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Workforce attachment after a congenital long QT syndrome diagnosis: a Danish nationwide study

Camilla H B Jespersen ,[1] Jawad Haider Butt,[1] Johanna Krøll,[1] Bo Gregers Winkel,[1] Jørgen K Kanters,[2] Gunnar Gislason,[3,4,5,6] Christian Torp-Pedersen,[7,8] Henning Bundgaard,[1] Henrik Kjærulf Jensen,[9,10] Lars Køber,[1] Jacob Tfelt-Hansen ,[1,11] Peter E Weeke[1]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/openhrt-2022-002056).

To cite: Jespersen CHB, Butt JH, Krøll J, *et al*. Workforce attachment after a congenital long QT syndrome diagnosis: a Danish nationwide study. *Open Heart* 2022;**9**:e002056. doi:10.1136/openhrt-2022-002056

JT-H and PEW contributed equally.

Received 9 May 2022
Accepted 15 June 2022

For numbered affiliations see end of article.

Correspondence to
Dr Camilla H B Jespersen; camillahbj@gmail.com

ABSTRACT

Objective To examine workforce attachment among patients with congenital long QT syndrome (cLQTS) following diagnosis and identify factors associated with workforce attachment.

Methods and results In this nationwide cohort study, all patients diagnosed with cLQTS in Denmark between 1996 and 2016 aged 18–60 years at diagnosis were identified using nationwide registries. Patients attached to the workforce at diagnosis were included. Attachment to the workforce 1 year after cLQTS diagnosis was examined and compared with a background population matched 1:4 on age, sex and employment status. Multiple logistic regression was performed to identify factors associated with 1-year workforce detachment among patients with cLQTS. 298 patients fulfilled the inclusion criteria. Six months after cLQTS diagnosis, 90.9% of patients with cLQTS were attached to the workforce compared with 95.0% in the background population (p=0.006 for difference). One year after diagnosis, 93.3% of patients with cLQTS were attached to the workforce compared with 93.8% in the background population (p=0.26). Among patients with cLQTS, a severe cLQTS disease manifestation was associated with workforce detachment 1 year after diagnosis (compared with asymptomatic patients; aborted cardiac arrest OR 20.4 (95% CI, 1.7 to 249.9); ventricular tachycardia/syncope OR 10.9 (95% CI, 1.1 to 110.5)). No other associated factors were identified.

Conclusions More than 90% of patients with cLQTS remained attached to the workforce 1 year after diagnosis, which was similar to a matched background population. Patients with a severe cLQTS disease manifestation were less likely to be attached to the workforce 1 year after diagnosis.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Workforce attachment is an important indicator of psychosocial well-being; however, data on social consequences after a congenital long QT syndrome (cLQTS) diagnosis, including attachment to the workforce, are limited.

WHAT THIS STUDY ADDS

⇒ Nine out of ten patients diagnosed with cLQTS remain attached to the workforce 1 year after diagnosis; however, a severe disease manifestation (ie, VT/VF or syncope) is a risk factor for workforce detachment.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The ability to pre-emptively identify which patients with cLQTS that are likely to be more severely affected by living with a potentially fatal disease can help guide physicians towards patients at risk, but importantly also reassure asymptomatic patients with cLQTS.

INTRODUCTION

Congenital long QT syndrome (cLQTS) is a hereditary cardiac disease associated with an increased risk of developing syncope, malignant ventricular arrhythmias and sudden cardiac death in often otherwise healthy individuals.[1] Although mortality rates among patients with cLQTS are low, being diagnosed with a potentially life-threatening disease can have a substantial impact on patients with cLQTS.[2] Previous studies have largely focused on risk stratification, occurrence of cardiac arrhythmias and mortality.[3–6] However, focusing on predominantly clinical outcomes does not provide a complete assessment of the psychological aspects or socioeconomic consequences of the disease. A more comprehensive assessment should include outcomes of function at home and in society including the ability to remain attached to the workforce in this group of relatively young patients. Besides being important financially, returning to work after being diagnosed with a chronic disease is also a marker of functional status and well-being.[7] Detachment from the workforce has previously been shown to be associated with both an increased risk of depression and mental health problems, and with an increased risk of suicide.[8 9] Moreover,

efforts aimed at preventing, for example, depression is of particular importance for patients with cLQTS, as many psychotropic agents are unsuitable for treating patients with cLQTS because of the associated proarrhythmic properties.[10]

To examine the ability of patients with cLQTS to remain attached to the workforce and identify factors associated with workforce detachment, we performed a nationwide cohort study on adult Danish patients diagnosed with cLQTS who were attached to the workforce at time of diagnosis.

METHODS

Registries

All Danish citizens receive a unique and permanent identification number through the Civil Registration System on birth or immigration making nationwide cross-linkage among the Danish registries on an individual level possible. All admissions to Danish somatic or psychiatric hospitals are registered in the Danish National Patient Registry (DNPR) and Psychiatric Central Register, respectively. For each admission and discharge, one primary and relevant secondary diagnoses are registered according to the International Classification of Diseases (10th revision (ICD-10)). All dispensed drug prescriptions from Danish pharmacies are by law registered in the Danish National Prescription Registry using the Anatomical Therapeutic Chemical (ATC) system.

Danish law prohibits reporting of low group numbers (n≤3) to avoid potential identification of individuals, and thus, such low group numbers were replaced with '≤3' throughout the paper. The exact numbers are known to the investigators.

Study population

We identified all Danish patients aged 18–60 years at the time of cLQTS diagnosis (1996–2016) who were also part of the workforce or eligible to work 30 days prior to their cLQTS diagnosis. Patients with cLQTS were identified through the DNPR by the ICD-10 diagnosis code I472E. In Denmark, all patients with cLQTS are followed at clinics specialising in inherited cardiac diseases, and the diagnosis is given according to current guidelines.[10] The diagnosis code is associated with a positive predictive value of 97.6%.[11]

Matched control population

To compare outcomes and clinical characteristics with the background population, we matched each patient with cLQTS on age, sex and employment status with four controls from the entire Danish population using a greedy matching algorithm. Controls were assigned index dates corresponding to the diagnosis date for the case they were matched on.

cLQTS disease manifestation

Additional clinical data obtained by manual review of medical records from routine visits to clinics specialising in inherited cardiac diseases including information on disease manifestation and genotype were available for a subset of the patients.[2] This was the case for patients followed at the clinics at Copenhagen University Hospitals, Rigshospitalet and Gentofte; Aarhus University Hospital, Aarhus; and Hospital of Southern Jutland, Aabenraa. For patients followed at other clinics than mentioned, chart review was not available, and for these patients we used solely registry data.

We based cLQTS disease manifestation on information from medical records and hospital discharge diagnoses from the DNPR for cardiac events related to time of cLQTS diagnosis. We categorised patients into four subgroups—asymptomatic, ventricular tachycardia (VT) or syncope, aborted cardiac arrest (ACA) or unspecified disease manifestation—as done previously.[12] Asymptomatic patients were defined as patients having neither any symptoms registered through chart review nor any in-hospital diagnoses for cardiac events prior to diagnosis. Patients with VT or syncope and patients with ACA were defined through chart review or hospital discharge codes. Patients with inconclusive disease manifestation according to registries and chart review were categorised as unspecified.

