



Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

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Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

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Abstract

Introduction: Patient reported health status, including symptom burden, functional status and quality of life, is an important measure of health. Differences in health status between diagnostic groups within cardiology have only been sparsely investigated. These outcomes may predict morbidity, mortality, labour market affiliation and health care utilization in various diagnostic groups. A national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population has been designed as the DenHeart survey.

Methods and analysis: DenHeart is designed as a cross-sectional survey with register based follow-up. All diagnostic groups at the five national Heart Centres are included during one year (April 15th 2013 to April 15th 2014) and asked to fill out a questionnaire at hospital discharge. The total eligible population, both responders and non-responders, will be followed in national registers. The following instruments are used: SF-12, HADS, EQ-5D, B-IPQ, HeartQoL and ESAS. The following variables are collected from national registers: action diagnosis, procedures, co-morbidity, length of hospital stay, type of hospitalisation, visits to GP and other agents in primary health care, dispensed prescription medication, vital status, and cause of death. Labour market affiliation, sick leave, early retirement pension, educational degree and income will be collected from registers. Frequency distributions and multiple logistic regression analyses will be used to describe and assess differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors. Cox proportional hazards regression models with age as the time scale will be used to investigate associations between patient reported outcomes at baseline and morbidity/mortality, labour market affiliation and health care utilization after one year.

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4 Ethics and dissemination: The study complies with the Declaration of Helsinki. The study
5
6 has been approved by the Danish Data Protection Agency: 2007-58-0015/30-0937. Study
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8 findings will be disseminated widely through peer reviewed publications and conference
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10 presentations.
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14 Trial registration: ClinicalTrials.gov: NCT01926145.
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Introduction

Patient reported health status, which includes symptom burden, functional status and quality of life, is an important measure of health. Validated patient health status surveys, including disease specific instruments for patients with cardiovascular disease, allow quantification of critical patient-centred outcomes and additional research is needed to better understand the determinants¹ and the predicting factors of patients' health status. Previous studies suggest an association between heart disease, self-reported health and morbidity and mortality, and that patient reported outcome measures can predict prolonged hospital stay, future quality of life, return to work, morbidity and mortality in cardiac patients.²⁻⁷ Quality of life scores seem to provide important prognostic information independent of traditional clinical data, as higher scores have been associated with longer survival in patients with ventricular arrhythmias and coronary artery disease.^{8,9} However no studies have included all diagnostic groups within cardiology and comparisons among diagnostic groups are lacking. The overall aim of the DenHeart survey is to gain knowledge about patient reported outcome measures regarding health among cardiac patients at hospital discharge. Knowledge about patients' own perception of their health status and predicting factors can help to guide inpatient practice and outpatient follow-up. Furthermore, a survey combined with register data can be used to evaluate differences among diagnostic groups and predicting factors for patient reported outcome measures at hospital discharge and long-term morbidity and mortality. Also, economic analysis of healthcare utilisation and work ability status in a large cohort of cardiac patients is needed. Therefore, the DenHeart study is designed as a national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population.

Objectives

The objectives of the DenHeart study are to describe: (i) differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors and (ii) patient reported outcomes at hospital discharge as a predictor of a) morbidity and mortality, b) labour market affiliation and c) health care utilization after one year.

Methods and analysis

Study design

The DenHeart study is designed as a cross-sectional survey with register based follow-up. All cardiac patients are asked to fill out a questionnaire at hospital discharge to evaluate patient reported outcomes. Furthermore, the total eligible population, both responders and non-responders, will be followed in national registers.

Setting and participants

The five Heart Centres in Denmark are including patients during a one year period, from April 15th 2013 to April 15th 2014. One centre began data collection later, May 1st 2013. Four heart centres have both medical and surgical wards, one centre medical wards only. All cardiac patients discharged or transferred to a local hospital from one of the Heart Centres are potential participants in the study. Patients are unselected and consecutively included at hospital discharge. Included patients are asked to complete and return a questionnaire before they leave the hospital or alternatively to do so at home within 3 days of discharge and return it by mail. Patients who are transferred to another hospital are given the questionnaire at discharge from the Heart Centre and asked to fill it out at the

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4 day of hospital discharge or alternatively to do so at home within 3 days of discharge and
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6 then return it by mail.
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8 9 *Eligibility criteria*

10 All diagnostic groups within cardiology are included. Patients with ischemic heart disease
11 (e.g. coronary angiography, percutaneous coronary intervention), heart failure (e.g.
12 coronary artery bypass graft, heart transplantation), arrhythmia (e.g. ablation, labyrinth,
13 pacemaker, implantable cardioverter defibrillator), heart valve disease (e.g. stent, valve
14 replacement), endocarditis and congenital heart disease (e.g. atrium septum defect, patent
15 ductus arteriosus, patent foramen ovale, coarctatio) are diagnosed and treated at the
16 Heart Centres. Infrequent conditions such as thorax-trauma are also included.
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28 Patients under 18 years of age and patients without a Danish civil registration number are
29 excluded from the study. For ethical reasons, patients who are unconscious when
30 transferred are also excluded.
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35 Reasons for non-response are recorded which allows for sub-analyses of these groups.

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37 On the front page of the questionnaire there is a box that enables the patient or nurse to
38 tick off the reason for non-response: "Does not wish to participate", "Not able to participate
39 because of illness", "Not able to participate because of language barrier", "Questionnaire
40 not handed out" and "Other".
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47 *Recruitment*

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49 Patients are recruited at hospital discharge (the same day or the day before discharge) by
50 the ward nurse in charge of the discharge of the individual patients or by a research nurse.
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52 All nurses at the centres, approximately 800, have been informed about the study and
53 procedures at ward meetings, guidelines have been distributed and a website created
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4 (www.DenHeart.dk). When informing patients about the study and handing out the
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6 questionnaire, nurses also distribute a postage pre-paid envelope to them to return the
7
8 questionnaire in, either at the ward or after discharge. No reminders are sent to patients as
9
10 the time window of three days post discharge makes it impossible. Distribution and return
11
12 rates are monitored to allow for interventions if the rates drop during data collection.
13

14 15 16 *Data sources/measurement*

17
18 The following patient reported outcome measures are used: Short-form 12 (SF-12),
19
20 Hospital Anxiety and Depression Scale (HADS), EQ-5D, Brief Illness Perception
21
22 Questionnaire (B-IPQ), HeartQoL and Edmonton Symptom Assessment Scale (ESAS).
23

