Towards an Effective Decision Support System for Diabetic Foot Ulcers Diagnostic and Treatment Assessment

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Abstract Diabetes mellitus (DM) is a fast-growing metabolic condition that threatens human population quality of living in the overcoming decades. One of its severe consequences is diabetic foot ulcers (DFU), which affect up to a quarter of the DM patients in their lifetime. This consequence leads to high health costs and significant decrease of the patients' quality of life and self-esteem. In order to cope with the rising demands of heath resources and shortage in clinical human assets intelligent computational tools are required to aid in the decision where a patient is in an early stage of a DFU development and on the appraisal of a DFU treatment. It is aim of this research to provide a critical overview of the existing decision support systems (DSS) and publicly available research datasets for diabetic foot ulcers early diagnosis and treatment assessment, and thus proposing a new infrastructure system to deal with it overcoming the past attempts. The existing DFU DSS failed in being introduced in clinical practice due to total discrepancy with current daily clinical practice with DFU and the publicly available DM research datasets are shorter in data for feeding a new DSS. This research presents the actual and promising future data required for effective decisions and discloses a proposed architecture for a DSS applicable to DFU early diagnosis and treatment evaluation. Implementing the proposed system will take time but it will definitely contribute to cope with the patient demands, associated cost reduction and promotion of patients care.

Keywords Big data · Clinical datasets · Decision support systems · Diabetic foot ulcers · Diagnostic tools · Multiple data sources · Treatment assessment

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1 Introduction

1.1 The Problem of Diabetic Foot Ulcers (DFU)

Diabetes mellitus (DM) is the most affecting metabolic disease, which majorly threatens the population quality of life, being this aggravated with aging and life expectancy evolution. It can present itself in three forms: type 1 (autoimmune reaction caused, no or low insulin is produced), type 2 (caused by aging and lifestyle habits, characterized by insulin resistance), and gestational (temporary, high blood glucose levels during pregnancy). The estimated worldwide incidence of DM according to the International Diabetes Federation (IDF) is 9.3% for adults aged 20–79 years old, which means one in eleven adults is affected, being the projected rates of 11% and 13.5% for the years of 2030 and 2050, respectively, meaning a 51% increase of the condition [1].

One of the known consequences of DM evolution is the Diabetic Foot Ulcers (DFU), which may affect up to 25% of the DM patients' population, being the risk of recurrence rate of 40% within the first year and up to 65% after five years of healing [2]. This resulting condition can lead in the most severe cases to amputations and consequent death and contributes to the major spending among DM patients' care [3]. With the demand of care caused by the rising of DFU and with limited resources in terms of clinical personal, new intelligent technological instruments are required to facilitate the early identification of DFU and to help on the assessment of its treatments to aid on act promptly to provide the best care possible.

The International Working Group on the Diabetic Foot (IWGDF) in 2019 has defined the guidelines for the classification of diabetic foot ulcers [4], which is an important source of the required data to early detect and characterize a healing DFU.

Since the introduction of Decision Support Systems in medicine in the mid 1950's with the MYCIN that technology proved to be a precious aid to the clinicians daily practice helping them cope with growing demands in clinical care decision, eliminating human error, reducing costs and contributing to provide better overall care to patients [5]. The first known DSS devoted to DFU diagnosis appeared in 2009 for predicting amputations [6].

1.2 Current DFU Diagnostic and Treatment Assessment Methods

The current practical guidelines of the IWGDF established in 2019 [4] determined that to deal with DFU the following procedures have to be implemented:

- Prevention of DFU in subjects with DM
- Offloading DFU in subjects with DM

- Diagnosis, prognosis and management of peripheral artery disease (PAD) in patients with a DFU and DM
- Diagnosis and treatment of DFU infection in subjects with DM
- Interventions to enhance healing of DFU in subjects with DM
- Classification of DFU.

The characterization of DFU patients has a wide spectrum, it involves different geographies, social classes, ages, not specific of a single gender, although it is consensual that it results from a subject with DM and simultaneously having two or more risk factors. The diabetic peripheral neuropathy and PAD usually playing a central role. The first leads to an insensitive and sometimes deformed foot, often causing abnormal loading of the foot. The PAD is characterized by poor circulation in the extremity.

In order to prevent DFU it is very important to Identify the foot at-risk, to regularly inspect and examine the foot at-risk, to educate the patient, his family, and the other healthcare professionals, to ensure routine wearing of appropriate footwear and at least but not less important to treat the risk factors for ulceration.

