Clinical Microbiology and Infection 31 (2025) 847–854

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Measuring the impact of hospitalization for infectious diseases on the quality of life of older patients in four European countries: the AEQUI longitudinal matched cohort study (2020–2023)

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ARTICLE INFO

Article history:
Received 6 September 2024
Received in revised form
9 January 2025
Accepted 13 January 2025
Available online 20 January 2025

Editor: A. Kalil

Keywords:
Aged
Frailty
Functioning
Hospitalization
Infectious disease
Quality of life

ABSTRACT

Objectives: To evaluate the impact of hospitalization for infectious diseases on the Health-Related Quality of life (HRQOL), multidimensional frailty, and functioning of older patients, we conducted a longitudinal matched cohort study in four European countries.

Methods: HRQOL, frailty, and functioning were assessed using validated questionnaires at inclusion, at discharge, and up to 6 months later in patients aged over 65 years hospitalized for severe acute respiratory or bloodstream infections, and matched controls hospitalized for non-infectious conditions. Comparative analyses employed multilevel mixed-effect linear or logistic models to assess changes from inclusion.

Results: Between 2020 and 2023, 1968 patients aged 65–100 years (mean, 81) were included; 1064 (54.1%) were male and 59 (3%) were institutionalized. Of these 1968 patients, 826 were hospitalized for infectious diseases and 1142 for non-infectious conditions. At inclusion, European Quality of Life 5 Dimensions and 3 Lines scores ranged from −0.7 to 1 (full HRQOL), with a median of 0.7 across all visits and groups. Compared with controls, patients hospitalized for infectious diseases had lower scores on the Activities of Daily Living (ADL) scale (median, 4.5 vs. 5.0; p 0.020) and the Instrumental ADL scale (median, 3.0vs. 4.0; $p < 0.001$). At discharge, Instrumental ADL scores were lower in patients hospitalized for infectious diseases than in controls (median, 4.0 vs. 5.0, p 0.003), indicating reduced functioning. The proportion of frail patients, determined by a Multidimensional Prognostic Index score between 0.67 and 1, was significantly higher among patients hospitalized for infectious diseases ($n = 113/801$, 14.1%) than controls ($n = 108/1111$, 9.7%; p 0.012). At six months, no statistically significant differences were observed between groups in changes from inclusion in HRQOL (European Quality of Life 5 Dimensions and 3 Lines, p 0.436), frailty (Multidimensional Prognostic Index, p 0.269), and functioning (ADL, p 0.993).

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[*] They would like to express their sincere gratitude to all the members of the AEQUI group are listed in the Acknowledgements section.

https://doi.org/10.1016/j.cmi.2025.01.009

Discussion: Hospitalization for infectious diseases and non-infectious diseases or conditions had a similar impact on HRQOL in non-institutionalized older adults. **Nicola Veronese, Clin Microbiol Infect 2025;31:847**

Introduction

As population ages in Europe and older adults are more frequently hospitalized than the general population, hospital services use is expected to rise over the next decades [1,2]. Infectious diseases, especially acute respiratory infections, are leading causes of hospitalization in older adults [3]. Age-related factors like immunosenescence and frailty make acute respiratory infections more severe in older adults, resulting in higher hospitalization and mortality rates [4]. Although less common, bloodstream infections (BSIs) significantly impact morbidity and mortality [5], ranking over among Europe's top seven causes of death [5]. BSIs are pauci-symptomatic in older adults, which delays diagnosis [6,7]. The rise of antibiotic-resistant bacteria makes their complete eradication difficult [8,9]. Finally, infectious diseases are frequently associated with long-term hospital stays in older adults [10].

Traditionally, the impact of infectious diseases has been assessed during the acute illness phase (e.g. hospital admissions). However, infectious diseases can adversely affect health-related quality of life (HRQOL) and functioning in older patients for months and may exacerbate frailty [11]. Several national observational studies have measured the effect of infectious disease-related hospitalizations on HRQOL, frailty, and functioning in older adults, but these studies usually focus on specific diseases such as severe acute respiratory infection (SARI) or specific pathogens (e.g. influenza) [12–18]. None measured the impact of infectious diseases using validated questionnaires assessing a wide range of endpoints related to HRQOL, frailty, and autonomy.

