GITMO
GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

Convegno Educazionale GITMO

LE TERAPIE CELLULARI IN EMATOLOGIA
TRA PASSATO, PRESENTE E FUTURO

Brescia, 28-29 novembre 2025

Centro Paolo VI

La nutrizione nel paziente trapiantato: un'arma per ridurre infezioni e GVHD?

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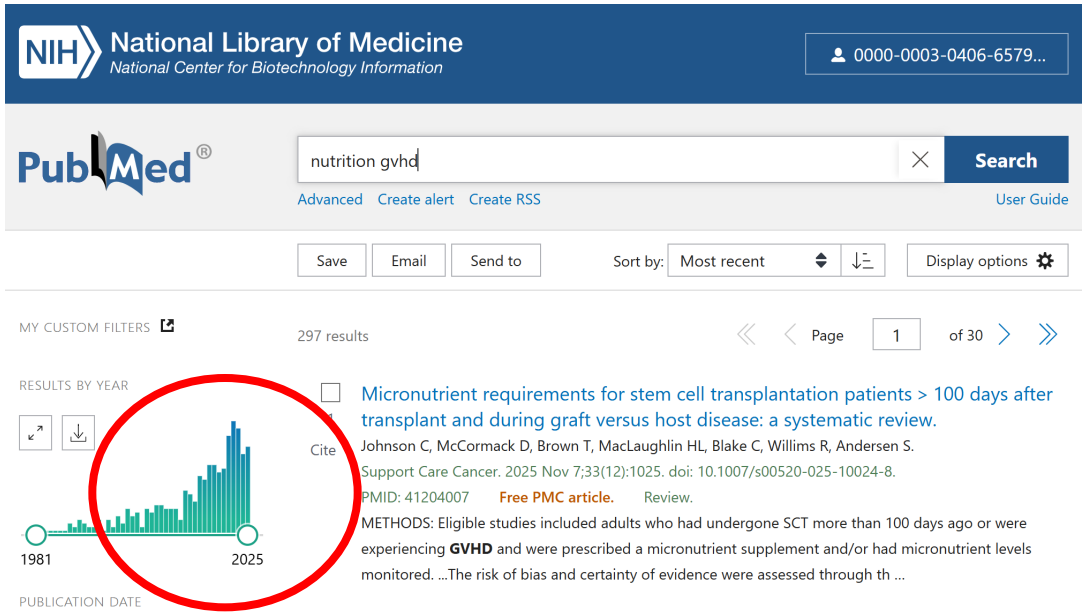
SSD Trapianto Midollo Osseo Adulti

Disclosures of Enrico Morello

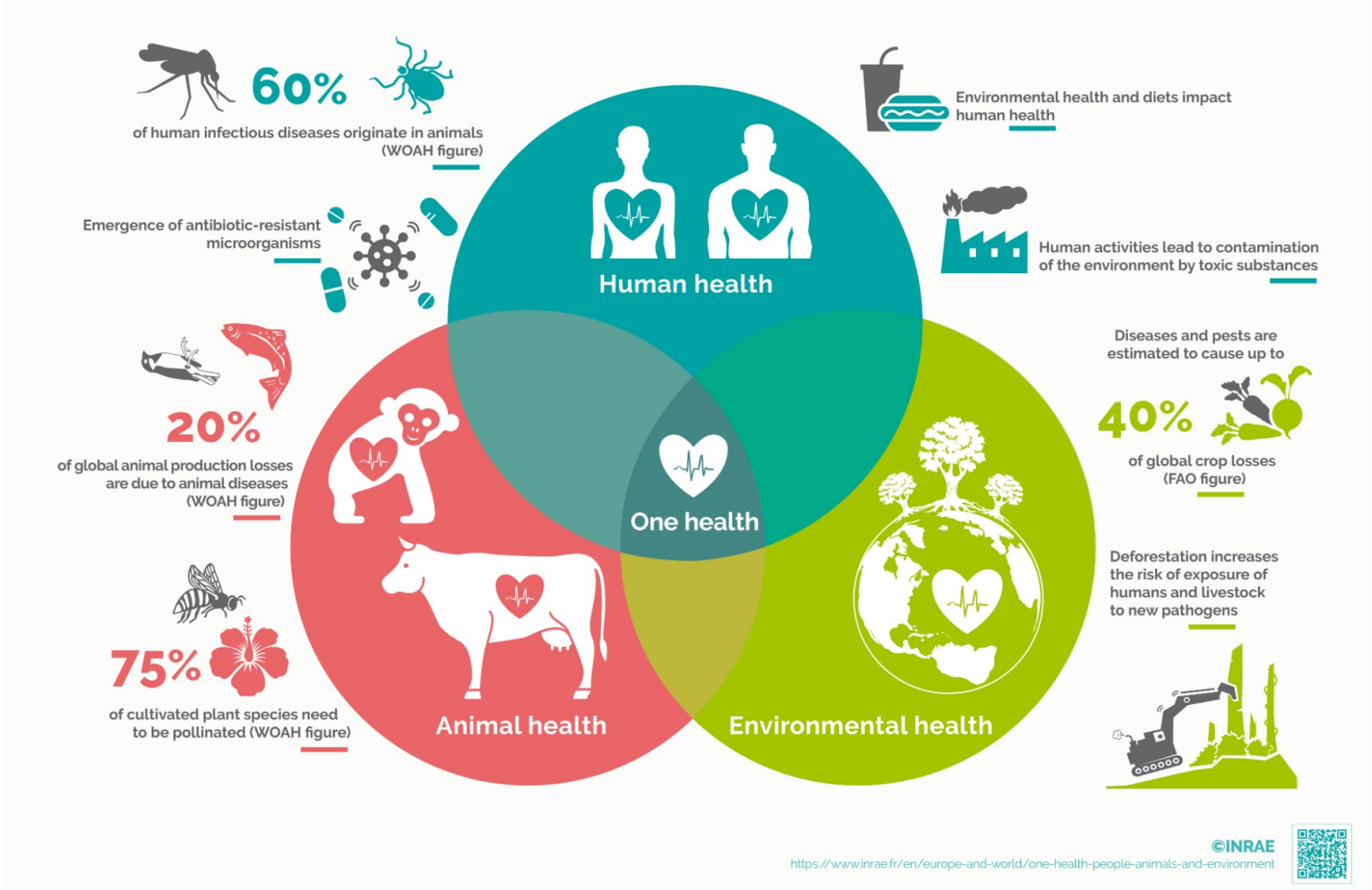
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Sanofi							(3000 Eur) EBMT2025 Travel grant
Nestlè	80000 Eur @ASST SCB (study support)						

Outline

- One-Health
- Eubiosi e Disbiosi
- Diete e impatto sulla salute
- Malnutrizione Disbiosi e Trapianto
- Come valutare la malnutrizione
- Disbiosi al trapianto
- Impatto sulle infezioni
- Impatto sulla GVHD
- Lattosio ed enterococchi
- Il ruolo del TGF-beta
- Proposte per il futuro



One-Health


60%
of human infectious diseases originate in animals (WOAH figure)
Emergence of antibiotic-resistant microorganisms
20%
of global animal production losses are due to animal diseases (WOAH figure)
75%
of cultivated plant species need to be pollinated (WOAH figure)
Human health
One health
Animal health
Environmental health
Environmental health and diets impact human health
Human activities lead to contamination of the environment by toxic substances
Diseases and pests are estimated to cause up to
40%
of global crop losses (FAO figure)
Deforestation increases the risk of exposure of humans and livestock to new pathogens
©INRAE
https://www.inrae.fr/en/europe-and-world/one-health-people-animals-and-environment

Eubiosi e Disbiosi = Salute e Malattia

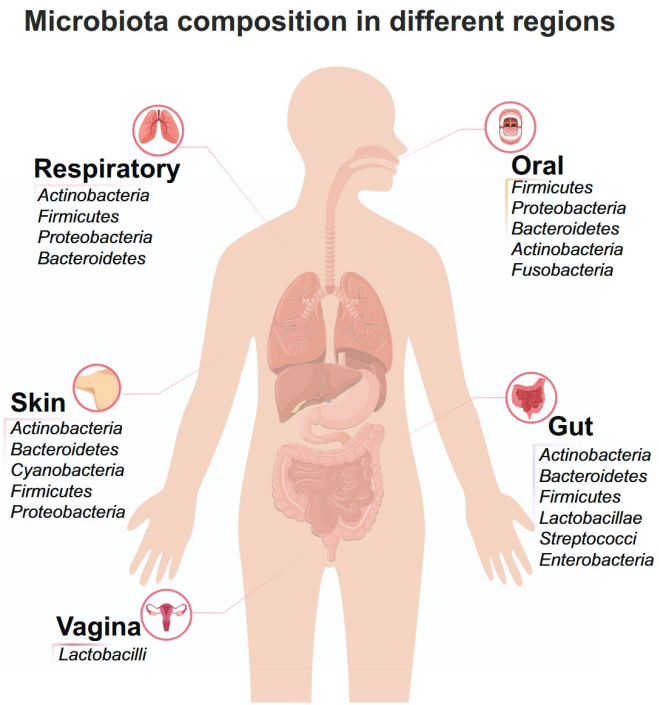


Fig. 1 Human microbiota composition in different locations. Predominant bacterial genera in the oral cavity, respiratory tract, skin, gut, and vagina are highlighted

