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A General Systems Theory Approach in Public Hearing Health: Lessons Learned From a Systematic Review of General Systems Theory in Healthcare

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ABSTRACT General Systems Theory (GST), as it was introduced by Karl Ludwig von Bertalannfy, had a significant, yet mostly unacknowledged influence on systems theory. The purpose of the current review is to highlight and assess the application of the aforementioned theory in the healthcare field and suggest a new approach to the public hearing healthcare sector. A systematic literature review has been conducted in the electronic databases of ScienceDirect, Pubmed and IEEEXplore covering the years of 2009-2019, following the PRISMA guidelines. The article selection was performed to identify GST-related frameworks in the healthcare field and was completed through a process of removing duplicates and non-available articles, analyzing the tittle and abstract, and then reviewing the full text of each selected article. In the final analysis, 47 studies were selected and were thoroughly analysed. Almost half of these articles showed a practical implementation of GST-inspired frameworks, following different types of research methodology. Analysis of these methodologies identified the limitations and positive effects of GST in the healthcare field. Although there is a significant number of references in GST in the healthcare field over the last 10 years, applications of it need to be further tested and explored before they are put into real-situation testing. Simulation models and evidence-based approaches on a micro-, meso- and macro-level of systems should be used to provide the contextual information needed for establishing GST as a driving force in the healthcare field. To this context, a paradigm of GST data framework applied to the hearing loss screening area is hereby presented and discussed. It is shown that a GST approach can be used to identify equilibria in all levels, to balance gain and prediction capacity over time and enhance public hearing health approaches for treatment and management strategies.

INDEX TERMS General systems theory, hearing healthcare, systemic approach, systematic review, public hearing health.

I. INTRODUCTION

A. RATIONALE

The underlying principles of General Systems Theory (GST) as they were described by von Bertalanffy [1] should seem largely intuitive to system-related fields. Topics related to the application of GST in the healthcare field have received limited attention in research. Theoretical models applied on GST can hint towards a holistic approach on healthcare related issues and problems, including those in the psychology and pharmacology field. The failure of linear models and reductionist approaches to explain variable outcomes for patients in several cases (e.g. neurodegenerative and musculoskeletal conditions) triggered researchers to look for explanations elsewhere.

GST and its most commonly used derivatives, the Biopsychosocial (BPS) model and Systems Biology, laid the appropriate grounds for such endeavors. The unification

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of systemic morphology under the domain of GST, simultaneously respected the differing disciplinary approaches and highlighted the dynamic interaction among them. This conceptual approach on the interrelations between varying systems in the natural world, extending from physical and biological to social sciences, emphasizes the need of humans to understand a system in a holistic manner.

As the healthcare field can be seen as a mega-system [2]–[4] consisting of subsystems, GST provides new opportunities to address the multiple challenges faced not only on a micro-level (e.g. hospital) but on a meso- (e.g. country) and macro (e.g. world) level as well. Especially nowadays that technological advancements, including big data analytics techniques and computational models [5] and public health informatics ([6], approach the health from a personalized and population perspective at the same time, application of GST in this field seems more than promising. It is therefore safe to assume that a reforming and reshaping of the healthcare field in a systemic manner will take place over the next years.

Putting into perspective the hearing healthcare field, it is widely accepted that it faces numerous challenges and is underutilized by those who need it, thus requiring a significant amount of effort, knowledge and coordination among its parts to be effective and efficient [7], [8]. It is the aim of this paper to change the perspective of current approaches and shift the view towards a general public hearing health policy framework. Application of a GST approach may identify and uncover the nature of the computations and information-processing systems, map the connectivity patterns and reveal the functional and structural activities of the hearing healthcare scene.

B. OBJECTIVES AND RESEARCH QUESTION

Given the aforementioned perspective, it is the purpose of this study to examine whether GST has played an active role in the healthcare field and whether GST-related frameworks have been applied, either on a theoretical or practical level. Although the auditory science is the main focus of this work, use of related keywords (e.g. 'hearing') returned minimal to none results, thus limiting the extent of a literature review on such a specific topic. Therefore, a systematic review was conducted to determine if and how GST has been applied in the healthcare realm over the last ten years.

The main research question of this study is to evaluate the application of GST, if any, in the healthcare field and identify the limitations and positive aspects of its practical application via the research methodology followed in its application.

II. METHODOLOGY

A. SEARCH STRATEGY

An electronic search was performed in April 2019 in three electronic databases with peer-reviewed publications. The search was conducted using the defined terms (''general systems theory'' AND ''health'') in each of the electronic databases' search field. Use of wildcards (e.g. ''general system* theory'' and ''health*'') was avoided as (a) ScienceDirect does not support the use of wildcards, so that would affect the common search criteria applied to the search engines and (b) it would yield a variety of results that are not relevant to General Systems Theory (e.g. ''systemic'' or ''systematic''), thus not providing answer to the research question of this study. We refrained from using other logical operators (e.g. OR) due to the generic nature of the concepts used. The years' range was set from 2009 to 2019 (last 10 years in the PubMed database). No other restrictions were applied.

B. DATA SOURCES AND ANALYSIS

The electronic databases of PubMed, IEEEXplore and ScienceDirect were identified as the main data sources. Other electronic databases, like ACM Digital Library, Cochrane or Web of Science Social Citations Citation Index (SSCI), were also explored but they returned zero (ACM) and one result (Cochrane, SSCI) accordingly. With the latters having already been identified in PubMed and ScienceDirect, they were both excluded from this report.

After yielding the results of the electronic search, we followed the PRISMA guidelines [9] for conducting a systematic literature review. Duplicates, articles not in English, as well as non-available articles were removed. The availability of the articles was defined by the access provided by the HEAL (Hellenic Academic Libraries Link) framework. After a first analysis of the tittle and abstract of each article, a full-text review was performed on the remaining papers. This review identified articles that were irrelevant to the field of healthcare, so they were also removed. The main reason behind these records not being eligible to be part of the reviewed corpus, was the reference of the term ''health'' only by-name. Many abstracts included sentences pointing out to the generic character of GST that could be expanded to other fields, including health, without further analyzing it, making the article not eligible for the final review. The finally selected articles composed the corpus of this review. A final full-text analysis was then performed on each of them, to assess them based on the research question.

III. RESULTS

A. FLOW DIAGRAM

B. STUDY SELECTION AND CHARACTERISTICS

The following studies were thoroughly examined and their main characteristics were extracted. Focus was given to recognizing whether a practical implementation of GST has taken place and in which healthcare field. Theoretical approaches of GST have been also identified; however, it was not in the scope of this review to further describe them. The articles presented hereinafter are divided into their relevant healthcare field.

1) HEALTH-RELATED CONCEPTS

Reference [10] presented a historical perspective regarding the influence of GST in medical sciences. The most important

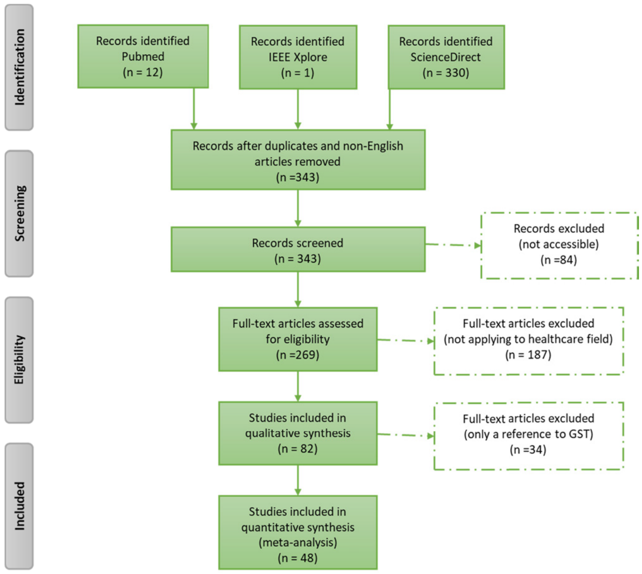

FIGURE 1. **Flow chart of the selection of papers.**

outcome of the paper is the "fuzzification of the state of health" and an attempt to express the concepts of health, illness, malady, patient-hood and disease in a fuzzy system way.

