Nutrition In Wounds And Tissue Regeneration

NUTRITIONAL SUPPORT AND WOUND HEALING

R. Stratton (UK)
Nutritional support and wound healing

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Inadequate nutrition and poor care still affecting patient lives in 2019

Nursing home had 'no record' of severe wound that caused elderly woman's death

By Jess Thompson
Posted 15 Jul 2019, 7:52am

Ms Aalberts-Henderson criticised both the quantity and quality of nutrition at the home, saying her mother's healing was hindered by a substandard diet.

She said her mother quickly lost weight because she was fed small meals of "no nutritional value."

PATIENT DIES OF BEDSORE IN JACKSON HOSPITAL DUE TO NEGLECT

SARA E. TELLER — JULY 4, 2019

Patient dies of bedsore in Jackson Hospital. Jury finds hospital responsible and awards the family $5 million.
Nutritional support is just one part of the care of patients with wounds.

Need the best possible intake from food where indicated.

Patient centred care model
Serena et al 2018
Why the need for nutritional support?

- Poor appetite
- Inadequate intake of energy, protein, micronutrients, fluid
- Low body weight / weight loss (loss fat, lean tissue)
- Reduced nutrient availability for wound healing
- Impaired immune system
- Limited feeding activity / ability

Nutritional support

- Improved intake of energy, protein, micronutrients, fluid
- To meet requirements
- Increased nutrient supply to improve wound healing (perfusion, repair/synthesis, cell multiplication, collagen & connective tissue synthesis etc.)
- Improved immune function
- Improved body weight (weight gain, less weight loss) (fat, lean tissue)
- Improved strength and mobility
### Types of nutritional support used

<table>
<thead>
<tr>
<th>Oral nutritional supplements</th>
<th>Enteral tube feeds</th>
<th>Feeds with specifically tailored formulations (orally or via tube)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Energy (fat, carbohydrate) – varying energy density</td>
<td></td>
<td>• Higher concentrations of micronutrients important for wound healing (e.g. vitamins B, C, E, Zn, Se, Cu, Mn)</td>
</tr>
<tr>
<td>• Protein (high protein, &gt; 20% energy)</td>
<td></td>
<td>• Higher content of specific amino acids or other ingredients important for wound healing</td>
</tr>
<tr>
<td>• Vitamins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Minerals</td>
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<tr>
<td>• Trace elements</td>
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</tbody>
</table>

**Parenteral nutrition**

*Food and drink is a fundamental part of the care of patients where indicated. Studies use nutritional support in combination with food. Little evidence base for dietary, food based strategies alone and wound healing.*
Under-use of nutritional support in patients, including those with pressure ulcers

Greater levels of under detection and undertreatment outside of hospitals

14th – 20th October 2019
@BAPENUK

UK MALNUTRITION AWARENESS WEEK
#MAW2019

% risk malnutrition (MUST)

- 0%
- 10%
- 20%
- 30%
- 40%

UK Hospitals (n 2700)

Intervention | PU patient
---|---
Energy/protein enriched diet | 18%
ONS | 9%
Enteral tube feeding | 3%
Parenteral nutrition | 4%
Dietetic referral | 28%

33 hospitals across Austria (n=71 with PU; only 40% malnutrition screening)

www.bapen.org.uk

Egsleer et al 2018
Large cost savings possible by managing malnutrition at a national level

‘Identifying and treating malnutrition can save at least £123,530 (€139,861) per 100,000 people

€73.6m net saving in England

Elia et al 2015; Stratton et al 2018
Nutritional support

• Where needed, use nutritional support – don’t wait. Importance of nutrient intake for the right amount of time/at the right time.

  • **Routine nutritional screening and assessment needs to be in place** *

• Typically use oral nutritional support, enteral tube feeding (parenteral nutrition).

