Rendiconto di assegnazione risorse 5 per 1000 ANNO 2021 Contributo percepito € 31.798,00
Enti della Ricerca Scientifica

ENTE*: FONDAZIONE INSIEME CON HUMANTAS

n. progressivo	titolo progetto	Fondi 5 per 1000 assegnati al progetto	Costo compelssivo del progetto	data indicativa di inizio progetto	durata prevista
1	Clinical pathways adapted to frailty in acute medical patients in Humanitas Research Hospital: study protocol for a before-and-after study	31.798,00 €	31.798,00 €	1.3.2023	18 mesi

Data: 11.10.2022

Legale Rappresentante
Dottoressa Rosa Clara De Bernardi

Si autorizza al trattamento dei dati ai sensi di d.lgs.196/2003

Legale Rappresentante
Dottoressa Rosa Clara De Bernardi

*Istituzione beneficiaria del contributo del 5 per 1000

Modulo rendiconto
ai sensi DPCM
23/06/2020
art. 16 comma 1

Ministero dell'Università e della Ricerca
Direzione Generale della Ricerca

Rendiconto di spesa fondi 5 per mille Enti della Ricerca Scientifica

ANNO FINANZIARIO 2021[1]

Ente beneficiario

Denominazione sociale	**FONDAZIONE INSIEME CON HUMANITAS ETS**
Codice fiscale	**97245860156**
Sede legale	**VIA MANZONI 56 – 20089 ROZZANO**
Indirizzo posta elettronica *(NO PEC)*	**fondazione.humanitas@pec.it**
Scopo dell'attività sociale	**Umanizzazione delle attività di assistenza, formazione e sviluppo della ricerca clinica e sperimentale presso l'Istituto Clinico Humanitas**
Nominativo legale rappresentante	**Rosa Clara De Bernardi**

Contributo percepito

Data percezione	**11 ottobre 2022**
Importo	**31.798**

[1] Indicare l'anno finanziario al quale si riferisce l'erogazione.

Ministero dell'Università e della Ricerca
Direzione Generale della Ricerca

Spese sostenute [2]

VOCI DI SPESA	COSTO COMPLESSIVO	QUOTA FINANZIATA CON FONDI 5 PER MILLE
DI FUNZIONAMENTO		
Risorse umane *Dettaglio spese:* 1. Personale reclutato al 100% sulle attività del progetto (Francesco Coletta – borsista)	18.700	18.700
Acquisto beni e servizi *Dettaglio spese:* 1. … 2. …	0,00	0,00
ALTRE VOCI DI SPESA [3]		
Dettaglio spese: 1. Costi indiretti (10%)	3.180	3.180
ACCANTONAMENTI PROGETTI PLURIENNALI [4]		
Dettaglio spese: 1. Proroga Borsa di Studio alla scadenza 2.	9.918	9.918
TOTALE	31.798	31.798

Il seguente rendiconto è pubblicato al seguente indirizzo web
www.insiemeconhumanitas.it

Luogo e data Rozzano 18 luglio 2023

Il Legale Rappresentante

Si autorizza al trattamento dei dati ai sensi del d.lgs.196/2003 e al Regolamento (UE) 2016/679 (GDPR).

Il Legale Rappresentante

[2] Evidenziare la loro riconduzione alle finalità ed agli scopi istituzionali del soggetto beneficiario.
[3] Altre voci di spesa comunque destinate ad attività direttamente riconducibili alle finalità e agli istituzionali del soggetto beneficiario.
[4] Eventuali accantonamenti delle somme percepite per la realizzazione di progetti pluriennali, con durata massima triennale, fermo restando l'obbligo di rendicontazione successive al loro utilizzo.