A whole-body systems-biology platform, loosely based on GST is presented in [11]. The suggested platform was proposed in order to modernize traditional Chinese medicine and explain the latter's theoretical framework in an evidence-based manner. However, the authors recognized a huge challenge in where and how to set up this platform for supporting their case.

Reference [12] used systems biology (a GST-based framework) for promoting the P4 (a personalized, predictive, preventive and participatory) medicine, as per the authors' words "this holistic or global approach allows us to comprehend the functions of biological systems (processes) and thoroughly research how their interactions, both internally as well as with other systems, result in the appearance of new emerging properties". The theoretical foundation described for P4 is explained in order to prepare the ground for it in a quantitative and modeled manner.

In [13], health information systems (HISs) and electronic health records were viewed in GST terminology, since they are considered to be sub-systems inside the healthcare system. A general methodology on the interoperability testing of HISs was fully analysed and described in order to provide the necessary concepts. These were then used to efficiently and extensively describe the interoperability framework of HISs and identify interaction patterns for a generic test system architecture.

Reference [14] suggests in his work an algorithm to support the application of systems-level (GST-based) thinking to clinical research and apply it to the health care systems. Costa expressed that algorithm in a simplified equation where it states "that the multiplicative interaction of personal genomics times systems pathology yields a personalized, predictive, precise, preventive and thus participatory medicine".

In [15], GST is used to assemble the components of the International Classification of Functioning, Disability and Health (ICF) framework to better illustrate interactions taking place. Concepts of the ICF such as interactivity, multidimensionality, holism, non-linearity, flux, and self-organization align with the GST framework. GST was used to depict the dynamic capability and enhance the capacity of the ICF framework in order to address concerns, criticism and issues with previous interpretation of it.

Reference [16] suggest a systems thinking approach for dealing with bioinformatics and biomedical problems, as complexity has risen over the last years, concluding that public health offers the real-world framework for integrating the molecular, physiologic and environmental perspectives on human health. Understanding the processes and interactions within that domain, complex thinking approaches offer plausibility to testable hypotheses and development to more sophisticated computational solutions.

Reference [17] present the Redox framework, a GST-inspired conceptual framework based upon the nature of electron exchange to explain "a multi-layered system in which intra/intercellular and inter-organ exchange processes essential to sensing and adaptation" of living organisms. The authors argue that such a framework can better explain the metabolic pathways and cellular bioenergetics for the Redox state of the human body in a multi-level holistic systems biology approach.

2) MENTAL HEALTH

Reference [18] developed a cross-sectional study based on family systems theory (which is in turn based on GST) to investigate features such as wholeness and circular causality in families with mentally ill members. Their results, from a family systems theory point of view, indicated factors to enhance the quality of life for these members, having a positive effect on the other family members as well.

Reference [19] presented an ecosystemic approach based on GST in counselling and psychotherapy sessions for special education children. The authors investigated the relationships and experienced feelings in stressful situations by the parents and teachers participating in their study, in order to get a better insight of various parameters, aspects, mechanisms and procedures of the issue discussed. The therapeutic intervention proposed in their work is suggested to be used as a tool to enhance teachers' understanding of the interactional processes in which they participate daily.

Reference [20] tested the "relationship of Communication Deviance in adoptive parents with adoptees having a high or low risk of schizophrenia in relation to the attributes of the adoptee and the adoptive parents themselves" on a GST base. Characteristics and parameters were checked and associated with different variables in a Finnish families sample. The findings of the study suggest that communication deviance can serve as an indicator for preventive interventions in the context of a child's development and health.

Reference [21] proposed a conceptual model for neurodegenerative diseases based on GST, considered to be "optimally suited to bring rapid changes in the current paradigms of discovery and validation of markers and therapy development". They identified that in order to validate such models for a multigenic diseases, the following three approaches are required: (a) identification of all key etiologic components, (b) understanding of the sequence interactions of crucial events, and (c) development of multiple strategies aimed at preserving/maintaining the functionality of the system. In the case study of Alzheimer's disease, the developed predictive models and biomarkers' patterns in conjunction with the identification of biochemical pathways were shown to provide the targeted therapeutic strategies for Alzheimer's disease treatment. This was achieved by enumerating and quantifying phenomena by means of integrated omics-based platforms and then by bioinformatics and statistical analyses. As per authors' suggestion, the use of GST should be encouraged for the understanding, conceptualization and operationalization of sub-systems and related mechanisms for major diseases, such as the Alzheimer's disease.

Reference [22] investigated the BPS model in psychogenic non-epileptic seizures as far as their biological and biomedical factors are concerned. Their retrospective, cross-sectional design included 689 patients from the Ohio State University and the data gathered were categorized into biological, psychological and social domains. This data recording allowed a better understanding of the seizures, however, the authors recognized that it was limited as far as both the cause and the effect of the factors were concerned.

In [23] there is a discussion on whether GST is fully exploited in the biopshychosocial model for mental health, introduced by Engel in 1977, as the latter "has failed to achieve what it set out to achieve". However, it is also mentioned that GST allows "multi-perspectival conceptualizations of any given mental health problem and multiple points of intervention, as well as a degree of freedom on the part of both the clinician and patient with respect to giving more or less preference to any given modality of treatment".

Reference [24] revisits the personality systems framework based on GST and systems thinking. Mayer recognizes the limiting nature of GST to describe the universal principles of systems, due to the uniqueness of each system. Therefore, Mayer develops the theory of personal intelligence along with the four domains of the personality framework (identification of personality, its parts, its organization and development) based on systems thinking, and argues over its advantage to better understand and navigate the personality domain.

Reference [25] examined the biobehavioural family model, which belong to the BPS family within a national representative sample of adults in the United States of America. They also tested the allostatic load as a physiological measure of the biobehavioral reactivity construct. The researchers found out that objective/physiological and subjective/emotional reports of biobehavioral reactivity were best measured as two distinct factors, as they have initially hypothesized. Moreover, they confirmed that by using a best-fitting measurement model, the pathways between variables identified were mostly correct.

The theoretical framework presented in [26] is based on family systems theory, an extension of GST. The study examined whether the behavioural health of adolescents aged 11 to 17 years' old who were involved with child welfare systems can be assessed with caregiver characteristics and family processes. Characteristics and baseline variables were used from previous studies, from which the control variables occurred, while dependent variables were assessed during the study. The final results were multivariable relationships leading to separate behavioural health models. The overall analysis contributed to a better understanding of factors affecting the caregiver-child relationships and interactions.

3) NURSING

The systems biology, an extension of GST, is proposed to be included in the nursing science in order to advance the mission of the National Institute for Nursing Research (NINR) in [27]. Suggestions towards use of inter-disciplinary teams, experiments design and interventions simulation are made to address the complexity, synthesis, modeling, and dynamics of the evolving systems biology framework and advance healthcare provision.

Reference [28] used GST and BPS for structuring the training of the nursing leaders in patient-centered practices on a medical ward. The results of their training showed an improvement in knowledge and self-efficacy in nurses. In continuation of this study there was the work of [29] where an updated comprehensive, evidence-based curriculum was constructed with recommendations for mental health and psychosocial training for internal medicine residents. The problem identified in the study was the lack of attention to patients' psychosocial and mental health problems. The developed models to address it were specifically behaviorally-defined, with some additional subset models in order to cover more areas. Application of these models in two general medicine faculties has been successful, leading to further training for the provision of improved care.

