Evidence Table H-3: Nutrition

Evidence Table H-3a. Nutrition trials

| **Author, year Country Overall Quality Rating** | **Eligibility Criteria** | **Exclusion Criteria** | **Number Screened/ Eligible/ Enrolled/ Analyzed** | **Age Sex Race** | **Intervention Type: Specify** | **Ulcer Type/Severity at Baseline (Intervention Onset)** | **Treatment A** | **Treatment B** | **Treatment C** | **Duration of Followup** | **Study Setting** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Benati, 200127  Italy  Poor | Patients with severe cognitive impairment and pressure ulcers | Unlikely to benefit from nutritional supplement-ation | NR/NR/36/16 | Age range: 72-91  44% female  Race NR | Nutrition: protein and arginine enriched supplements | NR | n=5  standard hospital diet | n=5  standard diet plus 2 x 200 ml aliquots/day of a high protein calorie supplementary feeding, providing an extra 500 kcal and approximately 37 g of proteins | n=6  standard diet and treatment B enriched with arginine (7.5g/day), zinc (25 mg) and antioxidants | 2 weeks | Health institution |
| Cereda, 200928 Italy Good | Residents of long-term care, age 65+; recent stage II, III and IV PU (NPUAP) | Presence of acute illness or chronic disease possibly affecting the nutritional intervention and healing process | 371/39/30/28 | Treatment A: mean age 82 69% female p=0.71 race NR  Treatment B: mean age 81 60% female race NR | Nutrition: 30 kcal/kg per day plus 400 mL oral supplement vs. 30 kcal/kg per day plus standard nutrition | Treatment A: PU n=13 15% stage II 31% stage III  54% stage IV  Treatment B: PU n=15 20% stage II  27% stage III  53% stage IV | 30 kcal/kg per day plus 400 mL oral supplement with 20% of calories from protein | 30 kcal/kg per day plus standard nutrition with 16% of calories from protein | NA | 12 weeks | 4 long-term care facilities |
| Chernoff, 199029  USA  Poor | Institutionalized tube feeding dependent with decubitus ulcer | NR | NR/NR/NR/12 | Mean age: 72  58% female  Race NR | Nutrition: high protein formula | NR | n=6  High protein (16% of calories) HP | n=6  Very high protein (25% of calories) VHP | NA | 8 weeks | Health institution |

| Evidence Table H-3a: Nutrition Trials, continued |  |  |  |  |  |  |  |  |  |  |  |
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| **Author, year Country Overall Quality Rating** | **Eligibility Criteria** | **Exclusion Criteria** | **Number**  **Screened/ Eligible/ Enrolled/ Analyzed** | **Age Sex Race** | **Intervention Type: Specify** | **Ulcer Type/Severity at Baseline (Intervention Onset)** | **Treatment A** | **Treatment B** | **Treatment C** | **Duration of Followup** | **Study Setting** |
| Desneves, 200530 Australia Poor | Bedridden elderly patients with stage II, III and IV PU. Comparator groups did not have PU, half were at high risk for developing PU and the other half were not bedridden nor were they at high risk for developing PU | Clinical suspicion or diagnosis of osteomyelitis; diabetes mellitus; receiving enteral or parenteral nutrition support; prescribed hydroxyurea or greater than 10 mg of steroids/day | NR/NR/16/16 | Treatment A:  mean age 63 33% female  race NR  Treatment B: mean age 76 40% female race NR  Treatment C:  mean age 83 40% female race NR | Nutrition; protein, arginine, vitamin C, zinc. | 75% with stage II PU  19% with stage III PU 6% with stage IV PU (Stages according to Australian Wound Management Association Clinical Practice Guidelines which are compatible with NPUAP) | Standard hospital diet | Standard hospital diet plus two TetraPaks of a high-protein, high-energy supplement providing an additional 500 kcal: 18g protein, 0g fat, 72mg vitamin C and 7.5mg zinc (brand name Resource Fruit Beverage) | Standard hospital diet plus two TetraPaks of a defined arginine-containing supplement supplying an additional 500 kcal: 21 g protein, 0g fat, 500mg vitamin C, 30 mg zinc and 9g arginine (brand name Resource Arginaid Extra) | 3 weeks | Hospital |