We conducted AEQUI (Aged European population QUality of life in Infectious diseases), a longitudinal matched cohort study across four European countries. Our study aimed to measure the impact of hospitalization for infectious diseases on HRQOL, frailty, and functioning inpatients aged 65 and over (65+) from hospital discharge up to 6 months later, compared with matched patients hospitalized for non-infectious conditions. Filling this gap would strengthen the evidence and guide public health policies on vaccination and other infection prevention strategies to promote healthy ageing.

Methods

Study design and participants

AEQUI was a prospective study conducted on 24 European sites (Table S1). Its protocol was approved by appropriate Ethical committees in each country. All participants signed an informed consent form before inclusion (Clinical trial NCT04825132).

All hospitalized male and female 65+ patients consenting to be contacted 3 (M3) and 6 months (M6) after hospital discharge were included. Bedridden or terminally ill patients, patients with persistent hemiplegia (stroke), blindness, or overt dementia, and patients who were not able to answer follow-up phone call assessments were excluded. Bedridden or terminally ill patients were defined by a score $\leq$2 on the Activities of Daily Living (ADL) questionnaire [19] or a score $\geq$8 on the Clinical Frailty Scale (CFS) [20].

Cases and controls

Cases comprised patients hospitalized for SARI, regardless of its aetiology, BSI, or both. SARI was defined using the WHO definition [21] and confirmed by chest X-ray or CT scan for lower respiratory tract infection. BSI was defined as a positive blood culture without catheter colonization or catheter-related infection. Per protocol, the number of cases of BSI was to be limited to a maximum of one in three inclusions and that of SARI because of COVID-19 in one in five inclusions for SARI. For each case, up to two matched controls were included. Matched controls were patients of the same sex and similar age (±3 years) hospitalized in the same setting during the same period (±1 month) but without suspicion of infection.

Clinical assessment and laboratory testing

Patients' characteristics were collected at inclusion (i.e. within the first 3 days of the hospital admission). Respiratory samples were analysed using multiplex PCR and blood samples through blood culture and/or matrix-assisted laser desorption ionization—time of flight. Morbidity and mortality were assessed at discharge, M3; and M6. Validated local-language versions of standardized questionnaires were completed at inclusion, discharge, M3 (European Quality of Life 5 Dimensions and 3 Lines [EQ-5D-3L] and CFS only) and M6. At inclusion, ADL and Instrumental Activities of Daily Living (IADL) were also completed retrospectively (15 days before inclusion: i.e. before admission).

The EQ-5D-3L measures HRQOL. Its score ranges from negative (poor health) to 1 (full health) [1,22]. The CFS quantifies the degree of disability from frailty [20]. Scores range from 'very fit' to 'terminally ill' [20]. The ADL and IADL measure functioning. Their scores range from 0 to 6 (ADL) or 0 to 8 (IADL), the higher score indicating better functioning. A battery of questionnaires was completed to calculate the Multidimensional Prognostic Index (MPI) [23] (Table S2). Its score ranges from 0 (lowest) to 1 (highest frailty).

Endpoints

The primary endpoint was the change from baseline (i.e. inclusion) in HRQOL throughout the study. The secondary endpoints were the following: changes from baseline (i.e. inclusion) in frailty; changes from baseline (i.e. inclusion or 15 days before inclusion) in functioning; aetiology of SARI or BSI; morbidity (housing and medications); mortality.

Statistical analysis and sample size

Statistical analysis was performed using Stata v16 (StataCorp LLC, TX). Descriptive analysis included reporting of statistics for continuous and categorical variables (Material S1). Missing data

were not imputed except for the EQ-5D-3L which was imputed as 0 in case of death during the study. EQ-5D-3L values were produced using the method based on the time trade-off valuation technique. Mixed linear effects models were used for comparisons between groups at baseline and at each time point after adjustment. The statistically significant threshold was set at 0.05.

For the comparison between groups in changes from baseline in HRQOL, frailty, and functioning, a multilevel mixed-effect model was used to account for the within-subject correlation. The models were linear for quantitative variables and logistic for qualitative variables. For CFS, worsening was defined as any transition between a better category to a worse category (1: 'Very fit/Well/Managing well', 2: 'Vulnerable/Mildly frail/Moderately frail' and 3: 'Severely frail/Very severely frail/Terminally ill'). It was defined as a 0.03 increment in score for MPI, and a decrease in score for ADL ($\geq$0.5) or IADL ($\geq$1).