In [30] an integrative framework for nurse absenteeism and turnover in hospitals was adopted from a multilevel perspective. The introduced JOINT (Job, Organization, Individual, National and inTerpersonal) model relied on a systemic analysis of reviewed variables in the same study along with a multi-level perspective. Micro- and macro-levels of interactions inside the proposed system can be used as a guiding framework by all interested stakeholders for investigating and managing attendance behavior in organizations.

Reference [31] described a variable restrictive framework based on GST for Nurse Residency Program in the United States. The proposed framework was adapted from on an earlier work of [32] which was also based in GST. The framework identified system-specific attributes and offered potential relationships among these attributes as these relate to patient outcomes. The outcomes of the study underscore that there is great variability among nurse residency programs and should a nurse decide which to choose, they should take into consideration the different variables of them.

Another GST-based conceptual framework was adopted in [33]. A systematically developed planned teaching program to help future nurses was designed to inform 60 adolescent girls in Mangalore about water-birth, including information about criteria, preparation, benefits and labour care. However, there are limited information regarding the GST methodology followed in this paper.

Founds revisited her theory showing the intersection of big data and prediction medicine with the systems biology with the P4 medicine [34]. This further enhances the application of it in nursing research, education, and practice, so that it can apply ongoing developments in omics and big data to a holistic precision health framework.

Reference [35] examined the nursing process as a GST framework. The authors proceeded with a descriptive non-experimental design to select the wards of the Lagos University Teaching Hospital and apply a questionnaire on application of nursing process and its affecting factors among nurses. It was found that application of nursing process yielded overall positive attitude on behalf of the nurses and it was suggested that hospital management keeps an active role in maintaining such processes.

4) PUBLIC HEALTH AND HEALTHCARE SERVICES

In [36] a parent-focused participatory intervention to promote physical activity in preschools in Germany and the procedures used to evaluate its effectiveness were designed along the GST framework. The proposed intervention was suggested so as to evaluate public health interventions in the pre-school context. A two-armed, controlled cluster-randomized trial ran among 37 South-German preschools, with the preschoolers' parents as the primary target group, including also the entire preschool community (parents, teachers, children, peers) as potential agents of behavioural change. Using a mixed-methods evaluation strategy after the trial enabled insights into factors that were seen as barriers or facilitators to successful implementation of the intervention suggested by the researchers.

Reference [37] presented the suitability of GST models for neonatal intensive care units, and proposed their theoretical model, which identifies mediating factors (i.e. family centered and developmental care) and medical/neurobehavioral outcomes. In their approach they compared the infant outcome in an open-bay versus a model-applied care unit along with their expected results.

Reference [38] used a GST-based cross-sectional and self-administered survey to describe the school environment and the teacher-led nutrition education instructional process in New York State's elementary schools in selected countries. 137 teachers participated in order to identify and describe the nature of the teacher-led nutrition education offered, along with a variety of factors that influence the scope of nutrition instruction in the classroom. As "school environments are mediated by federal, state, and district policies, community characteristics, school characteristics, and teacher characteristics", GST provided a snapshot of the underlying issues influencing ethnic and public health in the United States.

A stage-state approach to categorizing observational and quantitative data was presented in [39]. A five-stage maturity model was presented as a way to identify common sequences or patterns of response to health-related emergencies or disasters. The systems-nesting character (a GST attribute) of local public health agencies led to increased demands for information reporting and dissemination. The model which was introduced to pilot sites "demonstrated that adaptive responses by local health departments to emergencies can be documented by measuring internal organizational subunit deviation from normal day-to-day activities", improve preparedness planning and response management and lead to more refined understanding of underlying mechanisms of adaptation.

In [40] the need for a communication model based on GST was pinpointed. The suggested model aims to empower patients (children with long-term or life-threatening conditions) and their parents with knowledge regarding the healthcare system and the healthcare professionals to identify the specific needs of the individual patient. The proposed approach should also include economic, social and care-related services, putting the patients in its center in order to address their needs more effectively.

Reference [41] reviewed the biopsychosocial (BPS) model, where the physician integrates data from the human or psychological level with information from the biological and social level to construct the BPS description of each patient. The authors suggest a transformation of the general model into a specific model for each patient encounter, via a behaviorally defined, evidence-based interviewing method, as described in their paper.

Reference [42] presented "an illustration of how population-level dynamic models can be used to explore the complex causal pathways through which interventions influence population health trajectories" based on GST and other systemic approaches. The simulation models produced were used to explore alternative scenarios and demonstrate the impact of social determinants, important population health risk factors and health outcomes in the city of Toronto, Canada. For public health policy purposes this model can be used as a simulation tool for broad-based strategic analysis at a high level of abstraction and aggregation, along with the general trends associated with broad-based intervention tradeoffs for high-level strategies.

GST and information-processing theory are combined in a conceptual framework on interfaces in modular services, and more specifically long-term elderly care in [43]. Ten different types of interfaces were examined. These included continuous needs assessment, established communication lines, customer meetings, product books, pre-combined elements, planning rules for safety and smooth flow, organizational arrangements, work schedules and carrier dossiers. Their characteristics were used to form a typology in modular healthcare services. Authors identified also limitations in the generalizability of their framework, lacking external validity, however due to the nature of healthcare systems this can be further researched.

Reference [44] used quantitative instruments for preschool environment rating as templates for defining seven GST and Social Learning Theory domains of friendliness towards Physical Activity in German preschools. A multilevel model was built with covariates, followed by a descriptive analysis, with a final aim of developing an item battery for physical activity assessment. Authors concluded that a more comprehensive survey would enhance the importance of their approach.

In [45] GST is applied to a model designed to address end-of-life care barriers. The GST framework is applied to a practice program model, which aims to give the reader a better understanding of how the changes happening inside the systems defined influence several barriers regarding the end-of-life care. GST is also discussed along the framework of Symbolic Interactionism and how these two complement each other.

Reference [46] does not use a GST framework, rather than works towards defining one to identify the systemic vision for the Brazilian healthcare system. The qualitative study performed helped the researchers to identify the needs, perspectives and more specifically the interactions and relationships between patients, managers and health professionals as far as patient safety is concerned.

Reference [47] presented a possibilistic regression model for representing a GST framework for occupational health and safety management systems (OHSMSs) in Malaysia. The authors claimed that the implementation of possibilistic regression based on the convex hull approach can prove highly appropriate for analysis of the OHSMSs influential factors, and augment the related decision-making procedure. Their study can be seen as another visualization and outcome explanation method for policymaking.

5) HOSPITAL

Reference [48] used GST for a causal-loop diagrammatic and system dynamic approach for an N-echelon hospital supply chain. This structure consists of a collection of hospitals, distributors, and manufacturers in order to evaluate the impact information sharing has within a hospital supply chain. Their results suggest that the utilization of cloud-based information sharing in hospital supply chains may have several positive effects, such as inventory visibility, reduction in average inventory levels and variability, and improvement of customer service.

6) MUSCULOSKELETAL CONDITIONS

In the work of [49], GST was among the building principles in an evidence-informed approach for the prevention and management of the osteoarthritis case in the Australian WorkHealth Program Initiative. A program logic model for such a complex and multidimensional intervention was selected as the most appropriate to be presented to relevant stakeholders. The methodology and principle framework developed within the study may be further enhanced by evidence and evaluation supporting the implementation of such complex interventions.

A GST-inspired conceptualization of a Bone-Marrow/Hematopoietic stem-cell transplantation patient and their partners was explored in order to examine the dyadic adjustments of the patients and their caregivers in [50]. The model derived from the study was tested over a course of a 12-month treatment trajectory. After its completion, the results were consistent with the theoretical framework. There were, however, several restrictions including it not being able to use all available variables that could affect the relationships and behaviors of involved actors, as well as geographic and demographic-related issues.