Workforce attachment

The Danish registries have previously been used to describe workforce attachment in different patient groups.[13–15] As in these studies, we assessed workforce attachment through the Danish registry on public welfare benefits, which contains information on all residents who have received any public welfare benefits at any time on a weekly basis since 1991.[16] Patients were defined as being part of the workforce if they were employed, unemployed but capable of working (ie, not receiving paid sick leave or disability pension, and not on early retirement), students (ie, received standard Danish state educational grants) or on leave of absence (eg, maternity/paternity leave). Employment status 30 days prior to cLQTS diagnosis (ie, baseline employment status) was determined as the 5 weeks leading up to this date, and only patients who were a part of the workforce at this point were included. We used 5-week evaluation periods to reduce misclassification of short-term sick leave as detachment from the workforce. Only patients detached for at least three of the five evaluated weeks were classified as detached from the workforce. Our primary endpoint was workforce attachment 1 year after diagnosis.

The lowest state pension age in our study period was 65 years. As we limited our study population to patients up to 60 years old, no patient could per definition reach state pension age during follow-up.

Covariates

Information on patient comorbidity up to 5 years prior to cLQTS diagnosis was obtained through the DNPR and the Psychiatric Central Register. Concomitant pharmacotherapy in the 90 days leading up to diagnosis was

identified through the Danish National Prescription Registry. See supplemental appendix for specific ATC and ICD-10 codes.

Information on highest completed education at time of diagnosis and information on individual income regulated at 2015 index the year prior to diagnosis were obtained from Statistics Denmark.

Patient and public involvement

Patients and the public were not involved in the design of this study.

Statistical analysis

Patient characteristics were reported as frequencies with percentages or medians with IQR as appropriate. Differences between continuous variables were assessed using the Kruskal-Wallis test, and differences between categorical variables were tested using the χ^2 test or Fisher's exact test where appropriate.

Factors associated with detachment from the workforce 1 year after diagnosis among patients with cLQTS were identified using multivariable logistic regression. Variables included in the model were age (grouped 18–30, 30–45, 45–60), sex, year of diagnosis, disease manifestation, beta-blocker treatment, hypertension, diabetes, psychiatric comorbidity, income (quartiles), education at time of diagnosis, and living together or alone. All patients were followed from the date of cLQTS diagnosis and had minimum 12 months of follow-up. Patients who were not followed for one full year because of emigration or death were set as detached from the workforce in the logistic regression analysis, as done previously.[13–15] No significant interactions were identified.

Sensitivity analyses

We repeated the analysis on detachment from workforce restricting follow-up to 6 months after diagnosis to test if the effects were seen immediately after diagnosis. To test if there was a more long–standing effect, we examined detachment from the workforce 3 and 5 years after diagnosis. Furthermore, we repeated our analyses of detachment from the workforce defined as 2 or 4 weeks of the 5-week evaluation period rather than 3 weeks used in the primary analysis.

All analyses were performed using SAS statistical software package, V.9.4 (SAS Institute, Cary, NC) and R, V.4.0.3 (R Development Core Team). For all analyses, a two-sided p value<0.05 was considered statistically significant.

Ethics

Approval for this study was obtained from the Danish Data Protection Agency (P-2019-262). Registry-based analyses using de-identifiable data do not need an ethics approval in Denmark. Part of the present work was performed as part of a clinical quality control project.

Table 1 Employment status 30 days prior to cLQTS diagnosis in patients aged 18–60 and alive

	Patients with cLQTS aged 18–60 (n=342)
In the workforce	
Employed	230 (67.3)
Study, maternity leave, vacation	43 (12.6)
Unemployed	25 (7.3)
Not in the workforce	
Sick leave or subsidised job	23 (6.7)
Disability pension	21 (6.1)

cLQTS, congenital long QT syndrome.

RESULTS

Patient characteristics

We identified 342 patients diagnosed with a first-time cLQTS diagnosis at the predefined working age (18–60 years) at time of diagnosis. Of these, 298 patients with cLQTS were a part of or available for the workforce 30 days prior to cLQTS diagnosis and were included in the present study. Listed in table 1 is baseline employment status for all 342 patients with cLQTS at working age. A comparison of baseline characteristics between the 298 patients included and the 44 patients ineligible for the present study (ie, not part of the workforce) are listed in online supplemental table 1.

Baseline characteristics of the 298 included patients and the age-matched, sex-matched and employment status–matched control population are listed in table 2. Median age at diagnosis was 38.6 years (IQR 28.0–47.9) and patients were predominantly female (64.4%). Few significant differences between patients and matched controls were identified. Patients with cLQTS were significantly more likely to have diabetes (4.0% vs 0.8%), hypertension (10.4% vs 3.4%), epilepsy (1.3% vs 0.3%), atrial fibrillation (2.3% vs 0.3%), ischaemic heart disease (4.0% vs 0.6%) and psychiatric disease (7.7% vs 4.4%), as reported previously.[11] No differences in education level, income or living alone were identified (p>0.05 for all). The presenting disease manifestation was ACA for 9.1% (n=27), VT or syncope for 19.5% (n=58), asymptomatic for 27.9% (n=83) and unspecified for 43.6% (n=130). No significant differences were identified between subgroups based on disease manifestation for age, employment status or educational level before diagnosis (online supplemental table 2). Few patients with cLQTS were diagnosed with anoxic brain damage within 1 year of cLQTS diagnosis (n≤3). Moreover, only few patients and controls died during follow-up (n≤3).

Among patients with additional clinical information available (n=156), 26.3% had a *KCNQ1* mutation, 48.1% had a *KCNH2* mutation and 7.1% had an *SCN5A* mutation (online supplemental table 3). There were no significant differences in disease manifestation according to genotype (p=0.88) (online supplemental figure 1).

Table 2 Baseline characteristics, patients with cLQTS and age-matched, sex-matched and employment status–matched control population