Final models were reported as adjusted least squared mean differences for quantitative variables and ORs for qualitative variables. Point estimates were accompanied by their corresponding 95% CI. The main analysis was restricted to participants with an EQ-5D-3L score at M6, which included participants who died (see above for imputation). A sensitivity analysis was performed to assess the impact of including participants who did not provide EQ-5D-3L data at M6.

As the expected difference between cases and controls was unknown, the sample size calculation was based on the 95% CI accuracy of the difference in mean EQ-5D-3L scores between cases and controls with the following assumptions: inclusion of one case for two controls; attrition rate set of 30%; standard deviation for the mean score estimated at 0.35 and identical for cases and controls; EQ-5D-3L ranging from −0.158 to 1.000. The minimal sample size to observe a difference was 1215 patients (405 cases and 810 controls).

Results

The study lasted from 9 December 2020 to 11 December 2023. A total of 2361 patients were screened for eligibility and 2296 were included. As EQ-5D-3L scores at M6 were missing for 328 participants, the analysis population included 1968 participants: 826 cases and 1142 controls; 921 (46.8%) patients from Spain, 529 (26.9%) from Italy, 440 (22.4%) from France, and 78 (4.0%) from Germany (Fig. S1).

Participants

Patients (N = 1968) were aged 65 and 100 years; 1064 (54.1%) were male and 59 (3%) were institutionalized (Table 1). Polypharmacy was frequent. ADL scores 15 days before inclusion were similar in the two groups. Before inclusion, IADL scores were lower in cases than in controls, indicating reduced functioning. SARI was confirmed mainly by X-ray (N = 262, 90.0%) or CT scan (N = 73, 24.9%). The most frequently identified pathogens were SARS-CoV-2 and common human coronaviruses for SARI and *Escherichia coli* and *Staphylococcus aureus* for BSI (Table S3).

HRQOL, frailty, and functioning

No significant differences in EQ-5D-3L scores or changes from baseline in EQ-5D-3L scores were observed between groups throughout the study (Fig. 1 and Table 2). EQ-5D-3L scores ranged between −0.7 and 1.0, with a median of 0.7 across all visits and groups. The sensitivity analysis which included all patients did not find any significant difference between cases and controls in EQ-5D-3L scores (baseline, p 0.806; discharge, p 0.431; M3, p 0.584; M6, p 0.643) as well as in their changes from baseline (p 0.367; p 0.336; p 0.463).

Table 1
Main baseline sociodemographic and medical characteristics of participants (N = 1968)

Sociodemographic and medical characteristics		Cases (N = 826)	Controls (N = 1142)
Age (y) (a)	Mean (SD)	81.2 (7.8)	81.4 (7.3)
	Median (min; max)	82 (65; 100)	82 (65; 99)
Sex, male (b)	%	55.7%	52.9%
Vaccination			
Up-to-date, yes (c)	%	85.3	86.0
Pneumococcal vaccine, yes (d)	%	53.2	50.0
Influenza vaccine, yes (e)	%	82.1	81.8
Type of housing (f)			
Home, alone	%	50.8	52.7
Home, with care	%	45.4	44.9
Institutionalized[a]	%	3.8	2.5
CIRS score (g)	Mean (SD)	3.4 (2.1)	3.4 (2.0)
	Median (min; max)	3 (0; 10)	3 (0; 10)
Number of medications (h)[b]	Mean (SD)	7.5 (4.3)	7.3 (3.9)
	Median (min; max)	7 (0; 25)	7 (0; 24)
At least one of the following			
Cardiovascular (i)	%	85.0	85.5
Antiplatelet (j)	%	32.6	29.8
Anticoagulant (k)	%	34.7	37.5
Oral hypoglycaemic/insulin (l)	%	31.5	33.1
Immunosuppressant (m)	%	5.3	4.8
Corticosteroids (n)	%	23.6	12.9
NSAIDs (o)	%	12.0	18.7
Psychotropic (p)	%	30.8	30.0

Being 'Up-to-date' means that, at inclusion, the patient has received all vaccines recommended in their age group in their country.
Missing data: (a) 16 and 19; (b) 0 and 1; (c) 295 and 336; (d) 347 and 386; (e) 207 and 202; (f) 0 and 1; (g) 20 and 20; (h) 9 and 20; (i) 20 and 15; (j) 20 and 17; (k) 24 and 18; (l) 22 and 17; (m) 22 and 25; (n) 22 and 20; (o) 24 and 24; and (p) 27 and 21 for cases and controls, respectively.
CIRS, Cumulative Illness Rating Scale; max, maximum; min, minimum; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation.
[a] Living in a skilled nursing facility, residential care, or long-term care.
[b] Medications for chronic diseases taken before hospitalization.