The BPS theory was also described in [51] where it was found to be "well suited for public health and epidemiological studies on musculoskeletal conditions". One of the reasoning behind using the BPS theory was the selection criteria of variables used for the statistical models for musculoskeletal epidemiology. The wheel of causation was used as a conceptual model by the authors in order to integrate variables from the social, physical and biological environments of the host population. The main outcome of the study was to present another means of understanding the interactions between variables to enable researchers in the hypotheses' formulation as far as the musculoskeletal conditions are concerned.

7) IMAGING

Reference [52] applied GST in a mathematical sense for creating a hierarchical Bayesian model that provides subject and trial-specific estimates of precision-weighted prediction errors at different hierarchical levels of computation. They tested their model in computational fMRI studies of audio-visual learning and their findings indicated the importance of having precision-weighted prediction errors and their significance in the neuromodulatory transmitters' computational role.

Reference [53] developed a system dynamic simulation model for a part of the patient pathway of cutaneous malignant melanoma. The model describes the flow of patients from the appearance of the melanoma up to when it is diagnosed and can undergo treatment. From different values of population size and incidence, flows are distributed so that the volume in each of the suggested four categories can be determined. In order to build this GST-model, current research results and statistics have been adapted in a simulation model. The model had a positive reception by users, as the authors reported, "mainly for its ability to produce realistic results that can be based on flexible scenarios".

Reference [54] presents the VLC4WLIMES project, the goal of which is to realize the Wandering Logic Intelligence (WLI) and the Memory Evolutive Systems (MES) formalism in virtual oncology. The project aims to tackle current obstacles from a general system's perspective, since an oncology image is defined from different dynamics' perspective. Due to the fact that this is an ongoing project, no results were available and this work is better described as a position paper.

8) PHARMACOLOGY

Reference [55] describes how systems thinking applies in neuropharmacology medicine due to their multi-mechanistic features. The advantages offered by omics and computational models provide a systemic approach for biological and neuro-psychic related process, "incorporating the reality of a disturbed network of interactions". The review recognizes the role of GST in neuropharmacology and its promising outcomes.

The Quality by Design approach, a GST-based framework, and its applications upon the development of a dry powder inhaler and its overall clinical performance along with the interactions of it are presented in [56]. The authors provide a review regarding the application of the aforementioned approach and point out the missing elements to holistically understand the interactions and success of a pharmaceutical product.

Reference [57] gave an introduction to quantitative systems pharmacology, whose focus is to "provide a framework for integrating the synergies of low-level mechanisms to the high-level host defense mechanisms, and eventually the broader environmental and behavioral signals external to the host". The concepts and models presented in their chapter give options to researchers to explore complex clinical scenarios by mechanistically describing drug behavior at the tissue/organ level and at the molecular level.

C. SYNTHESIZED FINDINGS

Following the analysis of the characteristics of each article, the following table has been constructed in order to identify the effect of GST and its derivatives on the healthcare field. Table 1 also lists the research methodology followed in each practical application of GST and the healthcare field it refers to.

We can see from Table 1 that 22 out of 47 studies (46.8% of the corpus) presented a conceptual and theoretical model of GST and/or its derivatives, while 25 studies (53.2% of the corpus) offered a conceptualization method for GST frameworks. The most common field of application is mental health (10 studies) with healthcare/hospital-related services following (8 studies). Nursing has also a significant amount of research interest (7 studies), while public-health related issues are explored in 6 studies.

TABLE 1. Studies categorization.

Study	Practical Application of GST	Research Methodology	Healthcare Field
[10]	No	-	Health in general
[18]	Yes	Cross-sectional Study	Mental Health
[27]	No	-	Nursing
[19]	Yes	Case study	Psychotherapy
[36]	Yes	Cluster-randomized Trial	Physical Activity / Public Health
[49]	Yes	Case study	Osteoarthritis
[11].	No	-	Chinese Medicine
[37]	Yes	Randomised Control Trial	Neonatal Care
[20]	Yes	Cross-sectional Study	Schizophrenia
[28]	Yes	Longitudinal Study	Nursing education
[47]	Yes	Simulation modelling with real-time data analysis	Occupational Health and Safety Management Systems
[12]	No	-	Personalised Medicine
[13]	Yes	Case Studies	eHealth
[21]	No	-	Neurodegenerative Diseases
[38]	Yes	Cross-Sectional Study	Nutrition Education
[14]	No	-	Clinical research
[39]	Yes	Pilot study	Public Health
[50]	Yes	Longitudinal Study	Mental Health
[15]	No	-	Health Protocol
[40]	Yes	Case study	Health care services
[41]	No	-	Medical Interviewing
[51]	No	-	Musculoskeletal Health / Epidemiology / Public Health
[52]	Yes	Cross-sectional Study	Neuroimaging, fMRI
[42]	Yes	Simulation Model from population data	Public Health
[30]	No	-	Nursing
[31]	Yes	Cross-sectional study	Nursing
[43]	Yes	Case study	Elderly Care
[33]	Yes	Pilot study	Childbirth, Nursing
[44]	Yes	Mixed-methods study	Physical Activity, Public Health
[22]	Yes	Longitudinal study	Non-epileptic and Pseudo-Seizures
[29]	No	-	Mental Health
[23]	No	-	Mental Health
[24]	No	-	Psychology
[25]	Yes	Cross-sectional study	Physical/Mental Health
[53]	Yes	Simulation Modeling based on patient data	Skin Cancer
[45]	Yes	Case study	End-of-life care
[55]	No	-	Neuropharmacolog y
[54]	No	-	Virtual Oncology
[26]	Yes	Longitudinal Study	Mental Health

TABLE 1. ***(Continued.)*** **Studies categorization.**

Study	Practical Application of GST	Research Methodology	Healthcare Field
[16]	No	-	Biomedicine
[56]	No	-	Pharmacology
[34]	No	-	Nursing
[48]	No	-	Hospital
[57]	No	-	Pharmacology
[17]	No	-	Physiology
[46]	No	-	Patient Safety
[35]	Yes	Non-experimental Study	Nursing

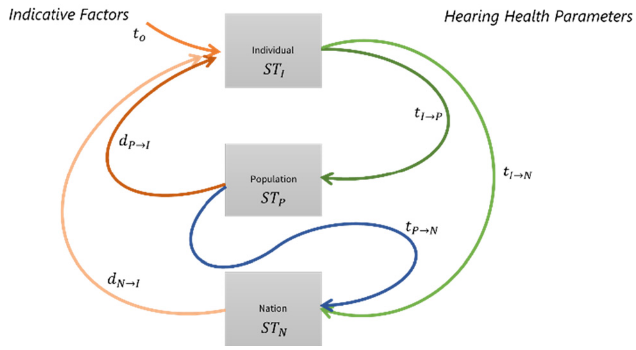

FIGURE 2. **Progressive (over time) and interactive (between patient, population and nation) diagram of factors affecting hearing health parameters in a GST-framework.**

The main research methodologies followed in each recognized practical application of GST from the selected papers were implemented via:

- a cross-sectional study in: [18], [20], [25], [31], [38], [52]
- a longitudinal study in: [22], [26], [29], [50]
- a mixed-methods study in:[44]
- a case study in: [13], [19], [40], [43], [45], [49]
- a pilot study in: [33], [39]
- a randomized trial in: [36], [37]
- a non-experimental study in: [35]
- a simulation based on real-world data: [42], [47], [53]

The core dimensions and findings of the selected articles provide a rich basis for the elaboration of specific issues. In the next section, we discuss the limitations and positive aspects of the GST application based on the findings of the research methodologies followed in these articles.

