabetes living in one country, for example). The study population will be either the total population in the area or in one selected locality. In general, studies of a whole population (or of a country, province, county, city, etc.) will have a lower risk of bias than those undertaken in subsets. Health insurance data are sometimes used to define a local population even though they may sometimes involve some selection. If observations are made on the total population in the area (i.e. including those both with and without diabetes), comparisons with other populations will not be possible unless the prevalence of diabetes in each is known.

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Defining the 'at risk' study population with diabetes: the denominator

Identification of people with diabetes The majority of countries lack either a national or regional database of people with diabetes, although the information may be available from statutory health insurance records or healthcare programmes or estimated from population-based health surveys. If, however, the chosen population is derived from records of glucose-lowering treatments, the data are of limited value if those managed with diet alone are excluded. These and other potential weaknesses may undermine the reliability of the data derived from existing electronic databases, as previously described [10].

Under-ascertainment of diabetes Under-ascertainment of diabetes can be owing to individuals with known disease that is not recorded in a healthcare record or, more frequently, because diabetes has not yet been diagnosed. Under-ascertainment will persist unless there exists a system for comprehensive, and repeated, population screening.

However, one consequence of the introduction of systematic screening for the detection of undiagnosed diabetes will be that the resultant diabetes population will initially contain an increased number of people with (predominantly type 2) diabetes of shorter duration and, hence, also with fewer complications predisposing to ulcer development. It follows that the incidence rate of amputation may be seen to fall in the early years after the start of screening and this could be misinterpreted as being the result of improved foot care. In practice, the fall could be followed by a rise after 10–15 years, when complications that predispose individuals to foot disease (such as peripheral arterial disease [PAD] and neuropathy) have become established.

Diabetes type There has previously been little evidence that diabetes type contributes to the overall incidence of amputation but a recent study from the USA has reported a rise in amputation incidence, which was most marked in those aged 18–44 years [11]. Such a trend could be the result either of a rise in type 1 diabetes or increasing emergence of type 2 diabetes at an earlier age, or both, and for such reasons, diabetes type should be specified if it is known (while bearing in mind the fact that the type recorded in electronic healthcare registers may not always be completely accurate) [10].

Former diabetes There is no consensus regarding the inclusion of people who have had diabetes effectively eradicated by dieting, bariatric surgery or islet cell transplantation. Not only can the diabetes recur in such people but their previous hyperglycaemia may have left a legacy of risk. On balance, it would seem better for people with 'previous' or 'cured' diabetes to be included and the broader implication is that their names should be retained on diabetes registers.

Studies of the incidence of amputation in diabetes require careful assessment

- While amputation is a relatively uncommon outcome for any new case of foot ulcer, it causes a considerable burden for both individuals and society
- There have been multiple studies of amputation incidence but there is great heterogeneity in both the methods used and the results obtained
- Estimates of amputation incidence should preferably use the population with diabetes as a denominator and not the whole population
- Estimates of the prevalence of diabetes in a study population may be affected by under-ascertainment resulting from either unreported or undiagnosed diabetes
- Estimates of the incidence of major and minor amputation should be kept separate; the two types of operation should not be combined
- The incidence of amputations depends largely on what is counted, which ranges in studies between all procedures to one amputation (first, highest, etc.) per person. Standardisation is needed with regard to the number of amputations included for each clinical episode. This may be difficult to implement because of the heterogeneous data sources

Identifying other details of the 'at risk' study population to enable case-mix adjustment

A number of factors are associated with increased risk of both new foot disease and of amputation and it follows that the study population should be characterised whenever possible in order to facilitate effective comparison with other groups. Specific population details that need to be considered are listed below.

Age and sex Increasing age and male sex are both well recognised as being associated with increased risk of both new foot disease and amputation in people with diabetes.

Socioeconomic position Numerous studies have demonstrated the association between diabetic foot disease, amputation and socioeconomic status, with poorer health outcomes being reported in people who are more socially deprived [12–15]. Several reasons have been identified for this association, including unhealthy lifestyle, restricted access to healthcare delivery and limitations in health literacy [16].

Ethnicity The role played by ethnicity in foot disease and amputation is complex. Some ethnic groups appear to have a racially-mediated increase in risk of both ulcers and amputation and these include indigenous groups in the USA [17], as well as in Australia [18] and New Zealand [19]. On the other hand, some ethnic groups appear to have reduced ulcer risk, possibly as the result of a lower incidence of distal neuropathy (e.g. in South Asians) [20, 21] or because of a reduced incidence of PAD (e.g. in South and Southeast Asians) [22, 23].

Any effect of ethnicity can, however, be either exaggerated or masked when a particular group is also an ethnic minority that is exposed to an independent effect of social deprivation. This is thought to underlie the apparent differences in the relationship between ethnicity and amputation risk between different countries, such as between the USA and UK [24].