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25 SF-12: The SF-12 is a 12-item version of the SF-36 and is a brief, reliable measure of
26
27 overall health. The questionnaire measures eight domains of health: physical function,
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29 role-physical, bodily pain, general health, vitality, social functioning, role-emotional and
30
31 mental health with higher scores indicating better health status. The items cover the
32
33 previous four weeks and results are expressed in terms of two summary scores: the
34
35 Physical Component Summary (PCS) and the Mental Component Summary (MCS).¹⁰ A
36
37 Cronbach's alpha of 0.87 and 0.84 for PCS-12 and MCS-12 respectively have been
38
39 reported in a population of coronary heart disease patients.¹¹ The SF-12 is a suitable for
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41 studies focusing on patient-based assessment of physical and mental health.¹⁰
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45 Furthermore it is used in the National Health Surveys and outcomes can be compared.
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49 HADS: HADS is a 14-item questionnaire that assesses levels of depression and anxiety in
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51 medically ill patients. The scale offers two scores, HADS-A and HADS-D, and consists of
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53 seven questions to assess anxiety and seven questions to assess depression.¹² For each
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55 of the questions the respondent chooses from four responses to indicate the extent to
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4 which each applies for the last week. HADS is a valid and internally consistent measure,
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6 with a mean Cronbach's alpha of 0.83 and 0.82 for the HADS-A and HADS-D
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8 respectively.¹³ Scores of 0 to 7 for either subscale are regarded as normal and scores of 8
9
10 to 10 suggest the presence of a mood disorder. Scores of 11 and above indicate the
11
12 probable presence of a mood disorder.¹⁴
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16 EQ-5D: The EQ-5D is a standardised instrument for measuring current health status that
17
18 provides a simple descriptive profile and a single index value that can be used in clinical
19
20 and economic evaluation of health care and in population health surveys. The
21
22 questionnaire covers five dimensions of health: mobility, self-care, usual activities,
23
24 pain/discomfort and anxiety/depression. Each dimension is divided into three levels: no
25
26 problems, some or moderate problems or extreme problems. The questionnaire consists
27
28 of a descriptive system produced in a standard layout that enables the respondent to
29
30 classify his/her health according to the five dimensions and a Visual Analogue Scale that
31
32 enables the respondent to provide a self-rating of his/her own health. Higher scores
33
34 indicate better health status.¹⁵ An overall Cronbach's alpha of 0.73 has been found in a
35
36 population of coronary heart disease patients.¹¹
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41 B-IPQ: B-IPQ is a short questionnaire that assesses cognitive and emotional
42
43 representations of illness on the basis of eight items. The eight items each represent a
44
45 dimension of the respondent's perception of his or her own illness. Five items assess
46
47 current cognitive representations of illness: consequences, timeline, personal control,
48
49 treatment control and identity. Two items assess emotional representations of illness:
50
51 concern and emotions. The last item assesses illness comprehensibility. A higher score on
52
53 the B-IPQ reflects a more threatening view of illness. B-IPQ has good test-retest reliability
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4 measured with Pearson correlations and has shown good predictive validity among
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6 patients recovering from myocardial infarction.¹⁶
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9 HeartQoL: HeartQoL is an illness specific questionnaire that measures quality of life (QoL)
10
11 in cardiac patients. The questionnaire covers the previous four weeks and produces a
12
13 global score and two subscales. A physical and an emotional scale with higher scores
14
15 indicating better QoL status. HeartQoL is a new questionnaire developed on the basis of
16
17 items from three widely used questionnaires for specific groups of cardiac patients (Seattle
18
19 Angina Questionnaire, MacNew Heart Disease Health-related Quality of Life Questionnaire
20
21 and Minnesota Living with Heart Failure questionnaire). The questionnaire has proven to
22
23 be a reliable instrument with a Cronbach's alpha between 0.80-0.91 for the global score
24
25 and each subscale and to be responsive in patients with a wide spectrum of diagnoses.¹⁷⁻¹⁹
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30 ESAS: ESAS is a 10 item questionnaire that allows patients to rate their current symptoms
31
32 on a visual numeric scale. The following symptoms are included: pain, tiredness, nausea,
33
34 depression, anxiety, drowsiness, appetite, well-being, shortness of breath and distress.
35
36 Higher scores indicate the presence and intensity of the symptoms. ESAS has proven to
37
38 be a valid instrument to measure cancer patients' self-reported symptoms with an overall
39
40 Cronbach's alpha of 0.79.²⁰ However, the scale has not yet been evaluated in cardiac
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42 patients.
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46 Besides the validated questionnaires, thirteen questions about health behaviour, sense of
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48 security and use of medicines are included in the questionnaire. This amounts to a total of
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50 62 items. The questionnaire was pre-tested for feasibility by 12 (10 male, 2 female)
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52 patients aged 52-81 years old (mean 65.9) on medical and surgical wards at three of the
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4 Heart Centres, and the introduction and layout was adjusted afterwards. The questionnaire
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6 takes about 20 minutes to complete.
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8 9 *Variables from registers*

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11 Because all Danish citizens have a unique personal identification number, linkage between
12
13 the national registers and other data sources is feasible. Therefore, the Danish registers
14
15 offer a great number of possibilities for national epidemiological studies.²¹
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18 For the DenHeart study, data are drawn at baseline and follow-up after one year from the
19
20 following registers:
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24 The Danish Civil Registration System:²² Gender, age, marital status.
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27 The Danish National Patient Register:²³ Action diagnosis, other diagnoses, procedures,
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29 length of hospital stay, type of hospitalisation (acute, heart related, other).
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32 The Danish National Health Service Register:²⁴ Contact with general practitioners and
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34 other agents in primary health care.
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37 Registers on personal labour market affiliation:²⁵ Labour market affiliation, sick leave, early
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39 retirement pension.
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43 Population Education Register:²⁶ Educational degree.
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46 The Income Statistics Register:²⁷ Income.
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48 49 *Data handling and record keeping*

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51 Questionnaires are mailed from the Heart Centres or from the patients' home to a
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53 scanning agency (Express A/S). Questionnaires are scanned and the file delivered to The
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55 National Institute of Public Health, University of Southern Denmark and placed on a secure
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4 hard drive. When the data collection is finished, the entire dataset will be reviewed in order
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6 to remove ineligible respondents, e.g. pulmonary trauma. Furthermore, the entire
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8 population of patients discharged from the Heart Centres during the data collection period
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10 will be drawn from the National Patient Register. This will be reviewed in order to remove
11
12 irrelevant discharges, in accordance with the inclusion criteria.
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14 15 16 *Data monitoring*

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18 In order to monitor trial conduct, reports are continuously delivered from the scanning
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20 agency in order to identify the need for adjustments. A data file is delivered every two
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22 weeks during the first three months and every month thereafter throughout the entire data
23
24 collection period. The data file includes a list of received questionnaires ranked by centre
25
26 and unit, and information on whether the questionnaire has been completed on the front
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28 page. The numbers are compared to the number of patients discharged at unit level in the
29
30 same period. Assessments of response rates are done and adjustments made if needed.
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32 Low response rates in a unit will lead to contact with the unit concerned to learn the reason
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34 why and actions to increase them. Returned questionnaires will be screened for
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36 systematic errors.
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40 41 *Study size*

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43 The study size is not derived statistically, as it consists of the total population of patients
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45 discharged from the five Heart Centres in the project period. The five Heart Centres
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47 diagnose and treat about 45,000 patients per year. These patients are diagnosed with
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49 numerous diseases and conditions and the aim is to describe differences, not only among
50
51 the most common diagnoses but also the infrequent ones. Thus, all patients discharged
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53 from national Heart Centres over one year are included in order to secure as high a level
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55 of specificity as possible. Furthermore, by including a large number of participants, a
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4 shorter follow-up time is needed. Besides the primary objectives, further ancillary and spin-
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6 off analyses will be prepared. Clearly, power calculations cannot be performed
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8 prospectively for all potential analyses based on data from the DenHeart study. Moreover,
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10 adverse outcomes have very different incident rates.

13 *Response rate*

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15 The final response rate is calculated based on discharge data from the National Patient
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17 Register. For calculating the actual number of eligible patients, the following are not
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19 included: patients without a Danish civil registration number, patients living in Greenland
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21 (no register follow-up possible), patients with two admissions within 24 hours, patients
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23 deceased in hospital and outpatient visits. Patients admitted for less than 24 hours without
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25 a procedure and readmitted with a procedure within one month are counted once.
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29 Patients who have filled out more than one questionnaire during the project period due to
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31 repeated hospitalizations will only be counted once (the first questionnaire returned) in the
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33 final count of the response rate. The repeated measurements may be included in sub-
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35 analyses.
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38 *Statistical methods*

