Supporting evidence-based practice in nutrition and hydration

KEY WORDS

- ▶ Dietitians
- **▶** Evidence
- **→** Guidance
- **>>** Hydration
- **▶** Nutrition

The aim of this review is to synthesise literature on food, nutritional status and wound healing to help inform those working in wound care. A literature search was performed on PubMed, Scopus and EMBASE databases. Studies were critically appraised and the findings were analysed by narrative synthesis. Nutritional assessment is important in practice as nutritional status can impact on wound healing in several ways (including affecting both healing time and susceptibility to infection). There is widespread recognition of the importance of nutritional assessment tools, however, completion can sometimes be overlooked in practice. Healthcare professionals also need to be aware that obesity may be accompanied by micronutrient deficiency causing low micronutrient levels, however, nutritional assessment tools using body mass index (BMI) and weight loss may not identify this. Although there are intervention studies using nutritional formulations, such as amino acids, to support wound healing, the results of this review suggest that future research around using food as therapy and specific nutritional supplementation is needed.

ound care currently represents a significant issue in healthcare in the UK. Over a decade ago, in 2008, Posnett and Franks estimated that the cost of caring for patients with chronic wounds in the UK from 2005-2006 was between £2.3-£3.1 billion a year. A few years later, it was reported that dressings alone accounted for at least £120million in primary care costs (National Prescribing Centre, 2010). Scallon et al also reported in 2013 that £400m was spent on venous leg ulcers in the UK. Moreover, wounds impact on the lives of hundreds of thousands of people. In 2004, Bennett et al (2004) estimated that 412,000 people in the UK develop a new pressure ulcer annually and estimate 150,000 people within the UK have active venous ulcers. Wound care is also an important issue due to ageing populations; this in itself places extra demands on healthcare resources whilst lessening the availability of revenue available to support healthcare through taxation (Phillips, 2005). This highlights the need for cost-effective strategies that both prevent complications and support recovery, reducing healing times where-ever possible.

AIMS

The aims of this review are to consider the relationship between wound healing and nutritional status in both acute and chronic wounds, including pressure ulcers and diabetic foot ulcers, in the hope of informing healthcare practice and increasing the awareness of the importance of consideration of nutrition in a multidisciplinary approach. With economic austerity in the UK through much of the last decade, ongoing healthcare funding issues and the increasing emphasis at a policy level on patient centred-care, prevention and minimisation of complications would undoubtedly be considered best practice. The author aims to demonstrate how assessment of nutritional status of patients combined with an awareness of the prevalence of nutritional deficiencies and how they may impact on wound healing are worthy considerations to inform clinical approaches.

APPROACH

A narrative approach has been used to synthesise findings from a literature search using search

JUSTINE BOLD

Programme Director of
Continuing Professional
Development in the Centre For
Medical Education, Medical
School, Cardiff University
Senior Lecturer School of Allied
Health & Community University
of Worcester



Figure 1. Eatwell Guide Source Public Health England in association with the Welsh Government, Food Standards Scotland and the Food Standards Agency in Northern Ireland (Public Health England, 2016)

terms such as wound healing and nutritional status, nutritional supplements and wound healing, nutritional assessment and wound healing, nutrition and pressure ulcers, nutritional status and pressure ulcers, nutrition and diabetic foot ulcers.

THE UK'S CURRENT NUTRITIONAL GUIDELINES AND REQUIREMENTS

Current nutritional recommendations are based on the Eat Well Guide (Figure 1). The National Diet and Nutrition Survey (NDNS) shows that not many adults currently meet nutritional guidelines and healthcare professionals would probably benefit from knowledge of this data (even at a population level) as it can help inform clinical approaches and highlight the importance of nutritional assessment.