Defining the amputation details to be documented: the numerator

Minor amputation, major amputation and 'lower extremity amputation' The term 'minor amputation' is usually taken to refer to transverse removal of part of the foot below the ankle joint, even though some clinicians have traditionally referred to some such operations as being 'major' because of the difficulty and cost involved. It is, however, less ambiguous to restrict the term 'major amputation' to any transverse removal of part of the limb undertaken above the ankle.

Minor amputation is an operation undertaken to promote resolution of disease localised to the foot, and to restore both the capacity for weight-bearing and for ambulation, depending on previous function. In this respect, the aim of minor amputation contrasts with that of a major amputation, which is undertaken because it is judged that the limb cannot be saved. It is because the two types of operation have fundamentally different aims and benefits that it is illogical to combine the two into a single entity, such as 'lower extremity amputation' (LEA), which has been common practice to date. The only purpose of combining both major and minor procedures into a single figure is to document the extent of the burden of all amputations on the healthcare service.

Limitations of amputation details in existing databases Amputation details should ideally be extracted from hospital databases, which document person-linked events; but, in many cases, the hospital activity records are not linked to individuals and their value is, therefore, limited to documenting the overall burden posed by amputation on healthcare activity. However, the required linkage of operative procedures to individuals with diabetes may be available if there is a diabetes register for the locality that includes the necessary detail.

How many amputations can be included in a single episode? Multiple operations may be undertaken during the same clinical episode. There may be one or more minor amputations prior to one or more major amputations on the same limb. Not infrequently, a person will have bilateral disease at presentation or may acquire a second ulcer as a result, for example, of being immobilised for one that they already had on the other foot. This inevitably leads to uncertainty as to how many of these operations should be counted as the consequence of any one episode. If the primary aim of the study is to assess the burden of diabetic foot disease on either healthcare services or the patient, then it is clear that all procedures need to be counted. If, however, the aim is to document outcomes of discrete disease episodes, then a decision has to be made concerning which operations to include. One option may be to select just one amputation—the highest—on each limb in a defined period (such as 12 months from presentation) but there is no current consensus.

When diabetes is a subsidiary cause of amputation Many studies of major amputation in people with diabetes exclude amputation triggered either by trauma or malignancy. While understandable, it is not completely logical because the presence of diabetes, either with or without associated active foot disease, may be a factor determining the decision to amputate in such cases [25]. As the numbers will also be comparatively small, it is arguably better to include people with these other primary causes of amputation.

Possible reasons for differences in amputation incidence between communities

Differences in the incidence of amputation between communities may relate to:

- Differences in the methodology adopted to document amputation incidence
- Differences in the population studied relating to age, sex, socio-demographic variables or ethnicity
- Differences in the accessibility of best quality care for: (1) diabetes; and (2) limb-threatening disease

Interpretation of findings

Do differences in incidence of amputation reflect differences in the relative effectiveness of care? Amputation is a treatment and not strictly a complication of the diabetes, and, as it is a

treatment, the decision to amputate or not (whether minor or major, or single or multiple operations) will almost inevitably be made as a result of discussion between the clinician and the patient (and family). When a decision is made to undertake a major amputation, it is usually a de facto acknowledgement of an inability to resolve the presenting problem and that the operation is a damage-limitation exercise. In this respect, major amputation is directly analogous to an operation undertaken for malignancy and it is very relevant that operations undertaken for malignancy are not usually used as measures of cancer outcome.

It follows that while amputation incidence is of value in assessing the impact of disease, it is not necessarily a good measure of the quality of care. Such care quality would be better assessed by measures that reflect the aims of management, such as time to healing, amputation-free survival, recurrence-free survival and, ideally, measures of function and well-being.

Interpretation of differences observed in the incidence of major amputation between different localities The main aim of audit in this field is currently to identify differences between populations that are well matched. When such differences exist between localities (which has been clearly demonstrated both in the UK and the USA [26–30]), this should prompt urgent enquiry into the reasons for these differences. Such enquiry should take note of known factors that could have been contributory to differences between populations, such as age, sex, ethnicity and socioeconomic position, as well as for diabetes comorbidities (notably PAD, neuropathy and nephropathy). If clear differences between populations persist after these are taken into account, then the explanation should be sought. It is possible that the differences may result from variable access to clinical care of the equivalent standard. Such differences in care provision may result from aspects of professional training and/or belief, as was first suggested 20 years ago [31]. The potential impact of professional belief and practice has also been suggested by evidence of 'clustering', demonstrated in the USA [27] and, more recently, in New Zealand [19]. There is some evidence that this may be an important factor in England, not least because the localities with a high incidence of major amputation in England are the same as those with a high incidence of minor amputations, and both are mirrored closely by the incidence of both major and minor amputations in people without diabetes [28, 30]. Further studies are needed to establish the extent of any contribution made by differing access to effective care to the incidence of amputation in different populations.

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