FRAME study protocol, advanced draft (Bernardini Bruno)

Clinical pathways adapted to frailty in acute medical patients in Humanitas Research Hospital: study protocol for a before-and-after study

1. Background

As the population ages, older people with multimorbidity and disability, including the frail, represent an increasing proportion of hospital users. Exposure to the hospital environment increases the risk of multiple adverse health events for the most vulnerable, including new disabilities, delirium, falls, infections, periprocedural complications, institutionalization, and death. In this scenario, one of the most challenging issues is the identification of the frail elderly to design tailored hospital clinical pathways that provide patients with the highest quality of care with the least possible harm.

Frailty is conceptualized as an age-related multisystem biophysiologic dysregulation that makes the elderly more vulnerable to a stressful event.[1] In several medical and surgical hospital populations, frailty has been shown to be associated with the chance of multiple adverse outcomes,[2,3,4,5,6] replacing chronological age as a risk factors for poor outcomes. Many current guidelines, particularly in surgery, recommend routine preoperative assessment of frailty to guide postoperative care.[7,8] In medicine, frailty has been the focus of geriatric and gerontologic research for at least thirty years.

Frail patients are not only at greater risk of complications, they often have complex care needs and require more time to return to pre-morbid function. As a result, they have longer hospital stays and often need to be transferred to rehabilitation, long-term care or palliative care facilities. Overall, the costs of caring for a frail person tend to be disproportionately higher than would be expected from the burden of the primary disease alone, or even from the comorbidities themselves. The optimal approach to frailty care in the hospital setting therefore necessarily requires a high degree of integration between the medical, nursing and multimodal rehabilitation components.

This study is the starting point of a quality program at our institution to create safer and more effective care pathways for vulnerable medical and surgical patients. Humanitas Research Hospital is a Joint Commission International (JCI)-accredited tertiary teaching hospital that, since 2016, has implemented an electronic health record to facilitate the monitoring of clinical behaviors (physicians, nurses, rehabilitation, and care professionals) for compliance with standards set by JCI.[9]

JCI's patient-centered standards address key processes across the hospital's continuum of care, covering international patient safety goals (IPSG), patient access and continuity of care (ACC), patient and family rights (PFR), patient assessment (AOP), patient care (COP), anesthesia and surgical care (ASC), medication management and use (MMU), and patient and family education (PFE).

Adherence to JCI standards ensures that the flow of information is consistent with teamwork and multidisciplinary collaboration across the continuum of care in our hospital and in transition to community-based settings. They are process and outcome-oriented and provide the framework and methodological basis for the development and integration of specific, transparent, and measurable pathways.

In this paper, we present the pathway project for frail patients admitted to the acute medicine ward, which we have named FRAME (Frailty-adapted Rehabilitation in Acute MEdicine), the result of a collaboration between the departments of Internal Medicine and Neurorehabilitation in our hospital. The FRAME path was designed using the Clinical Practice Improvement (CPI) approach recommended by Horn, a kind of high-quality controlled observational study that is as good as randomized trials at identifying and addressing factors predictive of poor outcomes. Horn explains: CPI *"is an observational study design whose measurement encompasses a comprehensive view of the care management process: (1) key patient characteristics, (2) all treatment and care processes, and (3) outcomes. All 3 classes of data are considered simultaneously. This comprehensive measurement framework provides a basis for meaningful analyses of significant associations between process and outcome(s), controlling for patient differences"*.[10]

The FRAME pathway more efficiently integrates medical and functional decision-making processes into patient co-management, changing only some aspects of the specific routines of medical and neurorehabilitation teams. Once its clinical utility is proven, the FRAME pathway can become a routine standard. The FRAME pathway involves the use of already validated indicators of complexity of care and a prognostic score, as well as the use of an original, purpose-built frailty assessment instrument, the rationale and validity of which are briefly explained.

The pilot study we conducted on 100 acute patients admitted from February to May 2023 made us confident that our methods will allow us to:

- Quantify pre-morbid frailty in acutely ill patients admitted to the internal medicine ward.
- Qualify care needs with markers of medical and functional complexity at admission and discharge
- Determine the incidence of complications during hospitalization (falls, urinary tract infections, delirium, pneumonia, sepsis)
- Detect functional dependency at discharge,
- Detect discharge destination for home or community facilities and services.
- Estimate the degree of association between premorbid frailty, complexity of care, and all outcomes.