MALNUTRITION

It is also important to bear in mind that around three million people in the UK are at risk of malnutrition (Allied Health Professionals (AHP) 2012 and British Dietetic Association (BDA) no date). The BDA estimate 93% of these are living in their own home, whilst 5% are living in care homes and only 2% of these are in hospital. Malnutrition is an established risk factor for both delayed wound healing but also infection and reduced immunity (BDA, 2019) and in-hospital stays it increases the chance of complications and re-admission (Frank et al, 2015). Malnutrition is associated with deprivation but might be the result of problems with dentition (as commonly seen in the elderly) or the result of changes in taste that can also be associated with both ageing and some medication. Mobility issues can also cause difficulties with accessing and preparing food. Some academics and researchers now view obesity as a state of malnourishment; indeed, the World Health Organization refer to this as the 'double burden of malnutrition'. Very simply, people may be malnourished through food and calorie deficit whilst others may be overfed in terms of energy

Wounds UK | Vol 16 | No 2 | 2020

Box 1. What is the 5-a-day recommendation?

Five x 80 g portions of fruits and vegetables, excluding starchy vegetable such as potato. This can include one small glass of juice and one portion of beans or pulses.

(Kcal) but deficient in one or more micronutrients.

MUST NUTRITIONAL ASSESSMENT

In the UK, the National Institute for Health and Clinical Excellence (NICE) has recommended for some time that nutritional screening tools such as MUST (Malnutrition Universal Screening Tool) be used on patients admitted to hospital (NICE, 2006). MUST is a five-step tool developed by British Association for Parenteral and Enteral Nutrition (BAPEN). Information and materials are available at www.bapen.org.uk. MUST should be undertaken weekly after hospital admission but can also be used in a community setting.

Healthcare professionals should be urged to remember the tool uses BMI and weight loss as the primary determinants of risk; hence may not be able to identify obese or overweight individuals with micronutrient deficiencies.

Moreover, data on completion of nutritional assessment has been reported, a cross-sectional study in one hospital was reported in 2012 (Dingwal et al, 2012). This study reported sub-optimal completion of MUST assessments and nutritional care plans. In the study, ten patients were randomly selected from ten wards across the hospital (100 patients in total). No wards had 100% completion of MUST assessments, whilst eight of ten of the wards had nutritional care plans, 45% of the 100 patients did not have a MUST score. Of the patients that did have a MUST score, 52% were found to be at a medium or high risk of nutritional deficiency.

Another study in the UK on 80 medical patients also reported that MUST screening did not reach 100%. The authors report 'high' levels of completion (but below the target level of 100%) but also state rates of completion drops off over the period of 4 weeks after admission as the results were 87% completion in week one, 89% in week two, 85% in week three and 84% in week four (Middleton et al, 2012). Another study reports similarly that the MUST tool was under-utilised on vascular wards, but the authors did state that usage of the tool increased following an education session (Tewari et al, 2013). Another author raises the issue of accuracy of completion of MUST assessment and recommends that future audits of MUST completion should assess not just levels of completion but also the accuracy of completion (Smith, 2014).

HYDRATION

The Eatwell Guide recommends 6–8 glasses of fluid a day such as water, low-fat milk, tea or coffee. Ousey et al (2016) report on the importance of hydration in skin healing to maintain dermal water balance as dehydration can delay wound healing. Fluids should, therefore, be considered too in the context of wound healing and hydration charts are also important in terms of assessing patients in hospital settings.

