Review

Evidence for the Domains Supporting the Construct of Intrinsic Capacity

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Abstract

Healthy ageing can be defined as “the process of developing and maintaining the functional ability that enables wellbeing in older age”. Functional ability (i.e., the health-related attributes that enable people to be and to do what they have reason to value) is determined by intrinsic capacity (i.e., the composite of all the physical and mental capacities of an individual), the environment (i.e., all the factors in the extrinsic world that form the context of an individual’s life), and the interactions between the two. This innovative model recently proposed by the World Health Organization has the potentiality to substantially modify the way in which clinical practice is conducted (3). Current models of care are designed to anticipate (through screening for specific disease biomarkers) or react to a disease when it is clinically manifest. In contrast, the healthy ageing approach is characterized by the longitudinal observation of the individual’s trajectories with the aim of supporting proactive and personalized interventions for the enhancement of capacities and abilities, independently of (i.e., all the factors in the extrinsic world that form the context of an individual’s life), and (iii) the interactions between the two (2).

This innovative model has the potentiality to substantially modify the way in which clinical practice is conducted (3). Current models of care are designed to anticipate (through screening for specific disease biomarkers) or react to a disease when it is clinically manifest. In contrast, the healthy ageing approach is characterized by the longitudinal observation of the individual’s trajectories with the aim of supporting proactive and personalized interventions for the enhancement of capacities and abilities, independently of

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clinical phenotypes. The core of this novel theoretical framework resides in the comprehensive assessment of the different domains of intrinsic capacity and functional ability. It is noteworthy that holistic approaches in the evaluation of older persons generate better outcomes compared to traditional disease-based model of care (4,5). At the same time, the model proposed by the WHO has great potential for supporting behavior modification toward healthy lifestyles by raising awareness about potentially deleterious declines in capacity, and empowering the individual to take earlier action as these become apparent. In fact, if the individual is enabled to understand and follow the trajectories of his/her health status (defined in terms of functions and personal values rather than as complex nosological entities), he/she may take responsibility for its maintenance at optimal levels.

However, before these concepts are translated into practice, it is necessary to define their constituent natures. In particular, the constituent elements of the central construct of intrinsic capacity have to be described in order to guide what to observe, measure, and monitor.

The purpose of the present article is to provide the framework for supporting the future assessment of intrinsic capacity in the clinical and research setting. Available evidence is used to identify and describe which health domains are the most useful for adequately and objectively measuring the individual’s intrinsic capacity.

Development of the Intrinsic Capacity Construct

As said, intrinsic capacity is the composite of all the physical and mental capacities of an individual. But which are the physical and mental capacities constituting intrinsic capacity? Which are these characteristics that can comprehensively describe the overall biological, personal, and psychological status of the individual?

The International Classification of Functioning, Disability and Health as Starting Point for the Framework of Intrinsic Capacity

In 2001, the WHO published the International Classification of Functioning, Disability and Health (ICF) (6). In this document, disability was described as the umbrella term for impairments, activity limitations, and participation restrictions. Disability denoted an impaired interaction of the individual affected by a health condition with contextual factors (both environmental and personal). The proposed framework (Figure 1) was constituted by multiple interacting elements determining the manifestation of the health status.

![Figure 1. The ICF model as basis for the development of the construct of intrinsic capacity. ICF = International Classification of Functioning, Disability and Health.](https://example.com/icf_model.png)

Moving the focus onto healthy ageing, the measurement of intrinsic capacity strongly promotes the transition from a reactive toward a preventive model of medicine. In fact, whereas the clinical manifestation of disease typically results in a medical alert and response, a reduction of intrinsic capacity (i.e., abnormal deviation of a trajectory) may lead to a remedial/recuperative intervention even in the absence of a specific clinical phenotype. Furthermore, the design of interventions based on multiple evaluations of the individual will be better tailored and more responsive to his specific needs and priorities.