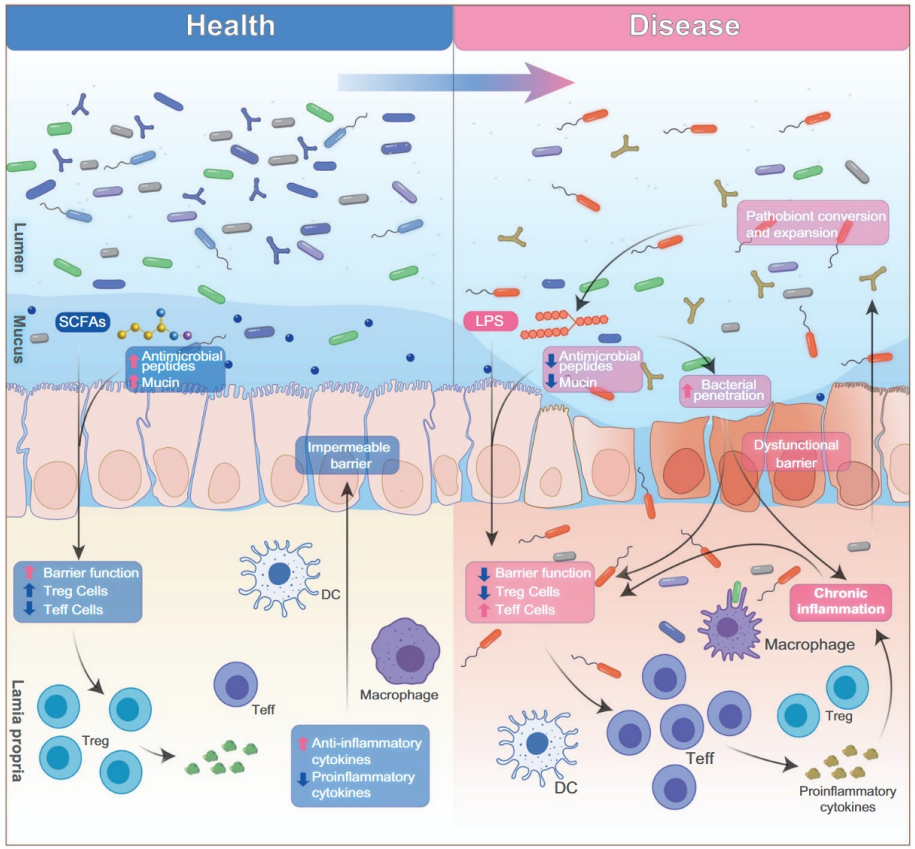


Fig. 3 Factors affecting microbiota-associated chronic inflammation in healthy and disease state

