UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

# FACULDADE DE MEDICINA

DEPARTAMENTO DE NUTRIÇÃO

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# DESEMPENHO DE INDICADORES NUTRICIONAIS ISOLADOS NO DIAGNÓSTICO DE DESNUTRIÇÃO EM PACIENTES COM CÂNCER DO TRATO GASTROINTESTINAL E DE CABEÇA E PESCOÇO

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Trabalho de Conclusão de Curso de Graduação apresentado como requisito parcial para obtenção de grau em bacharel em Nutrição, à Universidade Federal do Rio Grande do Sul, Faculdade de Medicina.

Orientadora: Prof<sup>a</sup>. Dr<sup>a</sup>. Thais Steemburgo Coorientadora: Me. Nutr. Giovanna Potrick Stefani

> Porto Alegre 2023

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**Parágrafo 1º** O TCC em formato de monografia deverá seguir as normas vigentes estabelecidas pela biblioteca da Faculdade de Medicina.

Parágrafo 2º O TCC em formato de artigo científico deverá conter:

1. Resumo estruturado (conforme as normas vigentes da biblioteca)

2. Revisão da literatura e lista de referências (conforme as normas vigentes da biblioteca)

3. Artigo original (no formato da revista de interesse)

4. Anexos necessários e normas da revista de interesse de submissão.

# DEDICATÓRIA

Dedico esse trabalho a minha avó que teve seus estudos interrompidos ainda no ensino fundamental e a minha mãe que concluiu o ensino superior com 42 anos.

#### RESUMO

**INTRODUÇAO:** Pacientes com câncer gastrointestinal e de cabeça e pescoço apresentam elevado risco nutricional e alta prevalência de desnutrição, condições que se associam a piores desfechos, como o maior tempo de internação hospitalar. Instrumentos de triagem e de avaliação nutricional possibilitam identificar precocemente o risco e estado nutricional beneficiando os pacientes com uma intervenção nutricional precoce e especializada. Neste sentido, algumas das principais ferramentas utilizadas para a avaliação do estado nutricional são a Avaliação Subjetiva Global (ASG), que é considerada um critério referência e, a Avaliação Subjetiva Global Produzida pelo Próprio Paciente (ASG-PPP) que é um instrumento especificio para pacientes com câncer. Além disso, os indicadores nutricionais isolados como Índice de Massa Corporal (IMC), Força do Aperto de Mão (FAM) e Circunferência da Panturrilha (CP) por serem rápidos, de baixo custo e de fácil aplicação também são utilizados para complementar a avaliação nutricional na prática clínica.

**OBJETIVO:** Avaliar em pacientes hospitalizados com câncer gastrointestinal e de cabeça e pescoço: (1) desempenho dos indicadores do estado nutricional: IMC, FAM e CP para o diagnóstico de desnutrição e, (2) associação destes indicadores e da desnutrição com o maior tempo de internação.

**MÉTODOS:** Estudo de coorte prospectivo realizado em 171 pacientes com câncer gastrointestinal e de cabeça e pescoço admitidos no Hospital de Clínicas de Porto Alegre (HCPA). O estado nutricional foi avaliado em até 48 horas após a internação por IMC, Força do Aperto de Mão (FAM), Circunferência da Panturrilha (CP), SGA e PG-SGA. As curvas ROC (*Receiver Operating Characteristic*) com intervalo de confiança (IC) de 95%, área sob a curva (AUC), sensibilidade, especificidade e valores preditivos positivo e negativo foram calculadas para avaliar o desempenho dos indicadores nutricionais (IMC, CP e FAM) na sua forma isolada comparados aos critérios de referência ASG ou ASG-PPP. O modelo de regressão logística múltipla, ajustado para fatores de confusão, foi utilizado para avaliar a associação de desnutrição com maior tempo de hospitalização.

**RESULTADOS:** Foram avaliados 171 pacientes (52% eram homens, média de idade 61,9 ± 12,9 anos e 64.3% eram idosos). O tratamento do câncer na maioria foi a cirurgia (58,5%), 33,3% estavam em estágio III e IV da doença e a presença da metástase foi observada em 26,9% dos pacientes. A mediana do tempo de internação foi 6 (3 - 11) dias e 56,7% ficaram hospitalizados  $\geq$  6 dias. A desnutrição foi identificada em 57,3% e 87,1% dos participantes, segundo a ASG e ASG-PPP, respecticamente. De acordo com os indicadores nutricionais, 13,5% estavam desnutridos (IMC <18,5 kg/m<sup>2</sup>), 46,2% apresentaram baixa FAM e 59,1% com valores reduzidos de CP. Todos os indicadores nutricionais apresentaram baixo desempenho (AUC <0,70) na identificação de desnutrição. No entanto, o baixo IMC (<18,5 kg/m<sup>2</sup>) demonstrou especificidade satisfatória (>80%) quando comparado ao ASG e ASG-PPP. Além disso, pacientes desnutridos, avaliados pela ASG e ASG-PPP tiveram uma chance de internação  $\geq$  6 dias em 3,60 e 2,70 vezes maior quando comparados aos pacientes bem nutridos.

**CONCLUSÃO:** Em pacientes com câncer gastrointestinal e de cabeça e pescoço, o IMC <18,5kg/m<sup>2</sup> apresentou uma especificidade adequada para o diagnóstico de desnutrição e pode ser complementar a avaliação nutricional neste grupo de pacientes. Ainda a desnutrição foi positivamente associada a maior tempo de internação hospitalar.

**DESCRITORES:** Câncer; Antropometria; Estado nutricional; Desnutrição; Tempo de internação.

#### ABSTRACT

**INTRODUCTION:** Patients with gastrointestinal and head and neck cancer have a high nutritional risk and a high prevalence of malnutrition, conditions that are associated with worse outcomes such as longer hospital stays. Screening and nutritional assessment instruments make it possible to identify risk and nutritional status at an early stage, benefiting patients with an early and specialized nutritional intervention. In this sense, some of the main tools used to assess nutritional status are the Subjective Global Assessment (SGA), which is considered a reference, and the Subjective Global Assessment Produced by the Patient (PG-SGA) which is a specific instrument for patients with cancer. In addition, isolated nutritional indicators such as Body Mass Index (BMI), Hand Grip Strength (HGS) and Calf Circumference (CC), as they are quick, inexpensive and easy to apply, are also used to complement the nutritional assessment in clinical practice.

**OBJECTIVE:** Evaluate in patients hospitalized with gastrointestinal and head and neck cancer: (1) performance of nutritional status indicators: BMI, HGS and CC for the diagnosis of malnutrition, and (2) association of these indicators and malnutrition with longer hospital stay.

**METHODS:** Prospective cohort study carried out in 171 patients with gastrointestinal and head and neck cancer admitted to Hospital de Clínicas de Porto Alegre (HCPA). Nutritional status was assessed within 48 hours after admission by BMI, Hand Grip Strength (HGS), Calf Circumference (CC), SGA and PG-SGA. The ROC (Receiver Operating Characteristic) curves with a confidence interval (CI) of 95%, area under the curve (AUC), sensitivity, specificity and positive and negative predictive values were calculated to evaluate the performance of the nutritional indicators (BMI, CC and HGS) in its isolated form compared to the SGA or PG-SGA reference criteria. The multiple logistic regression model, adjusted for confounding factors, was used to assess the association between malnutrition and longer hospital stays.

**RESULTS:** A total of 171 patients were evaluated (52% were men, mean age 61.9  $\pm$  12.9 years and 64.3% were older adults). The treatment of cancer in the majority was surgery (58.5%), 33.3% were in stage III and IV of disease and the presence of

metastasis was observed in 26.9% of patients. The median length of stay was 6 (3 - 11) days and 56.7% were hospitalized  $\geq$  6 days. The malnutrition was identified in 57.3% and 87.1% of the participants, according to the SGA and PG-SGA, respectively. According to nutritional indicators, 13.5% were malnourished (BMI <18.5 kg/m<sup>2</sup>), 46.2% had low HGS and 59.1% had reduced CC values. All nutritional indicators performed poorly (AUC <0.70) in identifying malnutrition. However, low BMI (<18.5 kg/m<sup>2</sup>) showed satisfactory specificity (>80%) when compared to SGA and PG-SGA. In addition, malnourished patients, assessed by SGA and PG-SGA, had a chance of hospitalization  $\geq$  6 days in 3.60 and 2.70 times higher when compared to well-nourished patients.

**CONCLUSION:** In patients with gastrointestinal and head and neck cancer, BMI <18.5kg/m<sup>2</sup> showed adequate specificity for the diagnosis of malnutrition and may complement nutritional assessment in this group of patients. Malnutrition was also positively associated with longer hospital stays.

**KEYWORDS:** Oncology; anthropometry; Nutritional status; Malnutrition; Length of stay.

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# ABREVIAÇÕES

## Revisão da Literatura

- OMS Organização Mundial da Saúde
- DCNT's Doenças Crônicas Não Transmissíveis
- ESMO European Society for Medical Oncology
- IMC Índice de Massa Corporal
- NRS 2002 Nutritional Risk Screening
- ASG Avaliação Subjetiva Global
- ASG-PPP Avaliação Subjetiva Global Produzida pelo Próprio Paciente
- SBNO Sociedade Brasileira de Nutrição Oncológica
- GLIM Global Leadership Initiative on Malnutrition
- ASPEN American Society for Parenteral and Enteral Nutrition
- ESPEN European Society for Clinical Nutrition and Metabolism
- FELANPE Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismo
- PENSA Parenteral and Enteral Nutrition Society of Asia
- CP Circunferência da Panturrilha
- FAM Força do Aperto de Mão

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### **1. REVISÃO DA LITERATURA**

#### Importância do problema

#### Câncer: definição e epidemiologia

O câncer é caracterizado pela formação e pelo crescimento anormal de células que interferem nas funções vitais do corpo (LÓPEZ-LÁZARO, 2018). O processo de formação de um câncer é o resultado de uma complexa interação entre fatores do hospedeiro, como características genéticas; fatores ambientais, como exposição a substâncias cancerígenas; e fatores comportamentais, que envolvem variáveis como alimentação, atividade física, etilismo e tabagismo (INCA, 2020).

Segundo a Organização Mundial da Saúde (OMS) no ano de 2022, as Doenças Crônicas Não Transmissíveis (DCNTs) foram responsáveis por 74% das mortes a nível mundial (*Noncommunicable Diseases Progress Monitor*, 2022). E, dentre as DCNTs, o câncer assume uma importante posição, já que a estimativa é de que essa doença se torne a principal causa de morte, bem como o principal obstáculo para o aumento da expectativa de vida em todos os países do mundo ao final do século 21 (BRAY et al., 2018).

A mais recente estimativa mundial de incidência e mortalidade do câncer elaborada para o ano de 2020 traz dados que contribuem para esse cenário preocupante (SUNG et al., 2021). A Global Cancer Statistics (2021) indica que a estimativa para o ano de 2020 é de 19,3 milhões de novos casos de câncer junto a, aproximadamente, 10 milhões de óbitos no mundo. Sobre a incidência conforme a localização primária do tumor, o mesmo documento destaca que o câncer de mama passou a ser o mais incidente no mundo (11,7%), seguido pelo câncer de pulmão (11,4%), câncer de próstata (7,3%) e câncer de pele não melanoma (6,2%) (SUNG et al., 2021). No Brasil, as estimativas para cada ano do triênio 2023 - 2025 preveem a incidência de 704,080 novos casos para cada 100 mil habitantes para todas as neoplasias malignas, os casos mais incidentes serão o câncer de mama em mulheres (30,1%) e, o de próstata em homens (30,0%). Na Região Sul, em mulheres, as três maiores incidências serão os cânceres de mama (27,8%), cólon e reto (10,1%) e traqueia, brônguio e pulmão (8,2%). Já em homens, a incidência maior será o câncer de próstata (20,4%), seguido por tumores de traqueia, brônquio e pulmão (11,3%) e o câncer colorretal ocupará a terceira posição neste grupo (9,6%). E, no Rio Grande do Sul, a taxa estimada para este mesmo triênio será de 189,22 novos casos para cada 100 mil habitantes, e os tumores de mama (3,720 novos casos) e de próstata (3,510 novos casos) manterão a liderança seguidos do câncer do tipo cólon e reto (3,120 novos casos em homens e mulheres) (INCA, 2022).