The current diagnosis is based in the patient history, medical examination of the foot appearance, the vascular status of the limb (which can have its levels of oxygen—O_2—monitored) and assessment of the Loss of protective sensation (LOPS). The LOPS can be monitored through the patient pressure perception using the Semmes–Weinstein 10 g monofilament test and/or the vibration perception: 128 Hz tuning fork test.

Based in this assessment the risk of the DFU can be established as presented in Table 1.

Through the history and clinical examination, and DFU can be classified as: neuropathic, neuro-ischemic or ischemic. The measurement of the ankle-brachial index (ABI) using a Doppler instrument is very important for identifying the presence of PAD or not, if it is not present then the DFU is only neuropathic.

For correctly classify the DFU it is important to know the type, cause, site and depth, signs of infection, and patient-related factors.

The severity of infection can be obtained from the IWGDF/ISDA classification criteria (Table 2) if the patient has no PAD but if he has the Wifi system (Table 3)

Table 1 The DFU Risk with the corresponding foot screening frequency by an expert [4]

Risk	Characteristics of the examination	Frequency of screening
Very low	No PAD and no LOPS	Once a year
Low	PAD and/or LOPS but no other signs in the foot	Once every 6/12 months
Medium	LOPS+PAD, or LOPS+foot deformity or PAD+foot deformity	Once every 3/6 months
High	LOPS or PAD, and one or more of the following: – history of a foot ulcer – a lower-extremity amputation (minor or major) – end-stage renal disease	Once every 1/2 months

Table 2 IWGDF/ISDA classification criteria [4]

Clinical manifestations	Infection severity
Wound lacking purulence or any manifestations of inflammation	Uninfected
Presence of ≥2 manifestations of inflammation (purulence, or erythema, tenderness, warmth, or induration), but any cellulitis/erythema extends ≤2 cm around the ulcer, and infection is limited to the skin or superficial subcutaneous tissues; no other local complications or systemic illness	Mild
Infection (as above) in a patient who is systemically well and metabolically stable, but which has ≥1 of the following characteristics: cellulitis extending >2 cm, lymphangitic streaking, spread beneath the superficial fascia, deep-tissue abscess, gangrene, and involvement of muscle, tendon, joint or bone	Moderate
Infection in a patient with systemic toxicity or metabolic instability (e.g., fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, severe hyperglycemia, or azotemia)	Severe

Table 3 Wifi system

Wound grade	DFU	Gangrene
0	No Ulcer	No Gangrene
	Clinical description: minor tissue loss. Salvageable with simple digital amputation (1 or 2 digits) or skin coverage	
1	Small, shallow ulcer(s) on distal leg or foot; no exposed bone, unless limited to distal phalanx	No gangrene
	Clinical description: minor tissue loss. Salvageable with simple digital amputation (1 or 2 digits) or skin coverage	
2	Deeper ulcer with exposed bone, joint or tendon; generally, not involving the heel; shallow heel ulcer, without calcaneal involvement	Gangrenous changes limited to digits
	Clinical description: major tissue loss salvageable with multiple (≥3) digital amputations or standard trans metatarsal amputation (TMA)±skin coverage	
3	Extensive, deep ulcer involving forefoot and/or midfoot; deep, full thickness heel ulcer±calcaneal involvement	Extensive gangrene involving forefoot and/or midfoot; full thickness heal necrosis with calcaneal involvment
	Clinical description: extensive tissue loss salvageable only with a complex foot reconstruction or non-traditional TMA (Chopart or Lisfranc); flap coverage or complex wound management needed for large soft tissue defect	

should be used for stratifying the possible amputation risk and revascularization benefit [4].

The DFU can be treated according with the status of the wound, it can be healed through pressure offloading and ulcer protection, restoration of tissue perfusion (surgery), infection treatment (clearance and debride of all necrotic tissue and

surrounding, oral antibiotic therapy, surgery), metabolic control and treatment of comorbidities (insulin and/or nutrition), local ulcer care (clearance, debride and/or dressings), and education of patient and relatives.

The DFU can be objectively assessed by using the Wagner scale [7, 8] or the University of Texas Diabetic Wound Classification scale [9]. When comparing the two, the second is more descriptive and complete, showing greater association with higher risk of amputation and likelihood of the healing process of ulcers, due to the combination of grade and stage characterization, whether the Wagner scale is simpler and easier to memorize as a visual method, although it does not consider the size, PAD, and LOPS.