Focus on Body Functions

The intrinsic capacity model is an evolution of previous WHO recommendations, namely the ICF framework (Figure 1) (11). As above discussed, the health conditions (i.e., diseases) included in the ICF model are clearly of limited interest for capturing the complexity of intrinsic capacity. Similarly, contextual factors are excluded from the construct of interest because part of the environment, interacting with intrinsic capacity for determining functional ability. Activities (i.e., the execution of a task or action by the individual) are also unsuitable as they are better considered as outputs of, rather than components of, intrinsic capacity. Thus, only the notion of body functions (i.e., the physiological functions of body systems) meets the defining criteria of intrinsic capacity as described in the
World Report on Ageing and Health (1). In fact, the interactions of the individual’s health characteristics (including pathophysiological patterns as well as health-related behaviors, traits, skills) determine his/her intrinsic capacity. If the individual’s body functions could be assessed and merged into a holistic entity, they might generate a powerful marker (i.e., intrinsic capacity) to track the individual’s health status and support proactive interventions with the aim of preserving function. In order to support this model, the intrinsic capacity definition should (i) optimally capture the multiple physiologival domains most influencing the health status of the individual, and (ii) feed the subsequent actions with insights about the components that more than others have determined the deviation of the trajectory in both quantitative (e.g., how much) and qualitative (e.g., how rapidly) terms.

Process Leading to the Identification of Defining Characteristics of Intrinsic Capacity

A nonsystematic literature review was conducted to investigate which body functions are more strongly determinant for the maintenance of independent and healthy life. In particular, special attention was focused at identifying those functions whose impairment was most strongly associated with incident functional loss and care dependence. The search of the evidence was made more definitive by including the list of body functions provided by the ICF. Analysis of the literature took advantage of the multiple and regularly updated systematic reviews exploring the risk factors for incident disability, functional loss, and/or care dependence in older persons. At the same time, the ICF body functions were individually searched in PubMed (updated up to February 2017) in combination with the keywords “disability”, “dependence”, or “functional loss” for retrieving potential articles of interest.

In 1999, Stuck and colleagues (12) conducted a systematic review of the literature aimed at measuring the strength of evidence linking different risk factors to functional decline in older persons. The study importantly contributed a few years later to the preparation of an evidence report by the WHO Regional Office for Europe (13). In particular, Stuck and colleagues (12) identified impairments in mood (i.e., depressive symptoms), sociality (i.e., participation in social activities), cognition, physical performance, homeostatic balance (i.e., weight loss, abnormal body mass index), and vision (i.e., reduced visual acuity) as strong predictors of care dependence. These results have been confirmed and consistently replicated in subsequent studies. Analyzing data from the Health and Retirement Study (n = 11,093, representing 34.5 million older Americans), Cigolle and colleagues (14) found that cognitive impairment, vision impairment, hearing impairment, and undernutrition were associated with activity of daily living (ADL) dependency. In 2010, Chaudhry and colleagues (15) reported that impairments in muscle strength, physical capacity, cognition, vision, hearing, and mood were found to be associated with an increased risk of incident mobility disability (i.e., severe difficulty or inability to climb 10 steps or walk ¼ of mile) and/or incident loss of ADL. More recently, a systematic review conducted by van der Vorst and colleagues (16) explored the risk and protective factors for the development of ADL limitation in community-dwelling older persons aged 75 years and older. After having screened almost 7,000 studies, the authors focused on 25 articles and identified a list of factors positively and negatively contributing to the disabling cascade. Here, several functions again emerged as predictive of subsequent onset of disability, in particular: social participation, mood, cognition, muscle strength and physical performance, body weight, nutritional status, hearing impairment, and vision impairment. Interestingly, similar results have also been reported from low- and medium-income countries. Data from population-based cohort studies conducted in Cuba, Dominican Republic, Venezuela, Mexico, Peru, India, and China showed that weight loss, slow gait speed, sensory impairment, and cognitive impairment were significant predictors of incident dependence in older people (17).

