Return to the workforce following infective endocarditis

A nationwide cohort study

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Return to the Workforce Following Infective Endocarditis – a Nationwide Cohort Study

Running title: *Butt et al.; Return to the workforce after IE*

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Abstract

Background: The ability to return to work after infective endocarditis (IE) holds important socioeconomic consequences for both patients and society, yet data on this issue are sparse. We examined return to the workforce and associated factors in IE patients of working age.

Methods and results: Using Danish nationwide registries, we identified 1065 patients aged 18-60 years with a first-time diagnosis of IE (1996-2013) who were part of the workforce prior to admission and alive at discharge. One year after discharge, 765 (71.8%) patients had returned to the workforce, 130 (12.2%) were on paid sick leave, 76 (7.1%) received disability pension, 23 (2.2%) were on early retirement, 65 (6.1%) had died, and 6 (0.6%) had emigrated. Factors associated with return to the workforce were identified using multivariable logistic regression. Younger age (18-40 versus 56-60 years; odds ratio, 2.85; 95% confidence interval, 1.71-4.76) and higher level of education (higher educational level versus basic school; 5.47,2.05-14.6) and income (highest quartile versus lowest; 3.17,1.85-5.46) were associated with return to the workforce. Longer length of hospital stay (>90 versus 14-30 days; 0.16,0.07-0.38), stroke during IE admission (0.38,0.21-0.71), and a history of chronic kidney disease (0.29,0.11-0.75), chronic obstructive pulmonary disease (0.31,0.13-0.71), and malignancy (0.39,0.22-0.69) were associated with a lower likelihood of returning to the workforce.

Conclusions: Seven out of ten patients who were part of the workforce prior to IE and alive at discharge were part of the workforce one year later. Younger age, higher socioeconomic status, and absence of major comorbidities were associated with return to the workforce.

Key words: Epidemiology; infective endocarditis; workforce attachment.

Introduction

Despite major advances in diagnostic imaging, antimicrobial therapy, and surgical treatment, infective endocarditis (IE) remains a disease with high morbidity and mortality.[1, 2] As survivors may be left with life-changing physical and mental disabilities, traditional outcome measures such as mortality, morbidity, and serious adverse events do not provide a complete assessment of the consequences of the disease.[3] Hence, a more comprehensive assessment should include outcomes of recovery and function at home and in society including quality of life and return to work.[4-6] Employment is important for physical and mental health, self-esteem, and social identity, but work capability also provides financial independence and economic contribution to the society.[7-11] Identifying patients at high risk of workforce detachment is of great importance and may aid in forestalling the aggravation of symptoms by providing better and more focused care. However, the ability to return to work after IE has only been sparsely investigated.[3] To address these issues, we conducted a nationwide cohort study in Denmark to examine return to the workforce and associated factors in patients with first-time IE of working age.

Methods

The Danish healthcare and social welfare systems

The Danish healthcare system, funded by taxes, provides free and equal access to healthcare for all residents regardless of employment status. Similarly, social welfare benefits and social services, also financed by taxes, are provided to residents whenever indicated. These benefits include, but are not limited to, state educational grants, unemployment benefits, and disability pension. In Denmark, all residents are offered a fully state-funded pension at the age of 65 or later depending on the date of birth.

Data sources

All residents in Denmark are assigned a unique and permanent civil registration number allowing accurate linkage of nationwide administrative registries at an individual level. The Danish registry on all public welfare benefits holds information on all Danish residents who have received public welfare benefits at any time on a weekly basis since 1991.[12, 13] The Danish National Patient Registry contains information on all hospital admissions since 1977 and all surgical procedures since 1996. Each admission is registered by one primary diagnosis and, if appropriate, one or more secondary diagnosis according to the International Classification of Diseases (ICD-8 until 1993 and ICD-10 from 1994) and operations are classified according to the NOMESCO Classification of Surgical Procedures (NCSP). The diagnosis of IE in patients below 60 years of age has been validated with a positive predictive value of 88% in the Danish National Patient Registry.[14] The Danish National Prescription Registry holds detailed information on all claimed drug prescriptions dispensed from pharmacies in Denmark.[15] Information on vital status was obtained from the Danish National Population Registry,[16] and data on education and household income was attained from the Statistics Denmark.[17, 18]

Study population

All Danish residents with a first-time diagnosis of IE between January 1, 1996 and December 31, 2013 were identified. Only patients of working age between 18 and 60 years, who were part of the workforce 30 days prior to admission and alive at discharge after IE were included and comprised the study population.