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40 Objective 1: For each diagnostic group, age (mean), sex distribution and patient reported
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42 outcomes at hospital discharge distribution will be reported. Differences between groups
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44 will be tested by use of ANOVA tests for continuous variables and chi-squared tests for
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46 categorical variables. Multivariate logistic regression will be used to investigate the
47
48 relationship between diagnostic group and patient reported outcomes when controlling for
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50 response date (number of days since hospital discharge), age, sex and other possible
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4 confounders, and in-hospital predicting factors (e.g. procedure, duration of index hospital
5 admission, acute/elective admission, stay at intensive care unit, complications).
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9 Objective 2a: For each diagnostic group, the crude associations between patient reported
10 outcome measures at hospital discharge and all-cause and cardiac morbidity and all-
11 cause and cardiac mortality after one year, will be described and assessed using ANOVA
12 tests for continuous variables and chi-squared tests for categorical variables. In addition,
13 multivariate Cox proportional hazards regression models, with age as the time scale, will
14 be used to examine the associations between patient reported outcome measures at
15 baseline and all-cause morbidity and mortality and cardiac morbidity and mortality when
16 adjusting for response date, sex, co-morbidity and other potential confounding factors at
17 baseline.
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30 Objective 2b: For each diagnostic group, the crude associations between patient reported
31 outcome measures at hospital discharge and labour market affiliation (employment status,
32 sick leave, early retirement pension) after one year will be described and assessed using
33 the ANOVA tests for continuous variables and chi-squared tests for categorical variables.
34 Multivariate Cox proportional hazards regression models, with age as the time scale, will
35 also be carried out to investigate the associations between patient reported outcome
36 measures at baseline and labour market affiliation when adjusting for potential
37 confounding factors (e.g. response date, sex, co-morbidity).
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48 Objective 2c: For each diagnostic group, the crude associations between patient reported
49 outcomes measures at hospital discharge and health care utilization (hospitalizations,
50 contact with general practitioner, medical specialist, and physiotherapist) after one year,
51 will be described and assessed using the ANOVA tests for continuous variables and chi-
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4 squared tests for categorical variables. Multivariate Cox proportional hazards regression
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6 models, with age as the time scale, will be used to analyse the association between
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8 patient reported outcome measures at baseline and health care utilization when adjusting
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10 for potential confounding variables (e.g. response date, sex, co-morbidity).
11

12 13 *Weighting*

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15 It is possible to link both respondents and non-respondents in the survey on an individual
16
17 level to different administrative registers. Thus, non-response weights will be computed
18
19 based on register information (e.g. sex and age) in order to reduce non-response bias.
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22 Patients with a low probability of response will be given a higher weight in the analyses to
23
24 represent the larger number of non-respondents with similar characteristics. Accordingly,
25
26 patients more likely to respond will be given a lower weight.
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28 29 *Spin-off projects*

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31 Several spin-off analyses will be prepared and conducted, e.g. a three year follow up
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33 analysis on the primary outcomes, the association between patient reported outcomes at
34
35 discharge and cardiac events over time, patient reported outcomes and medication
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37 compliance and patient reported outcomes as a screening tool in clinical practice. A follow-
38
39 up survey after two to five years is being considered.
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44 45 **Ethics and dissemination**

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47 The study is conducted in accordance with the Declaration of Helsinki. According to
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49 Danish legislation, surveys should not be approved by an ethics committee system but
50
51 only by the Danish Data Protection Agency, no. 2007-58-0015/30-0937. The DenHeart
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53 survey is approved by the Institutional Boards of the Heart Centres and registered at
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55 ClinicalTrials.gov (NCT01926145).
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4 The National Institute of Public Health stores data from the DenHeart survey. Access to
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6 data can only be provided to investigators after approval from the Publication Committee.
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8 All study results will be published in international research journals and conference
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10 presentations.
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12 13 **Discussion**

14 15 *Study population*

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17 The five Heart Centres treat the most critically ill cardiac patients in Denmark.
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20 Approximately 47 regional or local hospitals treat cardiac patients medically and care for
21
22 terminally ill cardiac patients. These patients are underrepresented in the DenHeart study.
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25 The patients in this study represent the patients with diagnoses where medical, invasive or
26
27 surgical treatment is possible, and patients with rare conditions such as heart transplant
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29 and congenital heart disease. Furthermore, four of the five Heart Centres have a local
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31 hospital function treating all cardiac diagnoses. One surgical unit did not wish to participate
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33 in the study.
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37 Patients who are hospitalised several times in the project period will be asked to fill out the
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39 questionnaire each time. Repeated measures will only be used in sub-analyses. For
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41 reporting of primary outcomes, patients will only be counted once (the first questionnaire
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43 returned).
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46 47 *Variables*

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49 The majority of the outcome measures included in the questionnaire is comprised of
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51 validated and standardised instruments to assess patient reported outcomes, which
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53 enhances the validity of the questionnaire. However, in the interpretation of the results, it
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4 must be taken into account that patients with different cardiac conditions differ regarding
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6 how much their health status has changed prior to admission to hospital, and that some of
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8 the instruments have long recall.
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10 11 *Confounding factors*

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14 From previous national health surveys, we know that age and socioeconomic position play
15
16 a significant role for non-response. Also, regional differences of about 15 % in response
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18 rates have been documented.^{28, 29} The patients treated at the Heart Centres are often aged
19
20 and severely ill, which may be reflected in the response rates. This will be accounted for
21
22 by reporting both actual responses as well as weighted data for the underrepresented
23
24 groups in the analyses. However, several different initiatives are being conducted by the
25
26 centres to optimize response rates. Nurses are reminded to hand out the questionnaires at
27
28 local meetings, by posters in the ward and logo-pens, and response rates are continuously
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30 shared with the ward nurses in order to secure motivation among the approximately 800
31
32 nurses involved in the distribution of questionnaires. Letters are sent to the local hospitals
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34 that receive patients from the Heart Centres asking to remind the patients to fill out the
35
36 questionnaire at discharge to home. Some centres are mailing questionnaires to patients
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38 after discharge when they are not handed out in hospital. As this is a national multicentre
39
40 study, regional differences in ways to enhance the response rates may occur. All of these
41
42 different strategies fall within the frame of the DenHeart study and timeframe for
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44 responding.
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50 51 **Contributorship**

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4 SKB conceived the study. SKB, AVC, MH, LT, BB, JS, AM, AL, AIC, KJ and OE initiated
5
6 the study design and implementation. KJ, AIC and OE provided statistical expertise in the
7
8 clinical trial design. All contributed to the refinement of the study protocol.
9

10 11 **Funding**

12
13
14 This work was supported by the five participating Heart Centres in Denmark. Further
15
16 funding will be applied for from external funds.
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19 20 **Competing interest**

21
22 No competing interests have been declared by the authors.
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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract Page 1 (b) Provide in the abstract an informative and balanced summary of what was done and what was found Page 2-3
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses Page 5
Methods		
Study design	4	Present key elements of study design early in the paper Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 5-6
Participants	6	<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants Page 6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Page 7-10
Bias	9	Describe any efforts to address potential sources of bias Page 11, 14, 16
Study size	10	Explain how the study size was arrived at Page 11-12
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Not applicable (analyses not done yet)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy

(e) Describe any sensitivity analyses

Page 12-14

Results		No results as this is a research protocol
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives Not applicable (no results yet)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 15-16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Not applicable (no results yet)
Generalisability	21	Discuss the generalisability (external validity) of the study results Not applicable (no results yet)
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Page 17

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at

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2 <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is
3 available at www.strobe-statement.org.
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BMJ Open

Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

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SCHOLARONE™
Manuscripts

Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

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Abstract

Introduction: Patient reported health status, including symptom burden, functional status and quality of life, is an important measure of health. Differences in health status between diagnostic groups within cardiology have only been sparsely investigated. These outcomes may predict morbidity, mortality, labour market affiliation and health care utilization in various diagnostic groups. A national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population has been designed as the DenHeart survey.