Taking into account and organizing the retrieved evidence, five different domains can be proposed as of primary interest for better defining the intrinsic capacity framework: (i) cognition, (ii) psychological (including mood and sociality), (iii) sensory function (including vision and hearing), (iv) vitality (i.e., homeostatic regulation, or balance between energy intake and energy utilization), and (v) locomotion (including muscular function).

Each of these five domains (depicted in Figure 2) will be individually examined in the following sections. However, it is necessary to acknowledge that the five components of intrinsic capacity should not be considered as standalone silos. In fact, each domain closely interacts with the others as part of a dynamically interrelated environment, the living organism. In other words, each specific domain will fail to provide an exhaustive picture of the health status of the individual, mainly because it would omit the information provided by the interactions across systems (10).

The Body Functions Defining the Construct of Intrinsic Capacity

Please note that in the scientific literature, the term “disability” is often used with a meaning different from the one described in the ICF, and frequently for indicating the impairment in ADLs. In the following sections describing the links between body functions and functional loss, the use of “disability” may reflect the sense coming from the literature, which might be narrower and more specific than what the ICF model implies.

Cognition

Cognitive function undergoes extremely heterogeneous patterns of modification with aging (18). Persons experiencing steeper declines in cognitive function are exposed to a higher risk of negative health-related outcomes (19). Thus, cognitive function may perfectly contribute to the design of an age-independent,
individual-specific, and dynamic risk profile. At the same time, cognition is influenced and can directly affect the other functions composing intrinsic capacity (20–23). It is also important to mention the large body of evidence showing how cognition is strongly affected by exogenous stressors (24). In fact, the environment plays a major role in determining the cognitive performance level. Acting on the environment may potentially enhance cognition (and consequently intrinsic capacity), thus improving the individual’s functional ability.

**Psychological**

Episodes of affective disorder become increasingly prevalent with older age. Differently from younger adults, older people often present depressive symptoms without meeting the diagnostic criteria for a depressive disorder (25), the so-called condition of “sub-threshold depression” (26). Depressive symptoms may have a strong relationship with the functional status of the individual (27). They may represent an independent risk factor for disability, or synergistically act with other conditions in the determination of the functional loss (28). The reciprocal and synergistic effects of depressive symptoms and disability have been described by Ormel and colleagues (29). The severity of depressive symptoms experienced by the older persons showed a gradient of risk for subsequent physical decline, even among individuals with no ADL or mobility disability (30). These findings suggest that the psychological assessment may support strategies for the early identification of individuals at risk of negative outcomes. Interestingly, secondary analyses conducted in the Women’s Health and Aging Study showed that emotional vitality could be preserved in the presence of severe disability (31). This implies that the capacity of the individual to maintain and develop social interactions may serve for differentiating health profiles and adequately contribute to a more comprehensive measure of intrinsic capacity.

**Sensory**

Sensory deficits (predominantly, vision impairment, and hearing loss) are associated with great disparities in health, activities, and social roles, especially when both are present (32). Thus, poor vision and hearing capacity have important implications for the health status and functioning of the individual (32).

A recent population-based study conducted in community-dwelling adults (age 57–85 years) reported that in two-thirds of the cases, sensory impairments are not isolated (33). Moreover, the simultaneous impairment of vision and hearing synergistically interfere with physical and cognitive function (34). In 2015, sense organ disorders represented the second leading cause of years lived with disability and counted for more than 68 million disability-adjusted life-years (35).

**Vision**

The prevalence of vision impairment significantly increases with age (14,36), and this trend is reported worldwide (37). Its detrimental effects are not only due to the presence of environmental barriers. In fact, vision impairment may be associated with negative health-related outcomes by acting on/enhancing different clinical mediators (e.g., depression (38), mobility impairment (36,39), falls (40)). Vision impairment has special implications for health policy and practice because it negatively impacts quality of life of the individual and substantially increases health care costs (41). Interestingly, the prevalence of vision impairment has been decreasing over the last 20 years in high—as well as in low-and-medium-income countries (37), suggesting the great potential for improving the populations’ health status by intervening on this attribute (35).

