Sistema Socio Sanitario
Regione Lombardia
ASST Lariana

Direzione Generale
Azienda Socio Sanitaria Territoriale Lariana

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Deliberazione n. 1085 del 19 settembre 2024

OGGETTO: Partecipazione di ASST Lariana al Bando competitivo per Progetti di Ricerca ai sensi del decreto Ministero della Salute del 06.02.23 "Criteri e modalità di utilizzazione dei fondi per la cura dei soggetti con disturbo dello spettro autistico per l'anno 2021" e della DGR n. XII/277 del 15/05/2023 – Progetto AUTINCA – Fondo anno 2021.

L'anno 2024, addì 19 del mese di settembre in Como, nella sede dell'Azienda Socio Sanitaria Territoriale Lariana, il Direttore Generale dott. Luca Filippo Maria Stucchi prende in esame l'argomento in oggetto e delibera quanto segue con l'assistenza del Direttore Amministrativo vicario avv. Gabriella Ceraulo, del Direttore Sanitario vicario dr. Roberto Pusinelli e del Direttore Sociosanitario ing. Maurizio Morlotti.

IL DIRETTORE GENERALE

Richiamato il Decreto del Ministero della Salute 6 febbraio 2023 riportante "Criteri e modalità di utilizzazione dei fondi per la cura dei soggetti con disturbo dello spettro autistico per l'anno 2021" pubblicato sulla GU serie generale n. 68 del 21 marzo 2023;

Richiamate la DGR XI/5415 del 25 ottobre 2021 "Approvazione del Piano Regionale Autismo" e la DGR XII/277 del 15 maggio 2023 "Determinazioni attuative del Decreto del Ministero della Salute 6 febbraio 2023 "Criteri e Modalità di utilizzazione dei fondi per la cura dei soggetti con disturbo dello spettro autistico per l'anno 2021" – approvazione del progetto regionale "la cura dei soggetti con disturbo dello spettro autistico: definizione di una rete territoriale che possa attuare un intervento precoce con una presa in carico volta a garantire la continuità di cura, l'integrazione e l'inclusione sociale e lavorativa dei soggetti con disturbo dello spettro autistico – progetto AUTINCA";

Richiamata la DGR n. XII/2049 del 18/03/2024 "Determinazioni in ordine al progetto regionale "AUTINCA" approvato con DGR n. XII/277/2023 in attuazione del Decreto del Ministro della salute 6 febbraio 2023 "criteri e modalità di utilizzazione dei fondi per la cura dei soggetti con disturbo dello spettro autistico per l'anno 2021 – obiettivo progetti di ricerca": criteri generali per l'approvazione del bando competitivo";

Visto il Decreto Direzione Generale Welfare n. 12032 del 02 agosto 2024 avente ad oggetto "Bando competitivo per progetti di ricerca ai sensi del decreto ministero della salute del 06.02.23 "criteri e modalità di utilizzazione dei fondi per la cura dei soggetti con disturbo dello spettro autistico per l'anno 2021" e la DGR n. XII/277 del 15/05/2023 "Progetto AUTINCA – Fondo anno 2021" ed in particolare l'allegato A riportante il testo del Bando;

Dato atto che l'ASST Lariana nel corso degli ultimi anni ha già implementato plurimi interventi per la cura dei soggetti con disturbo dello spettro autistico da ultimo sviluppando e concretizzando in sede territoriale gli obiettivi del Progetto AUTINCA sia con l'impegno delle risorse aziendali sia mediante il reclutamento di qualificati professionisti;

Considerata l'opportunità di partecipazione al Bando competitivo indetto con il D.D.G Welfare n. 12032 del 2 agosto 2024 mediante la presentazione del progetto aziendale denominato "PANDA – Personalized Approaches to Nutritional and Developmental Assessment in Autism" la cui realizzazione può rappresentare utile integrazione e rafforzamento delle iniziative aziendali già poste in essere;

Dato atto che il testo del Progetto è allegato al presente atto, di cui rappresenta parte integrante;