Methods and analysis: DenHeart is designed as a cross-sectional survey with register based follow-up. All diagnostic groups at the five national Heart Centres are included during one year (April 15th 2013 to April 15th 2014) and asked to fill out a questionnaire at hospital discharge. The total eligible population, both responders and non-responders, will be followed in national registers. The following instruments are used: SF-12, HADS, EQ-5D, B-IPQ, HeartQoL and ESAS. The following variables are collected from national registers: action diagnosis, procedures, co-morbidity, length of hospital stay, type of hospitalisation, visits to GP and other agents in primary health care, dispensed prescription medication, vital status, and cause of death. Labour market affiliation, sick leave, early retirement pension, educational degree and income will be collected from registers. Frequency distributions and multiple logistic regression analyses will be used to describe and assess differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors. Cox proportional hazards regression models with age as the time scale will be used to investigate associations between patient reported outcomes at baseline and morbidity/mortality, labour market affiliation and health care utilization after one year.

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4 Ethics and dissemination: The study complies with the Declaration of Helsinki. The study
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6 has been approved by the Danish Data Protection Agency: 2007-58-0015/30-0937. Study
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8 findings will be disseminated widely through peer reviewed publications and conference
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10 presentations.
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Introduction

Patient reported health status, which includes symptom burden, functional status and quality of life, is an important measure of health. Validated patient health status surveys, including disease specific instruments for patients with cardiovascular disease, allow quantification of critical patient-centred outcomes and additional research is needed to better understand the determinants¹ and the predicting factors of patients' health status. Previous studies suggest an association between heart disease, self-reported health and morbidity and mortality, and that patient reported outcome measures can predict prolonged hospital stay, future quality of life, return to work, morbidity and mortality in cardiac patients.²⁻⁷ Quality of life scores seem to provide important prognostic information independent of traditional clinical data, as higher scores have been associated with longer survival in patients with ventricular arrhythmias and coronary artery disease.^{8,9} However no studies have included all diagnostic groups within cardiology and comparisons among diagnostic groups are lacking. The overall aim of the DenHeart survey is to gain knowledge about patient reported outcome measures regarding health among cardiac patients at hospital discharge. Knowledge about patients' own perception of their health status and predicting factors can help to guide inpatient practice and outpatient follow-up. Furthermore, a survey combined with register data can be used to evaluate differences among diagnostic groups and predicting factors for patient reported outcome measures at hospital discharge and long-term morbidity and mortality. Also, economic analysis of healthcare utilisation and work ability status in a large cohort of cardiac patients is needed. Therefore, the DenHeart study is designed as a national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population.

Objectives

The objectives of the DenHeart study are to describe: (i) differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors and (ii) patient reported outcomes at hospital discharge as a predictor of a) morbidity and mortality, b) labour market affiliation and c) health care utilization after one year.

Methods and analysis

Study design

The DenHeart study is designed as a cross-sectional survey with register based follow-up. All cardiac patients are asked to fill out a questionnaire at hospital discharge to evaluate patient reported outcomes. Furthermore, the total eligible population, both responders and non-responders, will be followed in national registers.

Setting and participants

The five Heart Centres in Denmark are including patients during a one year period, from April 15th 2013 to April 15th 2014. One centre began data collection later, May 1st 2013. Four heart centres have both medical and surgical wards, one centre medical wards only. All cardiac patients discharged or transferred to a local hospital from one of the Heart Centres are potential participants in the study. Patients are unselected and consecutively included at hospital discharge. Included patients are asked to complete and return a questionnaire before they leave the hospital or alternatively to do so at home within 3 days of discharge and return it by mail. Patients who are transferred to another hospital are given the questionnaire at discharge from the Heart Centre and asked to fill it out at the

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4 day of hospital discharge or alternatively to do so at home within 3 days of discharge and
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6 then return it by mail.
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8 9 *Eligibility criteria*

10 All diagnostic groups within cardiology are included. Patients with ischemic heart disease
11 (e.g. coronary angiography, percutaneous coronary intervention), heart failure (e.g. heart
12 transplantation), arrhythmia (e.g. ablation, labyrinth, pacemaker, implantable cardioverter
13 defibrillator), heart valve disease (e.g. valve replacement), endocarditis and congenital
14 heart disease (e.g. atrium septum defect, patent ductus arteriosus, patent foramen ovale,
15 coarctatio) are diagnosed and treated at the Heart Centres. Infrequent conditions such as
16 thorax-trauma are also included. Patients are grouped by their primary action diagnose
17 and will only be included in one group.
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20 Patients under 18 years of age and patients without a Danish civil registration number are
21 excluded from the study. For ethical reasons, patients who are unconscious when
22 transferred are also excluded.
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25 Reasons for non-response are recorded which allows for sub-analyses of these groups.
26

27 On the front page of the questionnaire there is a box that enables the patient or nurse to
28 tick off the reason for non-response: "Does not wish to participate", "Not able to participate
29 because of illness", "Not able to participate because of language barrier", "Questionnaire
30 not handed out" and "Other".
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Recruitment

Patients are recruited at hospital discharge (the same day or the day before discharge) by the ward nurse in charge of the discharge of the individual patients or by a research nurse.

All nurses at the centres, approximately 800, have been informed about the study and procedures at ward meetings, guidelines have been distributed and a website created (www.DenHeart.dk). When informing patients about the study and handing out the questionnaire, nurses also distribute a postage pre-paid envelope for the return of the questionnaire, either at the ward or after discharge. No reminders are sent to patients as the time window of three days post discharge makes it impossible. Distribution and return rates are monitored to allow for interventions if the rates drop during data collection. No specific cut off is set for low rates calling for interventions. Instead monthly discussions on each site and in the national research group are undertaken allowing for discussions and ideas for reminding the staff to hand out the questioners. *Data sources/measurement*

The following patient reported outcome measures are used: Short-form 12 (SF-12), Hospital Anxiety and Depression Scale (HADS), EQ-5D, Brief Illness Perception Questionnaire (B-IPQ), HeartQoL and Edmonton Symptom Assessment Scale (ESAS). Both EQ5D and SF-12 are generic health instruments. SF-12 is included to be able to compare to a national general population and EQ5D is included due to a different scale composition.

SF-12: The SF-12 is a 12-item version of the SF-36 and is a brief, reliable measure of overall health. The questionnaire measures eight domains of health: physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health with higher scores indicating better health status. The items cover the previous four weeks and results are expressed in terms of two summary scores: the