We hypothesized that closer collaboration between medical and neurorehabilitation teams could improve decision-making and facilitate patients' transition to home or community-based services. Thus, the primary goal of this study is to significantly reduce the length of stay in the internal medicine ward without worsening patients' clinical and functional outcomes.

2. Methods

2.1 Study design and setting

This protocol describes a single-center, controlled, before-after study with an intention-to-treat design. A single clinical pathway was designed from admission of patients from the Emergency Department to the Internal Medicine-Nephrology (MN) ward of our institution until discharge.

MN ward is a 40-bed inpatient unit with an attached 10-bed outpatient dialysis unit. It admits non-critical acute patients from the emergency department, mainly with renal, infectious, oncological and immunological diseases. The main disease and comorbidities of patients will be identified with ICD-10 codes.

2.2 Patient Characteristics and Enrollment

All patients aged 50 years or older who are consecutively admitted to the MN ward will be enrolled in the FRAME study. Highly unstable patients, those requiring continuous monitoring or urgent dialysis will be enrolled in the FRAME study when clinically stable (i.e., green on the Early Warning Score[11,12,13]). Enrollment of patients considered to be terminally ill will be considered on a case-by-case basis.

Written informed consent will be obtained from all study participants at enrollment.

Due to the design of the study and the electronic medical record, it is not possible to blind participants, investigators, care providers, or outcome assessors in this study.

2.3 Original bedside tools of the FRAME study

2.3.1 The FLIGS frailty questionnaire

The construct of frailty, its quantification, and the prognostic contribution it can add to multivariable models remain controversial, and there is no consensus on which tool should be considered the reference standard for clinical use.[14,15]

One major problem is that most frailty assessment instruments have been limited to their predictive validity (i.e., their independent association with a negative health outcome), skipping psychometric validation (e.g., testing the consistency of the overall construct and the reliability of the salient scale indicators). A second problem is that scores on almost all frailty assessment instruments are used as a dichotomous (frail vs. non-frail) or three-category classification (non-frail, prefrail, and frail), which does not allow for a measure of "how" frail a person is. These inconsistencies can lead to widely biased estimates of frailty as different

instruments identify different people as frail, with non-negligible misclassification, and overall frailty scores cannot be compared or pooled.[16,17]

For these reasons, to assess frailty we developed an ad hoc questionnaire based on functional limitations and geriatric syndromes,[18] which we called the FLIGS Frailty Questionnaire (FLIGS-FQ). The FLIGS-FQ (**see Appendix 1**) is a patient-reported measure that details the patient's history over the past 30 days for the presence of functional limitations and geriatric syndromes. It consists of 23 dichotomous (no/yes) questions that can be easily administered by telephone or self-administered. The FLIGS-FQ produces an interval score ranging from 0 (no frailty) to 23 (failure to thrive), which can be traced to a z-score.

Preliminary results of the psychometric validation of the FLIGS-FQ confirmed the unidimensionality of the construct and a very good reliability. The FLIGS-FQ total score, used as a continuous scale, was found to be associated with adverse clinical events during hospitalization in a population of 261 patients admitted to the medical ward from the emergency department.

2.3.2 The FRIDA score

From a multicenter study including a very large case series that we coordinated, we recently validated a predictive score for individual risk of dependence in ambulation at the end of rehabilitation, which we called FRIDA (Functional Risk Index for Dependence in Ambulation).[20] The FRIDA score is based on the standardized process-outcome indicators of medical and functional complexity of the IPER-2.0 system.[19]

The FRIDA score is the first tool in the literature to combine both medical and functional elements into a single individual risk score. The score has very good predictive performance across major rehabilitation impairment categories and also across different rehabilitation facilities. As anticipated in our article, IPER-2.0 indicators (and therefore the FRIDA score) are suitable for monitoring the main medical and functional problems in rehabilitation and can provide a dynamic measure of the whole process of care for each individual patient.

