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Prevalenza e impatto della fragilità e dei suoi determinanti multidimensionali in pazienti anziani acuti ricoverati in diversi setting di cura – Studio MUFASA

Prevalence and impact of frailty and MUltidimensional Frailty determinants in older patients Admitted to different healthcare Settings for Acute conditions – MUFASA Study

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Table of Contents

List of Figures

List of Tables

Abbreviation list

ADL = Activities of Daily Living
AGW = acute geriatric ward
BADL = Basic Activities of Daily Living
BI = Barthel Index
BRASS = Blaylock Risk Assessment Screening Score
CAM = Confusion Assessment Method
CESD = Center for Epidemiological Studies – Depression scale
CFS = Clinical Frailty Scale
CGA = Comprehensive Geriatric Assessment
CHS = Cardiovascular Health Study
CI = Confidence Interval
CIRS = Cumulative Illness Rating Scale
CIRS-CI = Cumulative Illness Rating Scale – Comorbitidy Index
CIRS-SI = Cumulative Illness Rating Scale – Severity Index
COPD = Chronic Obstructive Pulmonary Disease
COVID-19 = Coronavirus Disease 2019
CRF = Case Report Form
CSHA = Canadian Study of Health and Aging
ED = Emergency Department
ELSA = English Longitudinal Study of Ageing
ESS = Exton-Smith Scale
FFP = Fried Frailty Phenotype
FI = Frailty Index
GIROT = Gruppi di Intervento Rapido Ospedale-Territorio
HADS = Hospital Anxiety and Depression Scale
HAC = Hospital-acquired complications
HaH = Hospital-at-Home
HAI = Healthcare-Associated Infection
IADL = Instrumental Activities of Daily Living
IQR = Interquartile Range, 25^{th} to 75^{th} percentile
LOS = length of stay
LTC = long-term care
MLTAQ = Minnesota Leisure Time Activity Questionnaire
MLTCF = Medium- or Long-Term Care Facility
MNA = Mini Nutritional Assessment ®
MOS-SSS = Medical Outcomes Study – Social Support Survey
MPI = Multidimensional Prognostic Index
NEWS2 = National Early Warning Score 2
NHANES = National Health and Nutrition Examination Survey
OPAT = Outpatient Parenteral Antimicrobial Therapy service
PASE = Physical Activity Scale for the Elderly
RCT = Randomized Controlled Trial
RR = Relative Risk
SD = Standard Deviation
SPMSQ = Short Portable Mental Status Questionnaire
STROBE = STrengthening the Reporting of OBservational studies in Epidemiology
TILDA = The Irish Longitudinal Study on Ageing
UK = United Kingdom
USA = United States of America

Summary

Introduction - Hospitalization is a major stressor for older adults, especially those who are frail, increasing risk of hospital-acquired complications (HAC), disability, institutionalization, and death. Hospital-at-Home (HaH) has been proposed as an alternative to in-hospital care for acutely-ill frail older adults, potentially reducing risks and reducing costs. However, data on frailty prevalence and its impact in the HaH setting remain limited.

Purpose - This Ph.D. project aims to assess the prevalence and prognostic role of frailty according to different definitions, and its interaction with healthcare setting on outcomes in older patients admitted to an HaH or an acute geriatric ward (AGW).

Methods - The MUFASA prospective observational study enrolled community-dwelling subjects aged ≥65 years admitted to the AGW and the HaH of the Molinette Hospital, Turin, Italy. Frailty at admission was evaluated according to Fried Frailty Phenotype (FFP), Clinical Frailty Scale (CFS), Frailty Index (FI), and Multidimensional Prognostic Index (MPI). In-hospital outcomes [mortality and HAC – delirium, healthcare-associated infections (HAIs), falls, and pressure injuries], and 6-month post-discharge outcomes (mortality, institutionalization, Emergency Department - ED visits or rehospitalization, and worsening functional status) were collected. The primary outcome was a composite or all-cause mortality or institutionalization at 6 months. Association of frailty definitions and healthcare setting with clinical outcomes were assessed by multivariable logistic regression adjusted for confounders.

Results – A total of 297 patients were enrolled (98 HaH, 198 AGW; median age 86 years, 52.2% female); admission diagnoses and acute illness severity were comparable across settings. Frailty prevalence ranged from 28.2% (MPI) to 67.7% (CFS) to 86.5% (FFP and FI). HaH patients showed higher prevalences of geriatric syndromes and frailty according to CFS (82.7% vs 60.3%) and MPI (40.7% vs 22.0%). Agreement among frailty tools was generally low, with the highest Cohen's κ in the overall sample between FI and FFP (0.53, moderate agreement) and between FI and CFS (κ 0.48); substantial agreement was reached between FI and CFS in HaH (κ 0.67).

During admission (median length of stay – LOS: 11 days), 5.7% of patients died (6.1% HaH vs 5.5% AGW) and 26.9% patients experienced at least one HAC (20.4% HaH vs 30.2% AGW); the most frequent HACs were HAI (15.2%) and delirium (10.8%). Transfer to the hospital was necessary for 6.5% of HaH patients. After adjusting for confounders (among others, comorbidity, functional and cognitive status, severity of acute illness, and LOS) frailty association with outcomes became nonsignificant, and HaH setting was associated with lower

odds of in-hospital death or any HAC, irrespective of frailty definition (aOR 0.29, 95% CI 0.14-0.59 – CFS adjusted). HaH was also independently associated with lower odds of any HAC (aOR 0.20, 95% CI 0.09-0.44), delirium (aOR 0.21, 95% CI 0.07-0.67), and HAI (aOR 0.32 (95% CI 0.12-0.88), in CFS-adjusted analyses; FI-adjusted analyses yielded similar results.

Among 280 patients discharged alive, 30.0% experienced the primary composite outcome of all-cause death or institutionalization (23.9% HaH vs 33.0% AGW). Mortality rates were similar among settings (20.7% HaH vs 22.3% AGW) while institutionalization was markedly higher in AGW (20.7% vs 3.3% HaH, p <0.001). ED visits/readmissions occurred in 35% of subjects (40.2% HaH vs 32.4% AGW), and 45.7% of the 219 survivors had significant functional decline at 6 months (43.8% HaH vs 46.6% AGW). Again, when adjusting for potential confounders (among others comorbidity, functional and cognitive status, caregiver availability, and HRC during admission), HaH setting was independently associated with lower odds of the primary outcome (aOR 0.41, 95% CI 0.20-0.84 in CFS adjusted analysis), whereas frailty defined by the CFS and FI retained their significance (aOR 3.52, 95% CI 3.52-8.09, and aOR 5.75 (95% CI 1.25-26.48), respectively). The results for the HaH setting were mainly due to reduced institutionalization risk. CFS frailty was independently associated with both institutionalization and mortality. Neither setting nor frailty were associated with ED visits/ readmissions or functional decline at follow-up, which were instead predicted, among others, by previous hospitalizations and low handgrip strength, respectively.

Conclusions - To the Ph.D. Candidate's knowledge, the MUFASA study is the first to systematically report prevalence of frailty in the HaH setting using four different definitions, and to explore the combined prognostic impact of healthcare setting and frailty in acutely ill older adults, representing an original contribution to the existing literature.

The study confirmed an extremely high prevalence of frailty and other geriatric syndromes in both settings, approaching ubiquity in the HaH population, with the exception of MPI frailty (possibly due to higher validated cutoffs). However, agreement between frailty tools was moderate at best. Results suggest that HaH care might play a protective role in the incidence of adverse clinical outcomes related to hospitalization of older adults, including delirium, HAIs, and institutionalization, mitigating the negative effects of frailty.

Future directions – Frailty should be routinely reported in studies on HaH targeting older subjects, and the CFS may represent a pragmatic choice due to its ease of use and predictive performance. Further studies exploring whether the benefits of HaH vary across different frailty severity levels could help inform patient selection and optimize resource allocation where HaH bed availability is still limited.

GENERAL INTRODUCTION

1. Frailty and Aging

During the last century, the gradual and widespread improvement in socioeconomic conditions, the adoption of primary and secondary prevention programs for infectious and chronic diseases, and advancements in diagnostic and therapeutic capabilities have led to a sharp increase in life expectancy, first in high-income countries and later in developing countries. This, along with declining birth rates, has resulted in and continues to drive a progressive aging of the population in these countries. Healthcare systems worldwide must thus respond to the increasingly complex needs of older adults, who are often affected by multiple chronic conditions and receiving complex therapies.[1–3] The overall health status of these patients derives from the interaction of biological, psychological, and socio-environmental factors and is strongly influenced by the presence of geriatric syndromes, including frailty, malnutrition, cognitive impairment, and falls, among others.[4,5]

Despite initial and ongoing challenges in reaching an agreement on frailty operationalization, a widespread consensus has been achieved in defining frailty as a geriatric syndrome that is related to but distinct from disability, that derives from the gradual accumulation of damage across multiple physiological systems, leading to a reduction in an individual's functional reserve and, ultimately, resulting in a less efficient response and increased vulnerability to even minor stressor events.[6–10] These seemingly minor insults (e.g., a mild infection, a new medication, a fall without direct clinical consequences, a planned minor surgical procedure) can trigger disproportionate changes in health status, including development of disability, cognitive deterioration, institutionalization, and death.[7,8,11] Therefore, frailty represents a relevant and emerging global health concern with profound clinical and social consequences, with the scientific community striving to find a common operational definition to facilitate early and effective identification and management of this condition.[3,6,10,12–14] Indeed, a wide range of operating criteria, tools, questionnaires, and scales have been proposed, each with different objectives (e.g., screening, identification, or treatment), settings of use (e.g., community, emergency department - ED, specialist-led clinics, in-hospital acute care, long-term care - LTC), and target populations (e.g., community-dwelling older adults, nursing home residents, candidates to specific interventions and treatments).[15]

1.1 Pathophysiology of frailty

Ageing is a complex process deriving from the interplay of genetic, epigenetic, and environmental factors, leading to a gradual accumulation of damages at the molecular, cellular, organ and system levels.[16,17] Despite this, in physiological ageing, the loss of homeostatic reserve is usually inapparent, and older adults can compensate for age and disease-related changes.

Frailty is considered a pathological condition resulting from an accelerated loss of physiological reserve in multiple systems, leading to homeostatic failure.[7,8,18,19] It is still unclear whether a threshold for damage in physiological systems exists at which frailty becomes manifest,[7] but, interestingly, it seems that the number of impaired systems is more relevant than which specific systems are affected; this supports a deficit accumulation theory in which an aggregate level of physiological decline culminates in frailty.[8,17,19,20]

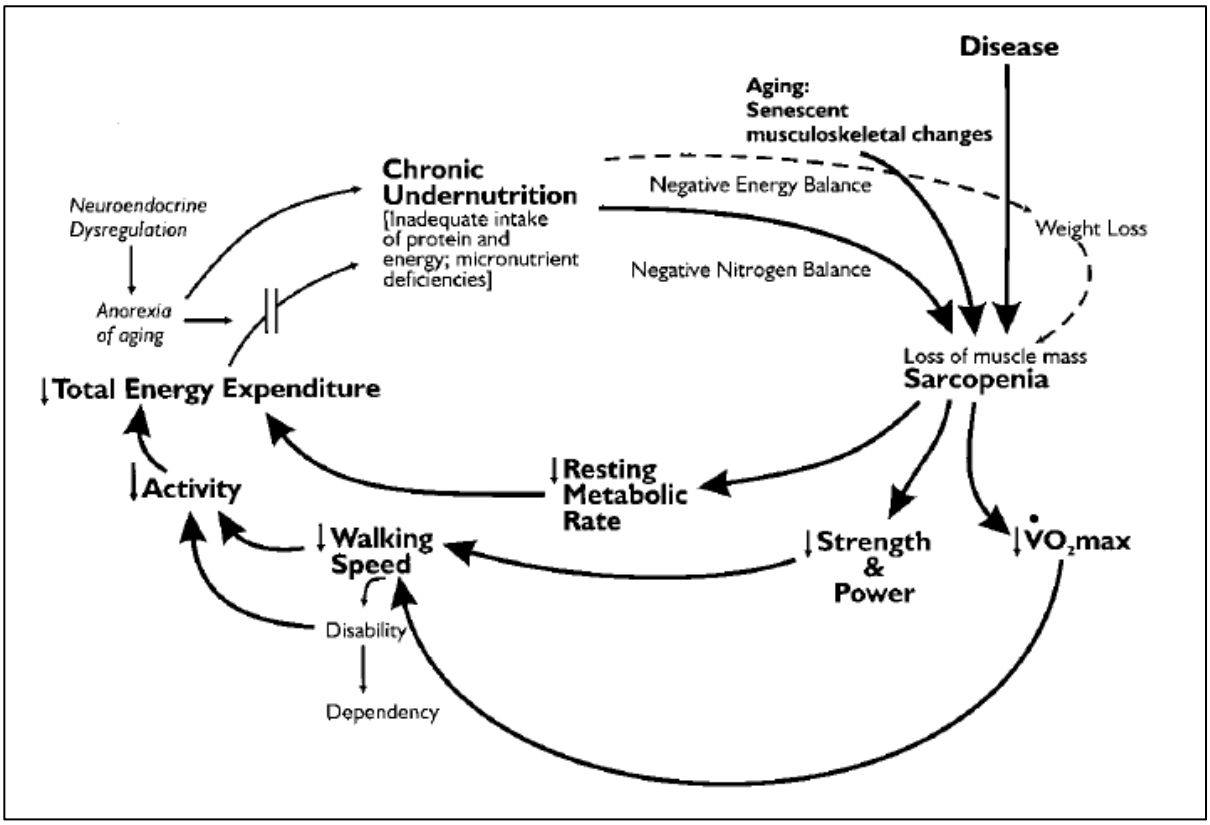
Despite many risk factors for frailty have been identified in recent years, including lifestyle, clinical, psychological and sociodemographic aspects,[8,21] the complexity of the multiple interconnected physiological processes that become dysregulated in frail older adults makes the biological pathways and mechanisms underlying frailty development still largely unknown.[7] Physical inactivity and malnutrition have been recognized as major risk factors for frailty onset and progression, and the beneficial effects of physical exercise and nutritional management on physiological systems implicated in frailty are well-documented.[22]

In recent years, the central role of sarcopenia in the pathogenesis of frailty has become clear.[17] Sarcopenia is a progressive and generalized condition characterized by reduced muscle strength and muscle mass, leading to impaired physical performance in its severe stages.[23] Therefore, sarcopenia, especially its obesity variant, is a formidable contributor to weakness, slowness, and functional deterioration, all key components of the frailty phenotype (*Figure 1*).[17,24]

It is believed that the initial frailty pathway derives from an accelerated accumulation of multiple damages (the so-called “allostatic load”) at the molecular, subcellular, cellular, and tissue levels that occur in physiological ageing.[25] A deregulated, sustained low-grade inflammatory response, driven by oxidative stress due to mitochondrial disfunction, appears to play a central role in the pathogenesis of frailty, due to the combined effects of chronic inflammation on anorexia and catabolism. This, in turn, leads to reduced humoral and cellular immune responses, as well as to skeletal muscle and adipose tissue wasting.[7,8,16,17,24,26–32] Indeed, increased levels of pro-inflammatory cytokines such as interleukin 6, C-reactive protein, and tumor necrosis factor-α, as well as of reactive oxygen species, have been identified

in patients with sarcopenia and frailty.[18,26,30–33] An increased inflammatory response has also been described within the central nervous system, where primed microglial cells might lead to neuronal dysfunction and loss.[34,35] Interestingly, both frailty and primed microglial cells have been linked to an increased incidence of delirium in older subjects.[35,36] Moreover, nervous system alterations might lead to increased sympathetic tone and loss of α-motor neurons, facilitating the loss of skeletal muscle mass and strength.[7]

Figure 1 – The cycle of physical frailty, according to prof. Linda Fried and colleagues.



Frailty has been associated with a deregulation in nutrient sensing and endocrine pathways, leading to an increase in cortisol secretion and a reduction in the production of sex hormones, as well as of growth hormone/insulin-like growth factor I.[7,17,33] This contributes to chronic inflammation, metabolic dysfunction, and anabolic-catabolic imbalance, ultimately leading to reduced neuronal plasticity and skeletal muscle dysfunction.[8,16]

Lastly, cellular senescence and stem cell exhaustion are other aspects that have been linked to the physiology of ageing and to the pathogenesis of frailty, contributing to energy failure, skeletal muscle anabolic resistance, reduced neuronal plasticity, and immunosenescence.[8,16]

1.2 Conceptual models of frailty

Despite the existence of various definitions, two main conceptual models of frailty have emerged over the last twenty years: the frailty phenotype model, which considers frailty as a geriatric syndrome impairing physical performance irrespective of multimorbidity and disability, and the deficit accumulation model, which sees frailty as a state of accumulated health deficits, also considering chronic diseases and functional impairments.[6–8,37,38] More recently, a third conceptual framework has been proposed, the multidimensional frailty model, which defines frailty as a state of impaired homeostasis due to imbalances across multiple bio-psycho-social domains.[21,39] Lastly, a positive and somewhat "reciprocal" approach, called "intrinsic capacity", has been introduced, that focuses on the residual resources in multiple health domains (namely, cognition, locomotion, sensorium, psychology, and vitality) of an individual.[3,40–42]

Although these concepts are different and identify distinct subpopulations, they share some common ground, as evidenced by a significant overlap in epidemiology, risk factors, and outcomes, irrespective of the definition employed.[7,8] Moreover, whatever the model adopted, frailty is recognized as a dynamic process, with an older adult capable of fluctuating between states of frailty, thereby paving the way for targeted interventions for frail subjects.[12,14,19]

1.2.1 FRAILTY PHENOTYPE MODEL

The frailty phenotype model (sometimes called "physical frailty" model) was developed by prof. Linda Fried and colleagues in the early 2000s through a secondary analysis of data from the Cardiovascular Health Study (CHS), which included 5,210 subjects aged 65 years and older, excluding subjects with neurological and psychiatric conditions (e.g., Parkinson's disease, dementia, stroke, and depression), and associated baseline characteristics with the risk of all-cause mortality over seven years.[37]

According to this phenotype model, frailty is a clinical syndrome characterized by the presence of at least three out of five key characteristics:[37]

- *Shrinking:* unintentional weight loss in the last year equal to or greater than 5% of the subject's body weight
- *Physical exhaustion*, as self-reported based on two items of the Center for Epidemiological Studies – Depression scale (CESD)[43]
- *Weakness* at the handgrip strength test, in the lowest quintile normalized according to sex and Body Mass Index

- *Slowness* at the gait speed test, in the lowest quintile normalized according to sex and body height
- *Reduced physical activity levels*, defined as a low energy expenditure based on the Minnesota Leisure Time Activity Questionnaire (MLTAQ) [44]

Although the order of appearance is not fundamental in defining the frailty phenotype, it has been noted that exhaustion and muscle weakness usually manifest first, followed by reduced gait speed and low physical activity levels, whereas weight loss tends to be the last one to become evident.[45] Subjects with none of these characteristics are deemed "robust", whereas those with one to two features are considered "pre-frail" and are at increased risk of becoming frail. All-cause mortality at seven years in the CHS increased sharply from 12% in robust subjects, to 23% in pre-frail subjects, peaking at 43% in frail subjects, with a 7-year adjusted Hazard Rate for mortality of 1.63 (95% CI: 1.27-2.08) in the frail group.[37] The presence of all five features indicates a critical transition, with the risk of death rising sharply and the chance of reversal diminishing.[46]

Despite its popularity, the frailty phenotype model has some conceptual and practical limitations. First, the five components were chosen *post hoc* for convenience from variables that were fortuitously available in a study not specifically designed to investigate frailty; consequently, potentially relevant factors such as cognitive or psychological status were not evaluated. This notwithstanding, gait speed is a well-known indicator of overall health status in older individuals, since the ability to walk independently and efficiently depends on the integrity of several interconnected physiological systems, and it has been linked with a variety of unfavorable clinical outcomes, including fall risk, disability, institutionalization, and death.[47–50] Moreover, with the recognition of sarcopenia as the clinical syndrome characterized by reduced muscle mass and muscle strength leading to reduced physical performance, the frailty phenotype model, despite being different from sarcopenia, appears to be highly interconnected with it, and, therefore, shares a common pathogenetic ground.[23]

Moreover, the inclusion of direct measures of muscle strength and gait speed, despite being highly informative, might have limited and continues to limit its widespread adoption in clinical practice, particularly in non-geriatric settings, and normative data on specific populations for frailty detection are frequently unavailable. Lastly, the use of the MLTAQ, which includes activities such as mowing the lawn, taking excursions, or playing tennis, to assess physical activity levels has been criticized for use in older subjects, particularly outside of the United States of America (USA). The Physical Activity Scale for the Elderly (PASE) has been deemed a more representative tool for the European geriatric context.[51–55]

1.2.2 DEFICIT ACCUMULATION MODEL

The deficit accumulation model was proposed by prof. Kenneth Rockwood and colleagues in the early 2000s as well, with the Frailty Index (FI) as a measure developed from a secondary analysis of data derived from the Canadian Study of Health and Aging (CSHA), which included 10,263 subjects with a mean age of 82 years to investigate the epidemiology and burden of dementia in Canada with five years of follow-up.[8,38,56]

According to the deficit accumulation model, frailty is a nonspecific syndromic state resulting from the accumulation of age-correlated conditions (not always pathological *per se*) in several physiological systems beyond a certain threshold at which physiological compensatory mechanisms are overwhelmed, leading to an increased susceptibility to negative clinical outcomes, such as death or institutionalization.[56,57] Frailty would therefore not directly derive from a specific pathological state (i.e., the *quality* of the health deficit), but rather be determined by the *quantity* of health deficits accrued over time by the older subject; the higher the number of deficits, the higher the risk of developing adverse events, irrespective of their nature.[8,38,56–58] In other words, "the more individuals have wrong with them, the more likely they are to be frail".[38] This model is clinically attractive, because it depicts frailty as a continuous, gradual condition, with different degrees of severity, rather than a binary (i.e., present or absent) syndromic state.[8,56,57]

The FI is defined as the proportion of deficits (signs and symptoms, diseases, disabilities, laboratory test abnormalities, and other health impairments) that the subject presents over the total number of deficits evaluated, ranging from 0 (complete absence of frailty deficits) to a theoretical maximum of 1.[38,56,59] It was originally developed considering 92, and later 70, items available in the CSHA dataset; however, subsequent studies have demonstrated that reducing the number of items to a total of 30 or 40 does not impair its ability to predict adverse events.[59,60]. Moreover, due to its focus on the quantity rather than the specific nature of deficits, the FI has proven to be a robust measure of frailty, allowing researchers to develop local frailty indices according to available datasets of deficits, provided that they respect some key characteristics - i.e., that they are acquired, have an impact on health, are age-associated but not universal after a certain age, and that they span different physiological systems.[59]

Despite the absence of a universally acknowledged FI cutoff for the diagnosis of frailty, a value of 0.25 has been proposed and is one of the most frequently suggested cutoffs. Moreover, it seems that FI values above 0.67 have rarely been observed (they are present in less than 1% of participants), probably identifying a critical level of deficit accumulation beyond which physiological system deterioration is rarely sustainable and survival is unlikely.[38,59–62]

Despite these characteristics and its high predictive ability for negative clinical outcomes in both hospital and community settings,[63,64] the FI can be time-consuming to evaluate, and its mathematical nature, although simple, renders it unpopular in the context of everyday clinical practice.[65] Various instruments derived from the FI have been developed to facilitate its use and derivation from routine Comprehensive Geriatric Assessment (CGA) data or Electronic Health Records.[7,8] Another approach to simplify the evaluation of frailty in everyday clinical practice was proposed in 2005 by prof. Kenneth Rockwood and colleagues with the Clinical Frailty Scale (CFS), a global "eyeball" summary of the deficits identified in a CGA that focuses on mobility, energy, physical activity and function. In its second revision, the CFS ranges from 1 to 9, with each score accompanied by a clinical vignette, with higher scores indicating more severe levels of frailty.[66,67]

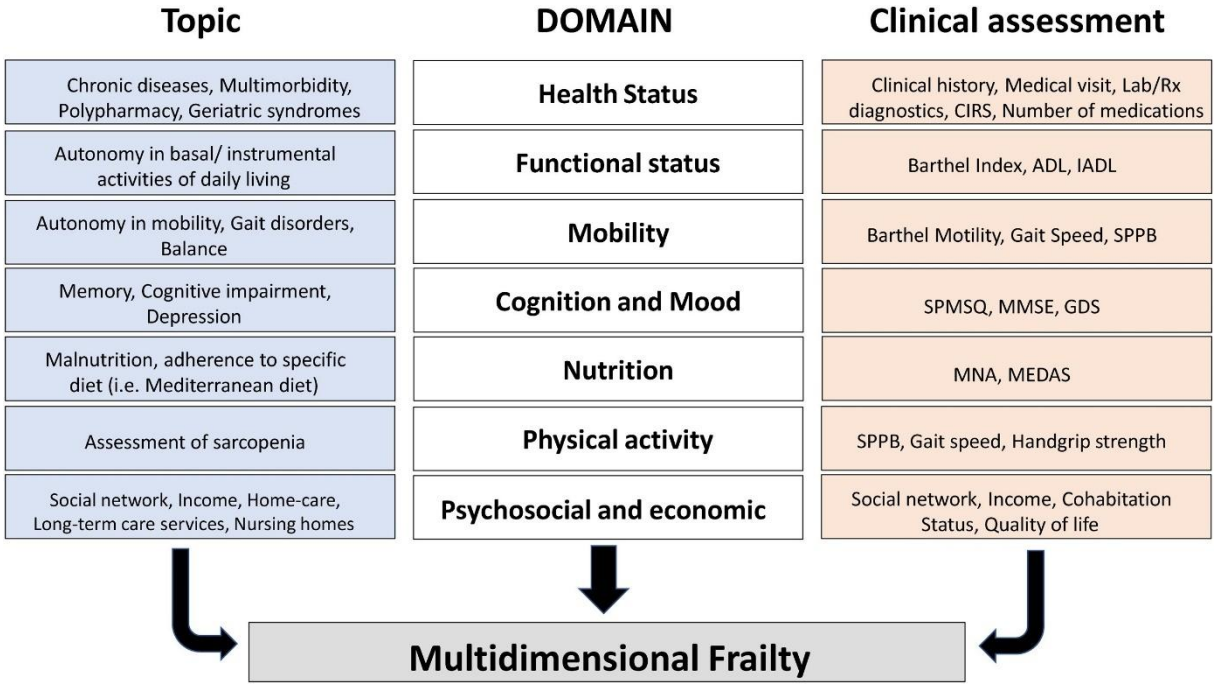
1.2.3 MULTIDIMENSIONAL MODEL

Recently, some researchers have proposed a new conceptual model of frailty, called the multidimensional (or integral) model of frailty, which highlights the importance of taking into account cognitive, psychological, and socioeconomic variables as both determinants and consequences of frailty.[9,21,39] According to this model, frailty is defined as the loss of harmonic interaction between multiple bio-psycho-social domains, leading to impaired homeostasis (*Figure 2*).[21,39] This approach places the biological dimension of frailty into the context of the older individual's life setting, including their social relationships and living environment, thereby highlighting potential areas for preventive interventions. The relevance of this perspective on frailty is underscored by the fact that, despite the numerous frailty operational tools available,[15] the CGA remains the gold standard tool for the evaluation and management of older subjects and frailty.[7,39,68–70] This was defined in 1991 by prof. Laurence Rubenstein as a multidimensional and interdisciplinary process that aims to determine the physical, psychological, and functional abilities in order to develop a coordinated and integrated management plan with and long-term follow-up of the older subject.[68] Among the various dimensions that can be evaluated during a CGA, there are functional abilities, cognition, nutrition, mood, mobility, polypharmacy, gait speed, comorbidity, geriatric syndromes (e.g., risk of falls, delirium, urinary incontinence, sensory impairment, oral health problems), disease specific scales (e.g., for Parkinson's disease and major neurocognitive disorders), social network and support, environmental and housing conditions (including home safety), economic status and financial problems, and advance care planning.[68,70]

When the results of a CGA are used to direct a focused multidisciplinary intervention in

the older adult, improved survival and better clinical outcomes have been demonstrated.[68] Moreover, as previously stated, and as implicitly recognized by the deficit accumulation model, multidimensional impairment is tightly linked with prognosis in older subjects, and the CGA is therefore a useful tool to estimate residual life expectancy and guide diagnostic and therapeutic decisions in geriatric patients. However, the CGA is time-consuming and requires a high level of expertise to be reliable and reproducible.[68–70]

Figure 2 – The domains of multidimensional frailty, according to prof. Alberto Pilotto and colleagues.



In an attempt to standardize and operationalize the results of a CGA into a numeric variable, the Multidimensional Prognostic Index (MPI) has been proposed as a tool to measure multidimensional frailty and its negative impact on one-year mortality.[39,71] This tool scores the absence or presence of problems in eight different domains from 0 (none) to 0.5 (minor) to 1 (major), including functional autonomy, cognitive and nutritional status, multimorbidity and polypharmacy, risk of pressure ulcer development, and living conditions, and the mean of these scores represents the total MPI score, with higher scores representing higher levels of risk and of multidimensional frailty severity.[71]

1.3 Operational definitions of frailty

Since the identification of the frailty construct, irrespective of the underlying conceptual model adopted, a host of frailty measurement tools has been proposed; a systematic review by

Buta and colleagues published in 2016 identified 67 different frailty instruments,[15] whereas another one found 51 instruments.[72] Among these instruments, no one has prevailed or has been identified as the "gold standard" for frailty assessment,[6] and this will probably never be the case, because different operational definitions might be more suitable for specific populations, conditions, settings or purposes. Some frailty tools may be used as screening tools in the general population, whereas others might be employed in specialized settings such as the ED, the acute ward, or the nursing home for case finding, diagnosis and management of frailty; other instruments might be more suitable for identifying frailty to predict one or more adverse events and to allocate resources.[7,8,12,14,15,72,73]

Unfortunately, extensive validation studies are lacking for a large share of frailty instruments and, even among those that have been validated, aspects such as reliability, cross-cultural validity, and responsiveness have not been thoroughly explored. For all these reasons, the field of frailty is moving toward the development of specific instruments for particular settings and populations, contributing to increased confusion over the term "frailty" among the general public.[8,12,13]

Among the most cited instruments for frailty assessment in the scientific literature are the Fried frailty phenotype criteria,[37] the FI,[56,59] the CFS,[66] the Vulnerable Elders Survey 13,[74] and the FRAIL questionnaire[75]. Other instruments include the Edmonton Frailty Scale,[76] the Tilburg Frailty Indicator,[77,78] the Groningen Frailty Indicator,[79] and the MPI[71,80] (*Table 1*).

Although the Fried frailty phenotype criteria and the FI have been shown to significantly converge in their identification of frailty,[81] with the FI exhibiting a greater discriminatory ability due to its continuous nature that can capture different levels of frailty severity,[82] many researchers suggest that these models should not be considered as alternative or interchangeable, but rather as complementary, allowing for the capture of different characteristics of the frail older subject.[83]

Lastly, physical performance measures have been proposed as proxies for frailty, focusing primarily on the physical dimension of frailty (i.e., the frailty phenotype model). These include gait speed at usual pace,[47] handgrip strength,[84] and the Short Physical Performance Battery, which, in addition to gait speed, includes balance tests and the chair stand test as measures of lower limb performance.[48] Undoubtedly, these measures have been linked to the development of disability and reduced survival, as well as other negative clinical outcomes.[47] This may be due to the fact that the evaluation of physical performance, in particular that of gait, allows for the detection of both recognized and unrecognized impairments in multiple physiological systems (e.g., musculoskeletal, sensory, cardiovascular, metabolic, nervous, and cognitive),

many of which affect survival and functional status. Moreover, slowness may induce a vicious circle of reduced mobility and deconditioning, which negatively impacts patients' health status and prognosis.

Table 1 –Most common frailty operational tools, along with their main characteristics, including frailty model of derivation.

Frailty Instrument	***Frailty Definition***	***Type of measure***	***N. of items***	***Cutoff***	***Model***
Fried Frailty Phenotype[37]	Number of phenotype characteristics among 5: unintentional weight loss, low physical activity, exhaustion, slowness, weakness	Ordinal Scale (3 levels)	5	≥3	FP
Frailty Index[56,59,61]	Ratio of number of health deficits on different physiological systems present on the total number of deficits evaluated	Continuous scale	Variable (30-92)	≥0.25 (suggested)	DA
Clinical Frailty Scale[66,67]	Global clinical evaluation of mobility, physical activity and function ranging from 1 (very fit) to 9 (terminally ill)	Ordinal scale (9 levels)	1	≥5 (suggested)	DA
Edmonton Frail Scale[76]	Evaluation of cognition, health, hospitalisation, social support, nutrition, mood, function, continence, medication use	Ordinal scale (5 levels)	11	>7	MD
Groningen Frailty Indicator[79]	Self-reported in 4 domains: physical, cognitive, social, psychological	Dichotomous scale	15	≥4	MD
Tilburg Frailty Indicator[77]	Self-reported in 3 domains: physical, psychological, social	Dichotomous scale	15	≥5	MD
Multidimensional Prognostic Index[71]	Derived from a CGA covering functional, cognitive, nutritional, and comorbidity aspects.	Continuous scale	8	>0.66	MD
Study of Osteoporotic Fractures Index[85]	Simplified tool assessing weight loss, inability to rise from a chair, and reduced energy levels	Ordinal scale (3 levels)	3		FP
FRAIL questionnaire[86]	A simple screening tool evaluating fatigue, resistance, ambulation, illnesses, and weight loss.	Ordinal scale (3 levels)	5	≥3	FP

Abbreviations: DA = Deficit Accumulation model, FP = Frailty Phenotype model, MD = Multidimensional model

1.4 Epidemiology of frailty

The global and local prevalence of frailty remains unclear, with wide variations reported across different studies, also when focusing on the same regions.[7,8,12,13] In a systematic review of 21 studies encompassing 61,500 community-dwelling older patients, Collard and colleagues reported a pooled frailty prevalence of 10.7% [95% Confidence Interval (CI): 10.5%-10.9%], but with a dramatic range among individual studies from 4.0% to 59.1%. When stratified according to frailty model, prevalence estimates became more consistent, with a prevalence of 9.9% (95% CI: 9.6-10.2) according to the frailty phenotype model and of 13.6% (95% CI: 13.2-14.0) using the "broad frailty phenotype" (i.e., the cumulative deficits model).[87]

Besides the heterogeneity of study setting, population, and inclusion criteria, undoubtedly a large share of this variation can be attributed to the aforementioned lack of a universally accepted operational definition of frailty, resulting in the use of different tools, frequently adapted to local realities.[7,8,12,13,52]

In a broader and more recent systematic review by O'Caoimh *et al.* of 240 population-based studies from 62 countries around the world, including 1,755,497 participants, frailty prevalence, irrespective of definition, was estimated at 17.0% (95% CI: 16.0-18.0). Furthermore, pooled prevalence estimates for physical frailty and for the deficit accumulation model were 12% (95% CI: 11-13) and 24% (95%CI: 22-26), respectively.[88] However, it is important to note that the actual prevalence of frailty worldwide remains largely unknown, due to the fact that most research on frailty has been conducted in high-income countries, and frailty prevalence in low- and middle-income countries might differ substantially.[13] One multi-country study, including China, Ghana, India, Mexico, South Africa, and Russia, applied both frailty phenotype and frailty index criteria, yielding prevalence estimates for the former from 8% to 15%, and for the latter from 13% to 56%.[89] A systematic review on frailty prevalence in low- and middle-income countries found the same striking variation on frailty prevalence figures, ranging from 3.9% to 59.4%.[90]

Frailty figures are understandably higher when focusing on specific clinical settings, such as acute hospital wards and LTC facilities, or in patients with clinical conditions like dementia, cancer, or end-stage renal disease, since sicker individuals are more likely to be also frail, regardless of the frailty assessment tool or definition employed.[12]

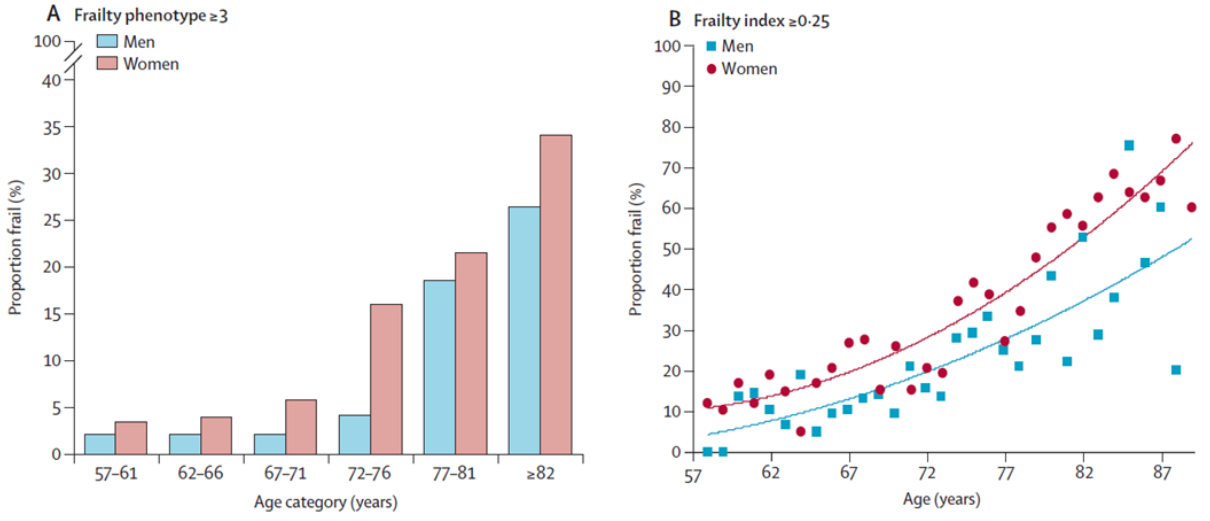
In a systematic review of 96 studies including 467,779 geriatric patients admitted to various in-hospital wards, overall frailty prevalence was 47.4% (95% CI: 43.7-51.1), rising to 66.5% (95% CI: 54.3-78.7%) in geriatric acute wards.[91] Specifically, frailty prevalence among geriatric inpatients was 42.9% (95% CI: 35.4-50.4%) when using the Frailty Phenotype, and

52.6% (95% CI: 38-67.1%) when using the Frailty Index.[91] Slightly lower estimates for older hospital inpatients from low- and middle-income countries in a recent systematic review and meta-analysis of 27 studies, finding a pooled total estimate of frailty of 39.1% (95% CI: 31.9-46.6%), varying from 52.2% (95% CI: 40.7-63.5%) when using the CFS to 36.2% (95% CI: 27.1-45.8%) with the Frailty Phenotype.[92] Among 1,373 LTC residents included in a recent systematic review by Kojima and colleagues, the pooled prevalence of frailty, irrespective of definition used, was 52.3% (95% CI: 37.9-66.5%).[93]

Despite the relatively more recent introduction of the concept of multidimensional frailty, systematic reviews on its prevalence among community-dwelling older people are also available. In a meta-analysis of 57 studies involving 56,407 older subjects across various clinical settings, Veronese *et al.* reported an overall prevalence of frailty and prefrailty according to the MPI of 26.9% (95% CI: 22.2-31.5) and 36.4% (95% CI: 33.1-39.7%), respectively.[80] Notably, the prevalence of multidimensional frailty was lowest in population-based studies (13.3%, 95% CI: 7.1-19.6%), increased to 29.8% (95% CI: 24.2-35.4) in hospitalized patients and peaked at 51.1% (95% CI: 50.0-53.1) among nursing home residents.[80] Furthermore, Qiu *et al* reviewed the prevalence of multidimensional frailty according to the Tilburg Frailty Indicator among 40,597 community-dwelling older subjects from 66 studies, finding a pooled prevalence of 42% (95% CI: 38-45%).[94]

Across all models, frailty is consistently more prevalent in women than in men (9.6% vs 5.2%, respectively), and increases steadily with age, from 3.2% among those aged 65-70 years to 25.7% among those aged 86-90 years (*Figure 3*).[7,12,87]

Figure 3 – Prevalence of frailty according to the Fried Frailty Phenotype (A) and the Frailty index (B), stratified by sex and age.



Moreover, although the prevalence of frailty across different ethnic groups and socioeconomic strata is less well-defined, evidence
suggests that this condition is more common among individuals with lower educational levels, lower income, or belonging to ethnic minority groups.[7,95–97]

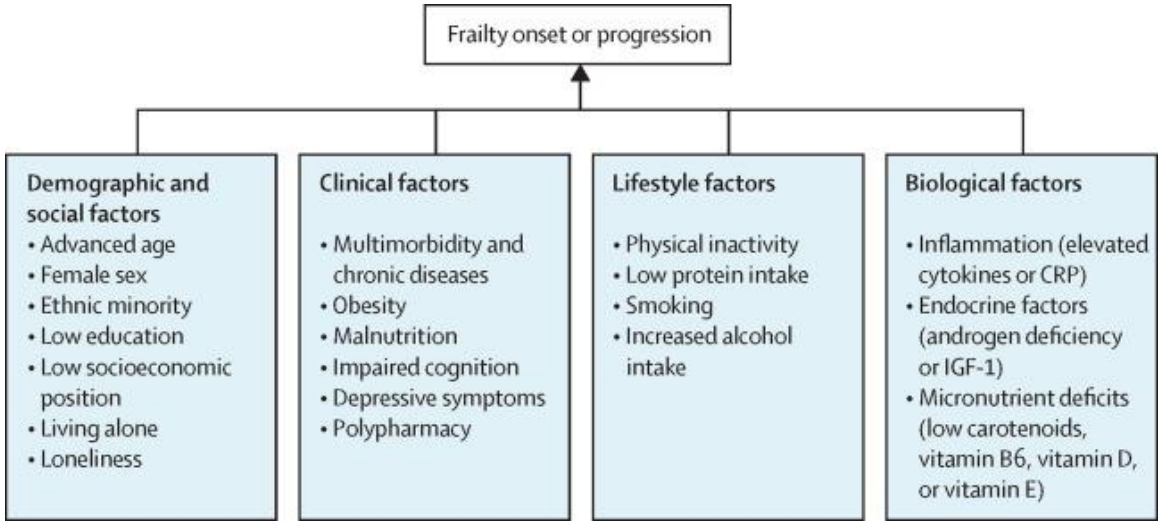
These epidemiological data, along with the aforementioned demographic projections of a global expansion of the older population, underscore the importance of recognizing and managing frailty as a core objective for healthcare, social and policy interventions. In particular, there is an urgent need to design, validate and implement more flexible and affordable healthcare models that optimize the management of chronic conditions, including frailty, to minimize their impact on functional autonomy, and increasing life expectancy free from disability.

1.5 Clinical factors associated with frailty

A recent umbrella review of systematic reviews of observational studies exploring factors associated with frailty (i.e., clinical correlates) in older adults has recently been published by Boucham and colleagues.[98] Due to its complex nature, frailty onset and progression is mediated by several potential risk factors interacting with one another, often in unpredictable ways, including biological and clinical factors, as well as demographic, socioeconomic and lifestyle factors (*Figure 4*).[12] In the previous section, it has already been shown that older age and female gender are among the most prominent factors associated with frailty.[7,12,87,94,98] Moreover, irrespective of the frailty conceptual model adopted, it is clear that both multimorbidity and disability are strictly correlated with it.[98] However, it is important to keep in mind that these are interconnected but distinct entities, and a frail subject might be free from chronic disease and completely autonomous, as demonstrated by prof Linda Fried, who showed that this is the case in 26.6% of frail subjects.[37,99,100]

Given the aforementioned central role of muscle wasting and low energy levels in the pathogenesis of frailty (particularly when defined according to the frailty phenotype model), it is also unsurprising that nutritional issues, including both malnutrition and malnutrition risk, as well as obesity and abdominal obesity, have been linked to frailty. Different dietary habits have been shown in smaller studies to be protective against frailty, such as adherence to the Mediterranean diet and higher protein intake.[98,101] Additionally, a sedentary lifestyle, low levels of physical exercise, and smoking have been associated with higher odds of being frail.

Figure 4 – Risk factors (i.e., clinical correlates) for frailty onset and progression.



An association between lower levels of education (either expressed in years of education or level of schooling) and frailty has been reported, which is noteworthy because it underscores once more the multidimensional determinants of frailty and the impact of non-biological factors on its development.[21,39,94,98] However, evidence on this topic is inconclusive, and the potential impact of confounders such as socioeconomic status and social support is difficult to fully account for. Undoubtedly, a higher income is inversely associated with frailty, likely due to better access to healthcare, a healthier lifestyle, higher education, and greater resources.[98,102]

On the other hand, living alone, and being single or widowed, have been linked to higher odds of frailty.[94,98,103,104] Regarding the psychological and cognitive domains, cognitive impairment, depression and depressive symptoms, and loneliness, as well as sensory impairments in both hearing and vision have been linked to frailty.[105,106] Moreover, poor quality of life and self-perceived health have been identified as potential correlates of frailty, despite difficulties in discerning whether these represent risk factors for frailty or consequences of frailty, or both.[98]

Other less consistent correlations with frailty have been reported, including, among others, ethnic background, pain, sleep disturbances, polypharmacy, and various chronic conditions and physiological alterations.[98]

1.6 Prognostic impact of frailty

Despite their differences, the three conceptual models of frailty agree on one key aspect, that is: frailty exposes older adults to a host of negative clinical outcomes when challenged by even minor life events, such as a minor infection or illness, hospitalization, or a fall. The risk appears to be proportional to the severity of frailty and frequently leads to worsening frailty

levels and overall health status. Thus, frailty represents a leading cause of death and disability in older people, constituting a major global health issue.[7,12,14,107] In one 10-year prospective cohort study on community-dwelling older subjects, frailty was identified as the most common cause of death (27.9% of subjects), followed by organ failure (21.4%), neoplasia (19.3%), and dementia (13.8%).[108] The association of frailty with mortality is well acknowledged and has been confirmed by several studies across different subpopulations and clinical settings, employing different frailty instruments, as shown by systematic reviews on the topic.[109–114]

Coherent with the key role of reduced muscle mass and strength in the development of frailty, this condition has been established as a risk factor for declining mobility,[37] as well as for falls and fractures.[115–117] Subsequently, frailty frequently leads to the development of disability in community-dwelling older people[118,119], and is a major risk factor for hospitalization[120,121] and institutionalization.[122]

Moreover, when frail older individuals are hospitalized, they exhibit a higher risk of adverse outcomes related to hospital admission, including falls, delirium, pressure ulcers, and healthcare-associated infections (HAIs).[123–129] Several frailty-associated factors may contribute to these hospital-acquired complications, with one condition increasing the risk of developing another, resulting in a spiral of worsening frailty, longer lengths of stay, increased readmission rates, and higher in-hospital and post-discharge mortality.[125,130,131] Reduced mobility predisposes individuals to both falls and pressure ulcer development, while increased susceptibility to adverse drug events raises the risk of falls and delirium; in turn, delirium management may require the use of sedative drugs, further increasing and to increased fall risk.[123,124,129] Poor nutritional status may lead to impaired wound healing and immune dysfunction, thereby elevating the risk of pressure ulcers and HAIs.[125–128]

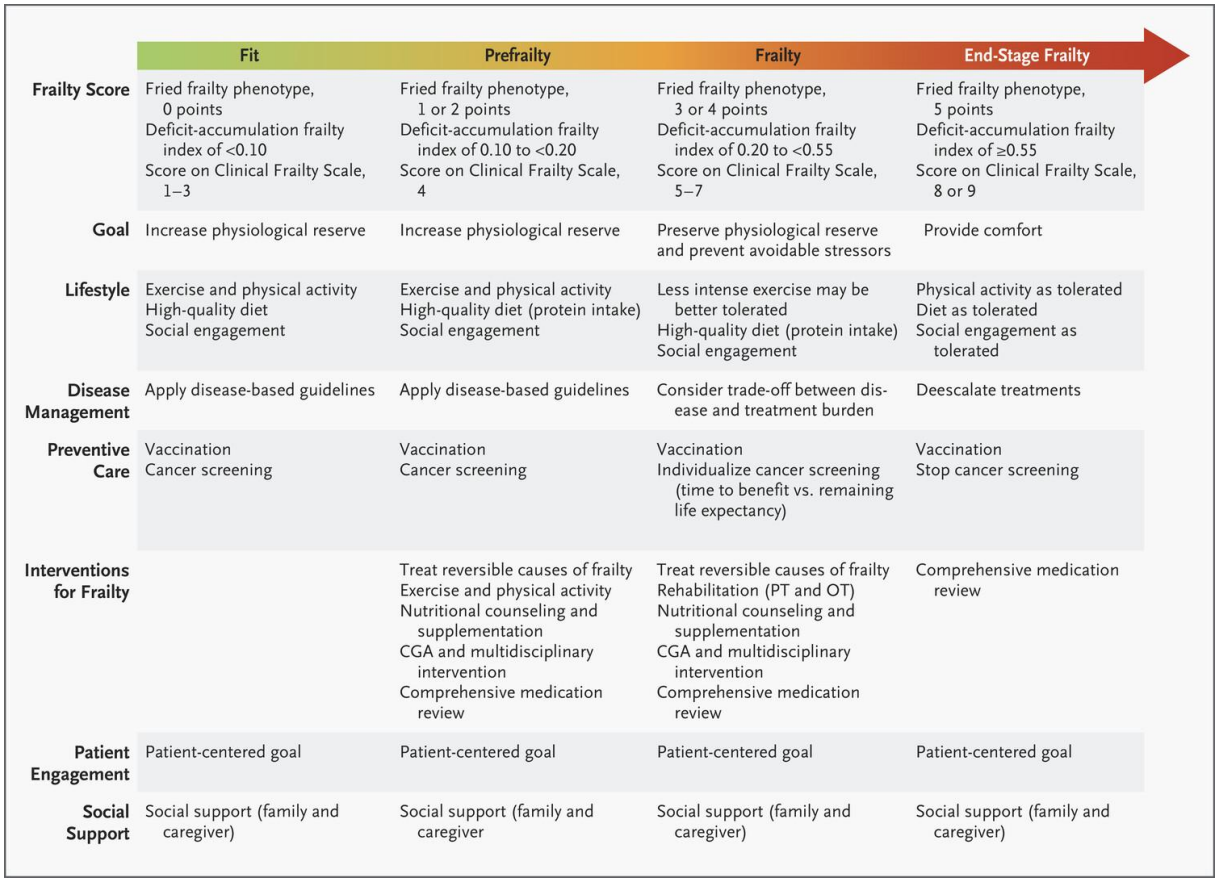
Frailty has also been linked to a broad range of other negative health outcomes, ranging from depression[132] and loneliness[105,133] to cognitive decline and dementia.[134,135] This ultimately underpins the association between frailty and lower quality of life.[136]

As previously stated, even though the association of frailty with negative health outcomes is widespread, different frailty instruments may be more suitable in specific clinical settings or for specific clinical purposes, or may more reliably predict certain clinical aspects than others. For example, frailty phenotype-based instruments have been proven to accurately predict risk of falls, fractures and disability, whereas tools stemming from the deficit accumulation model better predict the risk of hospitalization, disability and mortality. Multidimensional instruments can capture a variety of clinical outcomes, including declining quality of life and nursing home admission.[11]

1.7 Interventions for frailty

Since frail subjects show an increased risk of negative clinical outcomes, frailty frequently manifests as a progressive geriatric syndrome that leads to the development of disability and further worsening of frailty levels, thereby increasing the risk of complications. However, it has been demonstrated that frailty, like disability, is not always an irreversible condition: primary prevention strategies may prevent the progression from pre-frailty to overt frailty, whereas secondary interventions targeting functional and cognitive reserves may prevent further deterioration of frailty status and its unfavourable consequences, and, in some cases, reverse frailty to a pre-frailty state (*Figure 5*).[7,8,12,14] Proactive management of frailty can improve patient outcomes, enhance recovery, and reduce the overall burden on healthcare systems.[7,8,12,14,137,138]

Figure 5 – Lifelong prevention and management approach to the older adult first at risk of frailty development and, later on, with frailty of increasing frailty severity level.



	Fit	Prefrailty	Frailty	End-Stage Frailty
Frailty Score	Fried frailty phenotype, 0 points Deficit-accumulation frailty index of <0.10 Score on Clinical Frailty Scale, 1–3	Fried frailty phenotype, 1 or 2 points Deficit-accumulation frailty index of 0.10 to <0.20 Score on Clinical Frailty Scale, 4	Fried frailty phenotype, 3 or 4 points Deficit-accumulation frailty index of 0.20 to <0.55 Score on Clinical Frailty Scale, 5–7	Fried frailty phenotype, 5 points Deficit-accumulation frailty index of ≥0.55 Score on Clinical Frailty Scale, 8 or 9
Goal	Increase physiological reserve	Increase physiological reserve	Preserve physiological reserve and prevent avoidable stressors	Provide comfort
Lifestyle	Exercise and physical activity High-quality diet Social engagement	Exercise and physical activity High-quality diet (protein intake) Social engagement	Less intense exercise may be better tolerated High-quality diet (protein intake) Social engagement	Physical activity as tolerated Diet as tolerated Social engagement as tolerated
Disease Management	Apply disease-based guidelines	Apply disease-based guidelines	Consider trade-off between disease and treatment burden	Deescalate treatments
Preventive Care	Vaccination Cancer screening	Vaccination Cancer screening	Vaccination Individualize cancer screening (time to benefit vs. remaining life expectancy)	Vaccination Stop cancer screening
Interventions for Frailty		Treat reversible causes of frailty Exercise and physical activity Nutritional counseling and supplementation CGA and multidisciplinary intervention Comprehensive medication review	Treat reversible causes of frailty Rehabilitation (PT and OT) Nutritional counseling and supplementation CGA and multidisciplinary intervention Comprehensive medication review	Comprehensive medication review
Patient Engagement	Patient-centered goal	Patient-centered goal	Patient-centered goal	Patient-centered goal
Social Support	Social support (family and caregiver)	Social support (family and caregiver	Social support (family and caregiver)	Social support (family and caregiver)

Most trials on the topic have investigated the effectiveness of specific single- or multi-component interventions on the prevalence and severity of the frailty phenotype. Single molecules have been investigated for frailty prevention and management, based on the

aforementioned potential pathogenetic mechanisms; however, as might be expected, intervention studies have yielded inconclusive results due to the complex, multifactorial nature of this clinical syndrome. Vitamin D, n-3 fatty acid, sex hormone and growth hormone supplementation have been the most frequently studied single-molecule interventions.[139–145] However, despite evidence of beneficial effects in specific conditions, their use in the management of frailty remains controversial and, to date, not supported by high-quality, robust evidence.[8,146]

Not unexpectedly, when targeting physical frailty, the most consistent benefits have been demonstrated with physical exercise, including both resistance and aerobic training, as well as balance and coordination exercises.[147–158] These interventions, both alone and combined with nutritional interventions, prevent or improve frailty status according to Fried's frailty phenotype sriteria, and improve functional performance and mobility both in frail and non-frail older subjects, in the community and during hospital admission.[147–150,158] This might increase autonomy in Activities of Daily Living (ADL),[147,148,158] whereas the impact on fall risk is less certain.[148,150,158] Finally, some data suggest that exercise may increase bone density and reduce the risk of fall-related fractures.[159] However, heterogeneity in the type of intervention (e.g., frequency, intensity, and type of physical exercise), frailty measurement, and setting make it difficult to come up with conclusive evidence on the most effective exercise program; moreover, apparently, the net clinical benefit of this kind of intervention decreased with increasing severity of frailty.[8,160]

Nutritional interventions, mainly in the form of oral nutritional supplements or dietary programs providing 25 to 30 grams of protein per meal, might help counteract muscle loss in frail older subjects, and might have a role in reducing the risk or improving physical frailty, but evidence for an impact of nutritional interventions without combined physical exercise are of low quality.[147,161] Also, the impact of physical exercise without combined nutritional interventions seems to be less relevant. Therefore, a combination of physical exercise and nutritional supplementation (i.e., protein supplementation), seems to be the most effective multicomponent intervention when addressing physical frailty across a variety of settings.[8]

Moreover, the interventions that have been proved efficacious for the management of frailty in the ideal setting of clinical trials, might prove less effective in pragmatic routine care contexts.[162,163] The challenge of the future will be to understand the real-world effectiveness of these interventions and, most importantly, to determine how to implement and adapt them to obtain their benefits in specific populations with particular needs and habits.[13]

Despite the fact that most intervention studies have been directed toward community-

dwelling older individuals at risk of frailty or with frailty, the heightened risk of hospital-acquired complications in frail older subjects and their detrimental effect on overall health and frailty status make it essential to identify high-risk patients early, thereby enabling the implementation of preventive strategies such as delirium management protocols, early mobilization programs, infection control measures, and skin integrity preservation initiatives. A crucial aspect of frailty management is reducing the risks associated with routine care for frail older subjects. The first step is to proactively identify frail subjects among older patients accessing healthcare facilities, ensuring that they are not unnecessarily undertreated, but rather that patient-centered care is enabled, leading to better outcomes for all patients.[8,164]

For example, the adoption of coping strategies, such as maintaining a daily routine in a familiar environment and preserving a social network, as well as investing resources, might help frail patients to maintain basic and advanced ADL, thereby protecting their social role.[165]

Among more complex interventions, a CGA in both non-frail and frail community-dwelling older adults was shown to prevent or effectively ameliorate physical frailty, with a high level of certainty, besides reducing the risk of unplanned hospitalization.[163,166] In hospitalised older patients the well-known benefits of the CGA include the reduction of risk of nursing home admission and of hospital-associated complications such as falls, postoperative delirium and death, cognitive and functional decline.[163,166] However, patients with more severe frailty show seem to get smaller benefits.[167] Another complex intervention that has been studied for the prevention and management of frailty in older adults is medication optimization, including the use of explicit criteria for appropriate prescribing such as the STOPP/START criteria and Beers' Criteria.[168,169] Despite the potential major role of polypharmacy in the pathogenesis of frailty through inappropriate prescribing, adverse drug events and ED visits/hospitalizations,[170,171] results of medication optimization trials on older subjects across a variety of settings gave inconsistent results, probably due to the extreme heterogeneity of interventions, as well as a low level of adoption of suggested therapeutic changes.[172–175] Medication optimization probably reduces the risk of adverse drug events, including falls, and of unplanned ED visits and hospitalizations.[172–175] However, there is no evidence from randomized controlled trials on the impact of medication optimization on frailty.[8]

A different kind of approach to the management of frail older adults might be to focus on healthcare organizational aspects and models, rather than targeting specific conditions and risks in hospitalized frail older adults. In this perspective, care transitions and settings (i.e., care delivery at home and in outpatient clinics, ED visits, inpatient wards, hospital discharge and nursing home admission) are crucial moments in the older patient's frailty trajectory, given the

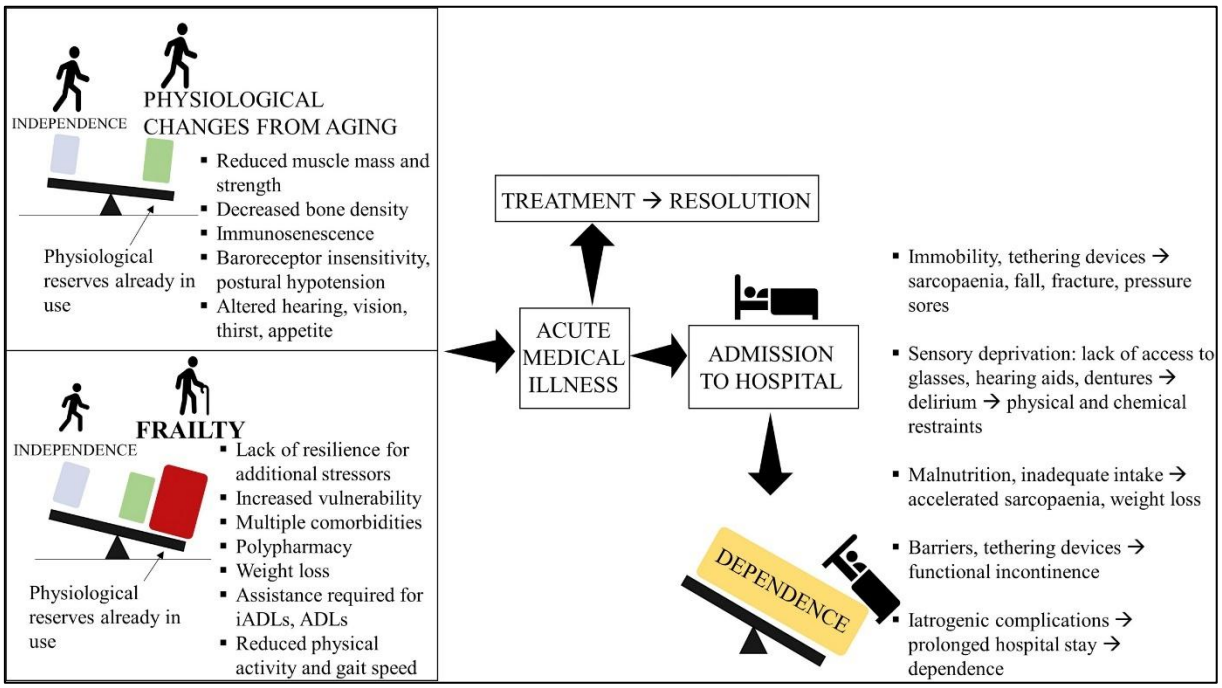
high risks of healthcare-associated harms. Unmet needs exist across the age spectrum, but given the high stakes and immediacy of consequences, enhancing hospital care safety for older adults with frailty should be regarded as a high priority.[8]

2. Management of acutely ill frail older adults

2.1 Hospital-acquired complications in frail older adults

Traditional in-hospital care, once considered the gold standard for treating acute illnesses, has long been associated with significant risks, especially for geriatric patients (*Figure 6*). Prolonged hospitalization can expose patients to hospital-acquired infections, an increased risk of falls, and other iatrogenic complications.[176,177] Older adults, who often have multiple comorbidities, are particularly vulnerable to the disorienting effects of an unfamiliar hospital environment, which can lead to delirium and further decline in functional status.[178,179] Moreover, a posthospital syndrome may develop as a result of deconditioning, malnutrition, sleep deprivation, and impaired mental status, thereby increasing the risk of short-term hospital readmission.[180] These risks, combined with the high cost of inpatient care, have spurred the exploration of alternative models that offer acute care in a more personalized and safer environment.