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4 Physical Component Summary (PCS) and the Mental Component Summary (MCS).¹⁰ A
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6 Cronbach's alpha of 0.87 and 0.84 for PCS-12 and MCS-12 respectively have been
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8 reported in a population of coronary heart disease patients.¹¹ The SF-12 is a suitable for
9
10 studies focusing on patient-based assessment of physical and mental health.¹⁰
11
12 Furthermore it is used in the National Health Surveys and outcomes can be compared.
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16 HADS: HADS is a 14-item questionnaire that assesses levels of depression and anxiety in
17
18 medically ill patients admitted to non-psychiatric hospital clinics. The scale offers two
19
20 scores, HADS-A and HADS-D, and consists of seven questions to assess anxiety and
21
22 seven questions to assess depression.¹² For each of the questions the respondent
23
24 chooses from four responses to indicate the extent to which each applies for the last week.
25
26 HADS is a valid and internally consistent measure, with a mean Cronbach's alpha of 0.83
27
28 and 0.82 for the HADS-A and HADS-D respectively.¹³ Scores of 0 to 7 for either subscale
29
30 are regarded as normal and scores of 8 to 10 suggest the presence of a mood disorder.
31
32 Scores of 11 and above indicate the probable presence of a mood disorder.¹⁴
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37 EQ-5D: The EQ-5D is a 6-item standardised instrument for measuring current health
38
39 status that provides a simple descriptive profile and a single index value that can be used
40
41 in clinical and economic evaluation of health care and in population health surveys. The
42
43 questionnaire covers five dimensions of health: mobility, self-care, usual activities,
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45 pain/discomfort and anxiety/depression. Each dimension is divided into three levels: no
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47 problems, some or moderate problems or extreme problems. . The sixth item a Visual
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49 Analogue Scale enables the respondent to provide a self-rating of his/her own health.
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51 Higher scores indicate better health status.¹⁵ An overall Cronbach's alpha of 0.73 has been
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53 found in a population of coronary heart disease patients.¹¹
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4 B-IPQ: B-IPQ is a short 8-item questionnaire that assesses cognitive and emotional
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6 representations of illness. The eight items each represent a dimension of the respondent's
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8 perception of his or her own illness. Five items assess current cognitive representations of
9
10 illness: consequences, timeline, personal control, treatment control and identity. Two items
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12 assess emotional representations of illness: concern and emotions. The last item
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14 assesses illness comprehensibility. A higher score on the B-IPQ reflects a more
15
16 threatening view of illness. B-IPQ has good test-retest reliability measured with Pearson
17
18 correlations and has shown good predictive validity among patients recovering from
19
20 myocardial infarction.¹⁶
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25 HeartQoL: HeartQoL is an 14-item illness specific questionnaire that measures quality of
26
27 life (QoL) in cardiac patients. The questionnaire covers the previous four weeks and
28
29 produces a global score and two subscales. A physical and an emotional scale with higher
30
31 scores indicating better QoL status. HeartQoL is a new questionnaire developed on the
32
33 basis of items from three widely used questionnaires for specific groups of cardiac patients
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35 (Seattle Angina Questionnaire, MacNew Heart Disease Health-related Quality of Life
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37 Questionnaire and Minnesota Living with Heart Failure questionnaire). The questionnaire
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39 has proven to be a reliable instrument with a Cronbach's alpha between 0.80-0.91 for the
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41 global score and each subscale and to be responsive in patients with a wide spectrum of
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43 diagnoses.¹⁷⁻¹⁹ ESAS: ESAS is a 10-item questionnaire that allows patients to rate their
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45 current symptoms on a visual numeric scale. The following symptoms are included: pain,
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47 tiredness, nausea, depression, anxiety, drowsiness, appetite, well-being, shortness of
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49 breath and distress. Higher scores indicate the presence and intensity of the symptoms.
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52 ESAS has proven to be a valid instrument to measure cancer patients' self-reported
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54 symptoms with an overall Cronbach's alpha of 0.79.²⁰ Even though ESAS was developed
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4 for palliative care in cancer patients, the ESAS has been used in cardiac populations and
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6 there was found modest correlation to NYHA class and heart failure questionnaires.
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8²¹Besides the validated questionnaires, 16 questions about health behaviour, cardiac
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10 symptoms, sense of security and use of medicines are included in the questionnaire. This
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12 amounts to a total of 80 items. The questionnaire was pre-tested for feasibility by 12 (10
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14 male, 2 female) patients aged 52-81 years old (mean 65.9) on medical and surgical wards
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16 at three of the Heart Centres, and the introduction and layout was adjusted afterwards.
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18 The questionnaire takes about 20 minutes to complete.
19

20 21 22 *Variables from registers* 23

24
25 Because all Danish citizens have a unique personal identification number, linkage between
26
27 the national registers and other data sources is feasible. Therefore, the Danish registers
28
29 offer a great number of possibilities for national epidemiological studies.²²
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32 For the DenHeart study, data are drawn at baseline and follow-up after one year from the
33
34 following registers:
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37 The Danish Civil Registration System:²³ Gender, age, marital status.
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40 The Danish National Patient Register:²⁴ Action diagnosis, other diagnoses, procedures,
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42 length of hospital stay, type of hospitalisation (acute, heart related, other).
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45 The Danish National Health Service Register:²⁵ Contact with general practitioners and
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47 other agents in primary health care.
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50 Registers on personal labour market affiliation:²⁶ Labour market affiliation, sick leave, early
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52 retirement pension.
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55 Population Education Register:²⁷ Educational degree.
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4 The Income Statistics Register.²⁸ Income.
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7 *Data handling and record keeping*
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9 Questionnaires are mailed from the Heart Centres or from the patients' home to a
10 scanning agency (Express A/S). Questionnaires are scanned and the file delivered to The
11 National Institute of Public Health, University of Southern Denmark and placed on a secure
12 hard drive. When the data collection is finished, the entire dataset will be reviewed in order
13 to remove ineligible respondents, e.g. pulmonary trauma. Furthermore, the entire
14 population of patients discharged from the Heart Centres during the data collection period
15 will be drawn from the National Patient Register. This will be reviewed in order to remove
16 irrelevant discharges, in accordance with the inclusion criteria.
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27 *Data monitoring*
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29 In order to monitor trial conduct, reports are continuously delivered from the scanning
30 agency in order to identify the need for adjustments. A data file is delivered every two
31 weeks during the first three months and every month thereafter throughout the entire data
32 collection period. The data file includes a list of received questionnaires ranked by centre
33 and unit, and information on whether the questionnaire has been completed on the front
34 page. The numbers are compared to the number of patients discharged at unit level in the
35 same period. Assessments of response rates are done and adjustments made if needed.
36 Low response rates in a unit will lead to contact with the unit concerned to learn the reason
37 why and actions to increase them. Returned questionnaires will be screened for
38 systematic errors.
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Study size

The study size is not derived statistically, as it consists of the total population of patients discharged from the five Heart Centres in the project period. The five Heart Centres diagnose and treat about 45,000 patients per year. These patients are diagnosed with numerous diseases and conditions and the aim is to describe differences, not only among the most common diagnoses but also the infrequent ones. Thus, all patients discharged from national Heart Centres over one year are included in order to secure as high a level of specificity as possible. Furthermore, by including a large number of participants, a shorter follow-up time is needed. Besides the primary objectives, further ancillary and spin-off analyses will be prepared. Clearly, power calculations cannot be performed prospectively for all potential analyses based on data from the DenHeart study. Moreover, adverse outcomes have very different incidence rates.

Response rate

The final response rate is calculated based on discharge data from the National Patient Register. For calculating the actual number of eligible patients, the following are not included: patients without a Danish civil registration number, patients living in Greenland (no register follow-up possible), patients with two admissions within 24 hours, patients deceased in hospital and outpatient visits. Patients admitted for less than 24 hours without a procedure and readmitted with a procedure within one month are counted once.

Even though patients are encouraged to fill out the questionnaire within 3 days all questionnaires completed within 4 weeks of discharge are included in the analyses.

Patients who have filled out more than one questionnaire during the project period due to repeated hospitalizations will only be counted once (the first questionnaire returned) in the

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4 final count of the response rate. The repeated measurements may be included in sub-
5
6 analyses.
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8 9 *Statistical methods*

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11 Objective 1: For each diagnostic group, age (mean), sex distribution and patient reported
12 outcomes at hospital discharge distribution will be reported. Differences between groups
13 will be tested by use of ANOVA tests for continuous variables and chi-squared tests for
14 categorical variables. Multivariate logistic regression will be used to investigate the
15 relationship between diagnostic group and patient reported outcomes when controlling for
16 response date (number of days since hospital discharge), age, sex and other possible
17 confounders, and in-hospital predicting factors (e.g. procedure, duration of index hospital
18 admission, acute/elective admission, stay at intensive care unit, complications).
19

20
21 Objective 2a: For each diagnostic group, the crude associations between patient reported
22 outcome measures at hospital discharge and all-cause and cardiac morbidity and all-
23 cause and cardiac mortality after one year, will be described and assessed using ANOVA
24 tests for continuous variables and chi-squared tests for categorical variables. In addition,
25 multivariate Cox proportional hazards regression models, with age as the time scale, will
26 be used to examine the associations between patient reported outcome measures at
27 baseline and all-cause morbidity and mortality and cardiac morbidity and mortality when
28 adjusting for response date, sex, co-morbidity and other potential confounding factors at
29 baseline.
30