• Formulation used will depend on the patient – wound type (pressure ulcer, leg ulcer etc), nutritional requirements/status, disease/condition

  * Energy density & source (30-35kcal/kg/d), protein (1.2-1.5g protein/kg/d) micronutrients, feeds available in your practice/country, national guidelines *

THINK: Prevention vs. treatment – high risk patients
Systematic review: Nutritional support and prevention of wounds (PU)

25% reduction, Number Needed to Treat 19

- Significant reduction in the prevalence of pressure ulcers using 1-2 supplements daily (liquid 1-1.5kcal/ml, mostly high protein, 2-26 weeks)

Stratton et al 2005
Economic benefit of reduction of pressure ulcers

‘the use of oral nutritional supplements in older patients at high risk of pressure ulcers produces a net cost benefit’

‘the magnitude and significance of which depend on the stage of the ulcer (£5 (stage I) to £460 (stage IV) net cost saving per patient)’

‘ the greatest cost benefit for prevention of stage III and IV pressure ulcers’

Per patient costs: Stage I £1064, II £4402, III £7313, IV £10,551
More recent systematic review on nutritional support and prevention of wounds (PU)

‘There was a reduction in the risk of pressure ulceration associated with nutritional ‘supplementation’*

(RR 0.84, 95% CI 0.74 to 0.96; P value = 0.01; $I^2 = 13\%$)

Langer et al 2014

* Included enteral tube feeding

SENATOR Overview of systematic reviews (2016): Pooling of the 4 trials could be done with low heterogeneity ($I^2 = 0\%$), and a significant benefit for nutrition intervention was found (RR 0.85, 0.74–0.98)
Other meta-analyses indicate nutritional support (ONS) reduces wound-related complications

<table>
<thead>
<tr>
<th>Model</th>
<th>Study</th>
<th>Setting</th>
<th>Odds ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beattie et al 2002</td>
<td>Hospital-Community</td>
<td>0.386</td>
<td>0.135</td>
<td>1.106</td>
<td>-1.772</td>
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<tr>
<td></td>
<td>Botella-Carretero et al 2008</td>
<td>Hospital-Community</td>
<td>1.308</td>
<td>0.473</td>
<td>3.615</td>
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<tr>
<td></td>
<td>Broquist et al 1994</td>
<td>Community</td>
<td>9.000</td>
<td>0.390</td>
<td>253.166</td>
<td>1.361</td>
<td>0.174</td>
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<tr>
<td></td>
<td>Dil et al 1990</td>
<td>Hospital-Community</td>
<td>0.383</td>
<td>0.194</td>
<td>1.492</td>
<td>-1.450</td>
<td>0.147</td>
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<tr>
<td></td>
<td>Eras et al 2004</td>
<td>Community</td>
<td>0.686</td>
<td>0.229</td>
<td>2.057</td>
<td>-0.672</td>
<td>0.501</td>
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<tr>
<td></td>
<td>Espau et al 2000</td>
<td>Hospital-Community</td>
<td>0.515</td>
<td>0.269</td>
<td>0.965</td>
<td>-2.006</td>
<td>0.045</td>
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<tr>
<td></td>
<td>Flynn et al 1987</td>
<td>Community</td>
<td>0.323</td>
<td>0.082</td>
<td>1.298</td>
<td>-1.620</td>
<td>0.105</td>
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<tr>
<td></td>
<td>Gariballa et al 2006</td>
<td>Hospital-Community</td>
<td>0.792</td>
<td>0.431</td>
<td>1.549</td>
<td>-0.754</td>
<td>0.461</td>
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<td></td>
<td>Gianetti et al 2002</td>
<td>Community</td>
<td>0.590</td>
<td>0.326</td>
<td>1.110</td>
<td>-1.940</td>
<td>0.056</td>
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<td></td>
<td>Gil-Gregorio et al 2003</td>
<td>Community</td>
<td>0.471</td>
<td>0.188</td>
<td>1.163</td>
<td>-1.603</td>
<td>0.109</td>
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<tr>
<td></td>
<td>Nayel et al 1992</td>
<td>Community</td>
<td>0.152</td>
<td>0.027</td>
<td>3.592</td>
<td>-1.172</td>
<td>0.241</td>
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<tr>
<td></td>
<td>Olte et al 1989</td>
<td>Community</td>
<td>0.825</td>
<td>0.147</td>
<td>4.628</td>
<td>-0.219</td>
<td>0.827</td>
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<tr>
<td></td>
<td>Sedner et al 2005</td>
<td>Community</td>
<td>1.192</td>
<td>0.465</td>
<td>3.057</td>
<td>0.365</td>
<td>0.715</td>
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<tr>
<td></td>
<td>Tidermark et al 2004</td>
<td>Community</td>
<td>0.464</td>
<td>0.111</td>
<td>1.940</td>
<td>-1.052</td>
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<tr>
<td>Fixed</td>
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<td></td>
<td>0.632</td>
<td>0.490</td>
<td>0.816</td>
<td>-3.529</td>
<td>0.000</td>
</tr>
<tr>
<td>Random</td>
<td></td>
<td></td>
<td>0.632</td>
<td>0.490</td>
<td>0.816</td>
<td>-3.529</td>
<td>0.000</td>
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</tbody>
</table>

Meta Analysis (14 RCT) (n1460) Complications (I² = 0.00)

ONS: ~600kcal/d 28g protein/d (most high in protein) 5d – 12 months, all community based.