	Patients with cLQTS aged 18–60 available for the workforce prior to diagnosis (n=298)	Matched control group (n=1192)	P value
Sex (female)	192 (64.4)	768 (64.4)	–
Age at diagnosis, years (median (IQR))	38.6 (28.0, 47.9)	38.6 (28.0, 47.9)	–
Social factors			
Education level at diagnosis			0.69
Basic school <10 years (ISCED 0–2)	62 (22.3)	276 (24.8)	
High school or vocational education (ISCED 3)	130 (46.8)	505 (45.4)	
Higher education (ISCED 5–8)	86 (30.9)	332 (29.8)	
Living alone	103 (35.0)	351 (31.2)	0.24
Employment status at baseline			
Employed	230 (77.2)	920 (77.2)	
Study, maternity leave, vacation	43 (14.4)	172 (14.4)	
Unemployed	25 (8.4)	100 (8.4)	
Income			0.85
1st quartile (lowest)	75 (25.2)	271 (23.6)	
2nd quartile	74 (24.8)	304 (26.5)	
3rd quartile	74 (24.8)	269 (23.5)	
4th quartile (highest)	75 (25.2)	302 (26.4)	
Disease factors			
Disease manifestation			
Aborted cardiac arrest	27 (9.1)	–	
VT or syncope	58 (19.5)	–	
Unspecified	130 (43.6)	–	
Asymptomatic	83 (27.9)	–	
Comorbidities prior to date of diagnosis			
Diabetes	12 (4.0)	9 (0.8)	<0.0001
Hypertension	31 (10.4)	41 (3.4)	<0.0001
Ischaemic heart disease	12 (4.0)	7 (0.6)	<0.0001
Atrial fibrillation	7 (2.3)	≤3	<0.0001
Epilepsy	4 (1.3)	≤3	0.02
Any psychiatric diagnosis	23 (7.7)	53 (4.4)	0.03
Concomitant pharmacotherapy, <90 days prior to date of diagnosis			
Beta-blockers	89 (29.9)	19 (1.6)	<0.0001
Calcium antagonists	7 (2.3)	18 (1.5)	0.45
ACE inhibitors	12 (4.0)	16 (1.3)	0.005
Thiazides	6 (2.0)	16 (1.3)	0.55
Lipid-lowering drugs	11 (3.7)	25 (2.1)	0.16
Antiepileptics	6 (2.0)	9 (0.8)	0.10
Antidepressants	14 (4.7)	44 (3.7)	0.52
Anxiolytics	10 (3.4)	22 (1.8)	0.17

cLQTS, congenital long QT syndrome; ISCED, International Standard Classification of Education; VT, ventricular tachycardia.

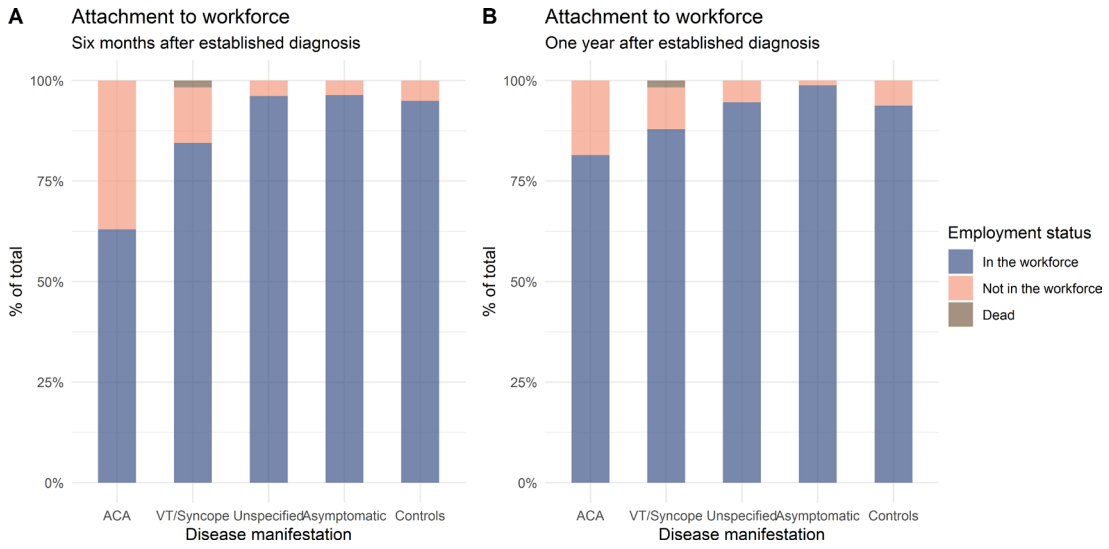

Figure 1 Workforce attachment after cLQTS diagnosis according to disease manifestation and age-matched, sex-matched and employment status–matched controls. Proportion of patients with cLQTS (stratified by disease manifestation) and matched control population attached to the workforce (A) 6 months and (B) 1 year after time of diagnosis (index date for controls). ACA, aborted cardiac arrest; VT, ventricular tachycardia.

Attachment to the workforce

Six months after diagnosis, 271 (90.9%) of the 298 patients with cLQTS were still attached to the workforce, compared with 95.0% of the age-matched, sex-matched and baseline employment status–matched control population (p=0.006). One year after diagnosis, 278 (93.3%) of the patients with cLQTS and 93.8% of the control population were attached to the workforce (p=0.26).

Among patients presenting with ACA, 17 (63%) were attached to the workforce 6 months after diagnosis and 22 (81.5%) were 1 year after diagnosis. In patients presenting with VT/syncope, 49 (84.5%) were attached to the workforce 6 months after diagnosis, and 51 (87.9%) were 1 year after diagnosis. Among patients who were asymptomatic at diagnosis, 80 (96.4%) and 82 (98.8%) patients were attached to the workforce 6 months and 1 year after diagnosis, respectively, and among patients with an unspecified disease manifestation, the corresponding numbers were 125 (96.2%) and 123 (94.6%) (figure 1).

Online supplemental tables 4 and 5 hold baseline characteristics of patients with cLQTS attached to the workforce and patients with cLQTS detached from the workforce or dead after 6 months and 1 year, respectively. No significant differences were found besides patients detached from the workforce or dead having a more severe disease manifestation at both time points (p<0.0001 and p=0.005, respectively). Among patients with clinical information available, we did not find any differences in genotype distribution between patients attached to and detached from the workforce 1 year after diagnosis (online supplemental figures 2 and 3).

Factors associated with attachment to the workforce

Patients with ACA or VT/syncope as presenting cLQTS disease manifestation were more likely to be detached from the workforce 1 year after diagnosis compared with asymptomatic patients (OR 20.4 (95% CI, 1.7 to 249.9) and OR 10.9 (95% CI, 1.1 to 110.5), respectively) (figure 2). No other factors in the multiple logistic regression model were significantly associated with workforce detachment after diagnosis including psychiatric comorbidity, education level and unemployment prior to diagnosis.

Sensitivity analyses

We found no substantial differences in the multiple logistic regression analysis when evaluating detachment 6 months after diagnosis (online supplemental figure 4).

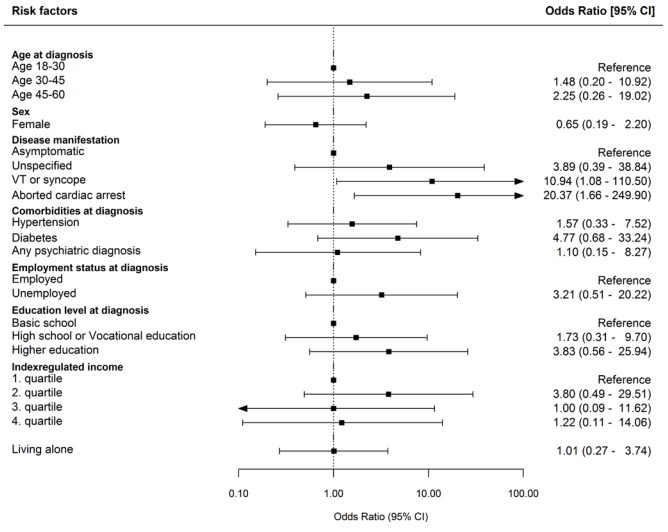

Figure 2 Factors associated with detachment from the workforce, 1 year after diagnosis. Forest plot showing OR of detachment from the workforce for different risk factors within the group of patients with cLQTS 1 year after diagnosis. cLQTS, congenital long QT syndrome; VT, ventricular tachycardia.