Dieta e microbiota: l'effetto delle scelte alimentari sulla nostra salute

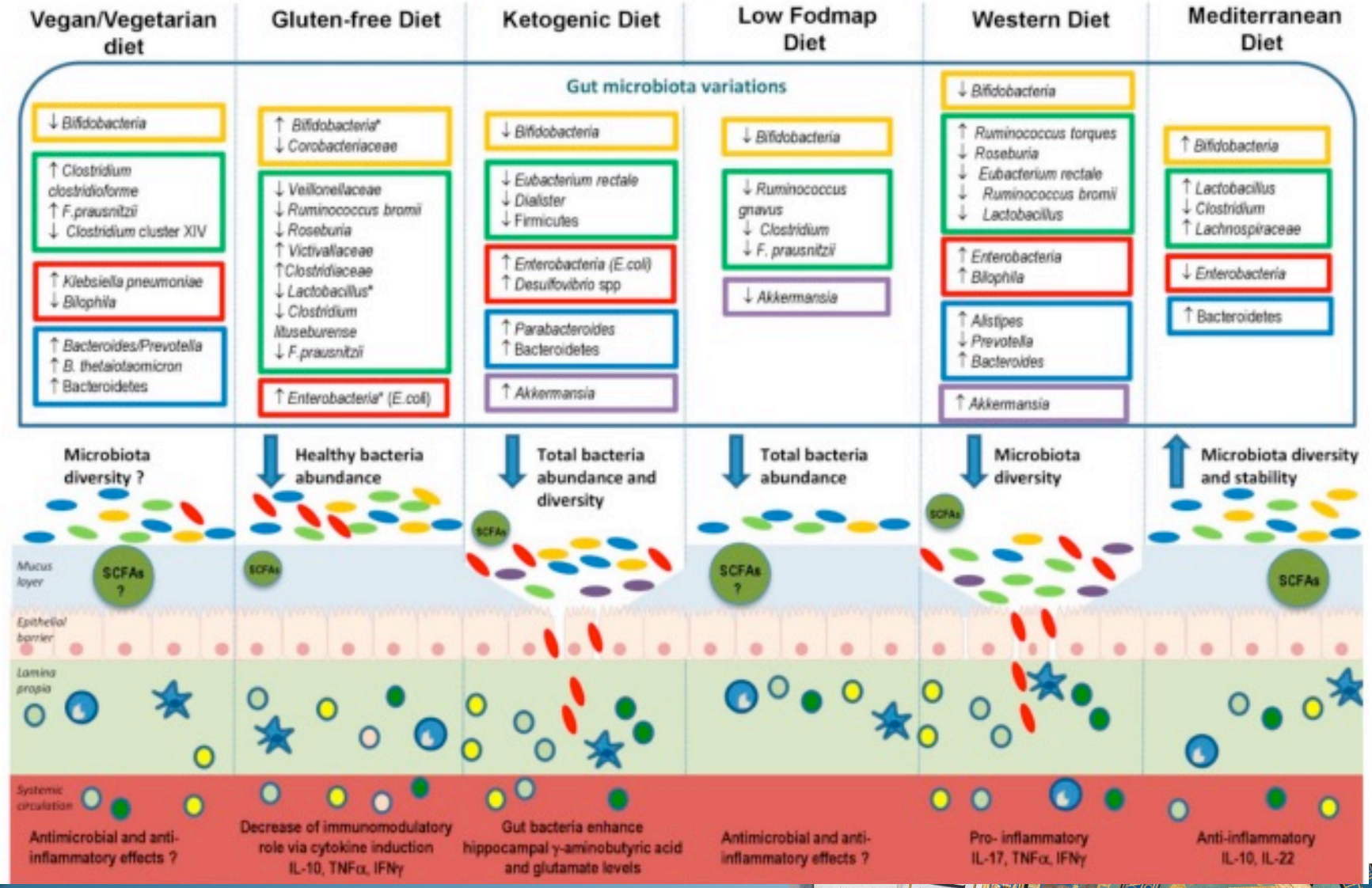
Microbiota

strato mucoso

epitelio

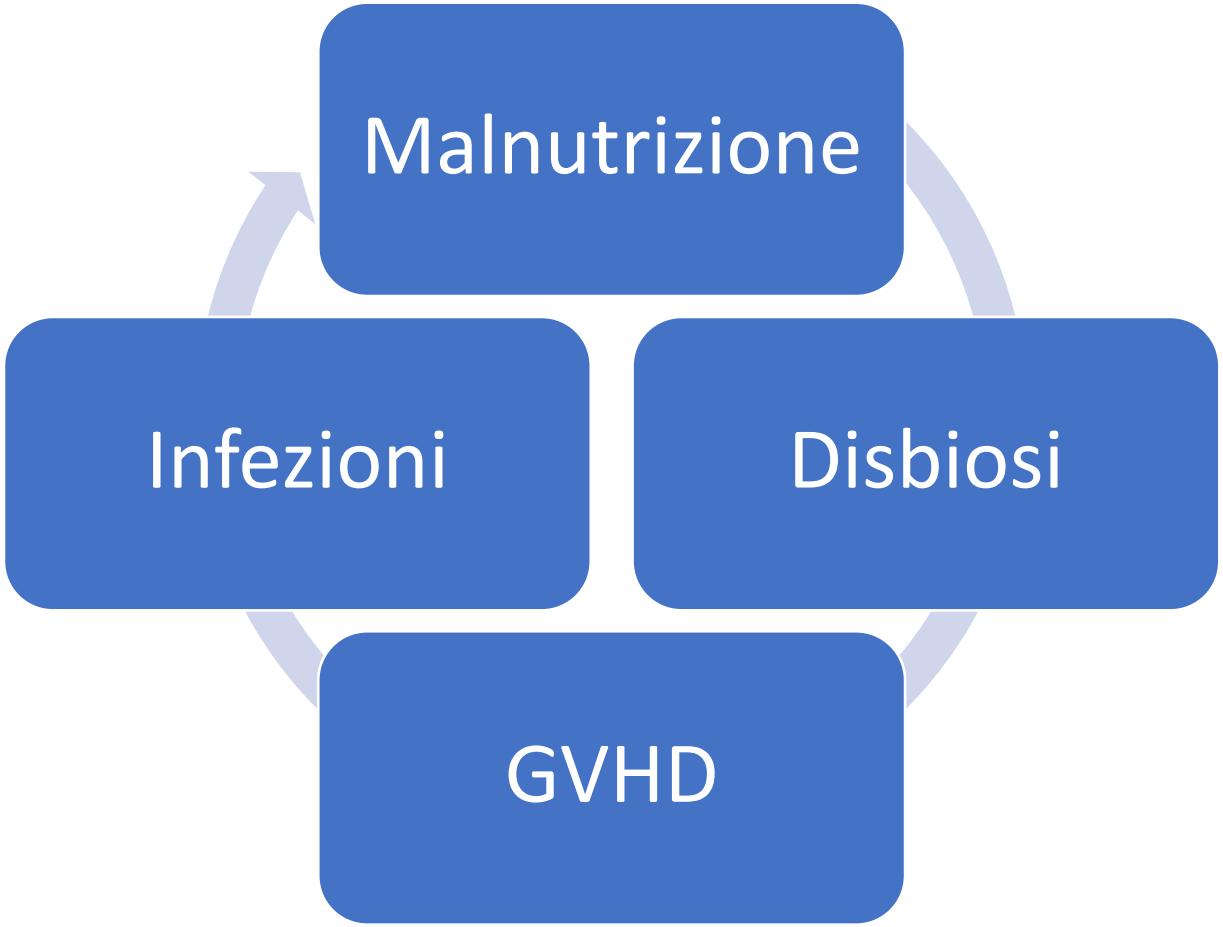
lamina propria

vasi



Renata Alleva, Terra Madre 2022

Un circolo, vizioso o virtuoso?



Malnutrizione, come valutarla (GLIM)

Screening → Assessment e Diagnosi nutrizionale

GLIM CRITERIA

Phenotypic criteria:

- **Unintentional weight loss** by time frame
- **Low body mass index (BMI; kg/m²)** according to age and ethnicity
- **Reduced muscle mass** based on valid body composition assessment methods
  - Examples: physical exam, dual-energy absorptiometry, bioelectrical impedance analysis, ultrasound, computed tomography, magnetic resonance imaging, mid upper arm circumference, or calf circumference

Etiologic criteria:

- **Reduced food intake or assimilation** based on quantitative or qualitative report
  - Examples: 3-day food record, food frequency questionnaire, or patient self-report
  - Considerations:
    - Gastrointestinal symptoms that impact food intake or absorption (e.g., dysphagia, nausea, vomiting, diarrhea, constipation, abdominal pain, etc.)
    - Presence of malabsorptive disorders (e.g., intestinal failure, pancreatic insufficiency, post-operative bariatric surgery, etc.)
    - Other relevant clinical situations affecting food intake (e.g., esophageal strictures, gastroparesis, intestinal pseudo-obstruction, etc.)
- **Inflammation and Disease Burden** from acute or chronic injury or disease
  - Acute: major infection, burns, trauma, or closed head injury
  - Chronic: malignant disease, chronic obstructive pulmonary disease, congestive heart failure, or chronic kidney disease
  - Supportive laboratory tests: C-reactive protein, albumin, or pre-albumin

HOW TO USE THE GLIM FRAMEWORK

	Phenotypic criteria	Check if present
Unintentional Weight loss (%)	> 5% within past 6 months	
	> 10% beyond 6 months	
BMI (kg/m²)	< 20 if < 70 years (Asia: < 18.5)	
	< 22 if ≥ 70 years (Asia: < 20)	
Muscle mass	Reduced	
	Etiologic criteria	**Check if present**
Reduced food intake	Ingestion ≤ 50% of needs from 1 to 2 weeks	
	Any reduction for > 2 weeks	
or	Any chronic GI condition that adversely impacts food assimilation or absorption	
Assimilation		
Disease burden/ Inflammation	Presence of acute disease/injury or chronic disease related	

Malnutrition: if at least one criterion was checked in each section

Determine Malnutrition Severity

Severity Grade	Phenotypic Criteria		
	Unintentional Weight Loss (%)	Low BMI (kg/m²) [a]	Reduced Muscle Mass
Stage 1: Moderate Malnutrition Patient requires 1 phenotypic criterion that meets this grade.	• 5-10% in 6 months; or • 10-20% in more than 6 months	• <20 if <70 years; or • <22 if ≥70 years	• Mild-to-moderate deficit (per validated assessment methods on previous page)
Stage 2: Severe Malnutrition Patient requires 1 phenotypic criterion that meets this grade.	• >10% in 6 months; or • >20% in more than 6 months	• 18.5 if <70 years; or • <20 if ≥70 years	• Severe deficit (per validated assessment methods on previous page)

Definitions and Footnotes:
ER= energy requirement; GI= gastrointestinal
[a] Further research is needed for consensus on reference body mass index data for Asian populations in clinical settings.

References:
Jensen, G.L., et al. (2018). *Journal of Parenteral and Enteral Nutrition*, 43(1), 32-40.
Keller, H.H., et al. (2020). *Journal of Parenteral and Enteral Nutrition*, 44(6), 992-1003.

Global Leadership Initiative on Malnutrition (GLIM)

Malnutrizione – PG-SGA, come si fa?

Valutazione soggettiva globale riportata dal paziente tramite punteggio
Scored Patient-Generated Subjective Global assessment (PG-SGA)

Anamnesi: Le sezioni da 1 a 4 sono strutturate per essere completate dal paziente. [Le sezioni da 1 a 4 vengono definite "PG-SGA Short Form (SF)"]

Storia del peso (a un mese e a sei mesi dal trapianto)

L'apporto di cibo

I sintomi (nausea, mucosite, disgeusia, vomito, diarrea….)

L'attività fisica

Le comorbilità

La presenza e l'entità di episodi febbrili (catabolismo)

La somministrazione di corticosteroidi (catabolismo)

L'esame obiettivo (stato muscolare, depositi di grasso e idratazione)

https://pt-global.org/pt-global/

Malnutrizione – PG-SGA

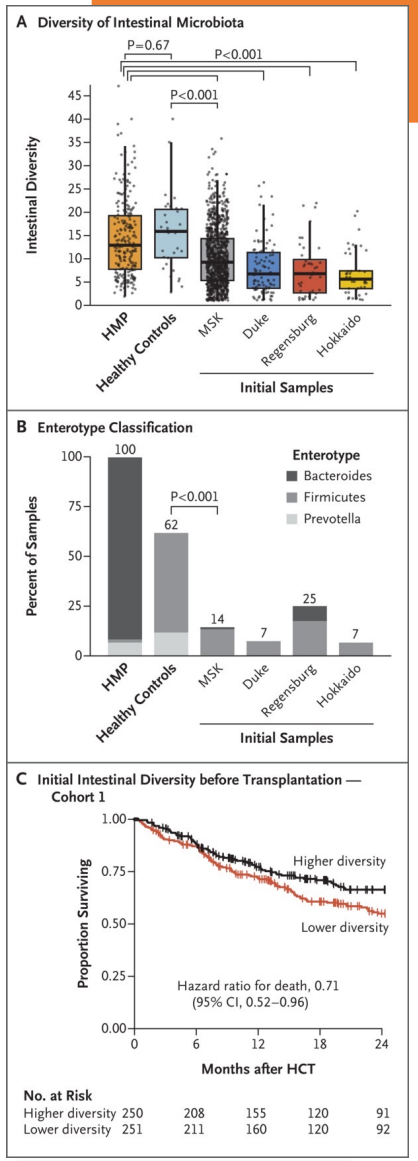
Strumento raccomandato soprattutto in oncologia per rilevare e classificare la malnutrizione.