2.4 Standard of care prior to the FRAME study

The standard of care prior to the present study was to activate multimodal rehabilitation treatment (physiotherapy, logopedic, speech therapy, neuropsychology, occupational therapy, as needed) after neuro-physiatric consultation requested at the discretion of the tutor physician of the patient.

2.5 FRAME study standard of care

The standard of care for this study will be based on the interdisciplinary meeting (internist, nurse, neurophysiologist and physical therapist, and other rehabilitation professionals if necessary) held every other day. During the interdisciplinary meeting, all new patients enrolled in the FRAME study and those undergoing rehabilitation will be discussed. For newly recruited patients, the FLIGS frailty score will be reviewed and discussed, and the FRIDA score will be calculated. The qualitative and quantitative analysis of the two instruments will serve as the basis for treatment planning and rehabilitation intervention. For patients in discharge, the Care Process Monitoring Chart will be updated and closed.

3. Study outcomes

The primary endpoint is length of stay (LOS). The incidence of adverse clinical events (i.e., delirium, falls, urinary tract infections, pneumonia, and sepsis), dependency in basic mobility at discharge, and failure to return home at discharge are considered as secondary outcomes.

4. Statistical analysis

The sample size was calculated based on the pilot study data. Based on the analysis of 100 patients admitted to the same medical ward from, the length of stay was 19±16 days. To reduce the average length of stay to 14 days, a 50-50 study requires 324 patients, or 162 patients per group. These calculations are based on 80% power with a two-sided significance level of 5%.

Starting in October 2023, the goal of including 162 patients in the prospective FRAME study appears achievable in about 7 months of enrollment. Patients in the prospective FRAME study will be compared with a group of patients treated between January 2020 and October 2022 in the same ward.

This control group was formed by applying the same inclusion and exclusion criteria used in the prospective FRAME study, and participated in rehabilitation programs according to the standard of care. All baseline characteristics and outcomes mentioned in the previous sections for the control group will be captured through retrospective review of medical records.

The end of data collection (prospective study and retrospective control group) can be completed by June 2024.

Descriptive statistics will be used to present the baseline characteristics. Differences in these characteristics between the control group and the FRAME group will be tested for statistical significance using Mann-Whitney's U test for continuous variables and Pearson's chi-square test or Fisher's exact test for categorical variables. A subgroup analysis will be performed to test for between-group differences in primary and secondary outcomes.

Statistical analysis will be performed with Stata 17 software. A two-sided p-value < 0.05 will be considered statistically significant. Data analysis will be performed according to the intention-to-treat principle.

This article was reported using the SPIRIT guidelines.[21]

Discussion

To do.

Strength

To our knowledge, this is the first study to use frailty and complexity of care as combined elements to define and monitor the individual care plan and outcomes in an acute care medicine ward.

Limitations

The design of the FRAME study makes the risk of bias quite high. Because of the before-and-after approach, randomization and blinding of patients and operators are impossible.

This study has a single-center design, which may limit its generalizability. However, the way it was set up and the original tools introduced at the bedside makes its implementation in other centers possible.

Financial support and sponsorship

This study is funded by Insieme con Humanitas Foundation.