FRUITS, VEGETABLES AND MICRONUTRIENTS

One of the main findings from the National Diet and Nutrition Survey (NNDS) over the last nine years is that in all age/sex groups mean intake of fruit and vegetables is below the 'Five A Day' recommendation (Box 1). Only about 30% of adults and around 10% of 11- to 18-year-olds meet the recommendation (British Nutrition Foundation [BNF], 2019). Fruits and vegetables are a source of many nutrients including Vitamin C. It is important to consider that fruits and vegetables also contain many other phytonutrients such as carotenes. Among others, carotenes have demonstrated to be useful for supporting skin health as they are antioxidants and can help protect the skin from UV light (Meléndez-Martínez et al, 2019). Another type of phytonutrients are flavonoids found in fruits, berries, soy products, red wine and legumes. They have been associated with improved microcirculatory parameters, however, trials on interventions with flavonoids have reported mixed results (Scallon et al, 2013) and further research is needed. Intervention studies using a randomised controlled model often assess the effect of a single nutrient or food component versus placebo or another component. It is difficult, therefore, to understand the combined synergistic effect of many foods such as fruits or vegetables in their natural state where they contain many nutrients and phytochemicals in combination. Consequently, it should be recognised that fruits and vegetables provide valuable sources of phytonutrients as well as vitamins and minerals.

VITAMIN C

Deficiency of Vitamin C causes scurvy, which affects the skin. Vitamin C is found in both the

dermis and epidermis of the skin (Shindo et al, 1994), though ageing causes levels to decline (Rhie et al, 2001). It is required for collagen synthesis and scurvy causes collagen production to decline which disrupts the connective tissue and makes blood vessels fragile. Recent case reports in the UK sadly indicate that this may be more prevalent than assumed (Mosdøl et al, 2008). Mosdøl et al reported on their study which demonstrated that 25% of men and 16% of women in the low-income/ materially deprived population had plasma Vitamin C concentrations indicative of a deficiency of Vitamin C (<11 micromol l(-1)). Fresh fruits and vegetables are generally perceived as expensive so we know food choice may be affected in financial hardship as there is a tendency to buy starchy foods that are perceived as more filling, as these are generally cheaper. Vitamin C requirements may be increased in smokers as smokers demonstrate low levels (Schectman et al, 1989). Health issues such as bleeding gums and easy bruising are associated with low levels of intake (BMJ Best Practice, 2020). The Reference Nutrient Intake (RNI) for Vitamin C in the UK is 40 mg/day for adults (set at a level to prevent deficiency in the majority 97.5% of the population). It is noteworthy that the EU Population Reference Intake is 110 mg/day for adult males and 95 mg/day for adult females because they have been derived from adequacy criteria (Gibney et al, 2009) as opposed to deficiency criteria as in the UK. Studies using interventions of Vitamin C supplements in wound healing have not yielded consistent results (Linus Pauling Institute, 2011), which probably highlights the importance of food sources of the nutrient.

VITAMIN D DEFICIENCY

Vitamin D deficiency is common in people who are housebound as it is made through sunlight exposure to the skin. Skin pigmentation also affects levels of production and skin with more pigmentation will produce less, so deficiency is more common in people with darker skin (Richard et al, 2017). Both obesity and diabetes are also associated with high rates of Vitamin D deficiency (Via, 2012). Patients with diabetes are at high risk of developing diabetic foot ulcers (Tatti and Barber, 2010). The aetiology of diabetes Type 2 is very complex and involves many issues

including genetic and behavioural/lifestyle factors, β-cell dysfunction in the pancreas, resistance to insulin and incretin hormone as well as injury from oxidative stress (Via, 2012). There is some indication that Vitamin D may play a role in insulin secretion and function as Vitamin D receptors are found in human pancreatic β-cells (Via, 2012). There have also been a few studies demonstrating positive results from intervention with Vitamin D supplementation, as it has been reported that Vitamin D supplements can improve both insulin signalling and glucose metabolism in patients with type 2 diabetes (Pittas et al, 2007). It is also worth noting in terms of infection risk in wound care that Vitamin D insufficiency may reduce immunity before other indicators of low levels are apparent (Miller et al, 2016). Moreover, it seems Vitamin D deficiency is relatively common in the UK as the recent NDNS analysis of the last 9 years reported that from January to March 19% of children aged 4 to 10 years, 37% of children aged 11 to 18 years and 29% of adults had low Vitamin D levels (25-OHD below 25 nmol/L) which is defined as the threshold indicating risk of deficiency.