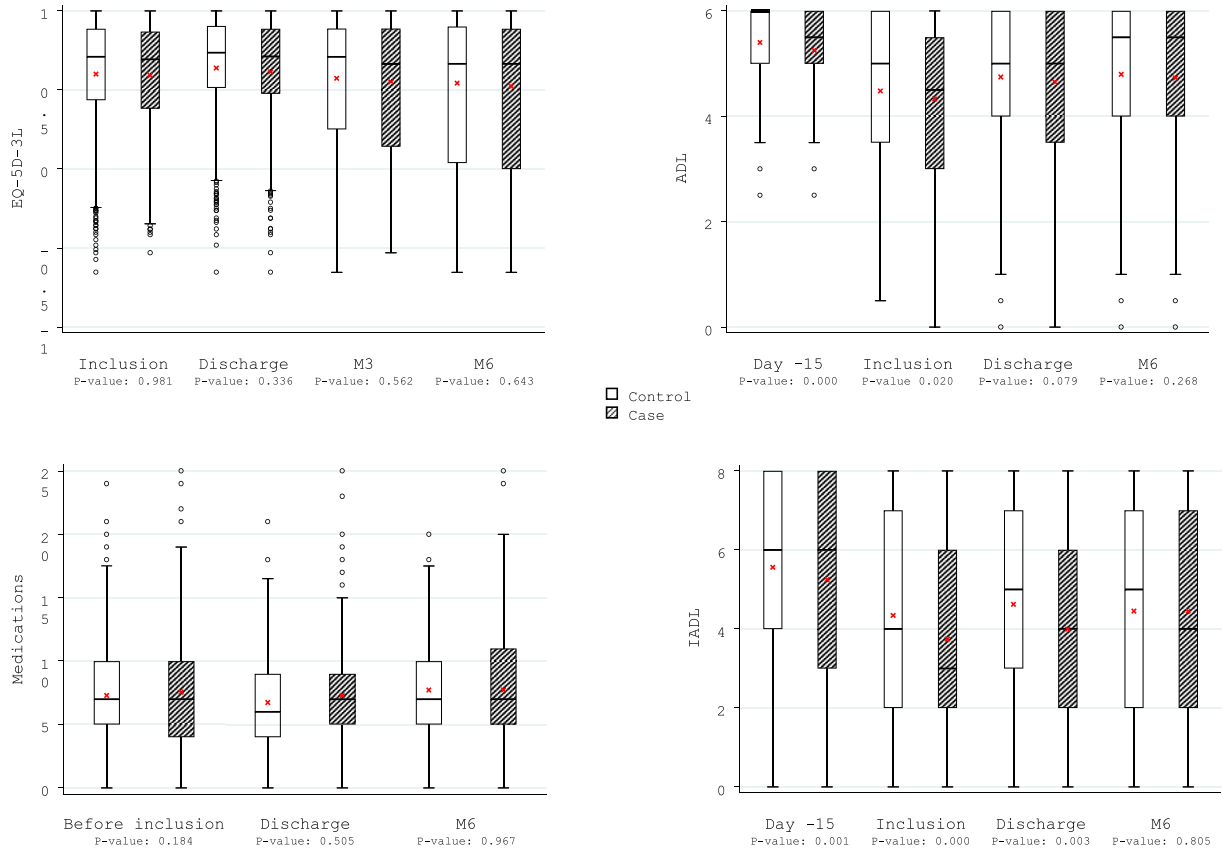

Fig. 1. Quality of life, functioning, and medication use throughout the study (N = 1968). The symbol X represents the mean for each group of patients. For medications, one patient with 55 medications at discharge was excluded from the graph. ADL, Activities of Daily Living; day -15, 15 days before inclusion; EQ-5D-3L, EuroQol 5 Dimension, 3-Level; IADL, Instrumental Activities of Daily Living; M, month. worsening in IADL case higher than control.