1.3 Promising Technological Instruments for DFU Diagnostic and Treatment Assessment Methods

Over the recent years, there were some technological advancements that proved their applicability, although those instruments are not yet fully available in daily clinical setting. Foot pressure loading monitoring is possible through the usage of a sensorial system and it aids to identify the point in which the patient may out more pressure and are more likely to generate a DFU [4] given the load and time of exposure, it can be recorded in rest of exercising. Like pressure load, monitoring the gait can also give important indications on the loss of equilibrium and neurological balance in DM patients [10], it can be performed using sensors such as 3 axis accelerometers and gyroscopes. These two information sources could enter as inputs for a DFU diagnostic SSD.

A recent research also proposed a set of biomarkers that can be of great importance for early detection of DFU [11].

Other important information is foot skin temperature, which is influence by both peripheral vascular and autonomic nervous system, it is known that an asymmetrical or variation to the close surroundings over 2.2 °C is an indicator of possibility of a DFU development one or two weeks before being visible [12]. This type of assessment can be performed using low-cost sensors that require contact [13, 14] or remote monitoring through infrared radiation, which are more expensive. There is also the possibility of using infrared thermal (IRT) imaging, which can measure the temperature of large areas of skin and provides a permanent record that can be used for further analysis, this technique has proved to be of importance either in aiding diagnosis through identifying risky areas (of neuropathic and vascular origin) [15] or through assess the outcome of a treatment [16].

In order to objectively assess DFU healing imaging techniques in visual spectrum can offer real estimation of area, volume, shape, and color of the wound [17, 18] providing a better characterization, along with the Pressure Ulcer Scale for Healing (PUSH) [19–21], already used for chronic wounds in clinical setting and accommodates the ulcer volume, the type of existing tissue and the amount of exudate, it can

aid and guide clinicians in a better treatment assessment and in case of poor outcome help to choose a different healing procedure.

Given this and with the recent developments in terms of data analysis and DSSs, it is of major importance to understand where the gaps and opportunities are for its implementation, which is the motivation for this research. The novelty and contribution of this piece of research is to identify the weaknesses of the existing DFU DSS and to disclose the required steps for the implementation of an effective DFU DSS system to give an adequate answer to the growing demand of DM patients care.

It is aim of this research to provide a critical overview of the existing decision support systems and publicly available research datasets for diabetic foot ulcers early diagnosis and treatment assessment, and thus proposing a new infrastructure system to deal with it overcoming the past attempts.

This manuscript is organized in five sections. The first, the current one, introduces the problem, the existing DFU clinical diagnostic and treatments assessment processes and the promising complementary emerging methods. It is followed by a characterization of the existing supportive technology in terms of freely available datasets and DSS implemented and mitigated. In section three a proposal of a new effective DFU DSS is made, it is followed by a discussion between what is proposed and the existing implementations, which is remarked with the conclusions.

2 Existing Supportive Technology

In this section, the existing available DM datasets are characterized and the mitigated DFU decision support systems are object of critical assessment.

2.1 Existing DM Datasets Available for Research

In Table 4 are described the DM open available datasets that can be used for research, the purpose of its storage, the number of records, and the attributes of each are presented.

It can be easily observed that mostly insulin and blood glucose levels are the only common attributes to all the datasets, this could be explained by the different nature of the original purpose of the dataset, but it is also possible to note that even the more detailed have insufficient data to classify or predict a DFU.