#### Desnutrição no paciente com câncer

Entre os pacientes hospitalizados, àqueles acometidos pela presença câncer têm a maior prevalência de desnutrição (MUSCARITOLI et al., 2019). Dados do Inquérito Brasileiro de Avaliação Nutricional (IBRANUTRI), estudo multicêntrico que incluiu quatro mil pacientes hospitalizados, demonstrou que a presença de desnutrição em pacientes oncológicos foi superior quando comparada a pacientes não oncológicos (66,3% vs. 42,9%, respectivamente) (WAITZBERG et al., 2001).

De fato, a prevalência da desnutrição em pacientes oncológicos pode alcançar taxas que variam de 30 a 50% (MUSCARITOLI et al., 2019). Ainda, a desnutrição impacta negativamente nos desfechos clínicos e o prognóstico dos pacientes com câncer. Dentre os desfechos clínicos negativos associados à desnutrição, está a diminuição da resposta ao tratamento oncológico, a redução da qualidade de vida, o aumento de risco para complicações pós-operatórias, aumento do tempo de hospitalização, morbidade e mortalidade (CRESTANI, et al., 2022). De fato, a mortalidade é um desfecho desfavorável observado entre 10 e 20% dos pacientes com câncer e que pode estar associada ao estado de desnutrição e não à doença maligna em si (ARENDS et al., 2017).

Pacientes com câncer apresentam alto risco para desnutrição porque tanto as características da doença quanto os efeitos do tratamento antitumoral ameaçam o estado nutricional (ARENDS et al., 2017; MUSCARITOLI et al., 2021). Quanto às características da doença que contribuem para quadros de desnutrição, podemos citar a ativação da inflamação sistêmica que leva a piora da anorexia e do catabolismo, além de contribuir para a depleção dos estoques de tecido adiposo e para a degradação da massa magra e, consequentemente, para a perda de peso corporal (GOMES e MAIO, 2015; ARENDS et al., 2017; CEDERHOLM et al., 2017).

Sobre os tratamentos mais utilizados para o câncer, evidenciam-se o tratamento cirúrgico, quimioterápico e radioterápico. Bem reportados, os efeitos adversos decorrentes do tratamento oncológico clínico (quimioterapia e radioterapia) intensificam o declínio do estado nutricional porque são, em maioria, sintomas que

impactam a ingestão de alimentos: náuseas, vômitos e anorexia (TSUNADA et al., 2019). Por sua vez, a desnutrição pode acentuar ainda mais a toxicidade das terapias, reduzindo a tolerância e a resposta do paciente ao tratamento antineoplásico (SMIDERLE e GALLON, 2012; GOMES e MAIO, 2015).

#### Principais tipos de câncer que causam impacto nutricional

Pacientes com câncer frequentemente desenvolvem sintomas de impacto nutricional que limitam ou impedem o paciente de se alimentar como resultado das alterações fisiológicas provocadas pela patologia em si e também pelo tratamento (ROCHA et al., 2016; ARENDS et al., 2017). Já em pacientes com a doença em estágio avançado, os sintomas nutricionais são muito comuns, atingindo até 50% destes indivíduos (TSUNADA et al., 2019). Em pacientes oncológicos submetidos à quimioterapia, os eventos adversos – como náusea e vômito – afetam a maioria dos pacientes em algum momento durante o curso do tratamento (KUDERER et al., 2022).

Também já está descrito que pacientes com câncer gastrointestinal ou de cabeça e pescoço apresentam risco nutricional aumentado e alta prevalência de desnutrição devido ao déficit nutricional causado por esses tipos de câncer (MARSHALL et al., 2019; DEFTEREOS et al., 2021; SIMON et al., 2021). De fato, o câncer gastrointestinal causa um efeito direto de obstrução mecânica pelo tumor, com consequente má absorção de nutrientes (AVERSA et al., 2017; SOUSA et al., 2022).

Em cânceres gastrointestinais é comum a presença dos seguintes sintomas de impacto nutricional: náuseas, vômitos e anorexia. Já especificamente no câncer colorretal é comum a alteração do hábito intestinal com a ocorrência de constipação ou diarreia, anemia, cólica abdominal, sangramento pelo reto e sensação de evacuação incompleta. Em cânceres de cabeça e pescoço os principais sintomas são disfagia, mucosite, dificuldades de mastigação e odinofagia (SCHIESSEL et al., 2020).

Os sintomas de impacto nutricional podem contribuir com o desenvolvimento de duas condições desfavoráveis ao prognóstico do paciente com câncer: a caquexia e a sarcopenia (SCHIESSEL et al., 2020; ARENDS et al., 2021).

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A caquexia é uma síndrome multifatorial caracterizada pela perda involuntária do peso corporal, com perda contínua de massa muscular com ou sem perda de massa gorda (ARENDS et al., 2017). Conduzida por uma combinação variável de mudancas metabólicas, bem como pela redução da ingestão de alimentos, a caquexia pode levar o paciente oncológico ao estado de desnutrição (SCHIESSEL et al., 2020). Essa síndrome leva ao comprometimento funcional progressivo, compreendido em três fases: pré-caquexia, caquexia e caquexia refratária. A diretriz de prática clínica sobre a caquexia do câncer em pacientes adultos do European Society for Medical Oncology de 2021 (ESMO) define como critério diagnóstico para caquexia a perda de peso >5% ou IMC <20 Kg/m<sup>2</sup> associado à perda de peso >2% (ARENDS et al., 2021). Visto isso, em pacientes com caquexia os sintomas de impacto nutricional mais comuns são anorexia e saciedade precoce, náuseas, distensão abdominal, alterações do paladar, xerostomia, disfagia e constipação. A caquexia tem sido fortemente associada a tipos específicos de tumores: pancreáticos, esofágicos, gástricos, pulmonares e hepáticos. Da mesma forma pacientes com essas neoplasias têm o maior grau de perda de peso (FREIRE et al., 2020).

A sarcopenia, segundo a mesma diretriz do ESMO, refere-se à combinação de baixa força muscular com baixa quantidade de massa muscular (ARENDS et al., 2021). Ainda, a sarcopenia está associada à baixa qualidade muscular e apesar de ser entre pessoas de idade avançada, também pode ocorrer mais cedo (CRUZ-JENTOFT et al., 2019). A sarcopenia pode ser detectada em pacientes com câncer que apresentam baixo, normal ou aumentado índice de massa corporal (IMC) e apresenta consequências severas nas complicações cirúrgicas, na toxicidade induzida por quimioterapia e na sobrevida (BOSSI et al., 2021). Em uma recente meta-análise que incluiu 81,814 pacientes com tumores sólidos, a prevalência da sarcopenia foi observada em aproximadamente 35,3% destes pacientes (SUROV e WIENKE, 2022).

#### Importância da avaliação nutricional no paciente com câncer

Como apresentado anteriormente, é frequente a presença da desnutrição em pacientes com câncer (GOMES e MAIO, 2015). Surge desse modo a necessidade de uma intervenção nutricional precoce nessa população, uma vez que esta pode vir a contribuir para a manutenção ou recuperação de um estado nutricional e funcional

normal do paciente (MUSCARITOLI et al., 2019). Neste sentido, para que se possa intervir antecipadamente com a terapia nutricional adequada, é preciso identificar o estado nutricional do paciente oncológico. E, essa identificação é realizada por meio da avaliação nutricional individualizada e completa (ARENDS et al., 2017).

A avaliação nutricional em pacientes oncológicos é de extrema relevância, já que o déficit nutricional nesses pacientes está intimamente relacionado à diminuição da resposta ao tratamento do câncer e menor qualidade de vida, bem como a presença de efeitos adversos da terapia (CRESTANI et al., 2022). A partir disso, o estado nutricional do paciente deve ser avaliado e monitorado para melhor resposta ao tratamento (MUSCARITOLI et al., 2019). Também para evitar que o paciente passe por algum procedimento hospitalar em déficit nutricional (SMIDERLE e GALLON, 2012).

#### Instrumentos de avaliação nutricional para o diagnóstico de desnutrição:

A avaliação nutricional completa consiste em: (1) na identificação do risco nutricional (através de instrumentos de triagem nutricional) e (2) na elaboração do diagnóstico nutricional (através de ferramentas validadas). A avaliação nutricional irá permitir uma intervenção nutricional adequada e específica (MENDES et al., 2019).

O Consenso Nacional de Nutrição Oncológica de 2021 recomenda a avaliação nutricional em um período de até 48 horas após a hospitalização do paciente com câncer. Sugere a utilização do *Nutritional Risk Screening 2002* (NRS-2002), Avaliação Subjetiva Global (ASG) ou Avaliação Subjetiva Global Produzida pelo Paciente (ASG-PPP) para triagem e avaliação nutricional de pacientes com câncer, respectivamente (SBNO, 2021). Mais recentemente, o *Global Leadership Initiative on Malnutrition* (GLIM), recomenda uma avaliação diagnóstica de estado nutricional em pacientes hospitalizados com e sem câncer mais precisa e completa na identificação da presença da desnutrição (CEDERHOLM et al., 2019).

O NRS-2002 foi desenvolvido pela Associação Dinamarquesa de Nutrição Parenteral e Enteral (DAPEN), baseado em 128 ensaios clínicos randomizados, com propósito de detectar, no ambiente hospitalar, a presença de desnutrição e o risco do desenvolvimento desta, em pacientes adultos, independentemente do diagnóstico clínico (KONDRUP et al., 2003). Os critérios de avaliação do risco nutricional incluem: (I) gravidade do impacto da doença primária no estado nutricional, (II) perda de peso recente (1-3 meses), (III) diminuição da ingestão alimentar dentro de uma semana, (IV) índice de massa corporal (IMC), e (V) idade superior a 70 anos (KONDRUP et al., 2003). Através da pontuação gerada é possível quantificar o risco nutricional. Os doentes são classificados como sem risco = 0, risco baixo = 0 a 1, risco médio = 3 a 4, e risco elevado ≥4. Ao final um escore ≥3 pontos já é indicativo de risco nutricional (KONDRUP et al., 2003). Em pacientes oncológicos hospitalizados, aplicando a NRS 2002, 32% dos pacientes apresentaram risco nutricional, sendo 18% com escore =3 e 14% com escore >3 pontos (BOZZETT et al., 2012). Estudo prospectivo controlado com 212 pacientes oncológicos hospitalizados mostrou aumento na ingestão alimentar e menor tempo de internação em pacientes que receberam intervenção nutricional após serem classificados como apresentando risco nutricional pela NRS- 2002 (HUMANN e CUNNINGHAM, 2005).

A ASG foi desenvolvida por Detsky et al. em 1987, com o propósito de não apenas diagnosticar a presença de desnutrição, mas sim identificar aqueles pacientes com maior risco de complicações associadas ao estado nutricional durante sua internação, sendo assim um instrumento tanto prognóstico, como diagnóstico (DETSKY et al., 1987). A ASG é considerada o critério referência para o diagnóstico nutricional e avalia a perda de peso, a alteração da ingestão alimentar, a presença de sintomas gastrointestinais e a alteração da capacidade funcional. Também exige a execução de um exame físico com objetivo de avaliar a perda de gordura e a perda de músculo, além da retenção de líquidos. Os pacientes recebem uma classificação de A, B ou C, indicando bem nutrido, moderadamente desnutrido ou com suspeita de desnutrição e gravemente desnutrido, respectivamente (DETSKY et al., 1987). Em estudo coorte que avaliou 234 pacientes com câncer colorretal, pacientes com ASG A (bem nutridos) apresentaram maior tempo de sobrevida que os pacientes com ASG B ou C (desnutrição moderada ou severa), sendo a ASG um instrumento adequado para aplicação em pacientes oncológicos (GUPTA et al., 2005).