References

1. Morley JE, Vellas B, Abellan van Kan G, et al. Frailty consensus: A call to action. *J Am Med Dir Assoc*. 2013;14(6):392-397. doi:10.1016/j.jamda.2013.03.022
2. Gill TM, Murphy TE, Gahbauer EA, Leo-Summers L, Becher RD. Geriatric vulnerability and the burden of disability after major surgery. *J Am Geriatr Soc*. 2022;70(5):1471-1480. doi:10.1111/jgs.17693
3. Rothenberg KA, Stern JR, George EL, et al. Association of frailty and postoperative complications with unplanned readmissions after elective outpatient surgery. *JAMA Netw Open*. 2019;2(5). doi:10.1001/jamanetworkopen.2019.4330
4. Gouda P, Wang X, Youngson E, McGillion M, Mamas MA, Graham MM. Beyond the revised cardiac risk index: Validation of the hospital frailty risk score in non-cardiac surgery. *PLoS One*. 2022;17(1 January):1-12. doi:10.1371/journal.pone.0262322
5. Lin HS, Watts JN, Peel NM, Hubbard RE. Frailty and post-operative outcomes in older surgical patients: A systematic review. *BMC Geriatr*. 2016;16(1). doi:10.1186/s12877-016-0329-8
6. Lee JH, Park YS, Kim MJ, et al. Clinical Frailty Scale as a predictor of short-term mortality: A systematic review and meta-analysis of studies on diagnostic test accuracy. *Acad Emerg Med*. 2022;29(11):1347-1356. doi:10.1111/acem.14493
7. Hamaker M, Lund C, te Molder M, et al. Geriatric assessment in the management of older patients with cancer – A systematic review (update). *J Geriatr Oncol*. 2022;13(6):761-777. doi:10.1016/j.jgo.2022.04.008
8. Witjes JA, Bruins HM, Cathomas R, et al. European Association of Urology Guidelines on Muscle-invasive and Metastatic Bladder Cancer: Summary of the 2020 Guidelines. *Eur Urol*. 2021;79(1):82-104. doi:10.1016/j.eururo.2020.03.055
9. Joint Commission International., Joint Commission on Accreditation of Healthcare Organizations. *Joint Commission International Accreditation Standards for Hospitals. 6th Edition.*; 2017.
10. Horn SD, DeJong G, Ryser DK, Veazie PJ, Teraoka J. Another look at observational studies in rehabilitation research: going beyond the holy grail of the randomized controlled trial. *Arch Phys Med Rehabil*. 2005;86(12 Suppl 2):S8-S15. doi:10.1016/j.apmr.2005.08.116
11. Alam N, Hobbelink EL, van Tienhoven AJ, van de Ven PM, Jansma EP, Nanayakkara PWB. The impact of the use of the Early Warning Score (EWS) on patient outcomes: A systematic review. *Resuscitation*. 2014;85(5):587-594. doi:10.1016/j.resuscitation.2014.01.013
12. Covino M, Sandroni C, Della Polla D, et al. Predicting ICU admission and death in the Emergency Department: A comparison of six early warning scores. *Resuscitation*. 2023;(March):109876. doi:10.1016/j.resuscitation.2023.109876
13. Royal College of Physicians. National Early Warning Score (NEWS) 2 Standardising the assessment of acute-illness severity in the NHS Updated report of a working party Executive summary and recommendations The Royal College of Physicians. 2017;(2017):3.
14. Akner G. Critical Appraisal of the Concept Frailty: Rating of Frailty in Elderly People has Weak Scientific Basis and should not be Used for Managing Individual Patients. *Aging Dis*. 2023;14(1):21. doi:10.14336/ad.2022.0506
15. Haren A, Lal R, Walker D, Nair R, Partridge J, Dhesi J. Frailty assessment in older urological patients prior to surgery: a systematic review and narrative synthesis. *Ther Adv Urol*. 2020;12:1-12. doi:10.1177/1756287220916614
16. Xue QL, JingTian, Walston JD, Chaves PHM, Newman AB, Bandeen-Roche K. Discrepancy in frailty identification: Move beyond predictive validity. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2020;75(2):387-393. doi:10.1093/gerona/glz052
17. Nguyen QD, Moodie EM, Keezer MR, Wolfson C. Clinical correlates and implications of the reliability of the frailty index in the Canadian longitudinal study on aging. *Journals Gerontol - Ser A Biol Sci Med Sci*. 2021;76(11):E340-E346. doi:10.1093/gerona/glab161
18. Carlson C, Merel, Susan E YM. Geriatric Syndromes and Geriatric Assessment for the Generalist. *Med Clin North Am*. 2015;99:263-279. doi:10.1016/j.mcna.2014.11.003
19. Bernardini B, Gardella ML V. *IPER 2 Indicatori Di Processo Esito in Riabilitazione, Versione 2. Uno*

Strumento per l'audit Clinico e Il Controllo Di Gestione.; 2012.

