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Background

The increased prevalence of diabetes mellitus (DM) and its comorbidities form serious health care problems (fig. 1).¹ Ulceration is a common complication of wounds which would otherwise heal and close, but instead evolve into chronic lesions due to the pathologic factors of DM. Diabetic foot ulcers (DFUs) precede 84% of all diabetes-related lower-leg amputations as they often present persistent infection.² The current rise in antibiotic resistance worsens the global outcome of pathogen persistence in diabetic wounds.³ Therapies working independent of resistance profiles are invaluable. Fortunately, medical grade honey (MGH) formulations become more and more popular in the healthcare sector.

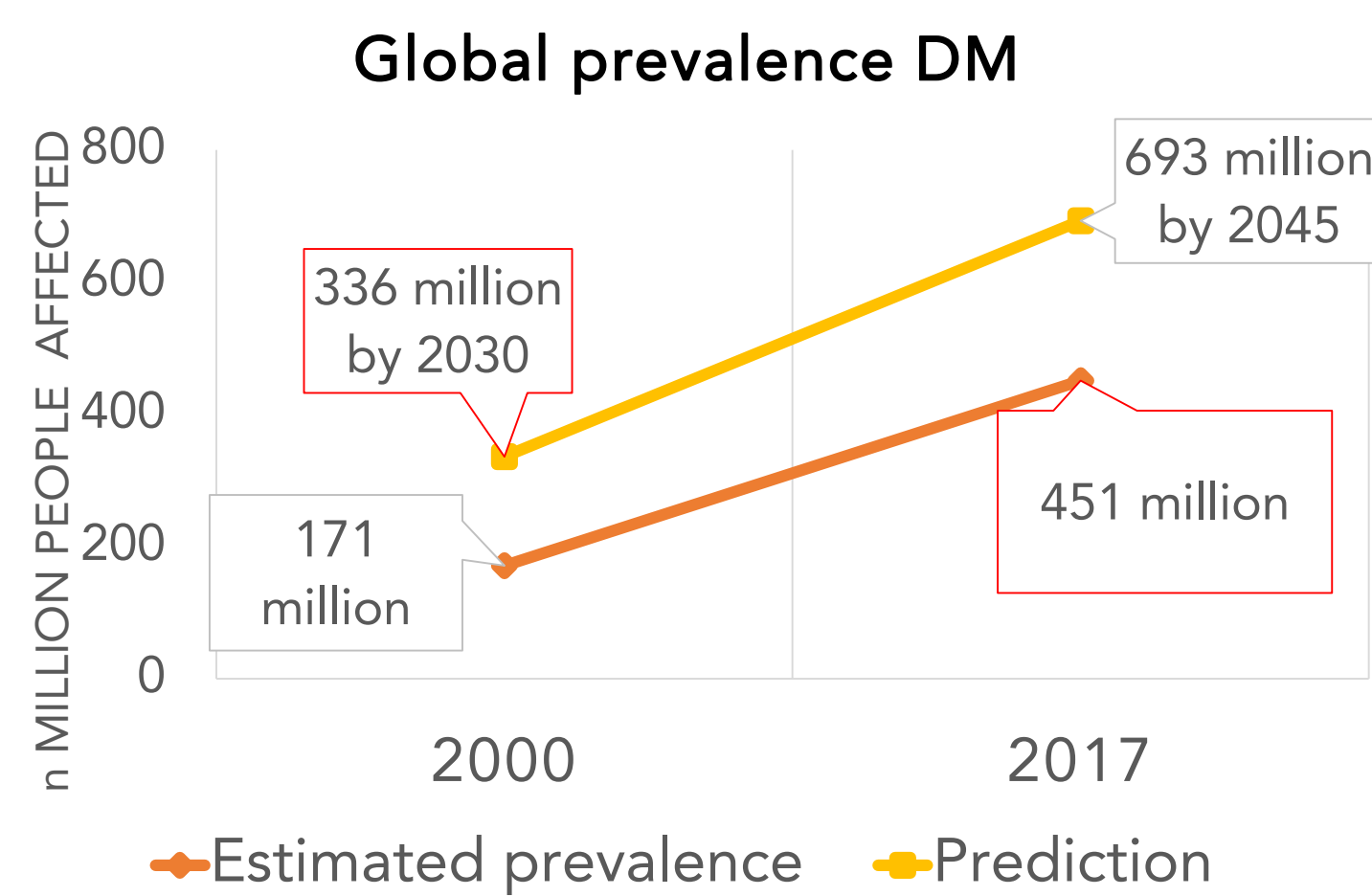
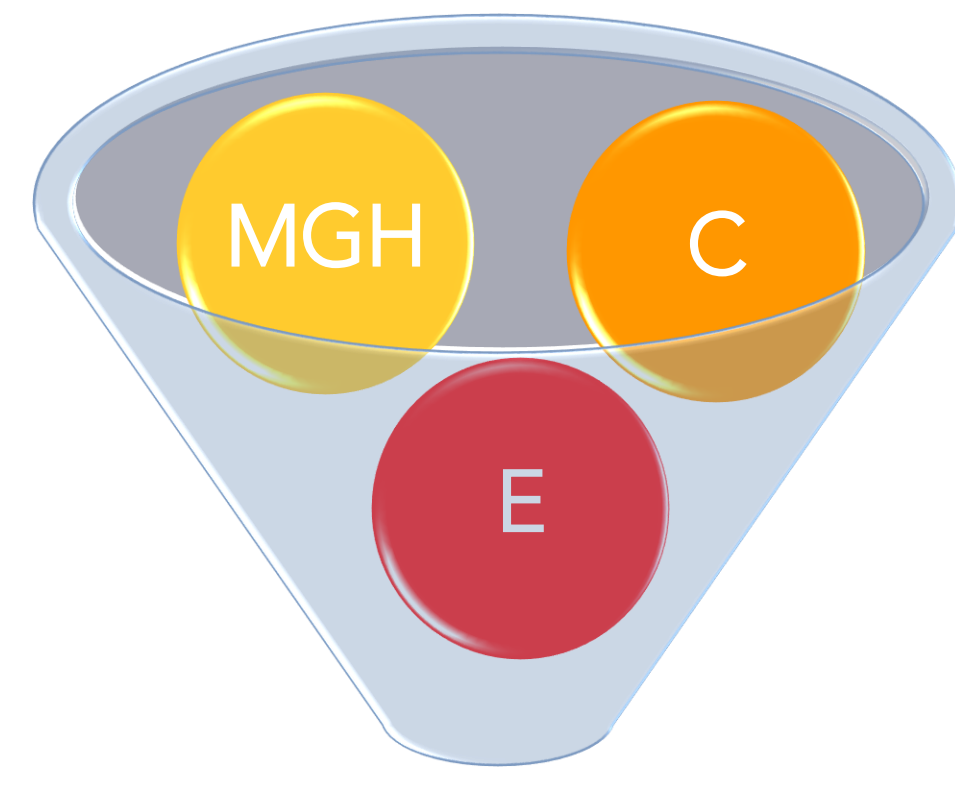