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32 Objective 2b: For each diagnostic group, the crude associations between patient reported
33 outcome measures at hospital discharge and labour market affiliation (employment status,
34 sick leave, early retirement pension) after one year will be described and assessed using
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4 the ANOVA tests for continuous variables and chi-squared tests for categorical variables.
5
6 Multivariate Cox proportional hazards regression models, with age as the time scale, will
7
8 also be carried out to investigate the associations between patient reported outcome
9
10 measures at baseline and labour market affiliation when adjusting for potential
11
12 confounding factors (e.g. response date, sex, co-morbidity).
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16 Objective 2c: For each diagnostic group, the crude associations between patient reported
17
18 outcomes measures at hospital discharge and health care utilization (hospitalizations,
19
20 contact with general practitioner, medical specialist, and physiotherapist) after one year,
21
22 will be described and assessed using the ANOVA tests for continuous variables and chi-
23
24 squared tests for categorical variables. Multivariate Cox proportional hazards regression
25
26 models, with age as the time scale, will be used to analyse the association between
27
28 patient reported outcome measures at baseline and health care utilization when adjusting
29
30 for potential confounding variables (e.g. response date, sex, co-morbidity).
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33

34 *Weighting*

35
36 It is possible to link both respondents and non-respondents in the survey on an individual
37
38 level to different administrative registers. Thus, non-response weights will be computed
39
40 based on register information (e.g. sex and age) in order to reduce non-response bias.
41
42

43 Patients with a low probability of response will be given a higher weight in the analyses to
44
45 represent the larger number of non-respondents with similar characteristics. Accordingly,
46
47 patients more likely to respond will be given a lower weight.
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50 *Spin-off projects*

51
52 Several spin-off analyses will be prepared.
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54

55 **Ethics and dissemination**

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4 The study is conducted in accordance with the Declaration of Helsinki. According to
5
6 Danish legislation, surveys should not be approved by an ethics committee system but
7
8 only by the Danish Data Protection Agency, no. 2007-58-0015/30-0937. The DenHeart
9
10 survey is approved by the Institutional Boards of the Heart Centres and registered at
11
12 ClinicalTrials.gov (NCT01926145). Patients sign informed consent stating that participation
13
14 is voluntary and that further information from patient records may be obtained.
15
16

17
18 The National Institute of Public Health stores data from the DenHeart survey. Access to
19
20 data can only be provided to investigators after approval from the Publication Committee.
21
22 All study results will be published in international research journals and conference
23
24 presentations.
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26

27 28 **Discussion**

29 30 *Study population*

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32 The five Heart Centres treat the most critically ill cardiac patients in Denmark.
33
34 Approximately 47 regional or local hospitals treat cardiac patients medically and care for
35
36 terminally ill cardiac patients. These patients are underrepresented in the DenHeart study.
37
38 The patients in this study represent the patients with diagnoses where medical, invasive or
39
40 surgical treatment is possible, and patients with rare conditions such as heart transplant
41
42 and congenital heart disease. Furthermore, four of the five Heart Centres have a local
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44 hospital function treating all cardiac diagnoses. One surgical unit did not wish to participate
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46 in the study.
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52 Patients who are hospitalised several times in the project period will be asked to fill out the
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54 questionnaire each time. Repeated measures will only be used in sub-analyses. For
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4 reporting of primary outcomes, patients will only be counted once (the first questionnaire
5
6 returned).
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8 9 *Variables*

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11
12 The majority of the outcome measures included in the questionnaire is comprised of
13
14 validated and standardised instruments to assess patient reported outcomes, which
15
16 enhances the validity of the questionnaire. However, in the interpretation of the results, it
17
18 must be taken into account that patients with different cardiac conditions differ regarding
19
20 how much their health status has changed prior to admission to hospital, and that some of
21
22 the instruments have long recall.
23
24

25 26 *Confounding factors*

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28
29 From previous national health surveys, we know that age and socioeconomic position play
30
31 a significant role for non-response. Also, regional differences of about 15 % in response
32
33 rates have been documented.^{29, 30} The patients treated at the Heart Centres are often aged
34
35 and severely ill, which may be reflected in the response rates. This will be accounted for
36
37 by reporting both actual responses as well as weighted data for the underrepresented
38
39 groups in the analyses. However, several different initiatives are being conducted by the
40
41 centres to optimize response rates. Nurses are reminded to hand out the questionnaires at
42
43 local meetings, by posters in the ward and logo-pens, and response rates are continuously
44
45 shared with the ward nurses in order to secure motivation among the approximately 800
46
47 nurses involved in the distribution of questionnaires. Letters are sent to the local hospitals
48
49 that receive patients from the Heart Centres asking to remind the patients to fill out the
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51 questionnaire at discharge to home. Some centres are mailing questionnaires to patients
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53 after discharge when they are not handed out in hospital. Mailed questionnaires are sent
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4 with overnight post service allowing the questionnaire to be filled out within the 3 days. As
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6 this is a national multicentre study, regional differences in ways to enhance the response
7
8 rates may occur. All of these different strategies fall within the frame of the DenHeart study
9
10 and timeframe for responding.
11

12 13 **Contributorship**

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16
17 SKB conceived the study. SKB, AVC, MH, LT, BB, JS, AM, AL, AIC, KJ and OE initiated
18
19 the study design and implementation. KJ, AIC and OE provided statistical expertise in the
20
21 clinical trial design. All contributed to the refinement of the study protocol.
22
23

24 25 **Funding**

26
27
28 This work was supported by the five participating Heart Centres in Denmark. Further
29
30 funding will be applied for from external funds.
31

32 33 **Competing interest**

34
35
36 No competing interests have been declared by the authors.
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Patient reported outcomes at hospital discharge from Heart Centres, a national cross-sectional survey with register based follow-up: The DenHeart study protocol.

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Field Code Changed

Abstract

Introduction: Patient reported health status, including symptom burden, functional status and quality of life, is an important measure of health. Differences in health status between diagnostic groups within cardiology have only been sparsely investigated. These outcomes may predict morbidity, mortality, labour market affiliation and health care utilization in various diagnostic groups. A national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population has been designed as the DenHeart survey.

Methods and analysis: DenHeart is designed as a cross-sectional survey with register based follow-up. All diagnostic groups at the five national Heart Centres are included during one year (April 15th 2013 to April 15th 2014) and asked to fill out a questionnaire at hospital discharge. The total eligible population, both responders and non-responders, will be followed in national registers. The following instruments are used: SF-12, HADS, EQ-5D, B-IPQ, HeartQoL and ESAS. The following variables are collected from national registers: action diagnosis, procedures, co-morbidity, length of hospital stay, type of hospitalisation, visits to GP and other agents in primary health care, dispensed prescription medication, vital status, and cause of death. Labour market affiliation, sick leave, early retirement pension, educational degree and income will be collected from registers. Frequency distributions and multiple logistic regression analyses will be used to describe and assess differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors. Cox proportional hazards regression models with age as the time scale will be used to investigate associations between patient reported outcomes at baseline and morbidity/mortality, labour market affiliation and health care utilization after one year.

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8 Ethics and dissemination: The study complies with the Declaration of Helsinki. The study
9 has been approved by the Danish Data Protection Agency: 2007-58-0015/30-0937. Study
10 findings will be disseminated widely through peer reviewed publications and conference
11 presentations.
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16 Trial registration: ClinicalTrials.gov: NCT01926145.
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Introduction

Patient reported health status, which includes symptom burden, functional status and quality of life, is an important measure of health. Validated patient health status surveys, including disease specific instruments for patients with cardiovascular disease, allow quantification of critical patient-centred outcomes and additional research is needed to better understand the determinants¹ and the predicting factors of patients' health status. Previous studies suggest an association between heart disease, self-reported health and morbidity and mortality, and that patient reported outcome measures can predict prolonged hospital stay, future quality of life, return to work, morbidity and mortality in cardiac patients.²⁻⁷ Quality of life scores seem to provide important prognostic information independent of traditional clinical data, as higher scores have been associated with longer survival in patients with ventricular arrhythmias and coronary artery disease.^{8, 9} However no studies have included all diagnostic groups within cardiology and comparisons among diagnostic groups are lacking. The overall aim of the DenHeart survey is to gain knowledge about patient reported outcome measures regarding health among cardiac patients at hospital discharge. Knowledge about patients' own perception of their health status and predicting factors can help to guide inpatient practice and outpatient follow-up. Furthermore, a survey combined with register data can be used to evaluate differences among diagnostic groups and predicting factors for patient reported outcome measures at hospital discharge and long-term morbidity and mortality. Also, economic analysis of healthcare utilisation and work ability status in a large cohort of cardiac patients is needed. Therefore, the DenHeart study is designed as a national survey aiming to include all cardiac diagnostic groups from a total Heart Centre population.