Study covariates

Comorbidity was defined using hospital discharge diagnoses any time prior to and including index hospitalization for IE (Supplementary Table 1 for ICD-8 and ICD-10 codes). Patients with diabetes and hypertension were identified using claimed drug prescriptions as done previously.[19, 20] Stroke during admission was defined using hospital discharge diagnoses during index hospitalization. In addition, Charlson Comorbidity Index was calculated as described previously to quantify the burden of comorbidities at discharge (Supplementary Table 2 for the weight of each comorbidity).[21] Patients with a Charlson Comorbidity Index greater than 2 were considered as having significant comorbidities. Surgical procedures were assessed prior to and during index hospitalization. Concomitant pharmacotherapy was defined by claimed prescriptions within 180 days prior to admission for IE (Supplementary Table 3 for ATC codes). The number of hospital admissions within the first year after discharge for IE was determined based on hospital discharge diagnosis. The highest level of completed education prior to admission for IE was classified according to the International Standard Classification of Education (i.e. basic school, high school, vocational education, short/medium length higher education, and long higher education or research). Average 5-year household income prior to admission for IE was calculated and graded in quartiles.

Workforce attachment

Patients were classified as part of the workforce if they were employed, unemployed but capable of working (i.e. not receiving paid sick leave or disability pension or not on early retirement), or received state educational grants, paid maternity leave, or other leave of absence. Employment status 30 days prior to admission for IE was assessed based on the five weeks leading up to this date, and only patients who were part of the workforce were included in the study. Five-week evaluation periods were applied in order to reduce misclassification, i.e. to ensure that patients with short-term sick leave were not classified as

detached from the workforce as described previously.[22, 23] Therefore, only patients with sick leave of at least three out of the five evaluated weeks were classified as detached from the workforce. Our study design ensured that no patients could reach the state pension age during the study follow-up period. Further, it was possible for patients to change status (i.e. attachment or detachment from the workforce) at later evaluations during follow-up.

Outcomes

The primary endpoint of the study was return to the workforce estimated in the five-week period one year after discharge for IE. Outcomes, i.e. part of the workforce, detached from the workforce, and death, were assessed every 6 months for a total of two years after IE.

Sensitivity analysis

To test the robustness of our results, we varied our definition of detachment from the workforce to two and four out of five weeks, respectively. Further, we examined return to work among patients, who were employed (i.e. patients in employment and not receiving any social benefits) 30 days prior to IE.

Statistical analyses

Descriptive data were reported as frequencies and percentages or medians with interquartile range (IQR) as appropriate. Baseline characteristics were summarized separately for age groups (18-40, 41-55, 56-60 years) and differences between age groups were tested by applying the chi-square test for categorical variables. Factors associated with return to the workforce one year after IE were identified using logistic regression, adjusted for age, gender, income, education, comorbidities, admission characteristics, hospital admissions within the first year post-discharge, and year of IE. Patients who were not followed for one

year due to emigration or death were set as detached from the workforce in the logistic regression analysis. Relevant interactions were tested by likelihood ratio test and found not significant, unless otherwise stated. All statistical analyses were performed with SAS statistical software (SAS 9.4, SAS Institute, Cary, North Carolina, USA), and a two-sided p-value <0.05 was considered statistically significant.

Ethics

Approval for this study was obtained by the Danish Data Protection Agency (No. 2007-58-0015; internal reference: *GEH-2014-014*, I-Suite no. 02732). In Denmark, register-based studies in which individuals cannot be identified do not require ethical approval. No extramural funding was used to support this work.