Acquisito il parere favorevole del Direttore Amministrativo vicario, del Direttore Sanitario vicario e del Direttore Sociosanitario

DELIBERA

Per le motivazioni in premessa riportate:

1. di prendere atto del progetto ASST Lariana denominato "PANDA – Personalized Approaches to Nutritional and Developmental Assessment in Autism" predisposto dal DSMD autorizzando la presentazione dello stesso al fine della partecipazione al Bando competitivo regionale di cui alla D.D.G Welfare n. 12032 del 2 agosto 2024;

2. di precisare che il progetto che verrà presentato nella procedura selettiva regionale è quello allegato alla presente deliberazione, di cui rappresenta parte integrante;

3. di dare atto che il presente atto non determina spese a carico del bilancio aziendale e che la realizzazione del Progetto "PANDA – Personalized Approaches to Nutritional and Developmental Assessment in Autism" è subordinata alla assegnazione di risorse regionali e nel limite delle risorse stesse.

IL DIRETTORE AMMINISTRATIVO
vicario
f.to avv. Gabriella Ceraulo

IL DIRETTORE SANITARIO
vicario
f.to dr. Roberto Pusinelli

IL DIRETTORE SOCIOSANITARIO
f.to ing. Maurizio Morlotti

IL DIRETTORE GENERALE
f.to dott. Luca Filippo Maria Stucchi

Documento firmato digitalmente ai sensi della normativa vigente. Il documento originale è conservato digitalmente presso gli archivi informatici dell'ASST Lariana - Ospedale Sant'Anna di Como dai quali il presente è estratto

Responsabile del procedimento: dr.ssa Patrizia Conti
Referente per l'istruttoria della pratica: dott. Massimo De Ponti

Sistema Socio Sanitario
Regione Lombardia
ASST Lariana

Direzione Socio Sanitaria
Direttore ing Maurizio Morlotti

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FORMAT PROGETTUALE

PROJECT TITLE

PANDA - Personalized Approaches to Nutritional and Developmental Assessment in Autism

Project duration (months*): 24 months*

Project Keywords:

1. *Autism Spectrum Disorder (ASD)*
2. *Nutrition*
3. *Developmental profile*
4. *Efficacy*
5. *Brain-gut axis*

OPERATIVE UNITS (da 1 a 4)

	INSTITUTION	Department/Division/Laboratory	Role in the project
1	Asst lariana	Child and adolescent Neuropsichiatric team	lead researcher
2	Centro Progetti educativi - Soc. Coop. Soc.	Neuropsycological team	partner researcher
3	Centro Progetti educativi - Soc. Coop. Soc.	Nutritional team	partner researcher

INVESTIGATORS, INSTITUTION AND ROLE IN THE PROJECT (1 Key personnel per UO)

	Key Personnel	Institution/Org./Pos.	Role in the project
1	Dr.ssa Patrizia Conti	ASST Lariana	Scientific Director
3	Dr. Salvatore Russolillo	Centro Progetti educativi - Soc. Coop. Soc.	Nutritional team Coordinator

4	Dr.ssa Antonella Mazzillo	Centro Progetti educativi - Soc. Coop. Soc.	Neuropsycologist Team Coordinator

The research develops a field to choose among these:

1) clinical trials to identify the efficacy and safety profile of the intervention and identification of the predictors and moderators of the response aimed at improving the available therapies (rif letter b) del DM);
2) procedures for the evaluation and management of co-occurring disorders/conditions (rif lettera c) del DM);
3) identification and evaluation of the outcomes of the paths envisaged by the guidelines (rif lettera h) del DM).

Our research would develop point 1: clinical trials to identify the efficacy and safety profile of the intervention and identification of the predictors and moderators of the response aimed at improving the available therapies (rif letter b) del DM).