Objectives

The objectives of the DenHeart study are to describe: (i) differences in patient reported outcomes at hospital discharge between diagnostic groups and in-hospital predicting factors and (ii) patient reported outcomes at hospital discharge as a predictor of a) morbidity and mortality, b) labour market affiliation and c) health care utilization after one year.

Methods and analysis

Study design

The DenHeart study is designed as a cross-sectional survey with register based follow-up. All cardiac patients are asked to fill out a questionnaire at hospital discharge to evaluate patient reported outcomes. Furthermore, the total eligible population, both responders and non-responders, will be followed in national registers.

Setting and participants

The five Heart Centres in Denmark are including patients during a one year period, from April 15th 2013 to April 15th 2014. One centre began data collection later, May 1st 2013. Four heart centres have both medical and surgical wards, one centre medical wards only. All cardiac patients discharged or transferred to a local hospital from one of the Heart Centres are potential participants in the study. Patients are unselected and consecutively included at hospital discharge. Included patients are asked to complete and return a questionnaire before they leave the hospital or alternatively to do so at home within 3 days of discharge and return it by mail. Patients who are transferred to another hospital are given the questionnaire at discharge from the Heart Centre and asked to fill it out at the

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8 day of hospital discharge or alternatively to do so at home within 3 days of discharge and
9 then return it by mail.

11 *Eligibility criteria*

12 All diagnostic groups within cardiology are included. Patients with ischemic heart disease
13 (e.g. coronary angiography, percutaneous coronary intervention), heart failure (e.g.
14 ~~coronary artery bypass graft~~, heart transplantation), arrhythmia (e.g. ablation, labyrinth,
15 pacemaker, implantable cardioverter defibrillator), heart valve disease (e.g. ~~stent~~, valve
16 replacement), endocarditis and congenital heart disease (e.g. atrium septum defect, patent
17 ductus arteriosus, patent foramen ovale, coarctatio) are diagnosed and treated at the
18 Heart Centres. Infrequent conditions such as thorax-trauma are also included. [Patients are
19 grouped by their primary action diagnose and will only be included in one group.](#)

20 Patients under 18 years of age and patients without a Danish civil registration number are
21 excluded from the study. For ethical reasons, patients who are unconscious when
22 transferred are also excluded.

23 Reasons for non-response are recorded which allows for sub-analyses of these groups.

24 On the front page of the questionnaire there is a box that enables the patient or nurse to
25 tick off the reason for non-response: "Does not wish to participate", "Not able to participate
26 because of illness", "Not able to participate because of language barrier", "Questionnaire
27 not handed out" and "Other".

28 *Recruitment*

29 Patients are recruited at hospital discharge (the same day or the day before discharge) by
30 the ward nurse in charge of the discharge of the individual patients or by a research nurse.
31 All nurses at the centres, approximately 800, have been informed about the study and

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8 procedures at ward meetings, guidelines have been distributed and a website created
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10 (www.DenHeart.dk). When informing patients about the study and handing out the
11 questionnaire, nurses also distribute a postage pre-paid envelope ~~for the to them to~~ return
12 ~~of~~ the questionnaire ~~in~~, either at the ward or after discharge. No reminders are sent to
13 patients as the time window of three days post discharge makes it impossible. Distribution
14 and return rates are monitored to allow for interventions if the rates drop during data
15 collection. No specific cut off is set for low rates calling for interventions. Instead monthly
16 discussions on each site and in the national research group are undertaken allowing for
17 discussions and ideas for reminding the staff to hand out the questioners.

25 *Data sources/measurement*

26
27 The following patient reported outcome measures are used: Short-form 12 (SF-12),
28 Hospital Anxiety and Depression Scale (HADS), EQ-5D, Brief Illness Perception
29 Questionnaire (B-IPQ), HeartQoL and Edmonton Symptom Assessment Scale (ESAS).
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33 Both EQ5D and SF-12 are generic health instruments. SF-12 is included to be able to
34 compare to a national general population and EQ5D is included due to a different scale
35 composition.

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39 SF-12: The SF-12 is a 12-item version of the SF-36 and is a brief, reliable measure of
40 overall health. The questionnaire measures eight domains of health: physical function,
41 role-physical, bodily pain, general health, vitality, social functioning, role-emotional and
42 mental health with higher scores indicating better health status. The items cover the
43 previous four weeks and results are expressed in terms of two summary scores: the
44 Physical Component Summary (PCS) and the Mental Component Summary (MCS).¹⁰ A
45 Cronbach's alpha of 0.87 and 0.84 for PCS-12 and MCS-12 respectively have been
46 reported in a population of coronary heart disease patients.¹¹ The SF-12 is a suitable for
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8 studies focusing on patient-based assessment of physical and mental health.¹⁰

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10 Furthermore it is used in the National Health Surveys and outcomes can be compared.

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12 HADS: HADS is a 14-item questionnaire that assesses levels of depression and anxiety in

13
14 medically ill patients [admitted to non-psychiatric hospital clinics](#). The scale offers two

15
16 scores, HADS-A and HADS-D, and consists of seven questions to assess anxiety and

17
18 seven questions to assess depression.¹² For each of the questions the respondent

19
20 chooses from four responses to indicate the extent to which each applies for the last week.

21
22 HADS is a valid and internally consistent measure, with a mean Cronbach's alpha of 0.83

23
24 and 0.82 for the HADS-A and HADS-D respectively.¹³ Scores of 0 to 7 for either subscale

25
26 are regarded as normal and scores of 8 to 10 suggest the presence of a mood disorder.

27
28 Scores of 11 and above indicate the probable presence of a mood disorder.¹⁴

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30 EQ-5D: The EQ-5D is a [6-item](#) standardised instrument for measuring current health

31
32 status that provides a simple descriptive profile and a single index value that can be used

33
34 in clinical and economic evaluation of health care and in population health surveys. The

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36 questionnaire covers five dimensions of health: mobility, self-care, usual activities,

37
38 pain/discomfort and anxiety/depression. Each dimension is divided into three levels: no

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40 problems, some or moderate problems or extreme problems. ~~The questionnaire consists~~

41
42 ~~of a descriptive system produced in a standard layout that enables the respondent to~~

43
44 ~~classify his/her health according to the five dimensions and a~~. ~~The sixth item a~~ Visual

45
46 Analogue Scale ~~that~~ enables the respondent to provide a self-rating of his/her own health.