**Hearing**

Multiple age-related modifications occur in the peripheral auditory system, potentially leading to deficits in perception (42). Compared to vision problems, hearing impairment is more prevalent in the older population, but has a weaker association with physical function loss (14). Nevertheless, hearing impairment is still directly and independently involved in the process determining the disabling cascade (43). By challenging communication, hearing impairment might lead to social isolation and generate a vicious cycle characterized by a sense of inadequacy, anxiety, depression, cognitive decline, and physical function loss (44,45). Systematic reviews and meta-analyses have also demonstrated that amplification is beneficial in individuals with untreated sensorineural hearing loss in terms of quality of life by acting on the reduction of psychological, social, and emotional burdens of the condition (46,47).

**Vitality**

With the term “vitality” is intended, the body functions devoted to metabolizing dietary intakes in order to produce the required amount of energy for the maintenance of an optimal homeostatic level. Modifications occurring in energy expenditure and metabolism are part of the aging process (48). A decline of energy expenditure (due to the parallel reductions of resting metabolic rate and activity energy expenditure) occurs with age across species (49). In order to maintain proper functioning, the organism needs to adequately balance the energy intake and expenditures, and markers of malnutrition (e.g., weight loss, low body mass index, overweight/obesity) are frequently indicated as targets of intervention for preventing the disabling cascade (12,50).

It is also noteworthy that malnutrition may be caused by social (e.g., isolation, poverty, reliance on others), physiological (e.g., diseases, anorexia, dysphagia), and psychological (e.g., poor motivation, depressive symptoms) conditions affecting the eating process (51). Diseases (e.g., cardiorespiratory conditions, hormonal abnormalities) also affect the energy homeostasis of the organism by influencing nutrition-related mechanisms (e.g., increasing metabolism, reducing appetite, generating swallowing difficulties, producing malabsorption) (52).

Interventions focused on nutrition and aimed at restoring the metabolic balance are able to delay care dependency, reverse frailty, and potentially improve intrinsic capacity (1). Modifications of the energy and protein intake have shown to directly affect the biological mechanisms of aging, probably through anti-inflammatory and antioxidative effects (53).

**Locomotion**

Mobility is a function common to the largest part of living beings (54), and strongly associated with the health status of the organism across species (55,56). Measures of mobility, such as the gait speed, present a linear relationship with the risk of negative health-related outcomes (57). In pooled analyses of nine cohort studies, Studenski and colleagues (58) demonstrated that it is possible to accurately estimate the life expectancy of an older individual by simply knowing age, gender, and gait speed. Consistent findings have also been reported for other outcomes, including incident disability and care dependence (59). A large body of evidence
Intrinsic Capacity in Relation to Other Theoretical Constructs of Health in Older People

The concept of intrinsic capacity is designed to have a “positive” connotation, focusing on the measurement of the residual biological capacities of the organism rather than on its impairments/deficits. In the present article, the putative domains in the intrinsic capacity model are supported by data showing how their impairment becomes deleterious for the health status. Such apparent contradiction is mainly due to the fact that traditional medicine and related research is specifically focused on the identification and treatment of deficits (being reactive) rather than at the residual wellness of the organism (primary interest in the healthy ageing preventive approach).

The impairments in the domains identified as potentially relevant for the construct of intrinsic capacity have repeatedly been advocated as components of frailty (50,67-70). However, the intrinsic capacity model should not be perceived as the mere reciprocal of frailty (Table 1). Within the intrinsic capacity model are indeed nested and reorganized multiple aspects of the various frailty theories and operationalizations proposed over the last two decades. For example, the multidimensional nature of the intrinsic capacity model can be found in the comprehensive approach proposed by Rockwood and Mitnitski (71). At the same time, intrinsic capacity as part of the healthy aging model perhaps includes the biological state that underpins the frailty phenotype proposed by Fried and colleagues (72). The definition of the healthy aging trajectory taking into account the clinical, biological, and environmental specificities of the individual is consistent with the integrated Bio-Psycho-Social model proposed by Gobbens and colleagues (73).