| Lee, 200631 US Poor | Residents of long-term care facilities with stage II, III or IV PU | Terminal diagnosis; hospice care; protein-restricted diet due to renal insufficiency; active metabolic or gastrointestinal diseases; food allergies; use of corticosteroids or antibiotics for wound infection; failure to provide informed consent | 295/89/89/71 | NR | Nutrition: collagen protein hydrolysate supplement vs. placebo | Treatment A: n=44  PU n=75 65% stage II 17.8% stage III 17.2% stage IV (NPUAP)  Treatment B: n=27  PU n= 33 51% stage II 26.2% stage III 22.8% stage IV | Standard care plus concentrated, fortified, collagen protein hydrolysate supplement (Pro-Stat) 15g in a 45mL dose | Standard care plus placebo: noncaloric liquid indistinguishable from study product | NA | 8 weeks | Long-term care facilities |
| Leigh, 201232  Australia  Good | Stage II, III or IV PU not showing healing signs; oral diet without arginine-containing supplement | Evidence of sepsis; acute gastrointestinal surgery; receiving dialysis; receiving hydroxyurea or >10mg of prednisolone or 1.5mg dexamethasone/day | 29/29/29/23 | Treatment A:  n=12  mean age 70  33% female  race NR  Treatment B:  n=11  mean age 68  45% female  race NR | Nutrition: arginine supplement | Treatment A:  PU n=17  76% stage II  18% stage III  6% stage IV  Location:  sacrum 24%  heel 35%  ischium 29%  knee 12%  Treatment B:  PU n=14  71% stage II  21% stage III  7% stage IV  Location:  sacrum 43%  heel 21%  ischium 14%  ankle/elbow 14%  trochanter 7% | Standard hospital diet plus 4.5 g arginine (one sachet of Arginaid, Nestle Medical Nutrition) | Standard hospital diet plus 9g arginine (two sachets of Arginaid) | NA | 3 weeks | Tertiary care facilities |
| Meaume, 200933 Bulgaria France Germany Italy Romania Spain Fair | Over 60 years; written informed consent; heel PU stage II or III in process of recovery with early signs of granulation tissue, after accidental immobilization (NPUAP) | Confined to bed 24 hours/day before development of PU; PU entirely covered by necrosis or fibrin, infected ulcer; poorly controlled type I or II diabetes; dialyses patient; active neoplastic disease; parenteral nutrition serum albumin <22g/I advanced peripheral arterial occlusive disease | 194/165/165/ 160 | Treatment A:  n=85 mean age 81 p=0.760 66% female p=0.017 race NR  Treatment B:  n=75 mean age 81 47% female race NR | Nutrition: ornithine alpha-ketoglutarate vs. placebo | Treatment A: 38.8% stage II 47.1% stage II or III p=0.656 14.1% stage IIITreatment B: 32.0% stage II 53.3% stage II or III 14.7% stage III | 10g of ornithine alpha-ketoglutarate per day with 200ml of water or with food at lunch | Placebo of similar aspect and taste administered in the same way | NA | 6 weeks | Hospital |
| Myers, 199034 US Poor | Patients with non-surgically debrided PU, admitted to medical center over 2 year period | NR | 80/80/80/80 | Mean age 70  43% female Race NR | Nutrition: oral supplements vs. wound care | 7.5% stage I 41.2% stage II 20% stage III 31.2% stage IV (stage criteria not specified whether it is NPUAP or otherwise; criteria is compatible with NPUAP) | Treatment A: wound care | Treatment B: Prescribed nutritional support including oral supplements, tube feedings, parenteral nutrition, vitamins and trace elements | Treatment C: wound care and nutritional support  Treatment D: Standard hospital care | 7 days | Hospital |
| Ohura, 201135 Japan Poor | Tube-fed patients; NPUAP stage III-IV PU in the sacral, coccygeal, trochanteric, or calcaneal region;  Albumin (Alb) 2.5-3.5 g/dL, Braden scale 9-17 | Current condition or history of serious liver or renal disorder; severe diabetes mellitus; arteriosclerosis obliterans; or a malignant tumor (within the past 5 years); unmanageable severe general condition; unevaluable pressure ulcer wounds | NR/NR/60/50 | Treatment A:  n=21 age: 81 p=0.738 sex: 71% female p=0.658 race: NR Treatment B: n=29  age: 81  sex: 66% female race: NR | Nutrition: calorie supplementation | Stage III and IV PU  (NPUAP) | Administered calories accordingly. Standard tube-feeding formula (Brand name Racol) at mean of 1384kcal/day | Standard tube-feeding formula (Brand name Racol) at mean of 1092kcal/day | NA | 12 weeks | Hospital |