A partir da ASG, Ottery criou em 1996 uma adaptação específica para a população oncológica: a ASG- produzida pelo próprio paciente (PPP) (OTTERY, 1996). Esse instrumento é considerado um método padrão para avaliação do estado nutricional em paciente oncológicos, em razão de sua sensibilidade e predição de complicações (SANTOS et al., 2017). Mais recentemente, uma revisão sistemática de 29 estudos mostrou que o ASG-PPP é uma ferramenta eficaz para avaliar

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desfechos clínicos desfavoráveis em pacientes hospitalizados com câncer (CRESTANI et al., 2022). Esse instrumento consiste em duas seções: (1) seção de quatro perguntas preenchidas pelo paciente e uma seção para o profissional de saúde. A seção preenchida pelo paciente considera o histórico de peso, presença de sintomas relacionados à nutrição, ingestão de alimentos e nível de capacidade funcional; (2) as seções preenchidas por um profissional de saúde incluem uma avaliação da demanda metabólica, presença de doença e sua relação com as necessidades nutricionais, em conjunto com os elementos do exame físico. Além disso, a ferramenta fornece uma pontuação numérica que orienta o nível de intervenção nutricional necessária com uma pontuação mais alta indicando maior risco de desnutrição (OTTERY, 1996).

Já os critérios para diagnóstico de desnutrição do GLIM foram estabelecidos a partir de um consenso entre representantes das principais sociedades de nutrição clínica globais: American Society for Parenteral and Enteral Nutrition (ASPEN), European Society for Clinical Nutrition and Metabolism (ESPEN), Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismo (FELANPE) e Parenteral and Enteral Nutrition Society of Asia (PENSA), ao longo de diversos encontros entre os anos 2016/2018. O objetivo foi desenvolver critérios globais, baseados em evidência e de fácil aplicação por todos os profissionais de saúde para o diagnóstico de desnutrição em pacientes adultos no cenário clínico (CEDERHOLM et al., 2019). A aplicação dos critérios GLIM é feita em duas etapas. Inicialmente é realizada a triagem nutricional do paciente, utilizando ferramenta validada que mais se adéque ao contexto clínico. Posteriormente é realizada avaliação diagnóstica e classificação da gravidade da desnutrição. Os critérios de classificação da desnutrição são divididos em fenotípicos (perda de peso não voluntária, índice de massa corporal (IMC) e massa muscular reduzida) e etiológicos (ingestão alimentar reduzida e inflamação ou gravidade da doença). Sendo necessária presença de pelo menos um critério fenotípico e um critério etiológico para diagnóstico de desnutrição. Finalmente, os critérios fenotípicos são utilizados para classificação do grau de desnutrição (CEDERHOLM et al., 2019). Mais recentemente, o GLIM discute técnicas de avaliação, em pacientes hospitalizados, da massa e função muscular como critérios fenotípicos (COMPHER et al., 2022).

Estudos em diferentes grupos vêm demonstrando a identificação da desnutrição através dos critérios GLIM. Em pacientes hospitalizados com diferentes

diagnósticos clínicos a prevalência da desnutrição, segundo o GLIM foi de 41,6% e este instrumento apresentou validade satisfatória para diagnosticar desnutrição nestes pacientes (BRITO et al., 2021). Em pacientes com câncer, o GLIM foi uma ferramenta eficaz para avaliar o estado nutricional e prever a sobrevida (ZHANG et al., 2021; ZHANG et al., 2021). Além disso, o diagnóstico de desnutrição de acordo com o GLIM foi associado a maiores custos de internação e tempo de internação (YIN et al., 2021).

#### Indicadores nutricionais e desnutrição

# Índice de massa corporal, circunferência da panturrilha e força do aperto de mão.

O índice de massa corporal (IMC) é utilizado para avaliar a proporção entre peso e estatura (OMS, 2000). Calculado a partir da relação entre o peso dividido pelo quadrado da estatura, o IMC um índice simples e fácil de usar, comumente usado para classificar desnutrição, sobrepeso e obesidade. Sendo assim, é amplamente utilizado na prática clínica e no contexto hospitalar, visto que avalia, mesmo que indiretamente, o estado nutricional (GARCIA et al., 2013). Os pontos de corte para adultos definidos pela OMS possibilitam a seguinte classificação: IMC < 18,5 kg/m² para baixo-peso; IMC entre 18,5 kg/ m² e 24,99 kg/m² para eutrofia; IMC entre 25,0 kg/m² e 29,99 kg/m² para sobrepeso e IMC ≥ 30 kg/m² como obesidade e seus progressivos graus (OMS, 1995). No entanto, o IMC pode apresentar limitação de baixa acurácia na discriminação de massa gorda e massa magra e, por isso, possa ser um confundidor quanto à classificação do estado nutricional de pacientes oncológicos (FERREIRA et al., 2013).

A circunferência da panturrilha (CP) é uma medida antropométrica altamente associada à massa muscular esquelética e, portanto, é indicada para diagnóstico de sarcopenia e foi, recentemente, sugerida como item essencial para kit de ferramentas do profissional da saúde (PRADO, et al., 2022). A medida é de realização fácil e rápida, além de possuir baixo custo por utilizar apenas fita antropométrica inelástica para aplicação. Para realização da medida o paciente deve estar sentado, com as pernas formando um ângulo de 90° graus e com os pés apoiados firmemente no chão. É medido no ponto de maior diâmetro da perna. A CP tem como ponto de corte para baixa massa muscular os valores de ≤34 cm para homens e ≤33 cm para mulheres (BARBOSA-SILVA et al., 2016). A CP foi associada de forma positiva para detectar alteração na massa muscular de pacientes hospitalizados, identificando aproximadamente 55% dos indivíduos com mudança no quantitativo de músculo da panturrilha (PEIXOTO et al., 2016). Mais recentemente, de acordo com os critérios do GLIM a medida também foi considerada como um importante critério fenotípico para avaliação de massa muscular para o diagnóstico de desnutrição (COMPHER et al., 2022). Ainda, é de importância ressaltar que os valores de CP devem ser ajustados pelo IMC do indivíduo, a fim de ajudar a remover os efeitos de confusão da adiposidade, da seguinte forma: redução do valor medido em 3 cm (IMC, 25-30 kg/m<sup>2</sup>) ou 7 cm (IMC, 30 – 40 kgm<sup>2</sup>) (GONZALEZ et al., 2021). Em pacientes com câncer, baixos valores de CP podem predizer o risco de mortalidade nesta coorte de pacientes e, por isso, a medida pode ser utilizada para rastrear rapidamente pacientes em risco de morte que poderiam se beneficiar de cuidados direcionados para melhorar seu prognóstico (SOUSA et al., 2020).

A força do aperto de mão (FAM) é medida por meio de um dinamômetro a partir da medida de força máxima voluntária da mão. É uma avaliação simples, rápida, não invasiva e que avalia em curtos períodos de tempo as mudanças nutricionais funcionais antes das mudanças antropométricas e bioquímicas (KILGOUR et al., 2013). É utilizada na prática clínica com o objetivo de avaliar a função muscular e a capacidade funcional, além de complementar a avaliação nutricional dos indivíduos, visto que pacientes desnutridos apresentam depleção de massa magra e baixa força muscular (SCHLUSSEL et al., 2008; GARCIA et al., 2013). Os pontos de corte de FAM variam de acordo com o sexo: mulheres que apresentam ≤16 Kg e homens ≤27 Kg são considerados com função muscular baixa (CRUZ-JENTOFT et al., 2019). Em pacientes oncológicos o baixo índice de FAM na admissão hospitalar foi associado com diminuição de cerca de três (3) vezes na probabilidade de alta (MENDES et al., 2014). Em um estudo transversal realizado em 76 pacientes como cânceres de tumores sólidos e hematológicos hospitalizados, demonstrou que a baixa capacidade funcional, avaliada por dinamometria foi associada com pior estado nutricional, avaliado pela ASG (STEEMBURGO et al., 2018). Estudo em 112 pacientes com doença renal crônica e em hemodiálise, a baixa FAM foi observada tanto em homens como em mulheres (CHA et al., 2021).

#### 2. JUSTIFICATIVA E OBJETIVO DO ESTUDO

A desnutrição é uma condição frequentemente identificada no paciente oncológico hospitalizado e está associada a desfechos clínicos negativos, como a diminuição da resposta ao tratamento oncológico, a redução da qualidade de vida, o aumento de risco para complicações pós-operatórias, o aumento do tempo de hospitalização, morbidade e mortalidade. Este cenário ainda é pior em pacientes com tumores sólidos do tipo gastrointestinal e de cabeça e pescoço, já que estes tipos de cânceres causam grande impacto nutricional.

Assim, os instrumentos de avaliação nutricional possibilitam identificar precocemente o risco e estado nutricional beneficiando os pacientes com uma intervenção nutricional precoce e especializada. A ferramenta de triagem nutricional, NRS-2002, e os de avaliação da desnutrição como ASG (considerada critério de referência), ASG-PPP (específica para pacientes oncológicos) e o GLIM permitem a realização do diagnóstico nutricional em pacientes com câncer. Ainda, existem os indicadores nutricionais que podem contribuir para uma avaliação da nutrição mais completa como o IMC, a CP e FAM. De fato, já é descrito que os valores reduzidos da CP e FAM são medidas em destaque porque estão fortemente relacionadas à desnutrição em pacientes com câncer.

As evidências científicas vêm demonstrando que a presença da desnutrição, avaliada por distintos instrumentos, está associada positivamente a piores desfechos clínicos em pacientes com diferentes tipos de cânceres. Contudo, os estudos direcionados a pacientes com tumores sólidos do tipo gastrointestinal e de cabeça e pescoço ainda são escassos. E, até o momento, não há estudo que avaliou o desempenho dos principais indicadores nutricionais amplamente utilizados na prática clínica para o diagnóstico de desnutrição e sua associação com o tempo de internação prolongada.

Sendo assim, o objetivo deste estudo foi avaliar em pacientes hospitalizados com câncer do trato gastrointestinal e de cabeça e pescoço: (1) desempenho dos indicadores do estado nutricional: IMC, FAM e CP para o diagnóstico de desnutrição e, (2) associação destes indicadores e da desnutrição com o maior tempo de internação.

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#### 3. ARTIGO ORIGINAL

# Performance of isolated nutritional indicators in malnutrition diagnosis in patients with gastrointestinal and head and neck cancer: A prospective cohort study.

Short title: isolated nutritional indicators in patients with cancer

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Keywords: Oncology; anthropometry; nutritional status; Malnutrition; Length of stay.

The study protocol was approved by the Ethics Commission of Hospital de Clínicas de Porto Alegre (protocol number #2019.0708).

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#### **Conflict of interest**

The authors declare no conflicts of interest.

#### Authorship

TS and MSC conceived and designed the study. CHS, MSC, GPS and LMS contributed to data acquisition. CHS and TS analyzed and interpreted the data. CHS, GPS and TS drafted the initial manuscript. All authors critically revised the manuscript and approved the final version. TS is the guarantor and attests that all listed authors meet authorship criteria and that no others who meet these criteria have been omitted.

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## Key points

- The prevalence of malnutrition is high in patients with gastrointestinal and head and neck cancer.
- During hospitalization, nutritional isolated markers such as Body Mass Index (BMI), Handgrip Strength (HGS), Calf Circumference (CC) and tools as Subjective Global Assessment (SGA), and Patient-Generated Subjective Global Assessment (PG-SGA) are widely used to diagnose malnutrition in patients with cancer.
- We identified that these indicators alone did not demonstrate a good performance to diagnose malnutrition. However, they can be used (in particular, the low BMI) combined with the SGA and PG-SGA in patients with gastrointestinal and head and neck cancer.

#### Abstract

**Background:** Patients with gastrointestinal and head and neck cancer have an increased risk of malnutrition. Body Mass Index (BMI), Subjective Global Assessment (SGA), and Patient-Generated Subjective Global Assessment (PG-SGA) are widely used for the nutritional assessment of patients with cancer, as they are inexpensive methods. We aimed to analyze the performance of isolated nutritional indicators in malnutrition diagnosis and their association with length of hospital stay (LOS).

**Methods:** A prospective cohort study was conducted on 171 gastrointestinal and head and neck cancer. Nutritional status was evaluated within 48 hours of hospital admission by BMI, Handgrip Strength (HGS), Calf Circumference (CC), SGA, and PG-SGA. Area Under the receiver operating characteristic Curve (AUC) was used to identify the performance of each nutritional indicator using SGA and PG-SGA as the reference methods. The multiple logistic regression model, adjusted for confounders, was utilized to assess the association of malnutrition with LOS.