1. Overall Summary - Summary description (max 1.000 characters)

Autism spectrum disorders generally arise during early childhood and affect the neurodevelopment of those affected to varying degrees (around 4 children out of a thousand). It is a range of disorders with a multifactorial origin, the multiple causes of which are still being explored and whose symptoms range from difficulties in social contact and the emotional sphere to repetitive behaviours, to problems in communication and language. A lesser-known symptom associated with autism, recently identified, is the occurrence of intestinal disorders that worsen the clinical picture of young patients and, above all, alteration of the intestinal flora (called microbiota). A detail of no small importance: intestinal bacteria can in fact influence some brain activities through the secretion of substances or the regulation of the immune system, and it is no coincidence that we often talk about the gut-brain axis. The intestinal microbiota, when well-balanced in its components, has a beneficial effect on health, while when it is altered (dysbiosis) it can cause intestinal permeability, inflammation and trigger a series of diseases, not only intestinal.

2. Background / State of Art (max 1.500 characters)

In the ATS Insubria[1], between 2016 and 2022, 3,794 subjects with ASD had at least one access to health or social health services, highlighting a growing attention to the diagnosis and treatment of neurodevelopmental disorders. The distribution of cases is in line with what is observed at a national level. The average age of male patients is 9.8 years, while in females it rises to 16.4 years, with a distribution unbalanced towards males. The M/F ratio is 3.3:1, confirming the male prevalence. The overall prevalence rates for ASD stand at 2.6 per 1,000 inhabitants, with significant differences between genders: 4.1 for males and 1.2 for females. Furthermore, most diagnoses concern very young subjects, with 44% of new cases identified in children under 5 years old, and another 25% in the age group between 5 and 9 years old. Overall, approximately 90% of patients are under 20 years old, with a prevalence among foreigners. The analysis highlights an average of approximately 500 new cases of ASD per year, with a fluctuating trend: there was a peak in new cases in 2018, followed by a slight decline in 2019 and 2020, likely linked to the effects of the pandemic, with a subsequent increase starting from 2021. In terms of territorial distribution, ASST Lariana has a higher prevalence rate with 2.84 cases, against an average of 2.61 per 1,000 inhabitants, suggesting a greater concentration of diagnoses in the area.

3. Hypothesis and Specific AIMS (max 20.000 characters)

In light of the above, it is believed that it is possible to evaluate the effects of a clinical customization model that includes the nutritional aspect of the rehabilitation pathway.

[1]source: https://www.ats-insubria.it/attachments/category/313/Autismo_Epidmiologia_Report.pdf

Autism spectrum disorder (ASD) is a multifactorial neurodevelopmental disorder, characterized by deficits in social interactions, communication and the presence of restrictive and repetitive behaviours, interests and activities. ASD is an etiologically heterogeneous disorder involving multiple factors, such as environmental and environmental factors, including pre- and/or post-natal factors. Among the comorbidities of ASD, gastrointestinal (GI) symptoms are of particular interest, given their prevalence and correlation with ASD severity. Gastrointestinal symptoms include abdominal pain, constipation, diarrhea, bloating, and gastroesophageal reflux (GERD).

In the last decade, many studies have highlighted the role of the gut microbiota (GM) in neurodevelopmental disorders, particularly in autism spectrum disorders. In fact, GM is known to influence social behaviour and brain physiology through a diverse set of pathways, including immune activation, microbial peptide production, metabolites, and various neuromodulators and neurotransmitters. As is well known, the gut is connected to several brain functions that act on emotional and cognitive brain regions, such as the prefrontal cortex, the system. Thus, communication by cross-interaction between the central nervous system (CNS) and the gastrointestinal tract, called the "gut-brain axis," plays a key role in the pathophysiology of neurological diseases and appears to be driven by the ecology and function of GMOs.

Several studies have shown that the gut microbial composition of the ASD enterophenotype is characterized by an increase in harmful microbes and a decrease in those. In particular, few metagenomics-based studies have highlighted specific overrepresented ASD-related microbial signatures, such as Ruminococcus, Sutterella, Enterococcus, Prevotella, and Fecalibacterium prausnitzii.

However, GMOs also play a critical role in maintaining the integrity of the intestinal barrier, protecting against the passage of bacterial toxins into the bloodstream, a phenomenon related to peripheral inflammation and the induction of behavioral alterations and damage to the blood-brain barrier, as demonstrated in animal models.

