Evidence Table H-3: Nutrition

Evidence Table H-3a. Nutrition trials

| **Author, yearCountryOverall Quality Rating** | **Eligibility Criteria** | **Exclusion Criteria** | **Number Screened/ Eligible/ Enrolled/ Analyzed** | **AgeSexRace** | **Intervention Type:Specify** | **Ulcer Type/Severity at Baseline (Intervention Onset)** | **Treatment A**  | **Treatment B** | **Treatment C** | **Duration of Followup** | **Study Setting** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Benati, 200127ItalyPoor | Patients with severe cognitive impairment and pressure ulcers | Unlikely to benefit from nutritional supplement-ation | NR/NR/36/16 | Age range: 72-9144% femaleRace NR | Nutrition: protein and arginine enriched supplements | NR | n=5standard hospital diet | n=5standard 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=6standard diet and treatment B enriched with arginine (7.5g/day), zinc (25 mg) and antioxidants | 2 weeks | Health institution |
| Cereda, 200928ItalyGood | 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 8269% femalep=0.71race NRTreatment B:mean age 8160% femalerace 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=1315% stage II31% stage III 54% stage IV Treatment B:PU n=1520% 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, 199029USAPoor | Institutionalized tube feeding dependent with decubitus ulcer | NR | NR/NR/NR/12 | Mean age: 7258% femaleRace NR | Nutrition: high protein formula | NR | n=6High protein (16% of calories) HP | n=6Very high protein (25% of calories) VHP | NA | 8 weeks | Health institution |

| Evidence Table H-3a: Nutrition Trials, continued |  |  |  |  |  |  |  |  |  |  |  |
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| **Author, yearCountryOverall Quality Rating** | **Eligibility Criteria** | **Exclusion Criteria** | **Number** **Screened/ Eligible/ Enrolled/ Analyzed** | **AgeSexRace** | **Intervention Type:Specify** | **Ulcer Type/Severity at Baseline (Intervention Onset)** | **Treatment A**  | **Treatment B** | **Treatment C** | **Duration of Followup** | **Study Setting** |
| Desneves, 200530AustraliaPoor | 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 6333% female race NRTreatment B:mean age 7640% femalerace NRTreatment C: mean age 8340% femalerace NR | Nutrition; protein, arginine, vitamin C, zinc. | 75% with stage II PU 19% with stage III PU6% 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, 200631USPoor | 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=44PU n=7565% stage II17.8% stage III17.2% stage IV(NPUAP)Treatment B:n=27PU n= 3351% stage II26.2% stage III22.8% 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, 201232AustraliaGood | 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=12mean age 7033% femalerace NRTreatment B:n=11mean age 6845% femalerace NR | Nutrition: arginine supplement | Treatment A:PU n=1776% stage II18% stage III6% stage IVLocation: sacrum 24%heel 35%ischium 29%knee 12%Treatment B:PU n=1471% stage II21% stage III7% stage IVLocation: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, 200933BulgariaFranceGermanyItalyRomaniaSpainFair | 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=85mean age 81p=0.76066% femalep=0.017race NRTreatment B:n=75mean age 8147% femalerace NR | Nutrition: ornithine alpha-ketoglutarate vs. placebo | Treatment A:38.8% stage II47.1% stage II or IIIp=0.65614.1% stage IIITreatment B:32.0% stage II53.3% stage II or III14.7% 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, 199034USPoor | Patients with non-surgically debrided PU, admitted to medical center over 2 year period | NR | 80/80/80/80 | Mean age 70 43% femaleRace NR | Nutrition: oral supplements vs. wound care | 7.5% stage I41.2% stage II20% stage III31.2% 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 supportTreatment D: Standard hospital care | 7 days | Hospital |
| Ohura, 201135JapanPoor | 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=21age: 81 p=0.738sex: 71% femalep=0.658race: NRTreatment B:n=29age: 81 sex: 66% femalerace: 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, 199536The NetherlandsGood | 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=43stages II and III: 86% Treatment B:n=45stages 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 andHospital |
| van Anholt, 201037Czech Republic, Belgium, The Netherlands, CuracaoFair | 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=22mean age 76 64% femalerace: NR Treatment B:n=21mean age 7348% femalerace: 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 Supplement750 kcal/day85.2g carbohydrate60g protein (includes 9g arginine) 21g fat, several vitamins and minerals | Non-caloric flavored placebo | NA | 8 weeks | Health care centersHospitalsLong-term care facilities |