**Results:** Of the total patients, 13.5% were underweight, 46.2% had low HGS, 59.1% presented low CC, 57.3% and 87.1% were malnourished by SGA and PG-SGA, respectively. 56.7% were hospitalized for  $\geq$  6 days. All nutritional indicators showed poor performance (AUC <0.70) in identifying malnutrition. However, low BMI demonstrated satisfactory specificity (>80%) when compared to SGA and PG-SGA. According to SGA and PG-SGA, malnutrition increased the chance of LOS  $\geq$  6 days by 3.60 and 2.70 times.

**Conclusion:** In patients with gastrointestinal and head and neck cancer, BMI <18.5kg/m<sup>2</sup> presents adequate specificity for the diagnosis of malnutrition. Malnutrition was positively associated with a prolonged hospital stay.

#### Introduction

In patients with cancer, malnutrition is considered a risk factor for many complications such as longer length of stay (LOS), hospital readmission, lower response to treatment, and mortality.<sup>1-5</sup> In fact, involuntary weight loss can affect 50% to 80% of these patients, and the degree of weight loss depends on the type, location, and stage of the tumor.<sup>6</sup> In this sense, patients with gastrointestinal or head and neck cancer have an increased nutritional risk and a high prevalence of malnutrition due to the nutritional deficit caused by these types of cancer.<sup>7-9</sup> Indeed, gastrointestinal cancer causes a direct effect of mechanical obstruction by the tumor, with consequent malabsorption of nutrients.<sup>10,11</sup> In patients with head and neck tumors, the main symptoms observed are dysphagia, mucositis, difficulty chewing and odynophagia, resulting in decreased food intake.<sup>12</sup>

Considering that nutritional deficit is closely related to the reduced response to cancer treatment and lower quality of life, the assessment of nutritional status needs to be constantly monitored.<sup>13</sup> Tools such as the Subjective Global Assessment (SGA) and the Patient-Generated Subjective Global Assessment (PG-SGA) are validated nutritional assessment tools for the early identification of malnutrition in hospitalized patients with cancer.<sup>14</sup>

The SGA<sup>15</sup> is considered the reference method for assessing nutritional status, its diagnosis of poor nutritional status was associated with LOS and higher mortality rates.<sup>16-18</sup> The PG-SGA was developed specifically for individuals with cancer<sup>19</sup> and a malnutrition diagnosis according to this tool has also been significantly associated with longer LOS.<sup>20,21</sup>

Moreover, isolated nutritional indicators such as body mass index (BMI), calf circumference (CC), and hand grip strength (HGS) are also used to complement nutritional assessment in clinical practice because these measures are related to

malnutrition in patients with cancer.<sup>22-26</sup> BMI is commonly used to classify undernutrition, overweight, and obesity<sup>27</sup>, and an association has been observed between very low BMI (<18 kg/m2) with poor clinical outcomes, including increased risk of death.<sup>28,29</sup> CC is an anthropometric measure highly associated with skeletal muscle mass, and in cancer patients, it has been shown to be a good predictor of hospital readmission and mortality.<sup>24,25,30</sup> Finally, HGS is used in clinical practice to assess muscle function and functional capacity, and reduced HGS values have been associated with a three-fold decrease in the likelihood of hospital discharge.<sup>20,31-33</sup>

Thus, the purpose of this study was to evaluate in patients with gastrointestinal and head and neck cancer the performance of different nutritional indicators (BMI, CC, and HGS) in the diagnosis of malnutrition considering the SGA or the PG-SGA as the reference method.

## Methods

### Study design

This article was designed and reported according to the STROBE Statement providing all sections suggested to cohort studies.

## Participants

This prospective cohort study was conducted in patients with cancer admitted to a university hospital in southern Brazil, between May 2021 and March 2022. It was approved by [removed for blind peer review], and all participants provided informed consent prior to data collection. The inclusion criteria were patients of both sexes, aged  $\geq$  18 years with gastrointestinal or head and neck tumors who were lucid, coherent, and able to communicate and perform the HGS test or CC measure. Patients in the emergency room, intensive care unit, palliative care, or infected with COVID-19 were excluded. The patient selection flowchart is described in **Figure 1**.

#### Data collection

Data collection was conducted within 48 hours after the hospital admission at the patient's bedside, by trained researchers. Clinical and demographic data were obtained from the digital records at the hospital: age, sex, ethnicity, education, smoking history, previous treatment with surgery, chemotherapy, and/or radiotherapy cancer staging and presence of metastasis and chronic diseases. In relation to clinical outcomes, patients were followed up until hospital discharge to assess length of stay (LOS), hospital readmission (within 30 days) and in-hospital mortality.

#### Nutritional risk, diagnosis of malnutrition and nutritional indicators

The patients were weighed at admission. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m<sup>2</sup>).<sup>27</sup> At the time of the interview, the patient was asked about weight loss prior to hospitalization. Patient-reported normal weight was subtracted from the current weight. Nutritional screening was performed within a period of up to 48 hours after the hospitalization of patient by Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF). The PG-SGA SF is a specific nutritional screening tool for patients with cancer and consists of four boxes: (1) weight history; (2) food intake; (3) nutrition symptoms and (4) physical function. The PG-SGA SF generates a total score sourced from four boxes, which scores ≥4 indicating nutritional risk and <4 no risk.<sup>34</sup>

Malnutrition was diagnosed using 2 tools: SGA and PG-SGA. The SGA is considered the reference for nutritional diagnosis and assessment of weight loss, changes in food intake, presence of gastrointestinal symptoms, changes in functional capacity and muscle and subcutaneous fat loss. This tool classifies patients as A, B or C, indicating well-nourished, moderately malnourished or suspected malnourished and severely malnourished, respectively.<sup>15</sup> The PG-SGA is an instrument specific for subjects with cancer, since this tool has the best diagnostic performance in those

patients. It relies on patients' history (weight history, dietary intake, nutrition impact symptoms, physical function, metabolic stress), and physical assessment (body fat, muscle mass, fluid retention). The patients completed the patient component of PG-SGA, while the professional component was completed by the researchers. The individuals were categorized as well-nourished (category A), moderately malnourished or suspected malnourished (category B) or severely malnourished (category C).<sup>19</sup>

The nutritional indicators evaluated were BMI, hand grip strength (HGS) and calf circumference (CC). BMI was calculated and classified according to the WHO criteria: underweight (BMI <18.5kg/m<sup>2</sup>), normal range (BMI 18.5 kg/m<sup>2</sup> - 24,99 kg/m<sup>2</sup>) and overweight (BMI  $\geq 25 \text{ kg/m}^2$ )<sup>27</sup> were established for analysis as binary categorical variables. The HGS was collected with a Jamar® hand dynamometer (Sammons Preston, Inc., Bolingbrook, IL, USA), 3 consecutive times, each one with a duration of 3 seconds of contraction and a rest interval of 1 minute between each test, using the dominant hand while the patient was seated with the feet touching the floor and with the test arm comfortably at 90° on the armrest. After that, the average of the three tests was calculated, and HGS  $\leq$  16 Kg for woman and  $\leq$  27Kg for men was considered low muscle function.<sup>22</sup> The CC was measured with the patient seated, with the foot supported, and the leg flexed at an angle of 90° at the maximum circumference of the calf on the right leg. CC values were adjusted by BMI to help remove the confounding effects of adiposity: the measured value was decreased by 3 cm (BMI: 25-29.9 kg/m<sup>2</sup>) or 7 cm (BMI: 30-40 kg/m<sup>2</sup>)<sup>35</sup> and the cohort point for CC, which was considered as muscle loss, was ≤34 cm for men and ≤33 cm for women were considered as low muscle mass.<sup>36</sup>

## Statistical analysis

Sample size estimation was based on a previous Brazilian study of patients with cancer that found a prevalence of 53.9% by the PG-SGA.<sup>33</sup> Considering a power of 80% and 5% as level of significance, 171 cancer inpatients were necessary.

Data are presented as mean and standard deviation, median (p25-p75), or n (%). The Kolmogorov-Smirnov was used to test the normality of the variables. Moderate and severe malnutrition were grouped as with malnutrition for analysis.

The receiver operating characteristic (ROC) curves with 95% confidence intervals (CI), area under the curve (AUC), sensitivity, specificity and positive and negative predictive values were calculated to evaluate accuracy of the SGA or PG-SGA and nutritional indicators for malnutrition. The AUC values were: 0.5-0.6 as very bad; 0.6-0.7 as poor; 0.7-0.8 as moderate; 0.8-0.9 as good; and > 0.9 as excellent.<sup>37</sup> Sensitivity and specificity values > 80% were considered satisfactory concurrent validity.<sup>38</sup> The agreement between SGA or PG-SGA and the nutritional indicators for malnutrition was analyzed using the Kappa coefficient (k). The values used to assess agreement were: 0.01–0.20 (poor); 0.21–0.40 (fair); 0.41–0.60 (moderate); 0.61–0.80 (as substantial); 0.81–0.99 (almost perfect); and 1.00 as perfect.<sup>39</sup>

The differences in general characteristics between according to the median of LOS were evaluated using the Chi-square test for categorical variables, and independent t-test for continuous variables. Hospitalization  $\geq$  6 days was considered prolonged LOS (the median value was considered for this categorization).

A multiple logistic regression analysis also was used to calculate the odds ratio (OR) and respective 95% CIs, considering prolonged LOS ( $\geq$  6 days) as the dependent variable. All models were adjusted for age, sex, presence of metastasis and chronic diseases.

Data analysis was completed using Medcalc Software version 20.116 and IBM SPSS (Statistical Package for the Social Sciences, Chicago, Illinois, United States) software version 25.0. A significance level of 0.05 was considered statistically significant.

#### Results

#### General, clinical, and outcomes

A total of 171 patients were evaluated (52% male, mean age 61.9  $\pm$  12.9 years, 64.3% older adults, 87.7% white, 66.1% had ≤8 years of education, and 40.4% were smokers). About the types of cancer, 57.9% (n = 99) had gastrointestinal and 42.1% (n = 72) head and neck. Concerning to treatment type, 58.5% (n = 100) had undergone surgery, 8.8% (n = 15) had undergone chemotherapy, 1.8% (n = 3) had undergone to radiotherapy and 23.4% (n = 40) had undergone to a combined treatment. A total of 33.3% (n = 57) were diagnosed with advanced cancer (stage III or IV) and 26.9% (n = 46) had the presence of metastasis. About chronic diseases, 50.3%, 21.1% and 12.3% of the patients had hypertension, diabetes and cardiovascular disease, respectively. Regarding clinical outcomes, the median length of stay (LOS) was 6 (3 – 11) days, 56.7% remained hospitalized for ≥ 6 days, 20.5% were readmitted within 30 days, and in-hospital mortality was 7% (n = 12). These data are described in **Table 1**.

#### Prevalence of nutritional risk, malnutrition and nutritional indicators

**Table 2** describes the nutritional characteristics of the participants. Patients considered at nutritional risk according by the PG-SGA SF represented 72.5% (n = 124) of the sample. The presence of malnutrition was identified in 57.3% (SGA) and 87.1% (PG-SGA) of patients with gastrointestinal and head and neck cancer. Regarding to the nutritional indicators, 13.5% (n = 23), 43.3% (n = 74) and 43.3% (n

= 74) were classified underweight, normal, and overweight according to the BMI, respectively. In addition, 46.2% had a low HGS and 59.1% had low CC. Also, in this group of patients the main symptoms with nutritional impact observed were appetite loss (56.2%), xerostomia (25.1%), nausea (24%) and constipation (19.3%).

#### Performance of isolated nutritional indicators in diagnosing malnutrition

**Table 3** and **Figure 2** show the performance of the nutritional indicators (BMI, HGS, and CC) in identifying malnourished patients considering SGA and PG-SGA as the reference method. Using SGA, by AUC ROC, all nutritional indicators showed similar performance for diagnosing malnutrition: 0.593 (low BMI), 0.580 (low HGS) and 0.573 (low CC). However, the low BMI (<18.5kg/m<sup>2</sup>) demonstrated the best specificity (>80%) when compared to the other nutritional markers. When we evaluated the performance of the markers using the PG-SGA as a reference, the low HGS demonstrated the best performance among the markers (AUC ROC 0.635) and the BMI maintained its satisfactory specificity (>80%). In addition, no nutritional indicator showed significant agreement with the SGA and PG-SGA.