Thus, changes in intestinal permeability due to tight junction modulation may reflect low GM function, as well as low antibacterial defence. Zonulin is a well-known biomarker of permeability, usually related to chronic diseases, such as diabetes, celiac disease, inflammatory bowel disease or obesity, but also to comorbidities associated with ASD. Secretory IgA (sIgA) represents the first immune defence barrier in the intestine that protects the intestinal epithelium from pathogens and enteric toxins, thus mediating the innate immune defence mechanism at the level of the intestinal mucosa, as also reported in patients with ASD. Fecal lysozyme is an alkaline glycosidase secreted by granulocytes, macrophages, Paneth cells, Brunner's glands and normal cells of the crypt of the colon, which has an antimicrobial action by hydrolysis of specific glycosidic bonds of mucopolysaccharides from the wall of Gram-positive bacteria. Elevated levels of fecal lysozyme have been identified in patients with colonic IBD compared to controls, but also in patients with ASD.

Specific Aim 1

To evaluate nutritional interventions on minors with autism spectrum disorders in habilitative therapies.

Specific Aim 2

To examine the role of the gut-brain axis in the modulation of autistic symptoms and in the response to therapies.

Specific Aim 3

To develop personalized rehabilitation protocols.

Experimental Design Aim 1

Initial, ongoing and final evaluation of the functioning profile through observation in life contexts, environmental questionnaires, standardized tests, in order to evaluate the effectiveness of the rehabilitation paths combined with the nutritional therapeutic protocol.

Experimental Design Aim 2

Laboratory tests: Profile of the intestinal microbiota on urine and feces, evaluation of nutritional deficiencies. Food diary that aims to monitor daily eating habits and identify any correlations with behavioural symptoms. Personalized Diet:

Gluten and Casein Free Meal Plan (GFCF): To improve behavioural symptoms and gut health. Probiotic and Prebiotic Supplementation: To rebalance the gut microbiota and improve gastrointestinal function. Evaluation of Nutritional Outcomes: Monitoring of dietary changes and correlation with behavioural and gastrointestinal improvements.

Experimental Design Aim 3

Personalized rehabilitation pathways that include ecological interventions on the neuropsychomotor, neuropsychological, speech-communicative, psychoeducational side.

4. Methodologies and statistical analysis (max 2.500 characters)

Participants will be 40 children diagnosed with ASD (3 Level), aged between 3 and 18 years (3-6 / 7-12 / 13-18) including 15 males and 15 females and 15 observed and studied with placebo.

*The inclusion criteria for autism spectrum disorders: age, 3–12 years; diagnosis of ASD according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5); confirmation by the Autism Diagnostic Observation Schedule, second edition (**ADOS-2**) and, when available, by the Autism Diagnostic Interview Revised (ADI-R). Characterization of the main symptoms of ASD, cognitive level, and behavioural problems was conducted by qualified clinical psychologists and psychiatrists. All patients who did not meet the inclusion criteria were excluded. Confirmed diagnosis of ASD (DSM-5), absence of serious medical comorbidities, informed consent of parents.*

***Exclusion Criteria:** Presence of severe medical conditions that cannot be managed within the scope of the project. Participant metadata will include clinical, medical history, and nutritional data [e.g., presence of food selectivity (FS) such as: elimination diet, gluten-free, or casein-free], probiotic supplementation, and administration of. Study of clinical parameters (e.g.,*

weight, height) for the calculation of body mass index (BMI), body mass index (pBMI) percentiles taking into account the growth charts of the Centre for Disease Control and Prevention (CDCP) for children and adolescents aged 3 to 18 years. Urine samples will be collected and sent to a diagnostic laboratory.