Table 4 Characterization of the open available DM datasets

Size	Purpose	Attributes	References
442	Group different DM patients per attribute	Age (years), Sex, body mass index, bp (average blood pressure), s1 tc (T-Cells—a type of white blood cells), s2 ldl (low-density lipoproteins), s3 hdl (high-density lipoproteins), s4 tch (thyroid stimulating hormone), s5 ltg (lamotrigine), s6 glu (blood sugar level)	[22]
6742	Progression of diabetic kidney disease and trajectory of kidney function decline	BMI, End-stage renal disease in type 2 diabetics, Fasting insulin, Chronic kidney disease in type 2 diabetics, Coronary artery disease in type 2 diabetics, Coronary heart disease or stroke or peripheral vascular disease in type 2 diabetics, eGFR-creat (serum creatinine), HDL cholesterol, Height, HOMA-B, Insulinogenic index, LDL cholesterol, Microalbuminuria, Macroalbuminuria vs. controls, Total cholesterol, Triglycerides, Type 2 diabetes, Urinary albumin-to-creatinine ratio, Waist circumference	Jiang et al. [23]
768	Verify whether patient shows signs of diabetes according to WHO criteria	Number of times pregnant, Plasma glucose concentration 2 h in an oral glucose tolerance test, Diastolic blood pressure, Triceps skin fold thickness, 2 h serum insulin, Body mass index, Diabetes pedigree function, Age (years), Class variable	[24]
11,830	General patient data for characterization	ID,Description,Affected Status, Product, Source, Gene, Mutations, Sex, Age at Sampling, Race, Ethnicity	[25]
70	General DM data of country/region/world overtime	Country/Region/World, ISO, Sex, Year, Crude diabetes prevalence, Lower 95% uncertainty interval, Upper 95% uncertainty interval	[26]
45,000	70 sets of data recorded on diabetes patients	Date, Time, Code, Value, Regular insulin dose, NPH insulin dose, UltraLente insulin dose, Unspecified blood glucose measurement, Unspecified blood glucose measurement, Pre-breakfast blood glucose measurement, Post-breakfast blood glucose measurement, Pre-lunch blood glucose measurement, Post-lunch blood glucose measurement, Pre-supper blood glucose measurement, Post-supper blood glucose measurement, Pre-snack blood glucose measurement, Hypoglycemic symptoms, Typical meal ingestion, More-than-usual meal ingestion, Less-than-usual meal ingestion, Typical exercise activity, More-than-usual exercise activity, Less-than-usual exercise activity, Unspecified special event	[27]

(continued)

Table 4 (continued)

Size	Purpose	Attributes	References
1688	Demographic information, diabetes status, health indicators, health behaviors, and Problem	class, class_language, age, year, gender, insurance_category, medical_home_category, race_ethnicity, education_level, diabetes_status_yes_no, heart_disease_yes_no, high_blood_pressure_yes_no, tobacco_use_yes_no, previous_diabetes_education_yes_no, diabetes_knowledge, fruits_vegetable_consumption, sugar_sweetened_beverage_consumption, food_measurement, carbohydrate_counting, exercise, problem_area_in_diabetes_paid_scale_score, zip_code_address, zip_code_city, zip_code_state, zip_code_zip	[28]
225	Verify whether the use of continuous glucose monitoring (CGM) without blood glucose monitoring (BGM) measurements is as safe and effective	Blood Glucose, Glycated hemoglobin level, Insulin, Medications, Patient Demographics	Aleppo [29]
451	Test CGM as a technology to assist in diabetes care	Glycated hemoglobin level, Insulin, Patient Demographics	Tamborlane [30]
200	Identify factors associated with severe hypoglycemia in older adults (60+) with type 1 diabetes	Insulin, Medications, Patient Demographics	Weinstock [31]

2.2 *Existing DSS for DFU Diagnostic and Treatment Assessment Methods*

In Table 5 are present the existing decision support systems for DFU, divided by type of DSS, informing the purpose, the used data, and the achieved assessment results. It is important to note that ANN refers to Artificial Neural Networks, acc to accuracy, CNN to Conversional Neural Networks, LDA to Local Discriminant Analysis, SVM to Support Vector Machines, k-NN to k-Nearest Neighbor, GA to Genetic Algorithms, and AUC to Area Under the Curve.

From Table 5, it can be seen that the majority of the DFU DSS are concerned with the classification of the data, only one was applied to risk identification [32] and another to the prediction of amputation [33]. Apart from [44] most of the samples used are very small (<2500). Only four DSS assess the treatment outcome [35, 36,

Table 5 Characterization of the existing DFU for diagnostic and treatment assessment