Table 2
Change from baseline in quality of life, functioning, and medication use throughout the study (*N* = 1968)

Change in quality of life, functioning, and medication use from			Cases (*N*)	Controls (*N*)	LS adjusted between case-control difference (SE) (95% CI)[a]		p
Inclusion	EQ-5D-3L	Discharge	792	1102	−0.02 (0.02)	(−0.05 to 0.01)	0.242
		M3	802	1111	−0.01 (0.02)	(−0.05 to 0.02)	0.381
		M6	807	1117	−0.01 (0.02)	(−0.05 to 0.02)	0.436
	ADL	Discharge	785	1070	0.01 (0.07)	(−0.12 to 0.14)	0.894
		M6	645	906	−0.00 (0.07)	(−0.13 to 0.13)	0.993
	IADL	Discharge	208	280	0.13 (0.16)	(−0.19 to 0.45)	0.434
		M6	626	890	0.50 (0.11)	(0.28 to 0.72)	0.000
	Number of medications	Discharge	410	459	0.16 (0.15)	(−0.14 to 0.45)	0.302
		M6	807	1117	−0.32 (0.02)	(−0.57 to −0.06)	0.015
15 days before inclusion	ADL	M6	631	893	0.07 (0.07)	(−0.06 to 0.21)	0.271
	IADL	M6	597	863	**0.22** (0.11)	(0.01 to 0.42)	**0.041**

Baseline values were collected at inclusion in the study for EQ-5D-3L and at inclusion and retrospectively (15 days before inclusion) for ADL and IADL.
Bold signifies the n = number of participants ot analysis (as a reminder).
Negative least squared mean difference between cases and controls indicates that change from baseline (i.e. at inclusion or at inclusion and 15 days before inclusion for ADL and IADL) was lower in cases than controls.
ADL, Activities of Daily Living; EQ-5D-3L, EuroQol 5 dimensions - 3 levels; IADL, Instrumental Activities of Daily Living; M, month; SE, standard error.
[a] Reference category = controls. Differences are adjusted by country, age, sex, basal score value, Chronic obstructive pulmonary Disease (COPD) and type of housing.

Based on CFS, most patients were 'vulnerable', 'mildly frail', or 'moderately frail' throughout the study, with no significant difference between groups (Fig. 2). The risk of worsening (compared with baseline) was similar across all visits and groups (Table 3).

The percentage of patients with MPI scores between 0.67 and 1 was statistically significantly greater in cases than controls at baseline (p 0.012) but not at discharge or M6 (Fig. 2). The risk of worsening (compared with baseline) was similar in both groups at both visits (Table 3).

ADL scores were significantly lower in cases than controls, indicating that cases needed more help to perform self-care activities 15 days before inclusion (p < 0.001) and at inclusion (p 0.020), but not at discharge or M6 (Fig. 1). No statistically significant differences were observed between groups in changes from baseline in ADL scores at M6 independently of the baseline (Table 2), and no statistically significant difference was observed in the percentage of patients with ADL decline from 15 days before inclusion to M6 (Table 3).