***Gastrointestinal assessment**: Use of the questionnaire based on the Rome IV classification (Drossman and Hasler, 2016) to assess GI symptoms, such as the presence of abdominal pain, functional diarrhea, constipation, and vomiting disorders. In addition, the presence or absence of GERD will be considered (Wasilewska and Klukowski, 2015). Patients with ASD will be divided into subgroups based on the presence or absence of one or more GI disorders to identify possible relationships with GM differences based on ASD-related GI enterophenotypes. The two groups, namely, with and without GI symptoms, were considered for the differential description of GM ecology.*

***Determination of fecal markers of inflammation and intestinal permeability**: secretory IgA, and calprotectin will be performed on stool collected from 40 patients.*

***Neuropsychological assessment:** Cognitive level (smart quotient, IQ; and developmental quotient, QD) is assessed based on age, language level, compliance, and timing of IQ assessment by **WISC-IV** (Lang et al., 2015), nonverbal IQ by Leiter-3 (Roid et al., 2013), or general quotient (QG) by Griffiths Mental Development Scales Extended.*

*Autism symptoms are assessed using ADOS-2, a semi-structured direct assessment of communication, social interaction, play, or imaginative use of materials for individuals with a suspected diagnosis of ASD, based on language level and which ranged from nonverbal to verbal fluency. **ADOS-2** has been administered and evaluated by licensed clinicians with demonstrated clinical ability to use it. For some patients, the diagnosis was also confirmed by ADI-R, a semi-structured interview with parents. To assess the severity of ASD symptoms. Behavioural and psychopathological problems were assessed by the Achenbach System of Empirically Based Assessment (ASEBA) questionnaire, specifically using the Child Behaviour Checklist (CBCL) for children aged 1.5 to 5 years and the CBCL questionnaires for children aged 6 to 18 years, reported by parents.*

5. Expected outcomes (max 500 characters)

*A significant improvement is expected in terms of **Behaviour and communication:** reduction of problematic behaviours and increase in social and communication skills. Progress in the ability to adapt and greater independence of the participating children. Improvement of emotional regulation. At the same time, an optimization of the intestinal macrobiota and reduction of related symptoms is expected. To verify the multiple interactions between the host and gut microorganisms, between different microbial strains, fecal samples represent a source of information that should be studied as a whole. To try to find a relationship between dysregulated gut microbial strains and upregulated sncRNAs in ASD. The importance of a healthy and correct diet to untangle the host-microbiome dialogue to understand the role of dysbiosis in the onset of ASD and to design diagnostic tools and personalized therapeutic interventions. To demonstrate that GI functional symptoms, such as constipation, abdominal pain, flatulence and diarrhea, represent an important comorbidity in the broad autistic phenotype, when compared with*

typically developing children. To demonstrate, that intestinal inflammation related to the integrity of the intestinal barrier and the defence of the innate immune barrier exerted as an antimicrobial action against Gram-positive bacteria make the child with a genetic predisposition to ASD more at risk of manifesting the symptoms of this pathology. Furthermore, since the transmission of signals between the brain, the digestive system and the microbes that populate the intestine is known as the microbiota-gut-brain axis, it is intended to demonstrate that gut microbes also perform the task of stimulating the host's immune system by producing anti-inflammatory metabolites such as short-chain fatty acids and promoting the release of immune molecules. Finally, it is expected that gastrointestinal disorders in the case of ASD could be associated with an altered microbiota (intestinal dysbiosis), which in turn is related to a condition of inflammation, altered function and permeability of the intestine, commonly referred to as leaky gut syndrome.

6. Risk analysis, possible problems and solutions (max 1000 characters)

Risk of resistance to interventions by the minor involved: he/she may not respond immediately or be resistant to rehabilitation interventions, showing negative emotions or lack of participation. In this situation, a gradual introduction of interventions is expected, the increase of which, determined by the frequency and duration of the individual treatment, will be personalized in order to actively involve the minor.

Risk of lack of coordination between family and operators: we expect that in this case, regular coordination meetings between families and operators will be implemented. Personalized updates on the minor's progress and individualized plans with family input will also be encouraged.

Inadequate approach by operators in the rehabilitation pathways: from a prevention perspective, continuous training will be promoted, periodic updates on evidence-based techniques, with constant monitoring of the quality of interventions, as well as constant supervision.

At the risk of limited progress compared to that expected, we will intervene by constantly re-evaluating the rehabilitation interventions with adjustments that constantly support the evolution of skills.