Patients with ACA or VT/syncope had an OR 23.8 (95% CI, 4.7 to 119.5) and OR 5.0 (95% CI, 1.2 to 21.7), respectively, of being detached from the workforce, compared with asymptomatic patients.

We determined workforce attachment 3 and 5 years after diagnosis. We identified 258 patients with cLQTS with at least 3 years of follow-up. Here, 25 patients with cLQTS (9.7%) were detached from the workforce after 3 years compared with 6.3% of their matched controls (p=0.02). For the 5-year analysis, we identified 190 patients with cLQTS. Here, 23 patients (12.1%) and 72 of their controls (9.5%) were detached from the workforce (p=0.5). Online supplemental figure 5 depicts long-term workforce attachment stratified by disease manifestation.

Last, we tested detachment from the workforce using 2 or 4 weeks instead of 3 weeks of the 5-week span. This yielded similar results as the main analysis, as we found no difference in the proportion of patients attached to the workforce 1 year after diagnosis (92.9% and 91.3% for 2 and 4 weeks, respectively, compared with 93.3% for 3 weeks).

DISCUSSION

We performed a nationwide study on attachment to the workforce after diagnosis of cLQTS among patients with cLQTS attached to the workforce before diagnosis. Here, we found that patients with cLQTS were significantly less likely to be attached to the workforce 6 months after their diagnosis compared with an age-matched, sex-matched and baseline employment status–matched control population. However, there was no significant difference between the two groups after 1 year (93.3% and 93.8% workforce attachment, respectively). In addition, a severe cLQTS disease manifestation was significantly associated with detachment from the workforce both 6 months and 1 year after diagnosis compared with patients asymptomatic at diagnosis.

Determining patients' attachment to the workforce is a useful and valid method of evaluating functional status, being important for both mental well-being and in socioeconomic aspects.[7] The method has previously been used to assess patients following admissions for different cardiac diseases[13–15 17 18] as well as other patient groups.[19 20] However, the cLQTS diagnosis is different from these types of diseases being a diagnosis presenting the patient with an increased risk of potentially lethal arrhythmias, and treatment aims at reducing risk of arrhythmias and sudden cardiac death in patients who may never previously have experienced any cardiac symptoms. To our knowledge, no previous studies have assessed workforce attachment in patients with neither cLQTS nor similar inherited cardiac diseases.

In contrast to our findings of no significant difference in workforce attachment between patients with cLQTS and controls 1 year after diagnosis, other studies have shown lower workforce attachment in patients 1 year after admission for infective endocarditis (71.8%),[14] heart failure (67.7%)[13] or coronary artery bypass grafting (80.0%).[15] This is expected, as these patient groups tend to be older and have more comorbidity compared with patients included in the present study. In addition, they are defined by an index event with admission to a hospital in contrast to patients with cLQTS, who are often diagnosed through visits to an outpatient clinic not necessarily involving absence from work.

Patients with cLQTS presenting with ACA had a higher likelihood of detachment from the workforce 1 year after diagnosis compared with patients who were asymptomatic. Thus, of patients with cLQTS presenting with ACA, 63% and 81.5% were attached to the workforce 6 months and 1 year after diagnosis, respectively. Comparably, a Danish study from 2015 on return to work after all-cause out-of-hospital cardiac arrest (OHCA) including patients at work prior to OHCA and alive after 30 days showed a return-to-work-rate after 1 year of 58.4% and a total return-to-work-rate of 76.6%.[17] In patients with cLQTS and ACA as disease manifestation, ≤3/27 patients were diagnosed with anoxic brain damage within a year following their cLQTS diagnosis compared with 73/796 patients (9.2%) in the all-cause OHCA cohort.[17] At all time points after diagnosis, less patients with cLQTS symptomatic at diagnosis were attached to the workforce than asymptomatic patients. In this context, previous studies have shown symptomatic patients with cLQTS having an increased risk of developing depression and anxiety,[21] and asymptomatic patients with cLQTS not having a significantly different risk of developing depression and anxiety from a matched control population.[12] Workforce attachment is an important factor in psychological well-being, and patients receiving disability pension both have a higher risk of developing depression after detachment from the workforce and higher suicide and mortality rates than persons attached to the workforce.[8 22 23] Depression is associated with increased mortality[24] and young patients with a psychiatric disease have a four times increased risk of sudden cardiac death.[25] Speculatively, the physical consequences of being a symptomatic patient with cLQTS could impact work capability and thereby psychological health, and anxiety and psychologic health following diagnosis with a severe disease could be part of the reason for detachment from the workforce.

A lower proportion of patients with cLQTS were attached to the workforce compared with controls both 3 and 5 years after diagnosis. However, the difference was only significant after 3 years. This could indicate reasons for detachment from the workforce of a more persistent matter, rather than only an immediate effect of the diagnosis.

Limitations

This study is observational with some limitations to consider. We tried to eliminate confounders; however, there is a possibility of residual confounding. Although it was a nationwide study including all Danish patients, sample size was limited which may have influenced our

findings. Furthermore, we did not have access to clinical information for all patients making disease manifestation unspecified and genotype unknown for a subset of the patients.

We found small differences in comorbidities between cases and controls. Some of these differences could reflect the diagnostic process where patients with cLQTS are thoroughly examined, whereas healthy people in Denmark are not routinely screened for, for example, diabetes or hypertension unless presenting relevant symptoms or risk factors. Anoxic brain damage was previously assessed through use of diagnosis code[26]; however, some patients may have unregistered anoxic brain damage affecting their ability to work.

The Danish registry on public welfare benefits is an accurate register.[16] However, only persons having received a public welfare benefit at some point after the initiation of the registry are included in the registry. We assumed persons not included to be self-sufficient through work; however, some may be self-sufficient through, for example, a working spouse and not be available for the workforce themselves. We could not distinguish between full-time and part-time sick leave, resulting in possible misclassification of detachment from the workforce. We were not able to examine timing of arrhythmogenic events in relation to being at work through this registry.

Author affiliations
[1]Department of Cardiology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
[2]Department of Biomedical Sciences, University of Copenhagen, Copenhagen, Denmark
[3]Department of Cardiology, Copenhagen University Hospital Herlev and Gentofte, Hellerup, Denmark
[4]The Danish Heart Foundation, Copenhagen, Denmark
[5]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark
[6]The National Institute of Public Health, University of Southern Denmark, Copenhagen, Denmark
[7]Department of Cardiology, Nordsjaellands Hospital, Hillerød, Denmark
[8]Department of Public Health, University of Copenhagen, Copenhagen, Denmark
[9]Department of Cardiology, Aarhus University Hospital, Aarhus N, Denmark
[10]Department of Clinical Medicine, Health, Aarhus University, Aarhus N, Denmark
[11]Section of Forensic Genetics, Department of Forensic Medicine, Faculty of Medical Sciences, Univeristy of Copenhagen, Copenhagen, Denmark

Twitter Camilla H B Jespersen @CamJespersen and Jacob Tfelt-Hansen @JacobTfelt

Acknowledgements Visual summary created with BioRender.com.