Figure 6 – Effects of hospitalization in frail older adults.



For older adults an unplanned hospitalization can represent a particularly troublesome event since, irrespective of the severity of the main diagnosis at admission, the physical, psychological, and social stresses underlying an acute admission can precipitate the development of geriatric syndromes, frequently marking the transition from a prefrailty state to overt frailty, and ultimately leading to disability that further increases the risk of additional

complications.[181] Approximately one third of older inpatients become dependent in at least one ADL, and less than half of these patients regains their prior level of independence within one year of discharge.

Hospital-acquired complications are conditions influenced by, but not directly linked to, the acute disease. In fact, they depend on the direct or indirect negative consequences of the hospital environment and medical treatments in predisposed individuals.

These hospital-acquired complications arise from a combination of factors including reduced mobility (due to general conditions, staff shortages, medical tubing such as drip lines, oxygen supplementation, or urinary catheters, and inappropriate bed rest), difficulties in maintaining autonomy in toilet use and urinary and fecal continence, malnutrition (due to inappropriate dietary restrictions, poor acceptance of hospital meals, challenges with self-feeding and staff shortages), as well as poor sleep quality (because of environmental and organizational factors), sensory impairments and difficulties with time orientation due to the lack of reference points (e.g. clocks, calendars, natural sunlight).[182] Moreover, symptoms such as anxiety, depression, and loneliness, that are related both to the acute condition and to limited visiting hours, as well as uncontrolled pain, dizziness, constipation, and side effects from new medications, further contribute to the development of these complications and to deconditioning of frail older adults.

Among the most studied hospital-acquired complications in the older adults are delirium (as well as worsening of behavioral and psychological symptoms of dementia), falls, urinary and fecal incontinence, functional dependence, pressure ulcer development, and HAIs.[183] As noted in the previous chapter, the incidence of these complications increases with the presence and severity of frailty; moreover, their occurrence strongly impacts on the hospital course by prolonging the length of hospital stay, raising the risk of further hospital-acquired complications, and ultimately leads to institutionalization, hospital readmission, disability, and death.[184]

Early recognition of frailty in older patients, starting from their ED entry, is therefore fundamental. Prompt implementation of positive hospital practices, including early mobilization, effective pain management, reorientation strategies, reduced boarding time, and advanced discharge planning, can positively influence outcomes by reducing the incidence of negative events during hospital stay and after discharge.[185] The importance of frailty recognition and management in acutely hospitalized older inpatients has been widely demonstrated in randomized controlled trials showing that in-hospital CGA reduces hospital-acquired complications and, ultimately nursing home admission and death.[68,186–188] In this perspective,

frailty should not be seen as an excuse to withhold potentially beneficial treatments from older adults but rather as a tool to deliver the best patient-centered care with realistic outcomes, reducing unnecessary hospital admissions and high-risk procedures, thereby preventing the development of hospital-acquired complications. Accordingly, evaluating different healthcare settings for delivering therapies, including clinics, day hospitals, home-based healthcare and Hospital-at-Home (HaH), should be carefully considered to reduce the risks of hospitalization in frail older adults.[185]

2.1.1 DELIRIUM

Delirium is defined, according to the text revision of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association, as a condition characterized by a fluctuating disturbance in attention and awareness that develops acutely over a short period of time, accompanied by an additional disturbance in a cognitive domain (e.g., memory, orientation, language, visuospatial ability or perception), that is not explained by a neurocognitive disorder but is secondary to a medical condition, substance intoxication or withdrawal, or a medication side effect.[189,190]

Predisposing (i.e., intrinsic) and precipitating (i.e., extrinsic) factors for delirium are well known and must be addressed during the hospital admission of an acutely ill older subject. Intrinsic risk factors include advanced age, preexisting sensory or cognitive impairment, malnutrition, chronic medical illnesses, and notably, frailty—which markedly increases vulnerability to delirium regardless of definition used to define it. Additionally, a history of prior delirium episodes or underlying neuropsychiatric conditions further predisposes patients to this condition. Precipitating factors encompass acute medical events and environmental stressors such as prolonged ED stays, urinary catheter placement, mobility constraints, polypharmacy (especially the use of psychotropic medications), uncontrolled pain, infections, electrolyte imbalances, and abrupt changes in medication regimens. Environmental contributors include sleep disruption, excessive noise, and the absence of familiar cues (e.g., clocks, calendars, and natural lighting).[123,124,129,190,191]

The relationship between frailty and delirium during hospitalization is bidirectional, although often overlooked by clinicians.[192] It has been estimated that frailty prevalence ranges from approximately 14% to 60% among surgical inpatients and from 8% to 17% among ED patients. Frail subjects exhibit an almost threefold higher incidence of delirium compared to non-frail older adults, irrespective of the frailty assessment tool used (e.g., frailty phenotype, FI, or CFS), because of their impaired resilience to stressor events.[193]

Delirium incidence, in turn, can precipitate further functional decline, prolong hospital length of stay, contribute to worsening of frailty and accelerate progression towards disability, leading to increased mortality, institutionalization and reduced quality of life.[190,191] Among several tools proposed for delirium screening and diagnosis, the 4-AT scale is a rapid, easy-to-administer tool that does not require specialized training for healthcare professionals. It evaluates alertness (scoring 4 points if the patients is clearly hyperactive or markedly slowed down), mentation (by asking for the patient's age, date of birth, current year and place, with 1 point scored for 1 error or 2 points for two or more errors), and attention (by having the patient name the months of the year backwards, scoring 2 points if fewer than 7 months are correctly named). Finally, 4 points are given for a clearly acute presentation with a fluctuating course over the past 2 weeks that persists within the last 24 hours. A total score of 4 or more is suggestive for the presence of delirium.[190,191,194]

Prevention strategies for delirium focus on minimizing the impact of predisposing factors and avoiding or at least reducing the presence of precipitating factors. These include optimizing the patient's medical condition, ensuring proper hydration, nutrition, drug therapy and pain control, and modifying the hospital environment by recreating a familiar setting with easily visible time references such as calendars and clocks, and ensuring adequate daytime lighting. Moreover, frequent visits from family and friends are essential for reorientation and cognitive stimulation, as well as for psychological wellbeing and help with ADLs. Additionally, ensuring proper sleep hygiene, early mobilization, and the use of corrective devices (e.g., glasses and hearing aids) help mitigate sensory deficits and isolation.[129,190,191,195]

2.1.2 FALLS

Falls are defined as unintentional events in which an individual comes to rest on the ground or other lower level for a reason other than a violent blow, loss of consciousness, or sudden onset of paralysis (e.g., due to a stroke or an epileptic seizure).[196]

Falls are common events during hospital stays, with an incidence ranging from 1.1 to 15.7 per 1,000 bed-days. The etiology of falls is typically multifactorial, involving a combination of patient-related (i.e., intrinsic) and environment-related (i.e., extrinsic) factors. Maintaining a standing position and walking requires the integration of multiple physiological systems; therefore, frail individuals, frequently presenting reduced muscle strength, impaired balance, and cognitive deficits, present an almost threefold risk of falls even under normal circumstances. From this perspective, a fall can be seen as the failure of a vulnerable complex system.[197]

During hospitalization, a frail older patient is further exposed by a combination of extrinsic hazards such as unfamiliar room layouts (e.g., toilet location), slippery floors, inadequate support during ambulation, and use of medications that can further impair balance or cognition. Additionally, prolonged bed rest exacerbates muscle weakness and deconditioning, further elevating fall risk. It has been described a post-hospital syndrome, a period following hospitalization characterized by generalized deconditioning and physiological stress further increasing the risk of falls, even after discharge.[180] Although many falls occur without significant consequences, they can also result in serious injuries, such as fractures, head trauma, and death. Moreover, even a single fall, regardless of its immediate clinical consequences, can trigger a cascade of adverse outcomes in frail older adults including prolonged hospital stays, increased healthcare costs, and a higher risk of nursing home admission.[198]

Effective fall risk management requires the identification of at-risk individuals, whether through a history of falls within the last year, the use of risk assessment scales and questionnaires, or direct evaluation of lower limb strength and balance (e.g., gait speed, the Timed Up and Go test, or the Short Physical Performance Battery). Fall prevention strategies encompass a range of interventions: first-line interventions include the use of walking aids and of appropriate footwear, as well as environmental changes such as improving lighting and utilizing alarm systems; second-line interventions involve medication review and optimization (particularly reducing the use of high-risk drugs such as benzodiazepines, antipsychotics, opioids, and antihypertensives) and close monitoring for delirium and infections; third-line interventions directly target the underlying causes of previous falls.[199]

2.1.3 PRESSURE INJURIES

Pressure injuries, also known as pressure ulcers, are localized damages to the skin and underlying soft tissues that usually develop over bony prominences or in relation with medical devices as a result of intense and/or prolonged pressure or pressure in combination with shear forces. Influencing factors on the development of pressure injuries include the skin microclimate, perfusion, nutritional status, and the presence of comorbidities.[200] Pressure injuries are classified into four ascending stages of severity: stage 1 is characterized by intact skin with a localized area of non-blanchable erythema, whereas stage 4 is defined by full-thickness skin and tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage, or bone.[200] Pressure injuries share risk factors with other hospital-acquired complications, including geriatric syndromes such as frailty, urinary incontinence, delirium,

and prolonged immobility. When these factors coexist with poor nutritional status, use of sedative medications, and pro-inflammatory or catabolic conditions, the skin's resilience is compromised, thereby increasing the susceptibility to soft tissue injuries.[201]

Pressure injuries impose a substantial negative impact on healthcare systems, because of the high direct costs related to wound bed preparation and dressing, and to the increased risks of HAIs, chronic pain, and further loss of mobility and functional autonomy. This leads to increased length of stay, disability development and increased risk of nursing home admission. Because of the multifactorial nature of pressure injury development and the widespread availability of preventive strategies, pressure injury occurrence is frequently used as an indicator of the quality of care and the effectiveness of prevention programs.[202]

2.1.4 HEALTHCARE-ASSOCIATED INFECTIONS

HAIs are defined as local or systemic infections presenting later than 48 hours after hospital admission, thereby distinguishing them from community-acquired infections. These infections have been classified in 13 distinct groups according to anatomical site.[203] The most frequent HAIs include hospital-acquired pneumonia, gastrointestinal infections, surgical site infections, and device-related infections (e.g. urinary tract infections in patients with urinary catheters, and catheter-associated bloodstream infections in patients with central venous catheters).[204,205]

The impact of HAIs on older adults is particularly severe, as HAIs often lead to prolonged hospital stays, and adverse effects from broad-spectrum antibiotic use, including selection of multidrug-resistant organisms, and higher mortality rates.[204–206]

The interplay between HAIs and frailty is bidirectional. Frail older adults are characterized by diminished immune function, reduced physiological reserves, impaired skin integrity, and poor nutritional status; these intrinsic vulnerabilities increase susceptibility to HAIs, particularly when invasive procedures and other hospital-related stressors are present.[127] On the other hand, the occurrence of an HAI can trigger or exacerbate frailty by inducing a systemic inflammatory response, accelerating muscle wasting and deconditioning, and further impairing cognitive and functional status. Understanding this bidirectional relationship is critical, as it underscores the need for comprehensive strategies that address both the prevention of HAIs and the management of frailty. Early detection of frailty and strict infection control measures are essential to breaking this cycle and improving clinical outcomes for this high-risk population.

Effective prevention strategies for HAIs involve a comprehensive and multifaceted

approach that addresses both patient-specific vulnerabilities and environmental risks. Pathogen transmission risk in healthcare settings is well established, especially in areas with high care intensity, which tend to have higher rates of HAIs and multidrug-resistant microorganisms; Strict adherence to infection control practices is essential. This includes rigorous hand hygiene, proper use of personal protective equipment, and regular, thorough environmental cleaning. Additionally, minimizing the use of invasive devices and ensuring their timely removal, when possible, can substantially lower the risk of device-related infections. Nutritional status optimization and early mobilization can strengthen immune function and skin integrity. Finally, adopting patient-centered strategies, such as reducing unnecessary hospital stays, implementing isolation protocols, and leveraging telemedicine for remote monitoring, contributes to creating a safer care environment that minimizes exposure to infectious agents.[204,207,208]

2.2 The Hospital-at-Home as an alternative to the acute hospital ward for frail older adults

The challenges posed by the increasing number of older individuals affected by multiple chronic conditions, often requiring acute care with subsequent hospital overcrowding and soaring healthcare costs, have prompted healthcare systems worldwide to design, develop, and implement alternative healthcare delivery models to traditional "brick-and-mortar" in-hospital admissions.[2] This need is even more pressing for individuals living with geriatric syndromes, including frailty, due to their heightened risk of hospital-acquired complications.[126,178,180,209,210]

Over the past 20 years, the response to these challenges has been the expansion of out-of-hospital services aimed at reducing the negative impact of chronic disease exacerbations on patients' functional autonomy, increasing life expectancy free from disability, and reducing costs. Among these interventions, the Hospital-at-Home (HaH) model has long been proposed and studied as an alternative for providing hospital-level care to acutely ill, predominantly frail and older patients in their homes, patients that would have been otherwise admitted to the hospital.[211–217] This approach has been increasingly enabled by a cultural shift from disease-focused to patient-centered care,[218–221] and by advances in medical equipment and technology, including portable devices and telehealth solutions.[222,223]

2.2.1 First Hospital-at-Home experiences and Turin experience

The first HaH programs were developed and studied in the late 1970s, primarily in Europe (France, Italy, and the United Kingdom - UK).[224–226] The fundamental idea of the HaH model

was to replicate hospital-level care outside the traditional in-hospital setting, thereby providing patients with the benefits of comprehensive medical treatment while minimizing the inherent risks of hospitalization.[227]

Over time, HaH has evolved from isolated experimental programs into a more structured and integrated model, gaining momentum in the 1990s with pilot projects expanding beyond Europe to Australia, New Zealand, Israel, and the USA.[228–231]

The HaH project in Turin is based in the Geriatric Medicine Division of Molinette University Hospital in the A.O.U. Città della Salute e della Scienza di Torino. It represents one of the first HaH experiences worldwide, with its initial experimental phases dating back to 1985. In 2010, a Resolution by the Piemonte Regional Council (DGR 16 marzo 2010 n.85-1350) officially recognized the HaH model and defined its characteristics and reimbursement modalities by the Regional Healthcare Service.[232] It operates a mixed model, incorporating both AA-HaH and ESD-HaH. A hospital-based team delivers medical and nursing care at home throughout the duration of admission.

This team consists of five geriatric medicine consultants, three to four geriatric medicine residents, and fifteen nurses, including a nurse coordinator and a case-manager nurse responsible for case finding and discharge planning. A social worker, a nurse specialist for vascular access, and a physiotherapist also collaborate with the team; additionally, a home radiology service provides chest X-ray and ultrasound examinations, while consultants of other medical and surgical specialties are available for teleconsultation or in-hospital consultation as needed. The team is available 7 days a week, all year round, from 8 AM to 8 PM, for both scheduled and urgent home visits. Nighttime emergencies are managed by the territorial Emergency Medical Team, which, if possible, treats acute conditions at home; if this is not possible, patients are transferred to the Molinette Hospital ED and, when feasible, returned home upon clinical stabilization.

Among the procedures and treatments delivered by the Turin HaH are intravenous therapy (including antibiotics and parenteral nutrition), red blood cell and platelet transfusions, enteral nutrition, wound dressings for pressure injuries and other ulcers, stable venous catheter (i.e., Midline and Peripherally Inserted Central Catheter) placements, bedside ultrasound exams, and patient and caregiver education. Criteria for HaH admission at the Turin HaH include the need for hospitalization, absence of requirement for invasive or continuous monitoring, the presence of a continuous (i.e., 24/7) caregiver, and a home located within the HaH's catchment area.

Over its many years of work, the Turin HaH has proven to be a safe and effective alternative to traditional in-hospital stays for several conditions. [233–239] This notwithstanding,

the Turin HaH has long remained a unique experience within Italy and has yet to expand its catchment area. As in many other regions worldwide, the Coronavirus Disease 2019 (COVID-19) pandemic, with its tremendous demand for hospital beds to manage infected patients and the almost impossible task to maintain COVID-19-free wards,[240] has spurred the Italian healthcare system to expand and implement home-based and telemedicine-supported care models.[241–245] Among these, an initiative with similar yet not superimposable characteristics with the Turin HaH has been proposed in the Toscana Region, called "Gruppi di Intervento Rapido Ospedale e Territorio" (Groups of rapid intervention Hospital-Community - GIROT).[246,247]

2.2.2 General characteristics of the Hospital-at-Home

Despite considerable heterogeneity among HaH models worldwide in terms of organization (e.g., hospital-based vs community-based programs, number of home visits, and availability of after-hours support), healthcare professionals involved, levels of telemedicine adoption, types of interventions delivered (e.g., patient and/or caregiver education), and medical conditions treated, there is now a consensus to define HaH as an integrated healthcare model that delivers hospital-level care in patients' homes as a substitute for in-hospital stays, for a limited time.[213,215,227,248–253]

These HaH programs typically involve a multidisciplinary team that may include physicians, nurses, and allied health professionals (e.g., physiotherapists, occupational therapists, and social workers) who provide home visits, intravenous treatments (sometimes including transfusions or chemotherapy), laboratory and imaging exams, as well as oxygen supplementation.[213,215,249–253] When an occasional facility-based service (e.g., a computed tomography scan, magnetic resonance imaging, or endoscopy) is needed, round-trip transportation to a facility is arranged. The use of telemedicine tools, remote monitoring devices, and portable diagnostic equipment is common in HaH models, although practices vary due to factors such as costs, regulatory limitations, and organizational structure.[235,254,255] Despite these differences, it is now clear that HaH is not a transitional care model (since its primary focus is not on post-discharge recovery), nor is it an outpatient parenteral antimicrobial therapy (OPAT) service (because its services are more complex and home-based), and it is distinct from Home Health Care or Palliative Home Care (as its main objective is to provide acute care).[213,215,227,249,250,252,253]

There are two main models of HaH, which sometimes coexist within the same setting. The first model, known as Admission Avoidance HaH (AA-HaH), sometimes referred to as

"hospital substitution" HaH, entails the direct admission of patients from the community (e.g., via referrals from General Practitioners or Home-based Primary Care) or, more frequently, from the ED. This approach allows patients to completely avoid hospitalization, thereby reducing the risks of hospital-acquired complications, except from those directly associated with the initial clinical encounter or brief ED observation.[211,216,217,256] The second model is called Early Supported Discharge HaH (ESD-HaH) and enables patients who have been initially admitted to an acute hospital setting to reduce the length of their traditional hospital stay by completing their diagnostic and therapeutic process at home. By transitioning patients earlier to a home-based setting while maintaining hospital-level care, ESD-HaH not only reduces hospital-related risks but also enhances resource allocation within the healthcare system.[211,257,258]

Initially, HaH pilot programs and research studies focused on a limited number of acute medical conditions, such as exacerbations of chronic obstructive pulmonary disease (COPD) and congestive heart failure, as well as hip fracture.[233,234,259,260] However, it soon became clear that strict diagnosis-based eligibility criteria were overly restrictive and excluded patients who might have benefited from HaH care. Consequently, HaH models shifted patient selection criteria from condition-based to patient-based.[215,251] Current HaH eligibility criteria focus on a balance between clinical stability, management requirements, and medical need: patients must ill enough to require hospital level care but be not so critically ill that they cannot be safely managed at home.[213] This individualized selection process requires not only an evaluation and prediction of medical needs during HaH admission, but also an assessment of social and environmental factors that are fundamental for HaH safety and success, such as the presence of a reliable, continuous caregiving support, a supportive home infrastructure, and reasonable proximity to the hospital in case of clinical deterioration (i.e., a pre-specified location). Conversely, patients requiring continuous or invasive monitoring, high-intensity interventions, or those at imminent risk of clinical deterioration (i.e., clinically unstable) are generally excluded from HaH programs.[250,251]

2.2.3 Benefits of Hospital-at-Home admission

An expanding body of evidence, synthesized in multiple several systematic reviews on the topic, has demonstrated that, when supported by an appropriate infrastructure and coordination, HaH can provide acute care at home that is as safe and effective as inpatient management for selected patients with acute or acutely decompensated chronic conditions.[211,214,216,217,256,257,261,262] In fact, HaH might represent a better alternative for frail older subjects, as it significantly reduces the risk of hospital-acquired complications,[236,261,263,264]

enhances patient experience,[234,257,263–269] and lowers overall healthcare costs (*Figure 7*).[233,234,264,270–277] Both AA-HaH and ESD-HaH have been proven safe and effective; while ESD-HaH has been more extensively studied, AA-HaH appears to be particularly advantageous in terms of cost-effectiveness, hospital-acquired complications, mortality, and readmission rates.[211,216,256–258]

Figure 7 – Effects of Hospital at Home on patients, caregivers and healthcare organizations.

The positive effects of home hospitalization on physiological and psychological well-being are particularly relevant for frail older patients, given how disruptive an unfamiliar hospital environment can be for them.[178,278] Patients managed in their own homes retain better social engagement, lower levels of anxiety and depressive symptoms, and improved sleep quality, all of which contribute to faster recovery and overall better health status and quality of life.[233,234,237,256,279] From a nutritional perspective, malnutrition and risk of malnutrition are extremely common in acutely-ill older patients[280] and, despite hospital meals are specifically designed to meet medical needs, they often lack the familiarity and sensory appeal of homemade meals, a particularly important consideration for older individuals struggling with anorexia of aging.[281,282] HaH has been associated in some studies with higher caloric and fluid intake by mouth, and this may improve overall nutritional status and reduce the risk of dehydration (and thus of delirium, falls, and pressure injuries).[233]

In terms of mobility and functional independence, HaH offers a significant advantage over traditional hospitalization. While hospital environments often impose mobility restrictions, leading to deconditioning and increased risk of pressure injuries,[209,278,283] the home setting allows the patient to remain more active and retain independence in ADLs as much as possible within a familiar environment.[258,276,284] Although managing fall-related risks at home presents

challenges, home management also represents a unique opportunity to evaluate and effectively address environmental risk factors for falls.[285] Hospitalization is a well-known precipitant of behavioral and psychological symptoms of dementia, which can manifest as agitation, aggression, and delirium due to environmental change, disrupted routines, and sensory overstimulation. Managing these patients at home allows for continuity in daily routines, reducing behavioral disturbances and alleviating caregiver burden.[238,239] The ability to remain in a familiar setting is also a key factor in lower delirium incidence, as demonstrated by studies comparing delirium rates in home-managed versus hospital-managed patients.[236,261,264,286]

Finally, another critical advantage of HaH is the reduction in HAIs, particularly infections caused by multidrug-resistant organisms.[256,287] Traditional hospital environments pose a high risk of cross-contamination due to close patient proximity, frequent invasive procedures, and prolonged antibiotic exposure. By contrast, home-based care, including HaH, significantly mitigates exposure to nosocomial pathogens, thereby reducing the risk of hospital-acquired pneumonia, catheter-associated urinary tract infections, bloodstream infections, and *Clostridioides difficile* infections.[204,208]

Moreover, home hospitalization represents a unique opportunity for healthcare professionals to directly assess patients within their own home environment and in the familiar context. This allows the implementation of tailored interventions, including targeted education for both patients and caregivers, while preserving their autonomy in the management of their physiological and clinical needs, thus promoting patient empowerment and increasing trust in self-efficacy.[266,276,288,289] Such an approach can lead to reduced anxiety and depressive symptoms among patients receiving HaH care, and improved patient satisfaction, primarily due to increased feelings of safety, value, respect, personalized care, improved communication, and reduced burden of frequent hospital visits.[256,267,268] However, the impact on caregiver experience is mixed, as increased responsibilities at home can sometimes contribute to caregiver burden unless adequately supported through education, respite care, and ongoing assistance.[256,266,268,269,289–291]

The effect of home hospitalization on overall length of stay is controversial, with some studies showing a shorter length of stay,[216,254,257,258,264,272,274,275,292,293] whereas others highglighting an equal or even longer length of stay for patients managed in HaH.[233,234,256,276,294] While AA-HaH may reduce the duration of in-hospital stays, the total length of care might in fact be slightly longer, partly due to the difficulty in clearly distinguishing between the acute and post-acute care in patients managed at home. In traditional hospitalisations, patients are frequently transferred to lower-intensity healthcare facilities, a factor that is not taken into

account in length-of-stay calculations.

Nevertheless, HaH represents a viable modality for delivering complex, high-level healthcare at a significantly reduced daily cost compared with traditional inpatient care.[233,234,264,270–277] This has been attributed to lower costs of out of hospital management, apparently lower use of diagnostics and lower hospital-acquired complications. However, the cost-effectiveness of HaH programs enabled by use of high-end telemedicine and telemonitoring technology is unclear.[214] Moreover, several studies have shown lower ED accesses and lower readmission rates for patients managed in HaH, further contributing to cost savings for healthcare systems[233,234,256,263,272,277,292]; however, other studies reported similar rates of hospital readmission for HaH patients.[217,258,264,294]

Furthermore, HaH is associated with a lower risk of institutionalization, both at discharge and at six months post-discharge,[216,217,233,256,257] and there is some, albeit inconclusive evidence suggesting that HaH might slightly reduce mortality at 6 to 12 months from discharge.[216,295]

Finally, HaH might represent a valuable alternative for geriatricians and families of frail older subjects who face the frequent challenging decision between pursuing care intensification with traditional hospitalization and its inherent risks, or opting for treatment withdrawal. HaH not only provides a safer acute care environment but also offers the possibility of transitioning to in-home supportive and palliative care in case of treatment insuccess.[278]

2.2.4 CHALLENGES OF HOME HOSPITALIZATION

Despite its many advantages, the HaH model is not without challenges, and according to recent Cochrane reviews on the topic, addressing existing barriers to home hospitalization is paramount to rapidly and effectively scale up HaH programs beyond their foundational years to reach their full potential.[295,296] Key objectives in this sense include: i) increasing the number of virtual HaH beds, through better patient identification and referral, increased acceptance of HaH from patients and caregivers and addressing issues about equity of the model ii) standardizing training for healthcare professionals, and iii) ensuring the long-term economic sustainability of scaled up services also by addressing reimbursement issues. Many of these challenges could be addressed through comprehensive educational programs to raise awareness about the characteristics and potential benefits of the HaH model among both the lay public and healthcare workers.[295–298]

In a recent study investigating reasons for HaH acceptance or refusal from patients and caregivers, Saenger and colleagues found that the main drivers for HaH acceptance among patients include the greater comfort of the home environment, the proximity to family, the

ability to maintain an active lifestyle, as well as avoidance of exposure to nosocomial infections, previous negative experiences with traditional hospital admissions, and fear of not returning back home from the hospital.[299] Conversely, more than one third of patients who refused HaH admission did not give any specific reason, probably indicating poor comprehension or prejudices of how the HaH model works. Among the most commonly stated drawbacks for HaH admission are generic preferences for traditional hospital care, concerns about the adequacy of home care (supported by perceptions of higher quality and safety), and discomfort with having healthcare professionals in their homes.[266,288,297–300] Other factors that limit HaH uptake include fears of delayed access to care escalation in case of deterioration of patient's conditions, caregiver apprehensions about managing complex tasks (such as drip line management), and insufficient training of healthcare providers, which can lead to incomplete or inaccurate information being provided when HaH is proposed or even result in HaH being omitted as a care option. [266,288,297–300] Most of these fears and misconceptions about HaH could be properly addressed through targeted patient education, appropriate tight links with Emergency Medical Teams and EDs and continuing research.

Undoubtedly, one of the principal drawbacks of HaH is its reliance on caregivers to manage essential care tasks, ranging from meal preparation and personal hygiene assistance to clinical monitoring (including vital signs detection and management of venous lines) and communication with the clinical team. Such responsibilities, particularly during periods such as acute illness when patients' needs are heightened, can lead to increased caregiver burden and distress.[256,266,268,290,291] However, these challenges can be mitigated through robust caregiver education, training and support.[289,296] Still, increased caregiving demands during HaH may impose additional costs on families, thereby diminishing the overall economic benefits of home hospitalization.[291] This issue, combined with biased patient selection by HaH programs or the preferential adoption of HaH by commercial insurers, fuels concerns about potential increase of healthcare inequities favoring higher-income subjects.[292,301] Home hospitalization could in fact potentially benefit more patients of lower socioeconomic status by directly addressing key social determinants of health and frailty, such as suboptimal home environment, limited health literacy and inadequate caregiver education, and by ensuring smoother transitions between levels of care.[292] Patient selection criteria also require careful consideration; not all patients are suitable candidates for HaH, and factors such as the safety of the home environment and the presence of a supportive caregiver are critical.

From a scalability perspective, HaH infrastructure requirements, including the availability of reliable telemedicine systems and home-based diagnostic equipment, remain

significant hurdles, particularly in rural or underserved areas. Furthermore, transitioning from hospital-based to home-based care demands extensive training for medical personnel, who must adapt to new workflows and emerging technologies.[302] Economic sustainability, in terms of reimbursement models and long-term cost-effectiveness, continues to be an area that necessitates further policy development and research.[248]

Looking toward the future, the continued evolution of HaH will likely be shaped by advancements in technology, changes in healthcare policy, and the growing needs of an aging population. Innovations such as artificial intelligence, wearable health devices, and more sophisticated telehealth platforms and information technology solutions are poised to enhance the delivery of acute care in the home setting. From the perspective of geriatric patients, these technological advances offer the promise of more precise monitoring and timely interventions, potentially reducing hospital readmissions and improving quality of life.[235,255,289,303–305] From the HaH perspective, such advances could reduce unnecessary exposure of healthcare personnel to infectious risks, enhance caregiver education and support, and optimize patient identification and case management.[235,306–310]

PERSONAL RESEARCH

3. Research questions and methods

3.1 Knowledge gaps and study objectives

As discussed in previous sections, despite ongoing debate regarding frailty conceptualization and the absence of a universally accepted frailty operational tool, frailty is now widely recognized as a geriatric syndrome that predisposes older individuals to an increased risk of major adverse outcomes following even minor stressor events.[6–10]

Hospitalization, in particular, poses a significant risk in older adults because of the interaction between the acute illness and the unfamiliar hospital environment, with risk of deconditioning, malnutrition, sleep deprivation, and confusion. This often leads to hospital-acquired complications such as delirium, falls, pressure injuries and HAIs,[176–179] as well as to the emergence of a post-hospital syndrome characterized by worsened functional status and increased short-term risk of hospital readmission,[180] that may eventually lead to disability, institutionalization, and death.

Among alternative healthcare models to the traditional "brick-and-mortar" acute ward, HaH has emerged as a safe and effective modality for delivering acute care, particularly in older adults. HaH programs have shown potential in reducing the incidence of hospital-acquired complications, improving patient and caregiver satisfaction, and reduce healthcare costs.[211,213,214,216,257] However, despite the increasing adoption of HaH as an alternative or even preferable approach for managing frail older adults, data on frailty within this setting remain limited. Most available studies on HaH report mean values of frailty indices rather than prevalence estimates, often using screening instruments or non-validated measures.[276,311–316]

Therefore, given the existence of three different conceptual models of frailty and the lack of a consensus for its operationalization, the moderate agreement between available frailty tools, and the possibility that they might capture different aspects of the frail subject, significant knowledge gaps persist regarding both the prevalence of frailty across different healthcare settings, including the HaH, and their combined prognostic impact in acute older adults.

With the aim of addressing these evidence gaps, the present Ph.D. project proposes the following specific objectives:

1) To assess the prevalence of frailty according to different operational definitions derived from the three different conceptual models of frailty (i.e., frailty phenotype,

deficit accumulation and multidimensional models), in acutely ill older adults admitted to either an acute geriatric ward (AGW) or in a HaH service

2) To evaluate the agreement among different frailty definitions across different healthcare settings (AGW vs HaH)
3) To investigate the prognostic role and interaction of frailty (as defined by each operational tool) and healthcare setting (AGW or HaH) on outcomes:
    a. during admission, including all-cause mortality and hospital-acquired complications (i.e., delirium, falls, pressure injuries, and healthcare associated-infections)
    b. after discharge, including all-cause mortality, institutionalization, unplanned readmissions or ED visits, and worsening functional status.

3.2 Study design, setting and participants

The "*Prevalence and impact of frailty and MUltidimensional Frailty determinants in older patients Admitted to different healthcare Settings for Acute conditions*" (MUFASA) study was a monocentric, prospective observational cohort study conducted at the acute geriatric ward (AGW) and Hospital-at-Home (HaH) Service of the Geriatric Medicine Division of the Molinette University Hospital, A.O.U. Città della Salute e della Scienza di Torino, Turin, Italy. The Ph.D. Candidate had an active role in study conception, study protocol, case report form (CRF) and database design, data acquisition and analysis, as well as in the interpretation of results. The results of the MUFASA study are presented according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) recommendations.[317] The original (Italian language) study CRF is available in the *Appendix*.

Patients were enrolled in the MUFASA study from 20th April 2022 to 3rd June 2024. Patients admitted to the participating AGW and HaH units were screened for eligibility at least twice weekly according to predefined inclusion and exclusion criteria, and those providing written informed consent to the study were consecutively enrolled. Start of patient enrollment was deferred due to delayed Ethics Committee approval and was further slowed down by one of the final COVID-19 outbreaks in the participating units.

Patients meeting all the following inclusion criteria and none of the following exclusion criteria were considered eligible to participate in the MUFASA study:

- *Inclusion criteria:*
    - Age 65 years or older at admission

- Admission for any acute or decompensated chronic condition
- Written informed consent signed by the patient or their legal representative

- *Exclusion criteria:*
  - Residents of long-term care (LTC) facilities at admission
  - Planned admission solely to perform a single diagnostic or therapeutic procedure (e.g., venous catheter placement, blood transfusion)
  - Patient approaching the end of life due to a terminal illness at admission for whom a palliative approach has been decided.

3.3 Ethical approval

The MUFASA study was conducted in accordance with the "Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects" of the Declaration of Helsinki.[318] The study protocol was reviewed and approved by the Local Ethics Committee (Comitato Etico Interaziendale A.O.U. Città della Salute e della Scienza di Torino, A.O. Ordine Mauriziano di Torino, A.S.L. Città di Torino), under protocol reference number 35389 A/2.4.8 and case number 107/2022 Written informed consent was obtained from each participant or their legal representative prior to study inclusion, ensuring that all individuals were fully aware of the study procedures, risks, and benefits.

3.4 Baseline evaluation

At study enrollment, all study participants underwent a CGA that included frailty assessment as well as measures of physical performance and muscle strength. This evaluation was conducted by geriatric medicine residents supported by two geriatric medicine specialists.

Besides CGA data, sociodemographic information and variables related to hospital admission, including vital signs, mental status and main laboratory test results at AGW/HaH entry were recorded. A detailed description of the frailty definitions used in this study, along with other variables and measures is provided in the following sections.

3.4.1 FRAILTY ASSESSMENT

Frailty status at admission was assessed according to the Fried Frailty Phenotype (FFP), the Frailty Index (FI), the Clinical Frailty Scale (CFS) and the Multidimensional Prognostic Index (MPI).

FRIED FRAILTY PHENOTYPE

All items of the FFP were evaluated according to the original criteria published by Linda Fried in 2001,[37] except for the assessment of low activity levels. In this case, the MLTAQ was deemed inappropriate for Italian older adults; therefore, according to previously published suggestions, the PASE was used instead.[51–55,319–321]. In detail, the FFP items were evaluated as follows:

- *Shrinking,* defined as an unintentional weight loss of 4,5 kilograms or more in the last 12 months, as reported by the patient or their caregiver
- *Weakness,* assessed via handgrip strength using a Jamar handheld dynamometer according to published recommendations;[84] the highest value from repeated measures was recorded, and weakness was defined according to Fried's original cutoffs stratified by sex and BMI (**Table 2**)
- *Exhaustion,* considered to be present if the patient responded with "a moderate amount of time" or "most of the time" to either one of the following questions: "In the last week, I felt that everything I did was an effort" and "In the last week, I could not get going", derived from the CESD[43,322]
- *Slowness,* measured using a stopwatch as the time required for the patient to walk 4.57 meters at their usual pace; patients were allowed to use walking aids if needed, and the mean of two measurements was used. Slowness was defined according to Fried's original cutoffs, stratified by sex and height (*Table 2*). Patients who were unable to perform the walking test due to chronic conditions preceding the index hospital admission were considered positive for the slowness criterion, whereas those unable to perform the gait speed test within the first 48 hours from enrollment due to acute conditions were classified as missing
- *Low physical activity levels*, evaluated using the Italian version of the PASE, a scale that explores the frequency and duration of leisure and household activities of different intensity over the past week, with higher scores indicating higher levels of physical activity.[55,319] Subjects were classified as having low activity levels if their total PASE score was equal or lower than 55, corresponding to the published Italian cutoff for the 25th percentile of the Italian population of subjects aged 65 years and older.[323]

Patients were considered frail according to the FFP if they met at least three criteria, pre-frail if they met 1-2 criteria and robust if they met none.[37] Patients with missing items were considered frail if they met at least 3 criteria; otherwise, they were classified as missing and

handled accordingly in the statistical analyses, as described in the Statistical methods section. Pre-frail and robust patients were grouped as non-frail according to the FFP.

Table 2 – Handgrip strength and 4.5-meter walking time cutoffs for defining weakness and exhaustion according to the Fried Frailty Phenotype.

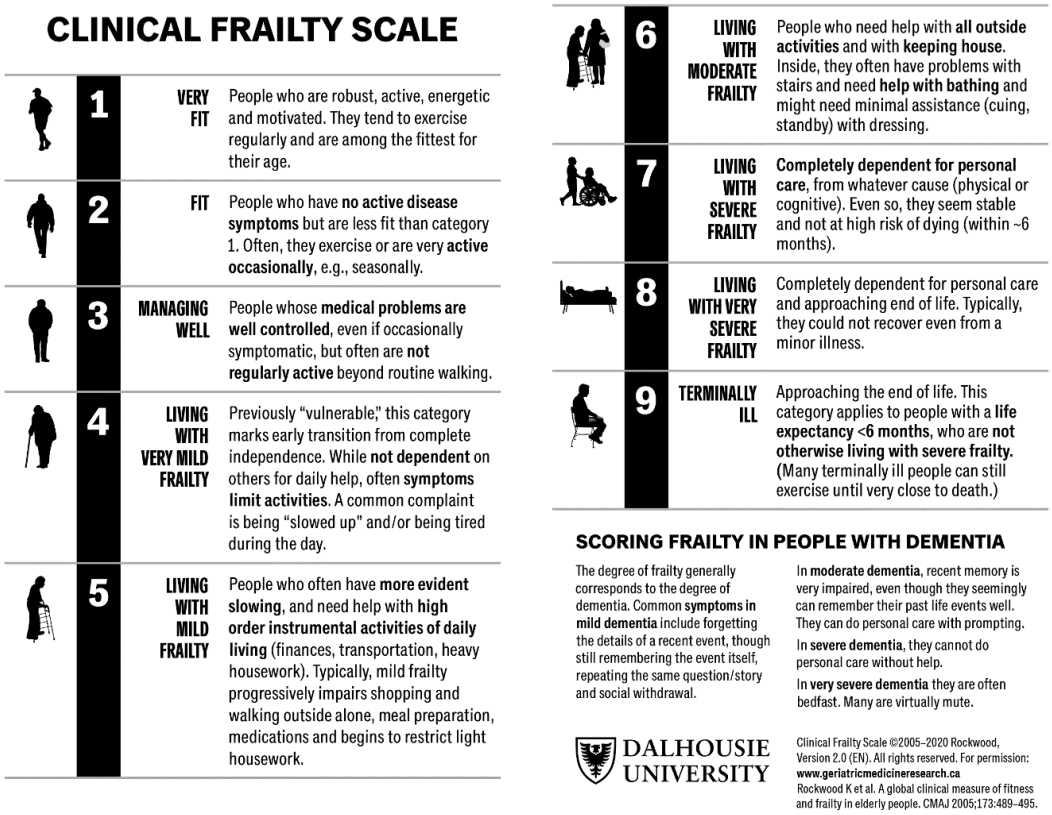
Handgrip strength test cutoffs for weakness, stratified according to BMI and sex			
BMI (kg/m^2)	*Male sex cutoff (kg)*	*BMI (kg/m^2)*	*Female sex cutoff (kg)*
≤24	≤29	≤23	≤17
24.1-26	≤30	23.1-26	≤17.3
26.1-28	≤30	26.1-29	≤18
>28	≤32	>29	≤21
4.5 meter walking time cutoffs for slowness (s), stratified according to height and sex			
Height (cm)	*Male sex cutoff (s)*	*Height (cm)*	*Female sex cutoff (s)*
≤173	≥7	≤159	≥7
>173	≥6	>159	≥6

Abbreviations: BMI = Body Mass Index

CLINICAL FRAILTY SCALE

The CFS version 2.0 (*Figure 8*) was scored by the study investigator who conducted the CGA, after performing the CGA.[67] If the study investigator was a geriatric medicine resident, a geriatric medicine specialist supervised the CGA and scoring process.

Figure 8 – The Cinical Frailty Scale version 2.0 Reproduced with permission n. 250417585



Patients were defined as frail according to the CFS if they had a CFS level of 5 ("living with mild frailty") or higher. Patients scoring 4 on the CFS ("living with very mild frailty", referred to as "vulnerable" in previous versions of the CFS) were not classified as frail to ensure comparability of results since most studies used a cutoff of 5 to identify frailty according to the CFS.[324,325] Patients with CFS levels of 7 or higher were classified as severely frail according to the CFS.[324,325]

FRAILTY INDEX

A frailty index (FI) was constructed according to published recommendations by evaluating 40 items derived from the baseline assessment, including living status, laboratory test results, chronic conditions, sensory impairments, functional autonomy, cognitive and mood status, physical performance measures, and self-rated health (*Table 3*).[59] Each item was scored from 0 (deficit absent) to 1 (deficit present); for items allowing gradation of deficits, a tripartite (i.e., 0–0.5–1) or quadripartite (i.e., 0–0.33–0.66–1) scoring scheme was adopted. The sum of the scores for all evaluated items was then divided by the total number of items assessed to obtain the FI. Patients with a FI of 0.25 or greater were considered as frail according to the FI, and patients with a FI of 0.45 or greater were considered as severely frail according to the FI.[326]

Table 3 – List of items evaluated to construct the Frailty Index in the present study and their respective scoring.

Item	***Evaluation***	***Score***
Living alone	No Yes	0 1
Low hemoglobin levels at admission (males <14.0 g/dl, females <12.0 g/dl)	Absent Present	0 1
Elevated serum TSH levels (>4.500 µIU/ml)	Absent Present	0 1
Creatinine clearance according to the Cockcroft-Gault formula	>60 ml/min 30-60 ml/min <30 ml/min	0 0.5 1
Low serum albumin levels (<3,5 g/dl)	Absent Present	0 1
Vision problems	Absent Mild-moderate Severe	0 0.5 1
Hearing problems	Absent Mild-moderate Severe	0 0.5 1
History of falls in the previous 12 months	Absent Present	0 1
Unintentional weight loss ≥4,5 kg in the last 12 months	Absent Present	0 1

Cardiac comorbidity (i.e., CIRS category 1 score ≥3)	Absent Present	0 1
Hypertension (i.e., CIRS category 2 score ≥3)	Absent Present	0 1
Respiratory comorbidity (i.e., CIRS category 4 score ≥3)	Absent Present	0 1
Hepatic comorbidity (i.e., CIRS category 8 score ≥3)	Absent Present	0 1
Genitourinary comorbidity (i.e., CIRS category 10 score ≥3)	Absent Present	0 1
Musculoskeletal comorbidity (i.e., CIRS category 11 score ≥3)	Absent Present	0 1
Neurological comorbidity (i.e., CIRS category 12 score ≥3)	Absent Present	0 1
Problems with feeding (according to BI item 1)	Absent (BI 10 pt) Mild-moderate (BI 5 pt) Severe (BI 0 pt)	0 0.5 1
Problems with dressing/undressing (according to BI item 2)	Absent (BI 10 pt) Mild-moderate (BI 5 pt) Severe (BI 0 pt)	0 0.5 1
Problems with moving from bed to chair (according to BI item 3)	Absent (BI 15 pt) Mild (BI 10 pt) Moderate (BI 5 pt) Severe (BI 0 pt)	0 0.33 0.66 1
Problems with personal hygiene (according to BI item 4)	Absent (BI 5 pt) Present (BI 0 pt)	0 1
Problems with bathing/showering (according to BI item 5)	Absent (BI 5 pt) Present (BI 0 pt)	0 1
Problems with using toilet (according to BI item 6)	Absent (BI 10 pt) Mild-moderate (BI 5 pt) Severe (BI 0 pt)	0 0.5 1
Problems with bowel continence (according to BI item 7)	Absent (BI 10 pt) Mild-moderate (BI 5 pt) Severe (BI 0 pt)	0 0.5 1
Problems with bladder continence (according to BI item 8 score)	Absent (BI 10 pt) Mild-moderate (BI 5 pt) Severe (BI 0 pt)	0 0.5 1
Problems with mobility (according to BI item 9 score)	Absent (BI 15 pt) Mild (BI 10 pt) Moderate (BI 5 pt) Severe (BI 0 pt)	0 0.33 0.66 1
Problems with climbing stairs (according to BI item 10 score)	Absent (BI 10 pt) Mild-moderate (BI 5 pt) Severe (BI 0 pt)	0 0.5 1
Problems with telephone use (according to IADL item 1)	Absent Mild Moderate Severe	0 0.33 0.66 1

Problems with going shopping (according to IADL item 2)	Absent Mild Moderate Severe	0 0.33 0.66 1
Problems with food preparation (according to IADL item 3)	Absent Mild Moderate Severe	0 0.33 0.66 1
Problems with housekeeping (according to IADL item 4)	Absent Mild Moderate Severe	0 0.33 0.66 1
Problems with transportation (according to IADL item 6)	Absent (1-2) Mild (3) Moderate (4) Severe (5)	0 0.33 0.66 1
Problems with taking own medications (according to IADL item 7)	Absent Mild-moderate Severe	0 0.5 1
Problems with handling finances (according to IADL item 8)	Absent Mild-moderate Severe	0 0.5 1
Cognitive impairment (according to SPMSQ)	Absent Mild Moderate Severe	0 0.33 0.66 1
Anxiety symptoms (according to HADS anxiety subscale)	Absent Borderline Present	0 0.5 1
Depressive symptoms (according to HADS depression subscale)	Absent Borderline Present	0 0.5 1
Problems with nutritional status (according to MNA)	None At risk Malnourished	0 0.5 1
Low handgrip strength test results (according to FFP criteria)	No Yes	0 1
Low gait speed (according to FFP criteria for 4,5 m walking test)	No Yes	0 1
Self-rated health compared with subjects with the same age (according to MNA item P)	Equal or better Worse or unknown	0 1

Abbreviations: BI = Barthel Index, CIRS = Cumulative Illness Rating Scale, FFP = Fried Frailty Phenotype, HADS = Hospital Anxiety and Depression Scale, IADL = Instrumental Activities of Daily Living, IU = International Units, MNA = Mini Nutritional Assessment, SPMSQ = Short Portable Mental Status Questionnaire, TSH = Thyroid-Stimulating Hormone

MULTIDIMENSIONAL PROGNOSTIC INDEX

The MPI was scored according to published criteria, based on data derived from the CGA (see following sections for further details).[71] Each of 8 dimensions was assigned a score of 0

(no problems), 0.5 (minor problems) or 1 (severe problems) according to scoring instructions. These dimensions included functional autonomy in Basic Activities of Daily Living (BADL) and Instrumental Activities of Daily Living (IADL), cognitive impairment as assessed by the Short Portable Mental Status Questionnaire (SPMSQ), comorbidity burden as measured by the Cumulative Illness Rating Scale Comorbidity Index (CIRS-CI), nutritional status evaluated by the Mini Nutritional Assessment ® (MNA®), risk of pressure injury development determined by the Exton-Smith Scale (ESS), number of medications and social support network/living conditions.[71]

The mean score of these 8 dimensions was then calculated to yield the total MPI score, which ranges from 0 (indicating the lowest risk of death and complete absence of frailty) to 1 (indicating the highest risk of death and maximal frailty severity). According to published cutoffs, patients were considered at low risk/robust for total MPI scores ranging from 0 to 0.33, moderate risk/pre-frail for scores from 0.34 to 0.66, and severe risk/frail for scores from 0.67 to 1.0.[71,80] In dichotomous analyses pre-frail and robust patients were grouped together as non-frail according to the MPI.

3.4.2 SOCIODEMOGRAPHIC VARIABLES

For each patient, in addition to sex and age at admission, data on years of education, highest education level achieved, and last occupation were recorded. Social support was explored by recording the patient's living condition (i.e., living alone without any help, living alone with help from friends or relatives, living with spouse or other relatives, or living with a paid caregiver), the number of cohabitants, and the presence or absence of a formal or informal caregiver with the daily hours of caregiving received. It was originally planned to further evaluate social support using the Medical Outcomes Study – Social Support Survey (MOS-SSS), a questionnaire that measures multiple dimensions of support (emotional/informational, tangible, affectionate, and positive social interaction) by asking subjects to rate 19 items on a scale from 1 (none support) to 5 (continuous support), thereby yielding scores for overall support and for specific support dimensions.[327,328] However, this tool soon proved to be too burdensome for our patient population, as more than half of participant refused to complete the MOS-SSS after the first couple of questions and most of provided inaccurate responses (e.g., rating all items uniformly as 5's or 3's). Therefore, the use of MOS-SSS was discontinued and not included in the data analysis.

For descriptive purposes it was also recorded whether the patient had a recognized legal disability ("*Invalidità civile*"), the level of disability, and whether the patient received a monthly

care allowance ("*Indennità di accompagnamento*", in 2024 this amounted in € 531.76 per month). Additionally, it was documented if the patient had previously undergone a CGA to access Geriatric Care ("*Unità Valutativa Geriatrica"*), and whether the patient had an appointed legal guardian.

The risk of discharge problems at admission was routinely evaluated through the Blaylock Risk Assessment Screening Score (BRASS), a tool that assesses patient age, social support, functional and cognitive status, behavior, mobility, sensory impairments, number of previous ED visits or hospital admissions, number of active clinical problems, and number of chronic medications used. Total BRASS scores range from 0 (indicating the lowest risk) to 36 (indicating the highest risk). Patients with scores between 0 and 10 are considered at low risk for discharge problems, those with scores between 11 and 19 at moderate risk, and those with scores of 20 or higher at high risk.[329]

3.4.3 COMORBIDITY AND POLYTHERAPY

A full medical history was obtained at admission, and the impact of both acute and chronic diseases on various organ systems was quantified using the Cumulative Illness Rating Scale (CIRS) in the modified version by Parmelee and colleagues.[330] This version assesses the level of impairment (i.e., treatment urgency and interference with normal activities) across 14 different organs/systems, namely: cardiac, hypertension, vascular, respiratory, eye/ear/nose/throat/larynx, upper gastrointestinal tract, lower gastrointestinal tract, hepatic, renal, other genitourinary, musculoskeletal/tegumental, neurological (excluding dementias), endocrine/metabolic, and psychiatric/behavioral (including dementias). Each organ/system is rated on a scale from 1 ("none, no impairment in that organ/system") to 5 ("extremely severe, impairment is life threatening, treatment is urgent or ineffective, and prognosis is grave"). Impairments with a rating of 3 ("moderate, impairment interferes with normal activities, treatment is needed, prognosis is good") or higher are considered clinically meaningful. Based on the CIRS evaluation, two indices are derived: a CIRS comorbidity index (CIRS-CI) and a CIRS severity index (CIRS-SI).[330] The CIRS-CI is calculated by counting the number of organ/system categories with clinically meaningful impairments (i.e., with a rating of 3 or higher), excluding the psychiatric/behavioral category, and thus ranges from 0 (no clinically meaningful impairments) to 13 (all organ/system categories meaningfully impaired). The CIRS-SI is the mean impairment score of the first 13 organ/systems categories (excluding psychiatric behavioral), thus ranging from 1 to 5, with higher scores indicating greater overall severity of impairments.

In addition, chronic medical therapy at admission was recorded, including the use of eye drops for glaucoma or other ophthalmic conditions, inhaled bronchodilators or corticosteroids for asthma and COPD, and long-term oxygen therapy. Polytherapy was defined as the regular use of 5 or more regular medications,[331,332] while hyperpolytherapy was defined as the use of more than 10 regular medications.[332]

3.4.4 FUNCTIONAL STATUS

Functional status prior to the current hospital admission was evaluated by interviewing the patient and/or their caregiver using the Barthel Index (BI),[333] and the Katz's BADL Index and Lawton's IADL scale.[334–336]

The BI evaluates the patient's autonomy across ten BADL domains, namely feeding, dressing/undressing, transferring from a (wheel)chair to a bed and return, personal toilet, getting on and off the toilet, bathing or showering, maintaining bowel continence, controlling the bladder, walking on a level surface (or propelling a wheelchair), and ascending and descending stairs. Each domain is scored to reflect varying levels of dependence, with higher scores indicating greater autonomy. The total BI score ranges from 0 (complete dependence) to 100 (complete independence).[333] It has been proposed that a total BI score of 100 indicates complete independence, scores of 91 to 99 indicate slight dependence, 61 to 90 moderate dependence, 21 to 60 severe dependence, and 20 or below total dependence.[337]

Katz's BADL Index assesses levels of dependence, categorized as none, partial, or complete in 6 BADLs, namely: bathing, dressing, toileting, transferring, continence, and feeding. Each activity is scored dichotomously; for instance, a patient who is partially dependent in transferring and toileting is considered dependent in those BADLs, whereas partial dependence in bathing, dressing, and feeding is considered equivalent to independence. Although there is no universal consensus regarding occasional continence issues, in this study patients with partial dependence in continence were considered as independent. Katz's Index thus quantifies the number of BADL functions lost, ranging from 0 (no loss) to 6 (loss of all functions).[334,335]

Lawton's IADL Scale evaluates autonomy in 8 IADLs, namely: telephone use, shopping, food preparation, housekeeping, laundry, transportation, responsibility for own medication, and handling of finances. For each IADL, different levels of autonomy are assessed, and in its original version they are scored dichotomously, by counting the number of functions maintained, yielding a total score from 0 (non-autonomous in all functions) to 8 (autonomous in all functions).[336]

3.4.5 COGNITIVE AND MOOD STATUS

Cognitive status at enrollment was evaluated using the SPMSQ, a 10-item questionnaire that assesses patient orientation (time, space, and self), long-term and short-term memory, and attention. Any incorrect or omitted answer is counted as a mistake.[338]

The total number of mistakes is recorded; for subjects with less than 8 years of education, one additional mistake is allowed, whereas for those with more than 8 years of education, one fewer mistake is allowed. The corrected SPMSQ score can thus range from 0 to 10 errors, with higher scores indicating more severe cognitive impairment. According to SPMSQ criteria, subjects with a corrected score of 0-2 are considered free from cognitive impairment, those scoring 3-4 as having mild cognitive impairment, scores of 5-7 indicate moderate cognitive impairment, and scores of 8 or higher indicate severe cognitive impairment.[338]

Mood status was assessed using the Hospital Anxiety and Depression Scale (HADS), a 14-item questionnaire designed to evaluate the frequency of anxiety and depressive symptoms experienced by the patient during the past week. The HADS employs a quadripartite response format, with each item rated from 0 (indicating minimal frequency of symptoms) to 3 (indicating higher frequency of symptoms). The total score of the seven odd-numbered items forms the HADS Anxiety subscale, whereas the sum of the seven even-numbered items forms the HADS Depression subscale. Each subscale can thus be scored from 0 to 21, with higher scores reflecting a greater burden of anxiety or depressive symptoms. Scores below 8 are considered normal, scores above 10 are regarded as abnormal, and scores between 8 and 10 are classified as borderline for each subscale.[339]

3.4.6 NUTRITIONAL STATUS

To investigate the nutritional status of enrolled patients, anthropometric measurements were obtained at enrolment, including weight, height, mid-arm circumference, and mid-calf circumference, according to the recommendations of the MNA User Guide.[340] BMI was then calculated by dividing the weight expressed in kilograms by the square of the height expressed in meters.

The full MNA was evaluated through a comprehensive review of medical charts and direct interviews with patients and/or their caregivers. The MNA is a validated malnutrition screening tool for older subjects. It comprises 18 items, covering anthropometric measures (including BMI, mid-arm, and mid-calf circumference), questions regarding appetite reduction and unintentional weight loss, evaluation of functional and cognitive status, assessment of living

conditions and medical therapy, history of acute illness or pressure injuries, inquiries about eating and drinking habits, and self-rated nutritional and overall health status. Each item is scored on a scale ranging from 0 to a maximum of 1, 2, or 3 points, depending on the item. The total MNA score ranges from 0 to 30, with lower scores indicating a higher risk of malnutrition. According to established cutoffs, a total MNA score lower than 17 identifies malnourished subjects, scores between 17 and 23.5 identifies subjects at risk of malnutrition, whereas subjects with total scores of 24 or higher are deemed to have normal nutritional status.[340–342]

3.4.7 Physical performance

Physical performance was evaluated, when feasible given the patients chronic and acute conditions by measuring handgrip strength and gait speed.

Handgrip strength was measured using a Jamar handheld dynamometer, with three repeated measures performed for each hand, and the best performance recorded according to published recommendations.[84]

Gait speed was assessed by timing the patient using a stopwatch as they walked a distance of 4.57 meters, a distance selected for convenience according to the published FFP criteria for slowness,[37] at usual walking speed. Patients were allowed to use walking aids, if needed; the mean time of two measures was used in this study.[47–49]

3.4.8 Sensory impairment and history of falls

Sensory impairments were self-reported by the patient and/or caregiver or directly verified from the medical history. Problems with vision and hearing were separately classified as follows: no problem, mild impairment (or amenable to correction with use of glasses or hearing aids), and severe impairment (or not amenable to correction). Additionally, a history of falls and the number of falls during the past 12 months were recorded.

3.4.9 Risk of pressure injury development

The risk of pressure injury development was evaluated using the ESS, also known as the Norton Scale.[343] The ESS evaluates five items, namely: general clinical conditions, mental status, ambulation, urinary and fecal continence, and mobility. Each item is scored from 1 to 4, where higher levels indicate better health status. The total ESS score ranges from 5 to 20. According to MPI classification criteria, scores from 5 to 9 identify a high risk of pressure injury development, whereas scores from 10 to 15 indicate moderate risk, and scores of 16 or

higher indicate low risk of pressure injury development.[71]

3.4.10 OTHER VARIABLES EVALUATED AT ENROLLMENT

At enrollment, the primary reason for admission and the source of admission (e.g., directly from a General Practitioner, from the ED, or from another hospital unit) were recorded. In the HaH setting, patients admitted directly from the General Practitioner or from the ED were classified as receiving AA-HaH, whereas those transferred from other hospital units were classified as receiving ESD-HaH.[211]

Severity of acute illness at admission according to the National Early Warning Score 2 (NEWS2)[344] was retrospectively evaluated from the first visit after admission in the AGW or HaH. The NEWS2 is an aggregate scoring system in which a score ranging from 0 (normal) to 3 (severely abnormal) is allocated to six physiological parameters, namely: respiration rate, peripheral oxygen saturation, systolic blood pressure, pulse rate, level of consciousness (categorized as Alert, Confused, Visual, Pain, Unresponsive) and body temperature. An additional weighting score of 2 is added if the patient requires oxygen supplementation to maintain their prescribed oxygen saturation range. The total NEWS2 score reflects the overall severity and risk of clinical deterioration of the patient's status, with scores of 1-4 denoting low severity/risk, 5-6 moderate severity/risk, and 7 or higher indicating high severity/risk. Patients with a single vital parameter scoring of 3 are particular cases, and were labelled as "low-medium" risk.[344]

3.5 Follow-up

Follow-up of enrolled patients was conducted at two timepoints to evaluate the incidence of clinical outcomes of interest: the first at discharge from the AGW or HaH, and the second at six months after discharge.

3.5.1 VARIABLES COLLECTED AT DISCHARGE

At discharge, study investigators retrieved relevant information by directly reviewing medical records and administrative discharge documents, and by interviewing healthcare professionals directly involved in patient care when necessary to resolve any unclear points.

Vital status at discharge, the discharge date and setting, and primary diagnosis at discharge were recorded, along with data on the use of medical equipment (e.g., venous cannulas, urinary catheters, oxygen therapy), administration of specific therapies (e.g., intravenous antibiotics,

new initiation of opioids, benzodiazepines, hypnotics, or antipsychotics), and the need for red blood cell or platelet transfusions.