Poor parental participation: we will respond to this risk with constant feedback and creating and constant support regarding management in a family environment, in a manner consistent with the therapies. Analysing the risks associated with our research, we identify four main issues: 1) Variability in individual results related to the treatment of intestinal microbiota, which may limit the effectiveness of the personalized diet for some participants; 2) Potential adverse reactions or intolerances to the new foods introduced, requiring continuous monitoring; 3) Difficulties in data collection and management due to the specific communication needs of the participants; 4) Possible incomplete adherence to the dietary plan by participants, which could affect the research outcomes. To address these issues, we will adopt a flexible and adaptive approach, with regular monitoring plans, involving experienced professionals, and using advanced technologies for data collection and analysis. Additionally, collaboration with caregivers and

specialists will ensure adequate support for participants, minimizing risks and optimizing results."

7. Significance and Innovation (max 1.000 characters)

Scientific research provides concrete and measurable data that can demonstrate the effectiveness of specific therapies. This is crucial to obtain the necessary endorsement for the acceptance of treatment plans by professionals and families, avoiding fewer effective treatments and focusing resources on proven interventions. Furthermore, identifying which aspects of nutritional interventions and speech and psychomotor therapies are most effective allows for improving and personalizing treatments, increasing the benefits for children with autism and allowing for more personalized and targeted treatments. From a social perspective, providing evidence of the effectiveness of treatments can influence health policies and access to services, improving opportunities for providing appropriate care. Research findings can also serve as a basis for the ongoing training of professionals working with children with autism, ensuring that the practices adopted are based on up-to-date scientific evidence.

8. Description of the complementary and synergy research team (max 1.000 characters)

The Complementary and Synergy Research Team would be composed of interdisciplinary experts whose combined expertise enhances the project. This team might include:

1. Clinical Researchers: Specialists in autism spectrum disorders (ASD) with experience in designing and conducting clinical trials.

2. Gastroenterologists: Experts in the gut-brain axis and its potential influence on neurodevelopmental disorders.

3. Psychologists and neuropsychiatrists: professionals working on behavioural therapies and psychomotor skills in ASD.

4. Nutritionists: to assess and guide dietary interventions supporting overall clinical outcomes.

5. Data Scientists/Statisticians: Responsible for analysing data and ensuring robust, statistically valid results.

This synergy ensures that all aspects of the project are covered comprehensively, leading to evidence-based results that can have a tangible impact on therapeutic protocols.

9. Bibliography (max 2.000 characters)

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10. Timeline (max 1.000 characters)

The project timeline is developed in three main phases, with a total duration of 24 months.

- ***Phase 1: Data Collection and Sample Selection (0-4 months)*** *- We begin with the selection of subjects, gathering clinical and anamnesis information. At the same time, we will conduct a literature review on diets and the microbiota in individuals with autism.*
  Development of development of personalized intervention plans end initial assessments (clinical, dietary, behavioural)

- ***Phase 2: Intervention and Monitoring (5-12 months)*** *- This phase involves the implementation of personalized diet plans developed by expert nutritionists. Participants will follow these diets for 12 months, during which we will monitor the gut microbiota through fecal analysis and collect data on behavioural changes and overall health. Start of psychomotor, behavioural, interventions. Data collection (bi-monthly). Monitoring progress through observational and standardized assessments*
- ***Phase 3: Mid-term Review (Months 13-15)*** *- Data analysis of preliminary results ends adjustments to interventions if necessary*
- ***Phase 4: Continuation and Data Collection (Months 16-21)*** *- Ongoing interventions and evaluations*
- ***Phase 5: Analysis and Dissemination (22-24 months)*** *- We will analyse the results to assess the effectiveness of the intervention. Finally, the findings will be published in a report and presented in seminars to raise awareness among practitioners and families.*

In the research project aimed at studying the effects of personalized nutrition and supplementation on children with autism spectrum disorder, various tools and resources can be crucial in ensuring a rigorous scientific approach and reliable results.