‘Malnourished and ‘non-malnourished’
Post surgery, cancer, acute illnesses

Significantly fewer complications inc. pressure ulcers, wound related complications – poor healing, infections  (OR 0.63 (95% CI 0.49-0.82), 14 RCT, n 1460)  

Stratton et al 2012

Nutritional support and wound healing – earlier reviews unclear

Ageing Research Reviews
Stratton et al 2005

‘Enteral nutrition support, particularly as high protein or disease specific formulas, may improve the healing of pressure ulcers but adequately powered, robust RCT conducive to meta-analysis are required to confirm this’

Cochrane Review
Langer et al 2014

‘There was no clear evidence of an improvement in pressure ulcer healing from the nutritional supplements evaluated in any of these individual studies’
Nutritional support and wound (PU) healing — examples of older trials of ‘standard’ formulations

Oral nutritional supplements

Elderly long term care patients (n 495), oral nutritional supplements (400kcal, 16% protein), up to 26 weeks vs standard care.

Ek et al 1991

![Bar chart showing healed and improved percentages for routine care and supplement](chart.png)

- Significant decrease in total truncal pressure ulcer surface area with high protein tube feed
- Significantly greater decrease in stage IV pressure ulcer areas with high protein vs. standard protein tube feed
- Change in total ulcer area correlated with dietary protein intake and energy intake per kg body weight

Tube feeding

Nursing home patients (n 28; high protein (24% energy) vs. 14% energy from protein tube feeding) (non randomised trial)

Breslow et al 1993
More recently: Evidence for nutritional support with a specially formulated feed and pressure ulcer healing

**A Nutritional Formula Enriched With Arginine, Zinc, and Antioxidants for the Healing of Pressure Ulcers: A Randomized Trial**

Emanuele Cereda, MD, PhD; Catherine Klersy, MD, MSc; Marcella Serioli, RD; Aldo Crespi, MD; Federico D’Andrea, MD; for the OligoElement Sore Trial Study Group *

- Randomised, controlled, blinded trial
- Adult, malnourished, long term care residents or receiving home care services – stage II, III, IV pressure ulcers
- Ad lib food intake (with dietary advice) plus 400ml specially formulated ONS (Cubitan: 500kcal, 40g protein, arginine, additional Zn, antioxidants etc.), 100ml boluses between meals, up to 8 weeks vs. isoenergetic, isonitrogenous control ONS
- Evidence-based wound care. PU area using Visitrak wound management system (Smith & Nephew)
Nutritional support – specific formulation improves PU healing. Results of a randomised, controlled trial

<table>
<thead>
<tr>
<th>End Point</th>
<th>Experimental Formula Group (n = 101)</th>
<th>Control Formula Group (n = 99)</th>
<th>Crude Treatment Effect</th>
<th><em>P</em> Value</th>
<th>Adjusted Treatment Effect</th>
<th><em>P</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Mean reduction in PU area at 8 wk, %</td>
<td>60.9 (54.3 to 67.5)</td>
<td>45.2 (38.4 to 52.0)</td>
<td>15.7 (3.2 to 28.1)‡</td>
<td>0.026§</td>
<td>18.7 (5.7 to 31.8)‡</td>
<td>0.017§</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
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<td></td>
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<tr>
<td>≥40% reduction in PU area at 8 wk, %</td>
<td>69.9 (59.5 to 79.9)</td>
<td>54.1 (42.7 to 65.5)</td>
<td>1.97 (1.11 to 3.50)‖</td>
<td>0.020§</td>
<td>1.98 (1.12 to 3.48)‖</td>
<td>0.018§</td>
</tr>
<tr>
<td>Complete healing, %</td>
<td>16.9 (8.2 to 25.6)</td>
<td>9.7 (2.1 to 17.3)</td>
<td>1.94 (0.88 to 4.28)‖</td>
<td>0.100</td>
<td>2.16 (0.88 to 5.39)‖</td>
<td>0.097</td>
</tr>
<tr>
<td>Mean reduction in PU area at 4 wk, %</td>
<td>37.2 (28.7 to 45.8)</td>
<td>29.3 (21.9 to 36.7)</td>
<td>7.9 (-9.5 to 25.4)‡</td>
<td>0.25</td>
<td>10.2 (-6.5 to 27.0)‡</td>
<td>0.149</td>
</tr>
</tbody>
</table>