Results

Between January 1, 1996 and December 31, 2013, a total of 5804 patients had a first-time diagnosis of IE and 1678 patients were of working age between 18-60 years and alive at discharge (Figure 1). Of these, 1065 (63.5%) were part of the workforce 30 days prior to admission and comprised the study population (Table 1). Baseline characteristics, admission characteristics, and hospital admissions within the first year post-discharge stratified according to age are summarized in Table 2 and 3, respectively. The median age of the study population was 48 years (IQR 18) and 73.6% were men. The median length of hospital stay was 43 days (IQR 21), and 42.0% underwent valve surgery during admission. Younger patients (age 18-40) were less likely to undergo valve surgery, had a shorter length of stay, had fewer comorbidities and were less likely to be men compared with older patients.

Return to the workforce following IE

One year after discharge for IE, 765 (71.8%) patients returned to the workforce, 130 (12.2%) were on paid sick leave, 76 (7.1%) received disability pension, 23 (2.2%) were on early retirement, 65 (6.1%) had died, and 6 (0.6%) had emigrated. The proportion of patients returning to the workforce at one-year follow-up ranged from 62.3% to 81.3% according to age groups and was lowest in the oldest age group. One-year mortality was comparable across age groups and ranged from 5.8% to 6.3%. Over time, there was a trend towards an increase in the proportion of patients who were part of the workforce one year after discharge for IE (71.0% in the period 1996-2001, 69.1% in the period 2002-2007, and 75.4% in the period 2008-2013), although this association was not statistically significant ($p = 0.16$)

The distribution of outcomes every 6 months for a total of two years after discharge for IE according to age is shown in Figure 2. The proportion of patients returning to the workforce over time elapsed since discharge for IE was comparable in the two youngest age groups and declined in the oldest age group.

The distribution of outcomes at one-year follow-up in patients with and without significant comorbidities at discharge is presented in Figure 3. 149 (14.0%) patients had significant comorbidities (Charlson Comorbidity Index > 2) at discharge. Regardless of age, patients with significant comorbidities were less likely to return to the workforce compared with those without significant comorbidities, and the difference was most prominent in patients aged 41-55 years (74.3% without versus 43.7% with significant comorbidities). Likewise, a higher mortality was observed among patients with significant comorbidities compared with those without significant comorbidities.

Factors associated with return to the workforce

Results from the multivariate logistic regression for return to the workforce one year after discharge for IE are shown in Figure 4. Factors associated with a higher likelihood of

returning to the workforce were younger age, and higher level of education and income. Stroke during admission, longer length of hospital stay, as well as a history of chronic kidney disease, chronic obstructive pulmonary disease, acute myocardial infarction, and malignancy, and more hospital admissions within a year post-discharge were associated with a lower likelihood of returning to the workforce. There was a trend in the association between lower likelihood of returning to the workforce and a history of heart failure, hypertension, peripheral vascular disease, and liver disease, although not statistically significant.

Sensitivity analyses

To test the robustness of our findings, we varied our definition of detachment from the workforce from three to two or four out of five weeks, respectively and found no difference in the proportion of patients returning to the workforce one year after discharge for IE (71.1% and 72.0% for two and four weeks, respectively). Further, we examined return to work (i.e. patients in actual employment and not receiving any social benefits) among those, who were employed prior to IE and alive at discharge. The proportion of patients returning to work one year after discharge for IE was similar as for patients returning to the workforce (67.5% versus 71.8%).

Discussion

In this nationwide cohort study, we examined return to the workforce in patients of working age between 18 and 60 years with a first-time diagnosis of IE. Our study yielded the following findings: First, seven out of ten patients who were part of the workforce prior to admission and alive at discharge returned to the workforce one year later and less than one out of ten died. Second, younger age and higher socioeconomic status were associated with a higher likelihood of returning to the workforce whereas comorbidities, stroke during

admission, longer length of hospital stay, and additional hospital admissions within a year post-discharge after IE were associated with a lower likelihood of returning to the workforce.