Figure 1: Prevalence of diabetes mellitus as estimates by Cho et al. (2017) *Diabetes Res Clin* and Wild et al. (2000) *Diabetes Care*.



Organic Medical Grade Honey (MGH)

- o Osmotic effect⁴
- o Cell migration⁵
- o Antibacterial⁶
- o Antiinflammatory⁷

Antioxidant vitamins

- o Collagen synthesis⁸⁻¹⁰
- o Tensile strength⁸⁻¹⁰
- o Antiinflammatory¹¹

Stimulating the wound healing trajectory without compromising bacterial susceptibility

Case 3 – polymicrobial infection

Foot ulcer of 64 y/o type 2 diabetic male

- 15 Days of prior treatment
- o Maggot therapy

Ampicillin and penicillin resistance

Total material costs for L-Mesitran treatment: €71,-* (1x 50 g Ointment and 7 pcs Hydro; 1x 15 g Soft and 4 pcs Tulle)



Case 4 – resistant *Ps. aeruginosa*

Foot ulcers of 52 y/o type 2 diabetic male
Noncompliant to diabetic medication and wound management, risk of amputation

- 3 Months of prior treatment
- o Hydrogels / SSD / NaCl-gel / alginate
- o Iodosorb powder
- o Metronidazole
- o Papase

Piperacillin/tazobactam and amoxicillin resistance

Total material costs for L-Mesitran treatment: €13,-* (1x 50 g Ointment)



Case 5 – resistant *Streptococcus B. / E. Coli*

Toe ulcers of 45 y/o type 2 diabetic female
Risk of amputation

- 13 Days of prior treatment
- o Hydrogel
- o Alginate
- o Film dressing

Ampicillin/tetracycline resistance

Total material costs for L-Mesitran treatment: €13,-* (1x 50 g Ointment)



Case 6 – resistant *Staph. aureus*

Feet and leg ulcers of 80 y/o type 2 diabetic female

- 15 Days of prior treatment
- o Povidone iodine
- o Neomycin sulphate
- o No coverage