An additional remark should be made in relationship to so-called “resilience” (Table 1). Considering that the focus of intrinsic capacity is on the residual biological reserves of the organism rather than on its deficits, intrinsic capacity may also be seen as sharing some commonalities with the concept of resilience (74-77). However, resilience is a concept that extends well beyond the biological status of the organism, and spreads over its social network, cultural background, economical capacities, and living environment.

Future Perspectives

The present article defines the components defining intrinsic capacity. To translate this first step into practice, it is necessary that validated measures for adequately capturing each intrinsic capacity domain will be identified. The WHO is currently working with several panels of experts for generating recommendations about the metrics of intrinsic capacity. This task is extremely challenging given the need to find among the multiple available instruments the most validated and acceptable tools that can be applied worldwide. In parallel, as recently exemplified (3), statistical approaches must be tested and optimized to enable easy computation of intrinsic capacity once the defining tools have been identified.

The novel construct of intrinsic capacity should also be considered in the context of the advancements and large-scale diffusion of technologies. Today, multiple devices commonly used in daily life (e.g., smartphones, actimeters) are able to automatically capture a wide range of data about our functions. Analysis of such information may inform public health actions (when used to observe population-matched data (78,79)) as well as potentially drive personalized interventions (if connected to other clinical information about the individual (80,81)). Moreover, in those regions where health care access might be more difficult, the possibility of measuring at distance the intrinsic capacity of the individual may serve for promoting the case finding of individuals experiencing abnormal functional trajectories.

Finally, the possibility of developing some disease paradigms into novel nosological conditions benefiting from the clustering of functional data should not be underestimated. In fact, the definition of the clinical profile might be improved by exploring the complex interactions of the individual’s functions allowing more personalized approaches.

### Table 1. Theoretical Definitions of Intrinsic Capacity, Frailty, and Resilience

<table>
<thead>
<tr>
<th>Construct</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Intrinsic capacity</td>
<td>- The composite of all the physical and mental capacities of an individual (1)</td>
</tr>
<tr>
<td>Frailty</td>
<td>- A progressive age-related decline in physiological systems that results in decreased reserves of intrinsic capacity, which confers extreme vulnerability to stressors and increases the risk of a range of adverse health outcomes (1)</td>
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<td></td>
<td>- Frailty is a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death (70)</td>
</tr>
<tr>
<td>Resilience</td>
<td>- The capacity of metals to resist deformation presaged interest in individual differences in the resiliency of people under stress (74)</td>
</tr>
<tr>
<td></td>
<td>- (Psychological) resilience refers to effective coping and adaptation although faced with loss, hardship, or adversity (75)</td>
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<tr>
<td></td>
<td>- The human ability to adapt in the face of tragedy, trauma, adversity, hardship, and ongoing significant life stressors (76)</td>
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<td>- (Physical) resilience is a characteristic at the whole person level which determines an individual's ability to resist functional decline or recover physical health following a stressor (77)</td>
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</table>
Conclusions

The intrinsic capacity model is extremely promising and potentially able to reshape the future medical approach. Its framework is, to date, still theoretical and needs to be translated into an operational instrument for feeding clinical and research practice. In order to render its objective, it is important to determine which body functions should be included in it. In this context, cognitive, psychological, locomotion, sensory, and vitality functions can be proposed as the components of intrinsic capacity corroborated (to date) by a larger body of evidence.

This first discussion about the construct of intrinsic capacity is proposed to stimulate exchanges among researchers and clinicians in order to consensually develop instruments for future health care, paying attention to generating models that can be adaptable worldwide independently of social, economic, and cultural diversities. The intrinsic capacity construct may indeed represent a unique opportunity for reorganizing our knowledge about age-related conditions, and designing instruments and models of care in support of improved person-centered integrated care approaches in our aging societies.

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Conflict of Interest

None reported.

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