IV. SUMMARY OF MAIN FINDINGS FROM REVIEW OF CURRENT LITERATURE

A. SUMMARY OF MAIN FINDINGS

Empirical and theoretical analyses of system-approached environments show that evidence and interpretation of relationships, patterns and interaction among components play a significant role in understanding a system as it is, as well as how it works. The complexity of phenomena occurring in and out of a system, whether it is a human body [54], a family [26], a preschool [44] or a whole country [42] depend on the view and the limitations of the observers. Not only in the previous articles, but in every article chosen for this review, did the authors try to classify and identify systemic features, operations, interactions and relationships, where previous theories or models failed to provide an explanation or an objective assessment of a system's structure and functionalities.

A full-text analysis of all articles, giving more weight to the ones presenting a practical implementation of a GST framework, showed two main limitations and two major positive aspects of GST in the healthcare field.

1) LIMITATIONS

- Although the framework of GST is full of promising elements for its future implementation in the healthcare field, the identified approaches on this field were found to be restricted as far as their scope was concerned. It is a common characteristic in the majority of the articles chosen in the current review that their authors consider the application of their proposed framework limited regarding the generalizability of the findings. This can be seen not only in conceptual models like the one in [46], but in practical models as well, like the ones proposed in 38] and [48]).
- Another restricting factor identified is the availability of data used to examine the potential influences of variables (e.g. in [25]) or the data size used (e.g. in [31]) limiting the understanding of how some effects occur in a relational context within a systemic approach.

2) POSITIVE ASPECTS

- On the other hand, use of simulation techniques based on real-time data has been proven to work and exhibit promising results as far as the applicability of GST in healthcare is concerned. For example, in [53] users found "positive the ability to produce realistic results that can be based on flexible scenarios", while users in [42] were enabled to "to identify, assess and develop effective policy alternatives to advance health equity" using the simulation scenarios.
- Moreover, GST and its derivatives offer a vast field of hypotheses testing where researchers can explore and realize essential attributes, relationships and interactions in previously unknown environments, thus getting a new insight on these systems. Characteristically, [51] propose the BPS model to explore the relation between back pain and smoking among other variables, while [56] suggest a framework (Quality by Design) to enhance and alter the dry powder inhaler development, embracing all the necessary knowledge and not conforming strictly to guidelines.

To tackle existing limitations and further enhance the positive aspects of GST in the healthcare field, we suggest a further integration of big data analytics and simulation models to understanding contemporary systems

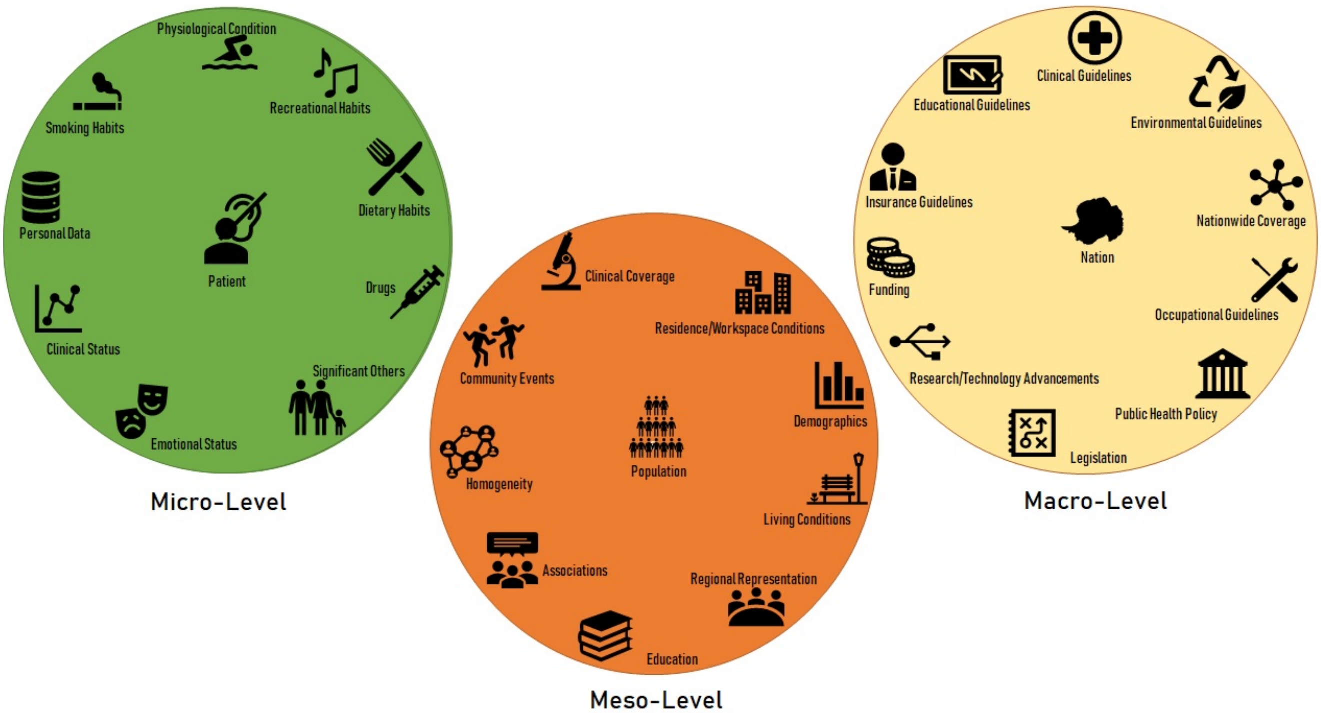

FIGURE 3. Indicative data requirements for patient, population and nation-level (micro, meso and macro-level) in a proposed GST-framework applied in Hearing Healthcare.

from a multi-perspective view. Evidence-based approaches on a micro-, meso- and macro-level need to be embedded in the conceptual and actual frameworks. At the same time, the need to reproach the epistemological and foundational concept of each health-associated system and provide an empirical knowledge base with direct reference to the environment, as this is defined by any observer to the system, will provide a hierarchy of systemic levels. This can be achieved when all relevant actors (e.g. organizations, patients, clinicians, public health policy makers and data scientists) identify and share their perspectives and observations, as these actors may be seen to play both an internal and external role to the system. It is the critical awareness and the methodological framework that should be maintained in order to give GST an action-framework, where the relational character of each system will lead to a further understanding and mapping of the components, interactions, relationships and patterns within a future healthcare concept.

B. LIMITATIONS

Limitations of the existing review are hereinafter mentioned: Not all existing electronic databases were used for the identification of potentially eligible studies. Only English-language articles were used, therefore articles in other languages have not been included, limiting the size of the corpus. Finally, the selection of studies for inclusion in the meta-analysis was based on quality and not on quantitative criteria, due to the nature of the GST framework.

V. APPLICATION OF A GST-FRAMEWORK IN HEARING HEALTHCARE

The evidence on how to link information related to the management of hearing loss healthcare onto appropriate, individualized management strategies is still lacking, particularly because treatment of hearing loss requires a better understanding and prediction of the challenges that hearing loss affected individuals face in different environments. This comes as a result of several factors beyond the sound characteristics of such environments, including, for example, the activities that individuals directly engage with or are faced with in these environments and other physiological, cognitive and medical conditions that they may have. Applying a GST methodological approach to the hearing healthcare system and given that a "system is a set of elements standing in interrelation among themselves and with the environment", we first have to construct the micro-, meso- and macro-perspectives of the system's related data. Information and material (i.e. data) in these systemic model-objects should characterize them from a "higher order statistics" point-of-view. The data presented in Fig. 3 are indicative and can be expanded or modified according to the sociological, geographical and cultural aspects of a viewer. However, they are all deemed necessary, as there are currently no longitudinal systemic data of hearing-affected patient cohorts, where patients can be seen as an "active personality system" opened to and affected by their social, cultural and material environment, which feeds on it in order to structure itself progressively, while remaining far from an "equilibrium" state. This approach can be also extended to other fields of healthcare.