Previous studies suggest that a substantial part of patients treated for IE may experience physical and cognitive difficulties such as fatigue, physical weakness, concentration difficulties, and memory loss, resulting in may have impaired health-related quality of life and poor self-perceived physical health post-discharge.[3, 24-28] Only a single questionnaire-based study has investigated employment status in 37 patients with IE and found that 65% were working one year after discharge.[3] To our knowledge, our study is the first to examine return to the workforce after first-time IE in a large unselected cohort of patients on a nationwide scale. Notably, we found that more than seven out of ten patients who were part of the workforce 30 days prior to first-time IE returned to the workforce one year after discharge. A recent study found a similar proportion of patients returning to the workforce one year after first-time hospitalization for heart failure (68%).[23] Among patients with infectious spondylodiscitis, 73% returned to the workforce within two years of follow-up.[29] In contrast, a higher proportion of patients returned to the workforce one year after community-acquired bacteremia (78%) compared with IE survivors in our study.[30] Likewise, a higher proportion of patients who survived pneumococcal meningitis and viral encephalitis were working one year after hospitalization (93% and 84%, respectively).[31] Thus, our findings reflect that patients who survive IE may be left with life-changing physical and mental disabilities due to the traumatic and potentially life-threatening character of the disease.

Employment has important socioeconomic consequences for both the patient and the society, but it can also enhance recovery and life satisfaction by consolidating self-esteem, confidence, and social identity.[7-11] In order to prevent detachment from the workforce to the extent possible, a better understanding of the obstacles that prevent return to work after

IE is warranted. Such information is potentially of great importance as it may help to suggest whether more intensive rehabilitation, psychological, educational, or some other therapeutic intervention may enable a successful reintegration into the workforce. Despite the major personal and economic costs to society of not returning to work, the literature is non-existent in the area of rehabilitation for patients following treatment for IE and both national and international guidelines for the management of IE do not include any recommendations on rehabilitation.[1, 2] Interventions that may impact patients' likelihood of returning to the workforce should be explored further in order to restore these as best possible and with a minimum of lost value for society. Currently, an ongoing randomized, multicenter clinical trial, CopenHeart IE, is investigating the effect of comprehensive cardiac rehabilitation versus usual care for patients treated with IE.[32] The results of this trial may therefore shed light on the effect of an integrated rehabilitation program on the physical and psychosocial functioning in patients treated for IE, including the ability to return to work.

The presence of comorbidities appears to have major impact on the likelihood of returning to the workforce in patients surviving IE. In our study, the proportion of patients returning to the workforce one year post-discharge was substantially lower if significant comorbidities were present at discharge. However, it is important to have in mind that the majority of the study population was free of significant comorbidities and even a substantial proportion of these patients failed to return to the workforce. We also found that higher socioeconomic status was associated with a higher likelihood of returning to the workforce; individuals with a higher level of education have more financial, social, and psychological resources and may have a less physically demanding job – factors which may facilitate a fast and successful reintegration into the workforce.[33, 34] Longer length of hospital stay and stroke during admission were associated with a lower likelihood of returning to the workforce as these factors reflect the severity of the course of the disease. However, valve surgery during

admission was not statistically significantly associated with a lower likelihood of returning to the workforce. Our findings may encourage a multidisciplinary approach in the management of patients treated for IE in order to increase the chance of returning to the workforce, particularly in patients identified as being at high risk of workforce detachment.