| ter Riet, 199536 The Netherlands Good | Residence in a nursing home or hospital; at least 1 existing pressure ulcer. Patients with stage II ulcers could only participate if de-epithelization had persisted for at least 7 days without interruption | Difficulties swallowing; frequent vomiting; osteomyelitis in the ulcer area; idiopathic hemochromatosis; thalassemia major; sideroblastic anemia; Cushing's syndrome or disease; pregnancy; radiotherapy in the ulcer area; use of antineoplastic agents or systemic glucocorticosteroids and a high probability to drop out and already taking vitamin C supplements in excess of 50mg/day | NR/NR/88/79 | NR | Nutrition: vitamin C supplementation | Treatment A:  n=43 stages II and III: 86%   Treatment B:  n=45 stages II and III: 78 %  (Study uses grade criteria to categorize PU) | Ascorbic acid, 500 mg twice daily | Ascorbic acid, 10 mg twice daily | NA | 12 weeks | Nursing home and Hospital |
| van Anholt, 201037 Czech Republic,  Belgium,  The Netherlands,  Curacao Fair | 18 to 90 years; one or more stage III to IV PU; receiving standard care and standard diet without nutritional supplements for at least 2 weeks before the study | Malnourished; severe medical conditions; non-pressure-related ulcers; life expectancy less than 6 months; receiving palliative care; use of corticosteroids;  dietary restrictions | NR/NR/47/43 | Treatment A:  n=22 mean age 76  64% female race: NR   Treatment B: n=21  mean age 73 48% female race: NR | Nutrition: calorie and vitamin/mineral supplementation | Treatment A:  stage III: 77%  stage IV: 23%  Treatment B: stage III: 67% stage IV: 33% (PU stages are in accordance with EPUAP, which are compatible with NPUAP) | Nutritional Supplement 750 kcal/day 85.2g carbohydrate 60g protein (includes 9g arginine) 21g fat, several vitamins and minerals | Non-caloric flavored placebo | NA | 8 weeks | Health care centers Hospitals Long-term care facilities |

| **Evidence Table  H-3a: Nutrition Trials, continued** |  |  |  |  |  |  |  |  |
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| **Author, year Country Overall Quality Rating** | **Outcomes: Complete Wound Healing** | **Outcomes: Wound Surface Area** | **Outcomes: Healing Time** | **Outcomes: Infection Rate** | **Outcomes: Osteomyelitis Rate** | **Outcomes: Recurrence Rate** | **Outcomes: Pain** | **Other Outcomes: Specify** |
| Benati, 200127  Italy  Poor | NR | Treatment A did not seem to have any considerable improving effect  Treatment B and C had a more rapid improvement | NR | NR | NR | NR | NR | NR |
| Cereda, 200928 Italy Good | Treatment A:  8% (n=1)  Treatment B:  NR | Treatment A: Pressure Ulcers decreased from 2,151mm2 to 701mm2 at 12 weeks. 68% improvement in wound surface area  Treatment B:  Pressure Ulcers decreased from 2,069mm2 to 1228mm2 at 12 weeks 41% improvement in wound surface area | Treatment A:  Area was reduced 40% at 6 weeks and 70% at 12 weeks  Treatment B  Area was reduced 30% at 6 weeks and 40% at 12 weeks | Treatment A:  23% (n=3)  Treatment B:  60% (n=9) p=0.07, Fisher exact test | NR | NR | NR | NR |
| Chernoff, 199029  USA  Poor | Treatment A: 0%  Treatment B: 67% (n=4) | Treatment A: 42% average decrease  Treatment B: 73% average decrease | NR | NR | NR | NR | NR | NR |
| Desneves, 200530 Australia Poor | NR | PUSH score at 3 weeks (lower is better)  A; 7  B: 6  C: 2.6  P<0.05 | Estimate  Treatment A:  16 weeks to completely heal  Treatment B: 15 weeks to completely heal  Treatment C: 5 weeks to completely heal | NR | NR | NR | NR | NR |
| Lee, 200631 US Poor | NR | Treatment A:  60% decrease in PUSH score  Treatment B:  48% decrease in PUSH score p<0.05 | Treatment A showed approximately twice the rate of healing  compared with  Treatment B | NR | NR | NR | NR | NR |
| Leigh, 201232  Australia  Good | Treatment A:  0%  Treatment B:  0% | Treatment A:  PUSH score decreased from 8.9 to 5.0  Treatment B:  PUSH score decreased from 9.0 to 5.9 | Treatment A:  Estimated time to complete wound healing 9 weeks  Treatment B:  Estimated time to complete wound healing 8 weeks | NR | NR | NR | NR | NR |