The first level is the micro-level which identifies the patient(s) as a system. The hearing data management approach of the patients are affected by their particular identity (e.g. personal, emotional and physiological data) and their interactions with other people (e.g. recreational activities, presence of significance others). The meso-level approaches a population (e.g. a patient cohort or a target group) in a similar manner. The GST approach in the meso-level pertains to the performance (e.g. education levels), structure (e.g. homogeneity) and behavior (e.g. patient associations) of a national or regional group of people. Finally, the macro-level treats a whole nation or a country as a system consisting of structures and communication (both internal and external) between public-health, clinical and business entities.

These micro-, meso- and macro- data collected over a period of time, provide a quantitative analysis of their nature in order to introduce expressions in a statistical form that can construct their relationships. By following a GST approach, we allow the possibility to unify hearing related phenomena not yet observed via a number of corroborating cases and settings which are independent of any model. Recent projects in the hearing healthcare field indicate the need for such data from a clinical and public health policy point-of-view [58], [59] to develop and promote quantifiable measures to assess and improve the quality of hearing healthcare services. Moreover, they will improve the compatibility and interoperability of hearing technologies with communications systems and the affordability of hearing healthcare services across federal, state, and private sectors. The evaluation and implementation of such a GST approach in hearing healthcare and public hearing policy will most likely improve access, quality, and affordability of services.

At the same time, it will promote individual, population and nationwide-based actions to support and manage hearing health and strengthen effective communication among all levels (Fig. 2) in a progressive and interactive manner.

Nomenclature for Fig. 2

$\boldsymbol{t_0}$: timepoint when an indicative factor affects an individual

$\boldsymbol{ST_x}$, ***where*** $\boldsymbol{x = \{I, P, N\}}$: transitional timeframe for a factor to be identified as parameter affecting hearing healthcare

$\boldsymbol{t_{x\to y}}$, ***where*** $\boldsymbol{x = \{I, P, N\}, y = \{I, P, N\}, x \to y = \{I \to P, I \to N, P \to N\}}$: timeframe over which a parameter affects another subsystem (used as input to another system)

$\boldsymbol{d_{y'\to x'}}$, ***where*** $\boldsymbol{y' \to x' = \{P \to I, N \to I\}}$: timeframe over which a parameter from an upper subsystem affects a lower-level system.

At this point, it should be noted that the aforementioned timeframes might not be mathematically interrelated with each other, i.e. relations like: $t_{I\to P} < t_{P\to N}$ are of relative nature and can only be assessed if data regarding these timeframes exist and can be applied when the timeframes are defined. This is due to the causality characteristics of the systems involved, as there is no effect without a cause. The suggested timeframes can be scaled to time instances (e.g. day) or even time periods (e.g. 4 years) and indicate when and how fast a cause (indicative factor) affects the state of a system (ST_x) and produces an effect (hearing health parameter) on another system ($t_{x\to y} or d_{y'\to x'}$). For these purposes we should also define a pointer j *with* $j = 0, 1, 2 \ldots,$ which points the number of cycles in one feedback where the applied effect takes place: $ST_{jx} \to ST_{(j+1)x}$ There might be a case of an indicative factor for example that takes two feedback cycles among an individual and population system before it has an effect on the national system.

The proposed concept can be considered as a vector of each subsystem for the aggregated timeframes the subsystem spends in a state, while changing its influence towards other subsystems. By using two different symbolisms (t, d) we take into account the time differences of when a system of a lower or upper level affects another subsystem. For example, individual-related factors might affect a population in a shorter time ($t_{I\to P}$) than the time it needs for the feedback mechanism from the population's side ($d_{P\to I}$) to introduce a new indicative factor to the individual system. Fig. 4 shows an indicative example of how the introduction of new factors into a subsystem is analyzed into relative timeframes to take into account the overlapping changes of the internal states of the subsystems of the general system.

Moving from point ($t_0 \to t_1$) on the time axis (OO'), we can identify a majority of changes happening inside and across the various subsystems of the proposed general system. Let us assume that initial states of the subsystems are $ST^0_{I,N,P} = [ST_{OI}, ST_{OP}, ST_{ON}]$.

At t_0 new hearing test is introduced to patients via a clinical trial at t_0. $ST_{1I} = (OA)$ is the time indicated by points O and A, where any changes happen inside the micro-level ($ST_{0I} \to ST_{1I}$). During that time no changes occur in the meso- or macro-level. After timepoint A, results might have indicated that a certain treatment should be proposed to these patients.

Following the treatment initiates a transition from $ST_{1I} \to ST_{2I}(AA')$, which is internal (it only happens on subsystem, I). After these changes take place in timepoint A', results show that larger groups of population (e.g. a specific group of patients with certain characteristics, such as tinnitus patients) could benefit from such an evaluation/treatment option. This is communicated ($A'B = t_{I\to p}$) and applied on a population level (B) . Changes happening at this meso-level occur from B to B' ($ST_{0P} \to ST_{1P}$), while the other subsystems retain their condition (patients are at ST_{2I} whereas nation is still at ST_{0N}).

The feedback (e.g. adjustments in treatment, introduction of new factors) provided by the application of such options on a population level is then communicated both to the patients in $(B'C) = d_{P\to I}$ time and the national stakeholders in $(B'D) = t_{P\to N}$ time. These two flows might have begun at

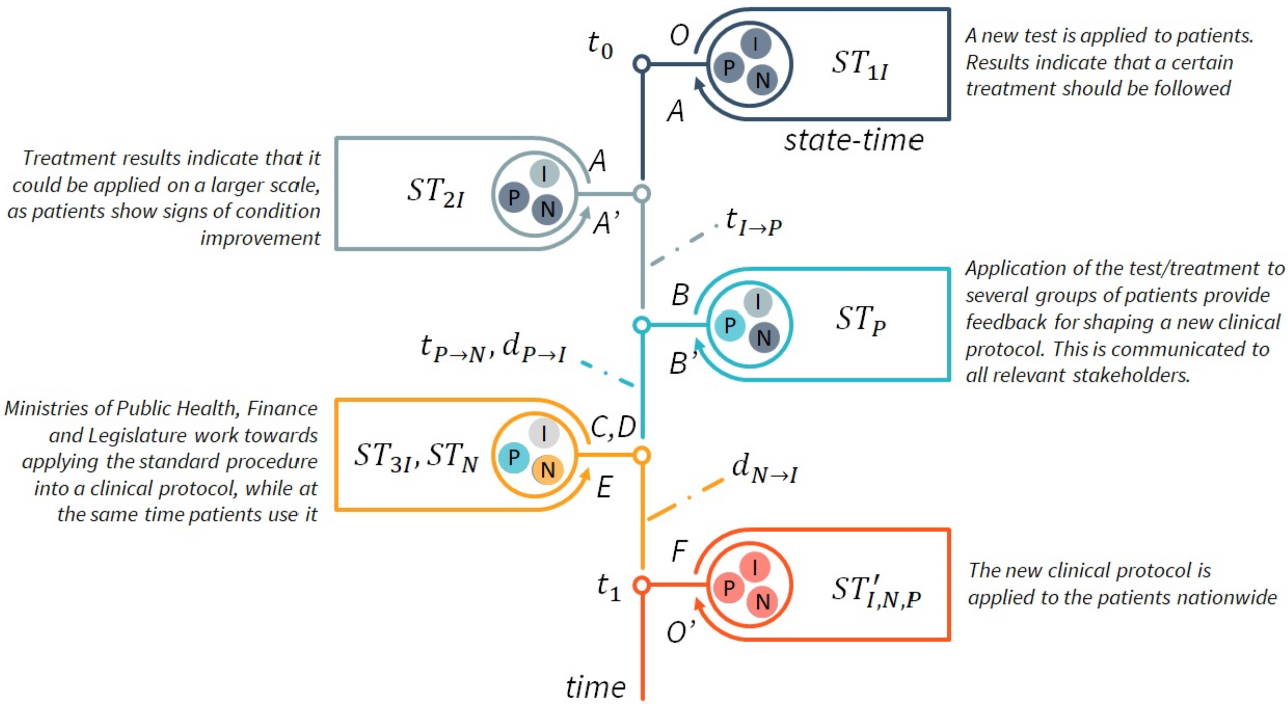

FIGURE 4. **An indicative timeseries analysis of the changes happening inside the proposed general system to identify the nature of the systemic phenomena.**

the same time, but their duration might be different, without the latter point being restrictive in any form. Supposing that government officials start working on applying the findings into a new clinical protocol, we have a status change in national level $ST_{0N} \rightarrow ST_{1N}(DE)$ and on a patient-level $ST_{2I} \rightarrow ST_{3I}(CE)$. E signifies the timepoint where the application of the new protocol takes place and is standardized $(EF) = d_{N\rightarrow I}$, leading the general system into a new state (with its subsystems at the following states: $ST'_{I,N,P} = [ST_{3I}, ST_{1P}, ST_{1N}]$ at t_1.