| **Evidence Table H-3a: Nutrition Trials, continued** |  |  |  |  |  |  |  |  |
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| **Author, yearCountryOverall 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, 200127ItalyPoor | NR | Treatment A did not seem to have any considerable improving effectTreatment B and C had a more rapid improvement | NR | NR | NR | NR | NR | NR |
| Cereda, 200928ItalyGood | 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 areaTreatment B:Pressure Ulcers decreased from 2,069mm2 to 1228mm2 at 12 weeks41% improvement in wound surface area | Treatment A:Area was reduced 40% at 6 weeks and 70% at 12 weeksTreatment BArea 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, 199029USA Poor | Treatment A: 0% Treatment B: 67% (n=4) | Treatment A: 42% average decreaseTreatment B: 73% average decrease | NR | NR | NR | NR | NR | NR |
| Desneves, 200530AustraliaPoor | NR | PUSH score at 3 weeks (lower is better)A; 7B: 6C: 2.6P<0.05 | EstimateTreatment A: 16 weeks to completely healTreatment B: 15 weeks to completely healTreatment C: 5 weeks to completely heal | NR | NR | NR | NR | NR |
| Lee, 200631USPoor | 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, 201232AustraliaGood | Treatment A:0%Treatment B:0% | Treatment A:PUSH score decreased from 8.9 to 5.0Treatment B:PUSH score decreased from 9.0 to 5.9 | Treatment A:Estimated time to complete wound healing 9 weeksTreatment B:Estimated time to complete wound healing 8 weeks | NR | NR | NR | NR | NR |
| Meaume, 200933BulgariaFranceGermanyItalyRomaniaSpainFair | 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 1.7cm2p=0.006 | Treatment A: Mean closure rate for PU (equal or less than 8cm2) was 0.07 cm2/dayTreatment B: Mean closure rate for PU (equal or less than 8cm2) was 0.04cm2/day p=0.007 | NR | NR | NR | NR | NR |
| Myers, 199034USPoor | NR | Treatment A:ulcer size mean change 2.76mm70% improvementTreatment B:ulcer size mean change 2.60mm70% improvementTreatment C:ulcer size mean change 2.34 mm65% improvementTreatment D: ulcer size mean change 2.70 mm50% improvement | NR | NR | NR | NR | NR | NR |
| Ohura, 201135JapanPoor | 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 cm²Wound surface improved 82% | Treatment A:Mean wound size decreased to 2cm² at 6 weeks and 0.5cm² at 12 weeksTreatment B:Mean wound size decreased to 9cm² at 6 weeks and 7cm² at 12 weeks | NR | NR | NR | NR | NR |
| ter Riet, 199536The NetherlandsGood | Treatment A: 40% (n=17) healed at 11 weeksTreatment B: 55% (n=25) healed at 12 weeks | Treatment A: Mean surface reduction:0.21cm²/week13.88%/week Treatment B: Mean surface reduction:0.27cm²/week22.85%/week | Treatment A: 30% (n=13) of ulcers healed at 6 weeks and 40% (n=17) at 11 weeksTreatment B: 30% (n=14) of ulcers healed at 6 weeks and 55% (n=25) at 12 weeks | NR | NR | NR | NR | NR |
| van Anholt, 201037Czech 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 2cm²Wound area improved 81%Treatment B: Mean ulcer size decreased from 11.5 to 3cm²Wound area improved 74% | Treatment A: 9% (n=2) healed at 4 weeks and 27% (n=6) at 8 weeksTreatment 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, YearCountryOverall 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, 200127ItalyPoor | NR | NR | NR | NR | NR | NR | NR | NR |
| Cereda, 200928ItalyGood | NR | NR | NR | NR | NR | NR | NR | Nutricia |
| Chernoff, 199029USAPoor | NR | NR | NR | NR | No adverse effects | NR | NR | NR |
| Desneves, 200530AustraliaPoor | NR | NR | NR | NR | NR | NR | NR | Windermere Foundation Ltd. |
| Lee, 200631USPoor | 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, 201232AustraliaGood | NR | NR | NR | NR | Side effects | 4% (n=1) | NR | NR |
| Meaume, 200933BulgariaFranceGermanyItalyRomaniaSpainFair | 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, 199034USPoor | NR | NR | NR | NR | NR | NR | NR | Ross Laboratories |
| Ohura, 201135JapanPoor | 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, 199536The NetherlandsGood | NR | NR | NR | NR | NR | Unclear if AE related to treatment | Unclear | The Netherlands Organization for Scientific Research |
| van Anholt, 201037Czech 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 |