Moreover, the incidence of the following complications during admission was recorded:

- *Delirium*, suspected on the basis of an acute and fluctuating change in alertness or the development of new behavioral symptoms documented by nursing or medical staff and confirmed by a geriatrician using the 4-AT scale (version 1.2) with a score of 4 or higher.[345–347] Use or medications for managing delirium during admission was also recorded
- *Falls*, defined as sudden losses of balance or support resulting in the patient's body landing on the ground, floor, or another object, as routinely documented in the medical record, along with any associated clinical consequences
- *New pressure injury development*, recording the number and highest stage of pressure injuries,[200] as reported in the medical records following daily inspections of patients by healthcare professionals
- *Healthcare-associated infections* (HAIs), defined as infections (bacterial, viral, or fungal) that occurr at least 48 hours after admission to the AGW or HaH, with symptoms confirmed by imaging and/or laboratory evidence; details such as the infection site, isolated microorganisms (if any), and antimicrobial therapy administered were also documented.

3.5.2 VARIABLES COLLECTED AT 6 MONTHS FROM DISCHARGE

At 6 months post-discharge, study investigators retrieved relevant information by telephone interviews with patients and/or their primary caregivers, and by reviewing regional public health archives (Archivio Unico Regionale Assistiti) and hospital discharge records.

For all enrolled patients, vital status at 6 months from discharge (including date and cause of death), institutionalization (i.e., admission to a LTC facility or nursing home), as well as unplanned ED visits and hospital or HaH readmissions (including date and main cause of admission) were recorded.

For patients alive at follow-up, additional data were collected on living conditions, including number of cohabitants and presence of a caregiver, as well as data on "Invalidità civile" and "Unità Valutativa Geriatrica" (as previously defined). Lastly, functional autonomy was re-evaluated through telephone interview by using the BI, as previously described.

3.6 Primary and secondary outcomes

The study primary outcome was defined as the composite of all-cause mortality and institutionalization at 6 months from discharge, in patients alive at discharge.

The study secondary outcomes were:

- Composite of complications during admission: in hospital death, delirium, falls, new pressure injury development, and HAIs (as previously defined)
- Any hospital-acquired complication, including delirium, falls, new pressure injury development, and HAIs (as previously defined), taken together and as single complications
- All-cause mortality at 6 months from discharge, in patients alive at discharge
- Institutionalization at 6 months from discharge, in patients alive at discharge
- ED visits or unplanned hospital/HaH admissions at 6 months from discharge, in patients alive at discharge
- Worsening functional status at 6 months from discharge, defined as a reduction of at least 10 points in the BI as compared to the baseline evaluation, in patients alive at discharge.[348–350]

3.7 Sample size calculation

Based on unpublished data from the same settings, the estimated frailty prevalence in the study population is approximately 60%. Moreover, the anticipated empirical incidence of the primary composite outcome is 45% in the frail group and 25% in the non-frail group.

Therefore, to detect a statistically significant difference in primary outcome incidence between these groups with a statistical power of 80% and a 5% type I error (alpha), a minimum sample size of 197 patients (74 not frail and 123 frail) with complete follow-up data is required. Accounting for an estimated 15% loss at follow-up (due to informed consent withdrawal or inability to adjudicate the primary outcome), the MUFASA study aimed to enroll at least 230 patients; additional enrollment was permitted to enable eventual subgroup analyses based on healthcare setting or other variables of interest.

3.8 Statistical analysis

Data for descriptive analyses are presented on available data as absolute and relative frequencies for dichotomous and categorical variables, and either mean and standard deviation

(SD) or median and interquartile range (IQR, 25th to 75th percentiles) for normally and not normally distributed continuous variables, respectively. The Kolmogorov-Smirnov test was used to assess whether a set of continuous data derived from a normal distribution or another probability distribution Differences among groups and univariate association analyses were evaluated on available data using the χ^2 test or Fisher's exact test for dichotomous and categorical variables, as appropriate, and using unpaired Student's *t*-test (parametric) or the Wilcoxon-Mann-Whitney test (non-parametric) for continuous variables, according to type of distribution. Frailty prevalence according to different frailty models, as well as outcome incidence in the overall study population and in selected subgroups are reported along with their 95% CIs.

Agreement among the four different frailty instruments was examined using Cohen's κ statistic. Agreement levels were defined as follows: κ 0.00-0.20 slight agreement, κ 0.21-0.40 fair agreement, κ 0.41-0.60 moderate agreement, κ 0.61-0.80 substantial agreement, κ 0.81-1.00 almost perfect agreement.[351,352] The overlap between the four frailty scales was explored also by constructing a Venn diagram using the web-based InteractiVenn tool.[48,49]

Missing values were handled as follows: for those variables in which missing values accounted for less than 5% of the overall sample (i.e., study title and education level, hemoglobin, creatinine clearance, SPMSQ, handgrip strength, PASE, falls and weight loss in the year prior to admission, BMI, mid-arm and mid-calf circumference), missing data were replaced with statistical summaries for those data; for those variables in which missing data was higher than 5% of the overall sample, (i.e., HADS in its anxiety and depression subscales, MNA, frailty according to FFP, and MPI) a Multiple Imputation using fully conditional specification methods was performed for a set of a priori selected variables.[355–357] Linear and logistic regression models were used for continuous and categorical variables, respectively.[356,357] The imputation model included auxiliary variables (e.g., age, sex, setting) that are strongly correlated with the dependent variable to obtain an efficient inference.[358] Imputed values were used to predict other variables with missing data (Multiple Imputation by chained equations). Thirty data sets were imputed, according to the recommendations for creating data sets in the presence of missing data to obtain more stable parameters estimates and better standard error estimates.[359] Derived variables were calculated after imputation for each imputed dataset.

Multivariable logistic regression analyses were conducted to explore associations of interest. For analyses focusing on clinical outcomes, four different analyses were conducted exploring frailty according to the four different frailty definitions (i.e., FFP, CFS, FI, and MPI)

and healthcare settings (i.e. HaH vs AGW). An adjusted analysis was first conducted using frailty and healthcare setting as predictors (Model 1); a multivariable analysis was then conducted adjusting for potential confounders selected according to clinical interest and previously published evidence. To check multicollinearity in the multivariable regression models, we examined the Variance Inflation Factor. Analyses on outcomes at 6-month follow-up were performed on the sample of patients alive at discharge from the AGW or the HaH, with the exception of analyses on worsening functional status at follow-up, which were restricted to patients alive at follow-up only, for which data on functional status according to the BI were available.

In order to evaluate the main secondary outcomes at 6-month follow-up (i.e., institutionalization and ED visit/unplanned rehospitalization), taking into account the competing event of all-cause death, we created for each event a secondary polytomic outcome by dividing the sample into 3 categories: "Outcome adjudicated at follow-up," "Dead without previously adjudicated outcome at follow-up," and "Alive and free from adjudicated outcome at follow-up". For both outcomes, we performed two multinomial models for each of the four frailty definitions, the first including as predictors frailty and healthcare setting, the second adjusting for potential confounders selected according to previously published evidence and clinical interest.[360] Results were expressed calculating the adjusted odds ratios (aORs) and their 95% CIs.

To explore the potential differential impact of healthcare setting on clinical outcomes of interest according to frailty severity levels, we conducted post-hoc sub-analyses repeating analyses on subjects with mild/moderate frailty and severe frailty according to the CFS and the FI as previously defined, as well as on subjects with moderate risk and high risk at the MPI.

For survival analysis, the Kaplan-Meier method to month 6 was applied, and the log-rank test was used to assess differences in survival curves; cumulative incidence curves of other outcomes were assessed considering death as a competing event using the Fine and Gray test.[361]

Statistical analyses were conducted using IBM SPSS Statistics for Windows software version 29.0.2.0 (© 2023, IBM Corporation, Armonk, NY, USA), Stata Statistical Software release 18 (© 2023 StataCorp LLC, College Station, TX, USA) and SAS for Windows software version 9.4 (© 2023, SAS Institute Inc, Cary, NC, USA). All statistical tests were two-sided, and statistical significance was set at a p value ≤ 0.05.

4. Study results

4.1 Prevalence of frailty at admission across different healthcare settings

4.1.1 GENERAL CHARACTERISTICS OF THE STUDY SAMPLE

A total of 297 patients were enrolled in the MUFASA study, with 199 in the AGW setting and 98 in the HaH setting (67.0% and 33.0% of the overall sample, respectively). Almost all patients in the AGW were admitted from the ED (96.5%); among HaH-admitted patients, 68 (69.4%) were directly admitted from the ED or upon the GP's request, representing AA-HaH, whereas the remaining 30 patients (30.6%) were transferred from other acute hospital wards to continue their therapies at home, representing ESD-HaH. The median age of participants was 86 years (IQR 81-90), with a maximum age of 101 years, and 52.2% were females.

Table 4 reports the general sociodemographic variables of the overall sample, and stratified according to healthcare setting, while *Table 5* presents the main aspects related to hospital admission.

Table 4 – General sociodemographic variables, in the overall sample and stratified by healthcare setting.

	Overall (n=297)	***AGW (n=199)***	***HaH (n=98)***	***P value***
Age (years), median (IQR)	86 (81-90)	86 (82-90)	87 (80-92)	0.333
Female sex, n (%)	155 (52.2)	101 (50.8)	54 (55.1)	0.481
Study title, n (%)*				0.057
- None	19 (6.5)	12 (6.1)	7 (7.4)	
- Primary school diploma	108 (37)	79 (39.9)	29 (30.9)	
- Middle school diploma	73 (25.0)	51 (25.8)	22 (23.4)	
- Professional school diploma	40 (13.7)	32 (16.2)	8 (8.5)	
- High school diploma	26 (8.9)	11 (5.5)	15 (16)	
- Bachelor's degree or higher	26 (8.9)	13 (6.5)	13 (13.8)	
Years of education, median (IQR)*	8 (5-11)	8 (5-10)	8 (5-13)	0.076
Living condition, n (%)				**<0.001**
- Alone without help	21 (7.1)	20 (10.1)	1 (1.0)	
- Alone with help	53 (17.8)	43 (21.6)	10 (10.2)	
- Living with spouse/relative	181 (60.9)	122 (61.3)	59 (60.2)	
- Living with paid caregiver	42 (14.2)	14 (7.0)	28 (28.6)	
Presence of a caregiver, n (%)	155 (52.2)	71 (35.7)	84 (85.7)	**<0.001**
- Paid caregivers, n (%)	81 (52.3)	32 (45.1)	49 (58.3)	
Continuous 24/7 caregiving, n (%)	102/155 (65.8)	35/71(49.3)	67/84 (79.8)	**<0.001**
Legal disability recognized, n (%)	137 (46.1)	76 (38.2)	61 (62.2)	**<0.001**
- With care allowance, n (%)	56 (40.9)	21 (27.6)	35 (57.4)	
Geriatric Assessment to access geriatric care, n (%)	35 (11.8)	13 (6.5)	22 (22.4)	**<0.001**
Presence of a legal guardian, n (%)	2 (0.7)	0	2 (2.0)	0.108

*Missing values <5%.
Abbreviations: AGW = acute geriatric ward, HaH = Hospital-at-Home, IQR = Interquartile Range

Less than one-third of enrolled individuals had an education level higher than a middle school diploma (31.5%). Most patients lived at home with family (60.9%). Overall, 52.2% of patients reported receiving paid or informal caregiving, with HaH patients reporting significantly higher rates of caregiving (85.7% vs 35.7% in the AGW); in 80% of cases a caregiver was available 24 hours a day before admission.

Table 5 – Hospital admission variables, in the overall sample and stratified by healthcare setting.

	Overall (n=297)	***AGW (n=199)***	***HaH (n=98)***	***P value***
At least one hospital admission in the preceding 3 months, n (%)	172 (57.9)	110 (55.3)	62 (63.3)	0.190
N. of hospital admissions in the preceding 3 months, n (%)				0.051
- 1	112 (37.7)	76 (38.2)	36 (36.7)	
- 2	42 (14.1)	27 (13.6)	15 (15.3)	
- 3	14 (4.7)	7 (3.5)	7 (7.1)	
- 4 or more	4 (1.3)	0	4 (4.1)	
Site of admission, n (%)				**<0.001**
- General Practitioner	17 (5.7)	0	17 (17.3)	
- Emergency Department	243 (81.8)	192 (96.5)	51 (52.1)	
- Other hospital ward	37 (12.5)	7 (3.5)	30 (30.6)	
Reason of admission, n (%)				**0.038**
- Respiratory tract infection	55 (18.5)	36 (18.1)	19 (19.4)	
- Acute heart failure	55 (18.5)	36 (18.1)	19 (19.4)	
- Fluid/electrolyte imbalance	29 (9.8)	20 (10.1)	9 (9.2)	
- Infection (other)	28 (9.4)	14 (7.0)	14 (14.3)	
- Urinary tract infection	24 (8.1)	11 (5.5)	13 (13.3)	
- Anemia/bleeding	19 (6.4)	15 (7.5)	4 (4.1)	
- Stroke/TIA	16 (5.4)	15 (7.5)	1 (1.0)	
- Uncontrolled BPSD	11 (3.7)	8 (4.0)	3 (3.1)	
- Other	60 (20.2)	44 (22.1)	16 (16.2)	
NEWS2 score, median (IQR)	2 (1-4)	1 (1-4)	2 (1-4)	0.572
NEWS2 score risk, n (%)				0.103
- Low risk	214 (72.1)	149 (74.9)	65 (66.3)	
- Low-medium risk	31 (10.4)	18 (9.0)	13 (13.3)	
- Medium risk	35 (11.8)	25 (12.6)	10 (10.2)	
- High risk	17 (5.7)	7 (3.5)	10 (10.2)	
Hemoglobin (g/dl), mean±SD*	11.7±2.2	11.7±2.3	11.8±2	0.648
ClCr (ml/min), median (IQR)*	38.4 (25.4-52.8)	39.6 (25.8-54.2)	35.2 (25.1-50.5)	0.337
BRASS, median (IQR)*	14 (10-19)	13 (10-17)	18 (13-23)	**<0.001**
BRASS risk, n (%)				**<0.001**
- Low	84 (28.7)	68 (34.9)	16 (16.3)	
- Medium	137 (46.7)	99 (50.7)	38 (38.8)	
- High	72 (24.6)	28 (14.4)	44 (44.9)	

*Missing values <5%

Abbreviations: AGW = acute geriatric ward, BPSD = behavioral and psychological symptoms of dementia, BRASS = Blaylock Risk Assessment Screening Score, ClCr = Creatinine Clearance, HaH = Hospital-at-Home, IQR = interquartile range, NEWS2= National Early Warning Score 2, TIA = Transient Ischemic Attack

More than half of the patients had experienced at least one hospitalization in the preceding 3 months (57.9%). The most frequent reasons for admission were infections (36.0%, predominantly pneumonia and respiratory tract infections), followed by acutely decompensated heart failure (18.5%) and dehydration or electrolyte imbalances (9.8%). Severity at admission and the risk of decompensation, evaluated according to the NEWS2 score, were similar across the different healthcare settings.

Per study protocol, all subjects underwent a standardized CGA during the first days of admission, which included evaluation of frailty. *Table 6* summarizes the results on the different domains explored in the CGA. The overall sample exhibited a high burden of comorbidity, with a median of 5 organ systems significantly impaired per patient, a finding that was reflected by a high prevalence of polytherapy (77.4%). Geriatric syndromes were also highly prevalent: 48.2% of subjects demonstrated severe or extremely severe functional impairment at the BI, 25.5% showed moderate to severe cognitive deficits on the SPMSQ, and 11.3% had severe vision and/or hearing impairments. Only 15.7% of subjects showed a normal nutritional status at the MNA®. The compromised nutritional status of the patients enrolled was reflected by poor physical performance measures and low physical activity levels (reported in 74.8% of the overall sample). Additionally, depressive and anxiety symptoms were present in 36.0% and 17.0% of subjects at admission, respectively. Notably, patients admitted to the HaH setting exhibited a significantly worse overall health status in almost every domain evaluated at the CGA (*Table 6*).

Table 6 –Comprehensive Geriatric Assessment variables at admission, in the overall sample and stratified by healthcare setting.

	Overall (n=297)	***AGW (n=199)***	***HaH (n=98)***	***P value***
Comorbidity burden				
CIRS-CI, median (IQR)	5 (4-6)	5 (4-6)	6 (4-7)	**0.019**
CIRS-SI, median (IQR)	2.2 (1.9-2.4)	2.1 (1.9-2.3)	2.2 (1.9-2.4)	**0.003**
Clinically significant comorbidities according to CIRS score ≥3				
Cardiac, n (%)	186 (62.6)	123 (61.8)	63 (64.3)	0.678
Hypertension, n (%)	235 (79.1)	164 (82.4)	71 (72.4)	**0.047**
Vascular and hematopoietic, n(%)	144 (48.5)	89 (44.7)	55 (56.1)	0.065
Respiratory, n (%)	104 (35.0)	67 (33.7)	37 (37.8)	0.488
Eyes,ears,nose,throat,larynx, n(%)	113 (38.0)	74 (37.2)	39 (39.8)	0.663
Upper gastrointestinal, n (%)	70 (23.6)	42 (21.1)	28 (28.6)	0.154
Lower gastrointestinal, n (%)	52 (17.5)	32 (16.1)	20 (20.4)	0.356
Liver, pancreas and biliary, n (%)	16 (5.4)	9 (4.5)	7 (7.1)	0.347
Renal, n (%)	159 (53.5)	100 (50.3)	59 (60.2)	0.106
Genitourinary, n (%)	92 (31.0)	60 (30.2)	32 (32.7)	0.661
Musculoskeletal and skin, n (%)	125 (42.1)	79 (39.7)	46 (46.9)	0.235
Neurologic, n (%)	103 (34.7)	69 (34.7)	34 (34.7)	0.997

Endocrine and breast, n (%)	195 (65.7)	127 (63.8)	68 (69.4)	0.342
Psychiatric (incl. dementia), n (%)	117 (39.4)	52 (53.1)	65 (32.7)	**<0.001**
Drug burden				
Drugs at admission, median (IQR)	7 (5-10)	7 (4-9)	7 (5-10)	0.267
Polytherapy, n (%)	230 (77.4)	148 (74.4)	82 (83.7)	0.071
Hyperpolytherapy, n (%)	56 (18.9)	35 (17.6)	21 (21.4)	0.426
Functional autonomy				
Barthel Index, median (IQR)	65 (35-90)	75 (50-95)	45 (15-75)	**<0.001**
Barthel Index disability level, n (%)				**<0.001**
- None	43 (14.5)	31 (15.6)	12 (12.2)	
- Mild	23 (7.7)	21 (10.6)	2 (2.0)	
- Moderate	88 (29.6)	71 (35.7)	17 (17.3)	
- Severe	89 (30.0)	57 (28.6)	32 (32.7)	
- Extremely severe	54 (18.2)	19 (9.5)	35 (35.8)	
Katz ADL (n. of functions lost), median (IQR)	2 (0-4)	1 (0-4)	4 (0.8-5)	**<0.001**
IADL (n. of functions kept), median (IQR)	2 (1-5)	3 (1-6)	1 (0-3)	**<0.001**
IADL autonomy category, n (%)				**<0.001**
- Autonomous	67 (22.5)	54 (27.1)	13 (13.3)	
- Partially autonomous	75 (25.3)	60 (30.2)	15 (15.3)	
- Non autonomous	155 (52.2)	85 (42.7)	70 (71.4)	
Cognitive impairment				
SPMSQ (n. of errors), median (IQR)*	2 (1-5)	2 (1-4)	3 (1-6)	0.058
Cognitive impairment SPMSQ, n(%)*				**0.009**
- None	148 (51.0)	109 (55.3)	39 (41.9)	
- Mild	68 (23.5)	46 (23.4)	22 (23.7)	
- Moderate	44 (15.2)	28 (14.2)	16 (17.2)	
- Severe	30 (10.3)	14 (7.1)	16 (17.2)	
Confused, wandering behavior	44 (14.8)	24 (12.1)	20 (20.4)	0.057
Mood status				
HADS anxiety, median (IQR)†	6 (4-9)	6 (4-9)	7 (5-9)	**0.016**
Anxiety levels at HADS, n (%)†				**0.031**
- Normal	161 (63.6)	123 (68.7)	38 (51.3)	
- Borderline	49 (19.4)	26 (14.5)	23 (31.1)	
- Abnormal	43 (17.0)	30 (16.8)	13 (17.6)	
HADS depression, median (IQR)†	9 (5-12)	8 (5-12)	9 (6-14)	**0.008**
Depression levels at HADS, n (%)†				**0.045**
- Normal	104 (41.1)	79 (44.1)	25 (33.8)	
- Borderline	58 (22.9)	43 (24.0)	15 (20.3)	
- Abnormal	91 (36.0)	57 (31.9)	34 (45.9)	
Physical performance and activity levels				
Best handgrip (kg), median (IQR)*	14 (9.9-20.0)	14.3(10.7-20.5)	12 (5.8-20.0)	0.075
Best handgrip (kg), males; median (IQR)*	19.8 (14-24.3)	19.9 (13.8-24.1)	20 (14.3-26.0)	0.829
Best handgrip (kg), females; median (IQR)*	11.6 (7.9-14.8)	12.0 (9.0-14.9)	10.0 (5.0-14.6)	**0.021**
Weakness at handgrip (FFP), n (%)	249 (86.8)	172 (88.7)	77 (82.8)	0.170
Unable to perform gait speed, n (%)	88 (38.3)	49 (36.6)	39 (40.6)	0.532
Gait speed (m/s), median (IQR)‡	0.54 (0.42-0.76)	0.54 (0.44-0.70)	0.54 (0.38-0.84)	0.950

Low gait speed (FFP), n (%)	105 (73.9)	65 (76.5)	40 (70.2)	0.402
Low gait speed or unable, n (%)**	193 (83.9)	114 (85.1)	79 (82.3)	0.571
PASE score, median (IQR)*	25 (0-57)	27.2 (0-75)	0 (0-27)	**<0.001**
Low activity levels at PASE, n (%)*	220 (74.8)	134 (68.4)	86 (87.8)	**<0.001**
Physical exhaustion, n (%)	221 (74.4)	145 (72.9)	77 (77.6)	0.384
Sensory impairment/balance				
Vision impairment, n (%)*				0.255
- None	69 (23.5)	51 (26.2)	18 (18.4)	
- Present, moderate	191 (65.2)	122 (62.6)	69 (70.4)	
- Present, severe	33 (11.3)	22 (11.2)	11 (11.2)	
Hearing impairment, n (%)*				**<0.001**
- None	146 (49.8)	113 (57.9)	33 (33.7)	
- Present, moderate	114 (38.9)	66 (33.9)	48 (49.0)	
- Present, severe	33 (11.3)	16 (8.2)	17 (17.3)	
History of falls in the previous year, n (%)*	112 (37.8)	76 (38.4)	36 (36.7)	0.783
Number of falls in the previous year, median (IQR)*	1 (1-2)	1 (1-2)	1.5 (1-2)	0.825
Nutrition				
BMI (kg/m^2), median (IQR)*	23.5 (20.8-26.7)	23.4 (20.8-26.2	23.9 (21.2-27.3)	0.864
Mid-arm circumference (cm), median (IQR)*	25.0 (23.0-27.5)	25.0 (23.0-28.0)	24.0 (22.0-27.0)	0.075
Mid-calf circumference (cm), median (IQR)*	31.5 (29.0-34.0)	31.5 (29.0-34.0)	31.5 (28.0-33.3)	0.232
MNA score, median (IQR)††	18.5 (14.5-22.0)	19 (15.8-23.0)	15.5 (12.0-20.0)	**<0.001**
Malnutrition risk at MNA, n (%)††				**<0.001**
- Normal	42 (15.7)	37 (19.6)	5 (6.3)	
- At risk	119 (44.4)	91 (48.1)	28 (35.5)	
- Malnourished	107 (39.9)	61 (32.3)	46 (58.2)	
Weight loss in the past 12 mo, n (%)*	140 (47.5)	87 (43.7)	53 (55.2)	0.064
Pressure injury development risk				
ESS, median (IQR)	16 (13-17.5)	16 (14-18)	14 (11-16.3)	**<0.001**
Risk of pressure injuries at ESS,				**<0.001**
- Low	154 (51.8)	120 (60.3)	34 (34.7)	
- Medium	125 (42.1)	72 (36.2)	53 (54.1)	
- High	18 (6.1)	7 (3.5)	11 (11.2)	

*Missing values <5%
†Missing values for 44 (14.8%) subjects
‡Missing values (unavailable or untestable) for 155 (52.2%) subjects
**Missing values for 67 (22.6%) subjects
††Missing values for 29 (9.8%) subjects

Abbreviations: ADL = Activities of Daily Living, AGW = acute geriatric ward, BMI = Body Mass Index, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, IADL = Instrumental Activities of Daily Living, ESS = Exton-Smith Scale, FFP = Fried Frailty Phenotype, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MNA = Mini Nutritional Assessment, mo = months, PASE = Physical Activity Scale for the Elderly, SPMSQ = Short Portable Mental Status Questionnaire,

4.1.2 PREVALENCE OF FRAILTY ACCORDING TO DIFFERENT CRITERIA

The burden of geriatric syndromes and comorbidities in the overall sample was reflected by a high prevalence of frailty across healthcare settings. Complete data for frailty evaluation using the FFP and the MPI were unavailable in 10.4% and 10.8% of patients, respectively, and were addressed via multiple imputation. *Table 7* presents frailty data for the overall sample and stratified according to healthcare setting, whereas *Table 8* displays frailty prevalence estimates after multiple imputation. Frailty prevalence varied depending on the definition used: patients were mostly frail according to the FFP and the FI (86.6% and 86.5%, respectively), whereas frailty prevalence estimates based on the CFS and the MPI were 67.7% and 28.2%, respectively.

Table 7 – Frailty assessment at admission according to different frailty definitions, in the overall sample and stratified by healthcare setting

	Overall (n=297)	***AGW (n=199)***	***HaH (n=98)***	***P value***
Fried Frailty Phenotype				
Frailty status according to FFP*				0.827
- Robust, n (%)	0	0	0	
- Pre-frail, n(%)	29 (10.9)	18 (10.6)	11 (11.5)	
- Frail, n (%)	237 (89.1)	152 (89.4)	85 (88.5)	
Clinical Frailty Scale				
CFS score, median (IQR)	6 (4-7)	5 (4-6)	7 (5-7)	**<0.001**
Frail according to CFS ≥5, (%)	201 (67.7)	120 (60.3)	81 (82.7)	**<0.001**
Frailty severity according to CFS				**<0.001**
- No frailty (CFS 1-4), n (%)	96 (32.3)	79 (39.7)	17 (17.3)	
- Moderate frailty (CFS 5/6), n (%)	106 (35.7)	77 (38.7)	29 (29.6)	
- Severe frailty (CFS≥7), n (%)	95 (32.0)	43 (21.6)	52 (53.1)	
Frailty index				
FI, median (IQR)	0.47 (0.32-0.61)	0.44 (0.33-0.54)	0.58 (0.42-0.64)	**<0.001**
Items evaluated at FI, mean±SD	38.8±1.4	38.9±1.3	38.7±1.7	0.828
Frail according to FI≥0.25, n (%)	257 (86.5)	170 (85.4)	87 (88.8)	0.427
Frailty severity according to FI				**<0.001**
- No frailty (FI <0.25), n (%)	40 (13.5)	29 (14.6)	11 (11.2)	
- Moderate frailty (0.25-0.44), n (%)	100 (33.7)	81 (40.7)	19 (19.4)	
- Severe frailty (FI≥0.45), n (%)	157 (52.9)	89 (44.7)	68 (69.4)	
Multidimensional Prognostic Index				
MPI score, median (IQR)†	0.50 (0.38-0.69)	0.43 (0.30-0.57)	0.58 (0.41-0.69)	**<0.001**
Frailty status according to MPI†				**0.003**
- MPI low risk, n (%)	59 (22.3)	48 (25.7)	11 (14.1)	
- MPI medium risk, n (%)	135 (50.9)	98 (52.4)	37 (47.4)	
- MPI high risk = frail, n (%)	71 (26.8)	41 (21.9)	30 (38.5)	

*Missing values for 31 (10.4%) subjects

†Missing values for 32 (10.8%) subjects

Abbreviations: AGW = acute geriatric ward, CFS = Clinical Frailty Scale, FI = Frailty Index, FFP = Fried Frailty Phenotype, HaH = Hospital-at-Home, IQR = interquartile range, MPI = Multidimensional Prognostic Index

Table 8 – Frailty prevalence at admission according to different frailty definitions, in the overall sample and stratified by healthcare setting

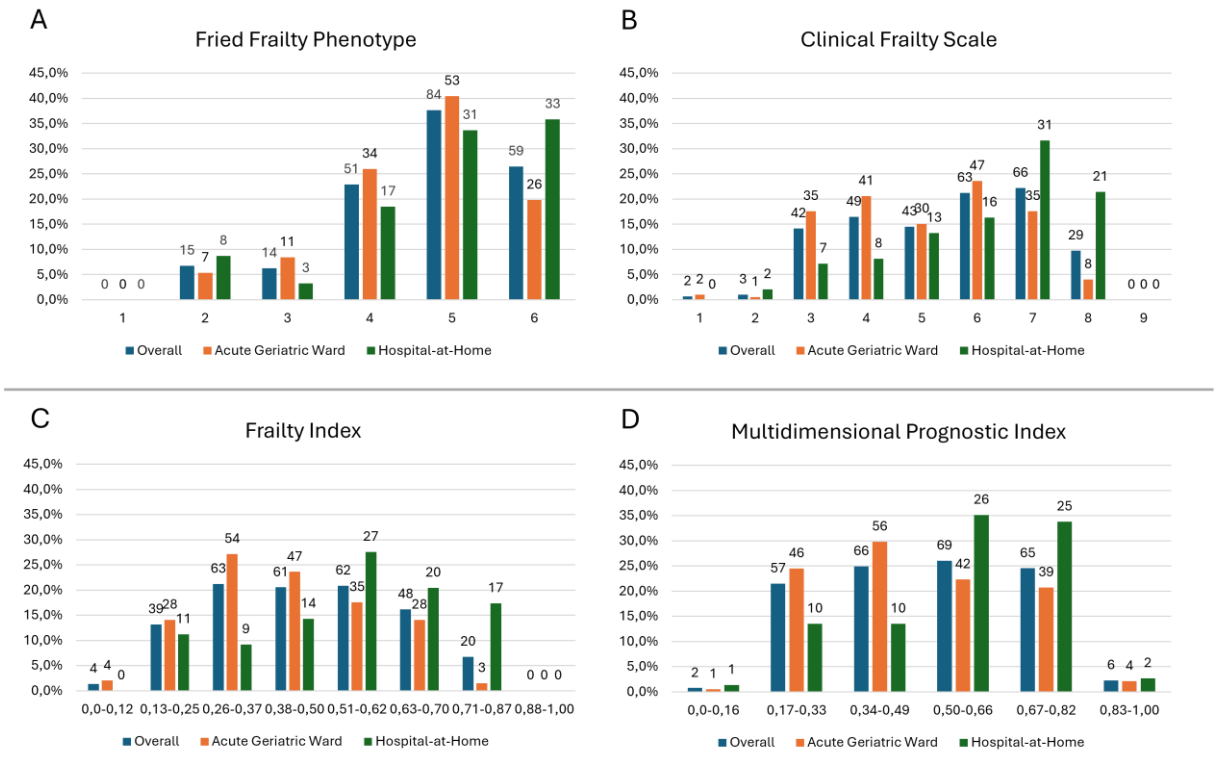
	Overall (n=297)	***AGW (n=199)***	***HaH (n=98)***	***p***
Fried Frailty Phenotype (FFP)*	86.6% (82.6%-90.5%)	85.5% (80.5%-90.4%)	88.8% (82.5%-95.0%)	0.415
Clinical Frailty Scale (CFS≥5)	67.7% (62.2%-72.7%)	60.3% (53.4%-66.8%)	82.7% (73.9%-89.0%)	**<0.001**
Frailty Index (FI≥0.25)	86.5% (82.2%-90.0%)	85.4% (79.8%-89.7%)	88.8% (80.8%-93.8%)	0.427
Multidimensional Prognostic Index (MPI≥0.66)*	28.2% (22.9%-33.4%)	22.0% (16.2%-27.8%)	40.7% (30.6%-50.9%)	**0.002**

*Results are presented after Multiple Imputation for missing values

Abbreviations: AGW =acute geriatric ward, CFS = Clinical Frailty Scale, FI = Frailty Index, FFP = Fried Frailty Phenotype, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index

Patients admitted to the HaH setting were more frequently frail than patients in the AGW according to the CFS and the MPI (82.7% vs 60.3% and 40.7% vs 22.0%, respectively). Moreover, mean frailty severity scores were also higher in HaH patients (see *Table 7*), reflected by 53.1% of patients considered as severely frail at the CFS (vs 21.6% in the AGW setting), and 69.4% of patients severely frail at the FI (vs 44.7% in the AGW setting), as presented in *Figure 9*.

Figure 9 – Distribution of frailty severity according to different frailty definitions, in the overall sample, and stratified by healthcare setting.



4.1.3 AGREEMENT BETWEEN DIFFERENT FRAILTY CRITERIA

Only a modest agreement between the different frailty definitions was observed in the overall sample. *Figure 10* illustrates the overlap among the four frailty tools used in the study, when taking the mode of frailty status after multiple imputation for the FFP and the MPI. Only 22 patients (7.4%) were classified as non-frail and 82 subjects (27.6%) as frail by all frailty tools, respectively. Among the 275 subjects identified as frail by at least one frailty tool, 29.8% were classified as frail by all four tools, whereas 39.6% were deemed frail by the FI, the CFS, and the FFP, but not by the MPI (39.6%). Additionally, 6.2% and 3.3% of frail subjects were classified as frail exclusively by the FFP or the FI, respectively, whereas no patient was identified as frail solely by the CFS or the MPI. When focusing on single healthcare settings, a higher agreement was found in the HaH setting, with 42.9% of HaH patients and 20.1% of AGW patients being classified as frail by all frailty tools (*Figure 11*).

Figure 10 – Venn diagram showing the overlap among frail subjects identified according to the Fried Frailty Phenotype (FFP, orange), the Clinical Frailty Scale (CFS, green), the Frailty Index (FI, blue), and the Multidimensional Prognostic Index (MPI, yellow). The proportion and absolute number of subjects classified as frail by one or more tools is reported in each overlapping section. Data for FFP and MPI are presented after multiple imputation for missing values.[354]

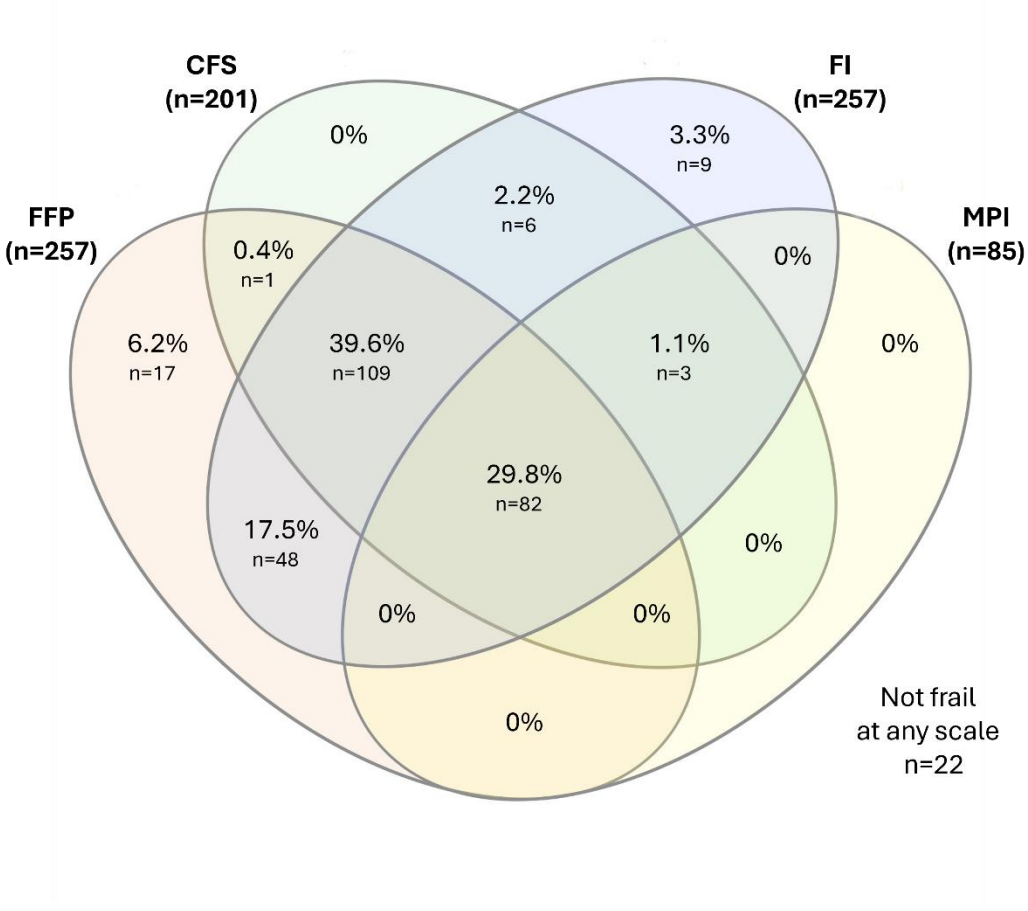


Figure 11– Comparison of Venn diagrams showing the overlap among frail subjects identified according to the Fried Frailty Phenotype (FFP, orange), the Clinical Frailty Scale (CFS, green), the Frailty Index (FI, blue), and the Multidimensional Prognostic Index (MPI, yellow) in the acute geriatric ward setting (left panel) and in the Hospital-at-Home setting (right panel). The proportion and absolute number of subjects classified as frail by one or more tools is reported in each overlapping section. Data for FFP and MPI are presented after multiple imputation for missing values.[354]

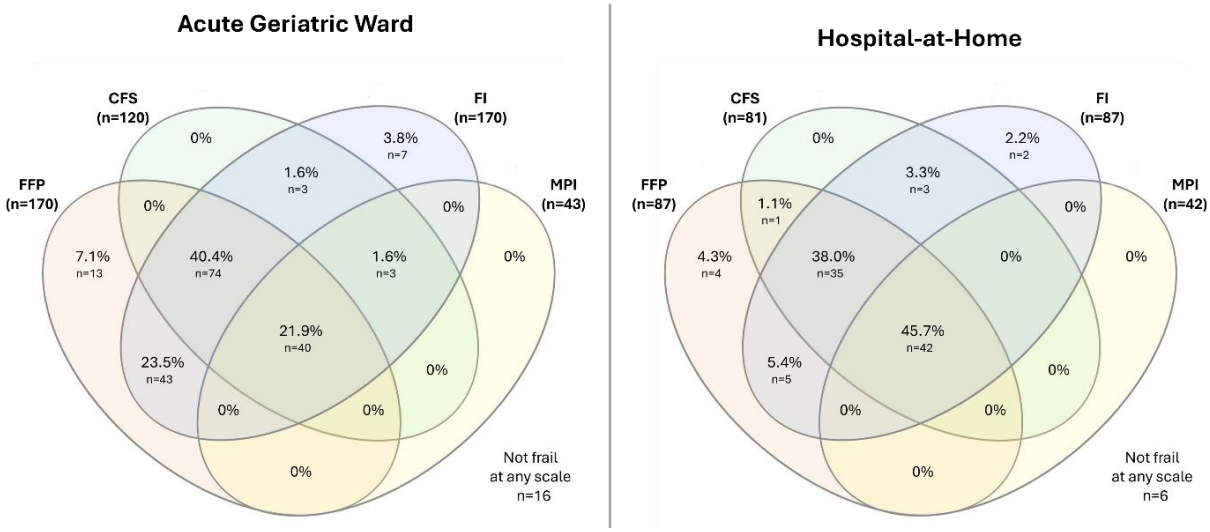


Table 9 reports data on the agreement between the different frailty operational tools, as measured by Cohen's κ, in the overall sample and stratified according to healthcare setting. In the overall sample, the highest level of agreement was moderate and was observed between the FI and the FFP (κ 0.53), with a wide 95% CI ranging from fair to substantial agreement. The FI also showed a moderate level of agreement with the CFS (κ 0.48), while other frailty tools demonstrated only slight to fair levels of agreement. When focusing on the HaH setting, the level of agreement increased substantially, with the highest agreement observed between the FI and the CFS (substantial agreement, κ 0.67), with the 95% CI ranging from moderate to almost perfect agreement. In contrast, in the AGW setting, agreement was generally lower and was highest between the FI and the FFP (moderate agreement, κ 0.55). These results did not differ substantially when using the mode of frailty status after multiple imputation for the FFP and the MPI (data not shown).

Table 9 – Agreement between different frailty definitions according to Cohen's kappa in the overall sample (panel A), in the acute geriatric ward (panel B), and in the Hospital-at-Home (panel C) settings, on available data. Data are presented as kappa (95% CI); at the bottom of the table is reported is the level of agreement according to κ.

A - Overall sample			
	FI	**CFS**	**MPI**[†]
FFP[*]	0.526 (0.365-0.687)	0.322 (0.202-0.442)	0.063 (0.022-0.104)
FI		0.473 (0.369-0.577)	0.112 (0.071-0.153)
CFS			0.312 (0.24-0.386)
B – Acute geriatric ward setting			
	FI	**CFS**	**MPI**[†]
FFP[*]	0.547 (0.351-0.743)	0.259 (0.132-0.386)	0.087 (0.048-0.126)
FI		0.412 (0.298-0.526)	0.040 (-0.009-0.890)
CFS			0.317 (0.225-0.409)
C – Hospital-at-Home setting			
	FI	**CFS**	**MPI**[†]
FFP[*]	0.487 (0.213-0.761)	0.502 (0.261-0.743)	0.116 (0.03-0.202)
FI		0.669 (0.459-0.879)	0.186 (0.076-0.296)
CFS			0.241 (0.116-0.366)

Almost perfect (κ 0.81-1.00)	**Substantial** (κ 0.61-0.80)	**Moderate** (κ 0.41-0.60)	**Fair** (κ 0.21-0.40)	**Slight** (κ 0.00-0.20)

[*]Missing values for 31 (10.4%) subjects
[†]Missing values for 32 (10.8%) subjects

Abbreviations: CFS = Clinical Frailty Scale, FI = Frailty Index, FFP = Fried Frailty Phenotype, MPI = Multidimensional Prognostic Index

4.1.2 Clinical correlates of frailty according to different criteria

Descriptive analyses of baseline data and outcomes at discharge, stratified by the presence of frailty as defined according to the FFP, CFS, FI, and MPI are presented in *Supplementary Tables S1-S4.* Almost every deficit identified during the CGA was significantly more prevalent in frail subjects, with only slight variations between the various frailty tools. In particular, functional, nutritional and cognitive status, as well as physical performance, were markedly worse in frail subjects, and the comorbidity burden was higher, with the exception of the FFP. This finding was not unexpected, also because several of these aspects are directly evaluated by some of the frailty tools used in the present study. Therefore, the association between frailty

(according to different definitions) and clinical variables of interest that have been previously reported as potentially associated with frailty, yet not directly included in the definition of these tools, was briefly explored.

Figure 12– Distribution of frailty prevalence according to different frailty definitions across age groups, in the overall sample. Results for the Fried Frailty Phenoype in Panel A and for the Multidimensional Prognostic Index in panel D are presented after multiple imputation for missing values.

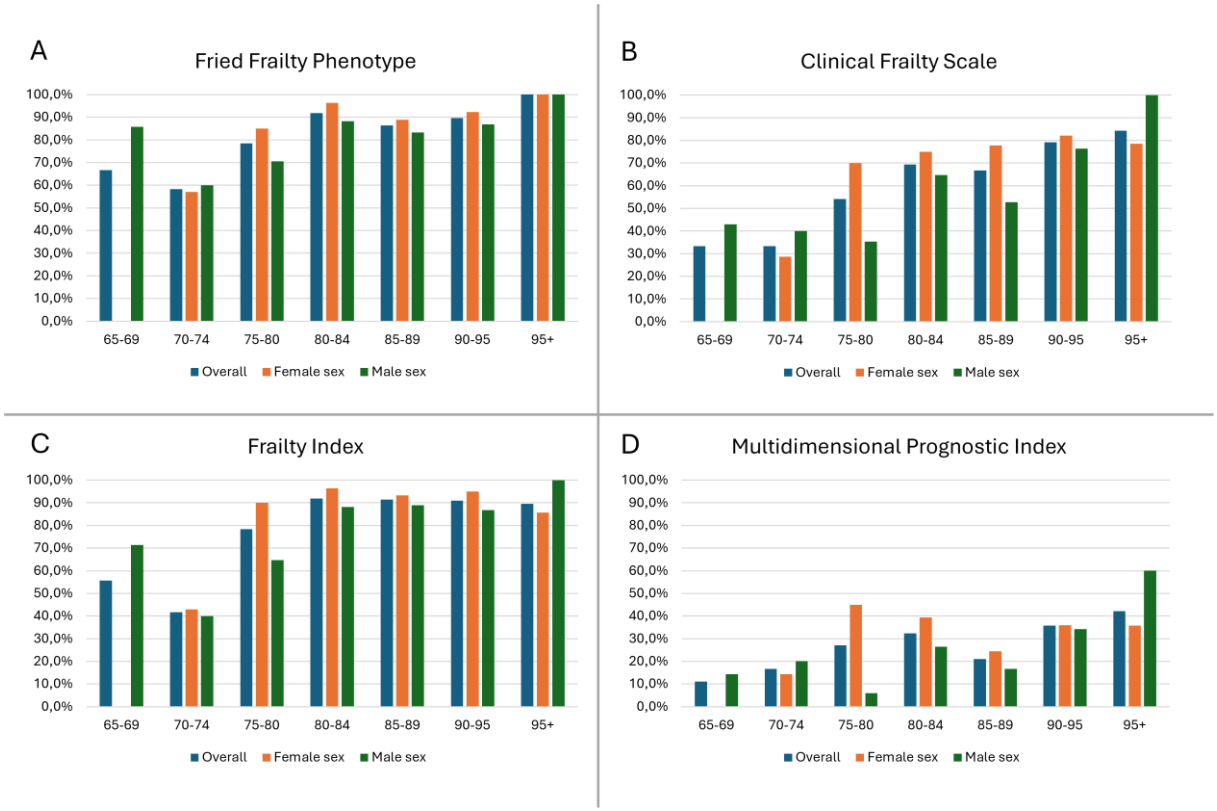


Table 10 – Clinical variables independently associated with frailty identified according to different frailty definitions. Results are expressed as aOR (95% CI).

	FFP*	CFS	FI	MPI*
Age, years	**1.09 (1.03-1.14)**	**1.08 (1.03-1.12)**	**1.08 (1.03-1.14)**	1.02 (0.97-1.06)
Female sex	1.16 (0.81-1.68)	**1.91 (1.11-3.30)**	1.48 (0.7-3.12)	1.27 (0.95-1.68)
Years of education	0.97 (0.89-1.05)	1.02 (0.95-1.08)	0.96 (0.88-1.04)	1.01 (0.94-1.07)
Any vision impairment	0.92 (0.60-1.4)	0.77 (0.42-1.42)	0.99 (0.44-2.19)	0.82 (0.6-1.13)
Any hearing impairment	1.02 (0.71-1.47)	**1.81 (1.06-3.11)**	1.67 (0.78-3.57)	**1.66 (1.25-2.22)**
Falls in the previous year	0.91 (0.63-1.32)	1.60 (0.932.78)	**2.49 (1.07-5.78)**	1.03 (0.78-1.36)

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, FFP = Fried Frailty Phenotype, FI = Frailty Index, MPI = Multidimensional Prognostic Index

Figure 12 presents data on frailty prevalence stratified by age class and sex, whereas *Table10* displays the results of multivariable analysis for factors associated with frailty. Frailty prevalence increased with age, and older patients in the overall sample had a higher risk of being frail according to all frailty definitions except the MPI. Female sex was associated with an increased odds of being frail only when using the CFS. Additionally, the presence of hearing impairment was inconsistently associated with frailty as defined according to the CFS and the MPI, whereas a history of falls in the previous year was significantly associated with frailty as defined by the FI.

4.2 Association of frailty with clinical outcomes during admission across different healthcare settings

4.2.1 INCIDENCE OF HOSPITAL-ACQUIRED COMPLICATIONS AND ALL-CAUSE MORTALITY DURING ADMISSION

All 297 enrolled patients had complete data regarding hospital admission, including details on medical devices and specific medication classes (see *Table 11*).

Table 11 – Use of medical devices and administration of specific medication classes during admission, in the overall sample and stratified by healthcare setting.

	Overall (n=297)	***AGW (n=199)***	***HaH (n=98)***	***P value***
Venous catheter use, n (%) - Midline/Long VC - PICC/CVC	282 (94.9) 74/282 (26.2) 16/282 (5.7)	196 (98.5) 33/196 (16.8) 9/196 (4.6)	86 (87.8) 41/86 (47.7) 7/86 (8.1)	**≤0.001** **≤0.001**
Venous catheter present at admission, n (%)	25/282 (8.9)	5/196 (2.6)	20/86 (23.2)	**≤0.001**
Urinary catheter use, n (%)	109 (36.8)	74 (37.4)	35 (35.7)	0.781
Urinary catheter present at admission, n (%)	24/110 (21.8)	6/74 (8.1)	18/35 (51.4)	**≤0.001**
Oxygen supplementation, n (%) - Nasal cannula - Venturi mask - NIV/HFNC	84 (28.3) 58/84 (69.0) 16/84 (19.0) 10/84 (11.9)	65 (32.7) 42/65 (64.6) 14/65 (21.5) 9/65 (13.8)	19 (19.4) 16/19 (84.2) 2/19 (10.5) 1/19 (5.3)	**0.017** **0.024**
Oxygen supplementation present at admission, n (%)	22/84 (26.2)	10/65 (15.4)	12/19 (63.2)	**≤0.001**
Intravenous antibiotic, n (%)	157 (52.9)	108 (54.3)	49 (50.0)	0.488
New opioid use, n (%)	25 (8.4)	16 (8.0)	9 (9.2)	0.911
New benzodiazepine use, n (%)	19 (6.4)	15 (7.5)	4 (4.1)	0.261
New other hypnotic use, n (%)	33 (11.1)	25 (12.6)	8 (8.2)	0.196
New antipsychotic use, n (%)	37 (12.5)	28 (14.1)	9 (9.3)	0.242

Abbreviations: AGW = acute geriatric ward, CVC = Central Venous Catheter, HaH = Hospital-at-Home, HFNC = High Flow Nasal Cannula, NIV = Non-Invasive Ventilation, PICC = Peripherally Inserted Central Catheter, VC = Venous Cannula

Almost all patients had a venous catheter, and 36.8% had a urinary catheter at some point during their admission (most of which were placed during admission), while 28.3% received oxygen supplementation. Patients managed in the AGW exhibited a higher proportion of newly inserted or used medical devices compared to those in the HaH setting. Regarding psychotropic medications, 11.1% of patients received a new hypnotic (mainly trazodone) and 12.5% received a new antipsychotic drug during admission, with no significant differences observed between healthcare settings.

Table 12 presents the incidence of hospital-acquired complications and other clinical outcomes during admission, for the overall sample and stratified by healthcare setting. During a median length of stay of 11 days (IQR 7-20, range 2-54), 17 patients (5.7%) died, and 80 patients (26.9%) experienced at least one hospital-acquired complication, resulting in 88 patients (29.6%) meeting the composite outcome of any hospital-acquired complication or in-hospital death (95% CI: 24.7%-35.1%). HAIs were the most frequent complication (accounting for 15.2% of patients, almost invariably requiring antimicrobial therapy), followed by delirium (10.8%, frequently managed with medications). Falls occurred in 9 patients, with two resulting in hip fractures (one in the AGW and one in HaH), and one resulting in a new vertebral fracture (in the AGW). Lastly, a new pressure injury or a worsening of previous pressure injury occurred in 20 patients (6.7%).

Patients in the HaH setting showed significantly lower rates of the composite outcome of hospital-acquired complication or death during admission than patients in the AGW [25.5% (95% CI 17.9%-35.0%) vs 31.7% (95% CI 25.6%-38.4%)], despite a significantly longer median length of stay [16 days (IQR 11-23) vs 9 (IQR 6-15) days]. During admission, 6 HaH patients died (6.1%) and 6 patients (6.1%) required an intensification of care with ED referral; the remaining HaH patients were all discharged at home, with or without community nurse services. In contrast, 11 patients (5.5%) in the AGW died during admission and 40 patients (21.3%) were discharged to a medium or LTC facility (MLTCF).

Data on outcomes at discharge stratified according to the presence of frailty according to different definitions are presented in *Supplementary Tables S1-S4*. Irrespective of the frailty definition, frail patients showed a significantly longer length of stay, and higher rates of the composite outcome of any hospital-acquired complication or in-hospital death (with the exception of the MPI). Moreover, patients considered frail according to the FFP and the FI were more frequently discharged to a MLTCF.

Table 12 – Hospital-acquired complications during admission and other clinical outcomes at discharge in the overall sample and stratified by healthcare setting.

	Overall (n=297)	***AGW (n=199)***	***HaH (n=98)***	***P value***
Length of hospital stay (days), median (IQR)	11 (7-20)	9 (6-15)	16 (11-23)	**<0.001**
Any hospital-acquired complication, including in-hospital death, n (%)	88 (29.6)	63 (31.7)	25 (25.5)	0.275
Death during admission, n (%)	17 (5.7)	11 (5.5)	6 (6.1)	0.836
Any hospital-acquired complication, n (%)	80 (26.9)	60 (30.2)	20 (20.4)	0.075
Delirium during admission, n (%) - Requiring use of medication	32 (10.8) 27/32 (84.4)	25 (12.6) 23/25 (92.0)	7 (7.1) 4/7 (57.1)	0.157 0.098
Fall during admission, n (%)	9 (3.0)	6 (3.0)	3 (3.1)	1.000
Pressure injury development during admission, n (%)	20 (6.7)	14 (7.0)	6 (6.1)	0.768
Healthcare-associated infection during admission, n (%)	45 (15.2)	33 (16.6)	12 (12.2)	0.327
Setting of discharge, n (%) - At home - MLTCF - ED	 234 (83.6) 40 (14.3) 6 (2.1)	 148 (78.7) 40 (21.3) -	 86 (93.5) - 6 (6.5)	**<0.001**

Abbreviations: AGW = acute geriatric ward, ED = Emergency Department, HaH = Hospital-at-Home, IQR = Interquartile Range, MLTCF = medium/long-term care facility

4.2.1 FACTORS ASSOCIATED WITH HOSPITAL-ACQUIRED COMPLICATIONS AND ALL-CAUSE MORTALITY DURING ADMISSION

The association between clinical variables – both at baseline and during hospital admission – and the incidence of the composite outcome of death or any hospital-acquired complication during admission, as well as its individual components, was then explored. *Supplementary Tables S9-S12* present data on selected clinical variables stratified according to the incidence of clinical outcomes during admission. In general, patients who experienced the composite outcome or any hospital-acquired complication were significantly older, had a higher NEWS2 score at admission and exhibited a greater burden of geriatric syndromes, including disability, cognitive impairment, and frailty. During admission, the use of medications and medical devices was significantly higher in patients who experienced hospital-acquired complications. These patients had also a significantly longer length of stay [19 (IQR 10-28) days vs 10 (IQR 6-15) days in patients that did not experience the composite outcome during admission], more frequently died during hospital stay (11.0% vs 3.7%), and when surviving, were more frequently discharged to a MLTCF (29.6% vs 9.1%).

Table 13 reports the results of analyses exploring the association between frailty and healthcare setting with the composite outcome of in-hospital death or any hospital-acquired

complication during admission.

In Model 1, frailty defined according to all four definitions was significantly associated with increased odds of experiencing the composite outcome during admission, regardless of healthcare setting. However, after adjusting for relevant clinical factors, including the presence of geriatric syndromes, the overall severity of acute illness and risk of clinical deterioration as measured by the NEWS2, and the length of hospital stay (Model 2), the association with frailty became nonsignificant. In contrast, the HaH setting proved to be independently associated with a lower risk of experiencing the composite outcome during admission, irrespective of frailty definition used [aOR 0.29 (95% CI 0.14-0.59) in the analysis with frailty defined according to the CFS]. A higher NEWS 2 score was also consistently associated with a higher risk of experiencing the composite outcome.

Table 13 – Factors independently associated with the composite outcome of in-hospital death or any hospital-acquired complication during admission. Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	**1.60 (1.02-2.53)**	**2.16 (1.20-3.89)**	**2.72 (1.1-6.75)**	**1.44 (1.08-1.92)**
HaH setting	0.85 (0.64-1.11)	0.63 (0.36-1.10)	0.72 (0.42-1.24)	0.8 (0.6-1.06)
Model 2				
Frailty	1.26 (0.76-2.07)	1.28 (0.57-2.86)	1.01 (0.34-3.04)	1.06 (0.66-1.72)
HaH setting	**0.71 (0.51-0.98)**	**0.29 (0.14-0.59)**	**0.29 (0.14-0.6)**	**0.70 (0.51-0.97)**
Age, years	1.04 (0.99-1.08)	**1.06 (1.01-1.11)**	**1.06 (1.01-1.11)**	1.04 (1-1.09)
Female sex	0.87 (0.66-1.14)	0.82 (0.45-1.47)	0.83 (0.46-1.49)	0.87 (0.67-1.09)
CIRS-CI	0.99 (0.84-1.16)	0.95 (0.8-1.13)	0.95 (0.80-1.13)	0.99 (0.84-1.16)
SPMSQ, errors	1.11 (0.99-1.25)	1.13 (0.99-1.28)	1.13 (0.99-1.28)	1.10 (0.97-1.25)
Barthel Index	1 (0.99-1.01)	1.00 (0.99-1.02)	1 (0.99-1.01)	1 (0.98-1.01)
Number of falls in the last year	**1.26 (1.03-1.53)**	1.23 (0.99-1.52)	1.23 (1-1.53)	**1.25 (1.03-1.52)**
NEWS2 score at admission	**1.15 (1.02-1.30)**	**1.15 (1.01-1.31)**	**1.15 (1.00-1.31)**	**1.16 (1.02-1.31)**
Length of stay, days	1.02 (0.99-1.04)	**1.1 (1.06-1.14)**	**1.1 (1.06-1.14)**	1.02 (0.99-1.05)

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index, NEWS2 = National Early Warning Score 2, SPMSQ = Short Portable Mental Status Questionnaire

The protective role of the HaH setting, irrespective of frailty, geriatric syndromes and acute illness severity, was also confirmed when considering hospital-acquired complications only [aOR 0.20 (95% CI 0.09-0.44) in the analysis using frailty defined according to the CFS], as reported in *Table 14*.

Table 14 – Factors independently associated with any hospital-acquired complication during admission. Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	1.50 (0.95-2.37)	**2.05 (1.12-3.75)**	**3.01 (1.13-8.01)**	**1.40 (1.04-1.89)**
HaH setting	0.76 (0.57-1.02)	0.51 (0.28-0.92)	0.57 (0.32-1.02)	0.72 (0.53-0.97)
Model 2				
Frailty	1.20 (0.72-2)	1.25 (0.54-2.93)	1.22 (0.37-4.01)	1.06 (0.64-1.74)
HaH setting	**0.62 (0.44-0.89)**	**0.20 (0.09-0.44)**	**0.20 (0.09-0.45)**	**0.62 (0.44-0.88)**
Age, years	1.03 (0.99-1.08)	**1.05 (1.00-1.11)**	**1.05 (1.00-1.11)**	1.03 (0.99-1.08)
Female sex	0.92 (0.7-1.22)	0.96 (0.52-1.77)	0.97 (0.52-1.79)	0.93 (0.70-1.23)
CIRS-CI	0.99 (0.84-1.16)	0.94 (0.78-1.13)	0.94 (0.78-1.11)	0.99 (0.84-1.17)
SPMSQ, errors	1.13 (1-1.28)	**1.16 (1.01-1.33)**	**1.16 (1.01-1.34)**	1.12 (0.98-1.28)
Barthel Index	1 (0.99-1.01)	1.00 (0.99-1.02)	1.01 (0.99-1.02)	1 (0.99-1.01)
Number of falls in the last year	**1.33 (1.09-1.63)**	**1.32 (1.05-1.65)**	**1.32 (1.05-1.65)**	**1.33 (1.09-1.62)**
NEWS2 score at admission	**1.14 (1.00-1.29)**	1.14 (0.99-1.31)	1.13 (0.98-1.30)	1.15 (1.01-1.3)
Length of stay, days	**1.03 (1.00-1.06)**	**1.12 (1.08-1.16)**	**1.12 (1.08-1.16)**	**1.03 (1.00-1.06)**

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index, NEWS2 = National Early Warning Score 2, SPMSQ = Short Portable Mental Status Questionnaire

Considering the slightly lower (although not statistically significant) incidence of delirium and HAIs in the HaH setting when compared to the AGW (7.1% vs 12.6% for delirium, and 12.2% vs 16.6% for infections), and in light of previous data suggesting a potential protective role of the HaH setting for these complications, a multivariable analysis also on these outcomes was conducted. This analysis was adjusted not only for geriatric syndromes, severity

of acute illness, and length of stay, but also for the use of urinary catheters during admission, a well-known risk factor for both delirium and HAIs. In the analysis focusing on delirium, comorbidity burden was substituted with the number of chronic medications used, given the well-documented detrimental impact of polypharmacy on delirium. The HaH setting was independently associated with lower odds of delirium only in the analyses where frailty was defined according to the CFS and the FI [aOR 0.21 (95% CI 0.07-0.67) and aOR 0.23 (95% CI 0.07-0.73), respectively]. Additionally, female sex was consistently associated with lower risk of incident delirium, whereas higher cognitive impairment at SPSMQ was independently associated with this outcome (see *Table 15*).