An example of GST Approach in Hearing Screening:

In order to show the possibilities of a GST-framework in hearing healthcare, an indicative example of GST applied in hearing screening will be presented.

Hearing screening is reported to "require better understanding of its longitudinal and indirect effects, alongside effective management and appropriate early identification programmes" [60]. Starting from universal newborn hearing screening [61] there is a need for an increase in the number of missed follow-up appointments and closer cooperation among healthcare units for the elimination of unnecessary tests and assurance of proper interventions. Hearing screening of preschool children has been known to suffer from "a lack of primary data and the variation in the variables used in modelling" [62] while there is also a "need for authorities to work together with health professionals to introduce hearing screening in areas where it is lacking" [63].

From a mathematical point of view and based on the mathematical foundations for GST [64] a general system for hearing screening (**HSGS**) can be defined as a pair of internally ordered sets $(\boldsymbol{M}, \boldsymbol{R})$. In such pairs, $\boldsymbol{M}$ is defined as a homogeneous set of system objects (e.g. M may refer to Individual, Population or Nation), while $\boldsymbol{R}$ is the set of relationships between elements of M, with respect to the content of information, the spatial structure and the various forms of interactions within the hearing screening system (e.g. relationships in the Population system object are $\boldsymbol{R_p}$). Equation (1) gives an overview of the mathematic formulation of such a system:

$$\mathbf{HSGS} = \begin{bmatrix} (\boldsymbol{M_I}, \boldsymbol{R_I}) \\ (\boldsymbol{M_P}, \boldsymbol{R_P}) \\ (\boldsymbol{M_N}, \boldsymbol{R_N}) \end{bmatrix} \quad (1)$$

The pairs and their respective relation sets, as seen in Equation (1) can be defined as follows (Table 2) along with some examples of these sets based on recent hearing screening bibliography:

Based on the aforementioned assumptions, a GST approach in hearing screening can be described as such:

1. Stocks indicate the elements of the system, which change over time and include the population of interest, risk population, treatment target and healthy populations.
2. Information-based relationships (flows) are signified by a 'drip-counter' icon and include the screening examinations, the evaluation of the condition and the treatment options offered, as well as the cognitive and functional assessment examinations
3. The purposes of the screening system are (a) to assess the hearing functionalities of the population and (b) have a

TABLE 2. General system sets and relation sets based on recent bibliography.

(set, relation set)	Definition of sets	Example sets
(M_I, R_I)	M_I: individual/patient-related R_I: relations concerning patient systems	Individuals (I) Hearing Screening Tests [65], [66] e.g. based on [65] we have: $(R_I) = (Pass\ when\ results\ of\ hearin$ $10-24)$
(M_P, R_P)	M_P: population related set R_P: relations concerning population systems	Preschool Children (P_1), Adolescents (P_2) Adolescent, Preschool Screening Examinations [63], [67]–[70] e.g. based on [67] we have $R_P = (Age$ $\leq 4\ less\ able\ to\ test, Age$ $> 4\ likely\ to\ pass, ethnicity\ d$
(M_N, R_N)	M_N: nation-related set R_N: relations concerning national systems	Newborn (N) Universal Hearing Screening Examinations [71]–[75] e.g. based on [75] we have: $(R_N) = (Pass\ Weight$ $= 2697.6 \pm 795.7g,$ $Pass\ Age$ $= 37.9 \pm 2.7\ weeks)$

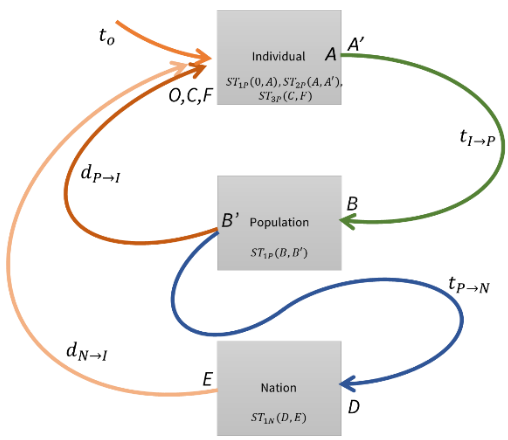

FIGURE 5. Time-points of reference based on Figure 3.

functional (e.g. cognitive-, speech-, social- and learning-enabled) population based on (a).

An initial version of the HSGS is depicted in Fig. 6 and can be read as such:

1. The population of interest (e.g. newborns or adults) is increased by any incoming member (e.g. a birth of a child or an adolescent turned into adult)
2. Screening examinations (e.g. otoacoustic emissions, auditory brainstem response or other type of tests identified in the relation sets of current bibliography in Table 2) are used to identify the hearing condition of the population and assess their capabilities.

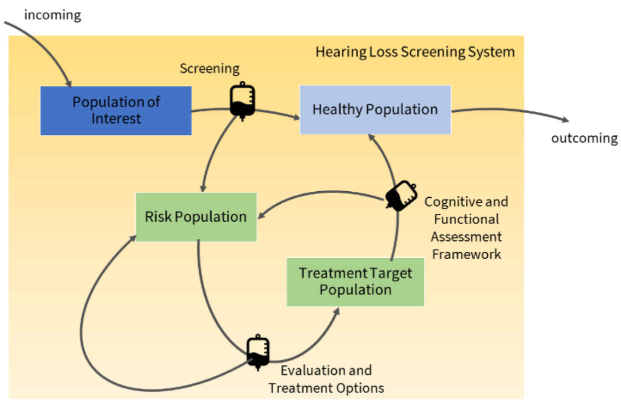

FIGURE 6. Initial view of the hearing screening general system.

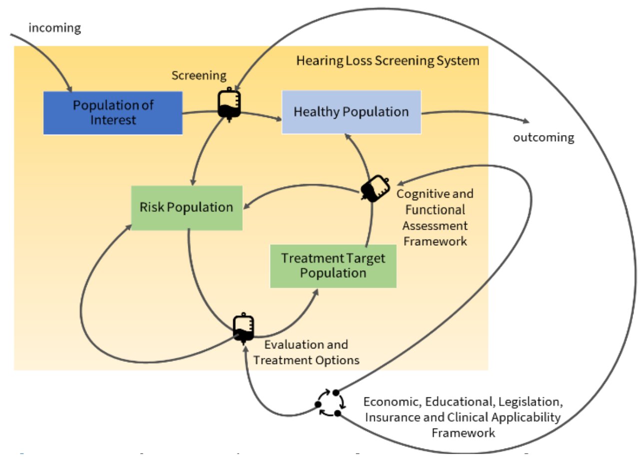

FIGURE 7. Modified view of the hearing screening general system.