**Mechanism?**

Effects of a combination of energy/source, PUFA, protein, arginine, zinc, vitamin C, other antioxidant micronutrients, synergistic effect?

*Cereda et al 2015*
Nutritional support – specific formulation improves PU healing. Results of a systematic review

‘This systematic review shows that the use of formulas enriched with arginine, zinc and antioxidants as oral nutritional supplements or tube feeds for at least 8 weeks are associated with improved PU healing compared with standard formulas’

Nutritional support should be at least 8 weeks long and primarily directed to malnourished patients.
Cost effectiveness of specifically formulated oral nutritional supplement for patients with pressure ulcers?

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Difference (Euros)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritional ('Disease-specific ONS' vs. standard)</td>
<td>€ 39.4 (31.6, 47.1)</td>
</tr>
<tr>
<td>Non-nutritional (Nurse, Physician, Dressings etc.)</td>
<td>-€113.7 (-162.9, -64.5)</td>
</tr>
<tr>
<td>Total</td>
<td>-€74.3 (-126.1, -22.5)</td>
</tr>
</tbody>
</table>

Significantly lower costs of PU care (P=0.013)

Cost-effectiveness plane (n =1000 bootstrap samples). The effect is expressed as percentage of reduction in ulcer area
What do the guidelines say on nutritional support? Pressure Ulcers

- Nutritional screening
- Nutritional assessment
- Care planning
- Energy intake
- Protein intake
- Hydration

**ESPEN geriatric guidelines:** Offer nutritional interventions to older people with PU to improve PU healing.
Less evidence for nutritional support and healing of other wounds: guidelines recommend nutritional support where malnourished

Guidelines for the treatment of venous ulcers

*Principle:* (B) Nutrition must be adequate to provide sufficient protein to support the growth of granulation tissue. Although most venous ulcer patients are ambulatory and not as nutritionally depleted as patients who require frequent or chronic hospitalization, nutritional support is required if an individual is undernourished.

*Evidence:*

Very little data on intervention. Cochrane review underway of nutritional support in treatment of venous leg ulcers
Less evidence for nutritional support and healing of other wounds: guidelines recommend nutritional support where malnourished

**Guidelines for the treatment of diabetic ulcers**

*Principle*: (4.1.B) Nutrition must be adequate to provide sufficient protein. Although most diabetic ulcer patients are ambulatory and not at the extremes of nutrition, nutritional support is required if an individual is undernourished.

**Evidence:**

*Maier et al 2013 systematic review*: Little data, no significant positive outcomes
Summary

1. **Nutrition** must be an integral part of the care of patients with or at risk of developing pressure ulcers, and other types of wounds.

2. **Malnutrition** should be routinely and regularly **screened** for and specific nutrient deficiencies identified and treated in all patients.

3. **Practical, evidence-based nutritional care plans** should be in place to enable appropriate and timely **nutrition support** to be given to patients with or at risk of developing wounds/poor wound healing– involve a dietitian if possible. **Don’t wait.**

4. Latest evidence and guidelines emphasise the important role of **high protein nutrition support for prevention** of PU in at risk patients, and use of a **specially formulated enteral feed for pressure ulcer healing.** Clinical and cost benefits. More evidence is needed for other wound types (and for other enteral formulations)
Let’s get the basics right and stop poor nutritional care in 2019

Ms Aalberts-Henderson criticised both the quantity and quality of nutrition at the home, saying her mother's healing was hindered by a substandard diet.

She said her mother quickly lost weight because she was fed small meals of "no nutritional value"
Acknowledgements

- Prof Marinos Elia, Dr Abbie Cawood, Dr Gary Hubbard
- All of the research teams
- OligoElement sore trial research team