Association of nutritional indicators and malnutrition in predicting prolonged hospitalization

**Table 4** shows the relation of clinical and nutritional with prolonged hospitalization. Patients who remained hospitalized  $\geq$  6 days represented 56.7% (n = 97). Older and patients with gastrointestinal cancer had longer LOS than adult and patients with head and neck cancer. Also was observed that patients at nutritional risk and malnutrition was related to hospitalization  $\geq$  6 days. Regarding nutritional indicators, patients with low BMI and low CC remained hospitalized longer. No differences were observed between treatment and cancer stage, as well as the presence of metastasis with length of hospitalization.

**Table 5** describe the association of nutritional indicators (BMI, HGS and CC) and malnutrition (by SGA and PG-SGA) with prolonged hospitalization ( $\geq$  6 days). In logistic regression model, adjusted by age, sex, presence of metastasis and chronic diseases. Patients diagnosed with malnutrition according to the SGA and PG-SGA showed a positive association with a higher a chance of hospitalization  $\geq$  6 days in 3.60 (p <0.001) and 2.78 times (p = 0.048), respectively. No associations were observed of nutritional indicators with hospitalization  $\geq$  6 days.

#### Discussion

The current study demonstrated that isolated nutritional indicators (BMI, HGS and CC) presented a poor performance (AUC <0.70) and agreement (Kappa <0.20) in identifying malnutrition when compared to SGA and PG-SGA. However, low BMI (<18.5 kg/m<sup>2</sup>) demonstrated satisfactory specificity (>80%) and this BMI cutoff point value could be used as a complementary indicator in nutritional assessment in patients with gastrointestinal and head and neck cancer. In addition, malnourished patients, according to the SGA and PG-SGA, had a more chance of hospitalization time when compared to well-nourished patients.

#### Prevalence of nutritional risk, malnutrition, and nutritional indicators

In hospitalized cancer patients, the prevalence of malnutrition is high and varies according to the location and stage of the tumor.<sup>40</sup> In this study we focused on the main types associated with malnutrition: gastrointestinal and head and neck tumors. In our sample, the nutrition risk by PG-SGA SF was 72.5% and the rate of malnutrition was identified in 57.3% (SGA) and 87.1% (PG-SGA) of patients. Previous studies in this group of patients collaborate with our findings.<sup>41-43</sup> In a multicenter study the risk of malnutrition (score  $\geq$  4) by PG-SGA SF was 60%.<sup>41</sup> In 64 patients with head and neck cancer the presence of malnutrition by SGA was

43.8%<sup>42</sup> and in subjects with gastrointestinal cancer, the malnutrition was 82.5% according to SGA<sup>43</sup>. Differences in the values of malnutrition can be found due to the specific characteristics of each tool. For example, the PG-SGA is specific for cancer patients as it also assesses symptoms caused by the oncological treatment.<sup>19</sup> In a multicenter study in patients with gastrointestinal and with head and neck cancer the malnutrition identified by PG-SGA was 61% and 40%, respectively.<sup>9</sup>

Isolated nutritional indicators (BMI, HGS and CC) can be used to complement the nutritional assessment and some studies in cancer patients have demonstrated associations of these indicators with negative outcomes.<sup>29,44</sup> In our study, 13.5% of patients had underweight according to WHO.<sup>27</sup> In a recent systematic review and meta-analysis in head and neck cancer demonstrated that underweight patients (BMI  $< 18.5 \text{ kg/m}^2$ ) had higher hazards of death compared to normal weight patients.<sup>29</sup> In fact, in patients this type tumor, being underweight at diagnosis was an independent, adverse prognostic factor.<sup>44</sup> HGS assesses muscle function and recently has been recommended as a complementary measure in hospitalized patients.<sup>45</sup> In our sample, the low HGS was observed in 46.2% of the participants. Similar data were found in studies in patients with cancer.<sup>18,33</sup> In malnourished with different type of cancer 47.9% had low HGS.<sup>33</sup> In subjects with advanced cancer, 37.9% had low HGS and this tool demonstrated be adequate to diagnose malnutrition and predicting six-month mortality.<sup>18</sup> Also, patients with low HGS had an approximately three-fold decrease in the likelihood of hospital discharge compared to patients with high HGS.<sup>20</sup> CC is considered an indicator of muscle mass<sup>24</sup> and in our sample 46.4% of patients had low CC, and these values were adjusted for BMI<sup>35</sup>. Similar rates were shown in patients with gastric and colorectal cancer, where the prevalence of low CC was 56.0%.<sup>11</sup> In addition, in patients with and without cancer reduced values of CC were associated with mortality<sup>25</sup> and hospital readmission<sup>30</sup>.

#### Performance of isolated nutritional indicators in diagnosing malnutrition

In our record, the BMI <18.5 kg/m<sup>2</sup> showed a poor performance (AUC <0.70) but a satisfactory specificity (> 80%) in identifying malnourished patients. In previous studies in individuals with different type of cancer the cutoff of BMI values diverges on diagnosing malnutrition.<sup>11,46,47</sup> In our patients with gastrointestinal and head and neck tumors, 13.5% had BMI <18.5 kg/m<sup>2</sup> and malnutrition rates ranged from 57% - 87%. In lung cancer patients in advance stage<sup>46</sup>, the mean BMI of severely malnourished patients, according to the SGA and PG-SGA, was 21.6 kg/m<sup>2</sup> which is considered normal by WHO<sup>27</sup>. In older patients with colorectal cancer 88% of patients malnourished by PG-SGA had a normal or high BMI (≥24 kg/m2).<sup>47</sup> In 178 gastric and colorectal cancer patients, 11% of patients had BMI <18.5 kg/m<sup>2</sup> and the low BMI when compared to SGA, also showed satisfactory specificity values (94.6%).<sup>11</sup>

In this study, low HGS indicated a poor agreement (kappa <0.2) and unsatisfactory sensitivity and specificity values (<80%) compared to SGA and PG-SGA for diagnosing malnutrition. It is known that patients malnourished and with cancer have impaired functionality due to loss of muscle function, and low HGS may reflect nutritional losses before changes in body composition can be identified.<sup>48</sup> However, in our study, the HGS was not able to identify patients with malnutrition when evaluated alone. In fact, a previous multicenter study, HGS had very low diagnostic value and accuracy for identifying severe malnutrition, and this can be explained because nutritional damage related to cancer can accelerate the decrease in HGS, but it is not the only cause either.<sup>49</sup>

Calf circumference (CC) is a measure that reflects body muscle mass and has prognostic value in clinical and oncology patients.<sup>24,25</sup> In our study, low CC did present a poor agreement with SGA (Kappa = 0.147) and PG-SGA (Kapa = 0.054) in

diagnosing malnutrition. In older patients with cancer, also was observed a fair agreement between low CC (cutoff point of < 31cm) and PG-SGA.<sup>25</sup> It is important to emphasize that in our study we used cutoff points according to gender<sup>36</sup> and the values of CC were adjusted for BMI, thus avoiding adiposity confounders.<sup>35</sup> In fact, this adjustment is appropriate, because can minimizes errors in which oncological patients with sarcopenic obesity are classified with normal CC values.<sup>50</sup> In our sample for example ~40% of patients had overweight.

# Association of nutritional indicators and malnutrition in predicting prolonged hospitalization

In our study, patients with at nutritional risk and malnutrition were related to LOS ( $\geq$  6 days). Also was found that patients with low BMI and low CC were hospitalized longer. These data collaborate with a meta-analysis in older patients with cancer, which suggests a relationship between BMI <18.5kg/m<sup>2</sup> and LOS<sup>28</sup>, and in adult's patients where low CC values were associated with prolonged hospitalization ( $\geq$  9 days)<sup>51</sup>. In this study, no association was observed between isolated nutritional indicators and LOS. However, malnourished patients according to SGA and SGA-PG were hospitalized 3.60 and 2.79 times when compared to well-nourished patients. In fact, patients with different type of cancer, the worse nutritional status is a factor that is associated with prolonged hospitalization.<sup>16-18,20,21</sup>

## Implications for clinical practice and limitations

Our findings suggests that nutritional indicators such as BMI, HGS and CC, commonly used in clinical practice, might be inappropriate if used alone to diagnose malnutrition. However, in patients with gastrointestinal and head and neck cancer the cutoff point for BMI <18.5 kg/m<sup>2</sup> can be combined with SGA or PG-SGA in nutritional assessments. This information is valid since BMI values can differ in different groups

of patients.<sup>11,47,48</sup> To assess muscle function, HGS is a measure that can complement nutritional assessment, it is associated with reduced functional capacity and malnutrition<sup>33</sup>, and this scenario is worse in older patients<sup>52</sup>. And indeed, in our study, approximately 65% were elderly. CC has been considered a sensitive anthropometric index to assess muscle mass and is an important measure to assess loss of muscle mass.<sup>27</sup> But it is suggested that your cutoff points be adjusted for BMI.<sup>35</sup>

Also in this study, we applied the PG-SGA, which is considered a specific instrument for cancer patients, and we also used it as a reference criterion to evaluate the performance of nutritional indicators in their isolated form. The use of this tool is important in this population since it evaluates signs and symptoms of treatment.<sup>19</sup> Indeed, we observed that the majority of our patients (56.2%) reported loss of appetite, which directly affects the nutritional status. Hospital LOS may also have negatively impacted the nutritional status of these patients, we observed that patients who presented malnutrition, regardless of the instrument used for the diagnosis, were hospitalized longer.

Among the limitations of this study, the heterogeneity of our sample, concerning to age and staging of cancer, can be cited. To minimize their effects, the logistic regression analyses were adjusted for sex, age, presence of metastasis and chronic disease. Nevertheless, this study presents important data on the high prevalence of malnutrition in hospital admission in subjects with gastrointestinal and head and neck cancer and reinforces the importance of early nutritional assessment together with nutritional indicators to reduce unfavorable clinical outcomes, such as longer hospitalizations.

## Conclusion

Our record showed that nutritional indicators (low BMI, low HGS and low CC) demonstrated a poor performance and agreement with SGA and PG-SGA and are not accurate alone for diagnosing malnutrition in patients with gastrointestinal and head and neck cancer. However, low BMI (<18.5kg/m<sup>2</sup>) should be used to complement nutritional assessment performed with SGA and/or PG-SGA.

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General	n (%)
Age (years)	61.9 ± 12.9
Older adults (≥ 60 years)	110 (64.3)
Sex (male)	89 (52)
Ethnicity, (white)	150 (87.7)
Education (≤8 years)	113 (66.1)
Smoking history (yes)	69 (40.4)
Clinics	
Prevalence	
Gastrointestinal	99 (57.9)
Head and neck	72 (42.1)
Treatment	
Surgery	100 (58.5)
Chemotherapy	15 (8.8)
Radiotherapy	3 (1.8)
Combined treatment	40 (23.4)
Tumor stage III/IV	57 (33.3)
Presence of metastasis (yes)	46 (26.9)
Chronic diseases	
Hypertension	86 (50.3)
Diabetes	36 (21.1)
Cardiovascular disease	21 (12.3)
Outcomes	
Length of stay (days)	6 (3 - 11)
≥ 6 days	97 (56.7)
Readmission in 30 days (yes)	35 (20.5)
Death (yes)	12 (7)

**Table 1.** Characteristics of patients with gastrointestinal and head and neck cancer (n = 171).

Data expressed as mean ± SD, median (p25-p75) or n (%). \*

Table 2. Nutritional characteristics of with gastrointestinal and head and neck cance	٢
(n = 171).	

	Values
Nutritional risk and status	n (%)
PG-SGA SF (score ≥ 4)	124 (72.5)
SGA (moderately and severely malnourished)	98 (57.3)
PG-SGA (moderately and severely malnourished)	149 (87.1)
Nutritional indicators	
BMI (kg/m²)	26.2 (5 - 41)
Underweight	23 (13.5)
Normal	74 (43.3)
Overweight	74 (43.3)
Low HGS (kg)*	79 (46.2)
Low CC (cm)**	101 (59.1)
Treatment symptoms and nutritional effects	
Appetite loss	96 (56.2)
Xerostomia	43 (25.1)
Nausea	41 (24)
Constipation	33 (19.3)

Data expressed as mean ± SD, median (p25-p75) or n (%).

NRS-2002 = Nutritional Risk Screening; MNA SF = Mini Nutritional Assessment Short Form; PG-SGA SF = Patient- Generated Subjective Global Assessment Short Form; SGA = Subjective Global Assessment; PG-SGA = Patient- Generated Subjective Global Assessment; BMI = Body Mass Index; HGS = hand grip strength; CC = calf circumference.