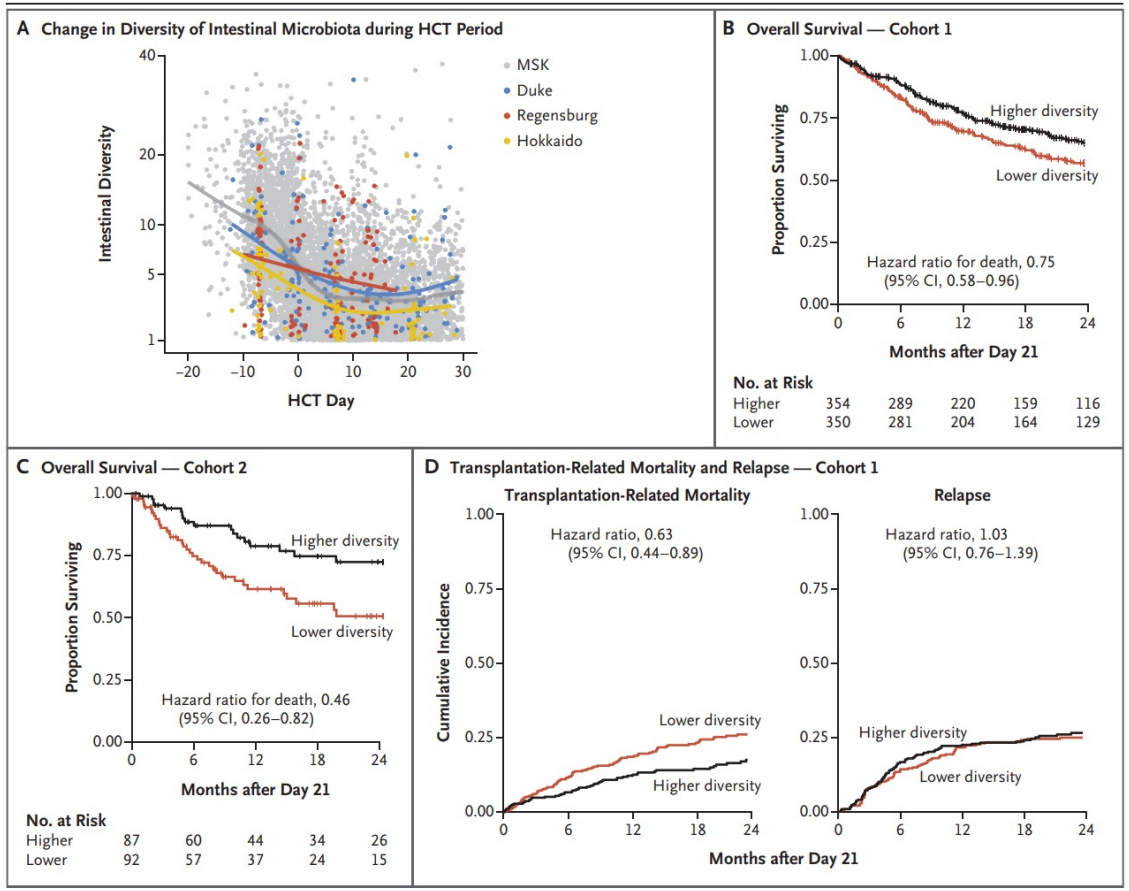
Include dati riferiti dal paziente (PRO) e valutazione clinica; risultato categorizzato in:

A: buono stato nutrizionale	B: moderata malnutrizione	C: grave malnutrizione.

Aiuta a identificare rapidamente i bisogni di intervento nutrizionale personalizzato.

Stato del microbiota pre-trapianto





The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Microbiota as Predictor of Mortality in Allogeneic Hematopoietic-Cell Transplantation

J.U. Peled, A.L.C. Gomes, S.M. Devlin, E.R. Littmann, Y. Taur, A.D. Sung, D. Weber,

Low Diversity = dysbiosis

LD @conditioning (Cohort1)

- Reduced OS

LD @engraftment

- Reduced OS
- Increased TRM
- = Relapse

Peled JU et al. N Engl J Med2020;382:822-834

Nutrizione e infezioni, quali evidenze?

EBMT www.nature.com/bmt

CORRESPONDENCE OPEN Check for updates

"The antibiotic paradox" in allogeneic stem cell transplantation

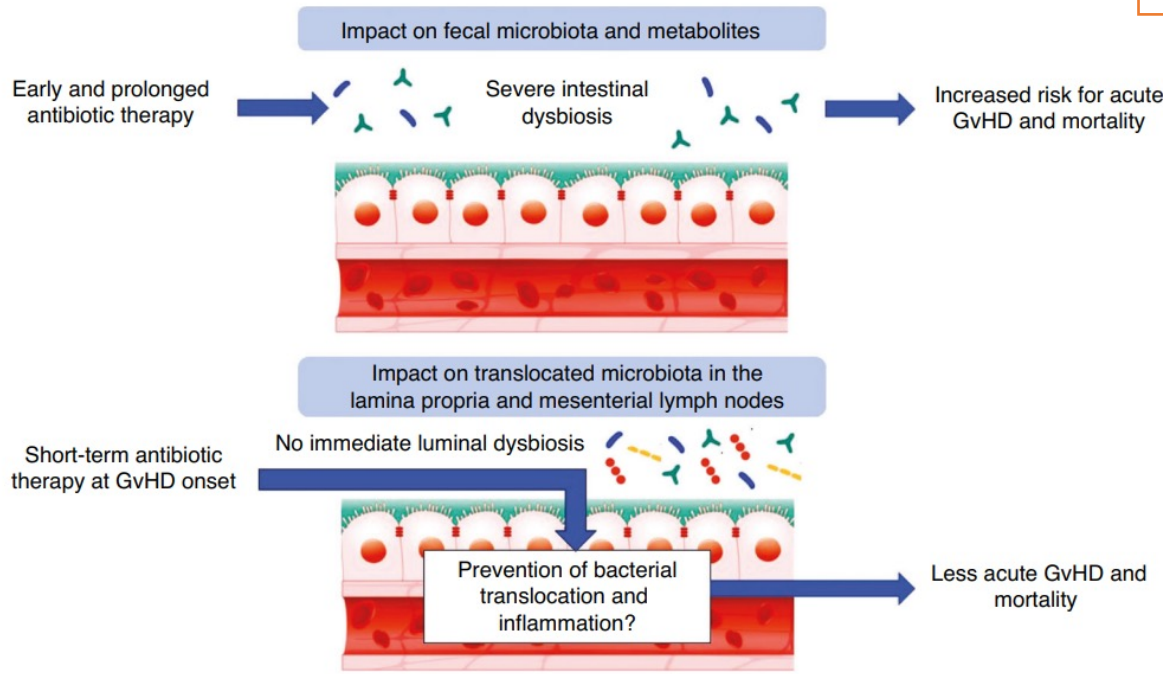


Fig. 1 The antibiotic paradox explained by differential microbial targets: Early and prolonged antibiotic therapy affects luminal microbiota composition resulting in severe intestinal dysbiosis and an increased risk for acute GI GvHD and associated mortality (evidence by Weber et al. [15] and Peled et al. [5]). Antibiotic administration at GvHD onset suppresses bacterial translocation as important co-stimulator of T cell activation and may dampen GvHD (evidence by van Bekkum et al. [10], Schwab et al. [11]).

- Storia microbiologica del paziente
- Storia antibiotica del paziente
- Antibiosi e Disbiosi
- GVHD onset

Bone Marrow Transplantation (2025) 60:1541–1543; https://doi.org/10.1038/s41409-025-02706-y

Nutrizione: diete restrittive e non

REGULAR ARTICLE

blood advances

Nonrestrictive diet does not increase infections during post-HSCT neutropenia: data from a multicenter randomized trial

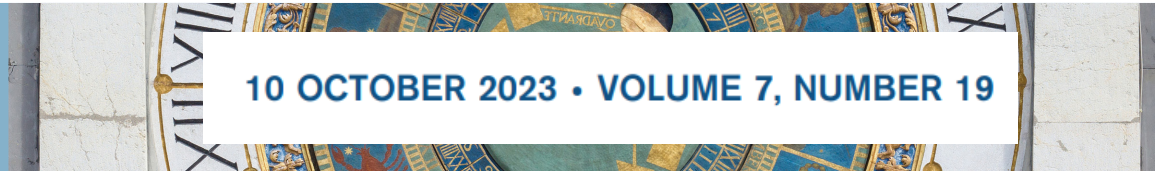
Federico Stella,[1,*] Vincenzo Marasco,[2,*] Giorgia Virginia Levati,[2] Anna Guidetti,[1,2] Annamaria De Filippo,[2] Martina Pennisi,[2] Cecilia Vismara,[1] Rosalba Miceli,[3] Silva Ljevar,[3] Cristina Tecchio,[4] Nicola Mordini,[5] Giorgia Gobbi,[2] Lucia Saracino,[2] and Paolo Corradini[1,2]

[1]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; [2]Division of Hematology and Bone Marrow Transplant and [3]Biostatistics for Clinical Research Unit, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale dei Tumori, Milan, Italy; [4]Department of Medicine, Section of Hematology and Bone Marrow Transplant Unit, University of Verona, Verona, Italy; and [5]Division of Hematology, Azienda Ospedaliera S. Croce e Carle, Cuneo, Italy

Table 1. Diet details

	PD	NRD
Fish and meat	Only well cooked	Only well-cooked
Vegetables	Only cooked above 80°C	Fresh vegetables allowed*
Fruit	Cooked or thick peel fruit washed and peeled	Fresh fruit allowed*
Milk	Only pasteurized	Only pasteurized
Cheese	Only pasteurized	Pasteurized and seasoned cheese without mold
Yogurt	No	Only pasteurized
Eggs	Only freeze-dried	Only cooked
Bread	Allowed	Allowed
Dessert and ice cream	Only industrial preparation	Only industrial preparation
Honey	No	Only pasteurized
Cold cuts and sausages	No	Yes single portioned

*Manipulated according to safe food handling procedures.