OTHER VITAMINS AND MINERALS

The NDNS data also showed a downward trend in intakes of most vitamins and minerals for any age/sex groups, for example, all age/sex groups showed a reduction in vitamin A and folate intake that was significant (BNF, 2019). Other micronutrients including riboflavin (vitamin B2), iron, calcium, iodine, potassium and zinc also demonstrated reductions in intakes and an increase in the proportion of people with low intakes (below the lower reference nutrient intake) (BNF, 2019). Zinc has an important role in protein metabolism and deficiency may be associated with a poor sense of taste and smell and delayed wound healing (Pisano and Hilas, 2016).

Those with higher incomes are closer to meeting nutritional recommendations, yet the data demonstrates that diets don't meet guidelines across a range of incomes. In terms of wounds, nutritional inadequacy is an established risk factor in the development of pressure ulcers (Carter and Lecko, 2018).

Vitamin A (like Vitamin C) has many important functions, including in immunity, and Vitamin A

Box 2. Examples of approximate protein content of food (SELF Nutrition Data, 2020)

- → 1 glass of milk (8 gms)
- → 1 egg (6.1 gms) 2 eggs (12.2 g)
- >> Cooked chicken breast 54 g
- → 1 cup yoghurt (7.9 gms)
- → 3 slices whole wheat bread (9 gms)
- → 1/2 cup carrots (2 gms)

(retinol) is important for skin and mucosal surfaces and involved in keratin production as retinoids help regulate keratin genes (Törmä, 2011). Previous NDNS data indicated that Vitamin A was above or close to the RNI in all age/sex groups except in children aged 11 to 18 years. The latest report indicates declining intakes and demonstrates a significant increase in the proportion with Vitamin A intake below the Lower Reference Nutrient Intake (LRNI).

PROTEIN

In the UK, the recommended intake of protein is less than 15% energy (Kcal) or 0.75g protein per kg body weight per day (for adults). Committee on Medical Aspects of Food and Nutrition (COMA) recommended 46g/day for adults (COMA, 1991). It is important to acknowledge that there is some disagreement in the scientific community about protein requirements and no consensus on what is considered a safe upper limit. There is also some evidence that vegetarians and vegans should eat slightly more because of factors affecting digestibility (Ciuris et al, 2019). It is acknowledged that those with wounds have higher requirements and this is where there can be a challenge in the elderly particularly as more elderly people, especially those with dental problems, might find protein foods such as meat or poultry too difficult to chew and this may affect intake. Moreover, deprived people may find it hard to afford protein-based foods. The human diet should include 'complete' proteins which have a good level of all the essential amino acids (EAAs). Foods such as meat, fish, poultry, eggs, dairy and soy are complete proteins and the diet should contain some of these foods (Box 2). This is because the EAAs have to be supplied by diet as they cannot be made in the body and they include isoleucine, tryptophan, leucine, phenylalanine, valine, methionine, lysine and threonine. For those on a restricted income, eggs and milk can be more affordable sources of complete proteins. Other good sources of vegetarian protein include nuts/seeds, nut butter, beans and pulses and protein powders such as whey protein. Whey is the protein from the liquid part of milk, once it has been separated from the curd (casein). There are different types of whey protein, including whey protein isolate and hydrolysed whey protein.

Proteins are made up of molecules called amino

acids and they are the building blocks for the body and they are used to make most body structures and blood cells, neurotransmitters antibodies and hormones. They also help to regulate the fluid balance in the body and to transport other nutrients around the body (they help transport iron to where it is needed for example) and are involved in other vital body processes such as clotting and regulating the pH of the body (Whitney et al, 2002). The amino acid arginine is a collagen precursor, it also stimulates insulin and growth hormone secretion and can enhance collagen accumulation. Bilsborough and Mann (2006) state the maximum protein intake based on bodily needs, weight control evidence, and avoiding protein toxicity would be approximately 25% of energy requirements at approximately $2-2.5g \times kg(-1) \times d(-1)$, which is a lot higher than the current UK recommendation as it corresponds to 176g protein per day for an 80kg individual on a 12,000 kJ/d diet. They define a maximum safe intake range for an 80kg person as 285-365 g/d (Bilsborough and Mann, 2006).