| Meaume, 200933 Bulgaria France Germany Italy Romania Spain Fair | Treatment A:  2% (n=2)  Treatment B:  4% (n=3) | Treatment A:  Mean decrease in area for PU (equal or less than 8cm2) was 2.3cm2  Treatment B:  Mean decrease in area for PU (equal or less than 8cm2) was 1.7cm2  p=0.006 | Treatment A:  Mean closure rate for PU (equal or less than 8cm2) was 0.07 cm2/day  Treatment B:  Mean closure rate for PU (equal or less than 8cm2) was 0.04cm2/day p=0.007 | NR | NR | NR | NR | NR |
| Myers, 199034 US Poor | NR | Treatment A: ulcer size mean change 2.76mm  70% improvement  Treatment B: ulcer size mean change 2.60mm  70% improvement  Treatment C: ulcer size mean change 2.34 mm  65% improvement  Treatment D: ulcer size mean change 2.70 mm  50% improvement | NR | NR | NR | NR | NR | NR |
| Ohura, 201135 Japan Poor | Treatment A:  24% (n=7)  Treatment B:  19% (n=4) | Treatment A:  Mean wound size decreased from 30 cm² to 0.5 cm²  Wound surface improved 83%  Treatment B:  Mean wound size decreased from 40 cm² to 7 cm² Wound surface improved 82% | Treatment A:  Mean wound size decreased to 2cm² at 6 weeks and 0.5cm² at 12 weeks  Treatment B:  Mean wound size decreased to 9cm² at 6 weeks and 7cm² at 12 weeks | NR | NR | NR | NR | NR |
| ter Riet, 199536 The Netherlands Good | Treatment A: 40% (n=17) healed at 11 weeks  Treatment B: 55% (n=25) healed at 12 weeks | Treatment A: Mean surface reduction: 0.21cm²/week 13.88%/week  Treatment B: Mean surface reduction: 0.27cm²/week 22.85%/week | Treatment A: 30% (n=13) of ulcers healed at 6 weeks and 40% (n=17) at 11 weeks  Treatment B: 30% (n=14) of ulcers healed at 6 weeks and 55% (n=25) at 12 weeks | NR | NR | NR | NR | NR |
| van Anholt, 201037 Czech Republic,  Belgium,  The Netherlands,  Curacao. Fair | Treatment A: 27% (n=6)  Treatment B: 24% (n=5) | Treatment A: Mean ulcer size decreased from 10.5 to 2cm² Wound area improved 81%  Treatment B: Mean ulcer size decreased from 11.5 to 3cm² Wound area improved 74% | Treatment A: 9% (n=2) healed at 4 weeks and 27% (n=6) at 8 weeks  Treatment B: 0% healed at 4 weeks, and 24% (n=5) at 8 weeks | NR | NR | NR | NR | NR |

| **Evidence Table  H-3a: Nutrition Trials, continued** |  |  |  | |  | |  |  |  | |  |
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| **Author, Year Country Overall Quality Rating** | **Harms: Dermatologic Complications** | **Harms: Bleeding** | | **Harms: Infection** | | **Other Harms: Specify** | **Severe Adverse Events** | **Withdrawal due to Adverse Events** | | **Overall Adverse Events Rate** | **Funding Source** |
| Benati, 200127  Italy  Poor | NR | NR | | NR | | NR | NR | NR | | NR | NR |
| Cereda, 200928 Italy Good | NR | NR | | NR | | NR | NR | NR | | NR | Nutricia |
| Chernoff, 199029  USA  Poor | NR | NR | | NR | | NR | No adverse effects | NR | | NR | NR |
| Desneves, 200530 Australia Poor | NR | NR | | NR | | NR | NR | NR | | NR | Windermere Foundation Ltd. |
| Lee, 200631 US Poor | NR | NR | | NR | | Discontinuations: hip fracture due to fall (2); changes in renal lab values (3); nausea or distention (4); death (2).  No difference between groups in rate of events. p>0.05 | NR | NR | | NR | Medical Nutrition, US, Inc |
| Leigh, 201232  Australia  Good | NR | NR | | NR | | NR | Side effects | 4% (n=1) | | NR | NR |
| Meaume, 200933 Bulgaria France Germany Italy Romania Spain Fair | NR | NR | | NR | | No serious adverse events related to treatment | Diarrhea, vomiting and nausea | NR | | 2% of AE related to treatment | CHIESI France and Italy |
| Myers, 199034 US Poor | NR | NR | | NR | | NR | NR | NR | | NR | Ross Laboratories |
| Ohura, 201135 Japan Poor | NR | NR | | NR | | NR | Treatment A: 38% (n=8)  Treatment B: 17% (n=5) | Treatment A: 5% (n=1)  Treatment B: NR | | Treatment A: 38% (n=8)  Treatment B: 17% (n=5) | Health and Labor Sciences Research Grants (Comprehensive Research on Aging and Health) |
| ter Riet, 199536 The Netherlands Good | NR | NR | | NR | | NR | NR | Unclear if AE related to treatment | | Unclear | The Netherlands Organization for Scientific Research |
| van Anholt, 201037 Czech Republic, Belgium,  The Netherlands, Curacao. Fair | NR | NR | | NR | | Higher rate of gastrointestinal symptoms in nutritional support group | Diarrhea, nausea, vomiting, constipation and dyspepsia | Treatment A: 9% (n=2)  Treatment B: 0 | | 5% (n=2) | Nutricia |