\*Low HGS = Male ( $\leq 27$  kg); Female ( $\leq 16$  kg)<sup>22</sup>

\*\*Low CC: Male ( $\leq$ 34 cm); Female ( $\leq$ 33 cm)<sup>36</sup>. CC values were adjusted by patient's BMI, in order to help to remove the confounding effects of adiposity<sup>35</sup>

**Table 3.** Performance of isolated nutritional indicators (body mass index, handgrip strength, and calf circumference) in diagnosing malnutrition in patients with gastrointestinal and head and neck (using SGA and PG-SGA as the reference method) (n = 171).

	Nutritional Indicators			
	Low BMI <sup>*</sup>	Low HGS**	Low CC***	
SGA as the reference				
Kappa (p-value)	0.165 (p = <0.001)	0.156 (p = 0.037)	0.147 (p = 0.054)	
Accuracy (%)	53.8	57.3	58.5	
AUC ROC (CI 95%)	0.593 (0.509 – 0.678)	0.580 (0.494 – 0.667)	0.573 (0.486 – 0.660)	
Sensitivity (%)	21.4	53.1	65.3	
Specificity (%)	97.3	63.0	49.3	
Positive predictive value (%)	91.3	65.8	63.4	
Negative predictive value (%)	47.9	50.0	51.4	
PG - SGA as the reference				
Kappa (p -value)	0.045 (p = 0.048)	0.114 (p = 0.018)	0.054 (p = 0.354)	
Accuracy (%)	26.3	53.2	59.1	
AUC ROC (CI 95%)	0.577 (0.462 – 0.692)	0.635 (0.517 – 0.752)	0.552 (0.422 – 0.682)	
Sensitivity (%)	15.4	49.7	60.4	
Specificity (%)	100.0	77.3	50.0	
Positive predictive value (%)	100.0	93.6	89.1	

Negative predictive value (%)

14.9

18.58

15.8

SGA: 57.3% malnutrition prevalence PG-SGA: 87.1% malnutrition prevalence

BMI = Body Mass Index; HGS = hand grip strength; CC = calf circumference

SGA = Subjective Global Assessment; PG-SGA = Patient- Generated Subjective Global Assessment.

\*Low BMI: according to WHO (<18.5 kg/m<sup>2</sup>)<sup>27</sup> \*\*Low HGS = Male ( $\leq 27$  kg); Female ( $\leq 16$  kg)<sup>22</sup> \*\*\* Low CC: Male ( $\leq 34$  cm); Female ( $\leq 33$  cm)<sup>36</sup>. CC values were adjusted by patient's BMI, in order to help to remove the confounding effects of adiposity<sup>35</sup>

Table 4. Relations of clinical and nutritional characteristics with hospitalization (≥ 6 days) in patients with gastrointestinal and head

and neck (n = 171).

Variables	Hospitalized patients <6 days	Hospitalized patients ≥ 6 days	p value
	(n = 74; 43.3%)	(n = 97; 56.7%)	
Age (years)	58.4 ± 14.4	64.5 ± 11.0	0.007
Older adults (≥ 60 years)	40 (36.4)	70 (63.6)	0.770
Cancer type			<0.001
Gastrointestinal	30 (30.3)	69 (69.7)	
Head neck	44 (61.1)	28 (38.9)	
Treatment / Stage / Metastasis			0.796
Surgery	46 (46)	54 (54)	
Chemotherapy	5 (33.3)	10 (66.7)	
Radiotherapy	1 (33.3)	2 (66.7)	
Tumor stage III/IV	22 (38.6)	35 (61.4)	0.181
Presence of metastasis (yes)	18 (39.1)	28 (60.9)	0.507
Nutritional risk and status			<0.01
PG-SGA SF (score ≥ 4)	44 (35.5)	80 (64.5)	
SGA (B and C)	28 (28.6)	70 (71.4)	
PG-SGA (B and C)	59 (39.6)	90 (60.4)	
Nutritional indicators			0.001
BMI (kg/m <sup>2</sup> )	27.7 ± 5.3	25.1 ± 5.2	

Underweight	6 (26.1)	17 (73.9)	
Normal	25 (33.8)	49 (66.2)	
Overweight	43 (58.1)	31 (41.9)	
Low HGS (Kg)*	29 (36.7)	50 (63.3)	0.108
Low CC (cm)**	37 (36.6)	64 (63.4)	0.035

Data expressed as mean ± SD, median (p25-p75) or n (%).

P-value with t independent test or Chi-square test

NRS-2002 = Nutritional Risk Screening; MNA SF = Mini Nutritional Assessment Short Form; PG-SGA SF = Patient- Generated Subjective Global Assessment Short Form; SGA = Subjective Global Assessment; PG-SGA = Patient- Generated Subjective Global Assessment; BMI = Body Mass Index; HGS = hand grip strength; CC = calf circumference.

B and C are patients classified moderately and severely malnourished, respectively. For analyses were grouped.

\*Low HGS = Male ( $\leq 27$  kg); Female ( $\leq 16$  kg)<sup>22</sup> \*\* Low CC = Male ( $\leq 34$  cm); Female ( $\leq 33$  cm)<sup>36</sup>. CC values were adjusted by patient's BMI, in order to help to remove the confounding effects of adiposity<sup>35</sup>

	OR <sup>a</sup>	95%CI	<i>p</i> value
Nutritional indicators			
Low BMI*	1.79	0.64 - 5.00	0.267
Low HGS <sup>**</sup>	1.53	0.77 – 3.02	0.218
Low CC***	1.71	0.88 – 3.31	0.111
Malnutrition <sup>b</sup>			
SGA (B and C)	3.60	1.83 – 7.09	<0.001
PG-SGA (B and C)	2.78	1.01 – 7.67	0.048

Table 5. Nutritional indicators and malnutrition associated with hospitalization (≥ 6 days) in patients with gastrointestinal and head and neck: Logistic regression model (n = 171).

BMI, Body Mass Index; CI, Confidence Interval; OR, Odds Ratio; SGA, Subjective Global Assessment; PG-SGA, Patient-Generated Subjective Global Assessment

Models adjusted by age, sex, presence of metastasis and chronic diseases.

Low BMI =  $< 18.5 \text{ kg/m}^2$ ) according to WHO<sup>27</sup>

<sup>\*\*</sup> Malnutrition: patients classified as moderately (B) and severely malnourished (C) were grouped. <sup>\*\*\*</sup> Low HGS = Male ( $\leq 27$  kg); Female ( $\leq 16$  kg)<sup>22</sup>; Low CC = Male ( $\leq 34$  cm); Female ( $\leq 33$  cm)<sup>36</sup>. CC values were adjusted by patient's BMI, in order to help to remove the confounding effects of adiposity<sup>35</sup>

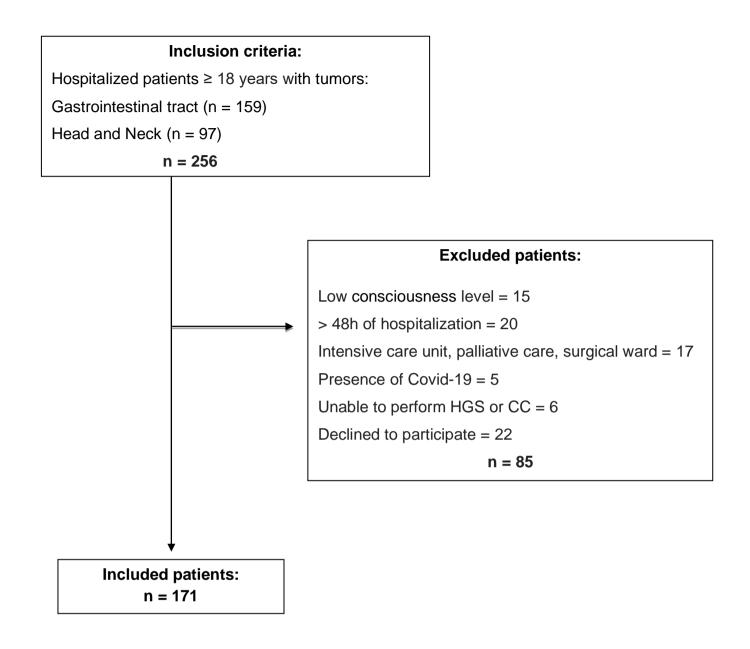
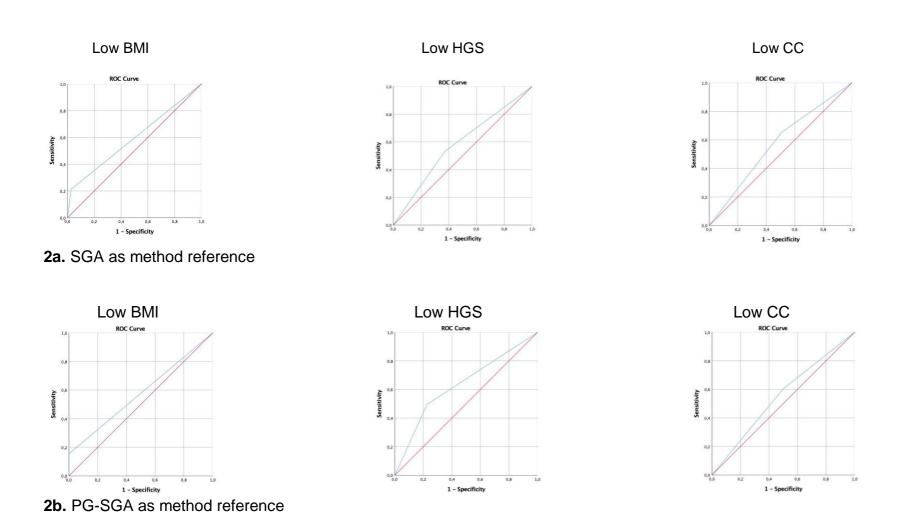


Figure 1. Flowchart of patient selection



**Figure 2.** Receiver operating characteristic (ROC) curves using nutritional indicators in diagnosing in patients with gastrointestinal and head and neck malnutrition (SGA and PG-SGA as the reference method). SGA = Subjective Global Assessment; PG-SGA = Patient-Generated Subjective Global Assessment; BMI = Body Mass Index; HGS = Hand Grip Strength; CC = Calf Circumference

Anexo 1 - Normas do periódico Journal of Human Nutrition and Dietetics

Author Guidelines

Aims and scope

Submission of manuscripts

Manuscript categories and requirements

Preparing a submission

Editorial processes and ethical considerations

Manuscript Referrals

Author licensing

Publication process post-acceptance

Article promotion

Contact details for submission enquiries

# 1. Aims and scope

*Journal of Human Nutrition and Dietetics* is an international peer-reviewed journal publishing papers in applied nutrition and dietetics. The scope of the journal recognises the multidisciplinary nature of nutrition and dietetic research and we will consider material from all facets employing a range of methodologies such as, public health, epidemiology, dietary assessment, dietary interventions, dietetic practice and nutritional biochemistry.

Papers are therefore welcomed on:

- Clinical nutrition and the practice of therapeutic dietetics
- Clinical and professional guidelines

- Public health nutrition and nutritional epidemiology
- Health promotion and intervention studies and their effectiveness
- Obesity, weight control and body composition
- Food intake, dietary patterns and nutritional status
- Lifecourse determinants of nutritional status, health and disease
- Malnutrition and food insecurity
- Determinants of healthy and unhealthy eating behaviour

The journal publishes the following types of article:

- Editorials (by invitation only)
- Reviews
  - Systematic reviews and meta-analyses
  - Scoping reviews
  - Narrative reviews (by invitation only)
- Original Research
  - Randomised controlled trials
  - Intervention studies
  - Cohort studies
  - Case-control studies
  - Cross-sectional studies
  - Basic science studies
  - Qualitative research studies
- Short reports
- Guidelines, endorsed by a learned society or professional body

# Please note that the journal does not publish animal research

# 2. Submission of manuscripts

New submissions should be made via the Research Exchange submission portal <u>https://wiley.atyponrex.com/journal/JHN</u>. Should your manuscript proceed to the revision stage, you will be directed to make your revisions via the same submission portal. You may check the status of your submission at any time by logging on to submission.wiley.com and clicking the "My Submissions" button. For technical help with the submission system, please review our <u>FAQs</u> or contact <u>submissionhelp@wiley.com</u>.