Methicillin resistance

Total material costs for L-Mesitran treatment: €121,-* (1x 50 g Ointment and 14 pieces Net; 1x 50 g Soft and 7 pieces of Tulle)



Materials and Methods

- o Local cleaning protocol
- o Implementation of medical grade honey (MGH)-based wound care products (L-Mesitran, Triticum Exploitatie B.V., Maastricht, The Netherlands) and dressing regime as described in Table 1
- o All patients received medication to control their diabetes
- o The patient in case 2 was hospitalised for 4 weeks and lost 50kg bodyweight during the treatment

Table 1: Wound management overview of each case and their respective L-Mesitran products. Ointment, a 48% MGH lanolin ointment, Soft, a 40% MGH wound gel, Net, a hydrocolloid net dressing containing 20% MGH, and Hydro, a hydrogel containing 30% MGH.

Case	Initial 1° dressing	Initial 2° dressing	Duration and dressing regime	1° dressing treatment change	2° dressing treatment change	Duration and dressing regime
1	Soft and Net	Sterile absorptive gauzes	4 weeks of daily changes	Soft	Sterile absorptive gauzes	48 weeks of daily changes following weekly application
2	Ointment and Net	Sterile absorptive gauzes	2 months of two changes per day	Soft	Sterile absorptive gauzes	6 months of daily changes
3	Ointment and Hydro	Fixative gauzes	7 weeks of daily changes	Soft and Tulle	Sterile absorptive gauzes	3 weeks of daily changes
4	Ointment	Film dressing	2 weeks of daily changes*	Ointment	Alginate and film dressing	10 weeks of daily changes*
5	Ointment	Film dressing	6 weeks of daily changes			
6	Ointment and Net	Sterile absorptive gauzes	3 weeks of daily changes	Soft and Tulle	Sterile absorptive gauzes	3 weeks of daily changes

Case 1 – resistant *Ps. aeruginosa / Streptococci*

Leg ulcer of 78 y/o type 2 diabetic male
Noncompliant to diabetic diet

- 21 Days of prior treatment
- o SSD
- o Enzyme products
- o Silicone sheets

Ciprofloxacin resistance

Total material costs for L-Mesitran treatment: €159,-* (4x 50 g Soft and 2x 10 pcs Net)



Case 2 – *Ps. aeruginosa*

Foot ulcer of 63 y/o type 2 diabetic male
Risk of amputation

- 1.5 Months of prior treatment
- o Sharp debridement
- o Maggot therapy
- o Systemic antibiotics

4 weeks of hospitalisation, 50kg weight loss

Total material costs for L-Mesitran treatment: €381,-* (11x 50 g Ointment, 28x 20 g Ointment; 5x 15 g Soft)



Results

On average, MGH controlled infection in 2.6 weeks. Granulation tissue formation occurred with an average of 3.5 weeks. Factors such as noncompliance, comorbid complications and weight loss possibly compromised the healing trajectory in cases 3, 4 and 5. Yet with time, all wounds including these three progressed towards healing and amputation could be avoided in all cases.

Table 2: Wound healing trajectory per case, including time to full healing, time to reduce inflammation and infection control.

Case	1	2	3	4	5	6
t _{Infection}	4 weeks	1 week	3 weeks	3 weeks	3 weeks	2 weeks
t _{Granulation}	4 weeks	4 weeks	3 weeks	3 weeks	3 weeks	4 weeks
t _{Healing}	52 weeks	32 weeks	10 weeks	12 weeks	6 weeks	6 weeks
Risk _{Amputation}		Yes		Yes	Yes	

Conclusion

In face of the rise in diabetes prevalence and complications related to DFUs, it's important to consider that medical grade honey formulation L-Mesitran..

- o is effective in controlling infection in diabetic ulcers
- o is easy to apply in the clinic as well as in home care
- o is a cost-effective modality for treating chronic diabetic ulcers

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* Retail prices averaged upon retrieval from webshops in the United Kingdom (www.farmaline.uk, www.amazon.co.uk, www.vetsend.co.uk), Germany (www.amazon.de, www.medpets.de, www.newpharma.de), France (www.nmmedical.fr, www.newpharma.fr, www.medpets.fr, www.amazon.fr), Sweden (www.djurfarmacia.se, www.med24.se), Austria (www.shop-apotheke.at, www.augegottes.at), The Netherlands (www.farmaline.nl, www.newpharma.nl, www.viata.nl), and Belgium (www.newpharma.be, www.farmaline.be) on 12 December 2018.