10 OCTOBER 2023 • VOLUME 7, NUMBER 19

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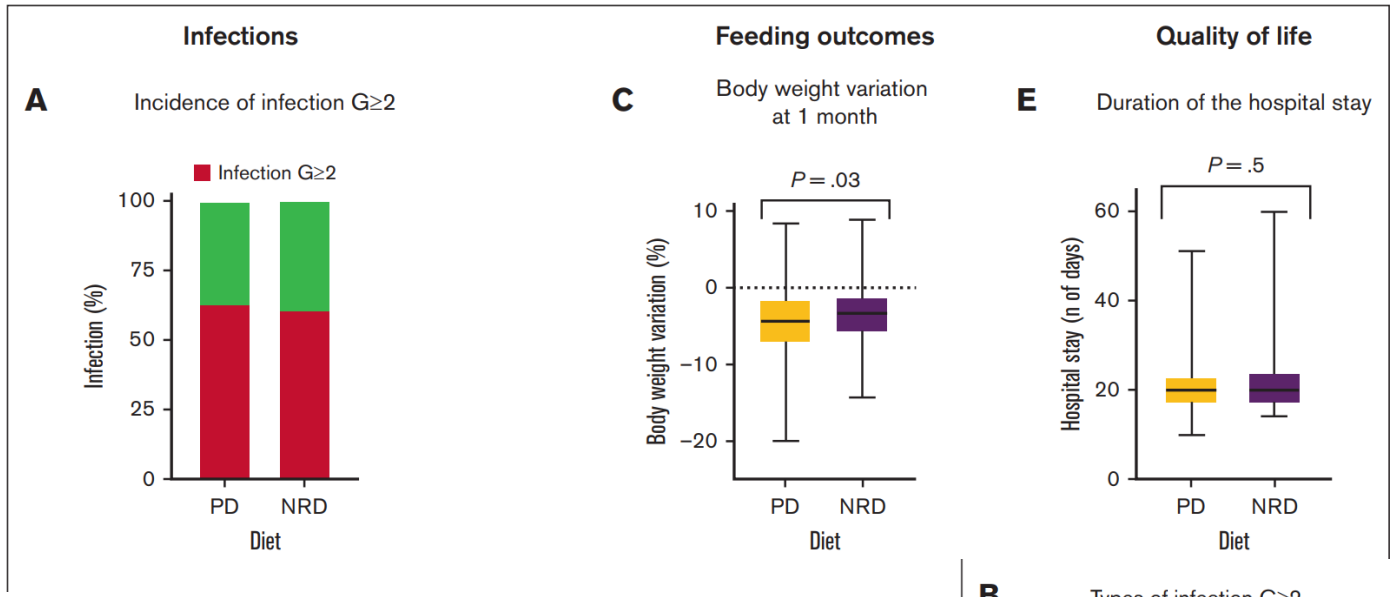
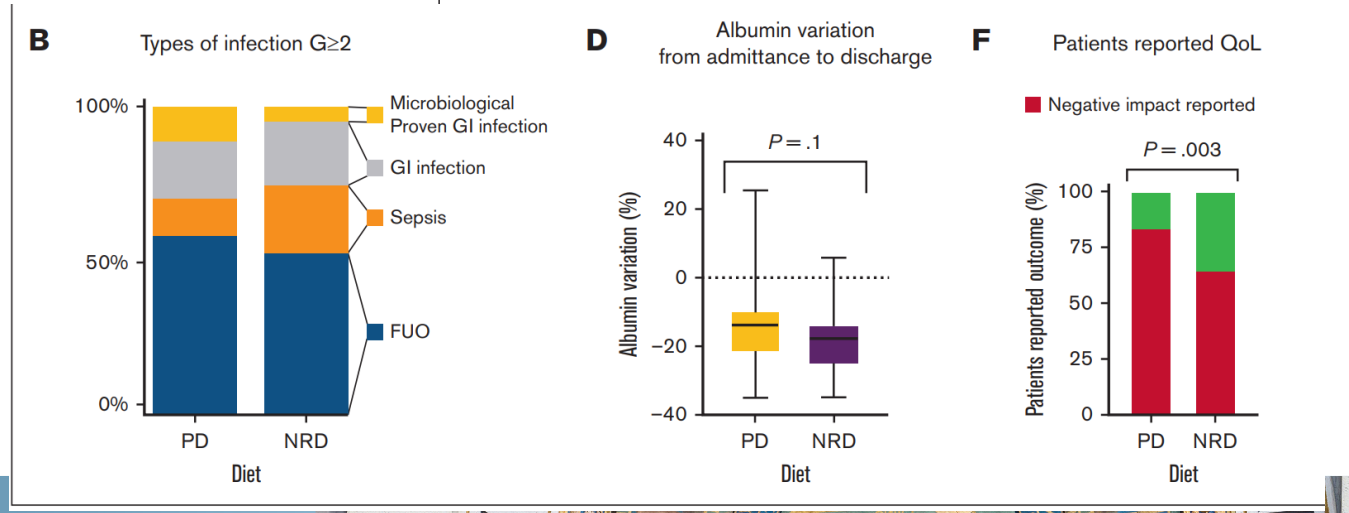




N=224
Allo HSCT: N=41 (20 PD, 21 NRD)
GVHD (>2): 20% vs 9.5% (NS)

Nutrizione e GVHD acuta, quali evidenze?

Non esistono studi randomizzati pubblicati che promuovano un intervento nutrizionale per ridurre l'incidenza di aGVHD come endpoint principale

Esistono metanalisi riguardo al tipo di nutrizione e incidenza di aGVHD?

- SI!

Se possibile usate la via enterale! → ↓ aGVHD

Transplantation and Cellular Therapy

journal homepage: www.tctjournal.org

ASTCT American Society for Transplantation and Cellular Therapy

Supportive Care

Enteral versus Parenteral Nutrition as Nutritional Support after Allogeneic Hematopoietic Stem Cell Transplantation: a Systematic Review and Meta-Analysis

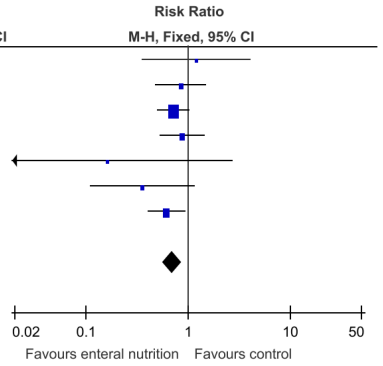
Daniele Zama[1], Davide Gori[2], Edoardo Muratore[1,*], Davide Leardini[1], Flavia Rallo[2], Silvia Turroni[3], Arcangelo Prete[1], Patrizia Brigidi[4], Andrea Pession[1], Riccardo Masetti[1]

[1] Pediatric Oncology and Hematology Unit "Lalla Seràgnoli", Department of Pediatrics, University of Bologna, Sant'Orsola Malpighi Hospital, Bologna, Italy
[2] Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy
[3] Unit of Microbial Ecology of Health, Department of Pharmacy and Biotechnology, University of Bologna, Bologna, Italy
[4] Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

A: aGvHD

Study or Subgroup	Enteral Nutrition Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Andersen 2015	3	5	2	4	2.0%	1.20 [0.36, 4.04]
Andersen 2020	10	20	13	22	10.9%	0.85 [0.48, 1.48]
Gonzales 2018	33	97	46	97	40.5%	0.72 [0.51, 1.02]
Guieze 2015	14	28	16	28	14.1%	0.88 [0.54, 1.43]
Hopman 2003	0	12	5	22	3.5%	0.16 [0.01, 2.68]
Papadopoulou 1998	3	20	8	19	7.2%	0.36 [0.11, 1.15]
Seguy 2012	34	94	16	27	21.9%	0.61 [0.40, 0.92]
Total (95% CI)		**276**		**219**	**100.0%**	**0.69 [0.56, 0.86]**
Total events	97		106			

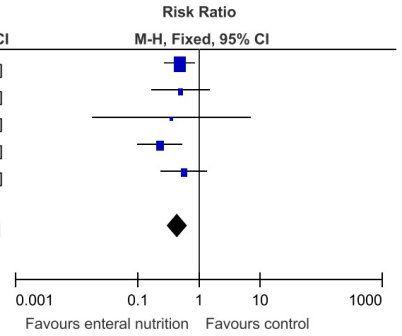
Heterogeneity: Chi² = 4.82, df = 6 (P = 0.57); I² = 0%
Test for overall effect: Z = 3.37 (P = 0.0007)



B: aGvHD III-IV

Study or Subgroup	Enteral Nutrition Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Gonzales 2018	15	97	31	97	44.9%	0.48 [0.28, 0.84]
Guieze 2015	4	28	8	28	11.6%	0.50 [0.17, 1.47]
Hopman 2003	0	12	2	22	2.6%	0.35 [0.02, 6.82]
Seguy 2012	8	94	10	27	22.5%	0.23 [0.10, 0.52]
Skaarud 2018	7	57	13	60	18.4%	0.57 [0.24, 1.32]
Total (95% CI)		**288**		**234**	**100.0%**	**0.44 [0.30, 0.64]**
Total events	34		64			

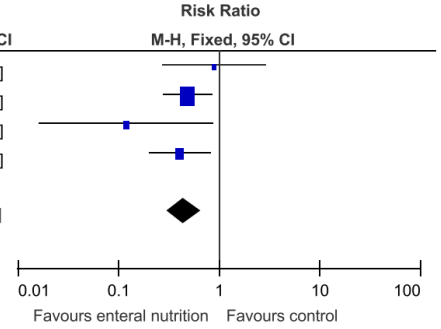
Heterogeneity: Chi² = 2.92, df = 4 (P = 0.57); I² = 0%
Test for overall effect: Z = 4.32 (P < 0.0001)