There are some small-scale studies of amino acidbased interventions. One study on twelve patients with recurrent diabetic foot ulcers was reported by Tatti and Barber in 2010. The study used a mixture of the amino acids glutamine and arginine and recommended a diet of around 20% of energy from protein (with overweight or obese patients having a 20% reduction in calories). All patients monitored blood glucose levels closely and the researchers monitored glycosylated haemoglobin and reported no difference before and after administration. Positive results were reported as ulcer duration was significantly decreased after supplementation (average 247 days before supplementation to 83 days after supplementation). Van Anholt et al (2010) also demonstrated an arginine enriched ready to drink formula was effective in treating pressure ulcers and positive findings were additionally reported from an arginine enriched oral supplement in a case report study on pressure ulcers, diabetic foot ulcers and leg ulcers (Neyens et al, 2017).

RECOMMENDATIONS

The first step is to identify those at risk of malnutrition, both in hospital and community settings, and consider this may be a possibility even if a patient is overweight or obese. A

GLOSSARY

Dietary Reference Values (DRVs)

DRVs are a set of values, including the Reference Nutrient Intake (RNI) and Lower Reference Nutrient Intake (LRNI) and Estimated Average Requirement (EAR), which can vary by age and gender. DRVs were set by the COMA in 1991 for the intake of nutrients, such as energy, carbohydrates including fibre and sugars as well as for micronutrients such as iron and Vitamin D. However, COMA has now been replaced by the Scientific Advisory Committee on Nutrition (SACN) and SACN has started to review and updated the DRVs (BNF, 2016). The DRVs are designed to be used at a population level to prevent deficiency diseases in the majority and do not take account of factors such as illness or individualised requirements, moreover, they are not set to encourage optimum health.

The Reference Nutrient Intake (RNI)

RNIs are mostly used for micronutrients, such as vitamins and minerals. The RNI is the amount of a nutrient that is enough to meet the needs for the 97.5% of the population. LRNI is the amount of a nutrient that meets the needs for a 2.5% of people who are considered to have low requirements (BNF, 2016). EAR tends to be used for energy and is set at being sufficient for 50% of the population.

The National Diet and Nutrition Survey (NDNS)

NDNS is a cross-sectional survey of around 1,000 people per year in the UK, that has been a continuous rolling programme since fieldwork started in 2008 and it collects quantitative data about foods consumed, the nutrient intake and nutritional status of participants. The sample is designed to be representative of the general population in the UK aged 1.5 years and over living in private households. Participants are interviewed and complete a 4-day estimated diet diary, plus there are physical measurements and both blood and urine samples are taken. Low levels in the NDNS can be a cause for potential concern, however, we must remember the survey only captures 4 days of participants' food intake so this does not necessarily mean low intakes are sustained over longer periods of time.

nutritional assessment such as a MUST should ideally be completed. If the patient is overweight or obese micronutrient deficiencies may still be present, so these should also be explored (especially in delayed wound healing). Dietetic advice will be required where patients cannot eat, so specialist feeding such as tube feed or parental feeding can be started if deemed necessary and appropriate for the patient. If a patient can eat it is important that healthcare professionals, carers and family recognise that there is an increased calorie need and also try to provide a higher protein diet. Kcal at 30-35 kcal/kg CURRENT weight is recommended by the Health Services Executive of the Republic of Ireland in their wound management guidelines which were published in 2018 (Health Services Executive, Republic of Ireland, 2018). A higher protein diet should be combined with 5 x 80g portions of fruits and vegetables, healthy fats such as olive oil, and oily fish and some starchy carbohydrates. Small frequent meals can be considered if food intake is poor or even a milky drink made with protein powder and 6-8 glasses of fluid should be consumed daily.