Strengths and limitations

The main strength of this study is the completeness of data in a nationwide unselected cohort of patients with a first-time diagnosis of IE followed in a real-world setting. To appreciate the findings of our study, it is important to acknowledge the limitations of our study. The accuracy of the data relies upon the coding in nationwide administrative registries, though these data have previously been validated.[14] The public health care and social benefits system in Denmark may hamper translation of our findings to countries with more restricted access to these services. Danish national guidelines for the management of patients with IE recommend that intravenous antibiotic therapy should be administered in-hospital, which may explain the long median length of hospital stay found in our study. This should be taken into account when translating our findings to countries with other practices. By design, no patients could reach the state pension age during the study follow-up period. However, the oldest patients did have the opportunity to retire early and receive early retirement benefits if the criteria for such were met; although accounting for only 2.3% of the study population, it is not unlikely that these patients did not return to the workforce due to lack of motivation and necessity rather than poor performance status. We did not have information on important prognostic factors such as microbiology and plasma creatinine levels or postoperative depression. However, this would only affect the results from the logistic regression and not our main findings. Patients who emigrated during the one-year follow-up period were set as

detached from the workforce in the logistic regression; this has most likely little to no impact on our results as only 0.3% of the study population emigrated.

Conclusion

One year after discharge, seven out of ten patients who survived first-time IE returned to the workforce and the proportion was substantially lower if significant comorbidities were present at discharge. A better understanding of the causes for not returning to the workforce is warranted and such information may suggest whether intensive rehabilitation, psychological or educational interventions may enable a successful reintegration into the workforce for patients treated for IE.

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Figure Legends

Figure 1. Flow chart of the study population selection process

Figure 2. Distribution of outcomes every 6 months for a total of two years

Figure 3. Distribution of outcomes at one-year follow-up according to comorbidities

C, Significant comorbidities; NC, No significant comorbidities.

Significant comorbidities were defined as Charlson Comorbidity Index > 2 (N=149) and no significant comorbidities as Charlson Comorbidity Index 0-2 (N=916).

Figure 4. Results from the multivariable logistic regression examining factors associated with return to the workforce one year after discharge for infective endocarditis

AMI, Acute myocardial infarction; COPD, Chronic obstructive pulmonary disease

Table 1. Employment status 30 days prior to first-time infective endocarditis in patients of working age and alive at discharge

	All patients N=1678	Age 18-40 N=458	Age 41-55 N=796	Age 56-60 N=424
In the workforce				
Employed	770 (45.9)	182 (39.7)	390 (49.0)	198 (46.7)
Study/maternity leave	32 (1.9)	21 (4.6)	4 (0.5)	32 (1.7)
Unemployed	263 (15.7)	140 (30.6)	89 (11.2)	263 (8.0)
Not in the workforce				
Sick leave	131 (7.8)	23 (5.0)	68 (8.5)	131 (9.4)
Disability pension	472 (28.1)	92 (20.1)	245 (30.8)	472 (31.8)
Early retirement	10 (0.6)	0 (0.0)	0 (0.0)	10 (2.4)

Table 2. Baseline characteristics of the study population

Characteristics	Age 18-40 N=343	Age 41-55 N=483	Age 56-60 N=239	P-value
Age (median [interquartile range])	32 (10)	49 (8)	58 (2)	
Male	233 (67.9)	361 (74.7)	190 (79.5)	< 0.01
Income group				< 0.01
Q1 (lowest)	176 (51.3)	63 (13.0)	19 (7.9)	
Q2	70 (20.4)	77 (16.0)	32 (13.4)	
Q3	57 (16.6)	144 (29.8)	91 (38.1)	
Q4 (highest)	40 (11.7)	199 (42.2)	97 (40.6)	
Education				< 0.01
Basic school	148 (43.2)	123 (25.5)	58 (24.3)	
High school	33 (9.6)	13 (2.7)	4 (1.7)	
Vocational education	86 (25.1)	193 (39.9)	100 (41.8)	
Short/medium higher education	30 (8.7)	79 (16.4)	40 (16.7)	
Long higher education	12 (3.5)	40 (8.3)	17 (7.1)	
Unknown	34 (9.9)	35 (7.2)	20 (8.4)	
Charlson Comorbidity Index				< 0.01
0-2	315 (91.8)	412 (85.3)	189 (79.1)	
> 2	28 (8.2)	71 (14.7)	50 (20.9)	
Comorbidities				
Stroke prior to IE admission	5 (1.5)	20 (4.1)	7 (2.9)	0.08
Heart failure	29 (8.5)	69 (14.3)	29 (12.1)	0.04
Atrial fibrillation	9 (2.6)	49 (10.1)	38 (15.9)	< 0.01
Myocardial infarction	4 (1.2)	17 (3.5)	20 (8.4)	< 0.01
Hypertension	32 (9.3)	124 (25.7)	104 (43.5)	< 0.01
Diabetes	7 (2.0)	23 (4.8)	22 (9.2)	< 0.01
Peripheral vascular disease	8 (2.3)	17 (3.5)	12 (5.0)	0.22
Malignancy	7 (2.0)	34 (7.0)	35 (14.6)	< 0.01
Chronic renal failure	9 (2.6)	11 (2.3)	11 (4.6)	0.20
Chronic obstructive pulmonary disease	5 (1.5)	14 (2.9)	11 (4.6)	0.08
Liver disease	10 (2.9)	17 (3.5)	12 (5.0)	0.40