C: gut aGvHD

Study or Subgroup	Enteral Nutrition Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Andersen 2020	4	20	5	22	8.0%	0.88 [0.27, 2.83]
Gonzales 2018	15	97	31	97	52.1%	0.48 [0.28, 0.84]
Papadopoulou 1998	1	20	8	19	13.8%	0.12 [0.02, 0.86]
Seguy 2012	14	94	10	27	26.1%	0.40 [0.20, 0.80]
Total (95% CI)		**231**		**165**	**100.0%**	**0.44 [0.30, 0.66]**
Total events	34		54			

Heterogeneity: Chi² = 3.20, df = 3 (P = 0.36); I² = 6%
Test for overall effect: Z = 4.04 (P < 0.0001)



Nutrizione, lattosio, microbiota e GVHD acuta

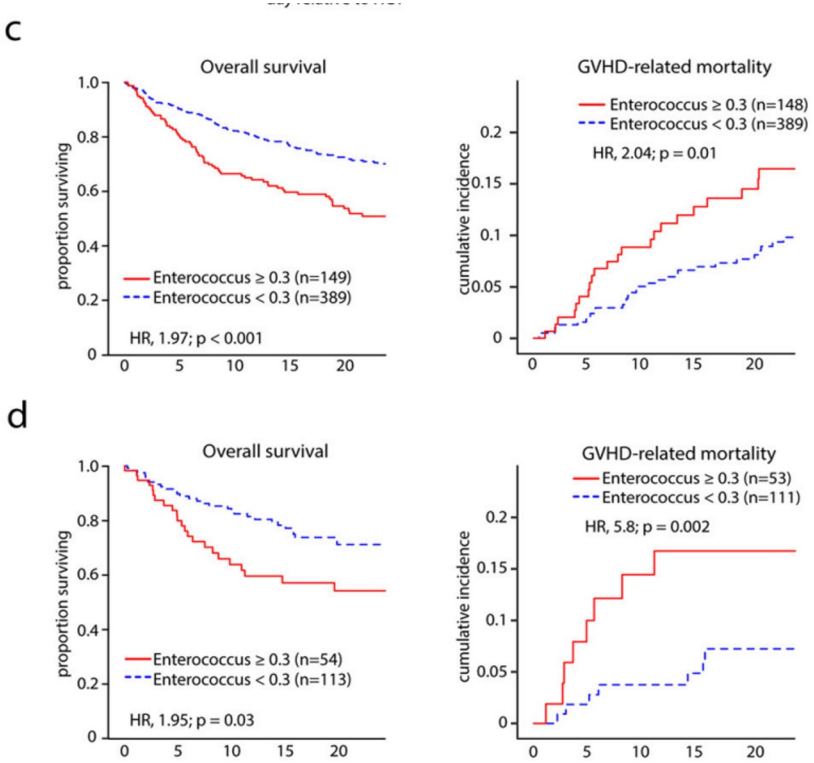
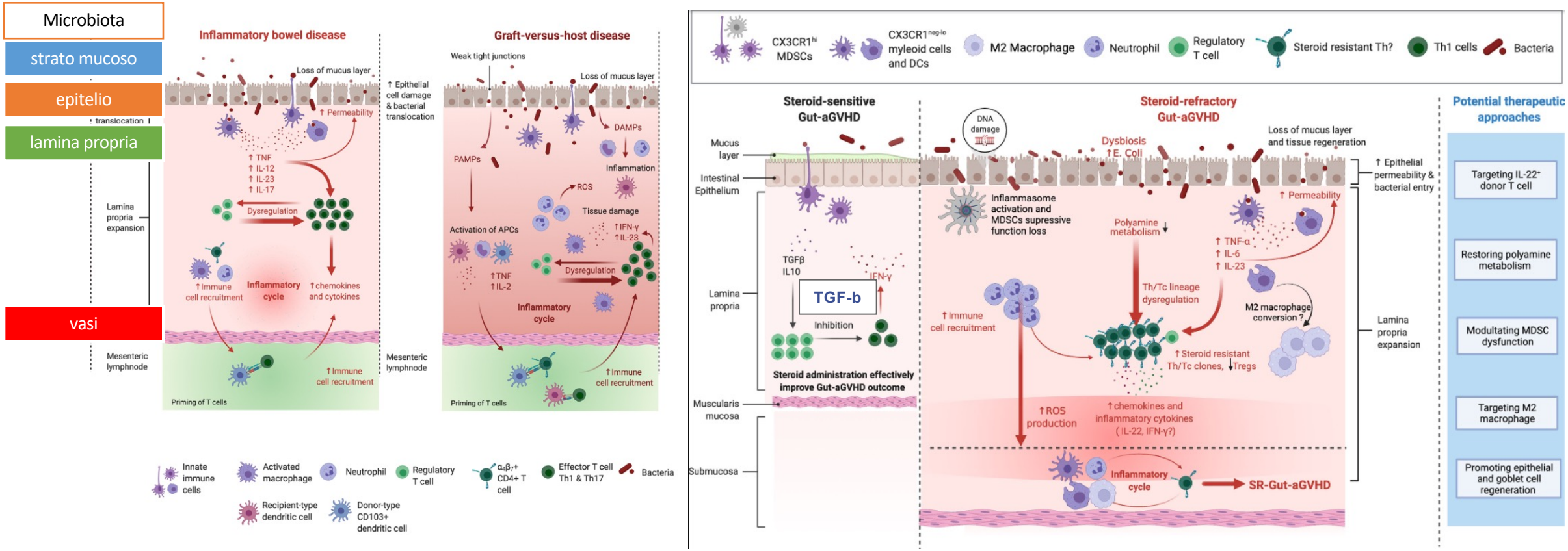


Fig. 1. *Enterococcus* domination occurs globally and increases risk of GVHD and mortality after allo-HCT.

IBD e GVHD, TGF-beta e disbiosi



Song et al., Frontiers in Immunology 2022

TGF-beta FSMP nel trapianto allogenico

- N=192
- TGF-FSMP (Food for Special Medical Purposes), proposto a tutti i pazienti sottoposti ad allo-HSCT
- Dose sufficiente per definire un effetto biologico: ≥50% della dose prescritta (Gruppo A, N112), vs 80 (Gruppo B <50%)
- Intervento nutrizionale: dose riportata in tabella 1
- Aggiustamento della dose 2 volte in settimana

Table 1
Calories recommended by TGF-β2 FSMP according to TDEE, BMI and PG-SGA.

	PG-SGA A	PG-SGA B	PG-SGA C	Calories by TGF-β2 FSMP of TDEE
If BMI <20	40 kcal/kg	42 Kcal/Kg	44 kcal/kg	20 %
If BMI 20–24.9	35 kcal/kg	39 kcal/kg	42 kcal/kg	15 %
If BMI 25–29.9	30 kcal/kg	33 kcal/kg	36 kcal/kg	12 %
If BMI >30	25 kcal/kg	28 kcal/kg	30 kcal/kg	10 %
		TDEE		

Clinical Nutrition ESPEN 69 (2025) 54–62

TGF-beta FSMP nel trapianto allogenico

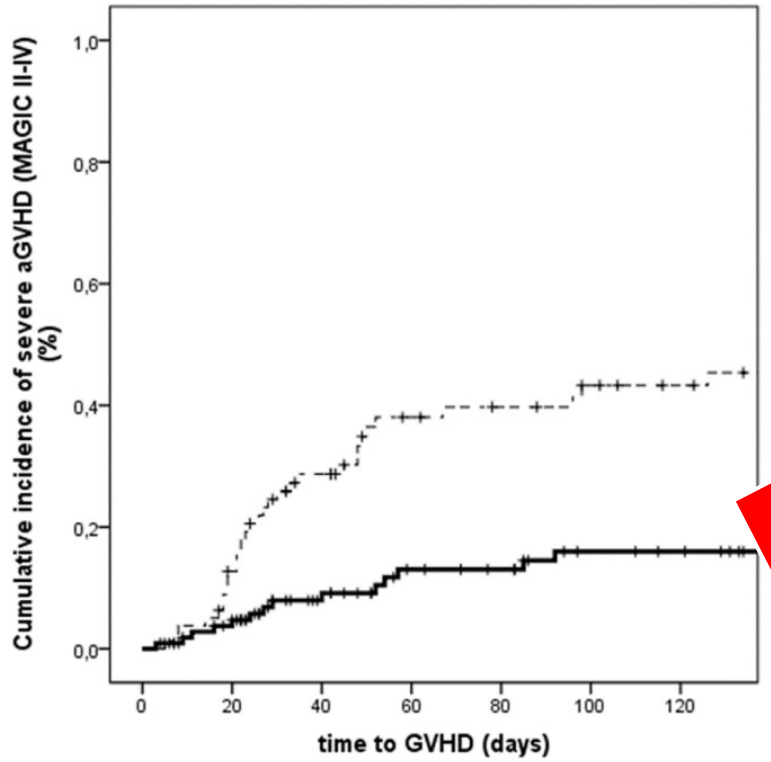


Fig. 2. CI of severe acute GVHD (MAGIC II-IV) according to TGF-β2 FSMP treatment group: Group A continuous line, Group B dotted line.