CONCLUSIONS

Malnutrition is a factor that can negatively affect wounds and wound healing.

Over 3 million people in the UK are at risk and many of these live in their own homes. Whilst there is widespread recognition of the importance of nutritional assessment tools, completion can sometimes be overlooked in practice. Healthcare professionals need to be aware that obesity may be accompanied by malnutrition in the form of micronutrient deficiency, and also be aware that nutritional assessment tools using BMI and weight may not identify this. There are some intervention studies using nutritional formulations, such as amino acids, to support wound healing, however, the results of this review suggest that future research around using food as therapy and specific nutritional supplementation is needed.

REFERENCES

Allied Health Professionals (2012) QIPP and ONS Toolkit. Available at: https://bit.ly/2XcXiMB(accessed 18.02.2020)

van Anholt RD, Sobotka L, Meijer EP et al (2010) Specific nutritional support accelerates pressure ulcer healing and reduces wound care intensity in non-malnourished patients. *Nutrition* 26(9):867–72

Bennett G, Deeley C, Posnett J (2004) The cost of pressure ulcers in the UK. Age Aging 33(3): 230–5

Wounds UK | Vol 16 | No 2 | 2020

- humans. Int J Sport Nutr Exerc Metab 16(2): 129-52
- British Dietetic Association (2019) Malnutrition Food Fact Sheet. Available at: https://bit.ly/36KsPIU (accessed 18.03.2020)
- BMJ Best Practice (2020) Scurvy. Available at: https://bestpractice.bmj.com/ topics/en-gb/632 (accessed 18.03.2020)
- British Nutrition Foundation (2016) Nutrition Requirements. Available at: https://bit.lv/2XxNzPO (accessed 18.03.2020)
- British Nutrition Foundation (2019) NDNS: Time Trend and Income Analyses for Years 1 to 9. Available at: https://bit.ly/2yEIFbe (accessed 18.03.2020)
- Carter R, Lecko C (2018) Supporting evidence-based practice in nutrition and hydration. Wounds UK 14(3): 18 - 21
- Ciuris C, Lynch HM, Wharton C, Johnston CS (2019) A comparison of dietary protein digestibility, based on DIAAS scoring, in vegetarian and nonvegetarian athletes. Nutrients 11(12): 3016
- Committee on Medical Aspects of Food Policy (1991) Dietary Reference Values for food energy and nutrients for the United Kingdom. London, Stationery Office Books
- Dingwal S, Shah S, Patel A et al (2012) PMO-037 Adult nutritional status assessment in a hospital: cross sectional study in a UK hospital. Gut 61(Suppl 2):A88-A89
- Frank M, Sivagnanaratnam A, Bernstein J (2015) Nutritional assessment in elderly care: a MUST! BMJ Qual Improv Rep 4(1): pii: u204810.w2031
- Gibney M, Lanham-New S, Cassidy A, Vorster H (2009) An Introduction to Human Nutrition. 2nd edition. Oxford, Wiley-Blackwell
- Health Services Executive, Republic of Ireland (2018) HSE National Wound Management Guidelines. Available at: https://healthservice.hse.ie/ filelibrary/onmsd/hse-wound-management-guidelines-2018.pdf (accessed 13.03.2020)
- Linus Pauling Institute (2011) Vitamin C and Skin Health. Available at: https:// bit.lv/2ZNA1lU (accessed 13.03.20)
- Meléndez-Martínez A J, Stinco CM, Mapelli-Brahm P (2019) Skin carotenoids in public health and nutricosmetics: the emerging roles and applications of the UV radiation-absorbing colourless carotenoids phytoene and phytofluene. Nutrients 11(5): 1093
- $Middleton\,J, Farnsworth\,H, Singh\,G\,(2012)\,PMO-034\,Compliance\,with\,the\,must$ screening tool for medical in patients. Gut 61: A87
- Mosdøl A, Erens B, Brunner EI (2008) Estimated prevalence and predictors of vitamin C deficiency within UK's low-income population. J Public Health (Oxf)30(4):456-60
- National Institute of Health and Clinical Excellence (2006) Nutrition Support for Adults: Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition. Clinical guideline [CG32]. Available at: https://www.nice.org.uk/ guidance/cg32 (accessed 13.03.20)
- National Prescribing Centre (2010) Evidence-Based Prescribing of Advanced Wound Dressings for Chronic Wounds in Primary Care. Available at: http:// www.npc.nhs.uk.abc.cardiff.ac.uk/merec/therap/wound/merec_ (accessed 13.03.20)
- Nevens J. Cereda E. Rozsos I. Molnár A et al (2017) Effects of an Arginine-Enriched Oral Nutritional Supplement on the Healing of Chronic Wounds in Non-Malnourished Patients; A Multicenter Case Series from the Netherlands and Hungary. Available at: https://bit.ly/3ccHyNC (accessed 13.03.20)
- Ousey K, Cutting KF, Rogers AA, Rippon MG (2016) The importance of $hydration\ in\ wound\ healing:\ reinvigorating\ the\ clinical\ perspective. \emph{JWound}$ Care 25(3): 122, 124-30
- Phillips CJ (2005) Health Economics: An Introduction for Health Professionals. Blackwell Publishing, Oxford
- Pisano M, Hilas O (2016) Zinc and Taste Disturbances in Older Adults: A Review of the Literature. Consult Pharm 31(5):267-70
- Pittas A G, Lau J, Hu F B, Dawson-Hughes B (2007) Re-view: the role of vitamin D and calcium in type 2 diabetes: a systematic review and meta-analysis. J Clin Endocrinol Metab 92(6): 2017-29
- Posnett J, Franks P (2008) The burden of chronic wounds in the UK. Nursing Times. 104(3): 44-45
- Public Health England (2016) Eat Well Guide. Available at: https://www.gov.uk/ government/publications/the-eatwell-guide (accessed 13.03.2020)