Contributors CHBJ, JTH and PW are responsible for the overall content, conception and design. CHBJ, JHB and PW are responsible for statistical analysis and interpretation of data. CHBJ is responsible for the first draft of the manuscript. All authors have been involved in critical revision of the manuscript. All authors have approved the final draft of the manuscript before submission. CHBJ acts as guarantor. JTH and PW hold joint senior authorship of this manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests CT-P reports grant from Bayer for randomised trials and from Novo Nordisk for epidemiological study, all unrelated to the present work. GG reports grants from Boehringer Ingelheim, Bristol-Myers Squibb and Pfizer, unrelated to the present work. HKJ is supported by grants from Novo Nordisk Foundation, Denmark (NNF18OC0031258 and NNF20OC0065151) and received lecture fees from Abbott, Denmark and Biosense Webster, Europe, all unrelated to the present work. JHB reports advisory honoraria from Bayer, outside the present work. LK reports honorarium form Novo, Novartis, AstraZeneca and Boehringer, unrelated to this manuscript. All remaining authors have declared no conflicts of interest.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and approval for the present study was obtained from the Danish Data Protection Agency (P-2019-262). Registry-based analyses using de-identifiable data do not need an ethics approval in Denmark. Registry-based study using de-identifiable data do not need informed consent from patients in Denmark.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. Due to restrictions related to Danish law and protecting patient privacy, the combined set of data used in this study can only be made available through a trusted third party, Statistics Denmark. Data will be shared on request to the corresponding author with permission from Statistics Denmark. More information regarding data access is available online (https://www.dst.dk/en/TilSalg/Forskningsservice).

ORCID iDs
Camilla H B Jespersen http://orcid.org/0000-0001-9664-9637
Jacob Tfelt-Hansen http://orcid.org/0000-0003-3895-9316

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Supplemental Material

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Abbreviations: ATC, anatomical therapeutic chemical system; CI, confidence interval; cLQTS, congenital long QT syndrome; ICD-10, international classification of diseases system, 10th revision; ISCED, international standard classification of education; IQR, interquartile range; VT, ventricular tachycardia

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Supplemental Table 1

Title: Baseline characteristics, patients with cLQTS attached to the workforce (cases) and patients with cLQTS not attached to the workforce (not included)

	cLQTS patients attached to the workforce (n=298)	cLQTS patients not attached to the workforce (n=44)	p-value
Sex (female)	192 (64.4)	29 (65.9)	0.98
Age at diagnosis, years (median (IQR))	38.6 [28.0, 47.9]	45.2 [39.8, 53.6]	0.0001
Social factors			
Education level			0.07
- Basic school <10 years (ISCED 0-2)	62 (22.3)	16 (36.4)	
- High school or vocational education (ISCED 3)	130 (46.8)	20 (45.5)	
- Higher education (ISCED 5-8)	86 (30.9)	8 (18.2)	
Living alone	103 (35.0)	17 (38.6)	0.77
Income			0.002
- 1. quartile (lowest)	75 (25.2)	5 (11.4)	
- 2. quartile	74 (24.8)	23 (52.3)	
- 3. quartile	74 (24.8)	8 (18.2)	
- 4. quartile (highest)	75 (25.2)	8 (18.2)	
Disease factors			
Disease manifestation			0.25
- Aborted cardiac arrest	26 (8.7)	6 (13.6)	
- VT or syncope	59 (19.8)	12 (27.3)	
- Unspecified	130 (43.6)	19 (43.2)	
- Asymptomatic	83 (27.9)	7 (15.9)	
Comorbidities prior to date of diagnosis			
Diabetes	12 (4.0)	≤3	1.00
Hypertension	31 (10.4)	14 (31.8)	0.0002
Ischemic heart disease or prior myocardial infarction	12 (4.0)	7 (15.9)	0.004
Atrial fibrillation	7 (2.3)	≤3	0.24
Epilepsy	4 (1.3)	≤3	1.00
Any psychiatric diagnosis	23 (7.7)	13 (29.5)	< 0.0001
Concomitant pharmacotherapy, <90 days prior to date of diagnosis			
Beta-blockers	89 (29.9)	20 (45.5)	0.06
Calcium antagonists	7 (2.3)	6 (13.6)	0.001
ACE inhibitors	12 (4.0)	6 (13.6)	0.02
Thiazides	6 (2.0)	≤3	0.61
Lipid lowering drugs	11 (3.7)	7 (15.9)	0.003
Antiepileptica	6 (2.0)	5 (11.4)	0.005
Antidepressants	14 (4.7)	9 (20.5)	0.0004
Anxiolytics	10 (3.4)	9 (20.5)	< 0.0001

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Supplemental Table 2

Title: Baseline characteristics, patients with cLQTS stratified by disease manifestation

	Aborted cardiac arrest (n=27)	VT or syncope (n=58)	Unspecified (n=130)	Asymptomatic (n=83)	p-value
Sex (female)	18 (66.7)	45 (77.6)	82 (63.1)	47 (56.6)	0.08
Age at diagnosis, years (median (IQR))	39.6 [26.6, 50.1]	39.1 [25.3, 49.8]	36.6 [28.8, 47.9]	38.5 [27.9, 45.9]	0.89
Social factors					
Education level at diagnosis					0.60
- Basic school <10 years (ISCED 0-2)	6 (26.1)	13 (23.6)	31 (25.6)	12 (15.2)	
- High school or vocational education (ISCED 3)	12 (52.2)	26 (47.3)	51 (42.1)	41 (51.9)	
- Higher education (ISCED 5-8)	5 (21.7)	16 (29.1)	39 (32.2)	26 (32.9)	
Living alone	13 (48.1)	24 (42.1)	47 (37.0)	19 (22.9)	0.03
Employment status at baseline					0.90
- Employed	22 (81.5)	43 (74.1)	102 (78.5)	63 (75.9)	
- Study, maternity leave, vacation	≤3	9 (15.5)	18 (13.8)	14 (16.9)	
- Unemployed	≤3	6 (10.3)	10 (7.7)	6 (7.2)	
Income					0.59
- 1. quartile (lowest)	10 (37.0)	17 (29.3)	29 (22.3)	19 (22.9)	
- 2. quartile	6 (22.2)	15 (25.9)	35 (26.9)	18 (21.7)	
- 3. quartile	≤3	15 (25.9)	31 (23.8)	25 (30.1)	
- 4. quartile (highest)	8 (29.6)	11 (19.0)	35 (26.9)	21 (25.3)	
Comorbidities prior to date of diagnosis					
Diabetes	≤3	≤3	6 (4.6)	≤3	0.83
Hypertension	≤3	9 (15.5)	15 (11.5)	4 (4.8)	0.20
Ischemic heart disease or prior myocardial infarction	≤3	≤3	8 (6.2)	0	0.12
Atrial fibrillation	≤3	≤3	≤3	0	0.008
Epilepsy	≤3	0	≤3	≤3	0.58
Any psychiatric diagnosis	≤3	6 (10.3)	11 (8.5)	5 (6.0)	0.66
Concomitant pharmacotherapy, <90 days prior to date of diagnosis					
Beta blockers	5 (18.5)	18 (31.0)	47 (36.2)	19 (22.9)	0.11
Calcium antagonists	0	≤3	4 (3.1)	≤3	0.63
ACE inhibitors	≤3	5 (8.6)	4 (3.1)	≤3	0.26
Thiazides	0	≤3	≤3	≤3	0.27
Lipid lowering drugs	≤3	≤3	7 (5.4)	≤3	0.56
Antiepileptica	≤3	≤3	≤3	0	0.004
Antidepressants	≤3	≤3	8 (6.2)	≤3	0.64
Anxiolytics	≤3	≤3	≤3	≤3	0.61