Table 15 – Factors independently associated with delirium during admission. Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	1.28 (0.68-2.37)	**2.62 (1.03-6.70)**	5.59 (0.74-42.3)	**1.98 (1.33-2.94)**
HaH setting	0.73 (0.47-1.13)	0.45 (0.18-1.09)	0.52 (0.21-1.24)	**0.62 (0.39-0.99)**
Model 2				
Frailty	0.98 (0.49-1.94)	1.91 (0.57-6.37)	3.38 (0.37-31.1)	1.97 (0.96-4.04)
HaH setting	0.63 (0.38-1.05)	**0.21 (0.07-0.67)**	**0.23 (0.07-0.73)**	0.65 (0.39-1.09)
Age, years	1.03 (0.97-1.10)	1.04 (0.97-1.12)	1.05 (0.97-1.12)	1.04 (0.97-1.11)
Female sex	**0.53 (0.34-0.82)**	**0.27 (0.11-0.67)**	**0.28 (0.11-0.69)**	**0.53 (0.34-0.83)**
Number of chronic medications	0.93 (0.82-1.05)	0.91 (0.8-1.03)	0.91 (0.8-1.04)	0.90 (0.79-1.03)
SPMSQ, errors	**1.26 (1.05-1.51)**	**1.3 (1.07-1.57)**	**1.30 (1.08-1.57)**	1.18 (0.97-1.43)
Barthel Index	0.99 (0.98-1.02)	1.01 (0.99-1.03)	1.01 (0.99-1.02)	1.01 (0.99-1.03)
NEWS2 score at admission	1.02 (0.84-1.22)	0.98 (0.81-1.2)	0.96 (0.79-1.16)	1.02 (0.84-1.23)
Urinary catheter during admission	1.09 (0.71-1.68)	0.89 (0.37-2.15)	0.91 (0.38-2.21)	1.1 (0.71-1.69)
Length of stay, days	1.01 (0.99-1.02)	**1.08 (1.04-1.12)**	**1.08 (1.04-1.12)**	1.01 (0.99-1.02)

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index, NEWS2 = National Early Warning Score 2, SPMSQ = Short Portable Mental Status Questionnaire

Frailty was not associated with the incidence of HAIs during admission. Conversely, the HaH setting was independently associated with lower odds of infection in analyses where frailty was defined according to the CFS and the FI [aOR 0.32 (95% CI 0.12-0.88) and aOR 0.33 (95% CI 0.12-0.9), respectively], even after accounting for the significant impact of urinary catheter use on this outcome [aOR 5.28 (95% CI 2.26-12.35) in the analysis with frailty defined according to the CFS] (*Table 16).*

Table 16 – Factors independently associated with healthcare-associated infections during admission. Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	1.27 (0.74-2.2)	1.51 (0.73-3.13)	1.75 (0.59-5.19)	1.17 (0.81-1.7)
HaH setting	0.83 (0.58-1.19)	0.64 (0.31-1.33)	0.69 (0.34-1.41)	0.81 (0.56-1.17)
Model 2				
Frailty	0.88 (0.47-1.65)	0.62 (0.20-1.91)	1.01 (0.24-4.12)	0.84 (0.44-1.62)
HaH setting	0.82 (0.54-1.25)	**0.32 (0.12-0.88)**	**0.33 (0.12-0.9)**	0.82 (0.54-1.25)
Age, years	1.01 (0.96-1.07)	1.04 (0.98-1.10)	1.04 (0.97-1.10)	1.01 (0.95-1.06)
Female sex	1.28 (0.9-1.83)	2 (0.9-4.46)	1.91 (0.87-4.21)	1.27 (0.89-1.82)
CIRS-CI	0.99 (0.80-1.23)	0.88 (0.69-1.13)	0.88 (0.68-1.12)	1.00 (0.81-1.24)
SPMSQ, errors	1.14 (0.98-1.33)	1.17 (0.99-1.38)	1.16 (0.98-1.37)	1.17 (0.98-1.39)
Barthel Index	1.01 (0.99-1.02)	1.01 (0.99-1.03)	1.01 (0.99-1.03)	1.01 (0.99-1.38)
NEWS2 score at admission	0.97 (0.83-1.14)	0.94 (0.78-1.13)	0.95 (0.79-1.14)	0.97 (0.83-1.14)
Urinary catheter during admission	**2.52 (1.7-3.76)**	**5.28 (2.26-12.35)**	**5.11 (2.19-11.94)**	**2.49 (1.68-3.68)**
Length of stay, days	1.02 (1-1.03)	**1.12 (1.08-1.17)**	**1.12 (1.08-1.17)**	1.01 (1-1.03)

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index, NEWS2 = National Early Warning Score 2, SPMSQ = Short Portable Mental Status Questionnaire

4.3 Association of frailty with clinical outcomes at 6 months from discharge from different healthcare settings

4.3.1 INCIDENCE OF CLINICAL OUTCOMES AT 6 MONTHS FROM DISCHARGE IN PATIENTS DISCHARGED ALIVE

All 280 patients discharged alive had complete follow-up data on all-cause mortality, institutionalization, and ED visits or unplanned rehospitalizations (*Table 17, Supplementary Tables S5-S8*). Over a median follow-up period of 182 days (IQR 162-189), 61 patients (21.8%) died, and 42 patients (15.0%) were institutionalized, resulting in 84 patients (30.0%) that met the primary composite outcome of all-cause mortality or institutionalization at 6 months post-discharge (95% CI: 24.9%-35.6%). Notably, 19 of the institutionalized patients (45.2%) died during follow-up. Access to urgent healthcare services was frequent, with 98 patients (35.0%) experiencing at least one ED visit or unplanned rehospitalization at follow-up (3 or more events occurred in 13 cases). Data on functional status at 6 months from discharge were available for the 219 patients who were alive at follow-up: of these, 100 (45.7%) experienced a clinically significant decline in the BI [95% CI 39.2%-52.3%, median reduction -20 (IQR -39 to -10)].

Table 17 – Outcomes at 6-month follow-up in patients discharged alive in the overall sample and stratified by healthcare setting.

	Overall (n=280)	***AGW (n=188)***	***HaH (n=92)***	***P value***
Length of follow-up (days), median (IQR)	182 (162-189)	182 (159-189)	183 (173-190)	0.519
All-cause mortality or institutionalization, n (%)	84 (30.0)	62 (33.0)	22 (23.9)	0.120
All-cause mortality, n (%)	61 (21.8)	42 (22.3)	19 (20.7)	0.748
Institutionalization, n (%)	42 (15.0)	39 (20.7)	3 (3.3)	**<0.001**
At least one ED visit or unplanned rehospitalization, n(%)	98 (35.0)	61 (32.4)	37 (40.2)	0.200
Number of ED visits or unplanned rehospitalizations, n (%) - 1 - 2 - 3 or more	 71 (25.4) 14 (5.0) 13 (4.6)	 43 (22.9) 9 (4.8) 9 (4.8)	 28 (30.4) 5 (5.4) 4 (4.3)	0.563
Worsening functional status, n (%)*	100/219 (45.7)	68/146 (46.6)	32/73 (43.8)	0.701
BI at follow-up, median (IQR)*	55 (25-90)	62.5 (30-91)	40 (15-72.5)	**0.002**
BI difference from baseline, median (IQR)*	-5 (-20-0)	-5 (-25-0)	0 (-10-0)	**0.037**

*Data available on 219 patients alive at follow-up (146 in the AGW setting and 73 in the HaH setting).

Abbreviations: AGW = acute geriatric ward, BI = Barthel Index, ED = Emergency Department, HaH = Hospital-at-Home, IQR = Interquartile Range

The incidence of the primary composite outcome or all-cause mortality or institutionalization was similar between the HaH and AGW settings (23.9% vs. 33.0%). However, only 3 patients (3.3%) discharged alive from the HaH were subsequently institutionalized, compared with 39 patients (20.7%) from the AGW. Conversely, the number of patients with ED visits or unplanned readmissions and the number of patients experiencing worsening functional status at 6 months follow-up did not differ significantly between the two healthcare settings.

Table 18 presents baseline and discharge characteristics of the 280 patients discharged alive, stratified according to the occurrence of the primary composite outcome of all-cause mortality or institutionalization at 6 months from discharge. Additional data on selected clinical variables stratified according to the incidence of other clinical outcomes at follow-up are reported in *Supplementary Tables S13-S17*. *Figure 13* shows cumulative incidence curves for the primary composite outcome and Kaplan-Meier survival curves in the overall sample and stratified by healthcare setting, while *Figures 14* and *15* present the same data according to frailty status as defined by the FFP, the CFS, the FI, and the MPI. *Supplementary Figures S1-S4* show cumulative incidence curves for institutionalization and for ED visits/unplanned hospitalizations considering death as a competing event, and stratified according to clinical setting and frailty status.

The median survival time in the overall sample was 58 days (IQR 1-138.5), with no significant differences between healthcare settings [HaH: 68 days (IQR 13-122); AGW: 53 days (IQR 21-130.5)] or according to frailty status. Similarly, median time to first event of the primary composite outcome was 118.5 days (IQR 28.3-182), again, with no significant differences between settings [HaH: 77.5 days (IQR 19-147.3); AGW: 126.5 days (IQR 30-183), $p = 0.124$). However, patients classified as frail according to the CFS showed a significantly shorter time to first event for the primary composite outcome [115.5 days (IQR 25.3-180.8) vs 169.5 days (IQR 57.3-208) in non-frail subjects, $p = 0.038$].

In general, patients who experienced the primary composite outcome had higher NEWS2 scores at admission and a greater burden of geriatric syndromes, including disability and reduced physical performance, cognitive impairment, malnutrition, depressive symptoms, and frailty (excluding the FFP definition). Interestingly, the incidence of hospital-acquired complications during the index admission was also significantly higher among these patients (35.7% vs 20.9% in those not meeting the primary outcome), particularly the incidence of delirium during hospital admission (see *Table 18*). Furthermore, patients that experienced the primary composite outcome more frequently required at least one ED visit or unplanned

hospitalization during follow-up (45.2% vs 30.6%). Similar results were observed in the analysis focused solely on all-cause mortality (*Supplementary Table S13*).

Table 18 - Descriptive analysis on patients discharged alive and stratified according to the primary composite outcome of all-cause mortality or institutionalization at 6 months from discharge.

	Alive at discharge (n=280)	***Absence of composite outcome at follow-up (n=196)***	***Presence of composite outcome at follow-up (n=84)***	***p***
Sociodemographic variables				
Age (years), median (IQR)	86 (80.5-90)	86 (81-90)	86 (80-90.5)	0.979
Female sex, n (%)	149 (53.2)	106 (54.1)	43 (51.2)	0.657
HaH setting, n (%)	92 (32.9)	70 (35.7)	22 (26.2)	0.120
- AA-HaH, n (%)	65 (70.7)	49 (70.0)	16 (72.7)	0.806
- ESD-HaH, n (%)	27 (29.3)	21 (30.0)	6 (27.3)	
Study title, n (%)*				0.108
- None	17 (6.1)	13 (6.6)	4 (4.8)	
- Primary school diploma	103 (36.8)	66 (33.7)	37 (44.0)	
- Middle school diploma	75 (26.8)	52 (26.5)	23 (27.4)	
- Professional school diploma	34 (12.1)	23 (11.7)	11 (13.1)	
- High school diploma	25 (8.9)	20 (10.2)	5 (6.0)	
- Bachelor's degree or higher	26 (9.3)	22 (11.2)	4 (4.8)	
Years of education, median (IQR)*	8 (5-11)	8 (5-11)	7.5 (5-8.6)	0.159
Living condition, n (%)				0.726
- Alone without help	21 (7.5)	14 (7.1)	7 (8.3)	
- Alone with help	50 (17.9)	32 (16.3)	18 (21.4)	
- Living with spouse/relative	172 (61.4)	123 (62.8)	49 (58.3)	
- Living with paid caregiver	37 (13.2)	27 (13.8)	10 (11.9)	
Presence of a caregiver, n (%)	145 (51.8)	96 (49.0)	49 (58.3)	0.151
- Paid caregivers, n (%)	73/145 (50.3)	51/96 (53.1)	22/49 (44.9)	0.349
Continuous 24/7 caregiving, n (%)	97 (66.9)	69 (71.9)	28 (57.1)	0.763
Legal disability recognized, n (%)	130 (46.4)	93 (47.4)	37 (44.0)	0.601
- With care allowance, n (%)	52/130 (40.0)	40/93 (43.0)	12/37 (32.4)	0.267
Geriatric Assessment to access geriatric care, n (%)	34 (12.1)	20 (10.2)	14 (16.7)	0.129
Presence of a legal guardian, n (%)	1	0	1	-
Hospital admission variables				
At least one hospital admission in the preceding 3 months, n (%)	162 (57.9)	108 (55.1)	54 (64.3)	0.154
N. of hospital admissions in the preceding 3 months, n (%)				0.176
- 1	104 (37.1)	70 (35.7)	34 (40.5)	
- 2	41 (14.6)	26 (13.3)	15 (17.9)	
- 3	13 (4.6)	9 (4.6)	4 (4.8)	
- 4 or more	4 (1.4)	3 (1.5)	1 (1.2)	
Site of admission, n (%)				0.103
- General Practitioner	15 (5.4)	14 (7.1)	1 (1.2)	
- ED	231 (82.5)	157 (80.1)	74 (88.1)	
- Other hospital ward	34 (12.1)	25 (12.8)	9 (10.7)	

Reason of admission, n (%)				**0.004**
- Respiratory tract infection	53 (18.9)	44 (22.4)	9 (10.7)	
- Acute heart failure	24 (8.6)	19 (9.7)	5 (6.0)	
- Fluid/electrolyte imbalance	27 (9.6)	19 (9.7)	8 (9.5)	
- Infection (other)	48 (17.1)	32 (16.3)	16 (19.0)	
- Urinary tract infection	14 (5.0)	9 (4.6)	5 (6.0)	
- Anemia/bleeding	28 (10.0)	23 (11.7)	5 (6.0)	
- Stroke/TIA	17 (6.1)	15 (7.7)	2 (2.4)	
- Uncontrolled BPSD	11 (3.9)	6 (3.1)	5 (6.0)	
- Other	58 (20.7)	29 (14.8)	29 (34.5)	
NEWS2 score, median (IQR)	2 (1-4)	1.5 (1-3)	3 (1-4)	**0.004**
NEWS2 score risk, n (%)				**0.049**
- Low risk	206 (73.6)	151 (77.0)	55 (65.5)	
- Low-medium risk	29 (10.4)	17 (8.7)	12 (14.3)	
- Medium risk	31 (11.1)	20 (10.2)	11 (13.1)	
- High risk	4 (5.0)	8 (4.1)	6 (7.1)	
Hemoglobin (g/dl), mean±SD*	11.8±2.2	11.8±2.2	11.6±2.1	0.441
ClCr (ml/min), median (IQR)*	38.5 (26.1-53.3)	38.5 (26.1-53.3)	38.6 (26.1-53.4)	0.767
BRASS, median (IQR)*	14 (10-19)	13 (9.5-18)	16 (13-20.5)	**0.001**
BRASS risk, n (%)				**0.001**
- Low	82 (29.3)	69 (35.2)	13 (15.5)	
- Medium	132 (47.1)	87 (44.4)	45 (53.6)	
- High	66 (23.6)	40 (20.4)	26 (31.0)	
Comprehensive Geriatric Assessment variables				
Comorbidity burden				
CIRS-CI, median (IQR)	5 (4-6)	5 (4-6)	5 (4-7)	0.747
CIRS-SI, median (IQR)	2.2 (1.9-2.3)	2.2 (1.9-2.3)	2.2 (2-2.4)	0.260
Clinically significant comorbidities according to CIRS score ≥3				
Cardiac, n (%)	173 (61.8)	122 (62.2)	51 (60.7)	0.809
Hypertension, n (%)	225 (80.4)	162 (82.7)	63 (75.0)	0.140
Vascular and hematopoietic, n(%)	131 (46.8)	92 (46.9)	39 (46.4)	0.938
Respiratory, n (%)	94 (33.6)	66 (33.7)	28 (33.3)	0.956
Eyes,ears,nose,throat,larynx, n(%)	107 (38.2)	75 (38.3)	32 (38.1)	0.979
Upper gastrointestinal, n (%)	65 (23.2)	45 (23.0)	20 (23.8)	0.877
Lower gastrointestinal, n (%)	52 (18.6)	32 (16.3)	20 (23.8)	0.140
Liver, pancreas and biliary, n (%)	15 (5.4)	8 (4.1)	7 (8.3)	0.157
Renal, n (%)	147 (52.5)	104 (53.1)	43 (51.2)	0.774
Genitourinary, n (%)	88 (31.4)	62 (31.6)	26 (31.0)	0.911
Musculoskeletal and skin, n (%)	119 (42.5)	79 (40.3)	40 (47.6)	0.257
Neurologic, n (%)	99 (35.4)	64 (32.7)	35 (41.7)	0.148
Endocrine and breast, n (%)	185 (66.1)	132 (67.3)	53 (63.1)	0.491
Psychiatric (incl. dementia), n (%)	113 (40.4)	70 (35.7)	43 (51.2)	0.016
Drug burden				
Drugs at admission, median (IQR)	7 (5-10)	7 (5-10)	6 (4-9)	0.063
Polytherapy, n (%)	215 (76.8)	157 (80.1)	58 (69.0)	**0.045**
Hyperpolytherapy, n (%)	54 (19.3)	39 (19.9)	15 (17.9)	0.692
Functional autonomy				
BI, median (IQR)	67.5 (35-90)	75 (40-95)	55 (25-80)	**<0.001**
BI disability level, n (%)				**<0.001**
- None	42 (15.0)	39 (19.9)	3 (3.6)	
- Mild	21 (7.5)	19 (9.7)	2 (2.4)	
- Moderate	83 (29.6)	56 (28.6)	27 (32.1)	

- Severe - Extremely severe	85 (30.4) 49 (17.5)	51 (26.0) 31 (15.8)	34 (40.5) 18 (21.4)	
Katz ADL (n. of functions lost), median (IQR)	2 (0-4)	1 (0-4)	3 (0.5-5)	**0.001**
IADL (n. of functions kept), median IQR)	2 (1-5)	3 (1-6)	1 (0-3.5)	**<0.001**
IADL autonomy category, n (%) - Autonomous - Partially autonomous - Non autonomous	 65 (23.2) 72 (25.7) 143 (51.1)	 55 (28.1) 53 (27.0) 88 (44.9)	 10 (11.9) 19 (22.6) 55 (65.5)	**0.001**
Cognitive impairment				
SPMSQ (n. of errors), median (IQR)*	2 (1-4)	2 (1-4)	3 (2-5)	**0.009**
Cognitive impairment SPMSQ, n(%)* - None - Mild - Moderate - Severe	 141 (51.3) 66 (24.0) 40 (14.5) 28 (10.2)	 107 (55.4) 46 (23.8) 23 (11.9) 17 (8.8)	 34 (41.5) 20 (24.4) 17 (20.7) 11 (13.4)	**0.016**
Confused, wandering behavior	39 (13.9)	22 (11.2)	17 (20.2)	**0.046**
Mood status				
HADS anxiety, median (IQR)†	6 (4-9)	6 (4-9)	6 (5-10)	0.316
Anxiety levels at HADS, n (%)† - Normal - Borderline - Abnormal	 152 (63.1) 49 (20.3) 40 (16.6)	 111 (63.8) 38 (21.8) 25 (14.4)	 41 (61.2) 11 (16.4) 15 (22.4)	0.472
HADS depression, median (IQR)†	8 (5-12)	8 (5-11)	10 (6-13)	**0.046**
Depression levels at HADS, n (%)† - Normal - Borderline - Abnormal	 101 (41.9) 56 (23.2) 84 (34.9)	 79 (45.4) 43 (24.7) 52 (29.9)	 22 (32.8) 13 (19.4) 32 (47.8)	**0.017**
Physical performance and activity levels				
Best handgrip (kg), median (IQR)*	14.1 (10-20)	14.9 (10-22)	12.8 (9.2-18.7)	**0.049**
Best handgrip (kg), males; median (IQR)*	19.8 (14.0-25.3)	20.0 (16.5-27.8)	17.1 (12.1-21.7)	**0.013**
Best handgrip (kg), females; median (IQR)*	11.6 (8-14.9)	11.9 (8.0-15.1)	11.0 (7.7-13.4)	0.368
Weakness at handgrip (FFP), n (%)	242 (86.4)	163 (83.2)	79 (94)	**0.015**
Unable to perform gait speed, n (%)	81 (28.9)	49 (25.0)	32 (38.1)	**0.027**
Gait speed (m/s), median (IQR)‡	0.5 (0.4-0.8)	0.5 (0.4-0.8)	0.6 (0.4-0.7)	0.765
Low gait speed (FFP), n (%)‡	100 (73.5)	75 (73.5)	25 (73.5)	1.000
Low gait speed or unable, n (%)**	181 (83.4)	124 (82.1)	57 (86.4)	0.439
PASE score, median (IQR)*	25 (0-57.2)	27.2 (0-72.2)	2.2 (0-28.6)	**0.001**
Low activity levels at PASE, n (%)*	208 (74.3)	134 (68.4)	74 (88.1)	**0.001**
Physical exhaustion, n (%)	209 (74.6)	149 (76.0)	60 (71.4)	0.418
Sensory impairment/balance				
Vision impairment, n (%)* - None - Present, moderate - Present, severe	 66 (23.6) 183 (65.4) 31 (11.1)	 42 (21.4) 129 (65.8) 25 (12.8)	 24 (28.6) 54 (64.3) 6 (7.1)	0.093
Hearing impairment, n (%)* - None - Present, moderate - Present, severe	 141 (50.4) 109 (38.9) 30 (10.7)	 99 (50.5) 75 (38.3) 22 (11.2)	 42 (50.0) 34 (40.5) 8 (9.5)	0.954
Falls in the previous year, n (%)*	109 (38.9)	69 (35.2)	40 (47.6)	0.051
Number of falls in the previous year, median (IQR)*	0 (0-1)	0 (0-1)	0 (0-1)	0.071

Nutrition				
BMI (kg/m^2), median (IQR)*	23.6 (20.8-26.3)	24.1 (21.5-26.7)	22.9 (19.8-25.7)	0.038
Mid-arm circumf. (cm), median(IQR)*	25 (23-27.3)	25 (23-27.5)	25 (22-27)	0.205
Mid-calf circumf. (cm), median(IQR)*	31.4 (29-34)	31.5 (29.8-34)	31 (28-33.3)	**0.030**
MNA score, median (IQR)††	18.5 (14.5-22)	19.3 (15.8-22.8)	15.8 (12.5-19.8)	**≤0.001**
Malnutrition risk at MNA, n (%)††				**≤0.001**
- Normal	40 (15.9)	37 (20.6)	3 (4.2)	
- At risk	112 (44.4)	83 (46.1)	29 (40.3)	
- Malnourished	100 (39.7)	60 (33.3)	40 (55.6)	
Weight loss in the past 12 mo, n (%)*	130 (46.4)	84 (42.9)	46 (54.8)	0.067
Pressure injury development risk				
ESS, median (IQR)	16 (13-18)	16 (14-18)	14 (12-16)	**≤0.001**
Risk of pressure injuries at ESS,				**≤0.001**
- Low	146 (52.1)	116 (59.2)	30 (35.7)	
- Medium	118 (42.1)	72 (36.7)	46 (54.8)	
- High	16 (5.7)	8 (4.1)	8 (9.5)	
Frailty assessment				
Fried Frailty Phenotype				
Frailty status according to FFP‡‡				0.104
- Robust, n (%)	0 (0)	0 (0)	0 (0)	
- Pre-frail, n(%)	29 (11.6)	24 (13.7)	5 (6.6)	
- Frail, n (%)	222 (88.4)	151 (86.3)	71 (93.4)	
Clinical Frailty Scale				
CFS score, median (IQR)	6 (4-7)	5 (4-7)	6 (5-7)	**≤0.001**
Frail according to CFS ≥5, (%)	190 (67.9)	118 (60.2)	72 (85.7)	**≤0.001**
Frailty severity according to CFS				**≤0.001**
- No frailty (CFS 1-4), n (%)	90 (32.1)	78 (39.8)	12 (14.3)	
- Moderate frailty (CFS 5/6), n (%)	102 (36.4)	64 (32.7)	38 (45.2)	
- Severe frailty (CFS≥7), n (%)	88 (31.4)	54 (27.6)	34 (40.5)	
Frailty index				
FI, median (IQR)	0.46 (0.31-0.6)	0.41 (0.28-0.58)	0.55 (0.41-0.64)	**≤0.001**
Items evaluated at FI, mean±SD	38.9±1.37	39.0±1.25	38.5±1.58	**0.006**
Frail according to FI≥0.25, n (%)	242 (86.4)	160 (81.6)	82 (97.6)	**≤0.001**
Frailty severity according to FI				**≤0.001**
- No frailty (FI <0.25), n (%)	38 (13.6)	36 (18.4)	2 (2.4)	
- Moderate frailty (0.25-0.44), n (%)	97 (34.6)	74 (37.8)	74 (37.8)	
- Severe frailty (FI≥0.45), n (%)	145 (51.8)	86 (43.9)	86 (43.9)	
Multidimensional Prognostic Index				
MPI score, median (IQR)***	0.5 (0.38-0.69)	0.44 (0.31-0.63)	0.56 (0.44-0.69)	**0.001**
Frailty status according to MPI***				**0.003**
- MPI low risk, n (%)	57 (22.7)	47 (26.3)	10 (13.9)	
- MPI medium risk, n (%)	127 (50.6)	93 (52.0)	34 (47.2)	
- MPI high risk = frail, n (%)	67 (26.7)	39 (21.8)	28 (38.9)	
Use of medical devices and medication classes during admission				
Venous catheter use, n (%)	265 (94.6)	185 (94.4)	80 (95.2)	1.000
- Midline/Long VC	67 (25.3)	40 (21.6)	27 (33.8)	**0.045**
- PICC/CVC	14 (5.3)	8 (4.3)	6 (7.5)	

Venous catheter present at admission, n (%)	23 (8.7)	14 (7.6)	9 (11.3)	0.328
Urinary catheter use, n (%)	96 (34.3)	62 (31.6)	34 (40.5)	0.153
Urinary catheter present at admission, n (%)	22 (22.7)	16 (25.4)	6 (17.6)	0.384
Oxygen supplementation, n (%) - Nasal cannula - Venturi mask - NIV/HFNC	73 (26.1) 52/73 (71.2) 13/73 (17.8) 8/73 (11.0)	52 (26.5) 39/52 (75.0) 7/52 (13.5) 6/52 (11.5)	21 (25.0) 13/21 (61.9) 6/21 (28.6) 2/21 (9.5)	0.093 0.311
Oxygen supplementation present at admission, n (%)	20 (27.4)	15 (28.8)	5 (23.8)	0.662
Intravenous antibiotic, n (%)	148 (52.9)	106 (54.1)	42 (50.0)	0.531
New opioid use, n (%)	20 (7.1)	10 (5.1)	10 (11.9)	**0.043**
New benzodiazepine use, n (%)	16 (5.7)	10 (5.1)	6 (7.2)	0.574
New other hypnotic use, n (%)	32 (11.5)	16 (8.2)	16 (19.3)	**0.008**
New antipsychotic use, n (%)	33 (11.8)	15 (7.7)	18 (21.7)	**<0.001**
Outcomes at discharge				
Length of hospital stay (days), median (IQR)	11.5 (7-19.5)	10 (6-18)	14 (9-24)	**0.001**
Any hospital-acquired complication, n(%)	71 (25.4)	41 (20.9)	30 (35.7)	**0.009**
Delirium during admission, n (%) - Requiring use of medication	28 (10) 24/28 (85.7)	13 (6.6) 11/13 (84.6)	15 (17.9) 13/15 (86.7)	**0.004** 1.000
Fall during admission, n (%)	8 (2.9)	3 (1.5)	5 (6.0)	0.055
Pressure injury development during admission, n (%)	16 (5.7)	11 (5.6)	5 (6.0)	1.000
Healthcare-associated infection during admission, n (%)	40 (14.3)	24 (12.2)	16 (19.0)	0.136
Setting of discharge, n (%) - At home - MLTCF - ED	 234 (83.6) 40 (14.3) 6 (2.1)	 182 (92.9) 10 (5.1) 4 (2)	 52 (61.9) 30 (35.7) 2 (2.4)	**<0.001**
Outcomes at 6 months from discharge				
Length of follow-up (days), median (IQR)	182 (162-189)	184 (177-193)	119 (29-182)	**<0.001**
All-cause mortality, n (%)	61 (21.8)	-	61 (72.6)	-
Institutionalization, n (%)	42 (15.0)	-	42 (50.0)	-
ED visit/unplanned rehospitalization, n (%)	98 (35.0)	60 (30.6)	38 (45.2)	**0.019**
N. of ED visit/rehospitalization, n (%) - 1 - 2 - 3 or more	 71 (25.4) 14 (5.0) 13 (4.6)	 45 (23.0) 8 (4.1) 7 (3.6)	 26 (31.0) 6 (7.1) 6 (7.1)	**0.014**

*Missing values <5%
†Missing values for 39 (13.9%) subjects
‡Missing values (unavailable or untestable) for 144 (51.4%) subjects
** Missing values for 63 (22.5%) subjects
†† Missing values for 28 (10.0%) subjects
‡‡ Missing values for 29 (10.4%) subjects
*** Missing values for 29 (10.4%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BI = Barthel Index, BMI = Body Mass Index, BPSD = behavioral and psychological symptoms of dementia, BRASS =

Blaylock Risk Assessment Screening Score, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, CVC = Central Venous Cannula, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, ESS = Exton-Smith Scale, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, HFNC = High Flow Nasal Cannula, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, NEWS2= National Early Warning Score 2, NIV = Non-Invasive Ventilation, PASE = Physical Activity Scale for the Elderly, PICC = Peripherally Inserted Central Catheter, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack, VC = venous cannula.

Most patients were institutionalized right after discharge, resulting in a median time to institutionalization of 0 days (IQR 0-60.3 – see *Supplementary Figure S1*). When comparing institutionalized patients with those living at home and alive at follow-up, the former were more often discharged from the AGW, were more frequently identified as frail at the CFS, FI, and MPI and showed a higher burden of geriatric syndromes. Interestingly, institutionalized patients had experienced more hospital-acquired complications during admission (40.5% vs 20.9%), and showed a greater decline in functional status at follow-up (73.9% vs 42.3%), as reported in *Supplementary Table S14*.

Figure 13– Cumulative incidence curves for the primary composite outcome of all-cause mortality or institutionalization after discharge in the overall sample (Panel A) and stratified by healthcare setting (Panel B), and Kaplan-Meier curves for overall survival after discharge in the overall sample (Panel C) and stratified by healthcare setting (Panel D). Curves are presented along with their respective 95% Confidence Interval (CI) areas.

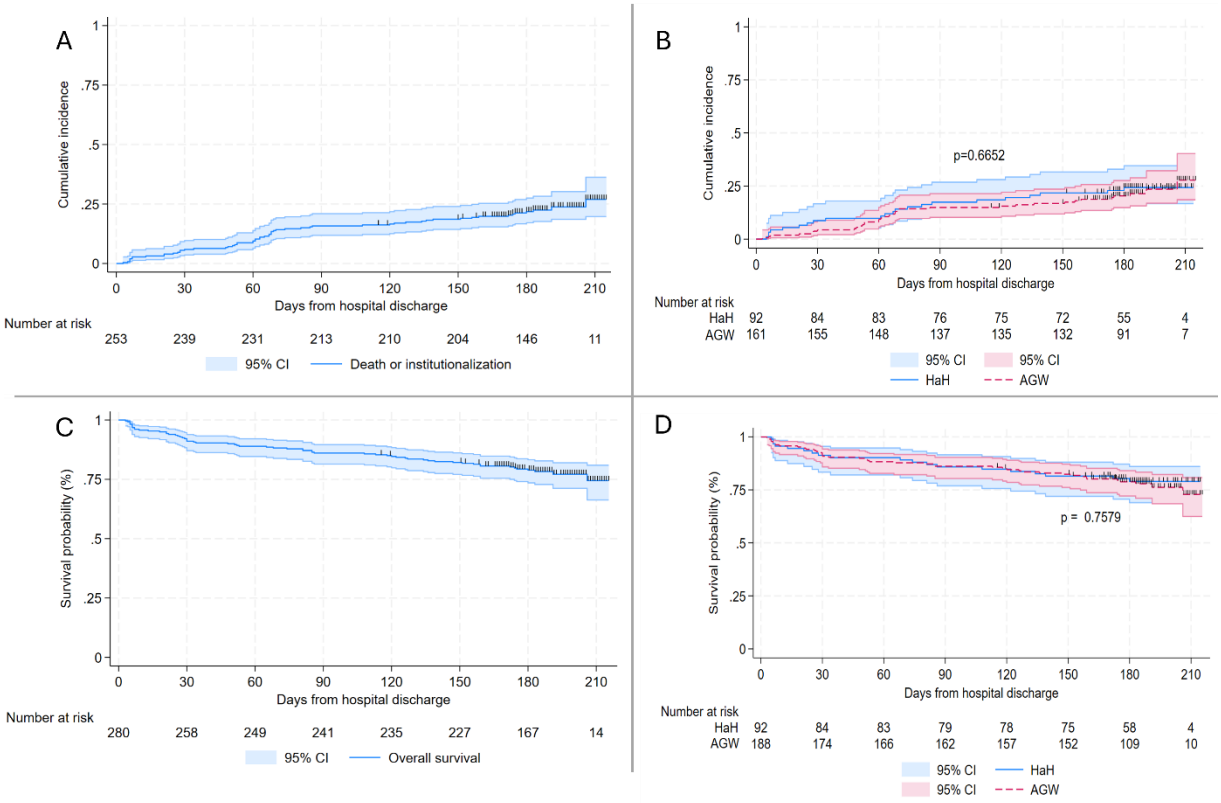
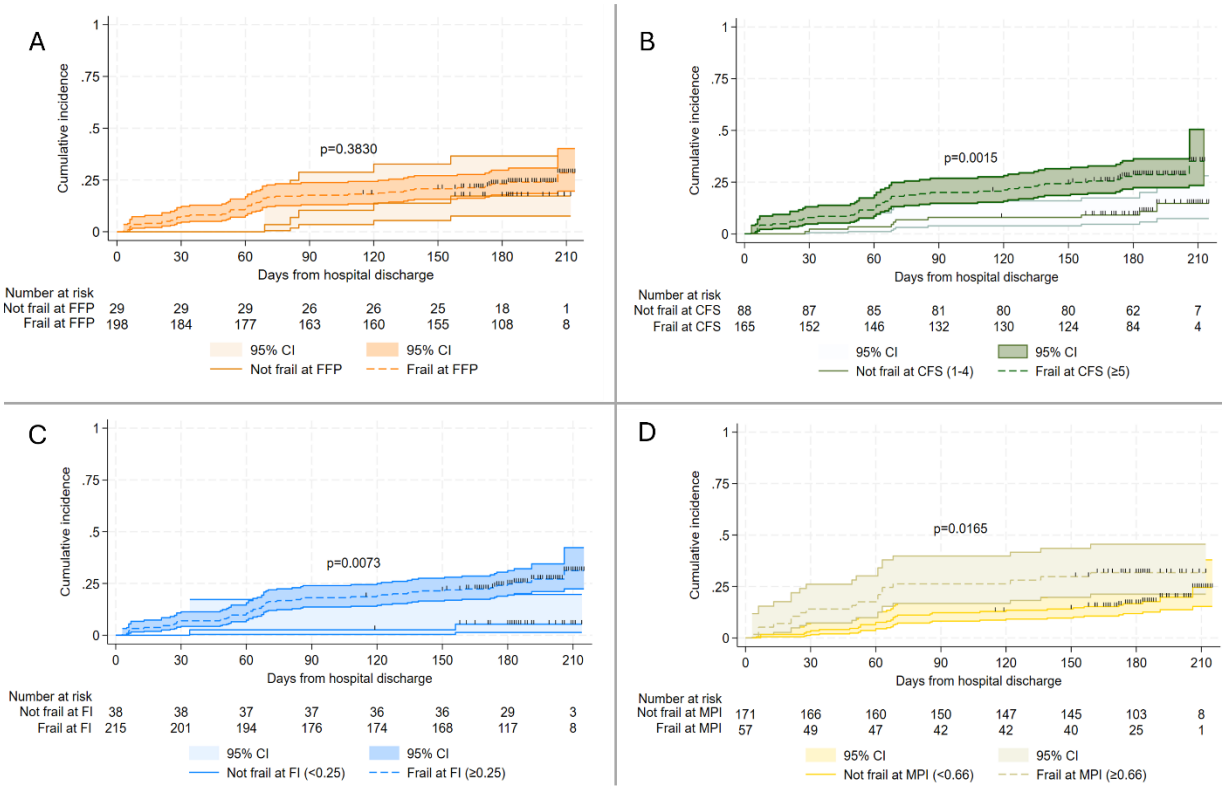


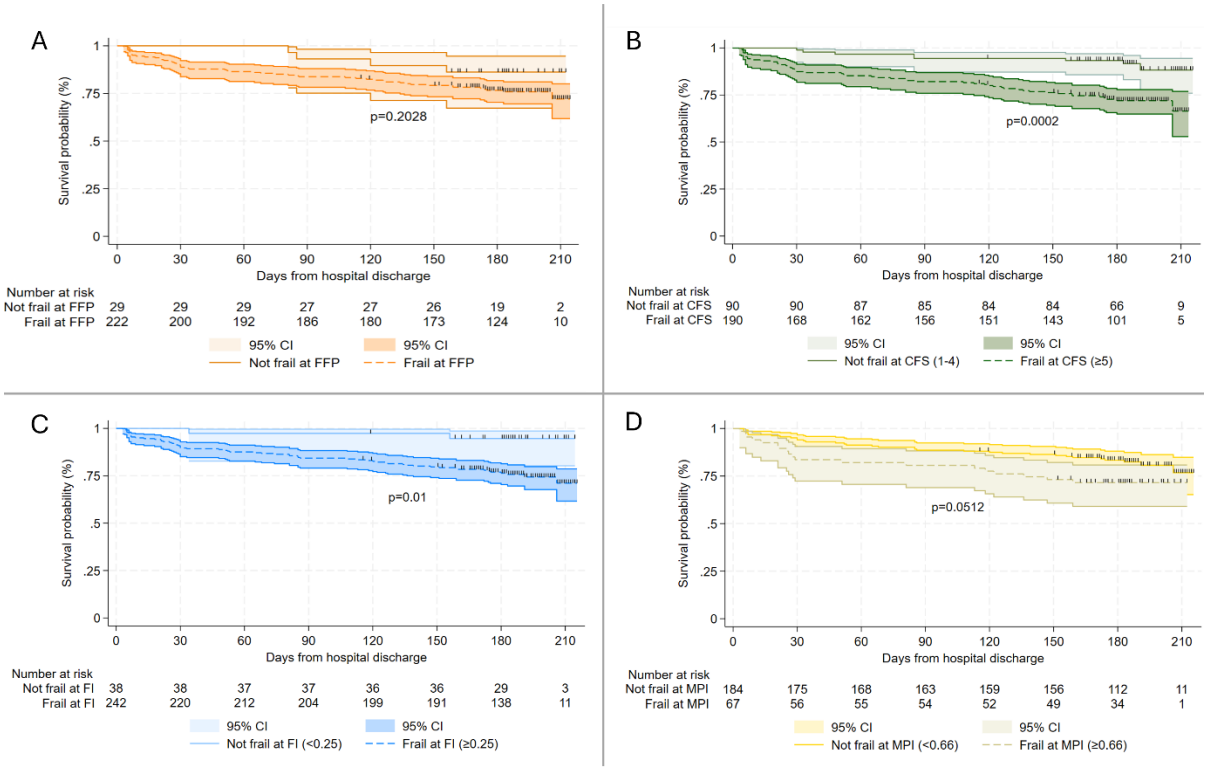
Figure 14 – Cumulative incidence curves for the primary composite outcome of all-cause mortality or institutionalization after discharge stratified according to frailty presence (dashed lines) or absence (solid lines) as defined by the Fried Frailty Phenotype (FFP, Panel A), the Clinical Frailty Scale (CFS, Panel B), the Frailty Index (FI, Panel C), or the Multidimensional Prognostic Index (MPI, Panel D). Curves are presented along with their respective 95% Confidence Interval (CI) areas.



The median time to first ED visit or rehospitalization was 57 days (IQR 17-114.3), with no significant differences according to healthcare setting or frailty status (*Supplementary Figures S3-S4***)**. Patients who experienced at least one further ED visit or unplanned hospitalization during follow-up had more frequently been hospitalized at least once in the three months prior to enrollment than those who did not require unplanned hospital care and were alive at follow-up (65.3% vs 52.0%). However, no significant differences in healthcare setting or frailty status were observed between these groups. Notably, patients that experienced at least one further ED visit or unplanned hospitalization showed a greater BI decline at follow-up (*Supplementary Table S15*).

Lastly, patients that experienced a clinically significant functional decline at 6-month follow-up were more frequently frail according to the CFS (74.0% vs 52.9%) and the FI (94.0% vs 74.8%) compared to those alive with preserved function at follow-up, as detailed in *Supplementary Table S16*.

Figure 15– Kaplan-Meier curves for overall survival after discharge, stratified according to frailty presence (dashed lines) or absence (solid lines) as defined by the Fried Frailty Phenotype (FFP, Panel A), the Clinical Frailty Scale (CFS, Panel B), the Frailty Index (FI, Panel C), or the Multidimensional Prognostic Index (MPI, Panel D). Curves are presented along with their respective 95% Confidence Interval (CI) areas.



4.3.2 FACTORS ASSOCIATED WITH CLINICAL OUTCOMES AT 6 MONTHS FROM DISCHARGE IN PATIENTS DISCHARGED ALIVE

Following these exploratory descriptive analyses, multivariable logistic regression analyses were performed to explore the association between frailty and healthcare setting also with clinical outcomes at follow-up.

Table 19 reports the results of analyses on the primary composite outcome of all-cause mortality or institutionalization during 6 months of follow-up. In Model 1, frailty defined according to all definitions except for the FFP was significantly associated with increased odds of experiencing the primary outcome, with wide variation in point estimates and wide 95% CIs. The HaH setting resulted independently associated with reduced odds of experiencing the primary outcome in analyses corrected for frailty defined according to the CFS and MPI [aOR 0.47 (95% CI 0.26-0.86) and aOR 0.72 (95% CI 0.54-0.98)]. After adjusting for relevant clinical factors in Model 2, including the presence of geriatric syndromes, the caregiving coverage and the incidence of any hospital-acquired complication during admission, the association with

frailty became nonsignificant while the HaH setting proved to be one, if not the only, independent predictor of reduced incidence of all-cause death or institutionalization at 6-month follow-up, irrespective of frailty definition used [aOR 0.41 (95% CI 0.20-0.84) in the analysis with frailty defined according to the CFS].

Table 19 – Factors independently associated with the composite outcome of all-cause mortality or institutionalization at 6-month follow-up in patients discharged alive. Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	1.35 (0.89-2.05)	**4.68 (2.34-9.34)**	**9.55 (2.24-40.76)**	**1.62 (1.20-2.17)**
HaH setting	0.79 (0.59-1.05)	**0.47 (0.26-0.86)**	0.61 (0.34-1.08)	**0.72 (0.54-0.98)**
Model 2				
Frailty	1.10 (0.7-1.74)	**3.52 (1.53-8.09)**	**5.75 (1.25-26.48)**	1.04 (0.65-1.67)
HaH setting	**0.65 (0.45-0.92)**	**0.41 (0.20-0.84)**	**0.46 (0.22-0.94)**	**0.64 (0.45-0.92)**
Age, years	0.97 (0.93-1.02)	0.97 (0.93-1.01)	0.97 (0.93-1.01)	0.97 (0.93-1.02)
Female sex	0.87 (0.66-1.15)	0.70 (0.4-1.24)	0.74 (0.42-1.3)	0.87 (0.66-1.15)
CIRS-CI	0.99 (0.85-1.17)	0.98 (0.83-1.15)	0.98 (0.83-1.15)	0.99 (0.84-1.17)
SPMSQ, errors	1.03 (0.91-1.16)	1.03 (0.91-1.15)	1.02 (0.91-1.15)	1.02 (0.90-1.16)
Barthel Index	**0.98 (0.97-0.99)**	0.99 (0.98-1.01)	0.99 (0.98-1.00)	**0.99 (0.97-1.00)**
Caregiver <24h vs no caregiver	1.50 (0.95-2.36)	1.90 (0.86-4.20)	1.86 (0.86-4.02)	1.49 (0.94-2.36)
Caregiver 24/7 vs no caregiver	0.91 (0.57-1.46)	1.24 (0.55-2.78)	1.2 (0.54-2.67)	0.92 (0.57-1.48)
Any hospital-acquired complication	1.31 (0.95-2.36)	1.63 (0.83-3.01)	1.68 (0.82-1.15)	1.31 (0.97-1.78)

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index, SPMSQ = Short Portable Mental Status Questionnaire

When focusing solely on all-cause mortality (*Table 20*), the association with frailty defined according to the CFS and the FI remained significant also at multivariable analysis [aOR 4.56 (95% CI 1.76-11.8) and aOR 4.86 (95% CI 1.03-22.9), respectively], whereas no association with healthcare setting was noted. Female sex confirmed to be an independent and consistent predictor of overall survival in our population.

Table 20 – Factors independently associated with all-cause mortality at 6-month follow-up in patients discharged alive. Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	1.46 (0.89-2.4)	**4.26 (1.91-9.51)**	**5.84 (1.36-25.01)**	1.34 (0.97-1.85)
HaH setting	0.94 (0.69-1.28)	0.71 (0.38-1.33)	0.88 (0.47-1.63)	0.90 (0.66-1.23)
Model 2				
Frailty	1.32 (0.78-2.24)	**4.56 (1.76-11.8)**	**4.86 (1.03-22.9)**	0.96 (0.57-1.63)
HaH setting	0.87 (0.6-1.28)	0.76 (0.35-1.65)	0.84 (0.39-1.83)	0.86 (0.59-1.26)
Age, years	0.97 (0.93-1.02)	0.97 (0.92-1.01)	0.97 (0.93-1.02)	0.98 (0.93-1.02)
Female sex	**0.69 (0.51-0.93)**	**0.43 (0.23-0.81)**	**0.47 (0.25-0.86)**	**0.69 (0.51-0.94)**
CIRS-CI	0.95 (0.80-1.13)	0.94 (0.79-1.12)	0.94 (0.79-1.12)	0.96 (0.81-1.14)
SPMSQ, errors	0.98 (0.86-1.11)	0.97 (0.86-1.11)	0.97 (0.86-1.10)	0.98 (0.87-1.69)
Barthel Index	**0.98 (0.97-0.99)**	0.99 (0.98-1.01)	0.99 (0.98-1.00)	**0.98 (0.97-0.99)**
Caregiver <24h vs no caregiver	1.17 (0.71-1.94)	1.08 (0.45-2.59)	1.10 (0.47-2.6)	1.19 (0.71-1.98)
Caregiver 24/7 vs no caregiver	0.87 (0.52-1.45)	0.86 (0.35-2.09)	0.85 (0.35-2.04)	0.86 (0.51-1.45)
Any hospital-acquired complication	1.21 (0.87-1.68)	1.35 (0.69-2.64)	1.41 (0.73-2.73)	1.21 (0.87-1.69)

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index, SPMSQ = Short Portable Mental Status Questionnaire

Tables 21 and 22 report results of multinomial analyses for institutionalization and for ED visits/unplanned readmissions at 6-month follow up, respectively, when compared to patients alive at follow-up and that did not experience the clinical outcome of interest, to account for the high competing event of death. Complete results of multivariable analyses, including comparisons between patients alive and deceased at follow-up and that did not experience the clinical outcomes of interest are reported in *Supplementary Tables S17-S18.*

When focusing solely on institutionalization (*Table 21* and *Supplementary Table S17*), the protective association with HaH setting remained significant in all models, irrespective of frailty definition, also when adjusted for relevant confounders such as comorbidity, functional and cognitive status, caregiver availability, and previous hospital-acquired complication [aOR 0.09 (95% CI 0.02-0.32) in CFS-adjusted analysis]. Frailty according to the CFS was also

independently associated with increased odds of institutionalization at fully adjusted analysis [aOR 3.36 (95% CI 1.10-10.20].

Table 21 – Factors independently associated with institutionalization at 6-month follow-up in patients discharged alive. Multinomial logistic regression analysis comparing patients that presented the outcome (n=42) with patients alive at follow-up and that did not present the outcome (n=196). Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	1.6 (0.85-2.99)	**5.57 (2.2-14.1)**	-†	**1.94 (1.33-2.83)**
HaH setting	**0.37 (0.2-0.67)**	**0.10 (0.03-0.34)**	**0.13 (0.04-0.44)**	**0.32 (0.17-0.59)**
Model 2				
Frailty	1.29 (0.65-2.54)	**3.36 (1.10-10.20)**	-†	1.26 (0.68-2.35)
HaH setting	**0.29 (0.15-0.56)**	**0.09 (0.02-0.32)**	**0.09 (0.03-0.35)**	**0.29 (0.15-0.56)**
Age, years	1 (0.94-1.06)	0.99 (0.94-1.06)	1 (0.94-1.06)	1.01 (0.95-1.07)
Female sex	1.15 (0.78-1.68)	1.25 (0.57-2.70)	1.30 (0.61-2.80)	1.16 (0.79-1.69)
CIRS-CI	1.02 (0.82-1.27)	1.01 (0.81-1.26)	1.01 (0.81-1.25)	1.01 (0.81-1.26)
SPMSQ, errors	1.09 (0.92-1.28)	1.07 (0.91-1.27)	1.08 (0.91-1.27)	1.06 (0.89-1.26)
Barthel Index	0.99 (0.97-1.00)	0.99 (0.98-1.01)	0.99 (0.98-1.01)	0.99 (0.97-1.01)
Caregiver <24h vs no caregiver	1.63 (0.91-2.93)	2.01 (0.77-5.25)	1.93 (0.75-4.94)	1.56 (0.86-2.83)
Caregiver 24/7 vs no caregiver	0.83 (0.43-1.59)	1.15 (0.39-3.39)	1.06 (0.37-3.05)	0.87 (0.44-1.72)
Any hospital-acquired complication	1.30 (0.88-1.93)	1.65 (0.74-3.67)	1.68 (0.76-3.71)	1.3 (0.87-1.93)

*Results are presented after Multiple Imputation for missing values
†Unable to estimate parameter due to quasi-complete separation of data

Abbreviations: CFS = Clinical Frailty Scale, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index, SPMSQ = Short Portable Mental Status Questionnaire

Neither frailty nor healthcare setting were significantly associated with the incidence of any ED visit or unplanned rehospitalization at follow-up, when compared to patients alive and not requiring urgent hospital care, both in Model 1 and in Model 2 (*Table 22* and *Supplementary Table S18)*. The only strong, consistent, independent predictor of ED visit or unplanned rehospitalization was the number of unplanned hospitalizations in the 3 months preceding the

index admission [aOR 1.34 (95% CI 1.00-1.79) in the analysis with frailty defined according to the CFS].

Table 22 – Factors independently associated with Emergency Department visits or unplanned hospital readmissions at 6-month follow-up in patients discharged alive. Multinomial logistic regression analysis comparing patients that presented the outcome (n=98) with patients alive at follow-up and that did not present the outcome (n=152). Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	1.26 (0.87-1.82)	1.31 (0.75-2.28)	1.27 (0.61-2.62)	1.12 (0.83-1.51)
HaH setting	1.16 (0.89-1.52)	1.36 (0.79-2.36)	1.43 (0.84-2.46)	1.15 (0.87-1.51)
Model 2				
Frailty	1.3 (0.87-1.93)	1.61 (0.78-3.33)	1.4 (0.6-3.28)	1.06 (0.65-17.2)
HaH setting	1.18 (0.88-1.6)	1.42 (0.78-2.59)	1.49 (0.82-2.71)	1.18 (0.87-1.59)
Age, years	1.01 (0.97-1.06)	1.01 (0.97-1.05)	1.01 (0.97-1.05)	1.02 (0.98-1.06)
Female sex	0.81 (0.62-1.07)	0.67 (0.39-1.16)	0.68 (0.4-1.18)	0.82 (0.63-1.08)
CIRS-CI	1.02 (0.88-1.19)	1.01 (0.87-1.18)	1.01 (0.87-1.18)	1.03 (0.89-1.20)
SPMSQ, errors	**1.14 (1.01-1.28)**	1.12 (1-1.27)	1.12 (0.99-1.26)	1.13 (0.99-1.28)
Barthel Index	1.01 (0.99-1.02)	1.01 (0.99-1.02)	1.01 (0.99-1.02)	1.01 (0.99-1.02)
N.of hospitalizations in the last 3 months	**1.38 (1.03-1.85)**	**1.34 (1.00-1.79)**	**1.35 (1.01-1.8)**	**1.37 (1.03-1.83)**
MLTCF discharge	1.20 (0.74-1.97)	1.17 (0.43-3.18)	1.23 (0.46-3.31)	1.22 (0.75-2.01)

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MLTCF = medium- or long-term care facility, MPI = Multidimensional Prognostic Index, SPMSQ = Short Portable Mental Status Questionnaire

Associations with worsening functional status at follow-up as compared to patients alive and without worsening functional status at follow-up were less consistent: frailty was associated with increased odds of experiencing worsening functional status at multivariable analyses only when defined according to the FI [aOR 3.29 (95% CI 1.19-9.11)], while healthcare setting was not associated with the outcome of interest. A higher handgrip strength test was consistently associated with lower odds of worsening functional status at follow-up [aOR 0.93 (95% CI 0.88-0.98) in the analysis with frailty defined according to the CFS], irrespective of frailty scale, and female sex was associated with lower odds only when frailty was defined according to CFS

[aOR 0.48 (95% CI 0.24-0.99)], as summarised in *Table 23*.

Since handgrip strength is associated with sex, interaction between these variables was explored but yielded non-significant results [*p* for interaction 0.5695 (FFP-adjusted), 0.5395 (CFS-adjusted), 0.6361 (FI-adjusted), 0.5598 (MPI-adjusted)]. Interestingly, when we explored aORs for interaction between sex and handgrip strength in datasets wit fully available data (i.e., with frailty defined according to CFS and FI), interaction between female sex and handgrip was nonsignificant, whereas interaction between male sex and handgrip was associated with lower odds of showing worsening functional status at follow-up [aOR HST 0.92 (95% CI 0.86-0.98) CFS-adjusted and aOR 0.92 (0.86-0.99) – FI-adjusted].

Table 23 – Factors independently associated with worsening functional status at 6-month follow-up in patients discharged alive. Multivariable logistic regression analysis comparing patients that presented the outcome (n=100) with patients alive at follow-up and that did not present the outcome (n=119). Results are expressed as aOR (95% CI).

	FFP*	***CFS***	***FI***	***MPI****
Model 1				
Frailty	1.91 (1.00-3.65)	**2.72 (1.50-4.90)**	**5.36 (2.12-13.5)**	1.76 (0.82-3.78)
HaH setting	0.79 (0.44-1.42)	0.72 (0.40-1.30)	0.84 (0.47-1.5)	0.88 (0.5-1.55)
Model 2				
Frailty	0.90 (0.58-1.42)	1.77 (0.88-3.58)	**3.29 (1.19-9.11)**	1.13 (0.73-1.76)
HaH setting	0.91 (0.66-1.25)	0.72 (0.38-1.37)	0.79 (0.41-1.5)	0.90 (0.65-1.24)
Age, years	1.02 (0.97-1.07)	1.02 (0.97-1.06)	1.02 (0.97-1.06)	1.02 (0.98-1.07)
Female sex	0.56 (0.25-1.22)	**0.48 (0.24-0.99)**	0.50 (0.24-1.03)	0.56 (0.26-1.24)
CIRS-CI	0.93 (0.78-1.11)	0.92 (0.77-1.10)	0.91 (0.76-1.09)	0.92 (0.77-1.10)
SPMSQ, errors	1.05 (0.94-1.17)	1.03 (0.92-1.15)	1.03 (0.92-1.15)	1.03 (0.9-1.17)
Handgrip strength	**0.92 (0.87-0.96)**	**0.93 (0.88-0.98)**	**0.93 (0.89-0.98)**	**0.92 (0.88-0.97)**
Any hospital-acquired complication	0.9 (0.64-1.25)	0.69 (0.35-1.39)	0.71 (0.35-1.42)	0.89 (0.63-1.24)

*Results are presented after Multiple Imputation for missing values

Abbreviations: CFS = Clinical Frailty Scale, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MPI = Multidimensional Prognostic Index, SPMSQ = Short Portable Mental Status Questionnaire

4.4 Exploratory analysis on frailty severity and clinical outcomes

To explore the potential differential impact of healthcare setting on clinical outcomes of interest according to frailty severity levels (mild/moderate vs severe), post-hoc sub-analyses for the CFS and the FI were performed, as well as a sub-analysis on subjects identified as moderate risk at MPI (MPI category 2, including subjects with MPI scores between 0.33 and 0.66).

With the exception of CFS, the inverse correlation of the HaH setting with the outcomes of all-cause death or any hospital-acquired complication during admission and with any hospital-acquired complication during admission only, was retained only in patients with higher levels of frailty severity according to both FI and MPI (*Table 24*).

For outcomes at 6-month follow-up associations with healthcare setting were less consistent and frequently non-significant, possibly due to reduced event rate when stratifying by frailty severity and/or correcting for the competing event of all-cause death (*Table 25*)

Table 24 – Post-hoc analysis stratified according to frailty severity for clinical outcomes during admission. Associations of the Hospital-at-Home setting as compared to the acute geriatric ward setting with the outcomes are reported as OR (95% CI).

	All-cause death or any hospital-acquired complication during admission		***Any hospital-acquired complication during admission***	
	Model 1* **OR (95%CI)**	**Model 2† aOR (95%CI)**	**Model 1*** **OR (95%CI)**	**Model 2† aOR (95%CI)**
Clinical Frailty Scale (CFS)				
Mild-moderate frailty (CFS 5-6, n=106)	0.51 (0.19-1.41)	**0.24 (0.06-0.9)**	0.58 (0.21-1.6)	**0.24 (0.06-0.09)**
Severe frailty (CFS 7-8, n=95)	0.88 (0.38-2.02)	0.55 (0.21-1.45)	0.56 (0.24-1.34	**0.29 (0.1-0.86)**
Frailty Index (FI)				
Mild-moderate frailty (FI 0.25-0.44, n=100)	0.50 (0.13-1.9)	0.3 (0.06-1.43)	0.50 (0.13-1.9)	0.3 (0.06-1.43)
Severe frailty (FI≥0.45, n=157)	0.74 (0.38-1.43)	**0.4 (0.17-0.93)**	0.57 (0.28-1.14)	**0.22 (0.08-0.59)**
Multidimensional Prognostic Index (MPI)‡				
Moderate risk (MPI 0.03-0.65,)	0.93 (0.61-1.39)	0.90 (0.58-1.4)	0.83 (0.54-1.28)	0.84 (0.53-1.35)
Severe risk = frail at MPI (MPI≥0.66)	0.73 (0.46-1.15)	**0.50 (0.27-0.94)**	0.64 (0.39-1.03)	**0.39 (0.2-0.78)**

*Univariate analysis

† Corrected for: age, sex, Cumulative Illness Rating Scale Comorbidity Index (CIRS-CI), Barthel Index, Short Portable Mental Status Questionnaire (SPMSQ), National Early Warning Score 2 (NEWS2) at admission, number of falls in the previous year, length of stay in days.

‡After multiple imputation of missing values

Table 25– Post-hoc analysis stratified according to frailty severity for clinical outcomes at 6-month follow-up in patients discharged alive. Associations of the Hospital-at-Home setting as compared to the acute geriatric ward setting with the outcomes are reported as OR (95% CI).