Concomitant medical treatment				
Oral anticoagulants	92 (26.8)	210 (43.5)	103 (43.1)	< 0.01
Beta-blockers	40 (11.7)	112 (23.2)	82 (34.3)	< 0.01
Calcium-blockers	16 (4.7)	61 (12.6)	43 (18.0)	< 0.01
Renin-angiotensin-system inhibitors	25 (7.3)	95 (19.7)	75 (31.4)	< 0.01
Procedures prior to IE admission				
Valve surgery	17 (5.0)	25 (5.2)	12 (5.0)	0.98
PM or ICD implantation	5 (1.5)	18 (3.7)	3 (1.3)	0.05

Categorical variables are presented as numbers and frequencies in percentages. Information on all covariates was obtained at discharge unless otherwise stated.

PM, pacemaker; ICD, implantable cardioverter defibrillator.

Table 3. Admission characteristics and hospital admissions within the first year post-discharge of the study population

Characteristics	Age 18-40 N=343	Age 41-55 N=483	Age 56-60 N=239	P-value
Procedures/complications during admission				
Valve surgery	107 (31.2)	224 (46.4)	116 (48.5)	< 0.01
PM or ICD implantation	10 (2.9)	30 (6.2)	12 (5.0)	0.09
Stroke	11 (3.2)	38 (7.9)	20 (8.4)	0.01
Length of stay				0.01
14-30 days	90 (26.2)	94 (19.5)	37 (15.5)	
31-60 days	206 (60.1)	306 (63.4)	150 (62.8)	
61-90 days	36 (10.5)	55 (11.4)	39 (16.3)	
> 90 days	11 (3.2)	28 (5.8)	13 (5.4)	
Hospital admissions within the first year after discharge				0.48
None	150 (43.7)	233 (48.2)	110 (46.0)	
1-2	136 (39.7)	162 (33.5)	84 (35.2)	
> 2	57 (16.6)	88 (18.2)	45 (18.8)	
Valve surgery within the first year after discharge	22 (6.4)	45 (9.3)	21 (8.8)	0.31

Categorical variables are presented as numbers and frequencies in percentages.

PM, pacemaker; ICD, implantable cardioverter defibrillator.