Supplemental Table 3

Title: *Findings in the patients with cLQTS with additional clinical information available*

	Patients with cLQTS (n=156)
Sex (female)	105 (67.3)
Age at diagnosis, years	38.3 [25.3, 46.9]
Proband	65 (41.7)
Relative	91 (58.3)
Genetics	
KCNQ1	41 (26.3)
KCNH2	75 (48.1)
SCN5A	11 (7.1)
Genonegative	18 (11.5)
Not tested	8 (5.1)
Disease manifestation	
ACA	20 (12.8)
VT/syncope	44 (28.2)
Unspecified	9 (5.8)
Asymptomatic	82 (53.2)

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Supplemental Table 4

Title: Baseline characteristics, patients with cLQTS attached to the workforce and patients with cLQTS not attached to the workforce or dead six months after diagnosis

	Attached to the workforce (n=271)	Not attached to the workforce or dead (n=27)	p-value
Sex (female)	174 (65.2)	18 (66.6)	0.97
Age at diagnosis, years (median [IQR])	38.2 [28.0, 47.8]	40.5 [28.8, 49.5]	0.63
Social factors			
Education level			
- Basic school <10 years (ISCED 0-2)	56 (22.0)	6 (25.0)	
- High school or vocational education (ISCED 3)	120 (47.2)	10 (41.7)	
- Higher education (ISCED 5-8)	78 (30.7)	8 (33.3)	0.87
Living alone	94 (35.2)	9 (33.3)	1
Employment status 30 days prior to date of diagnosis			
- Employed	208 (76.8)	22 (81.5)	
- Study, maternity leave, vacation	42 (15.5)	≤3	
- Unemployed	21 (7.7)	4 (14.8)	0.14
Income			
- 1. quartile (lowest)	66 (24.4)	9 (33.3)	
- 2. quartile	67 (24.7)	7 (25.9)	
- 3. quartile	69 (25.5)	5 (18.5)	
- 4. quartile (highest)	69 (25.5)	6 (22.2)	0.71
Disease factors			
Disease manifestation			
- Aborted cardiac arrest	17 (6.3)	10 (37.0)	
- VT or syncope	49 (18.1)	9 (33.3)	
- Unspecified	125 (46.1)	5 (18.5)	
- Asymptomatic	80 (29.5)	≤3	<0.0001
Comorbidities prior to date of diagnosis			
Diabetes	9 (3.3)	≤3	0.15
Hypertension	28 (10.3)	≤3	1
Ischemic heart disease or prior myocardial infarction	10 (3.7)	≤3	0.67
Atrial fibrillation	6 (2.2)	≤3	1
Epilepsy	≤3	≤3	0.81
Any psychiatric diagnosis	21 (7.7)	≤3	1
Concomitant pharmacotherapy, <90 days prior to date of diagnosis			
Beta blockers	80 (29.5)	9 (33.3)	0.85
Calcium antagonists	7 (2.6)	0	0.86
ACE inhibitors	10 (3.7)	≤3	0.67
Tiazides	5 (1.8)	≤3	1

Lipid lowering agents	11 (4.1)	0	0.60
Antiepileptics	4 (1.5)	≤3	0.17
Anxiolytics	8 (3.0)	≤3	0.51
Antidepressants	13 (4.8)	≤3	1

Supplemental Table 5

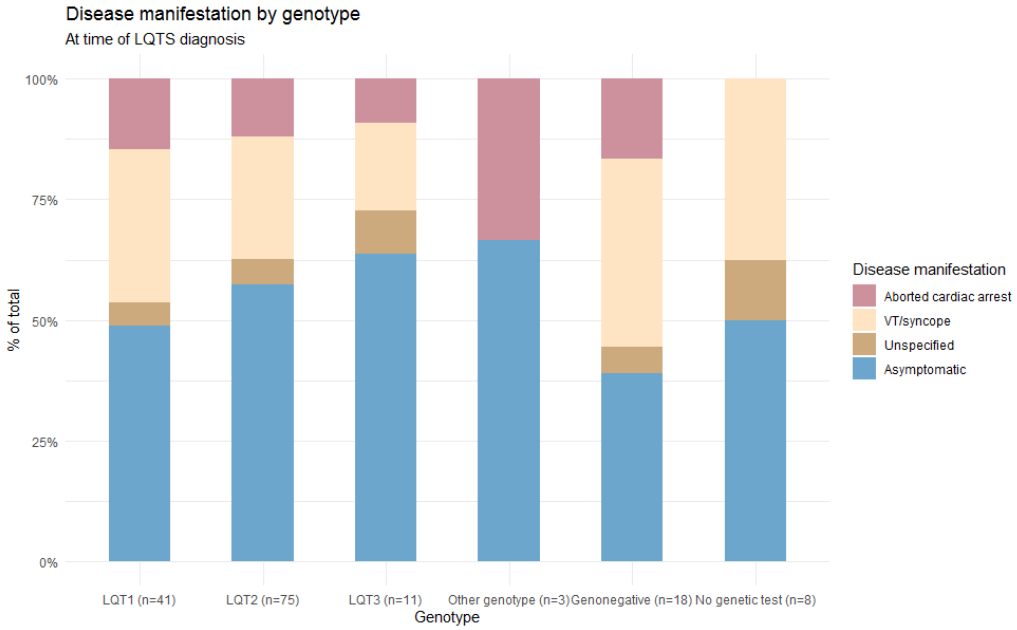
Title: Baseline characteristics, patients with cLQTS attached to the workforce and patients with cLQTS not attached to the workforce or dead one year after diagnosis