- Bilsborough S, Mann N (2006) A review of issues of dietary protein intake in Rhie G, Shin MH, Seo JY et al (2001) Aging- and photoaging-dependent changes of enzymic and nonenzymic antioxidants in the epidermis and dermis of human skin in vivo. JInvest Dermatol 117: 1212-17
 - Richard A, Rohrmann S, Quack Lötscher KC (2017). Prevalence of Vitamin D Deficiency and Its Associations with Skin Color in Pregnant Women in the First Trimester in a Sample from Switzerland, Nutrients 9(3): 260
 - Schectman G, Byrd JC, Gruchow HW (1989) The influence of smoking on vitamin Cstatus in adults. Am J Public Health 79(2): 158-162
 - Shindo Y, Witt E, Han D, Epstein W, Packer L. (1994) Enzymic and non-enzymic antioxidants in epidermis and dermis of human skin. J Invest Dermatol 102:
 - Smith A (2014) Potential barriers to effective MUST implementation. British Journal of Community Nursing 19: Sup11, S28-S31
 - Tatti P, Barber A (2010) Nutritional Supplement is associated with a reduction in healing time and improvement of fat free body mass in patients with diabetic footulcers. EWMA Vol 10 No 3
 - Tewari N, Rodrigues J, Bothamley L et al (2013) The utilisation of the MUST $nutritional\,screening\,tool\,on\,vascular\,surgical\,wards.\,BMJ\,Open\,Quality\,2(1):$ pii: u201374.w1122
 - Törmä H (2011) Regulation of keratin expression by retinoids. Dermatoendocrinology 3(3): 136-140
 - Via M (2012) The Malnutrition of Obesity: Micronutrient Deficiencies That Promote Diabetes. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC3313629/ (accessed 14.03.2020)
 - Whitney, Cataldo, Rolfes (2002). Understanding Normal and Clinical Nutrition. 6th edition, Wadsworth