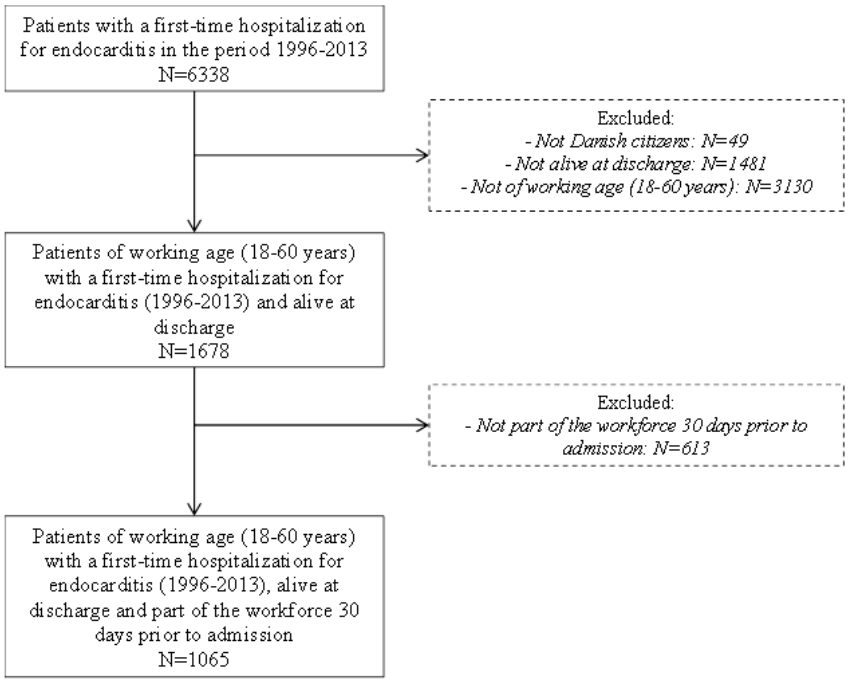

Figure 1

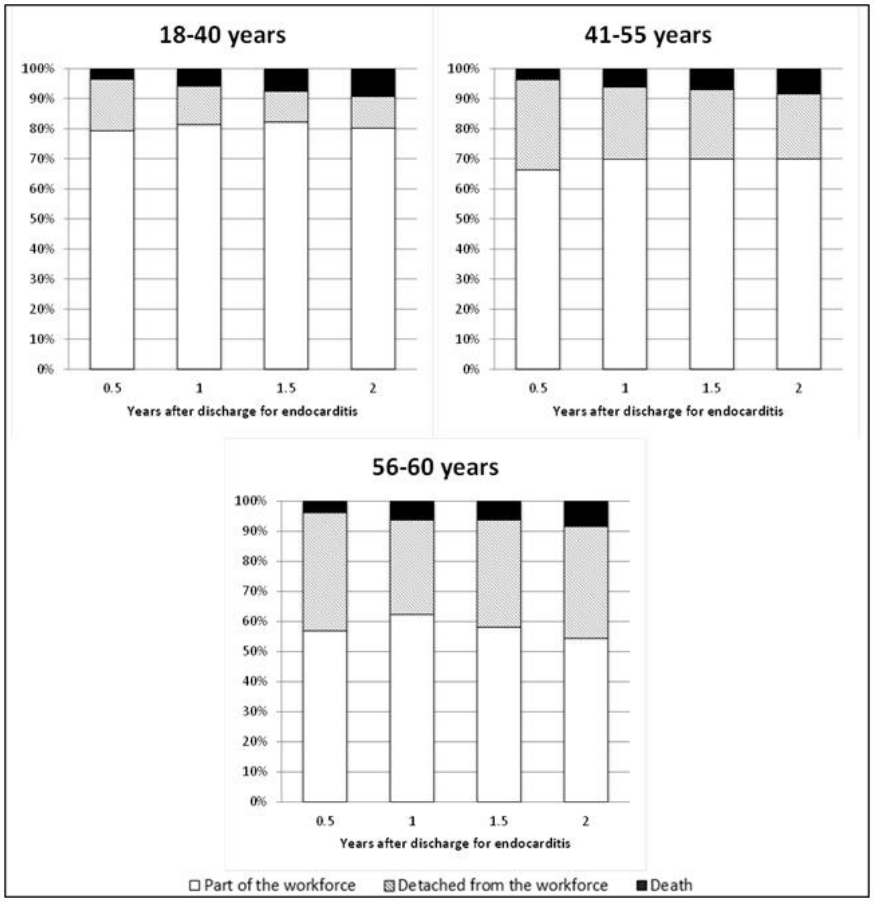

Figure 2