	All-cause death or institutionalization at follow-up		***All-cause death at follow-up***	
	Model 1* OR (95%CI)	**Model 2† aOR (95%CI)**	**Model 1* OR (95%CI)**	**Model 2† aOR (95%CI)**
Clinical Frailty Scale (CFS)				
Mild-moderate frailty (CFS 5-6, n=102)	0.68 (0.27-1.71)	0.83 (0.25-2.70)	1.28 (0.5-3.29)	1.86 (0.51-6.86)
Severe frailty (CFS 7-8, n=88)	**0.39 (0.16-0.95)**	0.38 (0.13-1.09)	0.50 (0.2-1.28)	0.54 (0.17-1.69)
Frailty Index (FI)				
Mild-moderate frailty (FI 0.25-0.44, n=97)	0.54 (0.14-2.06)	0.44 (0.09-2.14)	0.79 (0.20-3.06)	1.05 (0.20-5.49)
Severe frailty (FI≥0.45, n=145)	**0.42 (0.21-0.84)**	0.47 (0.20-1.1)	0.70 (0.33-1.47)	0.82 (0.32-2.07)
Multidimensional Prognostic Index (MPI)‡				
Moderate risk (MPI 0.03-0.65)	0.79 (0.51-1.23)	0.99 (0.97-1.01)	1.07 (0.68-1.68)	0.99 (0.97-1.01)
Severe risk = frail at MPI (MPI≥0.66)	0.61 (0.39-1)	**0.48 (0.25-0.9)**	0.75 (0.45-1.25)	0.55 (0.28-1.09)
	ED visit or unplanned hospitalization at follow-up**		***Worsening functional status at follow-up*****	
	Model 1* OR (95%CI)	**Model 2†† aOR (95%CI)**	**Model 1* OR (95%CI)**	**Model 2‡‡ aOR (95%CI)**
Clinical Frailty Scale (CFS)				
Mild-moderate frailty (CFS 5-6, n=102 | n=74)	2.31 (0.91-5.88)	1.97 (0.68-5.72)	0.48 (0.17-1.36)	0.42 (0.13-1.30)
Severe frailty (CFS 7-8, n= 88 | n=63)	1.31 (0.51-3.33)	1.35 (0.49-3.71)	1.4 (0.51-3.81)	2.27 (0.65-7.88)
Frailty Index (FI)				
Mild-moderate frailty (FI 0.25-0.44, n= 88| n=79)	1.29 (0.44-3.8)	1.15 (0.34-3.85)	1.25 (0.41-3.76)	1.71 (0.47-6.24)
Severe frailty (FI≥0.45, n= 124| n=104)	1.69 (0.82-3.48)	1.91 (0.84-4.36)	0.74 (0.34-1.60)	0.81 (0.35-1.90)
Multidimensional Prognostic Index (MPI)‡				
Moderate risk (MPI 0.03-0.65)	1.09 (0.73-1.64)	1.03 (0.64-1.65)	0.89 (0.39-2.06)	0.91 (0.57-1.44)
Severe risk = frail at MPI (MPI≥0.66)	1.34 (0.81-2.21)	1.39 (0.78-2.47)	1.03 (0.35-3.03)	0.94 (0.5-1.79)

*Univariate analysis

† Corrected for: age, sex, , Cumulative Illness Rating Scale Comorbidity Index (CIRS-CI), Barthel Index, Short Portable Mental Status Questionnaire (SPMSQ), caregiving level (24/7, <24 hours, no caregiving), any hospital-acquired complication during admission

‡After multiple imputation of missing values

**Multinomial analysis, showing results compared with patients alive at follow-up that did not experience the outcome of interest

††Corrected for: age, sex, , Cumulative Illness Rating Scale Comorbidity Index (CIRS-CI), Barthel Index, Short Portable Mental Status Questionnaire (SPMSQ), number of hospitalizations in the 3 months preceding index hospitalization, discharge to medium- or long-term care facility
‡‡Corrected for: age, sex, , Cumulative Illness Rating Scale Comorbidity Index (CIRS-CI), Barthel Index, Short Portable Mental Status Questionnaire (SPMSQ), handgrip strength test, any hospital-acquired complication during admission

5. Discussion

The MUFASA study prospectively investigated the prevalence and impact of frailty defined using four commonly adopted tools (FFP, CFS, FI, and MPI) in a cohort of 297 acutely ill older adults admitted from home to either a traditional in-hospital geriatric ward (AGW, n=199) or an alternative Hospital-at-Home program (HaH, n=98) at an Italian university hospital. The main findings of the MUFASA study can be summarized as follows:

1. Frailty prevalence in the study population was extremely high. Rates ranged from 86.6% (95% CI 82.6%-90.5%) for the FFP and 86.5% (95% CI 82.2%-90.0%) for the FI, to 67.7% (95% CI 62.2%-72.7%) for the CFS, and 28.2% (95% CI 22.9%-33.4%) for the MPI. This high frailty prevalence was paralleled by a high burden of geriatric syndromes, including functional and cognitive impairment, malnutrition, falls, and reduced physical performance.
2. Patients admitted to the HaH displayed a significantly worse overall health status, as indicated by a higher prevalence of severe or extremely severe disability (68.5% vs 38.1% in the AGW) and other geriatric syndromes, including frailty. More than 80% of HaH patients were frail according to the FFP, CFS, and FI. Frailty prevalence was significantly higher in the HaH compared to the AGW according to the CFS [82.7% (95% CI 73.9%-89.0%) vs 60.3% (95% CI 53.4%-66.8%)] as well as the MPI [40.7% (95% CI 30.6%-50.9%) vs 22.0% (95% CI 16.2%-27.8%)]. Severe frailty was also more frequent in the HaH according to the CFS (53.1% vs 21.6%) and the FI (69.4% vs 44.7%).
3. Agreement between the four frailty criteria was modest: only 29.8% of subjects classified as frail met all four definitions. Cohen's kappa statistics indicated a moderate level of agreement between the FI and FFP (κ 0.53, 95% CI 0.37-0.68) and between the FI and CFS (κ 0.47, 95% CI 0.37-0.58), whereas agreement across other pairings was only slight to fair. Notably, agreement was significantly higher in the HaH group, reaching substantial levels between the FI and CFS [κ 0.68 (95% CI 0.46-0.88)].
4. During a median length of stay that was significantly longer for HaH patients [16 days (IQR 11-23) vs 9 days (IQR 6-15) in the AGW], 26.9% of subjects experienced at least

one hospital-acquired complication (20.4% HaH vs 30.2% AGW), and 5.7% died (6.1% HaH vs 5.5% AGW). The most frequent complications were HAIs (15.2%) and delirium (10.8%). A return to the traditional in-hospital setting was required for 6.5% of patients admitted to the HaH. Notably, no HaH patient required post-acute institutionalization to a MLTCF, compared to 21.3% of AGW patients.

5. In adjusted analysis, frailty was associated with the composite outcome of in-hospital death or any hospital-acquired complication, whereas healthcare setting was not. However, after full adjustment for potential confounders (including, among others, severity of acute illness at admission, disability, multimorbidity, cognitive status, and length of stay), HaH admission was independently associated with lower odds of experiencing the composite outcome, irrespective of frailty definition [aOR 0.20 (95% CI 0.09-1.11) when frailty was defined by the CFS]. Moreover, in multivariable analyses adjusting for frailty according to the CFS, the HaH setting was also independently associated with lower odds of any hospital-acquired complication (aOR 0.20, 95% CI 0.09-0.44), delirium (aOR 0.21, 95% CI 0.07-0.67), and HAIs (aOR 0.32, 95% CI 0.12-0.88). Similar results emerged from analyses with frailty defined by the FI.
6. Among the 280 patients discharged alive, 30.0% experienced the primary composite outcome of all-cause mortality or institutionalization at 6-month follow up (95% CI: 24.9%-35.6%); 21.8% died and 15.0% were institutionalized, often immediately after discharge. After adjusting for potential confounders (including, among others, disability, multimorbidity, cognitive impairment, caregiver availability, and hospital-acquired complications), the HaH setting was associated with lower odds of experiencing the primary composite outcome, regardless of frailty definition [aOR 0.41 (95% CI 0.20-0.84) with CFS-defined frailty]. Frailty defined by the CFS and FI remained an independent predictor of the primary outcome in multivariable analysis [aOR 3.52 (95% CI 3.52-8.09) and aOR 5.75 (95% CI 1.25-26.48), respectively]. Discharge from HaH was not associated with overall survival, but was independently associated with reduced odds of being institutionalized as compared with being alive at home at 6 months from discharge [aOR 0.09 (95%CI 0.02-0.32) in CFS-adjusted analysis].
7. During the 6-month follow-up, 35% of subjects had at least one ED visit or unplanned readmission. The median time to first contact was 57 days (IQR 17-114). After accounting for the competing event of death through multinomial analysis, neither

frailty nor healthcare setting were associated with ED visits or unplanned readmissions. The only consistent predictor was the number of hospitalizations in the 3 months prior to study enrollment

8. Among the 219 patients alive at 6 months, 45.7% reported a clinically significant decline in functional status (95% CI 39.2%-52.3%), with a median decline of 20 points at the BI (IQR -39 to -10). Functional decline was not associated with healthcare setting, and associations with frailty were inconsistent. A higher handgrip strength at admission was consistently associated with a lower odds of functional decline, especially in males, although interaction analyses found no significant interaction between handgrip and sex.

To the best of the Candidate's knowledge, this is the first study to systematically investigate frailty prevalence using four different tools in the HaH setting, and to assess the combined prognostic impact of healthcare setting and frailty in acutely ill older adults.

The findings from MUFASA are highly relevant, since HaH has long been proposed as a safe and effective alternative to traditional "brick-and-mortar" hospital wards for treating frail older patients. This has been reflected by a recent systematic review stating that "*[AA-HaH] may be particularly beneficial for older people living with frailty […]"*,[216] and by institutional documents such as that of the National Health Service of England, which emphasizes that "*a HaH for frailty should be available as an option for clinicians to refer adults who have an acute exacerbation of a frailty-related condition*".[362] However, the supporting evidence is largely indirect: previous studies have often assumed that HaH patients were frail based on characteristics such as multimorbidity, functional dependence and cognitive impairment. Yet, direct data on frailty in the HaH setting remain limited and have been often reported as mean or median frailty scores rather than prevalence data.[214]

In a Randomized Controlled Trial (RCT) by Levine *et al*. involving 91 acute patients, among 43 patients allocated to HaH (median age: 80 years, 35% female) the median PRISMA-7 score was 4 (IQR 3), suggesting frailty at this screening tool (score ≥3).[276,363] Median CFS values in MUFASA HaH group (7, IQR 5-7) are consistent with those reported in four other HaH studies: one in a HaH rehabilitation service (mean age: 81.1, median CFS: 5),[312] two among patients admitted to a HaH for delirium (mean CFS: 6),[313,314] the last among 33 patients with severe COVID-19 managed at home (median CFS: 7).[311] Two congress abstracts reported multidimensional frailty data in HaH settings, one finding a mean MPI of 0.74 in 57 frail patients (mean age 87.4, 54% LTC residents),[315] another reporting a 70.5% frailty prevalence using the Groningen Frailty Indicator among 44 community-dwelling patients (mean age 80.9).[316] The lower median MPI in MUFASA (0.58, IQR 0.42-0.64) may reflect the exclusion

of LTC residents in the Turin HaH; also, the lower prevalence of multidimensional frailty (40.7%) could result from the high MPI cutoff used, based on previous literature.[80] If patients with moderate MPI risk (MPI category 2, classified as prefrail),[80] were also classified as frail, frailty prevalence among HaH patients would rise to 85.9%, closer to those measured by other tools.

Indeed, frailty prevalence in the present study was extremely high, and may be related to multiple factors, including advanced age of included patients, the inclusion of patients with cognitive impairment (frequently excluded from frailty studies), and the fact that patients referred to the Turin HaH usually present a higher burden of geriatric syndromes. Among AGW patients, prevalence of CFS-defined frailty (60.3%, 95% CI 53.4%-66.8%) was similar to the pooled prevalence of 64.2% (95% CI 57.3%-71.0%) among geriatric hospital inpatients reported in a recent systematic review of 18 studies.[91] Similarly, the prevalence of MPI-defined frailty in the overall sample (28.2%, 95% CI 22.9%-33.4%) was comparable to the 29.8% (95% CI 24.2%-35.4%) prevalence derived from a meta-analysis of 35 studies on 22,506 inpatients.[80] On the other hand, prevalences of FFP- and FI-defined frailty were significantly higher than those reported among AGW patients in a 2022 meta-analysis (86.6% vs 42.9% and 86.5% vs 52.6%).[91] This discrepancy may be due to several factors: for instance, the FFP, which heavily relies on physical performance tests, might have significantly overestimated frailty during the early acute phase of illness; also, it has been reported that FFP criteria modification can lead to significantly different frailty prevalence estimates,[52] therefore, the use of PASE scale instead of the more requiring MLTAQ to assess physical activity levels warrants cautious head-to-head comparisons. Lastly, the FI used in MUFASA was specifically designed based on 40 deficits from the CGA, with a significant focus on ADLs, likely contributing to the high FI-frailty rates observed in a population with a significant share of severe disability.

Our study confirmed that frailty prevalence increases with age, from 30-40% in subjects aged 70-75 years, to 80-85% at ages 95 years and older, and that older age is associated with increased odds of being frail (aOR for CFS 1.08, 95% CI 1.03-1.12), except when using the MPI. Interestingly, unlike what previously reported in community-based epidemiological studies, female sex was significantly associated with a lower prevalence of frailty only when using the CFS in our inpatient sample.[87]

Frail older subjects according to all four scales exhibited a significantly higher prevalence of multimorbidity, reduced physical performance and greater functional, nutritional, and cognitive deficits. These findings concur with previous systematic reviews,[98] and may partly reflect that some frailty tools directly include components of the CGA (e.g., physical

performance in the FFP, and MNA, ADL, IADL, and SPMSQ in the MPI and FI).[37,56,59,71] When focusing on variables not directly included in frailty tools, hearing impairment was independently associated with frailty by the CFS and MPI, as reported in previous systematic reviews,[106,364] while a history of falls was associated with frailty according to the FI. In contrast with some previous, inconclusive reports,[21,39,94,98] no significant correlation with education level was observed, possibly due to the limited sample size or the overall low median level of education (43.5% with primary school diploma or lower).

Results from MUFASA also confirm the observation of previous works about the poor agreement between different frailty instruments.[365–370] In a thorough study on 5,377 patients from the English Longitudinal Study of Aging (ELSA) comparing 35 different frailty instruments, 90% of measures showed a moderate or lower level of agreement ($\kappa < 0.60$), with the highest agreement among measures from the deficit accumulation model.[365] Similarly, in our study, the highest agreement was between the CFS and the FI in the HaH setting (κ 0.67), whereas in the overall sample the FFP-FI agreement was slightly higher (κ 0.53). Evidence on agreement between the FFP and the FI is inconclusive: in a study on 203 stroke patients, Tang *et al.* found an almost perfect FI-FFP agreement (κ 0.83),[366], whereas data from The Irish Longitudinal Study on Ageing (TILDA) showed only fair or moderate FI-FFP agreement (weighted κ 0.39 to 0.45)[367], and data from the National Health and Nutrition Examination Survey (NHANES) showed only slight agreement between the FI and modified 4-item FFP criteria (κ 0.17).[368] A low agreement between FI and FFP was also reported in a community-based study with a low overall prevalence of frailty (7% FFP and 8.3% FI), indicating higher agreement among subjects of older age and with higher comorbidity burden and reduced functional autonomy.[369] The higher frailty prevalence and the greater burden of comorbidities and geriatric syndromes may explain the observed higher agreement across all frailty scales in the HaH setting. In MUFASA, the MPI showed poor to slight agreement with all scales across healthcare settings; this could be due to the high frailty cutoff used, as previously illustrated, and, in the opinion of the Ph.D. Candidate, identifying severe frailty. However, even when considering prefrail and frail subjects at MPI (i.e., MPI categories 2 and 3) as frail, agreement with other definitions increased only slightly (data not shown).

These findings confirm once again that different frailty measures capture different, though overlapping, characteristics of the frail older adult, because different conceptual models focus on different aspects: physical function in the frailty phenotype model, overall health and functional status in the deficit accumulation model, and the bio-psycho-social context in the multidimensional model.[21,39,83] Therefore, different frailty tools may be useful for different

populations, in different settings, and for different purposes, urging caution against the indiscriminate interchangeable use of one frailty measure over another.

From this point of view, regardless of the frailty definition used, in MUFASA frail patients had significantly longer lengths of stay and higher rates of negative clinical outcomes, both during admission and at 6-month follow-up. Still, relevant differences in the association of different frailty definitions with outcomes at adjusted analysis should be noted. Many significant associations between frailty and outcomes observed in analyses adjusted only for healthcare setting became non-significant in fully adjusted models that accounted for other important prognostic factors in older adults, such as comorbidity, disability, and cognitive impairment. This may reflect the relatively higher prognostic impact of severe dementia and disability compared to the mere presence or absence of frailty (and not its severity), particularly in a population with poor overall health status.[4,371,372] Nonetheless, frailty defined by the FI and CFS retained an independent association with all-cause mortality at 6 months after discharge and with the primary composite outcome of all-cause mortality or institutionalization at 6 months (despite wide CIs). Frailty defined according to the FI was also predictive of increased odds of functional status deterioration at 6 months in survivors. The apparently higher prognostic ability of deficit accumulation model may stem from the inclusion of disability in such measures, as well as from limitations of other frailty definitions in our specific setting. First, in our population with reduced rates of low-risk patients, the MPI frailty cutoff may have yielded comparison groups that were actually composed both by frail subjects (moderately vs severely frail), thus flattening differences. Conversely, the prognostic ability of physical frailty models such as FFP in a sample with a high proportion of patients with severe mobility limitations may be weakened by the proportion of frail subjects approaching 90% of the overall sample, reducing discriminative capacity.

When taking into account the use of different frailty measures, their ability to predict clinical outcomes is crucial, but feasibility and reproducibility should also be taken into account.[73,373–375] Notably, the use of measures based on physical performance tests or on lengthy questionnaires is time-consuming, may be affected by the severity of acute illness in hospitalized patients, and can thus hinder complete frailty assessment.[73,373–375] In the overall study sample, for example, around 23% of subjects did not have a gait speed evaluation (despite not being bedridden), and 10% did not complete the MNA questionnaire; thus, frailty according to the FFP and MPI could not be assessed in almost 11% of subjects. Also, although the evaluation of frailty according to the FI is reproducible, based on CGA-derived data, and robust even in the presence of some missing values, it is time-consuming and its mathematical nature

can significantly hinder its practical application in clinical settings.[376] In this regard, the CFS has gained increasing attention thanks to its ability to rapidly (i.e., without formulas or mathematical computation) summarize CGA findings,[73,373–376] possibly incorporating the clinical judgment of the scorer, while retaining a good inter-rater reliability even when used by minimally trained personnel.[377]

The results of the MUFASA study, confirming both the feasibility and the predictive ability of CFS-based frailty assessment for a variety of adverse clinical outcomes even in severely frail older patients, support its standard adoption in HaH settings managing frail patients, as a means to better characterize their risk profiles while minimizing time requirements.

The high frequency of hospital-acquired complications and other adverse outcomes is consistent with the clinical profile of enrolled patients, and with prior literature on frail hospitalized older adults. When focusing on the impact of healthcare setting on clinical outcomes in acutely-ill older adults, findings from MUFASA confirm and expand on the evidence from previous systematic reviews and individual studies suggesting that HaH can be a safe and potentially protective alternative to traditional inpatient hospitalization, even for frail, complex patients.[214,216,233,234,236,237,246,254,256–258,261,263,264,276,277,286,287,313,378–383] Indeed, despite a higher prevalence of frailty and geriatric syndromes and a similar severity of acute illness and risk of clinical deterioration at admission (as evaluated by the NEWS2), patients admitted to HaH experienced comparable rates of in-hospital mortality, incidence of hospital-acquired complications (delirium, HAIs, pressure injuries, and falls), as well as 6-month all-cause mortality, ED visits or unplanned hospital readmissions, and functional deterioration. More significantly, when adjusting for frailty, age, sex and other relevant prognostic variables (including comorbidity burden, functional status, and cognitive impairment), multivariable analyses showed that admission to HaH was inversely associated with the incidence of several in-hospital and post-discharge outcomes, suggesting a potential attenuation of the negative impact of frailty in acutely ill older patients.

A prospective observational study on 2,095 patients admitted to an Australian HaH rehabilitation service (mean age: 81.1, median: CFS: 5) found that 23.9% experienced at least one negative event (including falls, infections, delirium, pressure injury, venous thromboembolism, and ED visit or transfer to hospital) during their HaH stay.[312] The most frequent negative events were transfer to hospital (14.1%) and falls (7.6%), whereas infections (4.4%), delirium (2.2%) and pressure injuries (1.1%) were less common.[312]

The rate of hospital-acquired complications in the MUFASA study was slightly lower

(20.4%), but incidence of HAIs, delirium, and pressure injuries was significantly higher (12.2%, 7.1%, and 6.1%, respectively), while transfer to in-hospital care and falls were lower (6.5% and 3.1%, respectively). These differences are plausibly explained by the different setting (acute vs rehabilitation): the Turin HaH provides acute-level care, whereas the Australian rehabilitation program is skilled in managing post-acute and chronic patients. Additionally, the higher rate of falls and lower rate of pressure injuries in the rehabilitation setting may be attributed to the significantly higher rate of ambulatory patients (98.9%).

The potential protective effect of the home environment during acute illness on hospital-acquired complications among older adults admitted to HaH has been explored in several studies.

In an RCT conducted in Australia involving 100 patients (mean age: 73), Caplan *et al.* reported a comparable rate of adverse events (including confusion, falls, urinary and fecal complications, phlebitis, and pressure injuries) between HaH and in-hospital groups (11.8% vs 16.3%), but a notably lower rate of confusion (0% vs 20.4%) and continence problems in the HaH group.[379] In another prospective quasi-experimental study conducted in the USA, the incidence of delirium was significantly lower in the HaH group (9% vs 24%, aOR 0.26, 95% CI 0.12-0.57), while nosocomial infections and falls did not differ significantly among groups.[264]

Levine *et al.* conducted an RCT in the USA on 91 acutely ill older adults (mean age: 80), with diagnoses at admission similar to those of MUFASA participants, and reported a lower rate of safety events in the HaH group (9% vs 15%), with no falls in the HaH group (vs 2%), and a compatible incidence of delirium (7% vs 8%).[276] The lower event rates and non-significant differences may be due to better baseline health status (median ADL: 6/6), and shorter length of stay (4.5 days HaH vs 3.8 days hospital), possibly preventing the emergence or observation of complications.[276]

Focusing on delirium, an RCT on HaH rehabilitation (mean age: 84) reported a significantly lower risk of delirium in the HaH group (0.6% vs 3.2%, OR 0.17, 95% CI 0.04-0.65) in the HaH setting.[286] Despite the higher delirium incidence registered in the present study, probably due to acute illness and the use of the 4-AT instead of the Confusion Assessment Method (CAM) to detect delirium, the aOR for delirium in HaH as compared to AGW was comparable (0.21, 95% CI 0.07-0.67 in CFS-adjusted analysis). Prior work by the Turin HaH team focused on delirium using CAM on 144 acutely ill patients (mean age: 86.1) also showed a reduced delirium incidence in the HaH setting (4.7% vs 16.6% AGW, adjusted relative risk - RR 0.26),[236] whereas delirium prevalence measured using the 4-AT scale among

391 Italian GIROT patients (mean age 88.4, 10.5% LTC residents) was 6.4%.[246]

Although the home environment may reduce pathogen exposure, few studies have specifically addressed HAIs in HaH realities. Besides the aforementioned non-significant differences reported by Leff and colleagues,[264] Patte *et al* evaluated the point prevalence of HAIs in 376 home care patients (40.7% aged ≥70, 25.2% ADL dependent), finding a 6.1% prevalence (95% CI 3.7%-8.5%), mainly due to urinary tract and skin infections. These were independently associated with urinary catheter use (OR 15.9, 95% CI 6.3-40.1), as similarly observed in our sample.

The impact of HaH on all-cause mortality and ED visits or rehospitalizations has been studied more extensively. In a UK RCT involving 150 patients with COPD exacerbation (mean age: 70), 3-month mortality and hospital readmission rates were similar between HaH and hospital groups (9% vs 8%; and 37% vs 34%, respectively).[380]

Another UK RCT in COPD patients with very short length of stay (1 day vs 3 days in-hospital) registered lower overall mortality but higher ED visit/rehospitalization at 3 months, likely reflecting early discharge and patient instability.[381] An RCT conducted in the Turin HaH on patients with exacerbation of COPD (mean age 80.1), with a high burden of geriatric syndromes, found comparable 6-month mortality between HaH and AGW (17% vs 23%), but significantly lower readmission rates (42% vs 87%) and longer time to readmission (mean 78 vs 37 days) in HaH.[234] The higher all-cause mortality observed in MUFASA can be related to both longer follow-up and the worse overall health status of frail older subjects admitted to geriatric units for a mix of conditions as compared to younger RCT participants with COPD alone. Lower readmission rates observed in the present study may relate to higher early readmission risk in COPD patients, and the high competing mortality risk in MUFASA.

In fact, when focusing on a similarly frail population as seen in the Italian GIROT cohort, 6-month hospital admission rate was 37.9%, similar to the 40.2% observed in the HaH sample of MUFASA, whereas all-cause mortality was significantly higher (53.8% vs 20.7%), likely due to the fact that 10.5% of patients in GIROT was institutionalized.[246]

Our study found no significant association between HaH admission and all-cause mortality or ED visits/unplanned hospital admission at 6 months, aligning with results from prior RCTs and meta-analyses.[216,256–258,261,382] In contrast, Levine *et al.* reported significantly lower ED visits and hospitalization rates at 30 days post-discharge in HaH-randomized patients (7% vs 23% and 7% vs 13%, respectively).[276]

One of the most significant findings of the present study was the independent association between HaH discharge and lower odds of institutionalization at 6 months, irrespective of age,

sex, frailty, disability, cognitive impairment, comorbidity, as well as caregiver availability and previous hospital-acquired complications. This reinforces evidence from systematic reviews reporting a reduced risk of institutionalization at 6 months in both AA-HaH (RR 0.53, 95% CI 0.41-0.69),[216] and ESD-HaH (RR 0.69, 95% CI 0.48-0.59).[257] Notably, most institutionalized patients in MUFASA were discharged directly from AGW to LTC, whereas none of the subsequently institutionalized HaH patients had been directly discharged to LTC, underscoring the potential vicious cycle of acute hospitalization, hospital-acquired complications, functional decline, and institutionalization.

When exploring the possible differential effect of HaH admission on patients with different frailty severity, a significant protective effect of HaH setting was observed in severely frail patients. Whether this reflects reduced statistical power in post-hoc sub-analyses or a true stratified benefit of HaH according to frailty severity remains unclear.

The MUFASA study presents some limitations that should be acknowledged to ensure adequate interpretation of its findings.

First, this was an observational study; therefore, although the association of HaH with reduced adverse outcomes remained significant after adjustment for confounding variables in multivariable analysis, causality cannot be inferred. Causal relationships could only be established through the implementation of an RCT comparing different models of acute care delivery. However, such an RCT may face substantial ethical and logistical challenges, given the growing body of evidence in favor of HaH programs, including studies that have been conducted in the Turin HaH.[233–239] Moreover, the Turin HaH has been in activity since the 1980s, and many patients, after their first HaH experience, prefer subsequent hospitalizations to be managed in the same setting, if clinically feasible.[265,266,291] Restricting access to HaH for research purposes would have been questionable from the perspectives of both physicians and patients/caregivers. From this point of view, the possibility of selection bias in patients admitted to the HaH cannot be entirely excluded. Propensity score-based analyses such as propensity score matching and inverse probability of treatment weighting were not conducted in the MUFASA study due to the high risk of model instability associated with the relatively small sample size and the substantial proportion of missing data in key covariates; these limitations could have paradoxically introduced greater bias and produced less accurate estimates, and matching could have reduced effective sample size, leading to a loss of statistical power and wider CIs.[384–386] Nonetheless, the exclusion of LTC residents and terminally-ill patients, along with similar admission diagnoses and severity of illness (as assessed by the NEWS2) across healthcare settings helps to mitigate this concern. Additionally, HaH patients showed a worse

overall health status, and multivariable analyses were adjusted for potential confounders, including geriatric syndromes and caregiver availability, among others.

Also, the study was conducted in a single center in Italy with a long-standing experience in geriatric HaH care, and its results may not be generalizable to other healthcare settings or regions. As previously reported, HaH programs vary significantly depending on national healthcare systems, organizational structures, types medical conditions treated and services delivered.[213,215,227,248–253] Pooling data from heterogeneous realities could introduce significant methodological challenges and prevent derivation of reliable results, undermining internal validity. Moreover, the only other Italian HaH experience (Regione Toscana GIROT) was still in its early development phases at the time of study initiation.[246,247]

Second, comparing HaH patients to those admitted to an AGW might limit generalizability of in-hospital outcomes, since patients admitted to internal medicine wards may have different risk profiles, especially concerning cognitive impairment and other geriatric syndromes.[387] Nevertheless, the protective association of HaH setting with hospital-acquired complications and post-discharge outcomes was independent from frailty, disability, cognitive impairment, and comorbidity, all of which were more prevalent in the HaH group compared to the AGW. Furthermore, the fact that both healthcare settings were geriatrician-led reduces the risk of detection bias due to different clinical sensibility and documentation for hospital-acquired complications such as delirium and pressure injuries.

Third, a wide array of self-reported and directly measured confounders were collected through a standardized CGA for all enrolled subjects; however, CGA length and administration at admission led to a non-negligible proportion of missing values because of the inability of acutely ill subjects to perform physical tests such as the gait speed or to respond to complex questionnaires such as the HADS and MNA. This prevented complete evaluation of frailty according to the FFP and MPI, effectively addressed through multiple imputation for missing values using a robust predictor set that allowed preservation of statistical power while minimizing bias. Additionally, as previously addressed, acute clinical status can have negatively impacted on physical performance, potentially leading to overestimation of FFP; however, comparable frailty prevalence estimates were observed when using the CFS and FI relying mainly or pre-admission data, supporting the robustness of these findings.

Also, it has been already highlighted that the FI used in MUFASA has not been previously validated; nonetheless, it was constructed according to standard recommendations for FI development,[59] and has demonstrated strong predictive validity for all-cause mortality at 6 months from discharge independent from age, sex, comorbidity burden, and functional or

cognitive impairment.

Lastly, patients in the AGW are continuously monitored by healthcare personnel, unlike those in the HaH setting, potentially introducing detection bias for certain hospital-acquired complications such as delirium and falls, that might have been underreported in the HaH setting. However, the Turin HaH program requires continuous caregiving during admission, ensures 12-hour telephone contact for bidirectional communication, and provides on average one daily visit by nurses and/or physicians, who routinely inquire about emerging issues. Thus, it is unlikely that clinically significant complications went undetected.

Despite these limitations, the MUFASA study has also some important strengths that merit consideration.

First, the study was conducted in the only long-standing Italian HaH program, therefore representing a unique study opportunity. The comparison with AGW patients within the same hospital division ensured consistency in organizational culture, clinical protocols, and staff expertise, minimizing potential biases related to institutional variability, and ensuring homogeneous data collection across settings with minimal differences in patient access to health services.

Second, the prospective design of the study allowed comprehensive data collection (including in-depth CGA data), that captured the multidimensional complexity of patients across healthcare settings and enabled adjustment for numerous clinical and social confounders. Moreover, it also allowed collection of events of interest during admission (e.g. administered medication, delirium and falls) that are inconsistently reported in administrative discharge documents and would have been difficult to retrieve in the absence of a fully integrated electronic health record.

Moreover, a mixed follow-up approach combining telephone interviews with data from public health archives and hospital databases ensured complete follow-up for the primary outcome and for other endpoints such as mortality and ED visits or rehospitalizations, virtually eliminating attrition bias, while also enabling the collection of nuanced outcomes like living conditions and functional status. Unfortunately, cause of death could not be explored due to its absence in administrative data.

Lastly, the complex interplay between frailty and healthcare setting was explored through the application of rigorous statistical methods, including multiple imputation for missing values and the construction of multivariable and multinomial logistic regression models, which adjusted for relevant confounders and accounted for the significant competing event of mortality.

The present study provides evidence with potential implications for optimizing care for geriatric patients. In fact, older subjects needing hospital-level care for acute disease or decompensated chronic conditions shares some common characteristics: very old age, moderate-to-severe frailty status, poor functional and cognitive performance, and frequent ED visits and/or hospitalizations, in many cases implying poor prognosis in the short term.[388] In these patients, conventional in-hospital care frequently implies unnecessary or disproportionate procedures and treatments,[389,390] high risk of hospital-acquired or iatrogenic complications (including, among others, delirium and HAIs), further mental and physical decline, resulting in increased risk of institutionalization.[176,178,179,179] The finding of MUFASA study provide a proof of evidence that in older patients with severe frailty moving acute care outside of the hospital walls in a HaH setting may represent a safer alternative to in-hospital stay, resulting in more comfortable care, with reduced rates of complications and institutionalization.

6. Conclusions

The MUFASA study demonstrated that frailty, like other geriatric syndromes, is highly prevalent among acutely ill older adults, regardless of the operational definition used, and that HaH admission within a comprehensive geriatric model, may attenuate the adverse clinical outcomes typically associated with traditional inpatient care in frail subjects. Despite a higher burden of frailty and other geriatric syndromes, HaH patients experienced similar or lower rates of hospital-acquired complications (particularly HAIs and delirium), as well as notably low rates of institutionalization at six months post-discharge. Furthermore, frailty defined according to the deficit accumulation model remained an independent predictor of long-term adverse outcomes in multivariable models, underscoring its prognostic value in this population.

The integration of HaH services into acute care pathways and home-based care for older adults with multiple chronic conditions represents a promising alternative to hospital-centric models of care, in terms of potential better health outcomes, increased patient satisfaction and probably reduced healthcare costs.

Future research on geriatric HaH models should prioritize large, multicenter prospective studies and pragmatic clinical trials that routinely collect and report data on frailty with robust yet feasible instruments, such as the CFS. Further exploration of the differential impact of HaH admission across different levels of frailty severity could help ongoing HaH services optimize patient selection and improve allocation of limited resources. Moreover, further evaluation of alternative healthcare models should encompass cost-effectiveness analyses, assessment of

patient-reported outcomes and caregiver experiences, and identification of barriers and facilitators to implementation across diverse healthcare contexts.

Collectively, these efforts will contribute to the development of patient-centered, efficient, and equitable care pathways for frail older adults, supporting the reduction of unnecessary hospitalizations and promoting aging in place.

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Supplementary information

S1 – Descriptive analyses and outcomes stratified by frailty

Supplementary Table S1 – Baseline data and outcomes at discharge of patients stratified by frailty status according to the Fried Frailty Phenotype (FFP). Results are presented on the 266 patients with complete data available for frailty status according to the FFP.

	Non-frail at FFP (n=29)	**Frail at FFP (n=237)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	80 (73.5-87)	87 (82-91)	**<0.001**
Female sex, n (%)	12 (41.4)	130 (54.9)	0.170
HaH setting, n (%)	11 (37.9)	85 (35.9)	0.827
- AA-HaH, n (%)	10/11 (90.9)	56/85 (65.9)	0.164
- ESD-HaH, n (%)	1/11 (9.1)	29/85 (34.1)	
Study title, n (%)*			0.075
- None	2 (6.9)	14 (6.0)	
- Primary school diploma	6 (20.7)	92 (39.5)	
- Middle school diploma	9 (31.1)	61 (26.2)	
- Professional school diploma	5 (17.2)	29 (12.4)	
- High school diploma	2 (6.9)	18 (7.7)	
- Bachelor's degree or higher	5 (17.2)	19 (8.2)	
Years of education, median (IQR)*	5 (8-13)	8 (5-10)	0.066
Living condition, n (%)			0.092
- Alone without help	3 (10.4)	16 (6.7)	
- Alone with help	7 (24.1)	40 (16.9)	
- Living with spouse/relative	19 (65.5)	140 (59.1)	
- Living with paid caregiver	0	41 (17.3)	
Presence of a caregiver, n (%)	7 (24.1)	136 (57.4)	**<0.001**
- Paid caregivers, n (%)	2/7 (28.6)	74/136 (54.4)	0.253
Continuous 24/7 caregiving, n (%)	4/7 (57.1)	90/136 (66.2)	0.623
Legal disability recognized, n (%)	8 (27.6)	119 (50.2)	0.066
- With care allowance, n (%)	0	54 (45.4)	
Geriatric Assessment to access geriatric care, n (%)	1 (3.4)	32 (13.5)	0.146
Presence of a legal guardian, n (%)	0 (0)	2 (0.8)	1.000
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	15 (51.7)	143 (60.3)	0.373
Site of admission, n (%)			0.249
- General Practitioner	0	17 (7.2)	
- ED	26 (89.7)	186 (78.5)	
- Other hospital ward	3 (10.3)	34 (14.3)	
Reason of admission, n (%)			0.198
- Respiratory tract infection	6 (20.7)	41 (17.3)	
- Decompensated heart failure	2 (6.9)	48 (20.2)	
- Fluid and electrolyte imbalance	3 (10.3)	23 (9.7)	
- Infection (other)	4 (13.8)	23 (9.7)	
- Urinary tract infection	3 (10.3)	19 (8.0)	
- Anemia/bleeding	0	18 (7.6)	
- Stroke/TIA	3 (10.3)	7 (3.0)	
- Uncontrolled BPSD	0	10 (4.2)	
- Other	8 (27.6)	48 (20.3)	
NEWS2 score, median (IQR)	1 (0-3)	2 (1-4)	**0.016**

NEWS2 score risk, n (%)			0.234
- Low risk	25 (86.2)	166 (70.0)	
- Low-medium risk	1 (3.4)	27 (11.4)	
- Medium risk	1 (3.4)	29 (12.2)	
- High risk	2 (6.9)	15 (6.4)	
Hemoglobin (g/dl), mean±SD*	12.2±2.2	11.6±2.2	0.147
ClCr (ml/min), median (IQR)*	49.3 (28.3-73.4)	36.2 (24.5-49.8)	**0.007**
BRASS, median (IQR)*	9 (6-11.5)	16 (11-21)	**<0.001**
BRASS risk, n (%)			**<0.001**
- Low	20 (69.0)	51 (21.8)	
- Medium	8 (27.6)	112 (47.9)	
- High	1 (3.4)	71 (30.3)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (3.5-6)	6 (4-7)	0.093
CIRS-SI, median (IQR)	2.08 (1.85-2.31)	2.15 (1.92-2.38)	0.088
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	17 (58.6)	150 (63.3)	0.623
Hypertension, n (%)	22 (75.9)	186 (78.5)	0.747
Vascular and hematopoietic, n(%)	12 (41.4)	122 (51.5)	0.305
Respiratory, n (%)	9 (31.0)	86 (36.3)	0.577
Eyes,ears,nose,throat,larynx, n(%)	5 (17.2)	99 (41.8)	**0.011**
Upper gastrointestinal, n (%)	9 (31.0)	56 (23.6)	0.381
Lower gastrointestinal, n (%)	5 (17.2)	45 (19.0)	0.820
Liver, pancreas and biliary, n (%)	2 (6.9)	14 (5.9)	0.689
Renal, n (%)*	13 (44.8)	135 (57.0)	0.214
Genitourinary, n (%)	11 (37.9)	75 (31.6)	0.495
Musculoskeletal and skin, n (%)	10 (34.5)	107 (45.1)	0.275
Neurologic, n (%)	9 (31.0)	83 (35.0)	0.670
Endocrine and breast, n (%)	20 (69.0)	157 (66.2)	0.769
Psychiatric (incl. dementia), n (%)	3 (10.3)	101 (42.6)	**<0.001**
Drug burden			
Drugs at admission, median (IQR)	8 (4.5-11)	7 (5-9)	0.408
Polytherapy, n (%)	22 (75.9)	185 (78.1)	0.788
Hyperpolytherapy, n (%)	8 (27.6)	43 (18.1)	0.223
Functional autonomy			
Barthel Index, median (IQR)	100 (77.5-100)	60 (25-85)	**<0.001**
Barthel Index disability level, n (%)			**<0.001**
- None	15 (51.7)	26 (11.0)	
- Mild	3 (10.3)	14 (5.9)	
- Moderate	8 (27.6)	65 (27.4)	
- Severe	3 (10.3)	78 (32.9)	
- Extremely severe	0	54 (22.8)	
Katz ADL (n. of functions lost), median (IQR)	0 (0-0.5)	3 (0-5)	**<0.001**
IADL (n. of functions kept), median (IQR)	6 (4.5-8)	2 (1-4)	**<0.001**
IADL autonomy category, n (%)			**<0.001**
- Autonomous	18 (62.1)	38 (16.0)	
- Partially autonomous	9 (31.0)	56 (23.6)	
- Non autonomous	2 (6.9)	143 (60.4)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	1 (0-2)	3 (1-5)	**<0.001**
Cognitive impairment SPMSQ, n(%)*			**0.004**
- None	23 (82.2)	109 (46.8)	
- Mild	2 (7.1)	59 (25.3)	
- Moderate	3 (10.7)	37 (15.9)	
- Severe	0	28 (12.0)	
Confused, wandering behavior	1 (3.4)	41 (17.3)	0.059

Mood status			
HADS anxiety, median (IQR)†	5 (3-8.5)	6 (4-10=	0.055
Anxiety levels at HADS, n (%)†			0.152
- Normal	21 (72.4)	120 (60.6)	
- Borderline	6 (20.7)	41 (20.7)	
- Abnormal	2 (6.9)	37 (18.7)	
HADS depression, median (IQR)†	6 (3-9)	9 (6-13)	**<0.001**
Depression levels at HADS, n (%)†			**<0.001**
- Normal	19 (65.5)	65 (32.8)	
- Borderline	7 (24.1)	49 (24.8)	
- Abnormal	3 (10.4)	84 (42.4)	
Physical performance and activity levels			
Best handgrip (kg), median (IQR)*	25 (19.7-32.0)	12.8 (8.1-18.0)	**<0.001**
Best handgrip (kg), males; median (IQR)*	28.2 (21.8-32.8)	18.0 (12.1-22.8)	**<0.001**
Best handgrip (kg), females; median (IQR)*	21.0 (16.9-30)	10.7 (7.3-13.6)	**<0.001**
Weakness at handgrip (FFP), n (%)	14 (48.3)	216 (92.7)	**<0.001**
Unable to perform gait speed, n (%)	1 (3.4)	86 (43.4)	**<0.001**
Gait speed (m/s), median (IQR)‡	0.80 (0.52-0.96)	0.51 (0.39-0.65)	**<0.001**
Low gait speed (FFP), n (%)‡	11 (39.3)	93 (83.0)	**<0.001**
Low gait speed or unable, n (%)**	12 (41.4)	179 (90.4)	**<0.001**
PASE score, median (IQR)	95.8 (63.1-134.6)	2.2 (0.0-39.4)	**<0.001**
Low activity levels at PASE, n (%)	3 (10.3)	204 (86.1)	**<0.001**
Physical exhaustion, n (%)	8 (27.6)	203 (85.7)	**<0.001**
Sensory impairment/balance			
Vision impairment, n (%)*			0.201
- None	8 (27.6)	52 (22.2)	
- Present, moderate	20 (69.0)	151 (64.5)	
- Present, severe	1 (3.4)	31 (13.3)	
Hearing impairment, n (%)*			0.118
- None	17 (58.6)	107 (45.7)	
- Present, moderate	11 (37.9)	98 (41.9)	
- Present, severe	1 (3.4)	29 (12.4)	
History of falls in the previous year, n (%)	11 (37.9)	91 (38.6)	0.948
Number of falls in the previous year, median (IQR)	2 (1-3)	1 (1-2)	0.645
Nutrition			
BMI (kg/m^2), median (IQR)*	24.3 (21.6-28.6)	23.4 (20.4-26.0)	
Mid-arm circumference (cm), median (IQR)*	26 (23.3-29.5)	25.0 (22.5-27.0)	**0.038**
Mid-calf circumference (cm), median (IQR)*	32.5 (30.5-36.0)	31.0 (28.0-34.0)	**0.009**
MNA score, median (IQR)††	23.5 (20.0-25.0)	17.0 (13.5-20.5)	**<0.001**
Malnutrition risk at MNA, n (%)††			**<0.001**
- Normal	12 (50.0)	21 (9.6)	
- At risk	9 (37.5)	93 (42.7)	
- Malnourished	3 (12.5)	104 (47.7)	
Weight loss in the past 12 mo, n (%)*	6 (20.7)	129 (54.7)	**<0.001**
Pressure ulcer development risk			
ESS, median (IQR)	18 (16.5-20)	15 (13-17)	**<0.001**
Risk of pressure injuries at ESS,			**<0.001**
- Low	26 (89.7)	105 (44.3)	
- Medium	3 (10.3)	114 (48.1)	
- High	0	18 (7.6)	
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	10 (5-15)	12 (7-20)	**0.046**
Any hospital-acquired complication, including in-hospital death, n (%)	2 (6.9)	74 (31.2)	**0.006**
Death during admission, n (%)	0 (0.0)	15 (6.3)	0.333
Any hospital-acquired complication, n (%)	2 (6.9)	66 (27.8)	**0.015**
Delirium during admission, n (%)	1 (3.4)	27 (11.4)	0.320
Requiring use of medication	1/1 (100)	22/27 (81.5)	1.000

Fall during admission, n (%)	2 (6.9)	6 (2.5)	0.213
Pressure injury development during admission, n (%)	0 (0.0)	19 (8.0)	0.230
Healthcare-associated infection during admission, n (%)	1 (3.4)	34 (14.3)	0.178
Setting of discharge, n (%) - At home - MLTCF - ED	 27 (93.1) 0 2 (6.9)	 184 (82.9) 34 (15.3) 4 (1.8)	**0.023**

*Missing values <5%
†Missing values for 39 (14.7%) subjects
‡Missing values (unavailable or untestable) for 126 (47.4%) subjects
**Missing values for 39 (14.7%) subjects
††Missing values for 24 (9.0%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BMI = Body Mass Index, BPSD = behavioral and psychological symptoms of dementia, BRASS = Blaylock Risk Assessment Screening Score, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, ESS = Exton-Smith Scale, FFP = Fried Frailty Phenotype, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MNA = Mini Nutritional Assessment, mo = months, MLTCF = medium/long-term care facility, mo = months, NEWS2= National Early Warning Score 2, PASE = Physical Activity Scale for the Elderly, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack.

Supplementary Table S2 – Baseline data and outcomes at discharge of patients stratified by frailty status according to the Clinical Frailty Scale (CFS).

	Non-frail at CFS (n=96)	Frail at CFS (n=201)	P
Sociodemographic variables			
Age (years), median (IQR)	84 (77.3-88)	87 (82-91)	**<0.001**
Female sex, n (%)	40 (41.7)	115 (57.2)	**0.012**
HaH setting, n (%)	17 (17.7)	81 (40.3)	**<0.001**
- AA-HaH, n (%)	17/17 (100)	51/81 (63.0)	**0.003**
- ESD-HaH, n (%)	0/17 (0)	30/81 (37.0)	
Study title, n (%)*			0.162
- None	6 (6.3)	13 (6.6)	
- Primary school diploma	30 (31.6)	78 (39.6)	
- Middle school diploma	23 (24.2)	50 (25.4)	
- Professional school diploma	18 (19)	22 (11.2)	
- High school diploma	8 (8.4)	18 (9.1)	
- Bachelor's degree or higher	10 (10.5)	16 (8.1)	
Years of education, median (IQR)*	8 (5-13)	8 (5-11)	0.271
Living condition, n (%)			**<0.001**
- Alone without help	17 (17.7)	4 (2.0)	
- Alone with help	15 (15.6)	38 (18.9)	
- Living with spouse/relative	63 (65.6)	118 (58.7)	
- Living with paid caregiver	1 (1.1)	41 (20.4)	
Presence of a caregiver, n (%)	24 (25.0)	131 (65.2)	**<0.001**
- Paid caregivers, n (%)	8/24 (33.3)	73/131 (55.7)	**0.049**
Continuous 24/7 caregiving, n (%)	14/24 (58.3)	88/131 (67.2)	0.401
Legal disability recognized, n (%)	23 (24.0)	114 (56.7)	**<0.001**
- With care allowance, n (%)	5/23 (21.7)	51/114 (44.7)	
Geriatric Assessment to access geriatric care, n (%)	0	35 (17.4)	**<0.001**
Presence of a legal guardian, n (%)	0	2 (1.0)	1.000
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	49 (51.0)	123 (61.2)	0.097
Site of admission, n (%)			**<0.001**
- General Practitioner	1 (1.0)	16 (8.0)	
- ED	90 (93.8)	153 (76.1)	
- Other hospital ward	5 (5.2)	32 (15.9)	
Reason of admission, n (%)			**0.024**
- Respiratory tract infection	17 (17.7)	38 (18.9)	
- Decompensated heart failure	22 (22.9)	33 (16.4)	
- Fluid and electrolyte imbalance	8 (8.3)	21 (10.4)	
- Infection (other)	8 (8.3)	20 (10.0)	
- Urinary tract infection	6 (6.3)	18 (9.0)	
- Anemia/bleeding	6 (6.3)	13 (6.5)	
- Stroke/TIA	11 (11.4)	5 (2.4)	
- Uncontrolled BPSD	0	11 (5.5)	
- Other	18 (18.8)	42 (20.9)	
NEWS2 score, median (IQR)	2 (1-4)	2 (1-4)	0.541
NEWS2 score risk, n (%)			0.398
- Low risk	73 (76.0)	141 (70.1)	
- Low-medium risk	4 (4.2)	27 (13.4)	
- Medium risk	16 (16.7)	19 (9.5)	
- High risk	3 (3.1)	14 (7.0)	
Hemoglobin (g/dl), mean±SD*	11.9±2.3	11.6±2.1	0.150
ClCr (ml/min), median (IQR)*	44.6 (28.7-63.6)	36.1 (24.7-49.5)	**0.008**
BRASS, median (IQR)*	9 (7-11)	17.5 (13.0-22.0)	**<0.001**

BRASS risk, n (%) - Low - Medium - High	 65 (68.4) 30 (31.6) 0	 19 (9.6) 107 (54.0) 72 (36.4)	**<0.001**
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	6 (4-7)	**0.001**
CIRS-SI, median (IQR)	2.08 (1.79-2.23)	2.23 (2.00-2.38)	**<0.001**
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	59 (61.5)	127 (63.2)	0.774
Hypertension, n (%)	83 (86.5)	152 (75.6)	**0.032**
Vascular and hematopoietic, n(%)	47 (49.0)	97 (48.3)	0.910
Respiratory, n (%)	32 (33.3)	72 (35.8)	0.674
Eyes,ears,nose,throat,larynx, n(%)	26 (27.1)	87 (43.3)	**0.007**
Upper gastrointestinal, n (%)	21 (21.9)	49 (24.4)	0.635
Lower gastrointestinal, n (%)	17 (17.7)	35 (17.4)	0.950
Liver, pancreas and biliary, n (%)	4 (4.2)	12 (6.0)	0.520
Renal, n (%)	44 (45.8)	115 (57.2)	0.066
Genitourinary, n (%)	29 (30.2)	63 (31.3)	0.843
Musculoskeletal and skin, n (%)	29 (30.2)	96 (47.8)	**0.004**
Neurologic, n (%)	25 (26.0)	78 (38.8)	**0.031**
Endocrine and breast, n (%)	55 (57.3)	140 (69.7)	**0.036**
Psychiatric (incl. dementia), n (%)	13 (13.5)	104 (51.7)	**<0.001**
Drug burden			
Drugs at admission, median (IQR)	6 (4-9)	7 (5-10)	0.075
Polytherapy, n (%)	70 (72.9)	160 (79.6)	0.197
Hyperpolytherapy, n (%)	14 (14.6)	42 (20.9)	0.193
Functional autonomy			
Barthel Index, median (IQR)	95 (85-100)	50 (20-75)	**<0.001**
Barthel Index disability level, n (%) - None - Mild - Moderate - Severe - Extremely severe	 40 (41.7) 15 (15.6) 36 (37.5) 5 (5.2) 0	 3 (1.5) 8 (4.0) 52 (25.9) 84 (41.8) 54 (26.8)	**<0.001**
Katz ADL (n. of functions lost), median (IQR)	0 (0-0)	4 (1-5)	**<0.001**
IADL (n. of functions kept), median (IQR)	6 (4-8)	1 (0-3)	**<0.001**
IADL autonomy category, n (%) - Autonomous - Partially autonomous - Non autonomous	 58 (60.4) 29 (30.2) 9 (9.4)	 9 (4.5) 46 (22.9) 146 (72.6)	**<0.001**
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	1 (0-3)	3 (2-6)	**<0.001**
Cognitive impairment SPMSQ, n(%)* - None - Mild - Moderate - Severe	 69 (74.2) 20 (21.5) 4 (4.3) 0	 79 (40.1) 48 (24.4) 40 (20.3) 30 (15.2)	**<0.001**
Confused, wandering behavior	1 (1.0)	43 (21.4)	**<0.001**
Mood status			
HADS anxiety, median (IQR)†	5 (3-7)	7 (5-10)	**<0.001**
Anxiety levels at HADS, n (%)† - Normal - Borderline - Abnormal	 73 (79.4) 13 (14.1) 6 (6.5)	 88 (54.6) 36 (22.4) 37 (23.0)	**<0.001**
HADS depression, median (IQR)†	5 (3-8)	10 (7-13)	**<0.001**

Depression levels at HADS, n (%)†			**<0.001**
- Normal	62 (67.4)	42 (26.1)	
- Borderline	18 (19.6)	40 (24.8)	
- Abnormal	12 (13.0)	79 (49.1)	
Physical performance and activity levels			
Best handgrip (kg), median (IQR)*	21.0 (14.7-26.2)	12 (7.5-17.5)	**<0.001**
Best handgrip (kg), males; median (IQR)*	23.2 (19.8-30.0)	17.1 (11.6-21.1)	**<0.001**
Best handgrip (kg), females; median (IQR)*	14.4 (11.0-20.2)	5.7 (10.0-13.2)	**<0.001**
Weakness at handgrip (FFP), n (%)	69 (74.2)	180 (92.8)	**<0.001**
Unable to perform gait speed, n (%)	2 (2.8)	86 (54.4)	**<0.001**
Gait speed (m/s), median (IQR)‡	0.6 (0.47-0.82)	0.47 (0.35-0.67)	**0.003**
Low gait speed (FFP), n (%)	48 (68.6)	57 (79.2)	0.150
Low gait speed or unable, n (%)**	50 (69.4)	143 (90.5)	**<0.001**
PASE score, median (IQR)	75.0 (39.4-103.6)	0 (0.0-27.2)	**<0.001**
Low activity levels at PASE, n (%)	37 (39.8)	183 (91.0)	**<0.001**
Physical exhaustion, n (%)	52 (55.2)	168 (83.6)	**<0.001**
Sensory impairment/balance			
Vision impairment, n (%)*			0.137
- None	24 (25.3)	45 (22.7)	
- Present, moderate	66 (69.5)	125 (63.1)	
- Present, severe	5 (5.2)	28 (14.2)	
Hearing impairment, n (%)*			**0.003**
- None	60 (63.2)	86 (43.5)	
- Present, moderate	27 (28.4)	87 (43.9)	
- Present, severe	8 (8.4)	25 (12.6)	
History of falls in the previous year, n (%)	29 (30.2)	83 (41.5)	0.948
Number of falls in the previous year, median (IQR)	1 (1.0-2.5)	1 (1-2)	0.645
Nutrition			
BMI (kg/m^2), median (IQR)*	24.5 (22-27.9)	23.3 (20.2-26.1)	**0.007**
Mid-arm circumference (cm), median (IQR)*	26 (24-28)	25 (22-27)	**0.006**
Mid-calf circumference (cm), median (IQR)*	32.3 (30.6-35.5)	31.0 (28.0-33.5)	**<0.001**
MNA score, median (IQR)††	22.5 (20.5-24.5)	16 (12.8-19.0)	**<0.001**
Malnutrition risk at MNA, n (%)††			**<0.001**
- Normal	36 (39.6)	6 (3.4)	
- At risk	50 (54.9)	69 (39.0)	
- Malnourished	5 (5.5)	102 (57.6)	
Weight loss in the past 12 mo, n (%)*	43 (44.8)	97 (48.7)	0.524
Pressure ulcer development risk			
ESS, median (IQR)	18 (17-20)	14 (12-16)	**<0.001**
Risk of pressure injuries at ESS,			**<0.001**
- Low	91 (94.8)	63 (31.3)	
- Medium	5 (5.2)	120 (59.7)	
- High	0	18 (9.0)	
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	9 (6-15)	13 (8-21)	**<0.001**
Any hospital-acquired complication, including in-hospital death, n (%)	20 (20.8)	68 (33.8)	**0.022**
Death during admission, n (%)	6 (6.3)	11 (5.5)	0.787
Any hospital-acquired complication, n (%)	19 (19.8)	61 (30.3)	0.055
Delirium during admission, n (%)	6 (6.3)	26 (12.9)	0.082
- Requiring use of medication	6/6 (100.0)	21/26 (80.8)	
Fall during admission, n (%)	2 (2.1)	7 (3.5)	0.767
Pressure injury development during admission, n (%)	2 (2.1)	18 (9.0)	**0.027**
Healthcare-associated infection during admission, n (%)	12 (12.5)	33 (16.4)	0.378
Setting of discharge, n (%)			0.072
- At home	80 (88.9)	154 (81.1)	
- MLTCF	7 (7.8)	33 (17.3)	
- ED	3 (3.3)	3 (1.6)	

*Missing values <5%
†Missing values for 44 (14.8%) subjects
‡Missing values (unavailable or untestable) for 155 (52.2%) subjects
**Missing values for 67 (22.6%) subjects
††Missing values for 29 (9.8%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BMI = Body Mass Index, BPSD = behavioral and psychological symptoms of dementia, BRASS = Blaylock Risk Assessment Screening Score, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, ESS = Exton-Smith Scale, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, NEWS2= National Early Warning Score 2, PASE = Physical Activity Scale for the Elderly, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack.

Supplementary Table S3 – Baseline data and outcomes at discharge of patients stratified by frailty status according to the Frailty Index (FI).