Type	Purpose	Used data	Assessment result	References
Risk analysis	Predicting the risk of DFU	255 samples of genotype data	ANN: 83% acc	Singh et al. [32]
Prediction	Predicting the amputation in DM patients with record of DFU	237 samples of amputation data	Logistic regression and Bayesian network AUC 0.765	Hüsers et al. [33]
Classification	Identify the extent of risk factors for major and minor amputations in patients with DFU	2321 samples of historical records of DM patient's medical history	Decision tree, validated the international guidelines	Widatalla et al. [6]
Classification	Feature extraction and consequent classification into ischemic and non-ischemic or infection and non-infection	1459 DFU images	Ensemble CNN, 90.3% acc ischemic 72.7% acc infection	McInnes et al. [34]
Classification	Classification of wound status	1000 samples of historical records of DM patient's medical history	logistic regression classifier, error of prediction of 2.8%	Yuan et al. [35]
Classification	Classification of microbial species from DFU	1750 samples	LDA+SVM 99.8% acc	Yusuf et al. [36]
Classification	Classify correctly the locations of the DFU in the thermal images	39 dynamic infrared images of DFU patients	SVM 87.5% acc	Vardasca et al. [37]
Classification	Automatic classification of the DFU according to their nature	54 infrared images of DFU patients	k-NN 93.4% acc	Vardasca et al. [38]
Classification	Early detection of DFU considering asymmetry	100 thermal images of DM patients	Otsu's method and GA, misclassification error of 0.034	Kaabouch et al. [39]
Classification	Classify into healthy and abnormal skin	754 foot images	SVM 94.5% acc	Alzubaidi et al. [40]
Classification	Classify pressure into healthy controls, DM controls and DM neuropathic	84 samples of dynamic plantar pressure	SVM 96.4% acc	Botros et al. [41]

(continued)

Table 5 (continued)

Type	Purpose	Used data	Assessment result	References
Classification	Classify into normal and abnormal skin	397 foot images	CNN 94.5% acc	Goyal et al. [42]
Classification	Localization of the DFU in the images	1880 foot images	CNN 91.8%	Goyal et al. [43]
Classification	Classifying into healing and non-healing wounds	53,354 samples of demographic and wound information	Gradient Boost Tree models, AUC 0.842	Jung et al. [44]
Classification	Wound classification into tissue types	50 wound images	SVM 88% acc	Wannous et al. [45]
Classification	Separate background from feet and identify correctly the DFU	76 thermal images of DM patient foot	Clustering k-means, 99.1% acc	Liu et al. [46]
Classification	Separate background from feet and identify correctly the DFU	26 visual spectrum and thermal images	Clustering k-means, 98.25%	Niri et al. [47]
Classification	Classify the risk of non-healing in DFUs	Hyperspectral images	PCA 0.66 AUC	Yang et al. [48]

44, 45], most are concerned with the diagnosis [6, 32–34, 37–42, 48] and other three with the correct location of the DFU in images [43, 46, 47]. The classification method that presents most application is the SVM, good accuracy (acc > 92%) is reported by most of the studies [36, 38, 40–42, 46, 47].

3 Proposed Intelligent Effective DSS for Diagnostic and Treatment Assessment Methods

From the previous section, it can be seen that the available datasets are insufficient for effectively aiding with DFU early diagnosis and treatment assessment, there are relevant data missing. Also, the existing DSS do not take into account the current IWGDF guidelines, which is the current clinical daily practice. Most of the used data by the previously implemented DSS was generated and read for the application, being small and dedicated.

In order to address the problematic, it is important to reformulate the data sources and make sure that is possible to achieve all the required data. The DM patient historic data is present on his electronic patient record (EPR), every time a patient undergoes a

expert examination because of a suspicious DFU, all the collected data on that consult should be stored in a regular consult DB, which can be linked with the EPR or not. Most patients nowadays use gadgets to monitor their health parameters, in special DM patients must verify their blood glucose level twice a day and they can record it along other parameters in an app in their smartphones with the possibility of having a cloud database to store that data. When they have a DFU that requires treatment, the general practitioner should document the intervention on a database. If any of the promising methods that were described in Sect. 1.3 are available, they can also be documented and stored in a database, it is important that the biomarkers due to its nature to be stored in a different data source. All this data stored in different sources is a challenge to a DSS implementation, it requires remote access to it and a lot of ETL and data preparation, in order to this be transformed and loaded into different data marts that will constitute the DFU data warehouse. Then intelligence will be added through Online Analytic Processing (OLAP) and Data Mining methods (which can be object of further research) to finally make knowledge visible in a dashboard through intelligent and simplified charts. This is the basis for the architecture proposed and present in Fig. 1.