11. Equipment and resources available (max 2.000 characters)

Diagnostic Evaluation Tools:

1. Clinical Questionnaires and Rating Scales: Use of standardized tools such as the Checklist for Autism in Toddlers (CHAT) and the Autism Diagnostic Observation Schedule (ADOS) to assess symptoms and the severity of autism spectrum disorder.

2. Nutritional Assessments: Software for evaluating food intake and nutritional analysis to personalize diets according to the specific needs of each child.

Technological Resources:

***1. Data Management Platforms**: Use of computer systems to securely collect and analyse data, complying with privacy regulations and the handling of personal data.*

***2. Scales and Measurement Tools:** Devices to measure weight, height, and other physical parameters, as well as equipment for blood analysis to monitor the nutritional status and metabolic profiles of participants.*

***3. S-DRIVE Device for epigenetic evaluation** through the analysis of the hair bulb of the subject.*

Professional Support:

1. Multidisciplinary Team: Collaboration between nutritionists, dieticians, psychologists, pediatricians, and neuropsychiatrists end specialists to personalize interventions and monitor progress.

2. Training and Workshops: Training sessions for healthcare professionals and families to raise awareness and educate on the importance of personalized nutrition and supplementation for children with autism.

Scientific Research Resources:

1. Access to Scientific Databases: Consultation of previous articles and studies on platforms like PubMed and ResearchGate to base the project on solid scientific evidence.

These tools and resources, combined with an evidence-based approach and a multidisciplinary team, can significantly contribute to the success of the project and the improvement of conditions for children with autism spectrum disorder.

12. Translational relevance and impact for the National Health System (SSN) (max 1.000 characters)

Scientific research on the effectiveness of speech, psychomotor and nutritional therapies for children with autism has fundamental translational relevance for the national health system. The results can guide the implementation of evidence-based clinical guidelines, optimize resource allocation and improve the training of professionals. Furthermore, they influence reimbursement policies and access to services, contributing to a more equitable distribution of treatments. They provide a basis for the development of informed health policies, allow continuous evaluation of interventions and stimulate further research. In summary, such research improves the quality of care and the efficiency of the health system, directly benefiting patients and their families.

13. Keys personal included the Scientific Coordinator (SC)

Key personnel in the project should include:

*1. **Scientific Coordinator:** Responsible for overseeing all aspects of the project, ensuring scientific rigor, coordinating between teams, and reporting to stakeholders.*

*2. **Lead Researchers**: Specialists in autism spectrum disorders, gut-brain axis research, and nutrition.*

*3. **Clinical and Behavioural Therapists:** Experts in delivering the tailored therapeutic interventions.*

*4. **Nutritional Experts:** To address and manage the dietary component of the project.*

*5. **Data Analysts:** Responsible for processing and analysing the collected data for scientific and clinical insights.*

Duly signed curriculae vitae shall be attached to the application using the model (All. n.2)

Overall proposed budget for all the research fields divided for Operative Units

Operative Unit 1 (Asst lariana)		
Items	**Rationale**	**Costs**
Personnel	-Psychological assessment -Funtional Assessment, monitoring	80.000
Total		80.000
Material, equipments, IT Services and Data Bases	-scales and instruments - *data base*	15.000
Total		15.000
Missions/travels	-*meeting , mission* - -	- *5.000* -
Total		5.000
Dissemination and conferences	-project presentation -	-5.000 -

	-	-
Total		5.000
Overheads	- *-neuropsychiatric team* -	- -1.000 -
Total		1.000
TOTAL OPERATIVE UNIT 1		106.000

Operative Unit 2 (Centro Progetti Educativi – Nutritional Team)		
Items	**Rationale**	**Costs**
Personnel	Team nutritional (salaries and consultancy fees)	50.000,00 €
	Assistants and support (e.g., monitoring and follow-up)	20.000,00 €
Total		70.000,00 €
Material, equipments, IT Services and Data Bases	Tools for nutritional assessments and monitoring (scales, laboratory instruments)	5.000,00 €
	Educational materials and resources for diet (e.g., dietary guides, special food items)	3.000,00 €
	Professional Scales: For accurate measurement of the children's weight.	600,00 €
	Height Measurement Tools: To monitor growth.	800,00 €
	Body Composition Analyzers: Such as calipers for measuring body fat and muscle mass	400,00 €