	Attached to the workforce (n=278)	Not attached to the workforce or dead (n=20)	p-value
Sex (female)	182 (65.5)	10 (50.0)	0.25
Age at diagnosis, years (median [IQR])	37.5 [27.9, 47.8]	44.5 [33.2, 50.4]	0.13
Social factors			
Education level at diagnosis			
- Basic school <10 years (ISCED 0-2)	59 (22.5)	≤3	
- High school or vocational education (ISCED 3)	123 (46.9)	7 (43.8)	
- Higher education (ISCED 5-8)	80 (30.5)	6 (37.5)	0.83
Living alone	95 (34.7)	8 (40.0)	0.81
Employment status 30 days prior to date of diagnosis			
- Employed	213 (76.6)	17 (85.0)	
- Study, maternity leave, vacation	43 (15.5)	0	
- Unemployed	22 (7.9)	≤3	0.11
Income			
- 1. quartile (lowest)	70 (25.2)	5 (25.0)	
- 2. quartile	66 (23.7)	8 (40.0)	
- 3. quartile	71 (25.5)	≤3	
- 4. quartile (highest)	71 (25.5)	4 (20.0)	0.38
Disease factors			
Disease manifestation			
- Aborted cardiac arrest	22 (7.9)	5 (25.0)	
- VT or syncope	51 (18.3)	7 (35.0)	
- Unspecified	123 (44.2)	7 (35.0)	
- Asymptomatic	82 (29.5)	≤3	0.005
Comorbidities prior to date of diagnosis			
Diabetes	10 (3.6)	≤3	0.41
Hypertension	28 (10.1)	≤3	0.75
Ischemic heart disease or prior myocardial infarction	11 (4.0)	≤3	1
Atrial fibrillation	6 (2.2)	≤3	0.96
Epilepsy	4 (1.4)	0	1
Any psychiatric diagnosis	21 (7.6)	≤3	1
Concomitant pharmacotherapy, <90 days prior to date of diagnosis			
Beta blockers	81 (29.1)	8 (40.0)	0.44
Calcium antagonists	7 (2.5)	0	1

ACE inhibitors	10 (3.6)	≤3	0.41
Tiazides	5 (1.8)	≤3	0.87
Lipid lowering agents	11 (4.0)	0	0.77
Antiepileptics	5 (1.8)	≤3	0.87
Anxiolytics	8 (2.9)	≤3	0.29
Antidepressants	12 (4.3)	≤3	0.54