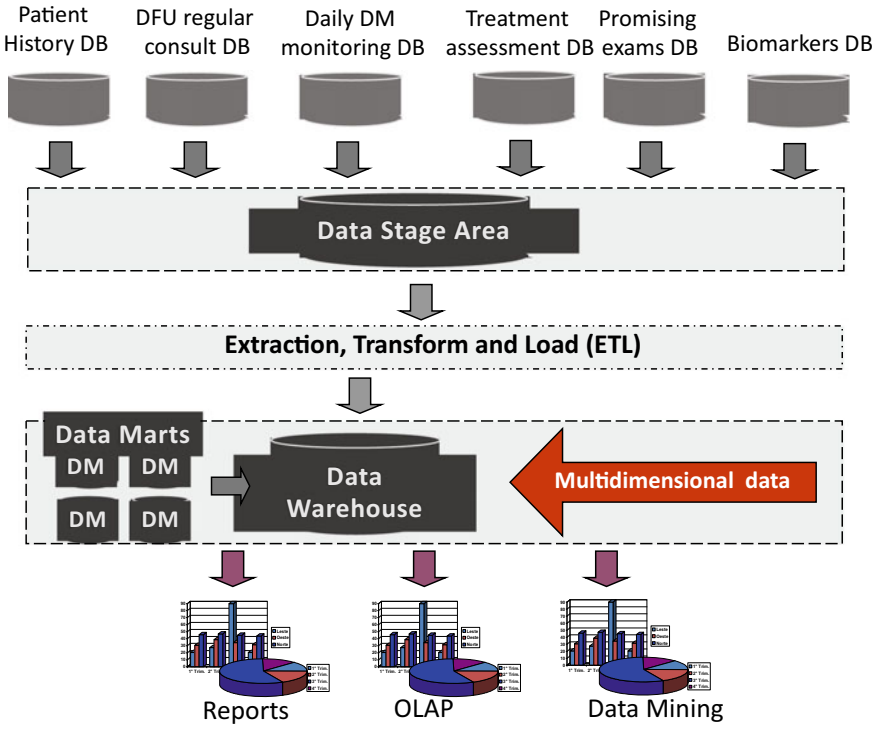

Fig. 1 The architecture of the proposed effective DSS for DFU diagnosis and treatment assessment

It is important to bear in mind that in the beginning there are two situations: we can be looking for the unknown and then unsupervised methods such as clustering, or aggregation rules should be used to implement the data mining models. On the other hand, if we have a hint and previous knowledge about the classification that we intend, depending on the data (continuous or discrete) and on how many classes are expected, SVM, ANN, k-NN, GA among other methods should be used. When trying to establish a prediction linear or logistic regression should be considered. It is not the intention of this research to propose combinations of data mining methods or suggesting models, or even suggesting implementation technologies, it would only make sense when the data sources were adequately available.

4 Discussion

The increase of DM and consequent DFU is a growing problem and burden to every health system, soon the demand will be so high that the health resource will find difficulties to cope with the care requirements, intelligent systems are needed to ease that scenario and to help reducing the associated costs. Preventing will always be cheaper than healing.

From this research, it can be observed that with the existing freely available datasets on DM it cannot be implemented an effective DSS for DFU diagnosis and treatment assessment. Also, the majority of the implemented and tested DFU DSS only addressed a specific question, being very simple to be of future value for the demanding. Most are resultant of academic research and will be difficult to be implemented in clinical daily practice, so the proposed open architecture is dynamic in allowing multiple questions, which through OLAP and data mining is possible to adjust to the required question. It was not found in the literature any implementation of this kind for dealing with DFU. This is first step toward a technological need. To date from the presented existing DSS it seems that developers are not aware of DFU daily practice in clinical setting and it is important to have in mind that is easier to adapt the computational tools to the health professional than the opposite, due to their afraid of losing a job to a smart system the show resistance in this systems adoption, so they have to feel that these tools are useful and only will act as facilitator in their practice.

5 Conclusion

The existing DFU DSS are insufficient for the early identification of feet at risk and to assess objectively the DFU treatments. The public available datasets are not in agreement with the current clinical information process required to make decisions nor with the emerging technologies and their objective data. A redefinition of new data sources in line with the IWGDF protocol is required, this along with new emerging related data sources would constitute DM to form a larger DW are essential for more

effective Data mining, data analysis, OLAP and Visual dashboards to aid effective DFU decision making.

Only with the implementation of a system as suggested it will definitely contribute to cope with the patient demands, associated cost reduction and promotion of patients care.

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