20. Bernardini B, Baratto L, Pizzi C, et al. A multicenter prospective study validated a nomogram to predict individual risk of dependence in ambulation after rehabilitation. *J Clin Epidemiol*. 2023;154:97-107. doi:10.1016/j.jclinepi.2022.10.021
21. Chan A, Tetzlaff JM, Altman DG. SPIRIT 2013 Statement : Defining Standard Protocol Items for Clinical Trials. *Ann Intern Med*. 2016;158(3):200-207. doi:10.7326/0003-4819-158-3-201302050-00583.Requests

FRAME study protocol, advanced draft (Bernardini Bruno)

APPENDIX 1

HUMANITAS
RESEARCH HOSPITAL

FLIGS (Functional Limitations and Geriatric Syndromes) FRAILTY QUESTIONNAIRE ver. 2.1a

(Bernardini B, Badalamenti S, et al)

INDICATORI

A. LIMITAZIONI FUNZIONALI	No	Si	Note
1. E' seguito/a da badante e/o da parenti per più di 6h/24			
2. Deve essere seguito o aiutato per fare il bagno o la doccia			
3. Deve essere aiutato per vestirsi			
4. Deve essere seguito o aiutato quando si muove all'interno della casa			
5. Ha bisogno di aiuto per gestire i farmaci			
6. Nelle attività usuali ha bisogno spesso di essere controllato			
7. Quando è necessario uscire di casa va sempre accompagnato			
8. Usa un bastone o altri ausili per camminare o muoversi fuori casa			
Sub-score Limitazioni Funzionali		0-8	

B. SINDROMI GERIATRICHE	No	Si
1. Ha spesso capogiri o disturbi dell'equilibrio		
2. Ha problemi seri di vista		
3. Ha problemi seri di udito o usa un apparecchio acustico		
4. Assume 5 o più farmaci al giorno (esclusi integratori e vitamine)		
5. Ha problemi importanti di memoria		
6. E' caduto negli ultimi 6 mesi		
7. Ha problemi a deglutire e tossisce quando beve		
8. E' dimagrito molto negli ultimi 6 mesi		
9. Si sente spesso giù di morale o depresso		
10. Ha problemi di incontinenza e usa assorbenti per non bagnarsi		
11. Soffre di insonnia		
12. Assume farmaci per dormire e/o tranquillanti		
13. Si lamenta spesso di dolori		
14. Si sente spesso debole e affaticato		
15. Ha disturbi del comportamento *		
Sub-score Sindromi Geriatriche		0-15

FLIGS-FQ score totale 0-23

*Questa domanda va posta ai caregiver in caso di noto deterioramento cognitivo del paziente.

ISTITUTO CLINICO HUMANITAS
Istituto di Ricovero e Cura a Carattere Scientifico

CARE PROCESSES MONITORING CHART

Complexity of care

Adverse Clinical Events

Medical Complexity Indicators

Time (to recovery)	A Early Warning Score	B reduced alertness	C Ongoing infection	D Depression	E Pain	F NGT / PEG	G Dysphagia	H Malnutrition	I Decubitus	L Urinary catheter	M Incontinence	N Venous line	O Drainage	P Respiratory Support/Tracheo
01														
02														
03														
04														
05														
06														
07														
08														
09														
10														
11														
12														
13														
14														

Functional Dependence Indicators

A Communicative disability	B Feeding	Basic mobility tasks C Supine to seat	D Sitting Balance	E Bed to Chair	F Sit to Stand	G Standing	H Walking

Adverse Clinical Events

A Delirium	B Fall	C UTI	D Pneumonia	E Sepsis	F Other

PAGE INTENTIONALLY LEFT BLANK