	Non-frail at FI (n=39)	Frail at FI (n=258)	P value
Sociodemographic variables			
Age (years), median (IQR)	82 (74-89)	86.5 (82-91)	**<0.001**
Female sex, n (%)	16 (41.0)	139 (53.9)	0.134
HaH setting, n (%)	11 (28.2)	87 (33.7)	0.495
- AA-HaH, n (%)	11/11 (100)	57/87 (65.5)	**0.017**
- ESD-HaH, n (%)	0	30/87 (34.5)	
Study title, n (%)*			**0.002**
- None	1 (2.6)	18 (7.1)	
- Primary school diploma	6 (15.4)	102 (40.3)	
- Middle school diploma	13 (33.3)	60 (23.7)	
- Professional school diploma	10 (25.6)	30 (11.9)	
- High school diploma	4 (10.3)	22 (8.7)	
- Bachelor's degree or higher	5 (12.8)	21 (8.3)	
Years of education, median (IQR)*	8 (8-13)	8 (5-11)	**0.004**
Living condition, n (%)			**<0.001**
- Alone without help	8 (20.5)	13 (5.0)	
- Alone with help	8 (20.5)	45 (17.4)	
- Living with spouse/relative	23 (59.0)	158 (61.2)	
- Living with paid caregiver	0	42 (16.3)	
Presence of a caregiver, n (%)	6 (15.4)	149 (57.8)	**<0.001**
- Paid caregivers, n (%)	2/6 (33.3)	79/149 (53.0)	0.426
Continuous 24/7 caregiving, n (%)	5/6 (83.3)	97/149 (65.1)	0.665
Legal disability recognized, n (%)	4 (10.2)	133 (51.5)	**<0.001**
- With care allowance, n (%)	1/4 (25.0)	55/133 (41.4)	
Geriatric Assessment to access geriatric care, n (%)	0	35 (13.6)	**0.007**
Presence of a legal guardian, n (%)	0	2 (0.8)	1.000
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	19 (48.7)	153 (59.3)	0.212
Site of admission, n (%)			**0.024**
- General Practitioner	0	17 (6.6)	
- Emergency Department	38 (97.4)	205 (79.4)	
- Other hospital ward	1 (2.6)	36 (14.0)	
Reason of admission, n (%)			0.397
- Respiratory tract infection	6 (15.4)	49 (19.0)	
- Decompensated heart failure	6 (15.4)	49 (19.0)	
- Fluid and electrolyte imbalance	6 (15.4)	23 (8.9)	
- Infection (other)	5 (12.8)	23 (8.9)	
- Urinary tract infection	3 (7.7)	21 (8.1)	
- Anemia/bleeding	4 (10.3)	15 (5.8)	
- Stroke/TIA	4 (10.3)	12 (4.7)	
- Uncontrolled BPSD	0	11 (4.3)	
- Other	5 (12.8)	55 (21.3)	
NEWS2 score, median (IQR)	1 (0-3)	2 (1-4)	0.002
NEWS2 score risk, n (%)			**0.044**
- Low risk	35 (89.7)	179 (69.4)	**0.005**
- Low-medium risk	3 (7.7)	28 (10.8)	
- Medium risk	1 (2.6)	34 (13.2)	
- High risk	0	17 (6.6)	
Hemoglobin (g/dl), mean±SD*	11.7±2.6	11.7±2.1	0.774
ClCr (ml/min), median (IQR)*	53.8 (25.4-67.5)	37.2 (25.4-54.9)	**0.011**
BRASS, median (IQR)*	7 (6-10)	15 (11-20)	**<0.001**

BRASS risk, n (%) - Low - Medium - High	 31 (79.5) 8 (20.5) 0	 53 (20.9) 129 (50.8) 72 (28.3)	**<0.001**
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	4 (3-6)	5 (4-7)	**<0.001**
CIRS-SI, median (IQR)	1.92 (1.77-2.15)	2.15 (1.92-2.38)	**<0.001**
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	22 (56.4)	164 (63.6)	0.389
Hypertension, n (%)	31 (79.5)	204 (79.1)	0.952
Vascular and hematopoietic, n(%)	22 (56.4)	122 (47.3)	0.288
Respiratory, n (%)	6 (15.4)	98 (38.0)	**0.006**
Eyes,ears,nose,throat,larynx, n(%)	10 (25.6)	103 (39.9)	0.087
Upper gastrointestinal, n (%)	6 (15.4)	64 (24.8)	0.196
Lower gastrointestinal, n (%)	5 (12.8)	47 (18.2)	0.409
Liver, pancreas and biliary, n (%)	1 (2.6)	15 (5.8)	0.704
Renal, n (%)	16 (41.0)	143 (55.4)	0.093
Genitourinary, n (%)	12 (30.8)	80 (31.0)	0.976
Musculoskeletal and skin, n (%)	9 (23.1)	116 (45.0)	**0.010**
Neurologic, n (%)	5 (12.8)	98 (38.0)	**0.002**
Endocrine and breast, n (%)	28 (71.8)	167 (64.7)	0.386
Psychiatric (incl. dementia), n (%)	3 (7.7)	114 (44.2)	**<0.001**
Drug burden			
Drugs at admission, median (IQR)	6 (4-10)	7 (5-10)	0.172
Polytherapy, n (%)	26 (66.7)	204 (79.1)	0.084
Hyperpolytherapy, n (%)	7 (17.9)	49 (19.0)	0.877
Functional autonomy			
Barthel Index, median (IQR)	100 (95-100)	60 (30-80)	**<0.001**
Barthel Index disability level, n (%) - None - Mild - Moderate - Severe - Extremely severe	 28 (71.8) 8 (20.5) 3 (7.7) 0 0	 15 (5.8) 15 (5.8) 85 (33) 89 (34.5) 54 (20.9)	**<0.001**
Katz ADL (n. of functions lost), median (IQR)	0 (0-0)	2 (0-4.3)	**<0.001**
IADL (n. of functions kept), median (IQR)	8 (7-8)	2 (1-4)	**<0.001**
IADL autonomy category, n (%) - Autonomous - Partially autonomous - Non autonomous	 33 (84.6) 6 (15.4) 0	 34 (13.2) 69 (26.7) 155 (60.1)	**<0.001**
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	1 (0-2)	3 (1-5)	**<0.001**
Cognitive impairment SPMSQ, n(%)* - None - Mild - Moderate - Severe	 32 (84.2) 6 (15.8) 0 0	 116 (46.0) 62 (24.6) 44 (17.5) 30 (11.9)	**<0.001**
Confused, wandering behavior	0	44 (17.1)	**0.005**
Mood status			
HADS anxiety, median (IQR)†	4 (3-6)	7 (4-10)	**<0.001**
Anxiety levels at HADS, n (%)† - Normal - Borderline - Abnormal	 32 (84.2) 5 (13.2) 1 (2.6)	 129 (60.0) 44 (20.5) 42 (19.5)	**0.010**
HADS depression, median (IQR)†	5 (2.8-7.3)	9 (6-13)	**<0.001**

Depression levels at HADS, n (%)†			**<0.001**
- Normal	29 (76.3)	75 (34.9)	
- Borderline	8 (21.1)	50 (23.2)	
- Abnormal	1 (2.6)	90 (41.9)	
Physical performance and activity levels			
Best handgrip (kg), median (IQR)*	24.1 (19.9-32.1)	13.1 (8.7-18.8)	**<0.001**
Best handgrip (kg), males; median (IQR)*	26.6 (22.6-33.2)	18.4 (13.1-22.7)	**<0.001**
Best handgrip (kg), females; median (IQR)*	14.6 (11.9-28.6)	11.0 (7.4-14.0)	**<0.001**
Weakness at handgrip (FFP), n (%)	22 (57.9)	227 (91.2)	**<0.001**
Unable to perform gait speed, n (%)	0	88 (44.0)	**<0.001**
Gait speed (m/s), median (IQR)‡	0.69 (0.54-0.89)	0.51 (0.37-0.68)	**0.001**
Low gait speed (FFP), n (%)‡	17 (56.7)	88 (78.6)	**0.015**
Low gait speed or unable, n (%)**	17 (56.7)	176 (88.0)	**<0.001**
PASE score, median (IQR)	93.7 (58.6-134.1)	6.8 (0.0-46.9)	**<0.001**
Low activity levels at PASE, n (%)	9 (23.7)	211 (82.4)	**<0.001**
Physical exhaustion, n (%)	15 (38.5)	206 (79.8)	**<0.001**
Sensory impairment/balance			
Vision impairment, n (%)*			0.208
- None	12 (30.8)	57 (22.4)	
- Present, moderate	21 (61.5)	167 (65.8)	
- Present, severe	3 (7.7)	30 (11.8)	
Hearing impairment, n (%)*			**0.015**
- None	27 (69.2)	119 (46.9)	
- Present, moderate	9 (23.1)	105 (41.3)	
- Present, severe	3 (7.7)	30 (11.8)	
History of falls in the previous year, n (%)	7 (19.7)	105 (40.9)	**0.006**
Number of falls in the previous year, median (IQR)	1 (1-2)	1 (1-2)	0.632
Nutrition			
BMI (kg/m^2), median (IQR)*	24.6 (21.9-29.3)	23.4 (20.7-26.1)	**0.034**
Mid-arm circumference (cm), median (IQR)*	25.3 (23.9-29.0)	25 (22.5-27)	0.085
Mid-calf circumference (cm), median (IQR)*	33 (31-36)	31 (28-34)	**<0.001**
MNA score, median (IQR)††	24.5 (22.0-25.8)	17.5 (14.0-20.5)	**<0.001**
Malnutrition risk at MNA, n (%)††			**<0.001**
- Normal	26 (70.3)	16 (6.9)	
- At risk	9 (24.3)	110 (47.6)	
- Malnourished	2 (5.4)	105 (45.5)	
Weight loss in the past 12 mo, n (%)*	15 (38.5)	125 (48.8)	0.227
Pressure ulcer development risk			
ESS, median (IQR)	19 (18-20)	15 (13-17)	**<0.001**
Risk of pressure injuries at ESS,			**<0.001**
- Low	38 (97.4)	116 (45.0)	
- Medium	1 (2.6)	124 (48.1)	
- High	0	18 (7.0)	
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	9 (5-15)	12 (7-20)	**0.013**
Any hospital-acquired complication, including in-hospital death, n (%)	6 (15.0)	82 (31.9)	**0.029**
Death during admission, n (%)	2 (5.0)	15 (5.8)	1.000
Any hospital-acquired complication, n (%)	5 (12.5)	75 (29.2)	**0.027**
Delirium during admission, n (%)	1 (2.5)	31 (12.1)	0.123
Requiring use of medication	1 (100.0)	26/31 (83.9)	1.000
Fall during admission, n (%)	0	9 (3.5)	0.480
Pressure injury development during admission, n (%)	0	20 (7.8)	0.137
Healthcare-associated infection during admission, n (%)	4 (10.0)	41 (16.0)	0.329
Setting of discharge, n (%)			**0.038**
- At home	35 (92.1)	199 (82.2)	
- MLTCF	1 (2.6)	39 (16.1)	
- ED	2 (5.3)	4 (1.7)	

*Missing values <5%
†Missing values for 44 (14.8%) subjects
‡Missing values (unavailable or untestable) for 155 (52.2%) subjects
**Missing values for 67 (22.6%) subjects
††Missing values for 29 (9.8%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BMI = Body Mass Index, BPSD = behavioral and psychological symptoms of dementia, BRASS = Blaylock Risk Assessment Screening Score, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, ESS = Exton-Smith Scale, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MLTFC = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, NEWS2= National Early Warning Score 2, PASE = Physical Activity Scale for the Elderly, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack.

Supplementary Table S4 – Baseline data and outcomes at discharge of patients stratified by frailty status according to the Multidimensional Prognostic Index (MPI). Results are presented on the 266 patients with complete data available for frailty status according to the MPI.

	Non-frail at MPI (MPI 1-2) (n=194)	**Frail at MPI (MPI 3) (n=258)**	**P value**
Sociodemographic variables			
Age (years), median (IQR)	86 (80-90)	87 (82-91)	0.184
Female sex, n (%)	96 (49.5)	44 (62.0)	0.071
HaH setting, n (%)	48 (24.7)	30 (42.3)	**0.006**
- AA-HaH, n (%)	36/48 (75.0)	18/30 (60.0)	0.163
- ESD-HaH, n (%)	12/48 (25.0)	12/30 (40.0)	
Study title, n (%)*			0.353
- None	12 (6.2)	6 (8.4)	
- Primary school diploma	71 (36.6)	27 (38.0)	
- Middle school diploma	48 (24.7)	20 (28.2)	
- Professional school diploma	27 (13.9)	8 (11.3)	
- High school diploma	18 (9.3)	4 (5.6)	
- Bachelor's degree or higher	18 (9.3)	6 (8.5)	
Years of education, median (IQR)*	8 (5-11)	8 (5-10)	0.664
Living condition, n (%)			**<0.001**
- Alone without help	18 (9.3)	2 (2.8)	
- Alone with help	29 (14.9)	15 (21.1)	
- Living with spouse/relative	30 (67.0)	34 (47.9)	
- Living with paid caregiver	17 (8.8)	20 (28.2)	
Presence of a caregiver, n (%)	80 (41.2)	53 (74.6)	**<0.001**
- Paid caregivers, n (%)	38/80 (47.5)	34/53 (64.2)	0.059
Continuous 24/7 caregiving, n (%)	50/80 (62.5)	34/53 (64.2)	0.847
Legal disability recognized, n (%)	72 (37.1)	52 (73.2)	**<0.001**
- With care allowance, n (%)	23 (31.9)	29 (55.8)	
Geriatric Assessment to access geriatric care, n (%)	11 (5.7)	21 (29.6)	**<0.001**
Presence of a legal guardian, n (%)	0	1 (1.4)	0.268
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	112 (57.7)	47 (66.2)	0.213
Site of admission, n (%)			**0.021**
- General Practitioner	7 (3.6)	7 (9.9)	
- ED	169 (87.1)	52 (73.2)	
- Other hospital ward	18 (9.3)	12 (16.9)	
Reason of admission, n (%)			0.113
- Respiratory tract infection	35 (18.0)	10 (14.1)	
- Decompensated heart failure	40 (20.6)	11 (15.5)	
- Fluid and electrolyte imbalance	17 (8.8)	8 (11.3)	
- Infection (other)	19 (9.8)	6 (8.5)	
- Urinary tract infection	11 (5.7)	10 (14.1)	
- Anemia/bleeding	14 (7.2)	5 (7.0)	
- Stroke/TIA	13 (6.7)	2 (2.8)	
- Uncontrolled BPSD	3 (1.6)	5 (7.0)	
- Other	42 (21.6)	14 (19.7)	
NEWS2 score, median (IQR)	2 (1-3)	3 (1-4)	0.024
NEWS2 score risk, n (%)			**<0.001**
- Low risk	156 (80.4)	44 (62.0)	
- Low-medium risk	9 (4.6)	15 (21.1)	
- Medium risk	24 (12.4)	6 (8.5)	
- High risk	5 (2.6)	6 (8.5)	
Hemoglobin (g/dl), mean±SD*	11.7±2.2	11.6±2.2	0.693
ClCr (ml/min), median (IQR)*	39.7 (25.8-53.9)	34.8 (21.3-55.8)	

BRASS, median (IQR)*	12 (9-15)	21 (18-24)	**<0.001**
BRASS risk, n (%)			**<0.001**
- Low	79 (40.9)	0	
- Medium	102 (52.9)	22 (31.4)	
- High	12 (6.2)	48 (68.6)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	6 (5-7)	**0.008**
CIRS-SI, median (IQR)	2.08 (1.92-2.25)	2.23 (2.00-2.46)	**0.006**
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	120 (61.9)	46 (64.8)	0.662
Hypertension, n (%)	157 (80.9)	53 (74.6)	0.264
Vascular and hematopoietic, n(%)	100 (51.5)	31 (43.7)	0.256
Respiratory, n (%)	66 (34.0)	22 (31.0)	0.642
Eyes,ears,nose,throat,larynx, n(%)	63 (32.5)	36 (50.7)	**0.007**
Upper gastrointestinal, n (%)	47 (24.2)	15 (21.1)	0.598
Lower gastrointestinal, n (%)	33 (17.0)	12 (16.9)	0.983
Liver, pancreas and biliary, n (%)	14 (7.2)	2 (2.8)	0.250
Renal, n (%)*	97 (50.0)	46 (64.8)	**0.032**
Genitourinary, n (%)	51 (26.3)	28 (39.4)	**0.038**
Musculoskeletal and skin, n (%)	80 (41.2)	34 (47.9)	0.333
Neurologic, n (%)	55 (28.4)	37 (52.1)	**<0.001**
Endocrine and breast, n (%)	122 (62.9)	52 (73.2)	0.116
Psychiatric (incl. dementia), n (%)	48 (24.7)	52 (73.2)	**<0.001**
Drug burden			
Drugs at admission, median (IQR)	7 (5-9)	8 (5-10)	0.360
Polytherapy, n (%)	151 (77.8)	57 (80.3)	0.668
Hyperpolytherapy, n (%)	36 (18.6)	15 (21.1)	0.638
Functional autonomy			
Barthel Index, median (IQR)	80 (60-95)	20 (10-45)	**<0.001**
Barthel Index disability level, n (%)			**<0.001**
- None	42 (21.7)	0	
- Mild	22 (11.3)	0	
- Moderate	77 (39.7)	3 (4.2)	
- Severe	46 (23.7)	32 (45.1)	
- Extremely severe	7 (3.6)	36 (50.7)	
Katz ADL (n. of functions lost), median (IQR)	0 (0-2)	5 (4-6)	**<0.001**
IADL (n. of functions kept), median (IQR)	4 (2-6)	1 (0-1)	**<0.001**
IADL autonomy category, n (%)			**<0.001**
- Autonomous	63 (32.5)	0	
- Partially autonomous	67 (34.5)	1 (1.4)	
- Non autonomous	64 (33.0)	70 (98.6)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (0-3)	5 (4-9)	**<0.001**
Cognitive impairment SPMSQ, n(%)*			**<0.001**
- None	132 (68.0)	8 (11.3)	
- Mild	45 (23.2)	17 (23.9)	
- Moderate	14 (7.2)	23 (32.4)	
- Severe	3 (1.6)	23 (32.4)	
Confused, wandering behavior	13 (6.7)	25 (35.2)	**<0.001**
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	6 (3-10)	0.286
Anxiety levels at HADS, n (%)†			0.112
- Normal	126 (67.4)	25 (55.6)	
- Borderline	35 (18.7)	10 (22.2)	
- Abnormal	26 (13.9)	10 (22.2)	
HADS depression, median (IQR)†	8 (5-11)	12 (8-15)	**<0.001**

Depression levels at HADS, n (%)[†]			**<0.001**
- Normal	90 (48.1)	9 (20.0)	
- Borderline	46 (24.6)	9 (20.0)	
- Abnormal	51 (27.3)	27 (60.0)	
Physical performance and activity levels			
Best handgrip (kg), median (IQR)[*]	17 (11-22)	10 (5—14)	**<0.001**
Best handgrip (kg), males; median (IQR)[*]	20.0 (17.3-25.5)	12.6 (6.7-16.9)	**<0.001**
Best handgrip (kg), females; median (IQR)[*]	12.0 (9.4-15.8)	7.2 (3.3-12.2)	**<0.001**
Weakness at handgrip (FFP), n (%)	163 (85.3)	67 (94.4)	**0.047**
Unable to perform gait speed, n (%)	36 (24.8)	41 (68.3)	**<0.001**
Gait speed (m/s), median (IQR)[‡]	0.54 (0.42-0.70)	0.46 (0.29-0.65)	0.219
Low gait speed (FFP), n (%)	82 (75.2)	16 (84.2)	0.560
Low gait speed or unable, n (%)[**]	118 (81.4)	57 (95.0)	**0.012**
PASE score, median (IQR)	31.4 (2.2-73.6)	0 (0-2.2)	**<0.001**
Low activity levels at PASE, n (%)[*]	132 (68.4)	67 (94.4)	**<0.001**
Physical exhaustion, n (%)	134 (69.1)	63 (88.7)	**0.001**
Sensory impairment/balance			
Vision impairment, n (%)[*]			0.762
- None	45 (23.3)	20 (28.6)	
- Present, moderate	130 (67.4)	41 (58.6)	
- Present, severe	18 (9.3)	9 (12.8)	
Hearing impairment, n (%)[*]			**<0.001**
- None	112 (58.0)	24 (34.3)	
- Present, moderate	65 (33.7)	36 (51.4)	
- Present, severe	16 (8.3)	10 (14.3)	
History of falls in the previous year, n (%)	73 (37.6)	28 (40.0)	0.726
Number of falls in the previous year, median (IQR)	1 (1-2)	1 (1-2)	0.298
Nutrition			
BMI (kg/m^2), median (IQR)[*]	24.2 (21.5-27.1)	22.3 (19.5-25.8)	**0.002**
Mid-arm circumference (cm), median (IQR)[*]	25 (23-28)	24 (22.3-26.3)	**0.019**
Mid-calf circumference (cm), median (IQR)[*]	32 (29.5-35.0)	30.0 (28.0-32.5)	**<0.001**
MNA score, median (IQR)	20 (17-22)	13.5 (9-15.5)	**<0.001**
Malnutrition risk at MNA, n (%)			**<0.001**
- Normal	41 (21.1)	0	
- At risk	109 (56.2)	9 (12.7)	
- Malnourished	44 (22.7)	62 (87.3)	
Weight loss in the past 12 mo, n (%)[*]	90 (46.4)	36 (50.7)	0.534
Pressure ulcer development risk			
ESS, median (IQR)	16.5 (15-18)	12 (10-14)	**<0.001**
Risk of pressure injuries at ESS,			**<0.001**
- Low	139 (71.6)	3 (4.2)	
- Medium	55 (28.4)	55 (77.5)	
- High	0	13 (18.3)	
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	10 (6-17)	14 (9-23)	**0.001**
Any hospital-acquired complication or in-hospital death, n (%)	50 (25.8)	27 (38.0)	0.052
Death during admission, n (%)	10 (5.2)	4 (5.6)	1.000
Any hospital-acquired complication, n (%)	46 (23.7)	24 (33.8)	0.099
Delirium during admission, n (%)	14 (7.2)	16 (22.5)	**<0.001**
Requiring use of medication	13/14 (92.9)	12/16 (75.0)	0.413
Fall during admission, n (%)	5 (2.6)	2 (2.8)	1.000
Pressure injury development during admission, n (%)	9 (4.6)	8 (11.3)	0.095
Healthcare-associated infection during admission, n (%)	27 (13.9)	10 (14.1)	0.972
Setting of discharge, n (%)	158 (85.9)	52 (77.6)	0.197
- At home	22 (12.0)	14 (20.9)	
- MLTCF	4 (2.2)	1 (1.5)	
- ED			

*Missing values <5%
†Missing values for 44 (12.5%) subjects
‡Missing values (unavailable or untestable) for 137 (51.7%) subjects
**Missing values for 60 (22.6%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BMI = Body Mass Index, BPSD = behavioral and psychological symptoms of dementia, BRASS = Blaylock Risk Assessment Screening Score, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, ESS = Exton-Smith Scale, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, MLTCF = Medium- or Long-Term Care Facility, NEWS2= National Early Warning Score 2, PASE = Physical Activity Scale for the Elderly, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack.

Supplementary Table S5 – Outcomes at 6 months from discharge in patients discharged alive and stratified by frailty status according to the Fried Frailty Phenotype (FFP). Results are presented on the 251 patients with complete data available for frailty status according to the FFP.

	Non-frail at FFP (n=29)	***Frail at FFP (n=222)***	***p***
Length of follow-up (days), median (IQR)	184 (165-192)	182 (158-188)	0.206
All-cause mortality or institutionalization, n (%)	5 (17.2)	71 (32)	0.104
All-cause mortality, n (%)	4 (13.8)	53 (23.9)	0.223
Institutionalization, n (%)	0 (0)	25 (11.3)	0.115
ED visit or unplanned rehospitalization, n(%)	9 (31)	80 (36)	0.596
Number of ED visits or unplanned rehospitalization,s n (%) - 1 - 2 - 3 or more	 5 (17.2) 2 (6.9) 2 (6.9)	 58 (26.1) 12 (5.4) 10 (4.5)	0.725
Worsening functional status at BI, n (%)	8 (27.6)	81 (36.5)	0.346
BI at follow-up, median (IQR)	0 (-10-0)	-5 (-20-0)	0.558
BI difference from baseline, median (IQR)	70 (40-100)	30 (20-70)	0.218

Abbreviations: BI = Barthel Index, ED = Emergency Department, FFP = Fried Frailty Phenotype, IQR = Interquartile Range

Supplementary Table S6 – Outcomes at 6 months from discharge in patients discharged alive and stratified by frailty status according to the Clinical Frailty Scale (CFS).

	Non-frail at CFS (n=90)	***Frail at CFS (n=190)***	***p***
Length of follow-up (days), median (IQR)	183 (178-195)	181 (150-187)	**<0.001**
All-cause mortality or institutionalization, n (%)	12 (13.3)	72 (37.9)	**<0.001**
All-cause mortality, n (%)	8 (8.9)	53 (27.9)	**<0.001**
Institutionalization, n (%)	4 (4.4)	23 (12.1)	**0.043**
ED visit or unplanned rehospitalization, n(%)	30 (33.3)	68 (35.8)	0.687
Number of ED visits or unplanned rehospitalization,s n (%) - 1 - 2 - 3 or more	 19 (21.1) 6 (6.7) 5 (5.6)	 52 (27.4) 8 (4.2) 8 (4.2)	0.578
Worsening functional status at BI, n (%)	26 (28.9)	74 (38.9)	0.101
BI at follow-up, median (IQR)	0 (-15-0)	-5 (-20-0)	0.353
BI difference from baseline, median (IQR)	70 (40-90)	25 (15-70)	0.051

Abbreviations: BI = Barthel Index, CFS = Clinical Frailty Scale, ED = Emergency Department, IQR = Interquartile Range

Supplementary Table S7 – Outcomes at 6 months from discharge in patients discharged alive and stratified by frailty status according to the Frailty Index (FI).

	Non-frail at FI (n=38)	***Frail at FI (n=242)***	***p***
Length of follow-up (days), median (IQR)	184 (180-199)	182 (159-189)	**0.021**
All-cause mortality or institutionalization, n (%)	2 (5.3)	82 (33.9)	**<0.001**
All-cause mortality, n (%)	2 (5.3)	59 (24.4)	**0.008**
Institutionalization, n (%)	1 (2.6)	26 (10.7)	0.201
ED visit or unplanned rehospitalization, n(%)	13 (34.2)	85 (35.1)	0.913
Number of ED visits or unplanned rehospitalization,s n (%) - 1 - 2 - 3 or more	 10 (26.3) 2 (5.3) 1 (2.6)	 61 (25.2) 12 (5.0) 12 (5.0)	0.938
Worsening functional status at BI, n (%)	6 (15.8)	94 (38.8)	**0.006**
BI at follow-up, median (IQR)	0 (-5-0)	-5 (-20-0)	0.121
BI difference from baseline, median (IQR)	70 (40-100)	35 (20-80)	0.308

Abbreviations: BI = Barthel Index, ED = Emergency Department; FI = Frailty Index, IQR = Interquartile Range

Supplementary Table S8– Outcomes at 6 months from discharge in patients discharged alive and stratified according by frailty status according to the Multidimensional Prognostic Index (MPI). Results are presented on the 251 patients with complete data available for frailty status according to the MPI.

	Non-frail at MPI (MPI 1-2) (n=184)	**Frail at MPI (MPI 3) (n=67)**	***p***
Length of follow-up (days), median (IQR)	182 (167-189)	180 (136-186)	0.069
All-cause mortality or institutionalization, n (%)	44 (23.9)	28 (41.8)	**0.006**
All-cause mortality, n (%)	33 (17.9)	19 (28.4)	0.071
Institutionalization, n (%)	13 (7.1)	12 (17.9)	**0.011**
ED visit or unplanned rehospitalization, n(%)	63 (34.2)	23 (34.3)	0.989
Number of ED visits or unplanned rehospitalization,s n (%) - 1 - 2 - 3 or more	 46 (25.0) 7 (3.8) 10 (5.4)	 17 (25.4) 4 (6.0) 2 (3.0)	0.766
Worsening functional status at BI, n (%)	65 (35.3)	26 (38.8)	0.612
BI at follow-up, median (IQR)	-5 (-20-0)	-5 (-15-0)	0.783
BI difference from baseline, median (IQR)	65 (35-80)	20 (10-25)	**0.028**

Abbreviations: BI = Barthel Index, ED = Emergency Department, IQR = Interquartile Range, MPI = Multidimensional Prognostic Index

S2 – Descriptive analyses stratified by incidence of clinical outcomes

Supplementary Table S9 – Descriptive analysis stratified according to the incidence of the composite outcome of in-hospital death or any hospital-acquired complication during admission.

	Absence of composite outcome at discharge (n=209)	**Presence of composite outcome at discharge (n= 88)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	85 (80-90)	88 (83.5-91)	**0.007**
Female sex, n (%)	110 (52.6)	45 (51.1)	0.814
HaH setting, n (%)	73 (34.9)	25 (28.4)	0.275
- AA-HaH/ESD-HaH, n (%)	50 (68.5)/23 (31.5)	18 (72.0)/7 (28.0)	0.743
Study title, n (%)*			0.787
- None	14 (6.7)	5 (5.7)	
- Primary school diploma	76 (36.4)	32 (36.4)	
- Middle school diploma	57 (27.3)	21 (23.9)	
- Professional school diploma	25 (12.0)	15 (17.0)	
- High school diploma	16 (7.7)	10 (11.4)	
- Bachelor's degree or higher	21 (10.0)	5 (5.7)	
Years of education, median (IQR)*	8 (5-11)	8 (5-12)	0.520
Living condition, n (%)			0.281
- Alone without help	12 (5.7)	9 (10.2)	
- Alone with help	36 (17.2)	17 (19.3)	
- Living with spouse/relative	134 (64.1)	47 (53.4)	
- Living with paid caregiver	27 (12.9)	15 (17)	
Presence of a caregiver, n (%)	107 (51.2)	48 (54.5)	0.598
- Paid caregivers, n (%)	49/107 (45.8)	32/48 (66.7)	**0.016**
Continuous 24/7 caregiving, n (%)	77 (72.0)	25 (52.1)	0.162
Legal disability recognized, n (%)	99 (47.4)	38 (43.2)	0.601
- With care allowance, n (%)	42/99 (42.4)	14/38 (36.8)	0.552
Geriatric Assessment to access geriatric care, n (%)	25 (12)	10 (11.4)	0.884
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	113 (54.1)	59 (67.0)	**0.039**
Site of admission, n (%)	10 (4.8)	7 (8.0)	0.541
- General Practitioner	172 (82.3)	71 (80.7)	
- Emergency Department	27 (12.9)	10 (11.4)	
- Other hospital ward			
Reason of admission, n (%)			0.606
- Respiratory tract infection	43 (20.6)	12 (13.6)	
- Decompensated heart failure	18 (8.6)	6 (6.8)	
- Fluid and electrolyte imbalance	22 (10.5)	6 (6.8)	
- Infection (other)	35 (16.7)	20 (22.7)	
- Urinary tract infection	9 (4.3)	7 (8.0)	
- Anemia/bleeding	19 (9.1)	10 (11.4)	
- Stroke/TIA	12 (5.7)	7 (8.0)	
- Uncontrolled BPSD	8 (3.8)	3 (3.4)	
- Other	43 (20.6)	17 (19.3)	
NEWS2 score, median (IQR)	2 (1-3)	3 (1-5)	**0.010**
NEWS2 score risk, n (%)			**0.001**
- Low risk	162 (77.5)	52 (59.1)	
- Low-medium risk	19 (9.1)	12 (13.6)	
- Medium risk	19 (9.1)	16 (18.2)	
- High risk	9 (4.3)	8 (9.1)	
Hemoglobin (g/dl), mean±SD*	11.8±2.2	22.6±2.2	0.392

ClCr (ml/min), median (IQR)*	38.5 (25.7-54.5)	37.5 (25.1-49.7)	0.270
BRASS, median (IQR)*	13 (10-18)	16 (11.5-21)	**0.001**
BRASS risk, n (%)			**0.003**
- Low	70 (33.5)	14 (15.9)	
- Medium	94 (45.0)	47 (53.4)	
- High	45 (21.5)	27 (30.7)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	6 (4-7)	0.483
CIRS-SI, median (IQR)	2.2 (1.9-2.3)	2.2 (1.9-2.4)	0.510
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	126 (60.3)	60 (68.2)	0.199
Hypertension, n (%)	171 (81.8)	64 (72.7)	0.078
Vascular and hematopoietic, n(%)	106 (50.7)	38 (43.2)	0.235
Respiratory, n (%)	74 (35.4)	30 (34.1)	0.828
Eyes,ears,nose,throat,larynx, n(%)	72 (34.4)	41 (46.6)	**0.049**
Upper gastrointestinal, n (%)	49 (23.4)	21 (23.9)	0.938
Lower gastrointestinal, n (%)	39 (18.7)	13 (14.8)	0.421
Liver, pancreas and biliary, n (%)	12 (5.7)	4 (4.5)	0.785
Renal, n (%)	103 (49.3)	56 (63.6)	**0.024**
Genitourinary, n (%)	64 (30.6)	28 (31.8)	0.839
Musculoskeletal and skin, n (%)	93 (44.5)	32 (36.4)	0.195
Neurologic, n (%)	69 (33.0)	34 (38.6)	0.353
Endocrine and breast, n (%)	138 (66.0)	57 (64.8)	0.835
Psychiatric (incl. dementia), n (%)	77 (36.8)	40 (45.5)	0.165
Drug burden			
Drugs at admission, median (IQR)	7 (5-10)	6 (4-8)	**0.014**
Polytherapy, n (%)	166 (79.4)	64 (72.7)	0.207
Hyperpolytherapy, n (%)	43 (20.6)	13 (14.8)	0.243
Functional autonomy			
Barthel Index, median (IQR)	75 (40-95)	57.5 (25-85)	**0.011**
Barthel Index disability level, n (%)			**0.007**
- None	38 (18.2)	5 (5.7)	
- Mild	17 (8.1)	6 (6.8)	
- Moderate	61 (29.2)	27 (30.7)	
- Severe	60 (28.7)	29 (33)	
- Extremely severe	33 (15.8)	21 (23.9)	
Katz ADL (n. of functions lost), median (IQR)	1 (0-4)	3 (0-5)	**0.014**
IADL (n. of functions kept), median (IQR)	3 (1-6)	2 (0-4)	**0.004**
IADL autonomy category, n (%)			0.054
- Autonomous	54 (25.8)	13 (14.8)	
- Partially autonomous	52 (24.9)	23 (26.1)	
- Non autonomous	103 (49.3)	52 (59.1)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (1-4)	3 (2-6)	**0.002**
Cognitive impairment SPMSQ, n(%)*			**0.002**
- None	116 (56.0)	32 (38.6)	
- Mild	48 (23.2)	20 (24.1)	
- Moderate	26 (12.6)	18 (21.7)	
- Severe	17 (8.2)	13 (15.7)	
Confused, wandering behavior	27 (12.9)	17 (19.3)	0.156
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	6 (3-10)	0.518
Anxiety levels at HADS, n (%)†			0.497
- Normal	116 (64.1)	45 (62.5)	
- Borderline	39 (21.5)	10 (13.9)	
- Abnormal	26 (14.4)	17 (23.6)	
HADS depression, median (IQR)†	8 (5-12)	9 (5-12.5)	0.964

Depression levels at HADS, n (%)[†]			0.676
- Normal	75 (41.4)	29 (40.3)	
- Borderline	43 (23.8)	15 (20.8)	
- Abnormal	63 (34.8)	28 (38.9)	
Physical performance and activity levels			
Best handgrip (kg), median (IQR)[*]	15 (10-21.6)	13.2 (9.9-18.8)	0.048
Best handgrip (kg), males; median (IQR)[*]	20.0 (14.1-26.0)	18.0 (12.1-22.8)	**0.038**
Best handgrip (kg), females; median (IQR)[*]	11.9 (8-16)	10.0 (7.0-13.6)	0.155
Weakness at handgrip (FFP), n (%)	175 (83.7)	84 (95.5)	**0.006**
Unable to perform gait speed, n (%)	53 (100.0)	35 (100.0)	
Gait speed (m/s), median (IQR)[‡]	0.6 (0.4-0.8)	0.4 (0.3-0.6)	**0.011**
Low gait speed (FFP), n (%)	83 (71.6)	22 (84.6)	0.170
Low gait speed or unable, n (%)[**]	136 (80.5)	57 (93.4)	**0.018**
PASE score, median (IQR)	25 (0-60)	20 (0-46.5)	0.223
Low activity levels at PASE, n (%)	151 (72.2)	72 (81.8)	0.082
Physical exhaustion, n (%)	156 (74.6)	65 (73.9)	0.888
Sensory impairment/balance			
Vision impairment, n (%)[*]			0.459
- None	51 (24.4)	22 (25.0)	
- Present, moderate	139 (66.5)	52 (59.1)	
- Present, severe	19 (9.1)	14 (15.9)	
Hearing impairment, n (%)[*]			0.959
- None	104 (49.8)	46 (52.3)	
- Present, moderate	85 (40.7)	29 (33.0)	
- Present, severe	20 (9.6)	13 (14.8)	
History of falls in the previous year, n (%)	74 (35.4)	38 (43.2)	0.207
Number of falls in the previous year, median (IQR)	0 (0-1)	0 (0-1.5)	0.107
Nutrition			
BMI (kg/m^2), median (IQR)[*]	23.5 (20.9-26.4)	23.9 (20.8-26.6)	0.539
Mid-arm circumference (cm), median (IQR)[*]	25 (23-27)	25.1 (22-28)	0.760
Mid-calf circumference (cm), median (IQR)[*]	31.4 (29-34)	31.5 (28.5-34)	0.767
MNA score, median (IQR)[††]	18.5 (15-22)	17.5 (13-21.5)	0.160
Malnutrition risk at MNA, n (%)[††]			0.248
- Normal	31 (16.4)	11 (13.9)	
- At risk	87 (46)	32 (40.5)	
- Malnourished	71 (37.6)	36 (45.6)	
Weight loss in the past 12 mo, n (%)[*]	94 (45)	47 (53.4)	0.184
Pressure ulcer development risk			
ESS, median (IQR)	16 (14-18)	14 (12-16)	**<0.001**
Risk of pressure injuries at ESS,			**0.005**
- Low	117 (56)	37 (42)	
- Medium	86 (41.1)	39 (44.3)	
- High	6 (2.9)	12 (13.6)	
Frailty assessment			
Fried Frailty Phenotype			
Frailty status according to FFP[‡‡]			**0.006**
- Robust, n (%)	0 (0)	0 (0)	
- Pre-frail, n(%)	27 (14.2)	2 (2.6)	
- Frail, n (%)	163 (85.8)	74 (97.4)	
Clinical Frailty Scale			
CFS score, median (IQR)	5 (4-7)	6 (5-7)	**0.006**
Frail according to CFS ≥5, (%)	133 (63.6)	68 (77.3)	**0.022**
Frailty severity according to CFS			**0.035**
- No frailty (CFS 1-4), n (%)	76 (36.4)	20 (22.7)	
- Moderate frailty (CFS 5/6), n (%)	74 (35.4)	32 (36.4)	
- Severe frailty (CFS≥7), n (%)	59 (28.2)	36 (40.9)	
Frailty index			
FI, median (IQR)	0.45 (0.3-0.59)	0.51 (0.37-0.63)	**0.006**

Items evaluated at FI, mean±SD	38.9±1.36	38.6±1.5	**0.033**
Frail according to FI≥0.25, n (%)	175 (83.7)	82 (93.2)	**0.029**
Frailty severity according to FI			**0.014**
- No frailty (FI <0.25), n (%)	34 (16.3)	6 (6.8)	
- Moderate frailty (0.25-0.44), n (%)	75 (35.9)	25 (28.4)	
- Severe frailty (FI≥0.45), n (%)	100 (47.8)	57 (64.8)	
Multidimensional Prognostic Index			
MPI score, median (IQR)***	0.47 (0.31-0.63)	0.56 (0.38-0.69)	**0.029**
Frailty status according to MPI***			**0.016**
- MPI low risk, n (%)	48 (25.5)	11 (14.3)	
- MPI medium risk, n (%)	96 (51.1)	39 (50.6)	
- MPI high risk = frail, n (%)	44 (23.4)	27 (35.1)	
Use of medical devices and medication classes during admission			
Venous catheter use, n (%)	197 (94.3)	85 (96.6)	0.565
- Midline/Long VC	42/197 (21.3)	32/85 (37.6)	**<0.001**
- PICC/CVC	7/197 (3.6)	9/85 (10.6)	
Venous catheter present at admission, n (%)	16 (8.1)	9 (10.6)	0.504
Urinary catheter use, n (%)	59 (28.2)	50 (56.8)	**<0.001**
Urinary catheter present at admission, n (%)	15 (25.0)	9 (18.0)	0.376
Oxygen supplementation, n (%)	49 (23.4)	35 (39.8)	**0.004**
- Nasal cannula	37/49 (75.5)	21/35 (60.0)	0.167
- Venturi mask	6/49 (12.2)	10/35 (28.6)	
- NIV/HFNC	6/49 (12.2)	4/35 (11.4)	
Oxygen supplementation present at admission, n (%)	17 (34.7)	5 (14.3)	**0.036**
Intravenous antibiotic, n (%)	99 (47.4)	58 (65.9)	**0.003**
New opioid use, n (%)	13 (6.2)	12 (3.6)	**0.036**
New benzodiazepine use, n (%)	11 (5.3)	8 (9.1)	0.222
New other hypnotic use, n (%)	15 (7.2)	18 (20.5)	**<0.001**
New antipsychotic use, n (%)	8 (3.8)	29 (33.0)	**<0.001**
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	10 (6-15)	18 (10-27)	**<0.001**
Setting of discharge, n (%)			**<0.001**
- At home	186 (89.0)	48 (67.6)	
- MLTCF	19 (9.1)	21 (29.6)	
- ED	4 (1.9)	2 (2.8)	

*Missing values <5%
†Missing values for 44 (14.8%) subjects
‡Missing values (unavailable or untestable) for 155 (52.2%) subjects
**Missing values for 67 (22.6%) subjects
††Missing values for 29 (9.8%) subjects
‡‡‡ Missing values for 31 (10.4%) subjects
*** Missing values for 32 (10.8%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BPSD = behavioral and psychological symptoms of dementia, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, CVC = Central Venous Cannula, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, HFNC = High Flow Nasal Cannula, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, NEWS2= National Early Warning Score 2, NIV = Non-Invasive Ventilation, PASE = Physical Activity Scale for the Elderly, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack, VC = venous cannula.

Supplementary Table S10– Descriptive analysis of selected clinical variables stratified according to the incidence of any hospital-acquired complication during admission.

	No incidence of hospital-acquired complication during admission (n=252)	**Any hospital-acquired complication during admission (n= 45)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	85 (80-90)	88 (83.5-90)	**0.007**
Female sex, n (%)	113 (52.1)	42 (52.5)	0.948
HaH setting, n (%)	78 (35.9)	20 (25)	0.075
- AA-HaH/ESD-HaH, n (%)	53 (67.9)/25 (32.1)	15 (75.0)/5 (25.0)	0.542
Presence of a caregiver, n (%)	113 (52.1)	42 (52.5)	0.948
Continuous 24/7 caregiving, n (%)	80 (70.8)	22 (52.4)	0.132
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	118 (54.4)	54 (67.5)	**0.042**
Site of admission, n (%)			0.728
- General Practitioner	12 (5.5)	5 (6.3)	
- Emergency Department	176 (81.1)	67 (83.8)	
- Other hospital ward	29 (13.4)	8 (10.0)	
Reason of admission, n (%)			0.589
- Respiratory tract infection	45 (20.7)	10 (12.5)	
- Decompensated heart failure	18 (8.3)	6 (7.5)	
- Fluid and electrolyte imbalance	22 (10.1)	6 (7.5)	
- Infection (other)	38 (17.5)	17 (21.3)	
- Urinary tract infection	9 (4.1)	7 (8.8)	
- Anemia/bleeding	19 (8.8)	10 (12.5)	
- Stroke/TIA	13 (6.0)	6 (7.5)	
- Uncontrolled BPSD	8 (3.7)	3 (3.8)	
- Other	45 (20.7)-	15 (18.8)-	
NEWS2 score, median (IQR)	2 (1-3)	3 (1-5)	**0.010**
NEWS2 score risk, n (%)		48 (60.0)	**<0.001**
- Low risk	166 (76.5)	11 (13.8)	
- Low-medium risk	20 (9.2)	14 (17.5)	
- Medium risk	21 (9.7)	7 (8.8)	
- High risk	10 (4.6)		
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	6 (4-7)	0.483
CIRS-SI, median (IQR)	2.2 (1.9-2.3)	2.2 (1.9-2.4)	0.510
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	131 (60.4)	55 (68.8)	0.185
Hypertension, n (%)	175 (80.6)	60 (75.0)	0.288
Vascular and hematopoietic, n(%)	114 (52.5)	30 (37.5)	**0.021**
Respiratory, n (%)	80 (36.9)	24 (30.0)	0.271
Eyes,ears,nose,throat,larynx, n(%)	76 (35.0)	37 (46.3)	0.077
Upper gastrointestinal, n (%)	50 (23.0)	20 (25.0)	0.724
Lower gastrointestinal, n (%)	39 (18.0)	13 (16.3)	0.729
Liver, pancreas and biliary, n (%)	13 (6.0)	3 (3.8)	0.448
Renal, n (%)	109 (50.2)	50 (62.5)	0.060
Genitourinary, n (%)	66 (30.4)	26 (32.5)	0.730
Musculoskeletal and skin, n (%)	95 (43.8)	30 (37.5)	0.331
Neurologic, n (%)	71 (32.7)	32 (40.0)	0.242
Endocrine and breast, n (%)	144 (66.4)	51 (63.8)	0.674
Psychiatric (incl. dementia), n (%)	80 (36.9)	37 (46.3)	0.142

Drug burden			
Drugs at admission, median (IQR)	7 (5-10)	6 (4-8)	**0.014**
Polytherapy, n (%)	172 (79.3)	58 (72.5)	0.216
Hyperpolytherapy, n (%)	44 (20.3)	12 (15.0)	0.302
Functional autonomy			
Barthel Index, median (IQR)	70 (35-95)	60 (30-85)	**0.011**
Barthel Index disability level, n (%)			**0.007**
- None	38 (17.5)	5 (6.3)	
- Mild	18 (8.3)	5 (6.3)	
- Moderate	62 (28.6)	26 (32.5)	
- Severe	62 (28.6)	27 (33.8)	
- Extremely severe	37 (17.1)	17 (21.3)	
IADL (n. of functions kept), median (IQR)	2 (1-6)	2 (0-4)	**0.004**
IADL autonomy category, n (%)			0.054
- Autonomous	55 (25.3)	12 (15.0)	
- Partially autonomous	53 (24.4)	22 (27.5)	
- Non autonomous	109 (50.2)	46 (57.5)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (1-4)	3 (2-6)	**0.002**
Cognitive impairment SPMSQ, n(%)*			**0.002**
- None	120 (56.1)	28 (36.8)	
- Mild	48 (22.4)	20 (26.3)	
- Moderate	27 (12.6)	17 (22.4)	
- Severe	19 (8.9)	11 (14.5)	
Confused, wandering behavior	32 (14.7)	12 (15.0)	0.956
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	6 (3-10)	0.518
Anxiety levels at HADS, n (%)†			0.497
- Normal	120 (64.5)	41 (61.2)	
- Borderline	39 (21.0)	10 (14.9)	
- Abnormal	27 (14.5)	16 (23.9)	
HADS depression, median (IQR)†	8.5 (5-12)	9 (5-12)	0.964
Depression levels at HADS, n (%)†			0.676
- Normal	76 (40.9)	28 (41.8)	
- Borderline	44 (23.7)	14 (20.9)	
- Abnormal	66 (35.5)	25 (37.3)	
Sensory impairment/balance			
Vision impairment, n (%)*			0.459
- None	53 (24.4)	20 (25.0)	
- Present, moderate	144 (66.4)	47 (58.8)	
- Present, severe	20 (9.2)	13 (16.3)	
Hearing impairment, n (%)*			0.959
- None	107 (49.3)	43 (53.8)	
- Present, moderate	89 (41.0)	25 (31.3)	
- Present, severe	21 (9.7)	12 (15.0)	
History of falls in the previous year, n (%)	75 (34.6)	37 (46.3)	0.065
Number of falls in the previous year, median (IQR)	0 (0-1)	0 (0-2)	0.107
Nutrition			
MNA score, median (IQR)‡	18.5 (14.5-22)	18 (14-22)	0.160
Malnutrition risk at MNA, n (%)‡			0.248
- Normal	32 (16.2)	10 (14.1)	
- At risk	88 (44.7)	31 (43.7)	
- Malnourished	77 (39.1)	30 (42.3)	
Weight loss in the past 12 mo, n (%)*	101 (46.5)	40 (50.0)	0.597

Frailty assessment			
Fried Frailty Phenotype			
Frailty status according to FFP**			**0.015**
- Robust, n (%)	0 (0)	0 (0)	
- Pre-frail, n(%)	27 (13.6)	2 (2.9)	
- Frail, n (%)	171 (86.4)	66 (97.1)	
Clinical Frailty Scale			
CFS score, median (IQR)	6 (4-7)	6 (5-7)	**0.006**
Frail according to CFS ≥5, (%)	140 (64.5)	61 (76.3)	0.055
Frailty severity according to CFS			**0.010**
- No frailty (CFS 1-4), n (%)	77 (35.5)	19 (23.8)	
- Moderate frailty (CFS 5/6), n (%)	76 (35.0)	30 (37.5)	
- Severe frailty (CFS≥7), n (%)	64 (29.5)	31 (38.8)	
Frailty index			
FI, median (IQR)	0.45 (0.3-0.6)	0.51 (0.37-0.62)	**0.006**
Items evaluated at FI, mean±SD	38.9±1.37	38.6±1.48	**0.042**
Frail according to FI≥0.25, n (%)	182 (83.9)	75 (93.8)	**0.027**
Frailty severity according to FI			**0.004**
- No frailty (FI <0.25), n (%)	35 (16.1)	5 (6.3)	
- Moderate frailty (0.25-0.44), n (%)	75 (34.6)	25 (31.3)	
- Severe frailty (FI≥0.45), n (%)	107 (49.3)	50 (62.5)	
Multidimensional Prognostic Index			
MPI score, median (IQR)††	0.5 (0.31-0.63)	0.53 (0.38-0.69)	**0.029**
Frailty status according to MPI††			**0.016**
- MPI low risk, n (%)	49 (25.1)	10 (14.3)	
- MPI medium risk, n (%)	99 (50.8)	36 (51.4)	
- MPI high risk = frail, n (%)	47 (24.1)	24 (34.3)	
Use of medical devices and medication classes during admission			
Venous catheter use, n (%)	205 (94.5)	77 (96.3)	0.766
- Midline/Long VC	45/205 (22.0)	29/77 (37.7)	**<0.001**
- PICC/CVC	8/205 (3.9)	8/77 (10.4)	
Venous catheter present at admission, n (%)	18 (8.8)	7 (9.1)	0.935
Urinary catheter use, n (%)	64 (29.5)	45 (56.3)	**<0.001**
Urinary catheter present at admission, n (%)	17 (26.2)	7 (15.6)	0.186
Oxygen supplementation, n (%)	53 (21.0)	31 (68.8)	**<0.001**
- Nasal cannula	39/53 (73.6)	19/31 (61.3)	0.201
- Venturi mask	7/53 (13.2)	9/31 (29.0)	
- NIV/HFNC	7/53 (13.2)	3/31 (9.7)	
Oxygen supplementation present at admission, n (%)	18 (34.0)	4 (12.9)	**0.034**
Intravenous antibiotic, n (%)	101 (46.5)	56 (70.0)	**<0.001**
New opioid use, n (%)	14 (6.5)	11 (13.8)	**0.044**
New benzodiazepine use, n (%)	12 (5.6)	7 (8.8)	0.319
New other hypnotic use, n (%)	15 (6.9)	18 (22.5)	**<0.001**
New antipsychotic use, n (%)	9 (4.2)	28 (35.0)	**<0.001**
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	10 (6-15)	19 (10-28)	**<0.001**
Death during admission, n (%)	8 (3.7)	9 (11.3)	**0.013**
Setting of discharge, n (%)			**<0.001**
- At home	186 (89.0)	48 (67.6)	
- MLTCF	19 (9.1)	21 (29.6)	
- ED	4 (1.9)	2 (2.8)	

*Missing values <5%
†Missing values for 44 (14.8%) subjects
‡Missing values for 67 (22.6%) subjects
** Missing values for 31 (10.4%) subjects
†† Missing values for 32 (10.8%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BPSD = behavioral and psychological symptoms of dementia, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, CVC = Central Venous Cannula, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, HFNC = High Flow Nasal Cannula, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, NEWS2= National Early Warning Score 2, NIV = Non-Invasive Ventilation, PASE = Physical Activity Scale for the Elderly, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack, VC = venous cannula.

Supplementary Table S11– Descriptive analysis of selected clinical variables stratified according to the incidence of healthcare-associated infections during admission.

	No incidence of infection during admission (n=252)	**Infection during admission (n= 45)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	86 (80-90)	88 (83-90)	0.244
Female sex, n (%)	128 (50.8)	27 (60.0)	0.655
HaH setting, n (%)	86 (34.1)	12 (26.7)	0.327
- AA-HaH/ESD-HaH, n (%)	59 (68.6)/27 (31.4)	9 (75.0)/3 (25.0)	0.652
Presence of a caregiver, n (%)	133 (52.8)	22 (48.9)	0.630
Continuous 24/7 caregiving, n (%)	90 (67.7)	12 (54.5)	0.239
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	145 (57.5)	27 (60)	0.758
Site of admission, n (%)			0.923
- General Practitioner	14 (5.6)	3 (6.7)	
- Emergency Department	206 (81.7)	37 (82.2)	
- Other hospital ward	32 (12.7)	5 (11.1)	
Reason of admission, n (%)			0.412
- Respiratory tract infection	50 (19.8)	5 (11.1)	
- Decompensated heart failure	21 (8.3)	3 (6.7)	
- Fluid and electrolyte imbalance	24 (9.5)	4 (8.9)	
- Infection (other)	46 (18.3)	9 (20)	
- Urinary tract infection	11 (4.4)	5 (11.1)	
- Anemia/bleeding	22 (8.7)	7 (15.6)	
- Stroke/TIA	15 (6)	4 (8.9)	
- Uncontrolled BPSD	10 (4)	1 (2.2)	
- Other	53 (21)	7 (15.6)	
NEWS2 score, median (IQR)	2 (1-4)	3 (1-4)	0.219
NEWS2 score risk, n (%)			0.367
- Low risk	184 (73)	30 (66.7)	
- Low-medium risk	26 (10.3)	5 (11.1)	
- Medium risk	28 (11.1)	7 (15.6)	
- High risk	14 (5.6)	3 (6.7)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	6 (4-7)	0.715
CIRS-SI, median (IQR)	2.2 (1.9-2.3)	2.2 (1.9-2.4)	0.596
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	156 (61.9)	30 (66.7)	0.543
Hypertension, n (%)	201 (79.8)	34 (75.6)	0.552
Vascular and hematopoietic, n(%)	126 (50.0)	18 (40.0)	0.216
Respiratory, n (%)	91 (36.1)	13 (28.9)	0.350
Eyes,ears,nose,throat,larynx, n(%)	89 (35.3)	24 (53.3)	**0.022**
Upper gastrointestinal, n (%)	60 (23.8)	10 (22.2)	0.817
Lower gastrointestinal, n (%)	47 (18.7)	5 (11.1)	0.220
Liver, pancreas and biliary, n (%)	15 (6.0)	1 (2.2)	0.307
Renal, n (%)	131 (52.0)	28 (62.2)	0.205
Genitourinary, n (%)	78 (31.0)	14 (31.1)	0.983
Musculoskeletal and skin, n (%)	108 (42.9)	17 (37.8)	0.525
Neurologic, n (%)	85 (33.7)	18 (40.0)	0.416
Endocrine and breast, n (%)	164 (65.1)	31 (68.9)	0.620
Psychiatric (incl. dementia), n (%)	97 (38.5)	20 (44.4)	0.452

Drug burden			
Drugs at admission, median (IQR)	7 (5-10)	6 (5-8)	0.144
Polytherapy, n (%)	196 (77.8)	34 (75.6)	0.743
Hyperpolytherapy, n (%)	47 (18.7)	9 (20.0)	0.831
Functional autonomy			
Barthel Index, median (IQR)	67.5 (35-90)	60 (35-85)	0.173
Barthel Index disability level, n (%)			0.091
- None	42 (16.7)	1 (2.2)	
- Mild	19 (7.5)	4 (8.9)	
- Moderate	72 (28.6)	16 (35.6)	
- Severe	76 (30.2)	13 (28.9)	
- Extremely severe	43 (17.1)	11 (24.4)	
IADL (n. of functions kept), median (IQR)	2 (1-5)	2 (0-4)	0.120
IADL autonomy category, n (%)			0.597
- Autonomous	58 (23.0)	9 (20.0)	
- Partially autonomous	64 (25.4)	11 (24.4)	
- Non autonomous	130 (51.6)	25 (55.6)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (1-4)	3 (2-6)	0.066
Cognitive impairment SPMSQ, n(%)*			**0.049**
- None	131 (52.8)	17 (40.5)	
- Mild	59 (23.8)	9 (21.4)	
- Moderate	36 (14.5)	8 (19.0)	
- Severe	22 (8.9)	8 (19.0)	
Confused, wandering behavior	40 (15.9)	4 (8.9)	0.224
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	6 (3-10)	0.368
Anxiety levels at HADS, n (%)†			0.640
- Normal	135 (62.8)	26 (68.4)	
- Borderline	44 (20.5)	5 (13.2)	
- Abnormal	36 (16.7)	7 (18.4)	
HADS depression, median (IQR)†	9 (5-12)	8 (5-13)	0.626
Depression levels at HADS, n (%)†			0.665
- Normal	86 (40.0)	18 (47.4)	
- Borderline	52 (24.2)	6 (15.8)	
- Abnormal	77 (35.8)	14 (36.8)	
Sensory impairment/balance			
Vision impairment, n (%)*			**0.036**
- None	64 (25.4)	9 (20.0)	
- Present, moderate	166 (65.9)	25 (55.6)	
- Present, severe	22 (8.7)	11 (24.4)	
Hearing impairment, n (%)*			0.792
- None	126 (50.0)	24 (53.3)	
- Present, moderate	102 (40.5)	12 (26.7)	
- Present, severe	24 (9.5)	9 (20.0)	
History of falls in the previous year, n (%)	95 (37.7)	17 (37.8)	0.992
Number of falls in the previous year, median (IQR)	0 (0-1)	0 (0-2)	0.690
Nutrition			
MNA score, median (IQR)‡	18.5 (14.5-22)	18.5 (14.5-23)	0.551
Malnutrition risk at MNA, n (%)‡			0.418
- Normal	35 (15.2)	7 (18.4)	
- At risk	101 (43.9)	18 (47.4)	
- Malnourished	94 (40.9)	13 (34.2)	
Weight loss in the past 12 mo, n (%)*	118 (46.8)	23 (51.1)	0.596

Frailty assessment			
Fried Frailty Phenotype			
Frailty status according to FFP**			0.144
- Robust, n (%)	0 (0)	0 (0)	
- Pre-frail, n(%)	28 (12.1)	1 (2.9)	
- Frail, n (%)	203 (87.9)	34 (97.1)	
Clinical Frailty Scale			
CFS score, median (IQR)	6 (4-7)	6 (4-7)	0.438
Frail according to CFS ≥5, (%)	168 (66.7)	33 (73.3)	0.378
Frailty severity according to CFS			0.403
- No frailty (CFS 1-4), n (%)	84 (33.3)	12 (26.7)	
- Moderate frailty (CFS 5/6), n (%)	89 (35.3)	17 (37.8)	
- Severe frailty (CFS≥7), n (%)	79 (31.3)	16 (35.6)	
Frailty index			
FI, median (IQR)	0.46 (0.31-0.6)	0.51 (0.35-0.63)	0.245
Items evaluated at FI, mean±SD	38.9±1.38	38.4±1.50	**0.037**
Frail according to FI≥0.25, n (%)	216 (85.7)	41 (91.1)	0.329
Frailty severity according to FI			0.370
- No frailty (FI <0.25), n (%)	36 (14.3)	4 (8.9)	
- Moderate frailty (0.25-0.44), n (%)	85 (33.7)	15 (33.3)	
- Severe frailty (FI≥0.45), n (%)	131 (52.0)	26 (57.8)	
Multidimensional Prognostic Index			
MPI score, median (IQR)††	0.5 (0.38-0.69)	0.5 (0.38-0.69)	0.703
Frailty status according to MPI††			0.744
- MPI low risk, n (%)	52 (22.8)	7 (18.9)	
- MPI medium risk, n (%)	115 (50.4)	20 (54.1)	
- MPI high risk = frail, n (%)	61 (26.8)	10 (27)	
Use of medical devices and medication classes during admission			
Venous catheter use, n (%)	238 (94.4)	44 (97.8)	0.483
- Midline/Long VC	56/238 (23.5)	18/44 (40.9)	**<0.001**
- PICC/CVC	10/238 (4.2)	6/44 (13.6)	
Venous catheter present at admission, n (%)	20 (8.4)	5 (11.4)	0.562
Urinary catheter use, n (%)	77 (30.6)	32 (71.1)	**<0.001**
Urinary catheter present at admission, n (%)	18 (23.1)	6 (18.8)	0.618
Oxygen supplementation, n (%)	64 (25.4)	20 (44.4)	**0.009**
- Nasal cannula	44/64 (68.8)	14/20 (70.0)	0.953
- Venturi mask	12/64 (18.8)	4/20 (20.0)	
- NIV/HFNC	8/64 (12.5)	2/20 (10.0)	
Oxygen supplementation present at admission, n (%)	20 (31.3)	2 (10.0)	0.059
Intravenous antibiotic, n (%)	121 (48.0)	36 (80.0)	**<0.001**
New opioid use, n (%)	18 (7.1)	7 (15.6)	0.078
New benzodiazepine use, n (%)	13 (5.2)	6 (13.3)	0.051
New other hypnotic use, n (%)	23 (9.2)	10 (22.2)	**0.010**
New antipsychotic use, n (%)	28 (11.2)	9 (20.0)	0.099
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	10 (7-17)	23 (11-32)	**<0.001**
Death during admission, n (%)	12 (4.8)	5 (11.1)	0.152
Setting of discharge, n (%)			0.107
- At home	205 (85.4)	29 (72.5)	
- MLTCF	30 (12.5)	10 (25.0)	
- ED	5 (2.1)	1 (2.5)	

*Missing values <5%
†Missing values for 44 (14.8%) subjects
‡Missing values for 67 (22.6%) subjects
** Missing values for 31 (10.4%) subjects
†† Missing values for 32 (10.8%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BPSD = behavioral and psychological symptoms of dementia, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, CVC = Central Venous Cannula, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, HFNC = High Flow Nasal Cannula, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, NEWS2= National Early Warning Score 2, NIV = Non-Invasive Ventilation, PASE = Physical Activity Scale for the Elderly, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack, VC = venous cannula.

Supplementary Table S12– Descriptive analysis of selected clinical variables stratified according to the incidence of delirium during admission.