Table 3
Comparison of mean values of lymphocyte subpopulations based on TGF-β2 FSMP Group.

Lymphocyte subpopulations	Group A (mean values)	Group B (mean values)	p-value
Lymphocytes at +28 days (cells/μL)	460.4 ± 44.4	333.8 ± 43.8	0.001
T-Helper Lymphocytes CD3+CD4+ at +28 (cells/μL)	100.4 ± 15.1	63.1 ± 11.1	0.020
NK Lymphocytes CD56+ at +28 (cells/μL)	155.3 ± 16.3	116.7 ± 23.6	0.012
NK Lymphocytes CD16+ at +28 (cells/μL)	130.1 ± 15.6	76.9 ± 17.1	0.002

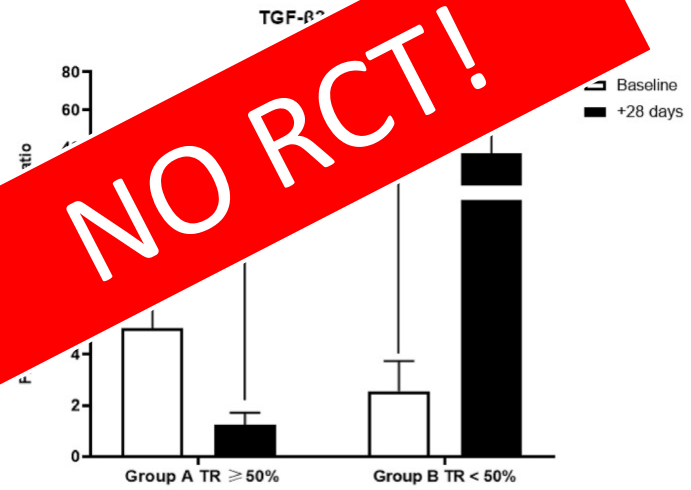


Fig. 4. Firmicutes/Bacteroidetes ratio according to TGF-β2 FSMP Treatment Ratio at baseline and after transplantation. * p-value = 0.011, Wilcoxon matched-pairs signed rank test. Data are shown as mean ± SEM.

NO RCT!

Gruppo A

- Ridotto rischio di grave malnutrizione (PG-SGA C)
- Ridotto rischio di TPN
- Ridotto rischio di aGVHD (II-IV)
- Ridotto rischio di GI aGVHD
- Ridotto rischio di polmoniti
- OS e NRM migliori
- Ridotta durata della degenza

Clinical Nutrition ESPEN 69 (2025) 54–62

TGF-Nutriallo Study

5.4.1 Inclusion Criteria

- Intact intestinal tract
- Life expectancy more than 12 weeks
- Allogeneic stem cell transplantation
- Signed informed consent

5.4.2 Exclusion Criteria

- Active hematological disease at the beginning of conditioning
- Personal history of inflammatory bowel diseases
- Personal history of bowel resection
- Personal history of gastric bypass procedures
- Enrolment in a competitive prospective study (malnutrition or GVHD as primary outcome)
- Subjects with known hypersensitivity to milk proteins or components of experimental FSMP

4.1 Study Plan

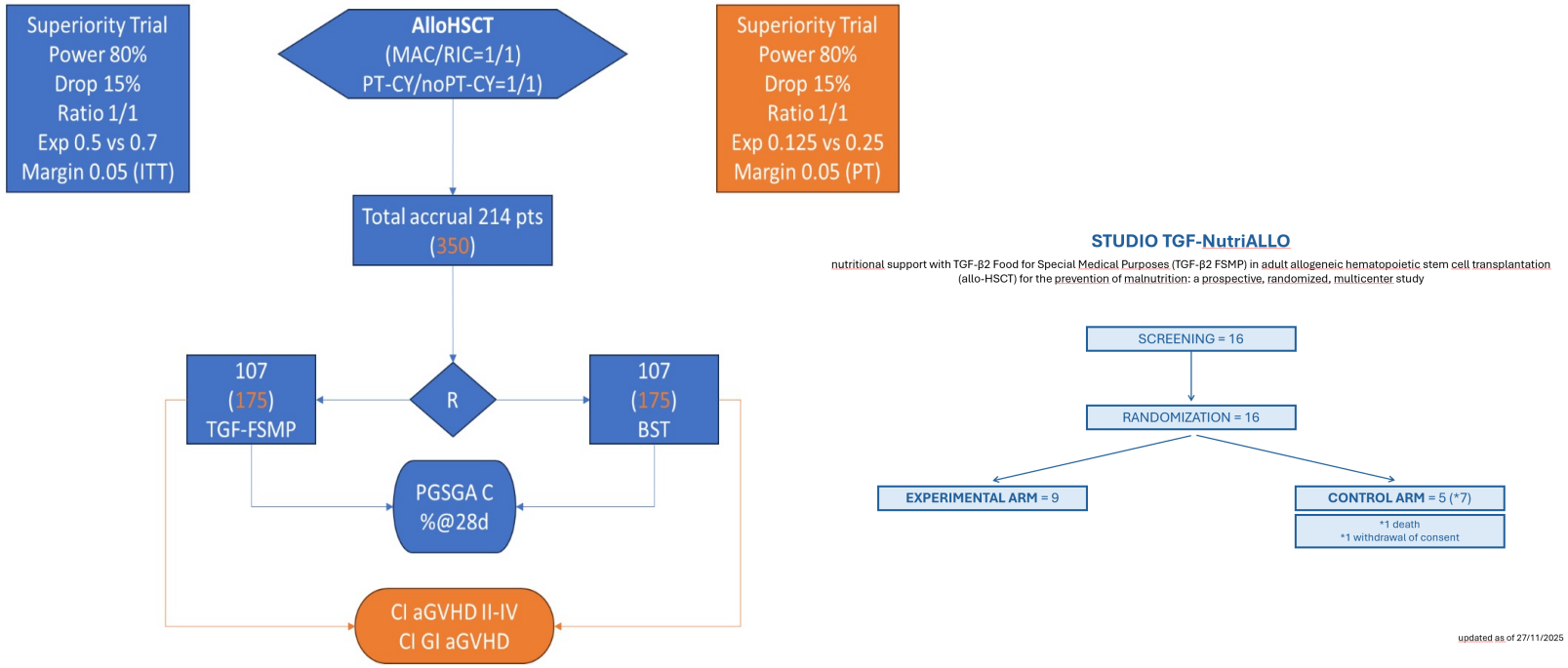


Figure 1 - Study plan: 214 patients will be enrolled and randomized 1:1 to receive TGF-β2 Food for Special Medical Purposes (FSMP) or the best supportive therapy (BST) from day -7 to day +28 post allo-SCT. The primary endpoint is the reduction from 70% to 50% of the malnutrition defined as PG-SGA C at +28. In the second phase, 68 more patients will be enrolled in each arm to assess the aGVHD cumulative incidence reduction from 25 to 12.5% at 100 days.

Nutrizione, microbiota e GVHD cronica

REVIEW · Volume 26, Issue 11, E265-E270, November 2020 · *Open Archive*

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Challenging and Practical Aspects of Nutrition in Chronic Graft-versus-Host Disease

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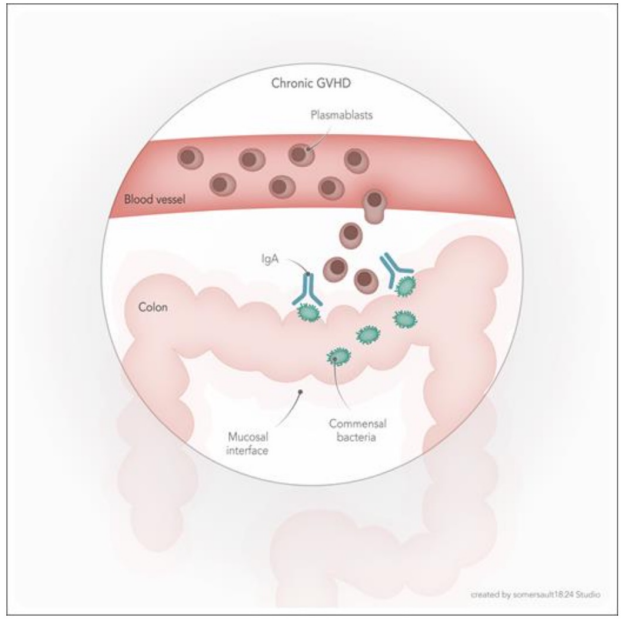
Highlights

- There are few studies on nutrition and chronic graft-versus host disease (GVHD).
- Many drugs used to treat chronic GVHD can lead to nutritional problems and metabolic syndrome.
- Monitoring and early nutritional measures of metabolic syndrome, osteoporosis, and loss of muscle mass could improve outcome and response to treatment in these patients.
- Zinc, vitamin A, vitamin D, omega 3, and probiotics could contribute to symptom reduction and nutritional improvement.