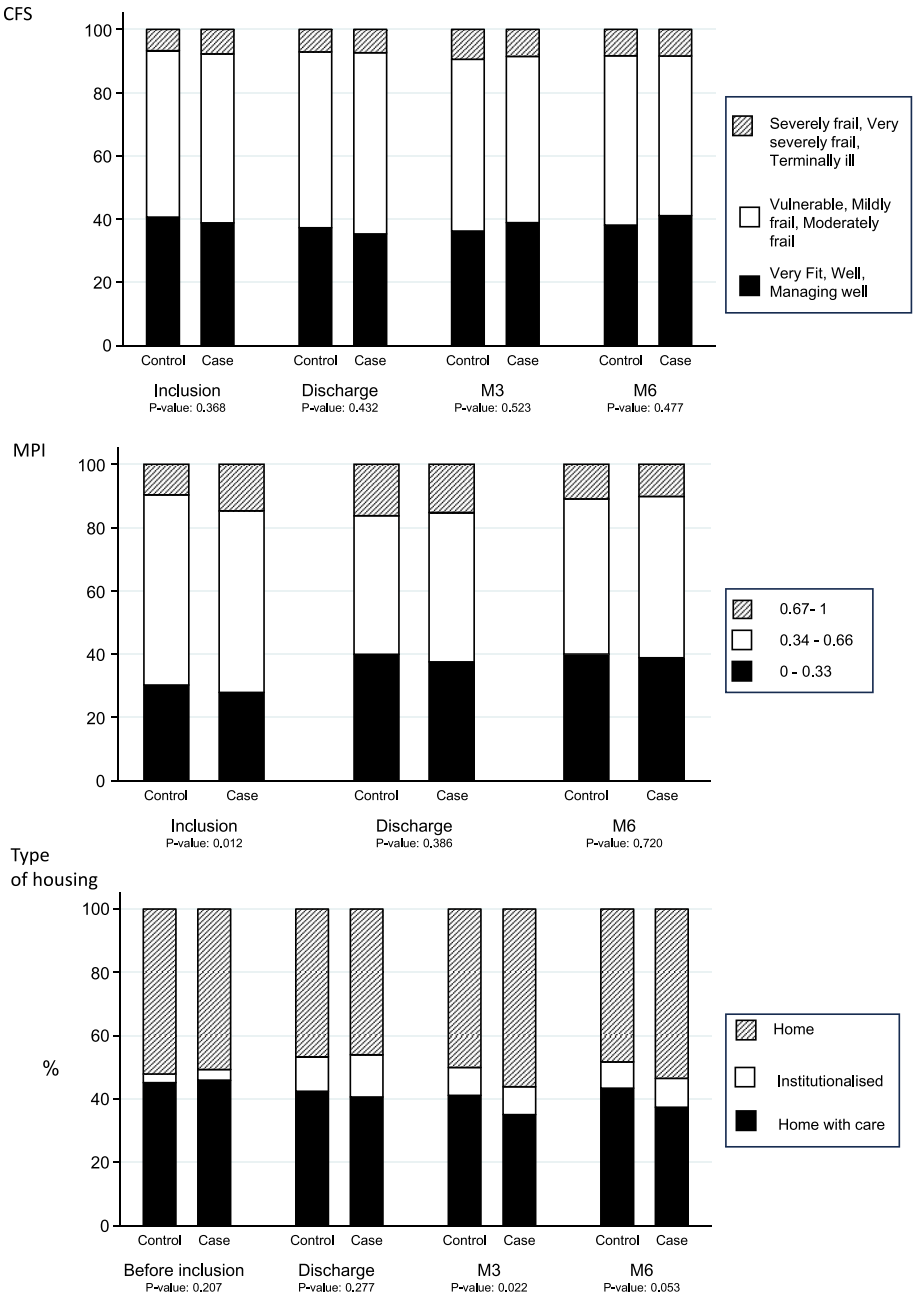

Fig. 2. Frailty and housing throughout the study ($N = 1968$). CFS, Clinical Frailty Score; M, month; MPI, Multidimensional Prognostic Index.

IADL scores were significantly lower in cases than controls 15 days before inclusion (p 0.001), at inclusion (p < 0.001), and discharge (p 0.003) (Fig. 1). At M6, the improvement in IADL scores was statistically significantly higher in cases than controls. The adjusted difference was +0.22 (p 0.041) when the baseline was 15 days before inclusion; it was +0.50 (p 0.000) with inclusion as the baseline (Table 2). However, IADL scores were lower at M6 than 15 days before inclusion in both groups (Fig. 1).

Clinical outcomes

In both groups, hospital stay lasted 6 days (median). During the hospital stay, percentages of patients admitted to intensive care unit (ICU) or intermediate care (5.5% vs. 3.5%), needing mechanical ventilation (5.5% vs. 1.7%), and with life-threatening complications (9.8% vs. 4.9%) were higher for cases than controls. Mortality rates were higher in cases than controls throughout the study: in-hospital, 5.2% vs. 3.1%; M3, 13.3% vs. 11.0%; M6, 19.6% vs. 17.3%.

The percentage of patients institutionalized was higher at discharge and after discharge than before hospital admission. The percentage peaked at discharge. It was statistically significantly greater for cases than controls at M3 (p 0.022) and marginally significantly at M6 (p 0.053) (Fig. 2). Cases had a higher risk of being institutionalized at M3 (p 0.012) or M6 (p 0.001) than controls (Table 3).

The number of medications taken by each patient was stable throughout the study, with no difference between groups (Fig. 1). At M6, the decrease in the number of medications from baseline (before hospital admission) was significantly lower for cases than controls (adjusted difference, −0.32; p 0.015) (Table 2).