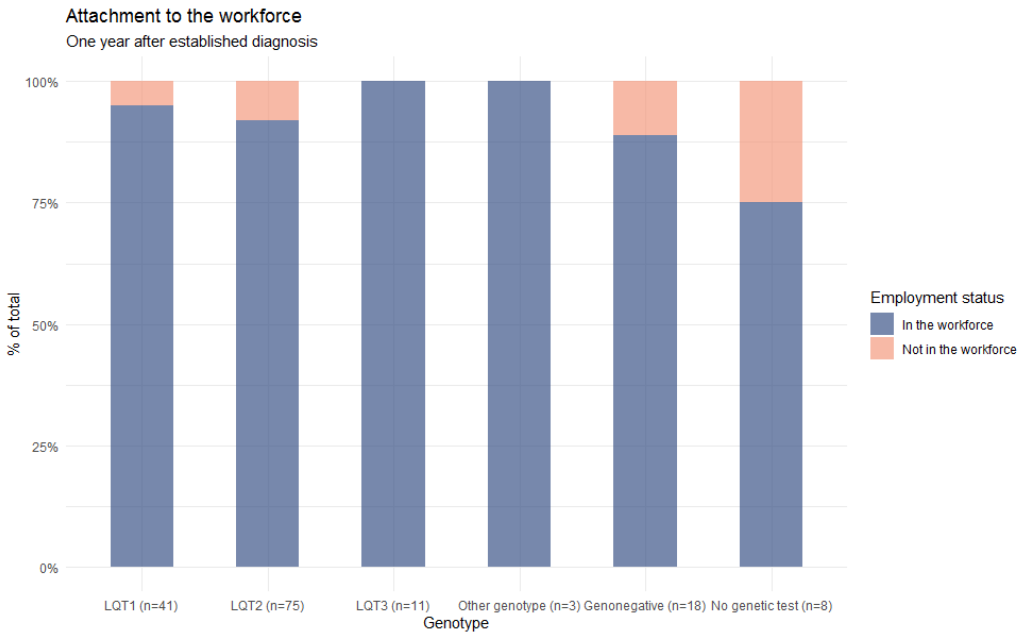
Supplemental Figure 1

Title: cLQTS disease manifestation according to genotype



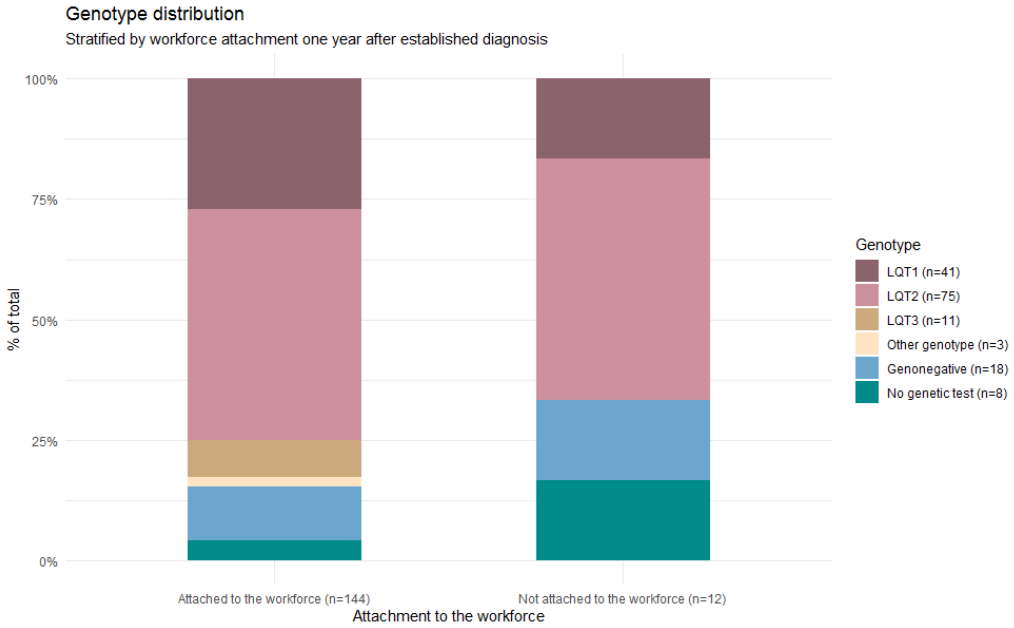
Supplemental Figure 2

Title: Workforce attachment according to genotype



Supplemental Figure 3

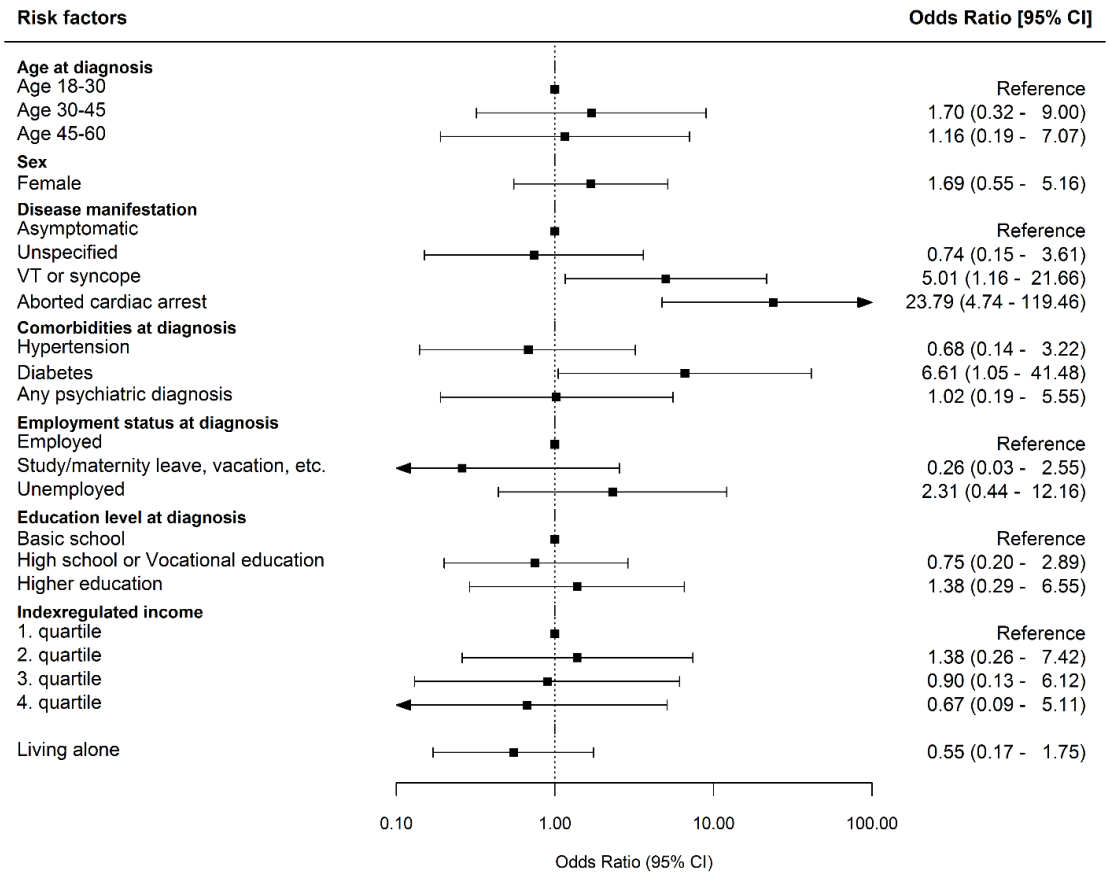
Title: Genotype distribution according to workforce attachment



Supplemental Figure 4

Title: Odds ratio of detachment from the workforce among patients with cLQTS, six months after diagnosis

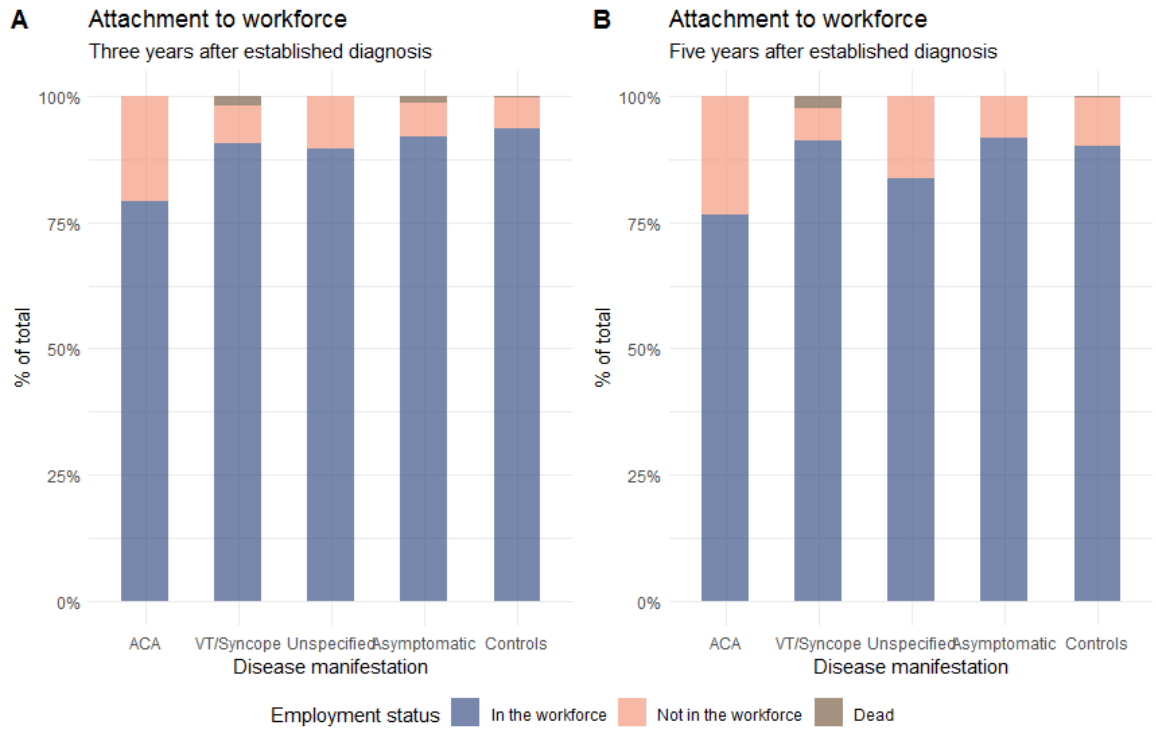
Legend: Forest plot showing odds ratio of detachment from the workforce for different risk factors within the group of cLQTS patients six months after diagnosis with cLQTS.



Supplemental Figure 5

Title: Workforce attachment after cLQTS diagnosis according to disease manifestation and age-, sex-, and employment status-matched controls

Legend: Bar chart showing proportion of patients with cLQTS (stratified by disease manifestation) and matched control population attached to the workforce (A)three years and (B)five years after time of diagnosis (index date for control population); ACA, aborted cardiac arrest; VT, ventricular tachycardia



Supplemental Appendix

Codes for treatment and diagnosis definition

Diagnoses/comorbidities	**ICD codes**
Aborted cardiac arrest	I469, I460, I490, I490B
Anoxic brain damage	G931
Any psychiatric disease	F
Atrial fibrillation	I48
Epilepsy	G40, G41
Ischemic heart disease or prior myocardial infarction	I20-25
Syncope	R559
Ventricular tachycardia	I470, I472, I472A, I472B, I472D
Therapy	**ATC codes**
ACE-inhibitors	C09A
Antiarrhythmic drugs	C01B
Antidepressants	N06A
Anxiolytics	N05B, N05C
β blockers	C07
Calcium channel blockers	C08
Lipid lowering drugs	C10
Loop diuretics	C03C
Thiazides	C03A
Comorbidities based (partly) on ATC codes	**ATC or ICD codes**
Diabetes[1]	Diagnosis code within 5 years of diagnosis of ICD10: E10-E14 *and/or* A dispensed prescription within 180 days of diagnosis of the following: ATC: A10
Hypertension[2]	2 or more dispensed prescriptions of the following within 180 days of diagnosis (ATC): α adrenergic blockers: C02A, C02B, C02C Non-loop diuretics: C02DA, C02L, C03A, C03B, C03D, C03E, C03X, C07B, C07C, C07D, C08G, C09BA, C09DA, C09XA52 Vasodilators: C02DB, C02DD, C02DG β blockers: C07 Calcium channel blockers: C07F, C08, C09BB, C09DB Renin–angiotensin system inhibitors: C09

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VISUAL SUMMARY Workforce attachment after a diagnosis with cLQTS