Intervento nutrizionale in GVHD cronica (Sindrome Metabolica)

Disbiosi e risposta IgA mediata



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Model for gut microbiota mediation of chronic GVHD. Early posttransplant IgA antibody response to commensal bacteria in the colon leads to clonal expansion of plasmablasts, associated with a higher risk for future cGVHD. The precise mechanism by which the process of bacterial recognition (and possibly immune-mediated clearance), IgA production, and clonal plasmablast expansion may lead to cGVHD is unknown.

TRANSPLANTATION | JUNE 26, 2025

Microbiota and chronic GVHD: a plasmablast link

Armin Rashidi

Check for updates

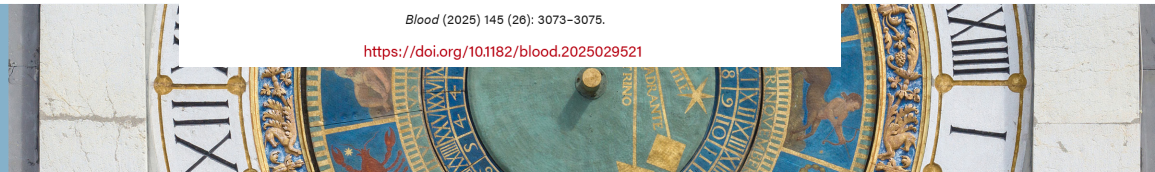
Blood (2025) 145 (26): 3073–3075.

https://doi.org/10.1182/blood.2025029521

Convegno Educazionale GITMO

LE TERAPIE CELLULARI IN EMATOLOGIA TRA PASSATO, PRESENTE E FUTURO

Brescia, 28-29 novembre 2025



Prospettive future: nutrizione e terapie cellulari

Two authors reviewed the title and abstracts of 1181 retrieved records; **however, no studies** were eligible for inclusion in this systematic review.

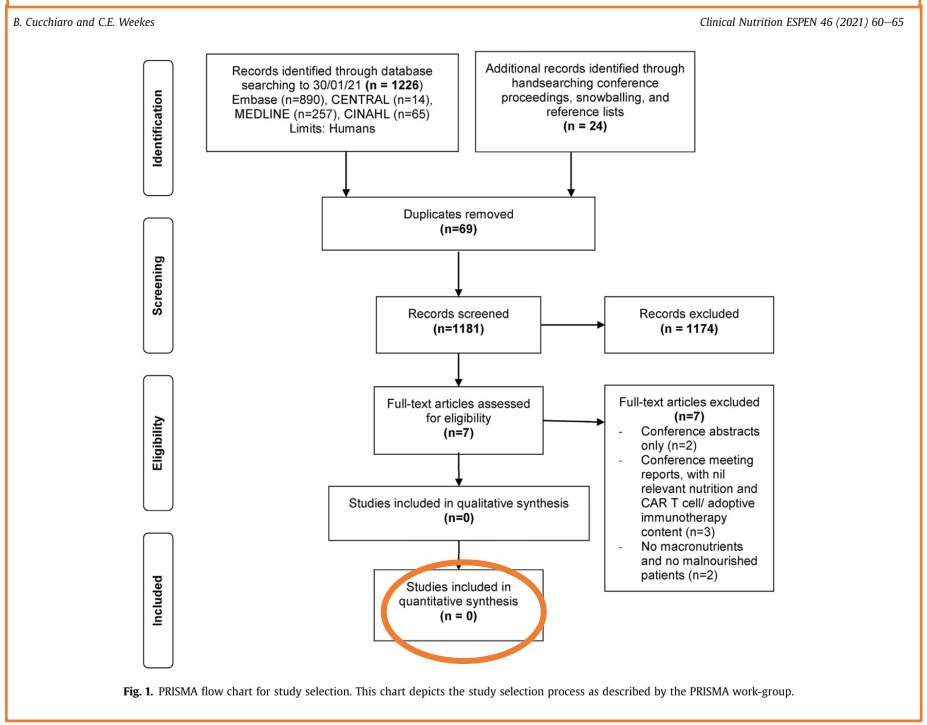


Fig. 1. PRISMA flow chart for study selection. This chart depicts the study selection process as described by the PRISMA work-group.

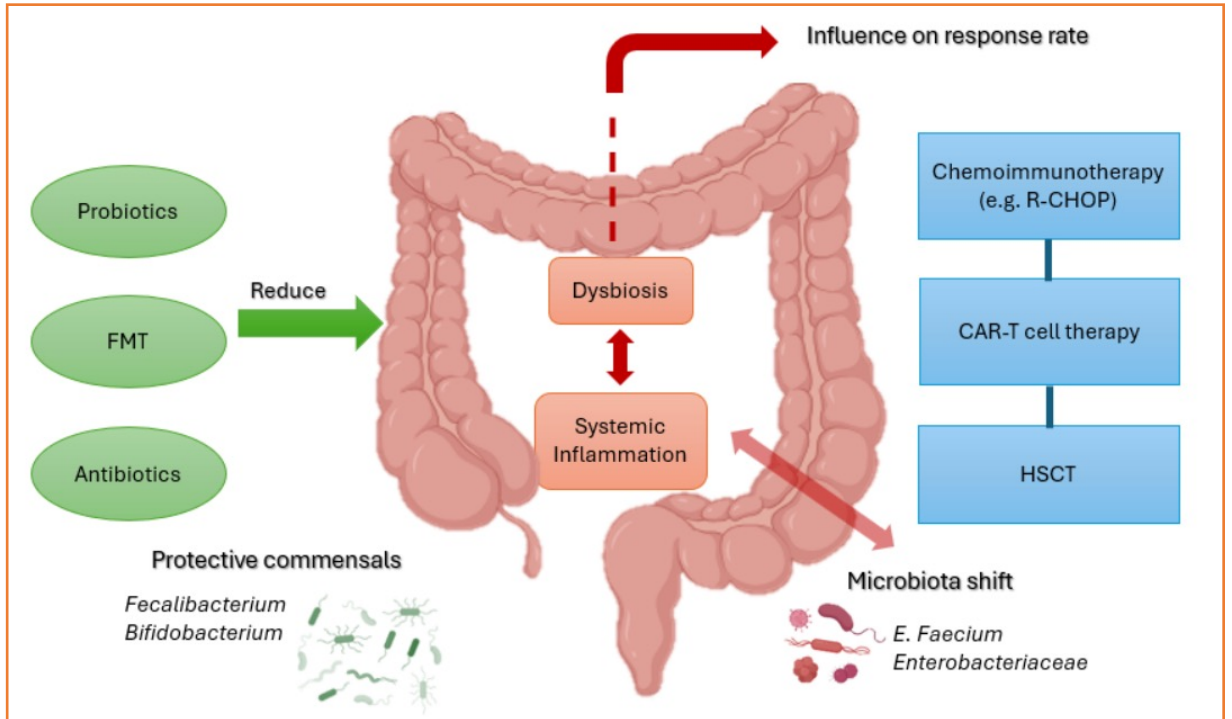


Figure 2. Schematic representation of the interplay between gut microbiota and treatment responses in B-cell NHL. Protective taxa (*Faecalibacterium*, *Bifidobacterium*) promote barrier integrity and immune regulation, while dysbiosis with *Enterococcus* and *Enterobacteriaceae* drives inflammation and toxicity. Interventions such as probiotics, FMT, and antibiotic stewardship may restore balance and improve outcomes with chemoimmunotherapy, CAR-T therapy, and HSCT. Created with BioRender. Santino Caserta. (2025) https://app.biorender.com/illustrations/68b5c44de87b2863610e44c6.

Ringraziamenti

Reparto TMO
Giulia Brambilla
Gabriele Magliano
Rachele Di Domenico
Silvia Zanon
Marco Galli
Elsa Cavagna

DH TMO
Vera Radici
Mirko Farina
Daniele Avenoso

Michele Malagola
Domenico Russo

Lab CREA
Simona Bernardi
Federica Re
Alessandro Leoni

Ematologia
Eugenia Accorsi Buttini

Lab Microbiologia
Simona Fiorentini
Sara Roversi
Gloria Bignotti

Data manager
Laura Vinati

Il team Infermieristico e OSS
Alice Valzelli
Chiara Renica

I futuri centri partecipanti!
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Slow Food®

IL NOSTRO CIBO È LA NOSTRA SALUTE. SOLO CON LA BIODIVERSITÀ SI NUTRE IL PIANETA

Il documento che illustra la posizione di Slow Food sulla relazione tra Cibo e Salute

Nella filosofia di Slow Food, che si impegna affinché tutti abbiano accesso a un cibo buono, pulito e giusto, la salute rappresenta uno dei valori chiave. Si può definire "sana" quella dieta che, oltre a risultare adeguata sul piano nutrizionale, favorisce la salute umana insieme a quella del pianeta; si deve quindi basare su una scelta ampia e diversificata di alimenti a base vegetale, integrali o per quanto possibile non processati, preferibilmente locali e ottenuti con metodi sostenibili. Oltre a ciò, è gradevole al palato.