	Laboratory Test Kits: For testing nutritional deficiencies and assessing vitamin and mineral status.	800,00 €
	Dietary Guides and Nutritional Manuals: Resources for creating personalized meal plans.	500,00 €
	Nutritional Planning Software: Programs for designing and tracking diets, such as MyFitnessPal or Nutrium.	1.000,00 €
	Educational Materials: Books, brochures, and information sheets to educate families and children about nutrition principles.	1.000,00 €
	Databases and Software	10.000,00 €
Total		23.100,00 €
Missions/travels	Nutritional meeting (travel, meeting and other costs related to Mission and Travel*)*	5.000,00 €
Total		5.000,00 €
Dissemination and conferences	Project presentation to press	2.500,00 €
	Press conference to disseminate results	5.000,00 €
Total		7.500,00 €
Overheads	Team nutritional	600,00 €
	Assistants and support	400,00 €
Total		1.000,00 €
TOTAL OPERATIVE UNIT 2		106.600,00 €

Operative Unit 3 (Centro Progetti Educativi – Neuropsycological team)		
Items	**Rationale**	**Costs**
Personnel	Team neuropsycological (salaries and consultancy fees))	60.000,00 €
	Assistants and support (e.g., monitoring and follow-up)	20.000,00 €
Total		80.000,00 €
Material, equipments, IT Services and Data Bases	Tools for neuropsycological assessments and monitoring (scales, laboratory instruments)	7.000,00 €
	Professional Scales: For accurate measurement of the children's development.	1.500,00 €
	Educational Materials: Books, brochures, and information sheets to educate families and children	1.000,00 €
	Databases and Software	10.000,00 €
Total		19.500,00 €
Missions/travels	Neuropsycological meeting (travel, meeting and other costs related to Mission and Travel*)*	4.000,00 €
Total		4.000,00 €
Dissemination and conferences	Project presentation to press	5.000,00 €
	Press conference to disseminate results	3.000,00 €
Total		8.000,00 €
Overheads	Team neuropsycological	600,00 €
	Assistants and support	400,00 €

Total	1.000,00 €
TOTAL OPERATIVE UNIT 2	112.500,00 €

Proposed total budget (max 361.704,35 euro)

Personnel	230.000
Material, equipments, IT Services and Data Bases	57.600
Missions/travels	14.000
Dissemination and conferences	20.500
Overheads (max 1%)	3.000
TOTAL	325.100

Timetable

Diagramma di Gantt	**1° year**												**2° year (until 15/10/2026)**									
Azioni	**I semestre**						**II semestre**						**I semestre**						**II semestre**			
	1	**2**	**3**	**4**	**5**	**6**	**1**	**2**	**3**	**4**	**5**	**6**	**1**	**2**	**3**	**4**	**5**	**6**	**1**	**2**	**3**	**4**
Starting project activities communication of acceptance of the financing by the assigned bodies no later than 5 days from the publication of the ranking																						
Acquisition of any opinions from the Ethics Committee, sending of the partnership agreement and start of the projects within 30 days of the publication of the ranking																						

Diagramma di Gantt	**1° year**												**2° year (until 15/10/2026)**									
Azioni	**I semestre**						**II semestre**						**I semestre**						**II semestre**			
	1	**2**	**3**	**4**	**5**	**6**	**1**	**2**	**3**	**4**	**5**	**6**	**1**	**2**	**3**	**4**	**5**	**6**	**1**	**2**	**3**	**4**
Development of project activities																						
Intermediate phase Interim reporting of activities carried out and expenses incurred by 31 October 2025																						
final phase Conclusion of project activities no later than 15 October 2026																						
Final reporting of the activities carried out with the results of the research projects conducted and reporting of all expenses incurred by 31 October 2026																						

Como, xxx/09/2024

SCIENTIFIC COORDINATOR

Dr.ssa Patrizia Conti