Table 3
Change from baseline in frailty, type of housing, and activities of daily living throughout the study ($N = 1968$)

Worsening in frailty, functioning, and housing from			Cases/total (%)		Controls/total, %		Adjusted OR (SE)[a] (95% CI)		p
Inclusion	CFS	Discharge	99/757	(13)	139/1073	(13)	1.00 (0.15)	(0.75–1.33)	0.988
		M3	122/703	(17)	206/996	(21)	0.80 (0.10)	(0.62–1.03)	0.089
		M6	124/659	(19)	200/930	(22)	0.84 (0.11)	(0.65–1.08)	0.175
	MPI	Discharge	309/774	(40)	463/1085	(43)	0.91 (0.09)	(0.75–1.11)	0.362
		M6	230/685	(34)	354/963	(37)	0.89 (0.10)	(0.72–1.10)	0.269
	Housing	Discharge	107/750	(14)	120/1069	(11)	1.28 (0.19)	(0.95–1.71)	0.105
		M3	135/706	(19)	133/990	(13)	1.44 (0.21)	(1.09–1.92)	0.012
		M6	119/651	(18)	105/921	(11)	1.65 (0.25)	(1.22–2.22)	0.001
15 days before inclusion	ADL	M6	205/631	(32)	298/893	(33)	0.94 (0.12)	(0.75–1.20)	0.647
	IADL	M6	297/597	(50)	465/863	(54)	0.79 (0.09)	(0.64–0.98)	0.035

Baseline values were collected at inclusion for CFS and MPI, before inclusion for housing, and retrospectively (15 days before inclusion) at baseline ADL and IADL.
Worsening was defined as a change to a worse category (i.e. achieving a greater level of care) for CFS and housing from inclusion, a 0.03-point increase in score for MPI from inclusion, and a 0.5-point decrease in ADL or 1-point decrease in IADL from inclusion or 15 days before inclusion. ORs>1 indicate worsening as compared with controls.
ADL, Activities of Daily Living; CFS, Clinical Frailty Score; IADL, Instrumental Activities of Daily Living; M, month; MPI, Multidimensional Prognostic Index; SE, standard error.

Discussion

Our longitudinal cohort study involved 65+ patients almost always not institutionalized. It evaluated the impact of hospitalization for infectious diseases on the HRQOL, frailty, and functioning of patients hospitalized for infectious diseases compared with matched patients hospitalized with non-infectious conditions. It found no statistically significant differences in HRQOL, frailty, and functioning or changes from baseline when assessed by the EQ-5D-3L, CFS, and ADL, respectively, and a few statistically significant differences in frailty and functioning when evaluated by the MPI and IADL, or in morbidity (housing or medications) and mortality 6 months after discharge. Finally, 6 months after discharge, the HRQOL, frailty, and functioning scores were similar in older patients hospitalized for infectious or non-infectious diseases.

Previous cohort studies have established that infectious diseases affect HRQOL and frailty [12,13,16,17]. Therefore, our results indicated that hospitalization for infectious and non-infectious diseases similarly impacted HRQOL, frailty, and functioning. This suggested that the hospitalization, rather than the infectious disease, affects these outcomes. Employing a control group (specifically matched on relevant characteristics) is essential when assessing the effect of diseases or interventions on HRQOL, frailty, or autonomy of older adults over various time frame.

Our results also possibly reflected the lack of sensitivity of the used instruments. The EQ-5D-3L, a commonly used generic HRQOL instrument, may not effectively discern differences in HRQOL among patients whose HRQOL has been impaired by hospitalization and disease. This was evidenced by the stable EQ-5D-3L scores observed in our study and corroborated by Zhang et al. [13] who found significant HRQOL differences (assessed by the Short-Form 36) between sepsis survivors and community controls, but not between sepsis survivors and non-septic critically ill controls. Phenotypical frailty as defined by CFS is less sensitive than a frailty index like the MPI in detecting minor frailty changes. The CFS identifies only obvious changes when MPI can detect smaller changes, as observed in our study. However, the differences noted using the MPI between patients hospitalized for infectious diseases and the other patients were transient. Regarding functioning, differences were observed between patients hospitalized for infectious diseases and the other patients when using the IADL, but not the ADL scale. This indicated that activities explored by the IADL declined earlier than the basic activities explored by the ADLs, explaining the ceiling effects reported with ADL scores.