# 3. Manuscript categories and requirements

Papers submitted to the journal for consideration for publication should be written in English and be written in a clear and concise manner. If English is not the first language of the authors, the paper should be checked by an English speaker prior to submission. Ensuring that manuscripts are in a form suitable for submission is solely the responsibility of the author.

<u>Wiley Editing Services</u> offers expert help with English Language Editing, as well as translation, manuscript formatting, figure illustration, figure formatting, and graphical abstract design – so you can submit your manuscript with confidence.

Also, check out our resources for **<u>Preparing Your Article</u>** for general guidance about writing and preparing your manuscript.

Authors who are considering submission to the journal should look at a current issue of the Journal of Human Nutrition and Dietetics and note the typographical conventions, layout of tables and figures and referencing style. If you are a first-time author the **Frequently Asked Questions** section may also be useful. The journal editors blog also has a series of articles on **'How to write'** which you may find useful. Typescripts should be prepared with 1.5 line spacing and wide margins (2 cm), the preferred font being Times New Roman size 12, or similar. At the ends of lines words should not be hyphenated unless hyphens are to be printed. Authors should provide line numbers on the manuscripts, with continuous numbering throughout the

# document.

Authors should be aware of the journal's commitment to the use of person-first, nonstigmatising language as described in a **2022 editorial**. For example, use a term such as 'person living with obesity or overweight' rather than 'obese individual'; 'person living with disability' rather than 'disabled person', etc. Avoid stigmatising and combative language when discussing health conditions, for example do not use words such as 'lacking will power', 'morbid obesity' or 'tackling obesity', respectively. Authors will be asked to provide a declaration that they have done this when a manuscript has been submitted, and reviewers will be instructed to check for stigmatizing language.

Manuscripts can be uploaded either as a single document (containing the main text, tables and figures), or with figures and tables provided as separate files. Should your manuscript reach revision stage, figures and tables must be provided as separate files. The main manuscript file can be submitted in Microsoft Word (.doc or .docx) format.

Your main document file should include:

- A short informative title containing the major key words. The title should not contain abbreviations
- The full names of the authors with institutional affiliations where the work was conducted, with a footnote for the author's present address if different from where the work was conducted;
- Acknowledgments;
- Abstract
- Up to six keywords;
- Main body;
- References;
- Tables (each table complete with title and footnotes);
- Figures: Figure legends must be added beneath each individual image during upload AND as a complete list in the text.

# 4. Preparing a submission

# 4.1 Format of submissions

The journal does not impose word limits on articles, but the length of original articles, systematic reviews and guidelines should not be excessive. Typically a paper would be expected to include no more than 6 tables or figures and approximately 3000-5000 words. Qualitative studies would normally be longer in order to fully present supporting evidence. Short reports should follow the same format for full papers, and in general should only be used for robust research that is in its infancy and which shows important results. A short report would be expected to comprise no more than 2 figure or table inclusions with supporting text. **Authors are strongly encouraged to submit data that is not central to their paper as supplementary material.** If accepted, this material will be free to access online, regardless of the open access status of the published paper.

Submitted manuscripts should include the following sections.

4.1.1 *Title page*: The manuscript title should be focused and succinct whilst giving sufficient information to encourage potential readers to read the paper. Where possible the title should be one complete sentence. The title should avoid excessive description of the location of the research (e.g. the city, country etc) unless it is important to the understanding of the paper.

The title should be followed by authors' names. These should be given without titles or degrees and one forename may be given in full. The name and address of the institution where the work was performed should be given, with the main working address for each author. The title page should also include up to six keywords and details of the role each of the author(s) undertook in the study. 4.1.2 *Abstract*: All papers should have an opening abstract of no more than 250 words. The journal requires a structured abstract for original research articles, setting out the background to the study, methodology, results and principal conclusions.

4.1.3 *Introduction*: The introduction should be a brief (no more than 2 pages A4 double spaced) overview of the key literature that is relevant to the stated aims or hypothesis for the study.

*4.1.4 Methods*: The methods section of the paper should clearly state the methodological approaches followed by the authors. Generally the level of detail should be sufficient to allow others to replicate the study. Where possible make reference to validated methodology, providing extensive information only where new methods were applied.

It is expected that authors will report data as summaries rather than providing individual data points. Methods of statistical analysis that are used should be clearly described, and references to statistical analysis packages included in the text. A statement of the number of samples/observations, average (mean or median as appropriate) values and some measure of variability (standard deviation, standard error of the mean, range) is a minimum requirement for quantitative studies. Manuscripts utilizing complex statistical analyses may be referred to a statistical editor as part of the review process.

4.1.5 *Results*: these should be reported as concisely as possible, making appropriate use of relevant figures or tables.

To be consistent with journal policy on equality and diversity, studies which include measures from mixed populations of men and women, or individuals of different ethnicity should present data split accordingly into sub-groups. This can be presented either in the main paper, or as supplementary files to be published with the paper. When presenting demographic data about a study population it should be presented using a logical system, for example listing ethnicities in alphabetical order.

*4.1.6 Discussion*: the discussion of the results should be presented as a separate section. The discussion should normally be no longer than four pages (A4 double spaced).

4.1.7 *Acknowledgments*: should be provided a single paragraph after the discussion. Acknowledgements are required to indicate sources of funding, declaration of any conflicts of interest and a brief statement of any contributions from individuals not listed as full authors. The Journal of Human Nutrition and Dietetics requires that sources of institutional, private and corporate financial support for the work within the manuscript must be fully acknowledged, and any potential conflicts of interest noted.

4.1.8 *Biographies:* Each author should provide a brief biography of no more than 30 words. This should refer to the author's role in their workplace, their qualifications and their general research interests.

4.1.9 *References:* Number references consecutively in the order in which they first appear in the text using superscript Arabic numerals in parentheses, e.g. 'These findings are consistent with previously published data  $(^{1,2-4})$ '. If a reference is cited more than once the same number should be used each time. Any references that are cited only in tables and figures or their legends should be numbered in sequence from the last number used in the text and in the order of mention of the individual tables and figures in the text.

References should be listed in a separate section at the end of the paper, in numerical order using the Vancouver system. If an article has more than three authors only the names of the first three authors should be given followed by 'et al.' Do not include issue in the reference. Titles of journals should appear in their abbreviated form as listed

# at http://www.ncbi.nlm.nih.gov/projects/linkout/journals/jourlists.fcgi?typeid=1 &type=journals&operation=Show.

References to books and monographs should include the town of publication and the number of the edition to which reference is made. References to material available on websites should include the full Internet address, and the date of the version cited. Examples of correct forms of references are given below. Authors using Endnote or Reference Manager to generate reference lists may find it useful to use their template files for *British Journal of Nutrition*.

## Journal articles

1. Thomas A, Sowerbutts AM, Burden ST. The impact of living with home enteral feeding: perspectives of people who have had a diagnosis of head and neck cancer. *J Hum Nutr Diet,* 2019; **32**: 676–683

Chalashika P, Essex C, Mellor D, *et al.* Birthweight, HIV exposure and infant feeding as predictors of malnutrition in Botswanan infants. *J Hum Nutr Diet*, 2017; **30**: 779–790

- 3. Langley-Evans SC. How to Write. J Hum Nutr Diet, 2019; 32: 551-558.
- Levey R, Ball L, Chaboyer W, *et al.* Dietitians' perspectives of the barriers and enablers to delivering patient-centred care. *J Hum Nutr Diet*, 2020; **33**: 106– 114

## Books and monographs

5. Langley-Evans SC. *Nutrition Health and Disease: A Lifespan Approach*. Chichester, UK: Wiley Blackwell; 2021.

# Sources from the internet

6. Public Health England (2014) Public Health England Obesity Statistics. http://www.noo.org.uk (accessed October 2014).

4.1.10 *Figure legends*: Figure legends should be provided separately to illustrations and must include the Figure title, description of figure content, definition of any

abbreviations and, if necessary, statistical information.

#### 4.1.11 Visual Abstracts

When you are invited to submit a revised version of your paper, we will ask you to provide a visual summary of your manuscript. Visual abstracts will be published on the journal website but will not be an element of the final published paper. Visual abstracts are a way of promoting your research findings in search engines, appealing to a broader range of readers and research users (including the public) and are a strong vehicle for article promotion through social media (**Ibrahim et al., 2017**). A number of studies have shown that using visual abstracts and infographics to accompany a paper increases the number of views of abstracts and Altmetric scores (**Thomas et al., 2018**)

A good visual abstract should be a concise summary of the main findings of an article and for greatest effect should be visually striking. It should give readers an understanding of the study methodology and principal findings. <u>See here</u> for some template options that you can use to prepare your visual summary. You can also generate a visual summary in your own format if you prefer. <u>Wiley Editing</u> <u>Services</u> offers expert help with visual summary design if desired.

Technical requirements for Graphical Abstracts include the following:

- Font: a sans-serif font such as Arial or Calibri. Minimum 12–16 points.
- Size: The submitted image should be 5.5 inches square at 300 dpi
- Preferred file types: TIFF, PNG, JPG

## Other requirements

- The image **must not** be identical to a figure or image included in the text itself
- Avoid excessive details
- Use simple labelling and avoid excessive text
- Highlight 1-3 key points; avoid trying to show too much

## 4.2 Professional guidelines papers

Professional practice guidelines that have been developed using a robust review

process and which are endorsed by a learned body are welcomed. The nature of guidelines varies considerably and therefore detailed information regarding how to structure them is difficult to provide. We suggest that you consult previous guideline published in the journal, and in particular recommend:

McKenzie YA, Bowyer RK, Leach H, *et al.* British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update). *J Hum Nutr Diet* 2016; **29**: 549-575.

The title of guidelines should follow the style used in the example above including the name of the endorsing society/body.

## 4.3 Qualitative research

High quality qualitative research studies that address important topics in nutrition and dietetics are welcomed. Authors must consider the epistemological and methodological issues in their research, and make particular reference to the methodological approach and the specific methods adopted to increase the rigour of their data. We strongly recommend that authors make use of standard texts in this area including:

Moisey L, Campbell KA, Whitmore C. Jack SM. Advancing qualitative health research approaches in applied nutrition research. J Hum

## Diet https://doi.org/10.1111/jhn.12989

Jack SM, Orr E, Campbell K, Whitmore C, Crammer A. A Framework for Selecting Data Generation Strategies in Qualitative Health Research Studies. https://onlinelibrary.wiley.com/doi/abs/10.1111/jhn.13134

# 4.4 Audit and service evaluation

Studies described as audit and service evaluation will only be eligible for publication if they provide very novel data and use gold-standard, validated techniques for data collection. Full papers that indicate they are audit or service evaluation that are thought to include components of research data, but which have not been approved by a research ethics committee / institutional review board will be rejected. We discourage the submission of clinical audits and service evaluations that only have relevance to the departments in which they were performed.

#### 4.5 Units

All unit terms should normally be expressed as SI units. If other units are used a conversion factor should be included. In the case of expression of energy intake or expenditure, kilojoules or megajoules should normally be used but kilocalories may be inserted as well as kilojoules if the author sees this as appropriate.

#### 4.6 Illustrations

Figures should not be larger than A4 and should be in a form suitable for reproduction.

Tables should be typed on separate sheets, numbered and have a title.

## **4.7 Electronic Artwork**

We would like to receive your artwork in electronic form. Please save vector graphics (e.g. line artwork) in Encapsulated Postscript Format (EPS), and bitmap files (e.g. half-tones) in Tagged Image File Format (TIFF). Ideally, vector graphics that have been saved in metafile (.WMF) or pict (.PCT) format should be embedded within the body of the text file. For more detailed information on our digital illustration standards please see <u>http://authorservices.wiley.com/bauthor/illustration.asp</u>

## 5. Editorial processes and ethical considerations

This journal adheres to the Committee on Publication Ethics (COPE) guidelines on research and publications

ethics: http://publicationethics.org/resources/guidelines.