	No incidence of delirium during admission (n=265)	**Delirium during admission (n= 32)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	86 (80-90)	88 (86-91)	**0.036**
Female sex, n (%)	144 (54.3)	11 (34.4)	**0.033**
HaH setting, n (%)	91 (34.3)	7 (21.9)	0.157
- AA-HaH/ESD-HaH, n (%)	64 (70.3)/27 (29.7)	4 (57.1)/3 (42.9)	0.466
Presence of a caregiver, n (%)	138 (52.1)	17 (53.1)	0.911
Continuous 24/7 caregiving, n (%)	94 (68.1)	8 (47.1)	0.239
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	152 (57.4)	20 (62.5)	0.578
Site of admission, n (%)			0.911
- General Practitioner	15 (5.7)	2 (6.3)	
- Emergency Department	217 (81.9)	26 (81.3)	
- Other hospital ward	33 (12.5)	4 (12.5)	
Reason of admission, n (%)			0.722
- Respiratory tract infection	50 (18.9)	5 (15.6)	
- Decompensated heart failure	21 (7.9)	3 (9.4)	
- Fluid and electrolyte imbalance	26 (9.8)	2 (6.3)	
- Infection (other)	50 (18.9)	5 (15.6)	
- Urinary tract infection	12 (4.5)	4 (12.5)	
- Anemia/bleeding	25 (9.4)	4 (12.5)	
- Stroke/TIA	16 (6)	3 (9.4)	
- Uncontrolled BPSD	10 (3.8)	1 (3.1)	
- Other	55 (20.8)	5 (15.6)	
NEWS2 score, median (IQR)	2 (1-4)	2 (1-4)	0.577
NEWS2 score risk, n (%)			0.150
- Low risk	195 (73.6)	19 (59.4)	
- Low-medium risk	25 (9.4)	6 (18.8)	
- Medium risk	29 (10.9)	6 (18.8)	
- High risk	16 (6.0)	1 (3.1)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	5 (4-7)	0.944
CIRS-SI, median (IQR)	2.2 (1.9-2.4)	2.1 (1.7-2.4)	0.475
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	162 (61.1)	24 (75.0)	0.126
Hypertension, n (%)	213 (80.4)	22 (68.8)	0.126
Vascular and hematopoietic, n(%)	135 (50.9)	9 (28.1)	**0.015**
Respiratory, n (%)	96 (36.2)	8 (25.0)	0.209
Eyes,ears,nose,throat,larynx, n(%)	99 (37.4)	14 (43.8)	0.482
Upper gastrointestinal, n (%)	61 (23.0)	9 (28.1)	0.520
Lower gastrointestinal, n (%)	48 (18.1)	4 (12.5)	0.430
Liver, pancreas and biliary, n (%)	15 (5.7)	1 (3.1)	0.548
Renal, n (%)	137 (51.7)	22 (68.8)	0.068
Genitourinary, n (%)	79 (29.8)	13 (40.6)	0.211
Musculoskeletal and skin, n (%)	113 (42.6)	12 (37.5)	0.578
Neurologic, n (%)	90 (34.0)	13 (40.6)	0.454
Endocrine and breast, n (%)	176 (66.4)	19 (59.4)	0.428
Psychiatric (incl. dementia), n (%)	101 (38.1)	16 (50.0)	0.194

Drug burden			
Drugs at admission, median (IQR)	7 (5-10)	5.5 (4-8)	**0.024**
Polytherapy, n (%)	209 (78.9)	21 (65.6)	0.090
Hyperpolytherapy, n (%)	52 (19.6)	4 (12.5)	0.331
Functional autonomy			
Barthel Index, median (IQR)	70 (35-90)	52.5 (17.5-85)	0.082
Barthel Index disability level, n (%)			0.070
- None	41 (15.5)	2 (6.3)	
- Mild	21 (7.9)	2 (6.3)	
- Moderate	79 (29.8)	9 (28.1)	
- Severe	79 (29.8)	10 (31.3)	
- Extremely severe	45 (17.0)	9 (28.1)	
IADL (n. of functions kept), median (IQR)	2 (1-5)	2 (0.5-3.5)	0.060
IADL autonomy category, n (%)			0.058
- Autonomous	64 (24.2)	3 (9.4)	
- Partially autonomous	67 (25.3)	8 (25)	
- Non autonomous	134 (50.6)	21 (65.6)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (1-4)	4 (2.5-7)	**<0.001**
Cognitive impairment SPMSQ, n(%)*			**<0.001**
- None	141 (54.4)	7 (22.6)	
- Mild	59 (22.8)	9 (29.0)	
- Moderate	35 (13.5)	9 (29.0)	
- Severe	24 (9.3)	6 (19.4)	
Confused, wandering behavior	37 (14.0)	7 (21.9)	0.288
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	3 (3-10)	0.057
Anxiety levels at HADS, n (%)†			0.436
- Normal	143 (62.7)	18 (72.0)	
- Borderline	46 (20.2)	3 (12.0)	
- Abnormal	39 (17.1)	4 (16.0)	
HADS depression, median (IQR)†	9 (5-12)	8 (4-12)	0.702
Depression levels at HADS, n (%)†			0.959
- Normal	93 (40.8)	11 (44.0)	
- Borderline	54 (23.7)	4 (16.0)	
- Abnormal	81 (35.5)	10 (40.0)	
Sensory impairment/balance			
Vision impairment, n (%)*			**0.025**
- None	59 (22.3)	14 (43.8)	
- Present, moderate	176 (66.4)	15 (46.9)	
- Present, severe	30 (11.3)	3 (9.4)	
Hearing impairment, n (%)*			0.612
- None	132 (49.8)	18 (56.3)	
- Present, moderate	104 (39.2)	10 (31.3)	
- Present, severe	29 (10.9)	4 (12.5)	
History of falls in the previous year, n (%)	98 (37)	14 (43.8)	0.456
Number of falls in the previous year, median (IQR)	0 (0-1)	0 (0-1)	0.623
Nutrition			
MNA score, median (IQR)‡	18.5 (14.5-22)	16 (11-21)	0.181
Malnutrition risk at MNA, n (%)‡			0.165
- Normal	38 (16.0)	4 (13.3)	
- At risk	109 (45.8)	10 (33.3)	
- Malnourished	91 (38.2)	16 (53.3)	
Weight loss in the past 12 mo, n (%)*	130 (49.1)	11 (34.4)	0.116

Frailty assessment			
Fried Frailty Phenotype			
Frailty status according to FFP**			0.332
- Robust, n (%)	0 (0)	0 (0)	
- Pre-frail, n(%)	28 (11.8)	1 (3.6)	
- Frail, n (%)	210 (88.2)	27 (96.4)	
Clinical Frailty Scale			
CFS score, median (IQR)	6 (4-7)	6 (5-7)	**0.024**
Frail according to CFS ≥5, (%)	175 (66.0)	26 (81.3)	0.082
Frailty severity according to CFS			**0.034**
- No frailty (CFS 1-4), n (%)	90 (34.0)	6 (18.8)	
- Moderate frailty (CFS 5/6), n (%)	95 (35.8)	11 (34.4)	
- Severe frailty (CFS≥7), n (%)	80 (30.2)	15 (46.9)	
Frailty index			
FI, median (IQR)	0.46 (0.31-0.6)	0.54 (0.36-0.64)	0.116
Items evaluated at FI, mean±SD	38.9±1.4	38.6±1.50	0.225
Frail according to FI≥0.25, n (%)	226 (85.3)	31 (96.9)	0.096
Frailty severity according to FI			0.227
- No frailty (FI <0.25), n (%)	39 (14.7)	1 (3.1)	
- Moderate frailty (0.25-0.44), n (%)	88 (33.2)	12 (37.5)	
- Severe frailty (FI≥0.45), n (%)	138 (52.1)	19 (59.4)	
Multidimensional Prognostic Index			
MPI score, median (IQR)††	0.5 (0.38-0.63)	0.69 (0.38-0.75)	**0.014**
Frailty status according to MPI††			**0.003**
- MPI low risk, n (%)	55 (23.4)	4 (13.3)	
- MPI medium risk, n (%)	125 (53.2)	10 (33.3)	
- MPI high risk = frail, n (%)	55 (23.4)	16 (53.3)	
Use of medical devices and medication classes during admission			
Venous catheter use, n (%)	250 (94.3)	32 (100.0)	0.167
- Midline/Long VC	62/250 (24.8)	12/32 (37.5)	0.149
- PICC/CVC	13/250 (5.2)	3/32 (9.4)	
Venous catheter present at admission, n (%)	21 (8.4)	4 (12.5)	0.504
Urinary catheter use, n (%)	93 (35.1)	16 (50.0)	0.098
Urinary catheter present at admission, n (%)	23 (24.5)	1 (6.3)	0.187
Oxygen supplementation, n (%)	73 (27.5)	11 (34.4)	0.656
- Nasal cannula	51/73 (69.9)	7/11 (63.6)	0.754
- Venturi mask	13/73 (17.8)	3/11 (27.3)	
- NIV/HFNC	9/73 (12.3)	1/11 (9.1)	
Oxygen supplementation present at admission, n (%)	19 (26.0)	3 (27.3)	1.000
Intravenous antibiotic, n (%)	137 (51.7)	20 (62.5)	0.248
New opioid use, n (%)	18 (6.8)	7 (21.9)	**0.010**
New benzodiazepine use, n (%)	16 (6.1)	3 (9.4)	0.444
New other hypnotic use, n (%)	19 (7.2)	14 (43.8)	**<0.001**
New antipsychotic use, n (%)	12 (4.5)	25 (78.1)	**<0.001**
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	11 (7-19)	19 (9-29.5)	**0.002**
Death during admission, n (%)	13 (4.9)	4 (12.5)	0.096
Setting of discharge, n (%)			**0.002**
- At home	216 (85.7)	18 (64.3)	
- MLTCF	30 (11.9)	10 (35.7)	
- ED	6 (2.4)	0 (0)	

*Missing values <5%
†Missing values for 44 (14.8%) subjects
‡Missing values for 67 (22.6%) subjects
** Missing values for 31 (10.4%) subjects
†† Missing values for 32 (10.8%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BPSD = behavioral and psychological symptoms of dementia, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, ClCr = Creatinine Clearance, CVC = Central Venous Cannula, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, HFNC = High Flow Nasal Cannula, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, NEWS2= National Early Warning Score 2, NIV = Non-Invasive Ventilation, PASE = Physical Activity Scale for the Elderly, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack, VC = venous cannula.

Supplementary Table S13 - Descriptive analysis of selected clinical variables on patients discharged alive stratified according to all-cause mortality at 6 months from discharge.

	Alive at follow-up (n=219)	**Deceased at follow-up (n=61)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	86 (81-90)	85 (80-91)	0.747
Female sex, n (%)	124 (56.6)	25 (41)	**0.030**
HaH setting, n (%)	73 (33.3)	19 (31.1)	0.748
- AA-HaH/ESD-HaH, n (%)	50 (68.5)/23 (31.5)	15 (78.9)/4 (21.1)	0.373
Presence of a caregiver, n (%)	112 (51.1)	33 (54.1)	0.683
Continuous 24/7 caregiving, n (%)	77 (68.8)	20 (60.6)	0.730
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	121 (55.3)	41 (67.2)	0.094
Site of admission, n (%)			0.329
- General Practitioner	14 (6.4)	1 (1.6)	
- ED	178 (81.3)	53 (86.9)	
- Other hospital ward	27 (12.3)	7 (11.5)	
Reason of admission, n (%)			**0.011**
- Respiratory tract infection	47 (21.5)	6 (9.8)	
- Decompensated heart failure	19 (8.7)	5 (8.2)	
- Fluid and electrolyte imbalance	20 (9.1)	7 (11.5)	
- Infection (other)	36 (16.4)	12 (19.7)	
- Urinary tract infection	12 (5.5)	2 (3.3)	
- Anemia/bleeding	24 (11.0)	4 (6.6)	
- Stroke/TIA	16 (7.3)	1 (1.6)	
- Uncontrolled BPSD	10 (4.6)	1 (1.6)	
- Other	35 (16.0)	23 (37.7)	
NEWS2 score, median (IQR)	2 (1-3)	3 (1-5)	**0.002**
NEWS2 score risk, n (%)			**0.007**
- Low risk	169 (77.2)	37 (60.7)	
- Low-medium risk	21 (9.6)	8 (13.1)	
- Medium risk	21 (9.6)	10 (16.4)	
- High risk	8 (3.7)	6 (9.8)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	5 (4-6)	0.942
CIRS-SI, median (IQR)	2.2 (1.9-2.3)	2.2 (1.9-2.4)	0.374
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	135 (61.6)	38 (62.3)	0.926
Hypertension, n (%)	182 (83.1)	43 (70.5)	**0.028**
Vascular and hematopoietic, n(%)	100 (45.7)	31 (50.8)	0.475
Respiratory, n (%)	73 (33.3)	21 (34.4)	0.873
Eyes,ears,nose,throat,larynx, n(%)	87 (39.7)	20 (32.8)	0.324
Upper gastrointestinal, n (%)	49 (22.4)	16 (26.2)	0.528
Lower gastrointestinal, n (%)	38 (17.4)	14 (23.0)	0.320
Liver, pancreas and biliary, n (%)	9 (4.1)	6 (9.8)	0.104
Renal, n (%)	117 (53.4)	30 (49.2)	0.557
Genitourinary, n (%)	67 (30.6)	21 (34.4)	0.569
Musculoskeletal and skin, n (%)	93 (42.5)	26 (42.6)	0.982
Neurologic, n (%)	77 (35.2)	22 (36.1)	0.896
Endocrine and breast, n (%)	144 (65.8)	41 (67.2)	0.831
Psychiatric (incl. dementia), n (%)	88 (40.2)	25 (41.0)	0.910
Drug burden			
Drugs at admission, median (IQR)	7 (5-10)	6 (4-9)	0.201

Polytherapy, n (%)	171 (78.1)	44 (72.1)	0.330
Hyperpolytherapy, n (%)	43 (19.6)	11 (18.0)	0.779
Functional autonomy			
Barthel Index, median (IQR)	70 (40-95)	55 (25-80)	**0.009**
Barthel Index disability level, n (%)			**0.011**
- None	39 (17.8)	3 (4.9)	
- Mild	19 (8.7)	2 (3.3)	
- Moderate	63 (28.8)	20 (32.8)	
- Severe	62 (28.3)	23 (37.7)	
- Extremely severe	36 (16.4)	13 (21.3)	
IADL (n. of functions kept), median (IQR)	3 (1-6)	2 (1-4)	**0.014**
IADL autonomy category, n (%)			**0.033**
- Autonomous	56 (25.6)	9 (14.8)	
- Partially autonomous	58 (26.5)	14 (23.0)	
- Non autonomous	105 (47.9)	38 (62.3)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (1-4)	3 (2-5)	0.200
Cognitive impairment SPMSQ, n(%)*			0.302
- None	115 (53.2)	26 (44.1)	
- Mild	49 (22.7)	17 (28.8)	
- Moderate	30 (13.9)	10 (16.9)	
- Severe	22 (10.2)	6 (10.2)	
Confused, wandering behavior	27 (12.3)	12 (19.7)	0.143
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	6.5 (5-9.5)	0.400
Anxiety levels at HADS, n (%)†			0.750
- Normal	122 (63.2)	30 (62.5)	
- Borderline	41 (21.2)	8 (16.7)	
- Abnormal	30 (15.5)	10 (20.8)	
HADS depression, median (IQR)†	8 (5-12)	10 (6-13)	0.045
Depression levels at HADS, n (%)†			**0.037**
- Normal	86 (44.6)	15 (31.3)	
- Borderline	46 (23.8)	10 (20.8)	
- Abnormal	61 (31.6)	23 (47.9)	
Sensory impairment/balance			
Vision impairment, n (%)*			0.121
- None	49 (22.4)	17 (27.9)	
- Present, moderate	142 (64.8)	41 (67.2)	
- Present, severe	28 (12.8)	3 (4.9)	
Hearing impairment, n (%)*			0.886
- None	110 (50.2)	31 (50.8)	
- Present, moderate	85 (38.8)	24 (39.3)	
- Present, severe	24 (11)	6 (9.8)	
History of falls in the previous year, n (%)	81 (37)	28 (45.9)	0.207
Number of falls in the previous year, median (IQR)	0 (0-1)	0 (0-1)	0.379
Nutrition			
MNA score, median (IQR)‡	19 (15.5-22.5)	15.3 (11.8-19.3)	**<0.001**
Malnutrition risk at MNA, n (%)‡			**<0.001**
- Normal	38 (19.0)	2 (3.8)	
- At risk	93 (46.5)	19 (36.5)	
- Malnourished	69 (34.5)	31 (59.6)	
Weight loss in the past 12 mo, n (%)*	91 (41.6)	39 (63.9)	**0.002**
Frailty assessment			
Fried Frailty Phenotype			
Frailty status according to FFP**			0.223
- Robust, n (%)	0 (0)	0 (0)	
- Pre-frail, n(%)	25 (12.9)	4 (7.0)	
- Frail, n (%)	169 (87.1)	53 (93.0)	

Clinical Frailty Scale			
CFS score, median (IQR)	5 (4-7)	6 (5-7)	**0.001**
Frail according to CFS ≥5, (%)	137 (62.6)	53 (86.9)	**<0.001**
Frailty severity according to CFS			**0.002**
- No frailty (CFS 1-4), n (%)	82 (37.4)	8 (13.1)	
- Moderate frailty (CFS 5/6), n (%)	74 (33.8)	28 (45.9)	
- Severe frailty (CFS≥7), n (%)	63 (28.8)	25 (41.0)	
Frailty index			
FI, median (IQR)	0.44 (0.3-0.59)	0.52 (0.39-0.65)	**0.003**
Items evaluated at FI, mean±SD	38.9±1.31	38.6±1.55	**0.049**
Frail according to FI≥0.25, n (%)	183 (83.6)	59 (96.7)	**0.008**
Frailty severity according to FI			**0.002**
- No frailty (FI <0.25), n (%)	36 (16.4)	2 (3.3)	
- Moderate frailty (0.25-0.44), n (%)	79 (36.1)	18 (29.5)	
- Severe frailty (FI≥0.45), n (%)	104 (47.5)	41 (67.2)	
Multidimensional Prognostic Index			
MPI score, median (IQR)††	0.5 (0.38-0.63)	0.56 (0.41-0.69)	0.075
Frailty status according to MPI††			0.077
- MPI low risk, n (%)	48 (24.1)	9 (17.3)	
- MPI medium risk, n (%)	103 (51.8)	24 (46.2)	
- MPI high risk = frail, n (%)	48 (24.1)	19 (36.5)	
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	11 (7-19)	14 (9-26)	**0.004**
Any hospital-acquired complication during admission, n (%)	51 (23.3)	20 (32.8)	0.132
Delirium during admission, n (%)	17 (7.8)	11 (18.0)	**0.018**
- Requiring use of medication	15/17 (88.2)	9/11 (81.8)	1.000
Fall during admission, n (%)	5 (2.3)	3 (4.9)	0.378
Pressure injury development during admission, n (%)	13 (5.9)	3 (4.9)	1.000
Healthcare-associated infection during admission, n (%)	29 (13.2)	11 (18.0)	0.344
Setting of discharge, n (%)			**<0.001**
- At home	195 (89.0)	39 (63.9)	
- MLTCF	20 (9.1)	20 (32.8)	
- ED	4 (1.8)	2 (3.3)	
Outcomes at 6 months from discharge			
Length of follow-up (days), median (IQR)	184 (178-194)	53 (21-127)	**<0.001**
Institutionalization, n (%)	23 (10.5)	19 (31.1)	**<0.001**
ED visit or unplanned rehospitalization, n(%)	67 (30.6)	31 (50.8)	**0.003**
N. of ED visit or unplanned rehospitalization, n (%)			**0.003**
- 1	49 (22.4)	22 (36.1)	
- 2	10 (4.6)	4 (6.6)	
- 3 or more	8 (3.7)	5 (8.2)	

*Missing values <5%
†Missing values for 39 (13.9%) subjects
‡Missing values for 28 (10.0%) subjects
** Missing values for 29 (10.4%) subjects
†† Missing values for 29 (10.4%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BPSD = behavioral and psychological symptoms of dementia, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, NEWS2= National Early Warning Score 2, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack.

Supplementary Table S14 – Comparison of selected clinical variables in patients alive and living at home at 6 months and in patients institutionalized at 6 months from discharge.

	Alive and living at home at follow-up (n=196)	**Institutionalized at follow-up (n=42)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	86 (81-90)	86 (82-90)	0.687
Female sex, n (%)	106 (54.1)	27 (64.3)	0.227
HaH setting, n (%)	70 (35.7)	3 (7.1)	**<0.001**
- AA-HaH/ESD-HaH, n (%)	49 (70)/21 (30)	1 (33.3)/2 (66.7)	0.232
Presence of a caregiver, n (%)	96 (49)	23 (54.8)	0.496
Continuous 24/7 caregiving, n (%)	69 (35.2)	11 (26.2)	0.262
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	108 (55.1)	25 (59.5)	0.600
Site of admission, n (%)			0.153
- General Practitioner	14 (7.1)	0 (0)	
- ED	157 (80.1)	38 (90.5)	
- Other hospital ward	25 (12.8)	4 (9.5)	
Reason of admission, n (%)			**0.013**
- Respiratory tract infection	44 (22.4)	5 (11.9)	
- Decompensated heart failure	19 (9.7)	2 (4.8)	
- Fluid and electrolyte imbalance	19 (9.7)	3 (7.1)	
- Infection (other)	32 (16.3)	6 (14.3)	
- Urinary tract infection	9 (4.6)	5 (11.9)	
- Anemia/bleeding	23 (11.7)	2 (4.8)	
- Stroke/TIA	15 (7.7)	1 (2.4)	
- Uncontrolled BPSD	6 (3.1)	4 (9.5)	
- Other	29 (14.8)	14 (33.3)	
NEWS2 score, median (IQR)	1.5 (1-3)	3 (1-4)	0.198
NEWS2 score risk, n (%)			0.776
- Low risk	151 (77.0)	31 (73.8)	
- Low-medium risk	17 (8.7)	6 (14.3)	
- Medium risk	20 (10.2)	4 (9.5)	
- High risk	8 (4.1)	1 (2.4)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	5 (4-7)	0.790
CIRS-SI, median (IQR)	2.15 (1.92-2.31)	1.92 (2.31-0)	0.512
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	122 (62.2)	24 (57.1)	0.538
Hypertension, n (%)	162 (82.7)	34 (81.0)	0.793
Vascular and hematopoietic, n(%)	92 (46.9)	18 (42.9)	0.630
Respiratory, n (%)	66 (33.7)	14 (33.3)	0.966
Eyes,ears,nose,throat,larynx, n(%)	75 (38.3)	16 (38.1)	0.984
Upper gastrointestinal, n (%)	45 (23.0)	9 (21.4)	0.830
Lower gastrointestinal, n (%)	32 (16.3)	13 (31.0)	**0.028**
Liver, pancreas and biliary, n (%)	8 (4.1)	3 (7.1)	0.391
Renal, n (%)	104 (53.1)	21 (50.0)	0.718
Genitourinary, n (%)	62 (31.6)	11 (26.2)	0.488
Musculoskeletal and skin, n (%)	79 (40.3)	19 (45.2)	0.556
Neurologic, n (%)	64 (32.7)	21 (50.0)	**0.033**
Endocrine and breast, n (%)	132 (67.3)	24 (57.1)	0.207
Psychiatric (incl. dementia), n (%)	70 (35.7)	26 (61.9)	**0.002**
Drug burden			
Drugs at admission, median (IQR)	7 (5-10)	5.5 (4-9)	**0.027**

Polytherapy, n (%)	157 (80.1)	24 (57.1)	**0.002**
Hyperpolytherapy, n (%)	39 (19.9)	8 (19.0)	0.900
Functional autonomy			
Barthel Index, median (IQR)	75 (40-95)	55 (35-85)	**0.011**
Barthel Index disability level, n (%)			**0.005**
- None	39 (19.9)	0 (0)	
- Mild	19 (9.7)	1 (2.4)	
- Moderate	56 (28.6)	15 (35.7)	
- Severe	51 (26.0)	20 (47.6)	
- Extremely severe	31 (15.8)	6 (14.3)	
IADL (n. of functions kept), median (IQR)	3 (1-6)	1 (1-3)	**0.001**
IADL autonomy category, n (%)			**0.001**
- Autonomous	55 (28.1)	3 (7.1)	
- Partially autonomous	53 (27.0)	9 (21.4)	
- Non autonomous	88 (44.9)	30 (71.4)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (1-4)	3.5 (2-5)	**0.004**
Cognitive impairment SPMSQ, n(%)*			**0.003**
- None	107 (55.4)	13 (31.0)	
- Mild	46 (23.8)	12 (28.6)	
- Moderate	23 (11.9)	12 (28.6)	
- Severe	17 (8.8)	5 (11.9)	
Confused, wandering behavior	22 (11.2)	10 (23.8)	**0.030**
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	6 (3-11)	0.823
Anxiety levels at HADS, n (%)†			0.510
- Normal	111 (63.8)	21 (61.8)	
- Borderline	38 (21.8)	4 (11.8)	
- Abnormal	25 (14.4)	9 (26.5)	
HADS depression, median (IQR)†	8 (5-11)	9 (6-13)	0.347
Depression levels at HADS, n (%)†			0.103
- Normal	79 (45.4)	12 (35.3)	
- Borderline	43 (24.7)	6 (17.6)	
- Abnormal	52 (29.9)	16 (47.1)	
Sensory impairment/balance			
Vision impairment, n (%)*			0.073
- None	42 (21.4)	15 (35.7)	
- Present, moderate	129 (65.8)	23 (54.8)	
- Present, severe	25 (12.8)	4 (9.5)	
Hearing impairment, n (%)*			0.778
- None	99 (50.5)	22 (52.4)	
- Present, moderate	75 (38.3)	16 (38.1)	
- Present, severe	22 (11.2)	4 (9.5)	
History of falls in the previous year, n (%)	69 (35.2)	22 (52.4)	**0.038**
Number of falls in the previous year, median (IQR)	0 (0-1)	1 (0-1)	**0.042**
Nutrition			
MNA score, median (IQR)‡	19.5 (16-23)	17 (14-20)	**0.013**
Malnutrition risk at MNA, n (%)‡			**0.012**
- Normal	37 (20.6)	1 (2.7)	
- At risk	83 (46.1)	18 (48.6)	
- Malnourished	60 (33.3)	18 (48.6)	
Weight loss in the past 12 mo, n (%)*	84 (42.9)	20 (47.6)	0.572
Frailty assessment			
Fried Frailty Phenotype			
Frailty status according to FFP**			0.055
- Robust, n (%)	0 (0)	0 (0)	
- Pre-frail, n(%)	24 (13.7)	1 (2.6)	
- Frail, n (%)	151 (86.3)	37 (97.4)	

Clinical Frailty Scale			
CFS score, median (IQR)	5 (4-7)	6 (5-7)	**0.003**
Frail according to CFS ≥5, (%)	118 (60.2)	36 (85.7)	**0.002**
Frailty severity according to CFS			**0.005**
- No frailty (CFS 1-4), n (%)	78 (39.8)	6 (14.3)	
- Moderate frailty (CFS 5/6), n (%)	64 (32.7)	19 (45.2)	
- Severe frailty (CFS≥7), n (%)	54 (27.6)	17 (40.5)	
Frailty index			
FI, median (IQR)	0.41 (0.28-0.58)	0.28 (0.58-0)	**0.001**
Items evaluated at FI, mean±SD	39.0±1.25	38.5±1.67	**0.016**
Frail according to FI≥0.25, n (%)	160 (81.6)	42 (100)	**0.003**
Frailty severity according to FI			**0.001**
- No frailty (FI <0.25), n (%)	36 (18.4)	0 (0)	
- Moderate frailty (0.25-0.44), n (%)	74 (37.8)	13 (31)	
- Severe frailty (FI≥0.45), n (%)	86 (43.9)	29 (69)	
Multidimensional Prognostic Index			
MPI score, median (IQR)††	0.44 (0.31-0.63)	0.31 (0.63-0)	**0.004**
Frailty status according to MPI††			**0.007**
- MPI low risk, n (%)	47 (26.3)	5 (13.5)	
- MPI medium risk, n (%)	93 (52.0)	16 (43.2)	
- MPI high risk = frail, n (%)	39 (21.8)	16 (43.2)	
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	10 (6-18)	12 (9-21)	**0.041**
Any hospital-acquired complication, n (%)	41 (20.9)	17 (40.5)	**0.007**
Delirium during admission, n (%)	13 (6.6)	8 (19)	**0.017**
- Requiring use of medication	1 (84.6)	8 (100)	0.515
Fall during admission, n (%)	3 (1.5)	3 (7.1)	0.070
Pressure injury development during admission, n (%)	11 (5.6)	4 (9.5)	0.311
Healthcare-associated infection during admission, n (%)	24 (12.2)	7 (16.7)	0.440
Setting of discharge, n (%)			**<0.001**
- At home	182 (92.9)	15 (35.7)	
- MLTCF	10 (5.1)	27 (64.3)	
- ED	4 (2.0)	0 (0)	
Outcomes at 6 months from discharge			
Length of follow-up (days), median (IQR)	184 (177-193)	171.5 (30-190)	0.001
ED visit or unplanned rehospitalization, n(%)	60 (30.6)	13 (31)	0.965
N. of ED visits or unplanned rehospitalizations, n (%)			0.425
- 1	45 (23.0)	7 (16.7)	
- 2	8 (4.1)	4 (9.5)	
- 3 or more	7 (3.6)	2 (4.8)	
Worsening functional status at Barthel Index, n (%)‡‡	83 (42.3)	17 (73.9)	**0.004**
BI at follow-up, median (IQR) ‡‡	60 (30-90)	20 (10-35)	**<0.001**
BI difference from baseline, median (IQR) ‡‡	0 (-15-0)	-45 (-25--5)	**0.001**

*Missing values <5%
†Missing values for 30 (12.6%) subjects
‡Missing values for 21 (8.8%) subjects
** Missing values for 25 (10.5%) subjects
†† Missing values for 22 (9.2%) subjects
‡‡ Missing values for 19 subjects dead at follow up after institutionalization

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BPSD = behavioral and psychological symptoms of dementia, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional

Prognostic Index, NEWS2= National Early Warning Score 2, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack.

Supplementary Table S15 – Comparison of selected clinical variables in patients alive and without Emergency Department visits or unplanned rehospitalizations and in patients with at least one Emergency Department visit or unplanned rehospitalization at 6 months from discharge.

	Alive and without ED visit or rehospitalization at follow-up (n=152)	**At least one ED visit or rehospitalization at follow-up (n=98)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	86 (80.5-90)	84.5 (80-90)	0.899
Female sex, n (%)	86 (56.6)	50 (51)	0.389
HaH setting, n (%)	45 (29.6)	37 (37.8)	0.180
- AA-HaH/ESD-HaH, n (%)	32 (71.1)/13 (28.9)	25 (67.6)/12 (32.4)	0.729
Presence of a caregiver, n (%)	75 (49.3)	54 (55.1)	0.374
Continuous 24/7 caregiving, n (%)	50 (32.9)	37 (37.8)	0.431
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	79 (52)	64 (65.3)	**0.038**
N. of hospital admissions in the preceding 3 months, n (%)			**0.014**
- 1	57 (37.5)	37 (37.8)	
- 2	12 (7.9)	22 (22.4)	
- 3	7 (4.6)	4 (4.1)	
- 4 or more	3 (2.0)	1 (1.0)	
Site of admission, n (%)			0.502
- General Practitioner	10 (6.6)	4 (4.1)	
- ED	126 (82.9)	80 (81.6)	
- Other hospital ward	16 (10.5)	14 (14.3)	
Reason of admission, n (%)			**0.229**
- Respiratory tract infection	36 (23.7)	14 (14.3)	
- Decompensated heart failure	16 (10.5)	5 (5.1)	
- Fluid and electrolyte imbalance	12 (7.9)	11 (11.2)	
- Infection (other)	20 (13.2)	22 (22.4)	
- Urinary tract infection	10 (6.6)	4 (4.1)	
- Anemia/bleeding	16 (10.5)	12 (12.2)	
- Stroke/TIA	11 (7.2)	5 (5.1)	
- Uncontrolled BPSD	6 (3.9)	4 (4.1)	
- Other	25 (16.4)	21 (21.4)	
NEWS2 score, median (IQR)	1 (1-3)	2 (1-3)	0.216
NEWS2 score risk, n (%)			0.130
- Low risk	121 (79.6)	69 (70.4)	
- Low-medium risk	11 (7.2)	14 (14.3)	
- Medium risk	14 (9.2)	10 (10.2)	
- High risk	6 (3.9)	5 (5.1)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-6)	5 (4-6)	0.972
CIRS-SI, median (IQR)	2.08 (1.92-2.31)	1.92 (2.31-0)	0.110
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	92 (60.5)	63 (64.3)	0.550
Hypertension, n (%)	126 (82.9)	76 (77.6)	0.295
Vascular and hematopoietic, n(%)	69 (45.4)	50 (51.0)	0.385
Respiratory, n (%)	53 (34.9)	31 (31.6)	0.597
Eyes,ears,nose,throat,larynx, n(%)	58 (38.2)	38 (38.8)	0.922
Upper gastrointestinal, n (%)	33 (21.7)	25 (25.5)	0.487
Lower gastrointestinal, n (%)	25 (16.4)	22 (22.4)	0.236
Liver, pancreas and biliary, n (%)	5 (3.3)	6 (6.1)	0.349

Renal, n (%)*	80 (52.6)	55 (56.1)	0.589
Genitourinary, n (%)	48 (31.6)	30 (30.6)	0.872
Musculoskeletal and skin, n (%)	64 (42.1)	42 (42.9)	0.907
Neurologic, n (%)	56 (36.8)	32 (32.7)	0.498
Endocrine and breast, n (%)	101 (66.4)	61 (62.2)	0.497
Psychiatric (incl. dementia), n (%)	61 (40.1)	37 (37.8)	0.707
Drug burden			
Drugs at admission, median (IQR)	7 (4.5-10)	8 (5-10)	0.180
Polytherapy, n (%)	114 (75.0)	82 (83.7)	0.104
Hyperpolytherapy, n (%)	30 (19.7)	20 (20.4)	0.897
Functional autonomy			
Barthel Index, median (IQR)	70 (35-95)	65 (40-90)	0.622
Barthel Index disability level, n (%)			0.688
- None	28 (18.4)	14 (14.3)	
- Mild	12 (7.9)	8 (8.2)	
- Moderate	43 (28.3)	28 (28.6)	
- Severe	42 (27.6)	34 (34.7)	
- Extremely severe	27 (17.8)	14 (14.3)	
IADL (n. of functions kept), median (IQR)	3 (1-6)	2 (1-4)	0.264
IADL autonomy category, n (%)			0.194
- Autonomous	39 (25.7)	22 (22.4)	
- Partially autonomous	44 (28.9)	22 (22.4)	
- Non autonomous	69 (45.4)	54 (55.1)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (1-4)	3 (1-4)	**0.032**
Cognitive impairment SPMSQ, n(%)*			0.063
- None	89 (59.7)	43 (44.3)	
- Mild	27 (18.1)	30 (30.9)	
- Moderate	19 (12.8)	15 (15.5)	
- Severe	14 (9.4)	9 (9.3)	
Confused, wandering behavior	13 (8.6)	16 (16.3)	0.061
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	7 (4-9)	0.395
Anxiety levels at HADS, n (%)†			0.376
- Normal	89 (65.9)	50 (59.5)	
- Borderline	26 (19.3)	20 (23.8)	
- Abnormal	20 (14.8)	14 (16.7)	
HADS depression, median (IQR)†	8 (5-11)	10 (6-13)	**0.023**
Depression levels at HADS, n (%)†			**0.034**
- Normal	62 (45.9)	30 (35.7)	
- Borderline	35 (25.9)	17 (20.2)	
- Abnormal	38 (28.1)	37 (44)	
Sensory impairment/balance			
Vision impairment, n (%)*			0.716
- None	39 (25.7)	18 (18.4)	
- Present, moderate	91 (59.9)	71 (72.4)	
- Present, severe	22 (14.5)	9 (9.2)	
Hearing impairment, n (%)*			0.960
- None	77 (50.7)	50 (51.0)	
- Present, moderate	60 (39.5)	37 (37.8)	
- Present, severe	15 (9.9)	11 (11.2)	
History of falls in the previous year, n (%)	54 (35.5)	41 (41.8)	0.316
Number of falls in the previous year, median (IQR)	0 (0-1)	0 (0-1)	0.281
Nutrition			
MNA score, median (IQR)‡	19.5 (15.5-23)	17.5 (14-21)	**0.024**
Malnutrition risk at MNA, n (%)‡			**0.034**
- Normal	30 (21.4)	10 (11.6)	
- At risk	64 (45.7)	38 (44.2)	
- Malnourished	46 (32.9)	38 (44.2)	

Weight loss in the past 12 mo, n (%)*	61 (40.1)	48 (49)	0.168
Frailty assessment			
Fried Frailty Phenotype			
Frailty status according to FFP**			0.359
- Robust, n (%)	0 (0)	0 (0)	
- Pre-frail, n(%)	19 (14.3)	9 (10.1)	
- Frail, n (%)	114 (85.7)	80 (89.9)	
Clinical Frailty Scale			
CFS score, median (IQR)	5 (4-7)	6 (4-7)	0.243
Frail according to CFS ≥5, (%)	94 (61.8)	68 (69.4)	0.223
Frailty severity according to CFS			0.365
- No frailty (CFS 1-4), n (%)	58 (38.2)	30 (30.6)	
- Moderate frailty (CFS 5/6), n (%)	50 (32.9)	38 (38.8)	
- Severe frailty (CFS≥7), n (%)	44 (28.9)	30 (30.6)	
Frailty index			
FI, median (IQR)	0.42 (0.28-0.58)	0.28 (0.58-0)	0.197
Items evaluated at FI, mean±SD	39.0±1.28	38.8±1.41	0.143
Frail according to FI≥0.25, n (%)	127 (83.6)	85 (86.7)	0.494
Frailty severity according to FI			0.250
- No frailty (FI <0.25), n (%)	25 (16.4)	13 (13.3)	
- Moderate frailty (0.25-0.44), n (%)	56 (36.8)	32 (32.7)	
- Severe frailty (FI≥0.45), n (%)	71 (46.7)	53 (54.1)	
Multidimensional Prognostic Index			
MPI score, median (IQR)††	0.5 (0.38-0.63)	0.38 (0.63-0)	0.493
Frailty status according to MPI††			0.807
- MPI low risk, n (%)	33 (23.7)	21 (24.4)	
- MPI medium risk, n (%)	73 (52.5)	42 (48.8)	
- MPI high risk = frail, n (%)	33 (23.7)	23 (26.7)	
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	10 (6-19)	12 (7-20)	0.296
Any hospital-acquired complication, n (%)	41 (27.0)	20 (20.4)	0.238
Delirium during admission, n (%)	17 (11.2)	6 (6.1)	0.176
- Requiring use of medication	15 (88.2)	6 (100.0)	1.000
Fall during admission, n (%)	2 (1.3)	6 (6.1)	0.060
Pressure injury development during admission, n (%)	10 (6.6)	3 (3.1)	0.221
Healthcare-associated infection during admission, n (%)	24 (15.8)	11 (11.2)	0.310
Setting of discharge, n (%)			0.366
- At home	134 (88.2)	83 (84.7)	
- MLTCF	16 (10.5)	11 (11.2)	
- ED	2 (1.3)	4 (4.1)	
Outcomes at 6 months from discharge			
Length of follow-up (days), median (IQR)	183.5 (179-194.5)	182 (151-189)	0.001
Institutionalization at follow-up, n (%)	16 (10.5)	13 (13.3)	0.509
Worsening functional status at Barthel Index, n (%)‡‡	64 (42.1)	36 (53.7)	0.111
BI at follow-up, median (IQR)‡‡	60 (25-90)	50 (25-85)	0.394
BI difference from baseline, median (IQR)‡‡	0 (-19-0)	-10 (-20-0)	**0.049**

*Missing values <5%
†Missing values for 31 (12.4%) subjects
‡Missing values for 24 (9.6%) subjects
** Missing values for 28 (11.2%) subjects
†† Missing values for 25 (10.0%) subjects
‡‡ Missing values for 31 subjects dead at follow up after ED visit or unplanned rehospitalization

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BPSD = behavioral and psychological symptoms of dementia, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness

Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, NEWS2= National Early Warning Score 2, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack.

Supplementary Table S16 – Comparison of selected clinical variables in patients alive and without worsening of functional status and in patients alive and with worsening functional status at 6 months from discharge.

	Alive and without worsening BI at follow-up (n=119)	**Alive and with worsening BI at follow-up (n=100)**	***P***
Sociodemographic variables			
Age (years), median (IQR)	85 (79-90)	87 (83-90)	0.056
Female sex, n (%)	66 (55.5)	58 (58.0)	0.706
HaH setting, n (%)	41 (34.5)	32 (32.0)	0.701
- AA-HaH/ESD-HaH, n (%)	29 (70.7)/12 (29.3)	21 (65.6)/11 (34.4)	0.641
Presence of a caregiver, n (%)	59 (49.6)	53 (53.0)	0.614
Continuous 24/7 caregiving, n (%)	43 (36.1)	34 (34.0)	0.742
Hospital admission variables			
At least one hospital admission in the preceding 3 months, n (%)	70 (58.8)	51 (51.0)	0.246
Site of admission, n (%)			0.352
- General Practitioner	5 (4.2)	9 (9.0)	
- Emergency Department	99 (83.2)	79 (79.0)	
- Other hospital ward	15 (12.6)	12 (12.0)	
Reason of admission, n (%)			0.632
- Respiratory tract infection	27 (22.7)	20 (20.0)	
- Decompensated heart failure	11 (9.2)	8 (8.0)	
- Fluid and electrolyte imbalance	14 (11.8)	6 (6.0)	
- Infection (other)	21 (17.6)	15 (15.0)	
- Urinary tract infection	6 (5.0)	6 (6.0)	
- Anemia/bleeding	13 (10.9)	11 (11.0)	
- Stroke/TIA	8 (6.7)	8 (8.0)	
- Uncontrolled BPSD	3 (2.5)	7 (7.0)	
- Other	16 (13.4)	19 (19.0)	
NEWS2 score, median (IQR)	1 (1-3)	2 (1-4)	0.205
NEWS2 score risk, n (%)			0.187
- Low risk	96 (80.7)	73 (73.0)	
- Low-medium risk	9 (7.6)	12 (12.0)	
- Medium risk	11 (9.2)	10 (10.0)	
- High risk	3 (2.5)	5 (5.0)	
Comprehensive Geriatric Assessment variables			
Comorbidity burden			
CIRS-CI, median (IQR)	5 (4-7)	5 (4-6)	0.831
CIRS-SI, median (IQR)	2.15 (1.92-2.31)	1.92 (2.31-0)	0.426
Clinically significant comorbidities according to CIRS score ≥3			
Cardiac, n (%)	73 (61.3)	62 (62.0)	0.921
Hypertension, n (%)	101 (84.9)	81 (81.0)	0.446
Vascular and hematopoietic, n(%)	58 (48.7)	42 (42.0)	0.319
Respiratory, n (%)	34 (28.6)	39 (39.0)	0.103
Eyes,ears,nose,throat,larynx, n(%)	42 (35.3)	45 (45.0)	0.144
Upper gastrointestinal, n (%)	24 (20.2)	25 (25.0)	0.393
Lower gastrointestinal, n (%)	25 (21.0)	13 (13.0)	0.119
Liver, pancreas and biliary, n (%)	0 (0)	9 (9.0)	**<0.001**
Renal, n (%)*	60 (50.4)	57 (57.0)	0.331
Genitourinary, n (%)	41 (34.5)	26 (26.0)	0.176
Musculoskeletal and skin, n (%)	51 (42.9)	42 (42.0)	0.898
Neurologic, n (%)	44 (37.0)	33 (33.0)	0.539
Endocrine and breast, n (%)	80 (67.2)	64 (64.0)	0.616
Psychiatric (incl. dementia), n (%)	43 (36.1)	45 (45.0)	0.183

Drug burden			
Drugs at admission, median (IQR)	7 (5-10)	7 (5-10)	0.993
Polytherapy, n (%)	92 (77.3)	79 (79.0)	0.763
Hyperpolytherapy, n (%)	24 (20.2)	19 (19.0)	0.828
Functional autonomy			
Barthel Index, median (IQR)	75 (35-100)	67.5 (45-85)	0.078
Barthel Index disability level, n (%)			0.062
- None	32 (26.9)	7 (7.0)	
- Mild	12 (10.1)	7 (7.0)	
- Moderate	24 (20.2)	39 (39.0)	
- Severe	29 (24.4)	33 (33.0)	
- Extremely severe	22 (18.5)	14 (14.0)	
IADL (n. of functions kept), median (IQR)	3 (1-7)	2 (1-4)	**0.011**
IADL autonomy category, n (%)			**0.003**
- Autonomous	40 (33.6)	16 (16.0)	
- Partially autonomous	31 (26.1)	27 (27.0)	
- Non autonomous	48 (40.3)	57 (57.0)	
Cognitive impairment			
SPMSQ (n. of errors), median (IQR)*	2 (0-4)	3 (1-5)	0.070
Cognitive impairment SPMSQ, n(%)*			0.090
- None	68 (58.1)	47 (47.5)	
- Mild	25 (21.4)	24 (24.2)	
- Moderate	15 (12.8)	15 (15.2)	
- Severe	9 (7.7)	13 (13.1)	
Confused, wandering behavior	9 (7.6)	18 (18.0)	**0.019**
Mood status			
HADS anxiety, median (IQR)†	6 (4-9)	6 (4-9)	0.951
Anxiety levels at HADS, n (%)†			0.737
- Normal	66 (61.7)	56 (65.1)	
- Borderline	25 (23.4)	16 (18.6)	
- Abnormal	16 (15.0)	14 (16.3)	
HADS depression, median (IQR)†	8 (5-11)	9 (5-13)	0.110
Depression levels at HADS, n (%)†			0.104
- Normal	51 (47.7)	35 (40.7)	
- Borderline	29 (27.1)	17 (19.8)	
- Abnormal	27 (25.2)	34 (39.5)	
Sensory impairment/balance			
Vision impairment, n (%)*			0.318
- None	27 (22.7)	22 (22)	
- Present, moderate	81 (68.1)	61 (61.0)	
- Present, severe	11 (9.2)	17 (17.0)	
Hearing impairment, n (%)*			0.851
- None	60 (50.4)	50 (50.0)	
- Present, moderate	47 (39.5)	38 (38.0)	
- Present, severe	12 (10.1)	12 (12.0)	
History of falls in the previous year, n (%)	42 (35.3)	39 (39)	0.571
Number of falls in the previous year, median (IQR)	0 (0-1)	0 (0-1)	0.654
Physical performance and activity levels			
Best handgrip (kg), median (IQR)*	17.3 (11.3-23.3)	12.5 (8.03-18.0)	**<0.001**
Best handgrip (kg), males; median (IQR)*	23.0 (18.4-31.3)	17.9 (12.8-22.2(	**<0.001**
Best handgrip (kg), females; median (IQR)*	12.3 (9.4-17.1)	10.4 (6.9-14.0)	**0.020**
Weakness at handgrip (FFP), n (%)	92 (77.3)	94 (94.0)	**<0.001**
Unable to perform gait speed, n (%)	29	29	
Gait speed (m/s), median (IQR)‡	0.58 (0.46-0.8)	0.51 (0.4-0.65)	0.277
Low gait speed (FFP), n (%)‡	42/61 (68.9)	38/47 (80.9)	0.158
Low gait speed or unable, n (%)**	71/90 (78.9)	67/76 (88.2)	0.112
PASE score, median (IQR)	40.3 (0-75.8)	25.0 (0-56.3)	**0.008**
Low activity levels at PASE, n (%)	77 (64.7)	75 (75.0)	0.100
Physical exhaustion, n (%)	90 (75.6)	77 (77.0)	0.812

Nutrition			
MNA score, median (IQR)[††]	20 (16-23.5)	18 (15.5-22)	0.11
Malnutrition risk at MNA, n (%)[††]			0.056
- Normal	26 (23.9)	12 (13.2)	
- At risk	50 (45.9)	43 (47.3)	
- Malnourished	33 (30.3)	36 (39.6)	
Weight loss in the past 12 mo, n (%)[*]	47 (39.5)	44 (44.0)	0.500
Frailty assessment			
Fried Frailty Phenotype			
Frailty status according to FFP[‡‡]			0.136
- Robust, n (%)	0 (0)	0 (0)	
- Pre-frail, n(%)	17 (16.2)	8 (9.0)	
- Frail, n (%)	88 (83.8)	81 (91.0)	
Clinical Frailty Scale			
CFS score, median (IQR)	5 (3-7)	6 (4-7)	**0.006**
Frail according to CFS ≥5, (%)	63 (52.9)	74 (74)	**0.001**
Frailty severity according to CFS			**0.017**
- No frailty (CFS 1-4), n (%)	56 (47.1)	26 (26.0)	
- Moderate frailty (CFS 5/6), n (%)	31 (26.1)	43 (43.0)	
- Severe frailty (CFS≥7), n (%)	32 (26.9)	31 (31.0)	
Frailty index			
FI, median (IQR)	0.38 (0.25-0.61)	0.25 (0.61-0)	**0.025**
Items evaluated at FI, mean±SD	39.0±1.37	38.9±1.24	0.338
Frail according to FI≥0.25, n (%)	89 (74.8)	94 (94.0)	**<0.001**
Frailty severity according to FI			**0.010**
- No frailty (FI <0.25), n (%)	30 (25.2)	6 (6.0)	
- Moderate frailty (0.25-0.44), n (%)	38 (31.9)	41 (41.0)	
- Severe frailty (FI≥0.45), n (%)	51 (42.9)	53 (53.0)	
Multidimensional Prognostic Index			
MPI score, median (IQR)[***]	0.44 (0.31-0.63)	0.31 (0.63-0)	0.170
Frailty status according to MPI[***]			0.153
- MPI low risk, n (%)	29 (26.9)	19 (20.9)	
- MPI medium risk, n (%)	57 (52.8)	46 (50.5)	
- MPI high risk = frail, n (%)	22 (20.4)	26 (28.6)	
Outcomes at discharge			
Length of hospital stay (days), median (IQR)	10 (6-19)	11 (7-17.5)	0.430
Any hospital-acquired complication, n (%)	28 (23.5)	23 (23.0)	0.926
Delirium during admission, n (%)	8 (6.7)	9 (9.0)	0.530
- Requiring use of medication	7 (87.5)	8 (88.9)	1.000
Fall during admission, n (%)	2 (1.7)	3 (3.0)	0.662
Pressure injury development during admission, n (%)	8 (6.7)	5 (5.0)	0.591
Healthcare-associated infection during admission, n (%)	15 (12.6)	14 (14.0)	0.762
Setting of discharge, n (%)			**0.004**
- At home	112 (94.1)	83 (83.0)	
- MLTCF	4 (3.4)	16 (16.0)	
- ED	3 (2.5)	1 (1.0)	
Outcomes at 6 months from discharge			
Length of follow-up (days), median (IQR)	184 (180-198)	183 (177-191.5)	0.300
Institutionalization at follow-up, n (%)	6 (5.0)	17 (17.0)	**0.004**
ED visit/unplanned rehospitalization at follow-up, n (%)	31 (26.1)	36 (36.0)	0.111
BI at follow-up, median (IQR)	80 (45-95)	35 (11-59)	**<0.001**
BI difference from baseline, median (IQR)	0 (0-5)	-20 (-39--10)	**<0.001**

*Missing values <5%
†Missing values for 26 (11.9%) subjects
‡Missing values for 111 (50.7%) subjects
**Missing values for 53 (24.2%) subjects
††Missing values for 19 (8.7%) subjects
‡‡Missing values for 25 (11.4%) subjects
***Missing values for 20 (9.1%) subjects

Abbreviations: AA-HaH = Admission Avoidance Hospital-at-Home, ADL = Activities of Daily Living, BPSD = behavioral and psychological symptoms of dementia, CFS = Clinical Frailty Scale, CIRS = Cumulative Illness Rating Scale, CIRS-CI = Cumulative Illness Rating Scale Comorbidity Index, CIRS-SI = Cumulative Illness Rating Scale Severity Index, IADL = Instrumental Activities of Daily Living, ED = Emergency Department, ESD-HaH = Early Supported Discharge Hospital-at-Home, FFP = Fried Frailty Phenotype, FI = Frailty Index, HADS = Hospital Anxiety and Depression Scale, HaH = Hospital-at-Home, IQR = interquartile range, MLTCF = Medium- or Long-Term Care Facility, MNA = Mini Nutritional Assessment, mo = months, MPI = Multidimensional Prognostic Index, NEWS2= National Early Warning Score 2, SD = standard deviation, SPMSQ = Short Portable Mental Status Questionnaire, TIA = Transient Ischemic Attack.

S3 - Analyses on outcomes at 6 months from discharge considering death as a competing event

Supplementary Table S17 – Variables associated with institutionalization at 6 months from discharge in patients discharged alive with competitive risk of mortality – multinomial logistic regression analyses with different frailty definitions. Results are presented after multiple imputation for missing values for the Fried Frailty Phenotype and the Multidimensional Prognostic Index.

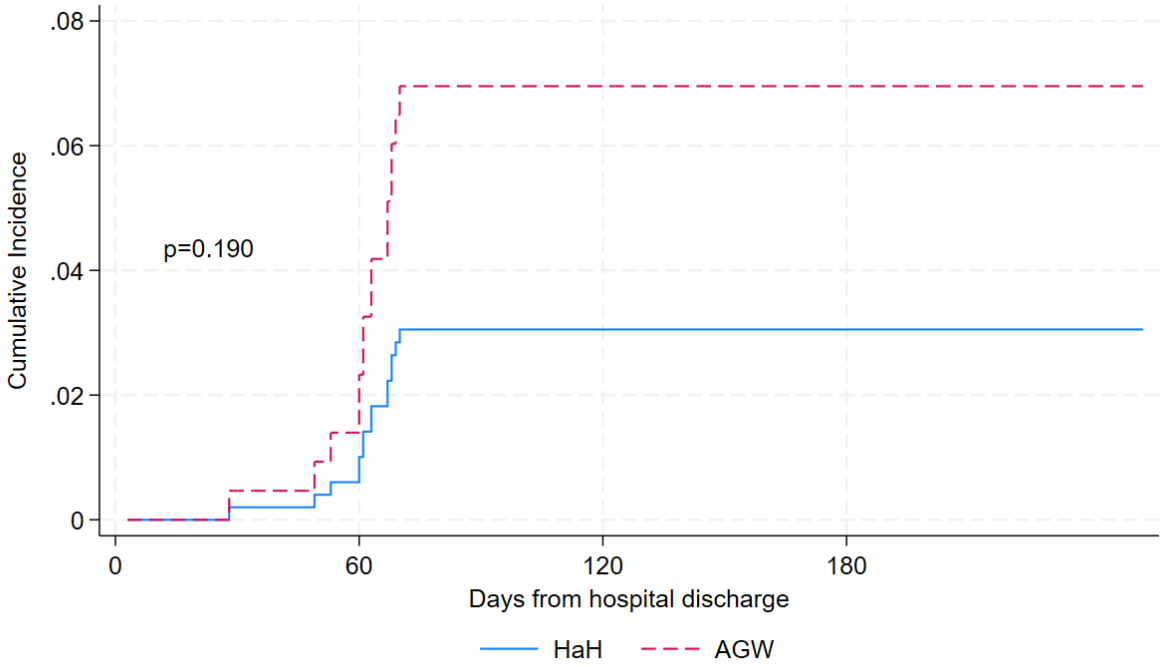
	Institutionalized at follow-up (n=42) vs Alive and living at home at follow-up (n=196)		**Dead without previous institutionalization (n=42) vs Alive and living at home at follow-up (n=42)**	
Fried Frailty Phenotype (FFP)*				
Variable	**aOR (95% CI)**	**P value**	**aOR (95% CI)**	**P value**
Model 1				
Frail according to FFP	1.6 (0.85-2.99)	0.1418	1.17 (0.71-1.95)	0.5367
HaH vs AGW setting	**0.37 (0.2-0.67)**	**0.0011**	1.21 (0.86-1.7)	0.2681
Model 2				
Frail according to FFP	1.29 (0.65-2.54)	0.4629	0.99 (0.57-1.73)	0.9819
HaH vs AGW setting	**0.29 (0.15-0.56)**	**0.0003**	1.02 (0.66-1.58)	0.9194
Age, years	1 (0.94-1.06)	0.9602	0.96 (0.91-1.01)	0.1216
Female sex	1.15 (0.78-1.68)	0.4764	**0.67 (0.47-0.97)**	**0.0323**
CIRS-CI	1.02 (0.82-1.27)	0.8628	0.97 (0.79-1.19)	0.7501
SPMSQ, errors	1.09 (0.92-1.28)	0.3179	0.99 (0.85-1.14)	0.8435
Barthel Index	0.99 (0.97-1.00)	0.1221	**0.98 (0.97-0.99)**	**0.0156**
Caregiver <24h vs no caregiver	1.63 (0.91-2.93)	0.1005	1.28 (0.70-2.34)	0.4138
Caregiver 24/7 vs no caregiver	0.83 (0.43-1.59)	0.5676	0.95 (0.53-1.7)	0.8548
Any hospital-acquired complication	1.30 (0.88-1.93)	0.1860	1.26 (0.85-1.87)	0.2494
Clinical Frailty Scale (CFS)				
Model 1				
Frail according to CFS	**5.57 (2.2-14.1)**	**0.0003**	**3.84 (1.52-9.73)**	**0.0045**
HaH vs AGW setting	**0.10 (0.03-0.34)**	**0.0002**	1.13 (0.56-2.27)	0.7383
Model 2				
Frail according to CFS	**3.36 (1.10-10.20)**	**0.0328**	**3.59 (1.18-10.89)**	**0.0243**
HaH vs AGW setting	**0.09 (0.02-0.32)**	**0.0003**	1.07 (0.44-2.6)	0.8845
Age, years	0.99 (0.94-1.06)	0.8816	0.95 (0.90—1.01)	0.0769
Female sex	1.25 (0.57-2.70)	0.5788	**0.42 (0.20-0.88)**	**0.0218**
CIRS-CI	1.01 (0.81-1.26)	0.9417	0.95 (0.77-1.17)	0.6221
SPMSQ, errors	1.07 (0.91-1.27)	0.3915	0.99 (0.85-1.14)	0.8684
Barthel Index	0.99 (0.98-1.01)	0.5767	0.99 (0.98-1.01)	0.2343
Caregiver <24h vs no caregiver	2.01 (0.77-5.25)	0.1673	1.40 (0.48-4.10)	0.5090
Caregiver 24/7 vs no caregiver	1.15 (0.39-3.39)	0.6811	1.07 (0.37-3.06)	0.8182
Any hospital-acquired complication	1.65 (0.74-3.67)	0.2174	1.46 (0.66-3.23)	0.3500

	ED visit/readmission (n=98) vs Alive and free from ED visit/readmission (n=152)		Dead without previous ED visit/readmission (n=30) vs alive and free from ED visit/readmission (n=152)	
Frailty Index				
Model 1				
Frail according to FI	-†	0.9614	**4.36 (1.01-18.91)**	**0.0493**
HaH vs AGW setting	**0.13 (0.04-0.44)**	**0.0010**	1.41 (0.72-2.79)	0.3199
Model 2				
Frail according to FI	-†	0.9620	3.31 (0.66-16.67)	0.1475
HaH vs AGW setting	**0.09 (0.03-0.35)**	**0.0004**	1.18 (0.48-2.88)	0.7155
Age, years	1 (0.94-1.06)	0.9665	0.96 (0.91-1.01)	0.0894
Female sex	1.30 (0.61-2.80)	0.4989	**0.45 (0.21-0.92)**	**0.0299**
CIRS-CI	1.01 (0.81-1.25)	0.9618	0.95 (0.78-1.16)	0.6125
SPMSQ, errors	1.08 (0.91-1.27)	0.3820	0.98 (0.85-1.14)	0.8141
Barthel Index	0.99 (0.98-1.01)	0.2776	0.99 (0.97-1.00)	0.0608
Caregiver <24h vs no caregiver	1.93 (0.75-4.94)	0.1580	1.39 (0.48-4.03)	0.5201
Caregiver 24/7 vs no caregiver	1.06 (0.37-3.05)	0.5825	1.08 (0.38-3.05)	0.8367
Any hospital-acquired complication	1.68 (0.76-3.71)	0.1983	1.53 (0.7-3.36)	0.2922
Multidimensional Prognostic Index*				
Model 1				
Frail according to MPI	**1.94 (1.33-2.83)**	**0.0006**	1.37 (0.93-2.02)	0.1155
HaH vs AGW setting	**0.32 (0.17-0.59)**	**0.0003**	1.14 (0.80-1.62)	0.4695
Model 2				
Frail according to MPI	1.26 (0.68-2.35)	0.4613	0.89 (0.47-1.66)	0.7101
HaH vs AGW setting	**0.29 (0.15-0.56)**	**0.0003**	1.02 (0.66-1.58)	0.9143
Age, years	1.01 (0.95-1.07)	0.8362	0.96 (0.91-1.01)	0.1134
Female sex	1.16 (0.79-1.69)	0.4583	**0.67 (0.47-0.97)**	**0.0338**
CIRS-CI	1.01 (0.81-1.26)	0.9248	0.97 (0.79-1.19)	0.7901
SPMSQ, errors	1.06 (0.89-1.26)	0.5396	0.99 (0.85-1.17)	0.9754
Barthel Index	0.99 (0.97-1.01)	0.3309	**0.98 (0.96-0.99)**	**0.0277**
Caregiver <24h vs no caregiver	1.56 (0.86-2.83)	0.1448	1.30 (0.71-2.39)	0.3900
Caregiver 24/7 vs no caregiver	0.87 (0.44-1.72)	0.6975	0.93 (0.52-1.68)	0.8138
Any hospital-acquired complication	1.3 (0.87-1.93)	0.1951	1.26 (0.85-1.87)	0.2550

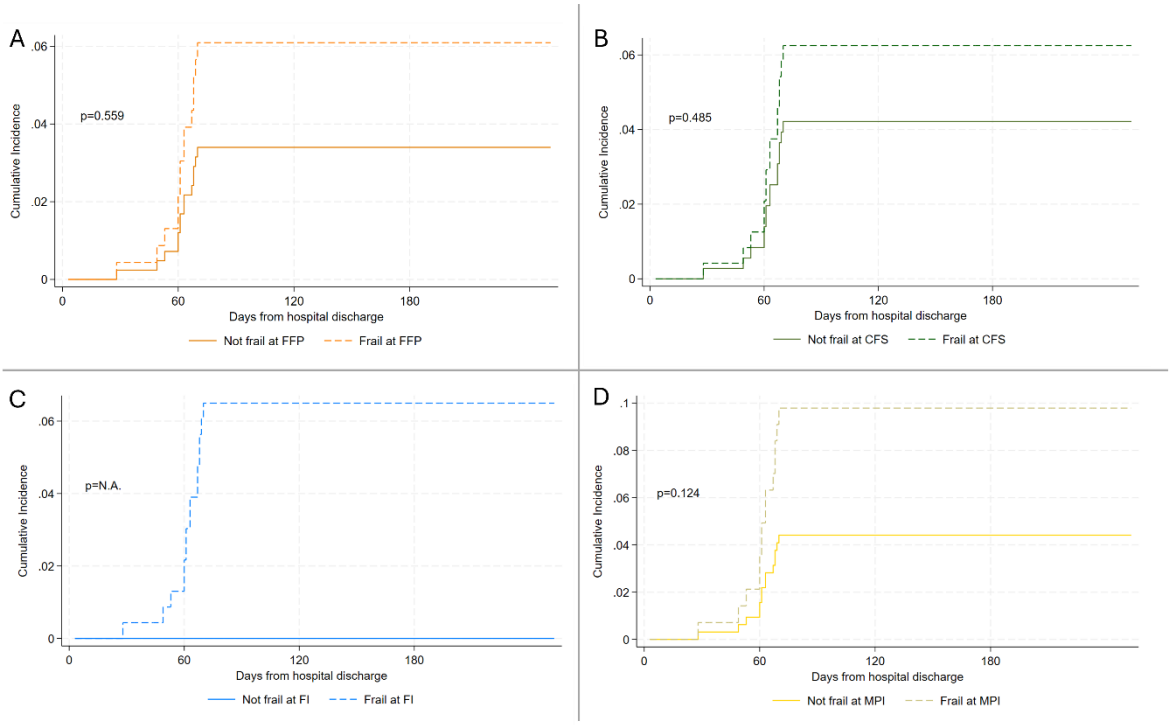
*After multiple imputation for missing values
†Unable to estimate parameter due to quasi-complete separation of data

Abbreviations: AGW = acute geriatric ward, aOR = adjusted Odds Ratio, CFS = Clinical Frailty Scale, CI = Confidence Interval, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, ED= Emergency Department, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MLTCF = medium- or long-term care facility, MPI = Multidimensional Prognostic Index, SPMSQ = Short Portable Mental Status Questionnaire

Supplementary Figure S1– Cumulative incidence curve for institutionalization at 6 months from discharge considering death as a competing event, stratified according to healthcare setting (Hospital-at-Home, HaH, or acute geriatric ward – AGW).