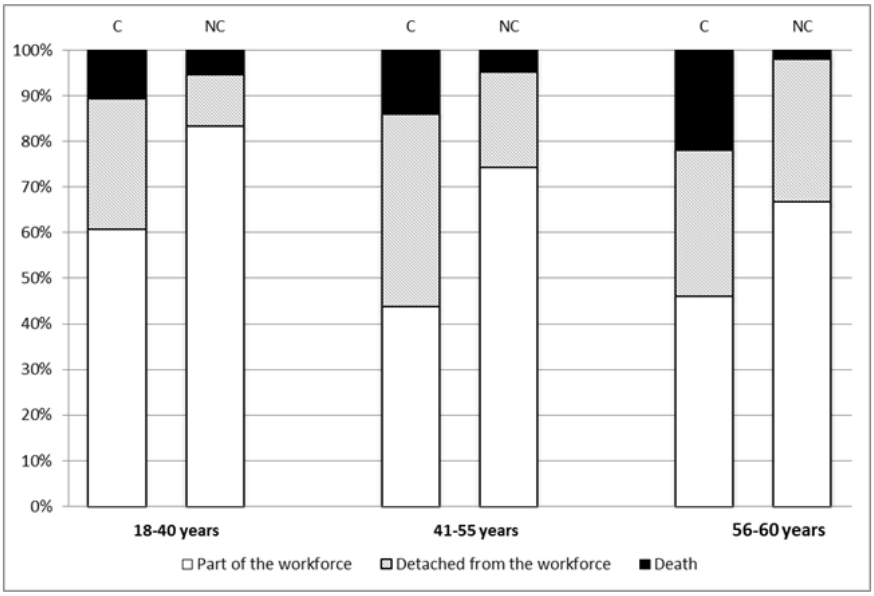

Figure 3

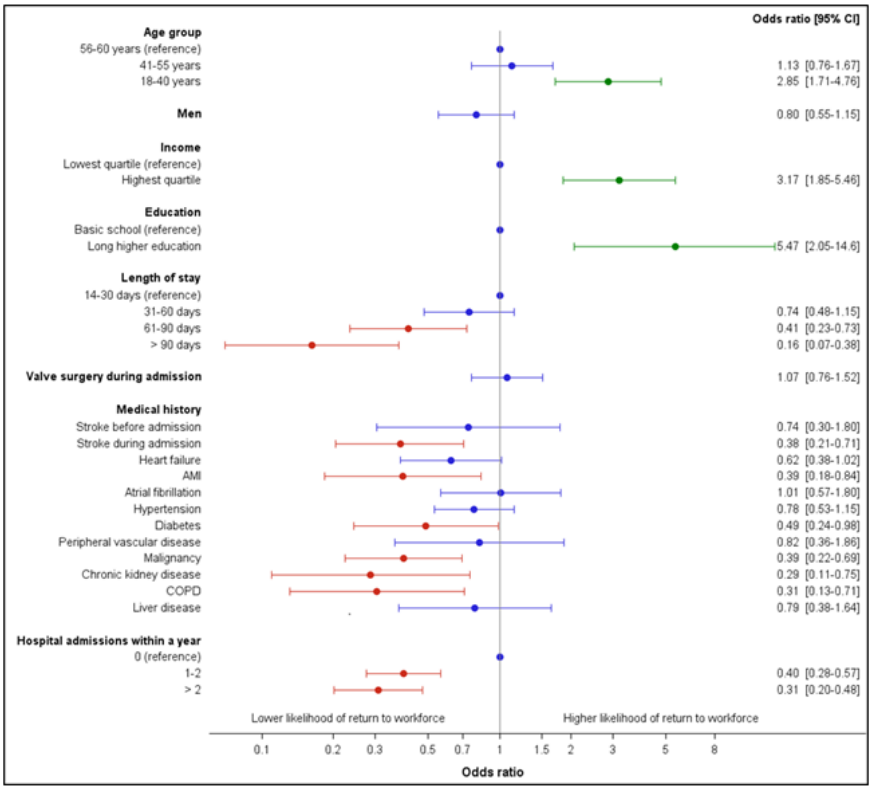

Figure 4