#### 5.1 Peer Review

Manuscripts will initially be evaluated by the Editorial Committee and an initial decision may be made without consultation with external reviewers. Papers which are sent for review will generally be considered by a minimum of two expert referees and the journal will aim to complete the review process within 6-8 weeks. The majority of manuscripts will not be accepted without authors making revisions in response to referee comments. If referees and editors require substantial revisions to a manuscript prior to acceptance, the authors will normally be given the opportunity to do this once only. Where revisions to manuscript are requested, these should normally be provided within 3 months. Beyond this period it may, on resubmission, be treated as a new paper and the date of receipt altered accordingly.

This journal is participating in a pilot on Peer Review Transparency. Authors choose if they prefer for their paper to undergo Transparent Peer Review. By reviewing for this journal, you agree that your finished comments to the author, along with the author's responses and the editor's decision letter, may be linked from the published article to where they appear on Publons, should the article be accepted. You have the choice to attach your name to the review if you wish. In case you have any concerns about participating in the Peer Review Transparency pilot, please reach out to the journal's editorial office at <u>akallaway@wiley.com</u>. Please indicate whether you would like your name to appear with your report on Publons by selecting 'yes' or 'no'.

### 5.2 Ethical approval

Human studies must have been approved by an ethics committee, but in questionable matters the Editor reserves the right to reject papers. Contributors are referred to the guidelines in the <u>World Medical Association (2000) Declaration of</u> <u>Helsinki: ethical considerations for medical research involving human</u> <u>subjects</u>.

#### 5.3 Transparent and accurate reporting of research studies

The Journal of Human Nutrition and Dietetics is committed to ensuring full and accurate reporting of research methods to ensure quality and integrity of the research we publish. The journal has a requirement for research manuscripts to conform to specific guidelines. Articles that do not fulfil this requirement will not be considered for publication. All submissions should include a section entitled '**Transparency Declaration**'. This section should state:

"The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported. The reporting of this work is compliant with CONSORT<sup>1/</sup>STROBE<sup>2/</sup>PRISMA<sup>3</sup> guidelines (delete as appropriate). The lead author affirms that no important aspects of the study have been omitted and that any discrepancies from the study as planned (please add in the details of any organisation that the trial or protocol has been registered with and the registration identifiers) have been explained.

#### <sup>1</sup>.Randomised controlled trials

We strongly welcome the submission of randomised controlled trials. Articles which are reporting the findings of randomised controlled trials involving human subjects must comply with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The guidelines can be accessed at <u>http://www.consort-</u> <u>statement.org</u> and authors should include a completed CONSORT checklist and flow diagram with their manuscript submission (the flowchart should be included as a figure within the paper, but the checklist will not be published) and include a statement about compliance with the guidelines within the Transparency Declaration section of the work. Manuscripts **must** include the term "randomised controlled trial" in their title.

Randomised controlled trials will not be considered for publication unless registered in a public trials registry. A clinical trial is defined by the ICMJE (in accordance with the definition of the World Health Organisation) as any research project that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Registration information must be provided at the time of submission, including the trial registry name, registration identification number, and the URL for the registry. Such registries include ICMJE-approved public trials registries

(<u>http://www.clinicaltrials.gov</u>, <u>http://www.anzctr.org.au/,http://www.isrctn.org</u>, <u>http://www.umin.ac.jp</u>, <u>http://www.trialregister.nl</u>). When submitting a manuscript please report the study ID number and the website where the clinical trial is registered in the manuscript, section Transparency Declaration. Registration claims will be audited as part of the editorial process. Authors may apply for an exemption from this requirement, but such exemptions will only be granted in exceptional circumstances and the justification will be reported in the journal..

#### <sup>2</sup>Observational Studies

Articles which report the findings of observational epidemiological studies (crosssectional, case-control, cohort studies) must comply with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. The guidelines can be accessed at <u>http://www.strobe-statement.org</u> and authors should include a completed STROBE checklist with their manuscript submission (this will not be published as part of the paper) and include a statement about compliance with the guidelines within the Transparency Declaration section of the work. For nutritional epidemiology studies we recommend the use of the specialised STROBEnut checklist, accessible at <u>https://www.equator-network.org/reporting-</u> <u>guidelines/strobe-nut/</u> and published in Plos Med 2016;13(6):e1002036. PMID: <u>27270749</u> Manuscripts should include the study design (e.g. a case-control study) within their title.

#### <sup>3</sup>Systematic reviews and meta-analyses

The journal publishes systematic review articles and meta-analyses and endorses the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement, a guideline to help authors report a systematic review and meta-analysis. Systematic review or meta-analysis should follow the PRISMA guidelines

(<u>http://prisma-statement.org</u>). Every systematic review/meta-analysis should be submitted along with a copy of the PRISMA checklist, that clearly indicates where in the manuscript each of the PRISMA recommendations are addressed. The PRISMA checklist can be downloaded from <u>http://www.prisma-</u>

statement.org/statement.htm . When submitting a systematic review/meta-analysis, the PRISMA checklist can be uploaded included in the covering letter to the editor. Please note, the checklist is a guide for the authors and peer-reviewers, but will not be published. Manuscripts should include the term "systematic review" or "meta-analysis" in their title. From January 1st 2018, the journal requires all systematic reviews to be registered with **PROSPERO**. Details of the registration, including registration identification number, should be provided in the Transparency Declaration. Registration claims will be audited as part of the editorial process.

## <sup>4</sup>Registration of investigations

*JHND* strongly encourages authors to register all clinical trials and observational studies in a public trials registry relevant to national organisations. Such registries include ICMJE-approved public trials registries

(<u>http://www.clinicaltrials.gov</u>, <u>http://www.anzctr.org.au/</u>, <u>http://www.isrctn.org</u>, <u>h</u> <u>ttp://www.umin.ac.jp</u>, <u>http://www.trialregister.nl</u>). When submitting a manuscript please report the study ID number and the website where the clinical trial is registered in the manuscript, section Transparency Declaration.

## 5.4 Conflicts of Interest

It is required that the authors of a paper should bring to the attention of the Editor, any conflicts of interest. This should be done at the point where the paper is first submitted. Conflicts of interest would include any existing financial arrangements between an author and an organisation that has provided funding for the research reported in the submitted manuscript, or between an author and a company whose products are mentioned prominently in the manuscript. All authors must declare any sources of funding for the research reported in their manuscript and report all potential conflicts of interest in a separate section in the manuscript. If an author has no conflicts of interest the statement "no conflicts of interest" should be included in the manuscript.

For authors, conflicts of interest might include:

1. Having a close relative or a professional associate with financial interest in the outcome of the research

2. Serving as an officer, director, member, owner, trustee, or employee of an organization with a financial interest in the outcome of the research

 Receiving financial support, including grants, contracts or subcontracts, with a company or organization having a financial interest in the research outcome
 Being employed, serving on an advisory board or owning shares in a company or organization that may have a financial interest in the outcome of the research

Individuals who are asked to review a manuscript should decline the invitation if they have a conflict of interest. Editors should also decline involvement in the processing of a manuscript if a conflict of interest is possible. Areas of concern would include the following, in addition to the conflicts of interests that pertain to authors:

- Receiving research grants, contracts or subcontracts, or consulting interests directly with one of the authors or their known collaborators
   Collaborating or publishing as a co-author with the author(s) of the manuscript during the past 3 years
   Serving as an advisor to the author(s) on the preparation of the manuscript;
  - 4. Being employed/prospective employment at the same institution as any of the authors of the manuscript within the last 12 months

Editors or Editorial Board members are never involved in editorial decisions about their own work. Journal editors, Editorial Board members and other editorial staff (including peer reviewers) withdraw from discussions about submissions where any circumstances might prevent them from offering unbiased editorial decisions.

## 5.5 Authorship

Full details of the roles of ALL authors must be included on the Title page of the manuscript. The name and address of the corresponding author to whom correspondence should be sent should be clearly stated, together with telephone and fax numbers and email address.

ALL named authors must have made an active contribution to the conception and design and/or analysis and interpretation of the data and/or the drafting of the paper and ALL must have critically reviewed its content and have approved the final version submitted for publication. Participation solely in the acquisition of funding or the collection of data does not justify authorship and, except in the case of complex large-scale or multi-centre research, the number of authors should not normally exceed 6 and **we would expect the maximum number of authors to be 25**.

Correction to authorship: In accordance with Wiley's <u>Best Practice Guidelines on</u> <u>Research Integrity and Publishing Ethics</u> and the <u>Committee on Publication</u> <u>Ethics</u>' guidance, *Journal of Human Nutrition and Dietetics* will allow authors to correct authorship on a submitted, accepted, or published article if a valid reason exists to do so. All authors – including those to be added or removed – must agree to any proposed change. To request a change to the author list, please complete the <u>Request for Changes to a Journal Article Author List Form</u> and contact either the journal's editorial or production office, depending on the status of the article. Authorship changes will not be considered without a fully completed Author Change form. Correcting the authorship is different from changing an author's name; the relevant policy for that can be found in <u>Wiley's Best Practice Guidelines</u> under "Author name changes after publication."

## 5.6 Plagiarism and falsification

The Journal will scrutinise all papers for evidence of plagiarism and falsified data using specialised software. Plagiarism can comprise the following:

- multiple submission (i.e. to several journals at the same time)
- redundant publication (i.e. when the same data are published repeatedly, especially when articles contain an unacceptable degree of overlap but some original data, or in the case of the first time data are published (followed by subsequent redundant publications);
- self-plagiarism
- reviewer misconduct (e.g. a reviewer making use of material obtained during review)
- changes to authorship after publication due to discovery of guest or ghost authors;
- deliberate omission of funding or competing interest information.

## 5.7 Serious Research Misconduct

Very rarely, the Editor may have cause to suspect serious research misconduct, based on comments received or editorial board review of a paper. In this case, the article in question will be held in abeyance until this matter is resolved. The Editor will contact authors and any appropriate third party to ascertain whether the grounds for investigation are justified. If serious research misconduct is discovered, the Editor will contact the authors' institutions after rejecting the paper.

Despite vigorous peer-review processes used by the journal, it is possible that a paper that is fraudulent in some manner may be published. If this is discovered, it will immediately be retracted and appropriate steps will be taken to notify readers of the journal, and the authors' institution. Retractions will include the word 'Retraction' in the title, so that they are identified as such on indexing systems, for example, PubMed.

In any case of serious research misconduct, all authors of such an article may be banned from future publication in *the Journal of Human Nutrition and Dietetics*.

# 6. Manuscript Referrals

This journal works together with Wiley's open access journals, <u>Food Science &</u> <u>Nutrition</u> and <u>Legume Science</u> to enable rapid publication of good quality research that is unable to be accepted for publication by our journal. Authors may be offered the option of having the paper, along with any related peer reviews, automatically transferred for consideration by the Editors of the alternative journals. Authors will not need to reformat or rewrite their manuscript at this stage, and publication decisions will be made a short time after the transfer takes place.

The Editors of *Food Science & Nutrition* and *Legume Science* will accept submissions that report well-conducted research which reaches the standard acceptable for publication. Both journals are Wiley Open Access Journal and article publication fees apply. For more information, please go

to *https://onlinelibrary.wiley.com/journal/20487177* or *https://onlinelibrary.wiley* .com/journal/26396181.

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If a paper is accepted for publication, the author identified as the formal corresponding author will receive an email prompting them to log in to Author Services, where via the Wiley Author Licensing Service (WALS) they are required to complete a copyright license agreement on behalf of all authors of the paper.

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**Self-Archiving definitions and policies.** Note that the journal's standard copyright agreement allows for self-archiving of different versions of the article under specific conditions. Please click <u>here</u> for more detailed information about self-archiving definitions and policies.

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Open access is available to authors of primary research articles who wish to make their article available to non-subscribers on publication, or whose funding agency requires grantees to archive the final version of their article. With open access, the author, the author's funding agency, or the author's institution pays an Article Publication Charge (APC) to ensure that the article is made available to nonsubscribers upon publication via Wiley Online Library, as well as deposited in the funding agency's preferred archive. For more information about Article Publication Charges, please visit the **Open Access page**.

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If the open access option is not selected the corresponding author will be presented with the copyright transfer agreement (CTA) to sign. The terms and conditions of the CTA can be previewed in the samples associated with the Copyright FAQs below:

# CTA Terms and Conditions <u>http://authorservices.wiley.com/bauthor/faqs\_copyright.asp</u>

# 7.3 For authors choosing Open Access

If the open access option is selected the corresponding author will have a choice of the following Creative Commons License Open Access Agreements (OAA):

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