The strengths of our study include the multicentric design across various European countries, the matched groups, and the use of several questionnaires. Our study also has limitations. First, we focused on SARI for its prevalence and BSI for its severity (BSIs related to central line infections excluded) [3–5]. Doing this may have introduced selection bias towards patients with milder infectious diseases, leading to shorter hospital stays and potentially minimal impact on HRQOL, frailty, and functioning. Second, patients were matched on age, sex, chonic obstructive pulomonary disease (COPD), town of residence, and type of housing, but not on their medical history. This omission means that some matched patients might have had recent infectious diseases. For instance, in winter, infectious diseases (e.g. influenza), and hospitalizations for hip fractures appear to be related in older adults [24,25]. Third, the analysis was performed on patients with EQ-5D-3L scores at M6, excluding patients who died during the study whereas the fatality rate was greater in patients hospitalized for infectious diseases than in the other patients. However, a sensitive analysis including all patients provided similar results. Finally, patient-reported outcome measures of HRQOL or disability may not fully capture the complexities of changes in HRQOL and functioning in older adults, particularly those with pre-existing limitations before hospitalization [12,26]. Previous research [12] indicates that survivors of severe sepsis hospitalization were at greater risk of additional functional limitations than patients hospitalized for non-sepsis general causes. Notably, the negative impact of sepsis hospitalization was observed in survivors with no or mild-to-moderate limitations before sepsis. In our study, patients were older and had severe limitations.

Healthy ageing is a challenge in all countries [27,28]. Although according to our study, hospitalization was the main factor impacting the HRQOL, frailty, and functioning of older patients hospitalized for infectious diseases, preventing infectious diseases is crucial in this population. Numerous infectious diseases, especially those leading to SARI or BSI, are vaccine preventable (e.g. influenza, COVID-19 and invasive pneumococcal disease) [29,30]. In this population, vaccine efficacy is compromised by immunosenescence, malnutrition, and comorbidity. Furthermore, vaccination coverage rates are low [4]. Sustained efforts to improve vaccine efficacy, vaccination coverage rates, and other infection prevention strategies are thus necessary to promote healthy ageing.

Conclusion

In non-institutionalized older adults, infectious diseases did not have a higher impact on HRQOL than other causes for hospital admission. However, such hospitalizations impact HRQOL, frailty, and functioning. Given that infectious diseases are a leading cause of hospitalization in this population, our study highlights the importance of their prevention.

Author contributions

All the authors have made substantial contributions to the conception or design of the work and the analysis or the interpretation of data for the work. They have reviewed the manuscript critically for important intellectual content and have approved the version submitted for publication. They agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. N.V. and M.C.P. contributed equally to this work.

Transparency declaration

Potential conflict of interest

N.V., J.Z., G.R.-C., A.B., A.L.-S., D.P., A.J.C.-J., and G.G. declare that they have no conflict of interest. M.C.P. reports grants or contracts from the German Ministry of Education and Research; royalties or licenses for the latest edition of 'Paziente Anziano - Paziente Geriatrico - Medicina della Complessità', EdiSES 2020 and 'Ratgeber Altern - Es ist nie zu spät', Elsevier 2021; consulting fees and participation on the Editorial Board Deutsche Medizinische Wochenschrift and the Editorial Board Ageing Research Reviews; payment or honoraria from Gilead. S.M. reports payment or honoraria from Sanofi, GSK, MSD, Moderna, Pfizer, BioNTech, and Viatris; support for attending meetings and/or travel from Moderna, BioNTech and Pfizer; participation on a Data Safety Monitoring Board or Advisory Board from Moderna, Pfizer and GSK. M.B. and P.B. are employees of Sanofi. J.D.A.-H. reports payment or honoraria from Ordesa, Fresenius, and Lundbeck. J.-P.L. reports grants or contracts from Paratek; payment or honoraria from Sanofi, Gilead, MSD, AEI, Pfizer, Tillots and ViiV Healthcare; payment for expert testimony from the French Police; support for attending meetings and/or travel from Overcome, Sanofi, Pfizer and Tillots; participation in an academic study.

Financial report

This study received funding from Sanofi. The founder had no role in the study's design, data collection, analysis, interpretation, manuscript writing, or the decision to publish the results.

Data availability

The protocol, study report, and data that support the findings of this study are available on request from the corresponding author.

Acknowledgements

The authors want to thank the VITAL consortium (members of WP1 and WP3) for their critical review of the study protocol and statistical analysis plan. They acknowledge the support of Abelia Science (Saint-Georges-sur-Baulche, France) for its assistance in medical writing. The manuscript was written online on MyPubli. They would like to express their sincere gratitude to all the members of the AEQUI group.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2025.01.009.

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