3. Based on the results and the effectiveness of these screening tests, members move either to the healthy population (which consists of functional members) or to the risk population for further examination
4. The risk population is evaluated of their condition (e.g. by follow-up visits or more thorough examinations) and they are being suggested of treatment options (e.g. no treatment, hearing aids). From that point onwards the flow directs the members of the risk population either back to it (feedback loop) or to the treatment target population.
5. Treatment target population gets reassessed based on their cognitive, speech, social and learning capabilities to identify whether the treatment has been successful or not and at what level. Should these capabilities be assessed, a member may return to the healthy population, otherwise it returns to the risk population (step 4).
6. The healthy population is reduced by the number of its outgoing members (e.g. a death or aging of its members)

Identifying a hierarchy H over time T among different timestamps of the hearing screening system (as neonates turn into children and adolescents, who then turn into adults)

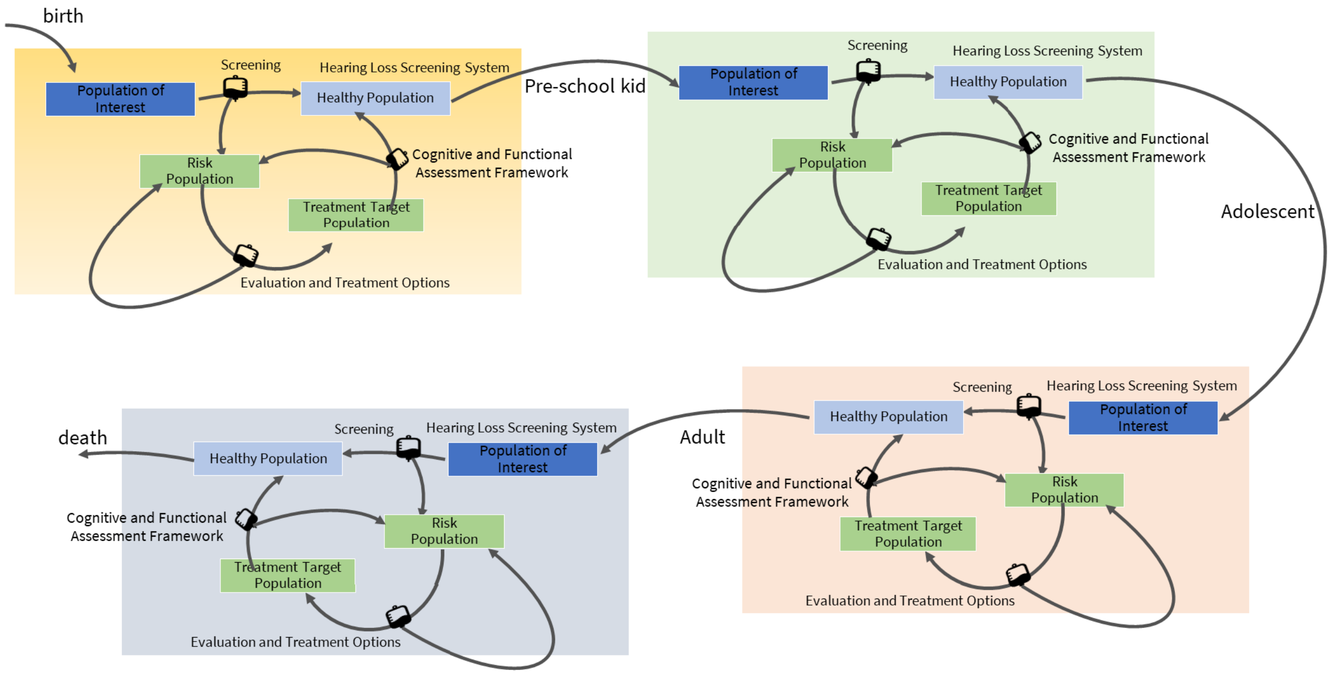

FIGURE 8. **In-series connection of the proposed *HSGS* over the lifetime of a patient (micro-scopic view).**

creates a linked time system:

$$\{H, m_s, T\}, \quad where\ s = \{N \rightarrow P_1, P_1 \rightarrow P_2, P_2 \rightarrow I\} \quad (2)$$

where m_s is the mapping from a macro- to meso- ($N \rightarrow P_1$), a meso- to meso- ($P_1 \rightarrow P_2$) and finally a meso- to micro- ($P_2 \rightarrow I$) view of the system respectively. Since the above sub-systems are group-related (neonates, children, adolescents and adults), the mapping m_s from one system into another imply a homomorhpism among these systems, especially if m_s corresponds to a behavior over time mapping, which is also the case here. This can also be seen taken from the time perspective of the patient lifetime (Fig. 8), where different instances of the HSGS are connected in series.

The above approach can be further extended and provide an indicative overview of how a general system model for hearing loss screening can be used for the prediction and assessment of its economic and social impact. For example, adding the economic/clinical framework as an external factor to the system (Fig. 7), we can see that it affects the evidence-based relationships for all stages (a better or worse clinical and economic status at any given time point affects the quality/quantity of the provided services). This is also reflected in current bibliography [76], [77] where the results of economic appraisal, cost-effectiveness analyses and economic assessments of costs and benefits related to newborn hearing screening appear to have played a decisive role to the adoption of related policies, proving it to be a cost-saving strategy compared with no screening. It is therefore safe to assume that introduction of such models can be used to identify equilibria when multiple interests are competing (i.e. public health policy and economic utility/viability of hearing loss treatment approaches) for actors to define their actions to balance gain and prediction capacity over time.

VI. CONCLUSION

The principles and the importance of considering relationships and interactions both among the components of a system and within a larger system-environment, is becoming a crucial issue over the last years, especially with the advent of the age of big-data. The organization, interaction and interdependence in a systems-oriented approach in the healthcare domain is getting more attention and shifts the interest to a holistic and dynamic point-of-view in different sub-fields. GST proposes a credible means and can be a driving force for the healthcare field, should it be applied in an evidence-based way.

The current paper critically reviewed existing GST approaches applied to the healthcare field, and highlighted the application of these approaches. Focus was given to real-world (practical) implementations of GST given the theoretical nature of GST. The paper identified 47 papers in total, where almost half of them had been applied in real-world settings. The research methodology followed in these papers helped us to identify both the limitations, as well as the positive aspects of GST application.

It is essential to note that addressing these limitations and focusing on the positive aspects of GST should gradually be incorporated into the healthcare field after excessive testing in simulations, model systemic environments, test systems and, finally, real-world experiments.

Building a knowledge exchange framework that acknowledges the reciprocity involved in developing evidence-informed interventions and carefully considers the needs of involved stakeholders, GST and its application will be directly relevant to the healthcare field. Therefore, simulation models and evidence-based approaches on a micro-, meso- and macro-level of under-research systems should be used to provide the contextual information needed for establishing GST as a driving force in the healthcare field of the future.

Based on the aforementioned points, a GST-inspired data framework is proposed for the hearing healthcare field, with an example given for the hearing screening management system. Based on recent hearing screening related papers, the key elements, relationships and purposes of a general hearing screening system have been identified. These were transformed into a GST point-of-view, indicating a paradigm change in how public health policy can transcend and be flexible at the spacious possibilities of evidence-based approaches. Practical interest in patient, population and nation systems along with information sharing and transmission mechanisms will allow the depiction and prediction of hearing-related phenomena in the arrow of time.

At this point of time, the specification of all individual relationships needed for the definition of such general system across time is not an easy task. We might often get glimpses of systemic elements, objects or relationships (e.g. via clinical or randomized trials and epidemiological studies), however we need additional data and information (e.g. meta-analysis, systemic reviews) as well as network modelling tools and techniques in order to construct such a complex concept. This combination of data and techniques from interdisciplinary approaches should be used to feed with information the elements of a general system, not only in hearing health but in other healthcare fields as well. The purpose of our paper is to show that the application and exploitation of data techniques in a very specialized and focused attempt can help to define the individual relationships, characteristics and interactions inside and outside a system towards its micro-, meso- and macroscopic validation.

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