Supplementary Figure S2 - Cumulative incidence curves for institutionalization at 6 months from discharge considering death as a competing event, stratified according to frailty presence (dashed lines) or absence (solid lines) as defined by the Fried Frailty Phenotype (FFP, Panel A), the Clinical Frailty Scale (CFS, Panel B), the Frailty Index (FI, Panel C), or the Multidimensional Prognostic Index (MPI, Panel D).



Supplementary Table S18 – Variables associated with Emergency Department visit or unplanned readmission at 6 months from discharge in patients discharged alive with competitive risk of mortality - multinomial logistic regression analyses with different frailty definitions. Results are presented after multiple imputation for missing values for the Fried Frailty Phenotype and the Multidimensional Prognostic Index.

	ED visit/readmission (n=98) vs Alive and free from ED visit/readmission (n=152)		**Dead without previous ED visit/readmission (n=30) vs alive and free from ED visit/readmission (n=152)**	
Fried Frailty Phenotype (FFP)*				
Variable	**aOR (95% CI)**	**P value**	**aOR (95% CI)**	**P value**
Model 1				
Frail according to FFP	1.26 (0.87-1.82)	0.2259	**3.16 (1.15-8.69)**	**0.0260**
HaH vs AGW setting	1.16 (0.89-1.52)	0.2733	1.08 (0.76-1.53)	0.6850
Model 2				
Frail according to FFP	1.3 (0.87-1.93)	0.2035	2.03 (0.70-5.85)	0.1916
HaH vs AGW setting	1.18 (0.88-1.6)	0.2711	1.10 (0.66-1.85)	0.7029
Age, years	1.01 (0.97-1.06)	0.5029	1.05 (0.98-1.12)	0.1642
Female sex	0.81 (0.62-1.07)	0.1355	**0.59 (0.38-0.92)**	**0.0188**
CIRS-CI	1.02 (0.88-1.19)	0.7667	0.94 (0.74-1.20)	0.6236
SPMSQ, errors	**1.14 (1.01-1.28)**	**0.0343**	1.2 (0.99-1.43)	0.0522
Barthel Index	1.01 (0.99-1.02)	0.1795	0.99 (0.98-1.02)	0.8014
N. of hospitalizations in the last 3 months	**1.38 (1.03-1.85)**	**0.0296**	**1.62 (1.02-2.58)**	**0.0428**
Discharge to MLTCF	1.20 (0.74-1.97)	0.4603	**2.29 (1.27-4.1)**	**0.0055**
Clinical Frailty Scale (CFS)				
Model 1				
Frail according to CFS	1.31 (0.75-2.28)	0.3389	**8.83 (2.01-38.80)**	**0.0039**
HaH vs AGW setting	1.36 (0.79-2.36)	0.2718	0.89 (0.38-2.1)	0.7949
Model 2				
Frail according to CFS	1.61 (0.78-3.33)	0.2013	**7.6 (1.46-39.6)**	**0.0160**
HaH vs AGW setting	1.42 (0.78-2.59)	0.2491	1.18 (0.43-3.26)	0.7525
Age, years	1.01 (0.97-1.05)	0.7216	1.04 (0.98-1.12)	0.2193
Female sex	0.67 (0.39-1.16)	0.1536	**0.33 (0.14-0.80)**	**0.0141**
CIRS-CI	1.01 (0.87-1.18)	0.8721	0.95 (0.74-1.20)	0.6442
SPMSQ, errors	1.12 (1-1.27)	0.0529	1.19 (0.99-1.42)	0.0606
Barthel Index	1.01 (0.99-1.02)	0.1171	1.01 (0.99-1.03)	0.4999
N. of hospitalizations in the last 3 months	**1.34 (1.00-1.79)**	**0.0485**	1.58 (0.99-2.52)	0.0540
Discharge to MLTCF	1.17 (0.43-3.18)	0.7522	**4.38 (1.36-14.1)**	**0.0131**

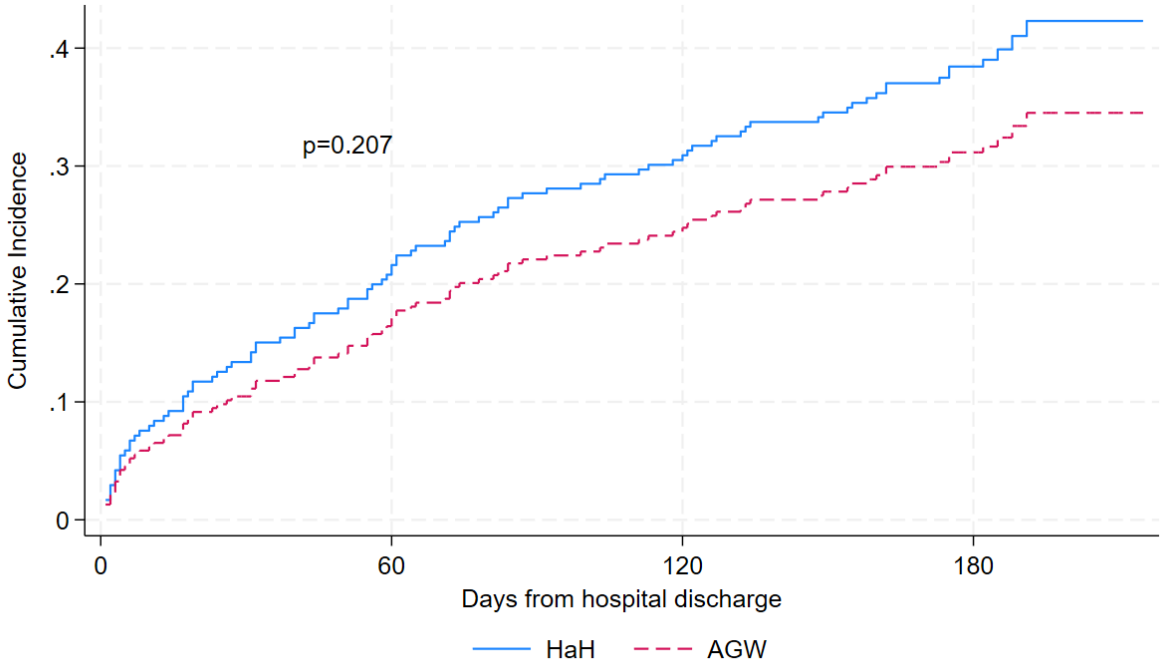
	ED visit/readmission (n=98) vs Alive and free from ED visit/readmission (n=152)		Dead without previous ED visit/readmission (n=30) vs alive and free from ED visit/readmission (n=152)	
Frailty Index				
Model 1				
Frail according to FI	1.27 (0.61-2.62)	0.5221	-†	0.9868
HaH vs AGW setting	1.43 (0.84-2.46)	0.1884	1.15 (0.5-2.68)	0.7404
Model 2				
Frail according to FI	1.4 (0.6-3.28)	0.4414	-†	0.9671
HaH vs AGW setting	1.49 (0.82-2.71)	0.1952	0.37 (0.15-0.87)	0.6274
Age, years	1.01 (0.97-1.05)	0.7026	1.05 (0.98-1.13)	0.1426
Female sex	0.68 (0.4-1.18)	0.1700	**0.37 (0.15-0.87)**	**0.0228**
CIRS-CI	1.01 (0.87-1.18)	0.8824	0.94 (0.74-1.2)	0.6230
SPMSQ, errors	1.12 (0.99-1.26)	0.0530	1.19 (0.99-1.43)	0.0605
Barthel Index	1.01 (0.99-1.02)	0.2060	1.00 (0.98-1.02)	0.9257
N. of hospitalizations in the last 3 months	**1.35 (1.01-1.8)**	**0.0437**	**1.63 (1.02-2.61)**	**0.0430**
Discharge to MLTCF	1.23 (0.46-3.31)	0.6868	**5.03 (1.59-15.9)**	**0.0060**
Multidimensional Prognostic Index*				
Model 1				
Frail according to MPI	1.12 (0.83-1.51)	0.4705	1.41 (0.98-2.05)	0.0650
HaH vs AGW setting	1.15 (0.87-1.51)	0.3239	1.03 (0.72-1.47)	0.8890
Model 2				
Frail according to MPI	1.06 (0.65-17.2)	0.8213	0.85 (0.41-1.77)	0.6715
HaH vs AGW setting	1.18 (0.87-1.59)	0.2812	1.11 (0.66-1.84)	0.6991
Age, years	1.02 (0.98-1.06)	0.3934	1.05 (0.98-1.06)	0.1375
Female sex	0.82 (0.63-1.08)	0.1587	**0.59 (0.38-0.92)**	**0.0199**
CIRS-CI	1.03 (0.89-1.20)	0.6829	0.97 (0.76-1.23)	0.7823
SPMSQ, errors	1.13 (0.99-1.28)	0.0598	1.21 (0.99-1.47)	0.0553
Barthel Index	1.01 (0.99-1.02)	0.3078	0.99 (0.97-1.01)	0.4725
N. of hospitalizations in the last 3 months	**1.37 (1.03-1.83)**	**0.0324**	**1.62 (1.02-2.57)**	**0.0400**
Discharge to MLTCF	1.22 (0.75-2.01)	0.4244	**2.46 (1.36-4.46)**	**0.0028**

*After multiple imputation for missing values

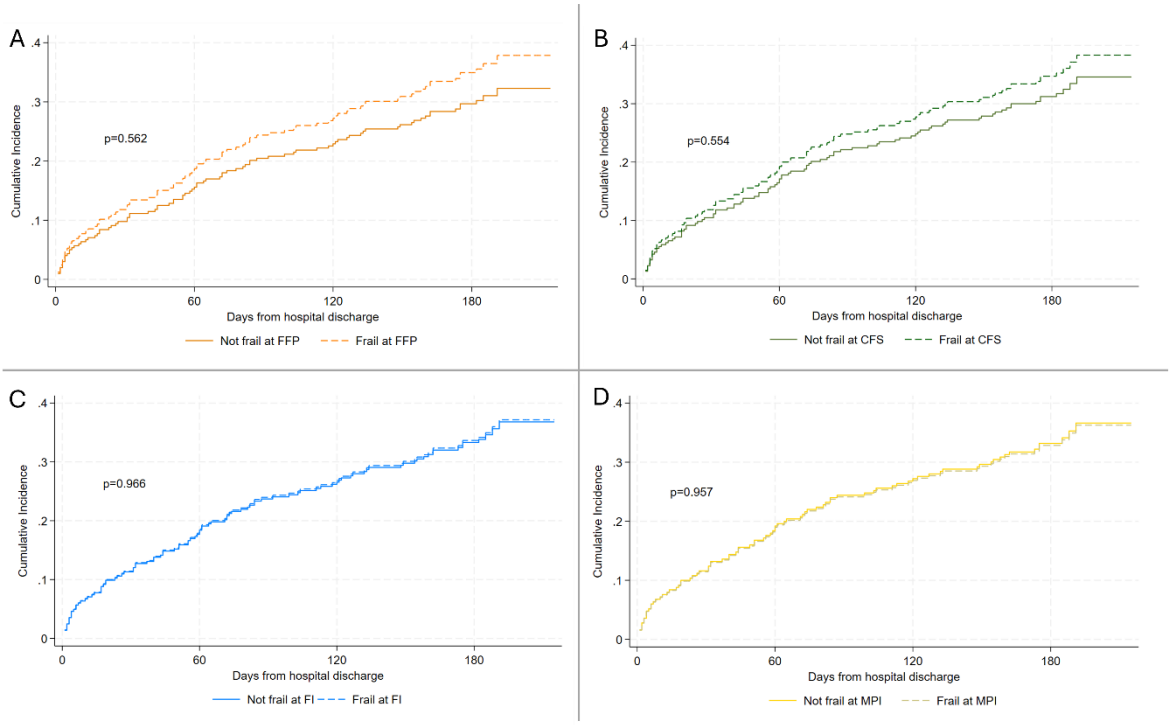
†Unable to estimate parameter due to quasi-complete separation of data

Abbreviations: AGW = acute geriatric ward, aOR = adjusted Odds Ratio, CFS = Clinical Frailty Scale, CI = Confidence Interval, CIRS-CI = Cumulative Illness Rating Scale – Comorbidity Index, ED= Emergency Department, FFP = Fried Frailty Phenotype, FI = Frailty Index, HaH = Hospital-at-Home, MLTCF = medium- or long-term care facility, MPI = Multidimensional Prognostic Index, SPMSQ = Short Portable Mental Status Questionnaire

Supplementary Figure S3 - Cumulative incidence curve for Emergency Department visit or unplanned readmission at 6 months from discharge considering death as a competing event, stratified according to healthcare setting (Hospital-at-Home, HaH, or acute geriatric ward – AGW).



Supplementary Figure S4 - Cumulative incidence curves for Emergency Department visit or unplanned readmission at 6 months from discharge considering death as a competing event, stratified according to frailty presence (dashed lines) or absence (solid lines) as defined by the Fried Frailty Phenotype (FFP, Panel A), the Clinical Frailty Scale (CFS, Panel B), the Frailty Index (FI, Panel C), or the Multidimensional Prognostic Index (MPI, Panel D).



Appendix

Original Case Report Form (Italian language)

Multidimensional Frailty in older patients Admitted to different healthcare Settings for Acute conditions" (MUFASA study)
CASE REPORT FORM – BASELINE

Valutazione dei criteri di inclusione e di esclusione dallo studio:

Inclusione (devono essere tutti presenti)

- □ Età al momento dell'arruolamento ≥65 anni
- □ Ricovero per qualsiasi patologia acuta o cronica scompensata
- □ Presenza di consenso informato scritto firmato dal paziente o dal rappresentante legale autorizzato

Esclusione (nessuno deve essere presente)

- □ Paziente residente in RSA o lungodegenza prima del ricovero ospedaliero
- □ Ricovero programmato (ad es. posizionamento di catetere venoso periferico, trasfusione di emocomponenti)
- □ Paziente in fine vita a causa di una patologia in stadio terminale al ricovero
- □ Paziente precedentemente reclutato in un altro episodio di ricovero nello stesso setting di cura
- □ Assenza di consenso informato scritto firmato dal paziente o dal rappresentante legale autorizzato

ID paziente _____ Data di reclutamento_____
Anni compiuti _____ Sesso: □ M □ F

Variabili socio-demografiche

Titolo di studio: □ Nessuno □ Licenza elementare □ Licenza media inferiore
□ Diploma professionale □ Diploma media superiore □Laurea o superiore
Anni di scolarizzazione: _____ Ultima professione esercitata _____

Stato abitativo:
□ vive solo senza sostegno □ vive solo con sostegno di amici e conoscenti
□ vive solo con sostegno di familiari □ vive con il coniuge
□ vive con altro familiare □ vive con badante
Numero di persone conviventi _____ Presenza di caregiver □ NO □ SI
Se SI □ professionale □ informale numero di ore di assistenza _____/24

Invalidità civile □ SI □ NO □ IN CORSO
Se SI percentuale riconosciuta: □ 100% □ <100%
Indennità di accompagnamento? □ SI □ NO
Pratiche di Unità Valutativa Geriatrica attivate prima del ricovero? □ SI □ NO
Presenza di tutore legale? □ SI □ NO
Numero di accessi in PS/ricoveri non programmati negli ultimi 3 mesi _____

Variabili correlate al ricovero

Data del ricovero _____

Provenienza: □ MMG □ accesso diretto da PS □ altro reparto ospedaliero

Principale causa del ricovero ospedaliero:

- □ Polmonite
- □ Infezioni delle alte vie aeree (compresa bronchite e BPCO riacutizzata)
- □ Infezione delle vie urinarie
- □ Altra infezione, specificare _____
- □ Insufficienza cardiaca scompensata
- □ Sindrome coronarica acuta
- □ Ictus cerebrale, specificare se ischemico o emorragico _____
- □ Tromboembolismo venoso
- □ Disidratazione e altri disturbi idro-elettrolitici
- □ Insufficienza renale acuta
- □ Subocclusione intestinale
- □ Emorragia, specificare _____
- □ Altra anemia, specificare _____
- □ Frattura, specificare _____
- □ Cancro, specificare _____
- □ Disturbi psico-comportamentali della demenza non controllati
- □ Scadimento delle condizioni generali
- □ Dolore non controllato, specificare _____
- □ Intossicazione da farmaci, specificare _____
- □ Altro, specificare _____

Parametri vitali <u>all'ingresso in reparto</u>:

- □ Frequenza respiratoria (FR) _____ atti/min
- □ Saturazione periferica di ossigeno (SpO2) _____% □ aria ambiente □ O2 _____ L/min
  - ○ Rischio di ipercapnia? Insufficienza respiratoria tipo II? □ SI □ NO
- □ Pressione arteriosa (PAS/PAD) _____ / _____ mmHg
- □ Frequenza cardiaca (FC) _____ min
- □ Stato di coscienza: □ Alert □ Confused (<u>new</u>) □ Voice □ Pain □ Unresponsive
- □ Temperatura corporea (in assenza di terapia antipiretica): _____ °C

Esami di laboratorio nei primi giorni di ricovero, se disponibili (meglio più precoci)

Emocromocitometrico			
WBC (leucociti)	x 10^9/L	AST	UI/L
Neutrofili	x 10^9/L	ALT	UI/L
Linfociti	x 10^9/L	GGT	UI/L
Monociti	x 10^9/L	Bilirubina totale	mg/dl
Eosinofili	x 10^9/L	Bilirubina diretta	mg/dl
Basofili	x 10^9/L	Bilirubina indiretta	mg/dl
RBC (eritrociti)	x 10^{12}/L	TSH	µUI/mlo
Hb (emoglobina)	g/dl	fT4	pg/ml
Hct (ematocrito)	%	fT3	pg/ml
MCV	fl	Ferro sierico	µg/dl
PLTS (trombociti)	x 10^9/L	Transferrina	mg/dl
Biochimica e endocrinologia		Ferritina	ng/ml
Creatinina sierica	mg/dl	Vitamina B12	pg/ml
Sodio sierico	mmol/L	Ac. folico	ng/ml
Potassio sierico	mmol/L	Pr. C reattiva	mg/L
Calcio tot (non corr)	mmol/L	Procalcitonina	mg/L
Fosforo	mmol/L	Troponina I hs	ng/L
Proteine totali	g/dl	NT-pro-BNP	ng/L
Albumina sierica	g/dl	HbA1c	mmol/mol

Altri esami ematochimici rilevanti per il ricovero (es. osteoporosi, EGA arteriosa e pH….)

_____

_____

Valutazione multidimensionale al ricovero

Problemi sensoriali

- Problemi di vista:
  - □ Assenti
  - □ presenti lievi/correggibili con lenti
  - □ presenti gravi/impattanti sulla vita quotidiana
- Problemi di udito:
  - □ Assenti
  - □ presenti lievi/correggibili con protesi acustiche
  - □ presenti gravi/impattanti sulla vita quotidiana

Cadute negli ultimi 12 mesi? □ NO □ SI Numero _____

Terapia farmacologica

Numero di principi attivi farmacologici assunti regolarmente, ovvero non al bisogno compresi colliri per glaucoma e terapie inalatorie per BPCO/asma prima del ricovero. Per farmaci con combinazione fissa contare il numero di principi attivi contenuti: _____

Principio attivo e dosaggio:

_____

_____

Cumulative Illness Rating Scale (vedi sotto istruzioni scoring) - specificare

	Categoria CIRS	**Gravità**					**Specificare**
1	Patologie cardiache (solo cuore)	1	2	3	4	5	
2	Ipertensione	1	2	3	4	5	
3	Patologie vascolari (vasi ed apparato emolinfopoietico) NB: per ematico non valutare la patologia indice ma solo le eventuali complicanze (anemia, leucopenia, trombocitopenia, alterazioni coagulative)	1	2	3	4	5	
4	Patologie respiratorie (sotto la laringe)	1	2	3	4	5	
5	O.O.N.G.L. (occhio, orecchio, naso, gola, laringe)	1	2	3	4	5	
6	Apparato GI superiore (esofago, stomaco, duodeno, albero biliare, pancreas)	1	2	3	4	5	
7	Apparato GI inferiore (intestino, ernie)	1	2	3	4	5	
8	Patologie epatiche (solo fegato – biliare in categoria 6)	1	2	3	4	5	
9	Patologie renali (solo rene)	1	2	3	4	5	
10	Patologie app. genito-urinario (ureteri, vescica, uretra, prostata, genitali)	1	2	3	4	5	
11	Sistema muscolo-scheletrico e cute (inclusa osteoporosi)	1	2	3	4	5	
12	Patologie sistema nervoso (SNC e SNP, non include demenze)	1	2	3	4	5	
13	Patologie endocrino-metaboliche, infezioni, intossicazioni	1	2	3	4	5	
14	Patologie psichiatriche e comportamentali (incluse demenze)	1	2	3	4	5	

Punteggio di gravità:
*1. **assente**: nessuna compromissione d'organo/sistema*
*2. **lieve**: la compromissione d'organo/sistema non interferisce con la normale attività; il trattamento può essere richiesto oppure no; la prognosi è eccellente (esempi possono essere abrasioni cutanee, ernie, emorroidi).*
*3. **moderato**: la compromissione d'organo/sistema interferisce con la normale attività; il trattamento è necessario; la prognosi è buona (esempi possono essere colelitiasi, diabete o fratture).*
*4. **grave**: la compromissione d'organo/sistema produce disabilità; il trattamento è indilazionabile; la prognosi può non essere buona (esempi possono essere carcinoma operabile, enfisema polmonare, scompenso cardiaco)*
*5. **molto grave**: la compromissione d'organo/sistema mette a repentaglio la sopravvivenza; il trattamento è urgente; la prognosi è grave (esempi possono essere infarto del miocardio; stroke; sanguinamenti gastro-intestinali; embolia).*
Indice di severità = media dei punteggi delle prime 13 categorie _____
Indice di comorbidità = il numero delle categorie nelle quali si ottiene un punteggio ≥3 (esclusa la 14)_____

Stato funzionale immediatamente precedente al ricovero

Barthel Index – ADL (immediatamente precedente al ricovero)

- □ *Alimentazione*
  - □ il pz può assumere un pasto se posto a distanza raggiungibile in un lasso di tempo ragionevole. È in grado di tagliare il cibo, usare sale/pepe, spalmare il burro.– 10 pt
  - □ il pz necessita di qualche aiuto (ad es. tagliare il cibo) – 5 pt
  - □ dipendente nell'alimentarsi– 0 pt
- □ *Vestirsi/svestirsi*
  - □ Il pz è in grado di indossare e rimuovere tutti gli indumenti, chiudere cerniere lampo, abbottonarsi, allacciare le scarpe, indossare corsetto o bretelle se necessario.– 10 pt
  - □ Il paziente necessita di aiuto nell'indossare, rimuovere o chiudere qualche indumento, ma svolge almeno metà del compito da solo in un tempo ragionevole. Per le donne non si valuta reggiseno/cintura salvo prescrizione medica – 5 pt
  - □ Dipendente in tutti gli aspetti precedenti – 0 pt
- □ *Spostarsi dalla sedia al letto e viceversa*
  - □ Indipendente: indipendente in tutte le fasi di questa attività. Il paziente può avvicinarsi in sicurezza al letto con la sua carrozzina, bloccare i freni, alzare i sostegni per i piedi, spostarsi in sicurezza nel letto, coricarsi, sedersi a bordo letto, cambiare posizione della carrozzina e trasferirsi in sicurezza se necessario. – 15 pt

- □ Minima assistenza, ricordo o supervisione per effettuare in sicurezza una o più attività di cui sopra – 10 pt
- □ Massima assistenza: il paziente può sedersi senza l'aiuto di una seconda persona ma necessita di essere alzato dal letto o si trasferisce con un aiuto sostanziale. – 5 pt
- □ Dipendente: totale necessità di aiuto, non ha equilibrio da seduto – 0 pt

□ *Igiene personale*

- □ Il pz può lavarsi mani e faccia, pettinarsi, spazzolarsi i denti e radersi. Può usare qualsiasi tipo di rasoio ma deve posizionare la lama o inserire la spina senza l'aiuto, così come prendere gli strumenti dal mobile. Le donne devono essere in grado di truccarsi, se abituate a farlo, ma non acconciarsi i capelli– 5 pt
- □ Il pz necessita di aiuto in almeno una delle precedenti funzioni – 0 pt

□ *Fare il bagno/la doccia*

- □ Il pz può usare la vasca da bagno, la doccia o lavarsi con la spugna in maniera completa eseguendo tutti i passaggi necessari senza presenza di un'altra persona – 5 pt
- □ Il pz non è in grado di effettuare tutti i passaggi come dettagliato sopra – 0 pt

□ *Utilizzo della toilette*

- □ Il pz è capace di sedersi ed alzarsi dal wc, alzarsi /abbassarsi gli indumenti, usare il wc senza sporcare e usare la carta igienica senza necessità di aiuto. Può usare maniglia o altro supporto se necessario. In caso di utilizzo di una padella, deve essere in grado di posizionarla correttamente, svuotarla e ripulirla – 10 pt
- □ Il pz necessita di aiuto per disequilibrio, gestire gli indumenti o usare la carta igienica – 5 pt
- □ Dipendente nell'uso della toilette – 0 pt

□ *Controllo sfinterico intestinale*

- □ Il pz è continente alle feci, usa supposta o clistere se necessario – 10 pt
- □ Il pz necessita di aiuto nell'usare supposta o clistere o ha occasionali incidenti - 5 pt
- □ Il paziente è completamente incontinente alle feci – 0 pt

□ *Controllo sfinterico vescicale*

- □ Il pz è continente alle urine giorno e notte. Pz che utilizzano dispositivi esterni e una sacca di raccolta urine a coscia devono poter posizionare, pulire e svuotare la sacca e di mantenersi asciutti giorno e notte. – 10 pt
- □ Il pz ha occasionali incidenti o non è in grado di attendere che gli venga fornita la padella o il pappagallo o necessita di aiuto nel posizionamento dello stesso. – 5 p
- □ Il pz è completamente incontinente alle urine – 0 pt

□ *Mobilizzazione in piano*

- □ Il pz può camminare >45 metri senza aiuto o supervisione. Può usare ausili ma non il girello antibrachiale. Deve poter mettere/togliere il freno, alzarsi/sedersi, usare gli ausili e posizionarli quando seduto – 15 pt
- □ Il pz necessita di qualche aiuto ma può camminare >45 metri con aiuto – 10 pt
- □ Il pz non è in grado di deambulare ma usa la carrozzina in maniera indipendente per > 45 m, può svoltare, cambiare direzione, avvicinarsi al tavolo, al letto, al wc– 5 pt
- □ Il pz non è in grado di utilizzare autonomamente la carrozzina come sopra – 0 pt

□ *Salire e scendere le scale*

- □ Il pz è in grado di salire e scendere una rampa di scale in sicurezza senza aiuto o supervisione. Può usare bastone o stampelle se necessario (trasportandoli) – 10 pt
- □ Il pz necessita di aiuto o supervisione per qualcuno degli item precedenti – 5 punti
- □ Completamente dipendente negli aspetti precedenti – 0 punti

Katz Index – ADL (immediatamente precedente al ricovero)

Fare il bagno/lavarsi		
Non riceve alcuna assistenza (entra/ esce dalla vasca autonomamente): 0	Riceve assistenza nel lavare una sola parte del corpo: 0	Riceve assistenza nel lavare più parti del corpo (o rimane non lavato): **1**
Vestirsi – preleva gli indumenti dall'armadio e dai cassetti, inclusa la biancheria intima; indossa gli abiti usando anche i fermagli (bretelle comprese)		
Prende gli abiti e si veste completamente senza assistenza: 0	Prende gli abiti e si veste senza assistenza, tranne per allacciare le scarpe: 0	Riceve assistenza nel prendere gli abiti o nel vestirsi (o rimane svestito): **1**
Uso dei servizi – va ai servizi per urinare e defecare, si pulisce e si riveste		
Va ai servizi, si pulisce e si riveste senza assistenza (sono consentiti ausili, sa usare padella e comoda): 0	Riceve assistenza nell'andare ai servizi, pulirsi, rivestirsi e usare la padella o la comoda: **1**	Non va ai servizi per i bisogni corporali: **1**
Spostarsi		
Entra ed esce dal letto, si alza e siede senza assistenza (può usare ausili): 0	Entra ed esce dal letto, si alza e si siede sulla sedia con assistenza: **1**	Non si alza dal letto: **1**
Continenza		
Controlla completamente da solo la minzione e la defecazione: 0	Ha occasionali incidenti: 0	Continenza condiz dalla sorveglianza, catetere o incontinenza: **1**
Alimentarsi		
Si alimenta da solo senza assistenza: 0	Si alimenta senza assistenza, tranne tagliare e spalmare: 0	Riceve assistenza nell'alimentarsi o riceve NE/NP: **1**

Lawton – IADL (immediatamente precedente al ricovero)

□ *Utilizzo del telefono*
- □ Usa il telefono di propria iniziativa, cerca i numeri e li compone: 1
- □ Compone solo alcuni numeri ben conosciuti: 1
- □ Risponde al telefono ma non è capace di comporre numeri: 1
- □ Non usa per nulla il telefono: 0

□ *Fare acquisti*
- □ Si occupa di tutte le proprie spese senza aiuto: 1
- □ Fa piccoli acquisti senza aiuto: 0
- □ Necessita di essere accompagnato per fare acquisti: 0
- □ Completamente incapace di fare acquisti: 0

□ *Preparazione dei pasti*
- □ Organizza, prepara e serve pasti adeguatamente preparati: 1
- □ Prepara pasti adeguati se gli vengono procurati gli ingredienti: 0
- □ Scalda e serve pasti preparati, o prepara pasti ma non mantiene una dieta adeguata: 0
- □ Ha bisogno di avere i pasti preparati e serviti: 0

□ *Governo della casa*
- □ Mantiene la casa da solo o con occasionale assistenza (ad es. per lavori pesanti): 1
- □ Esegue compiti quotidiani leggeri ma non mantiene un accettabile livello di pulizia: 0
- □ Ha bisogno di aiuto in ogni operazione di governo della casa: 0
- □ Non partecipa a nessuna operazione di governo della casa

□ *Lavaggio degli indumenti*
- □ Fa il bucato personalmente e completamente: 1
- □ Lava piccoli indumenti (sciacqua calzini, fazzoletti…): 1
- □ Tutta la biancheria deve essere lavata da altri: 0

□ *Utilizzo dei mezzi di trasporto*
- □ Si sposta da solo sui mezzi pubblici o guida la propria automobile: 1
- □ Organizza i propri spostamenti in taxi, ma non usa altri mezzi pubblici: 1
- □ Usa i mezzi pubblici se assistito o accompagnato da qualcun altro: 1
- □ Si sposta in taxi o automobile solo se assistito o accompagnato da qualcun altro: 0
- □ Non si sposta per niente: 0

□ *Responsabilità nell'uso dei farmaci*

- □ Assume le medicine prescritte al dosaggio corretto e all'orario corretto: 1
- □ Assume le medicine se preparate in anticipo e in dosi separate: 0
- □ Non è in grado di prendere le medicine da solo: 0

□ *Capacità di gestire le finanze*

- □ Maneggia le proprie finanze in modo indipendente (bilancio della casa, fa assegni, paga l'affitto o le bollette, va in banca), interessato al proprio reddito: 1
- □ Gestisce acquisti giornalieri ma necessita di aiuto per le questioni bancarie o per acquisti maggiori: 1
- □ È incapace di maneggiare il denaro: 0

Stato cognitivo - **Short Portable Mental Status Questionnaire** – *Fare indossare gli occhiali*

Domanda	*Risposta corretta*	*Risposta errata*
1) Che giorno è oggi? (giorno, mese, anno – tutti corretti)		
2) Che giorno della settimana?		
3) Qual è il nome di questo posto? (ok casa mia, città, nome ospedale)		
4) Qual è il suo numero di telefono (o indirizzo se non ha telefono)?		
5) Quanti anni ha?		
6) Quando è nato/a?		
7) Chi è l'attuale Papa (o Presidente della Repubblica)?		
8) Chi lo era precedentemente?		
9) Qual era il nome di sua madre prima di sposarsi?		
10) Sottragga 3 da 20 e ancora 3 da ogni numero fino a 2		

Orientamento spazio/tempo/sé:

- □ Sempre orientato
- □ Disorientato qualche volta in alcune sfere
- □ Disorientato sempre in tutte le sfere
- □ Disorientato qualche volta in tutte le sfere
- □ Disorientato sempre in tutte le sfere
- □ Coma

Stato comportamentale: □ Appropriato; □ wandering, agitazione, confusione

Rischio di lesioni da pressione – **scala di Exton-Smith**

- Condizioni generali: [4] Buone [3] Discrete [2] Scadute [1] Pessime
- Stato mentale: [4] Lucido [3] Apatico [2] Confuso [1] Stuporoso
- Deambulazione: [4] Normale [3] Si aiuta [2] Sedia a rotelle [1] Allettato
- Incontinenza: [4] Assente [3] Occasionale [2] Abituale [1] Doppia
- Mobilità: [4] Normale [3] Leggermente limitata [2] Molto limitata [1] Immobile

Stato nutrizionale: **Mini Nutritional Assessment (MNA) -** Vedi allegato 1 e relative istruzioni di somministrazione. Registrare il valore, NON SOLO IL CUTOFF di:

Peso corporeo _____ kg, altezza ____ cm, circ brachiale ____ cm, circ polpaccio _____ cm

Calo ponderale involontario (non dovuto a dieta o esercizio fisico) di ≥4,5 kg nell'ultimo anno o, al follow-up, di ≥5% del peso corporeo? □ SI □ NO

Performance fisica

Affaticabilità? Durante la scorsa settimana quanto spesso si è sentito nelle seguenti maniere?

Ho sentito che qualsiasi cosa che facevo era uno sforzo			
Mai o quasi (meno di 1 giorno)	Qualche volta (1-2 giorni)	Spesso (3-4 giorni)	Sempre o quasi (5-7 giorni)
[ ]	[ ]	[ ]	[ ]
Non ce la facevo ad ingranare			
[ ]	[ ]	[ ]	[ ]

Supporto sociale: **Medical Outcomes Study – Social Support Survey**

Le persone a volte cercano aiuto o supporto da parte di amici, parenti o di altre persone. **Quando ne ha bisogno, su quale tipo di aiuto sente di poter contare?** (*Ponga una crocetta sul numero che corrisponde a ciascuna delle Sue risposte).*

Posso contare su una persona	**Mai**	**Raramente**	**Qualche volta**	**Spesso**	**Sempre**
1. che mi aiuti quando sono malato/a					
2. a cui rivolgermi quando sento il bisogno di parlare.					
3. in grado di darmi un buon consiglio in caso di problemi.					
4. che possa accompagnarmi dal medico in caso di bisogno.					
5. che mi dimostri amore ed affetto.					
6. con cui passare bei momenti.					
7. i cui consigli possono aiutarmi a comprendere una situazione, un problema.					
8. con cui confidarmi o poter parlare dei miei problemi.					
9. che mi coccoli, che mi abbracci.					
10. con cui condividere momenti di svago.					
11. che mi prepari i pasti se non sono in grado di farlo.					
12. il cui parere sia importante per me					
13. che sia in grado di farmi distrarre.					
14. che sia in grado di aiutarmi nei problemi della vita quotidiana quando sono malato/a					
15. per condividere preoccupazioni, difficoltà, le paure più intime.					
16. a cui rivolgermi per ricevere suggerimenti e consigli.					
17. con cui fare cose piacevoli.					
18. che sia in grado di comprendere i miei problemi					
19. da amare o che mi faccia sentire amato/a					

Handgrip strength test

Fornire le seguenti istruzioni al paziente: far sedere il paziente con la schiena appoggiata allo schienale e l'avambraccio sul bracciolo. Il polso deve essere in posizione neutra, non appoggiato. Mostrare al paziente come usare il dinamometro facendo vedere che una stretta più forte registra valori più alti. Il pollice deve circondare la maniglia e lo strumento essere ben posizionato nella mano. Lo sperimentatore sorregge la base del dinamometro con la mano facendo attenzione a non impedire i movimenti del paziente. Incoraggiare il paziente a stringere il più forte e a lungo possibile, fintanto che l'ago sale. Iniziare la registrazione con la mano destra e alternare 3 misurazioni per mano. Registrare la migliore delle 6 misurazioni.

Dominanza manuale del paziente: □ destro □ sinistro □ ambidestro
Registrazioni (kg): mano destra: 1) _____ 2) _____ 3) _____
mano sinistra: 1) _____ 2) _____ 3) _____

Velocità del cammino su 4,5 metri

Fornire le seguenti istruzioni al paziente: camminare alla velocità di passo abituale, spedita, senza rischio cadute. Possono usare ausili se necessario. Fare 1 di prova, cronometrare 2 prove e registrare la migliore delle 2. Appuntare il tempo in secondi

Prova 1 _____ secondi Prova 2 _____ secondi

Clinical Frailty Scale (CFS) - Vedi allegato 2 e relative istruzioni di somministrazione _____

Hospital Anxiety and Depression Scale (HADS)

I medici sono consci del fatto che le emozioni giocano un ruolo importante nella maggior parte delle patologie. Se il suo medico è a conoscenza di queste emozioni sarà in grado di aiutarla in maniera più efficace. Questo questionario è disegnato per aiutare il suo dottore a comprendere come si sente. Legga ogni domanda e indichi per ogni affermazione la risposta più vicina a come si è sentito nell'ultima settimana. Non pensi troppo alla risposta da dare; la sua reazione immediata ad ogni domanda sarà probabilmente più accurata di una risposta molto ponderata.

1. Mi sento teso e molto nervoso
   [ ] Per la maggior parte del tempo [ ] Per molto tempo [ ] A volte [ ] Mai
2. Riesco ancora a provare piacere per le cose che ho sempre fatto volentieri
   [ ] Proprio come una volta [ ] Non proprio come una volta [ ] Solo in parte [ ] Per niente
3. Provo un sentimento di paura come se potesse accadere qualcosa di terribile
   [ ] Sicuramente e in maniera intensa [ ] Sì, ma in maniera non troppo intensa
   [ ] Un po' ma non da preoccuparmene [ ] Per niente
4. Riesco a ridere e a vedere il lato divertente delle cose
   [ ] Proprio come ho sempre fatto [ ] Non proprio come un tempo
   [ ] Sicuramente non come un tempo [ ] Per niente
5. Mi vengono in mente pensieri preoccupanti
   [ ] Per la maggior parte del tempo [ ] Per molto tempo [ ] A volte ma non troppo spesso [ ] Mai
6. Mi sento di buon umore
   [ ] Per niente [ ] Raramente [ ] A volte [ ] Per la maggior parte del tempo
7. Posso sedermi sentendomi rilassato e a mio agio
   [ ] Sempre [ ] Spesso [ ] Qualche volta [ ] Mai
8. Mi sento rallentato nei movimenti
   [ ] Quasi sempre [ ] Molto spesso [ ] A volte [ ] Mai
9. Mi sento nervoso, come con un senso di tensione allo stomaco
   [ ] Mai [ ] A volte [ ] Piuttosto spesso [ ] Molto spesso
10. Ho perso interesse per il mio aspetto fisico
    [ ] Completamente [ ] Non me ne prendo cura quanto dovrei
    [ ] Forse non me ne prendo cura abbastanza [ ] Me ne prendo cura come al solito
11. Mi sento irrequieto e incapace di stare fermo:
    [ ] Moltissimo [ ] Molto [ ] Non molto [ ] Per niente
12. Penso al futuro con ottimismo:
    [ ] Così come ho sempre fatto [ ] Un po' meno di una volta
    [ ] Sicuramente meno di una volta [ ] Per niente
13. Mi vengono improvvise crisi di panico:
    [ ] Molto spesso [ ] Piuttosto spesso [ ] Non molto spesso [ ] Mai
14. Ho provato piacere leggendo un buon libro o seguendo la radio o la televisione:
    [ ] Spesso [ ] A volte [ ] Non di frequente [ ] Molto raramente

Livelli di attività fisica – scala PASE

Le chiediamo negli ultimi 7 giorni se e quanto spesso ha svolto le seguenti attività

<u>Attività del tempo libero</u>

1. Leggere, guardare la televisione, fare qualche lavoretto stando seduto

[0] Mai	[1] Raramente (1-2 giorni)	[2] Qualche volta (3-4 giorni)	[3] Spesso (5-7 giorni)

Se Sì, in media, nei giorni indicati, quante ore ha dedicato alle suddette attività?

[1] Meno di 1 ora	[2] 1-2 ore	[3] 2-4 ore	[4] Più di 4 ore

2. Passeggiare (per qualsiasi ragione), portare il cane a spasso, andare in bicicletta

[0] Mai	[1] Raramente (1-2 giorni)	[2] Qualche volta (3-4 giorni)	[3] Spesso (5-7 giorni)

Se Sì, in media, nei giorni indicati, quante ore ha dedicato alle suddette attività?

[1] Meno di 1 ora	[2] 1-2 ore	[3] 2-4 ore	[4] Più di 4 ore

3. Attività fisica leggera, come ginnastica dolce (anche in acqua), pesca, bocce, yoga, tai chi ecc.

[0] Mai	[1] Raramente (1-2 giorni)	[2] Qualche volta (3-4 giorni)	[3] Spesso (5-7 giorni)

Se Sì, in media, nei giorni indicati, quante ore ha dedicato alle suddette attività?

[1] Meno di 1 ora	[2] 1-2 ore	[3] 2-4 ore	[4] Più di 4 ore

4. Attività fisica moderata, come ballo, caccia, tennis in doppio ecc.

[0] Mai	[1] Raramente (1-2 giorni)	[2] Qualche volta (3-4 giorni)	[3] Spesso (5-7 giorni)

Se Sì, in media, nei giorni indicati, quante ore ha dedicato alle suddette attività?

[1] Meno di 1 ora	[2] 1-2 ore	[3] 2-4 ore	[4] Più di 4 ore

5. Attività fisica pesante, come nuoto, corsa/jogging, ciclismo, ginnastica aerobica, trekking, calcio, tennis in singolo, sci (pista o fondo) ecc.

[0] Mai	[1] Raramente (1-2 giorni)	[2] Qualche volta (3-4 giorni)	[3] Spesso (5-7 giorni)

Se Sì, in media, nei giorni indicati, quante ore ha dedicato alle suddette attività?

[1] Meno di 1 ora	[2] 1-2 ore	[3] 2-4 ore	[4] Più di 4 ore

6. Esercizi di forza muscolare come ginnastica con attrezzi (pesi) e flessioni

[0] Mai	[1] Raramente (1-2 giorni)	[2] Qualche volta (3-4 giorni)	[3] Spesso (5-7 giorni)

Se Sì, in media, nei giorni indicati, quante ore ha dedicato alle suddette attività?

[1] Meno di 1 ora	[2] 1-2 ore	[3] 2-4 ore	[4] Più di 4 ore

<u>Attività domestiche</u>

7. Attività domestiche leggere come spolverare, lavare/asciugare i piatti, fare il bucato, stirare, preparare i pasti [0] NO [1] SI
8. Attività domestiche pesanti come spazzare e passare l'aspirapolvere, lavare i pavimenti, pulire le finestre, l'automobile, spostare mobili o la legna [0] NO [1] SI
9. Piccole riparazioni casalinghe (dare il bianco, tappezzeria, elettricità) [0] NO [1] SI
10. Eseguire lavori pesanti nell'orto (zappare, vangare) o nel giardino (tagliare il prato, curare il cortile, spalare la neve, rimuovere le foglie, tagliare la legna) [0] NO [1] SI
11. Effettuato attività di giardinaggio, cura dei fiori [0] NO [1] SI
12. Prestato assistenza ad altre persone (bambini, coniuge, altri adulti) [0] NO [1] SI

<u>Attività lavorativa non sedentaria</u>

13. Negli ultimi 7 giorni ha svolto attività lavorative pagate o di volontariato in cui si cammina o si richiede uno sforzo fisico? [0] NO [1] se sì, quante ore al giorno? _____

Reclutatore _____

Allegato 1

Mini Nutritional Assessment
MNA®

Nestlé NutritionInstitute

Cognome: Nome:

Sesso: Età: Peso, kg: Altezza, cm: Data:

Risponda alla prima parte del questionario indicando, per ogni domanda, il punteggio appropriato. Sommi il punteggio della valutazione di screening e, se il risultato è uguale o inferiore a 11, completi il questionario per ottenere una valutazione dello stato nutrizionale.

Screening

A Presenta una perdita dell' appetito? Ha mangiato meno negli ultimi 3 mesi? (perdita d'appetito, problemi digestivi, difficoltà di masticazione o deglutizione)
0 = grave riduzione dell'assunzione di cibo
1 = moderata riduzione dell'assunzione di cibo
2 = nessuna riduzione dell'assunzione di cibo ☐

B Perdita di peso recente (<3 mesi)
0 = perdita di peso > 3 kg
1 = non sa
2 = perdita di peso tra 1 e 3 kg
3 = nessuna perdita di peso ☐

C Motricità
0 = dal letto alla poltrona
1 = autonomo a domicilio
2 = esce di casa ☐

D Nell' arco degli ultimi 3 mesi: malattie acuteo stress psicologici?
0 = sì 2 = no ☐

E Problemi neuropsicologici
0 = demenza o depressione grave
1 = demenza moderata
2 = nessun problema psicologico ☐

F Indice di massa corporea IMC = peso in kg / (altezza in m)²
0 = IMC <19
1 = 19 ≤ IMC < 21
2 = 21 ≤ IMC < 23
3 = IMC ≥ 23 ☐

Valutazione di screening ☐☐
(totale parziale max.14 punti)

12-14 punti: stato nutrizionale normale
8-11 punti: a rischio di malnutrizione
0-7 punti: malnutrito

Per una valutazione più approfondita, continuare con le domande G-R

Valutazione globale

G Il paziente vive autonomamente a domicilio?
1 = sì 0 = no ☐

H Prende più di 3 medicinali al giorno?
0 = sì 1 = no ☐

I Presenza di decubiti, ulcere cutanee?
0 = sì 1 = no ☐

J Quanti pasti completi prende al giorno?
0 = 1 pasto
1 = 2 pasti
2 = 3 pasti ☐

K Consuma?
- Almeno una volta al giorno dei prodotti lattiero-caseari? sì ☐ no ☐
- Una o due volte la settimana uova o legumi? sì ☐ no ☐
- Oni giorne della carne, del pesce o del pollame? sì ☐ no ☐

0.0 = se 0 o 1 sì
0.5 = se 2 sì
1.0 = se 3 sì ☐.☐

L Consuma almeno due volte al giorno frutta o verdura?
0 = no 1 = sì ☐

M Quanti bicchieri beve al giorno? (acqua, succhi, caffé, té, latte...)
0.0 = meno di 3 bicchieri
0.5 = da 3 a 5 bicchieri
1.0 = più di 5 bicchieri ☐.☐

N Come si nutre?
0 = necessita di assistenza
1 = autonomamente con difficoltà
2 = autonomamente senza difficoltà ☐

O Il paziente si considera ben nutrito? (ha dei problemi nutrizionali)
0 = malnutrizione grave
1 = malnutrizione moderata o non sa
2 = nessun problema nutrizionale ☐

P Il paziente considera il suo stato di salute miglioreo peggiore di altre persone della sua età?
0.0 = meno buono
0.5 = non sa
1.0 = uguale
2.0 = migliore ☐.☐

Q Circonferenza brachiale (CB, cm)
0.0 = CB < 21
0.5 = CB ≤ 21 CB ≤ 22
1.0 = CB > 22 ☐.☐

R Circonferenza del polpaccio (CP in cm)
0 = CP < 31
1 = CP ≥ 31 ☐

Valutazione globale (max. 16 punti) ☐☐.☐
Screening ☐☐.☐
Valutazione totale (max. 30 punti) ☐☐.☐

Valutazione dello stato nutrizionale

24-30 da 24 a 30 punti ☐ stato nutrizionale normale
17-23.5 da 17 a 23,5 punti ☐ rischio di malnutrizione
meno 17 punti ☐ cattivo stato nutrizionale

Ref. Vellas B, Villars H, Abellan G, et al. *Overview of MNA® - Its History and Challenges.* J Nut Health Aging 2006; 10: 456-465.
Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for Undernutrition in Geriatric Practice: *Developing the Short-Form Mini Nutritional Assessment (MNA-SF).* J. Geront 2001; 56A: M366-377.
Guigoz Y. The Mini-Nutritional Assessment (MNA®) *Review of the Literature – What does it tell us?* J Nutr Health Aging 2006; 10: 466-487.

Per maggiori informazioni : www.mna-elderly.com

Allegato 2

CLINICAL FRAILTY SCALE

1 **VERY FIT** — People who are robust, active, energetic and motivated. They tend to exercise regularly and are among the fittest for their age.

2 **FIT** — People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g., seasonally.

3 **MANAGING WELL** — People whose **medical problems are well controlled**, even if occasionally symptomatic, but often are **not regularly active** beyond routine walking.

4 **LIVING WITH VERY MILD FRAILTY** — Previously "vulnerable," this category marks early transition from complete independence. While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up" and/or being tired during the day.

5 **LIVING WITH MILD FRAILTY** — People who often have **more evident slowing**, and need help with **high order instrumental activities of daily living** (finances, transportation, heavy housework). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation, medications and begins to restrict light housework.

6 **LIVING WITH MODERATE FRAILTY** — People who need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **LIVING WITH SEVERE FRAILTY** — **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~6 months).

8 **LIVING WITH VERY SEVERE FRAILTY** — Completely dependent for personal care and approaching end of life. Typically, they could not recover even from a minor illness.

9 **TERMINALLY ILL** — Approaching the end of life. This category applies to people with a **life expectancy <6 months**, who are **not otherwise living with severe frailty.** (Many terminally ill people can still exercise until very close to death.)

SCORING FRAILTY IN PEOPLE WITH DEMENTIA

The degree of frailty generally corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

In **very severe dementia** they are often bedfast. Many are virtually mute.

DALHOUSIE UNIVERSITY

Rockwood K et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–495.

CASE REPORT FORM - DIMISSIONE

ID paziente _____

Data di dimissione _____

Modalità e stato vitale in dimissione:

□ a domicilio□ a domicilio con attivazione di ADI □ a domicilio con attivazione di c. palliative
□ RSA □ in CAVS/lungodegenza □ riabilitazione □OAD □ hospice
□ PS □ deceduto/a

Diagnosi principale alla dimissione _____

Utilizzo di dispositivi medici durante il ricovero (crocettare se usato durante il ricovero, e informazioni riguardo a presenza all'ingresso e alla dimissione dal reparto)

- □ cateteri venosi; specificare: □ CVP □ Mini-Midline □ Midline □ PICC □ CVC □ PORT
  - presente prima del ricovero? □ SI □ NO
  - presente in dimissione? □ SI □ NO
- □ catetere vescicale
  - presente prima del ricovero? □ SI □ NO
  - presente in dimissione? □ SI □ NO
- □ sondino per nutrizione enterale; specificare: □SNG □PEG □ altro _____
  - presente prima del ricovero? □ SI □ NO
  - presente in dimissione? □ SI □ NO
- □ ossigenoterapia, specificare massimo livello raggiunto: □ cannule nasali □ Venturi □ Non rebreath □ alti flussi □ NIV
  - qualsiasi livello di ossigenoterapia presente prima del ricovero? □ SI □ NO
  - qualsiasi livello di ossigenoterapia presente in dimissione? □ SI □ NO
- □ altri dispositivi medici, specificare _____

Trattamenti particolari durante il ricovero?

- □ Trasfusioni di emazie concentrate, specificare numero _____
- □ Trasfusioni di piastrine, specificare numero _____
- □ Infusione di ferro, specificare molecola _____
- □ Nutrizione parenterale, specificare soluzione _____
- □ Antibiotici parenterali, specificare quali: _____

  _____
- □ Nuovo utilizzo di oppioidi? □ SI □ NO
- □ Nuovo utilizzo di benzodiazepine? □ SI □ NO
- □ Nuovo utilizzo di ipnoinducenti? □ SI □ NO
- □ Nuovo utilizzo di antipsicotici? □ SI □ NO

Incidenza di delirium durante il ricovero, sospettata sulla base di una variazione acuta dello stato di vigilanza o comparsa di disturbi del comportamento riferita dal personale medico-infermieristico e confermata mediante esecuzione della scala 4-AT da parte del geriatra

□ SI □ NO data _____

Utilizzo di terapia farmacologica per delirium? □ SI □ NO, specificare molecole, dosaggio e via di somministrazione _____

Cadute a terra registrate nella documentazione clinica? □ SI □ NO, data della prima caduta _____eventuali conseguenze cliniche della caduta più grave _____

Comparsa di nuove lesioni da pressione riscontrate dal personale sanitario durante la valutazione quotidiana dei pazienti e riportate in cartella clinica? □ SI □ NO

- □ Numero _____
- □ Sede _____
- □ Stadio di maggiore gravità durante il ricovero _____

Infezioni correlate all'assistenza definite come infezioni comparse almeno 48 ore dopo il ricovero in ospedale/ospedale a domicilio? □ SI □ NO

- □ Sede dell'infezione _____
- □ Microrganismo coinvolto _____
- □ Tipo e durata terapia effettuata_____

Sperimentatore dimissione _____

CASE REPORT FORM- FOLLOW-UP A 6 MESI

ID paziente _____ Data del follow-up _____

Colloquio con □ paziente □ caregiver

Stato vitale a 6 mesi: □ vivo/a □ deceduto/a

Data del decesso _____

Causa del decesso (essere il più specifici possibile, se disponibile consultare documentazione clinica) _____

Accessi in pronto soccorso/ricoveri non programmati negli ultimi 6 mesi □ SI □ NO

Data e causa

1) _____
2) _____
3) _____
4) _____

Stato abitativo:

1) A CASA □ solo senza sostegno □ solo con sostegno di amici e conoscenti □ solo con sostegno di familiari □ con il coniuge □ con altro familiare □ con badante
2) IN STRUTTURA _____

Numero di persone conviventi _____ Presenza di caregiver □ NO □ SI

Se SI □ professionale □ informale numero di ore di assistenza _____/24

Invalidità civile □ SI □ NO □ IN CORSO

Se SI percentuale riconosciuta: □ 100% □ <100%

Indennità di accompagnamento? □ SI □ NO

Pratiche di Unità Valutativa Geriatrica attivate? □ SI □ NO

Presenza di tutore legale? □ SI □ NO

Barthel Index – ADL

□ *Alimentazione*
- □ il pz può assumere un pasto se posto a distanza raggiungibile in un lasso di tempo ragionevole. È in grado di tagliare il cibo, usare sale/pepe, spalmare il burro.– 10 pt
- □ il pz necessita di qualche aiuto (ad es. tagliare il cibo) – 5 pt
- □ dipendente nell'alimentarsi– 0 pt

□ *Vestirsi/svestirsi*
- □ Il pz è in grado di indossare e rimuovere tutti gli indumenti, chiudere cerniere lampo, abbottonarsi, allacciare le scarpe, indossare corsetto o bretelle se necessario.– 10 pt
- □ Il paziente necessita di aiuto nell'indossare, rimuovere o chiudere qualche indumento, ma svolge almeno metà del compito da solo in un tempo ragionevole. Per le donne non si valuta reggiseno/cintura salvo prescrizione medica – 5 pt
- □ Dipendente in tutti gli aspetti precedenti – 0 pt

□ *Spostarsi dalla sedia al letto e viceversa*
- □ Indipendente: indipendente in tutte le fasi di questa attività. Il paziente può avvicinarsi in sicurezza al letto con la sua carrozzina, bloccare i freni, alzare i sostegni per i piedi, spostarsi in sicurezza nel letto, coricarsi, sedersi a bordo letto, cambiare posizione della carrozzina e trasferirsi in sicurezza se necessario. – 15 pt
- □ Minima assistenza, ricordo o supervisione per effettuare in sicurezza una o più attività di cui sopra – 10 pt

- □ Massima assistenza: il paziente può sedersi senza l'aiuto di una seconda persona ma necessita di essere alzato dal letto o si trasferisce con un aiuto sostanziale. – 5 pt
- □ Dipendente: totale necessità di aiuto, non ha equilibrio da seduto – 0 pt

□ *Igiene personale*

- □ Il pz può lavarsi mani e faccia, pettinarsi, spazzolarsi i denti e radersi. Può usare qualsiasi tipo di rasoio ma deve posizionare la lama o inserire la spina senza l'aiuto, così come prendere gli strumenti dal mobile. Le donne devono essere in grado di truccarsi, se abituate a farlo, ma non acconciarsi i capelli– 5 pt
- □ Il pz necessita di aiuto in almeno una delle precedenti funzioni – 0 pt

□ *Fare il bagno/la doccia*

- □ Il pz può usare la vasca da bagno, la doccia o lavarsi con la spugna in maniera completa eseguendo tutti i passaggi necessari senza presenza di un'altra persona – 5 pt
- □ Il pz non è in grado di effettuare tutti i passaggi come dettagliato sopra – 0 pt

□ *Utilizzo della toilette*

- □ Il pz è capace di sedersi ed alzarsi dal wc, alzarsi /abbassarsi gli indumenti, usare il wc senza sporcare e usare la carta igienica senza necessità di aiuto. Può usare maniglia o altro supporto se necessario. In caso di utilizzo di una padella, deve essere in grado di posizionarla correttamente, svuotarla e ripulirla – 10 pt
- □ Il pz necessita di aiuto per disequilibrio, gestire gli indumenti o usare la carta igienica – 5 pt
- □ Dipendente nell'uso della toilette – 0 pt

□ *Controllo sfinterico intestinale*

- □ Il pz è continente alle feci, usa supposta o clistere se necessario – 10 pt
- □ Il pz necessita di aiuto nell'usare supposta o clistere o ha occasionali incidenti - 5 pt
- □ Il paziente è completamente incontinente alle feci – 0 pt

□ *Controllo sfinterico vescicale*

- □ Il pz è continente alle urine giorno e notte. Pz che utilizzano dispositivi esterni e una sacca di raccolta urine a coscia devono poter posizionare, pulire e svuotare la sacca e di mantenersi asciutti giorno e notte. – 10 pt
- □ Il pz ha occasionali incidenti o non è in grado di attendere che gli venga fornita la padella o il pappagallo o necessita di aiuto nel posizionamento dello stesso. – 5 p
- □ Il pz è completamente incontinente alle urine – 0 pt

□ *Mobilizzazione in piano*

- □ Il pz può camminare >45 metri senza aiuto o supervisione. Può usare ausili ma non il girello antibrachiale. Deve poter mettere/togliere il freno, alzarsi/sedersi, usare gli ausili e posizionarli quando seduto – 15 pt
- □ Il pz necessita di qualche aiuto ma può camminare >45 metri con aiuto – 10 pt
- □ Il pz non è in grado di deambulare ma usa la carrozzina in maniera indipendente per > 45 m, può svoltare, cambiare direzione, avvicinarsi al tavolo, al letto, al wc– 5 pt
- □ Il pz non è in grado di utilizzare autonomamente la carrozzina come sopra – 0 pt

□ *Salire e scendere le scale*

- □ Il pz è in grado di salire e scendere una rampa di scale in sicurezza senza aiuto o supervisione. Può usare bastone o stampelle se necessario (trasportandoli) – 10 pt
- □ Il pz necessita di aiuto o supervisione per qualcuno degli item precedenti – 5 punti
- □ Completamente dipendente negli aspetti precedenti – 0 punti

Sperimentatore follow-up _____

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"A *garden's beauty never lies in one flower."*
Matshona Dhliwayo

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"*La bellezza di un giardino non sta mai in un solo fiore."*
Matshona Dhliwayo