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48 Higher scores indicate better health status.¹⁵ An overall Cronbach's alpha of 0.73 has been

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50 found in a population of coronary heart disease patients.¹¹

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8 B-IPQ: B-IPQ is a short [8-item](#) questionnaire that assesses cognitive and emotional
9 representations of illness ~~on the basis of eight items~~. The eight items each represent a
10 dimension of the respondent's perception of his or her own illness. Five items assess
11 current cognitive representations of illness: consequences, timeline, personal control,
12 treatment control and identity. Two items assess emotional representations of illness:
13 concern and emotions. The last item assesses illness comprehensibility. A higher score on
14 the B-IPQ reflects a more threatening view of illness. B-IPQ has good test-retest reliability
15 measured with Pearson correlations and has shown good predictive validity among
16 patients recovering from myocardial infarction.¹⁶

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26 HeartQoL: HeartQoL is an [14-item](#) illness specific questionnaire that measures quality of
27 life (QoL) in cardiac patients. The questionnaire covers the previous four weeks and
28 produces a global score and two subscales. A physical and an emotional scale with higher
29 scores indicating better QoL status. HeartQoL is a new questionnaire developed on the
30 basis of items from three widely used questionnaires for specific groups of cardiac patients
31 (Seattle Angina Questionnaire, MacNew Heart Disease Health-related Quality of Life
32 Questionnaire and Minnesota Living with Heart Failure questionnaire). The questionnaire
33 has proven to be a reliable instrument with a Cronbach's alpha between 0.80-0.91 for the
34 global score and each subscale and to be responsive in patients with a wide spectrum of
35 diagnoses.¹⁷⁻¹⁹

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45 ESAS: ESAS is a [10-item](#) questionnaire that allows patients to rate their current symptoms
46 on a visual numeric scale. The following symptoms are included: pain, tiredness, nausea,
47 depression, anxiety, drowsiness, appetite, well-being, shortness of breath and distress.
48 Higher scores indicate the presence and intensity of the symptoms. ESAS has proven to
49 be a valid instrument to measure cancer patients' self-reported symptoms with an overall
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8 Cronbach's alpha of 0.79.²⁰ ~~However, the scale has not yet been evaluated in cardiac~~
9 ~~patients~~ Even though ESAS was developed for palliative care in cancer patients, the ESAS
10 ~~-has been used in cardiac populations, and there was found modest correlation to NYHA~~
11 ~~class and heart failure questionnaires.~~²¹
12
13 Besides the validated questionnaires, ~~thirteen~~ 16 questions about health behaviour,
14 ~~cardiac symptoms,~~ sense of security and use of medicines are included in the
15
16 questionnaire. This amounts to a total of ~~80~~ 62 items. The questionnaire was pre-tested for
17
18 feasibility by 12 (10 male, 2 female) patients aged 52-81 years old (mean 65.9) on medical
19
20 and surgical wards at three of the Heart Centres, and the introduction and layout was
21
22 adjusted afterwards. The questionnaire takes about 20 minutes to complete.
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28 *Variables from registers*

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30 Because all Danish citizens have a unique personal identification number, linkage between
31
32 the national registers and other data sources is feasible. Therefore, the Danish registers
33
34 offer a great number of possibilities for national epidemiological studies.²²
35

36 For the DenHeart study, data are drawn at baseline and follow-up after one year from the
37
38 following registers:
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41 The Danish Civil Registration System:²³ Gender, age, marital status.
42

43 The Danish National Patient Register:²⁴ Action diagnosis, other diagnoses, procedures,
44
45 length of hospital stay, type of hospitalisation (acute, heart related, other).
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48 The Danish National Health Service Register:²⁵ Contact with general practitioners and
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50 other agents in primary health care.
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8 Registers on personal labour market affiliation:²⁶ Labour market affiliation, sick leave, early
9 retirement pension.

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12 Population Education Register:²⁷ Educational degree.

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15 The Income Statistics Register:²⁸ Income.

16 17 *Data handling and record keeping*

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19 Questionnaires are mailed from the Heart Centres or from the patients' home to a
20 scanning agency (Express A/S). Questionnaires are scanned and the file delivered to The
21 National Institute of Public Health, University of Southern Denmark and placed on a secure
22 hard drive. When the data collection is finished, the entire dataset will be reviewed in order
23 to remove ineligible respondents, e.g. pulmonary trauma. Furthermore, the entire
24 population of patients discharged from the Heart Centres during the data collection period
25 will be drawn from the National Patient Register. This will be reviewed in order to remove
26 irrelevant discharges, in accordance with the inclusion criteria.

27 28 *Data monitoring*

29
30 In order to monitor trial conduct, reports are continuously delivered from the scanning
31 agency in order to identify the need for adjustments. A data file is delivered every two
32 weeks during the first three months and every month thereafter throughout the entire data
33 collection period. The data file includes a list of received questionnaires ranked by centre
34 and unit, and information on whether the questionnaire has been completed on the front
35 page. The numbers are compared to the number of patients discharged at unit level in the
36 same period. Assessments of response rates are done and adjustments made if needed.

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39 Low response rates in a unit will lead to contact with the unit concerned to learn the reason

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8 why and actions to increase them. Returned questionnaires will be screened for
9 systematic errors.

11 *Study size*

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14 The study size is not derived statistically, as it consists of the total population of patients
15 discharged from the five Heart Centres in the project period. The five Heart Centres
16 diagnose and treat about 45,000 patients per year. These patients are diagnosed with
17 numerous diseases and conditions and the aim is to describe differences, not only among
18 the most common diagnoses but also the infrequent ones. Thus, all patients discharged
19 from national Heart Centres over one year are included in order to secure as high a level
20 of specificity as possible. Furthermore, by including a large number of participants, a
21 shorter follow-up time is needed. Besides the primary objectives, further ancillary and spin-
22 off analyses will be prepared. Clearly, power calculations cannot be performed
23 prospectively for all potential analyses based on data from the DenHeart study. Moreover,
24 adverse outcomes have very different incidence rates.

35 *Response rate*

36
37 The final response rate is calculated based on discharge data from the National Patient
38 Register. For calculating the actual number of eligible patients, the following are not
39 included: patients without a Danish civil registration number, patients living in Greenland
40 (no register follow-up possible), patients with two admissions within 24 hours, patients
41 deceased in hospital and outpatient visits. Patients admitted for less than 24 hours without
42 a procedure and readmitted with a procedure within one month are counted once.

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49 [Even though patients are encouraged to fill out the questionnaire within 3 days all](#)
50 [questionnaires completed within 4 weeks of discharge are included in the analyses.](#)
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8 Patients who have filled out more than one questionnaire during the project period due to
9 repeated hospitalizations will only be counted once (the first questionnaire returned) in the
10 final count of the response rate. The repeated measurements may be included in sub-
11 analyses.
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15 16 *Statistical methods*

17
18 Objective 1: For each diagnostic group, age (mean), sex distribution and patient reported
19 outcomes at hospital discharge distribution will be reported. Differences between groups
20 will be tested by use of ANOVA tests for continuous variables and chi-squared tests for
21 categorical variables. Multivariate logistic regression will be used to investigate the
22 relationship between diagnostic group and patient reported outcomes when controlling for
23 response date (number of days since hospital discharge), age, sex and other possible
24 confounders, and in-hospital predicting factors (e.g. procedure, duration of index hospital
25 admission, acute/elective admission, stay at intensive care unit, complications).
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34 Objective 2a: For each diagnostic group, the crude associations between patient reported
35 outcome measures at hospital discharge and all-cause and cardiac morbidity and all-
36 cause and cardiac mortality after one year, will be described and assessed using ANOVA
37 tests for continuous variables and chi-squared tests for categorical variables. In addition,
38 multivariate Cox proportional hazards regression models, with age as the time scale, will
39 be used to examine the associations between patient reported outcome measures at
40 baseline and all-cause morbidity and mortality and cardiac morbidity and mortality when
41 adjusting for response date, sex, co-morbidity and other potential confounding factors at
42 baseline.
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8 Objective 2b: For each diagnostic group, the crude associations between patient reported
9 outcome measures at hospital discharge and labour market affiliation (employment status,
10 sick leave, early retirement pension) after one year will be described and assessed using
11 the ANOVA tests for continuous variables and chi-squared tests for categorical variables.
12
13 Multivariate Cox proportional hazards regression models, with age as the time scale, will
14
15 also be carried out to investigate the associations between patient reported outcome
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17 measures at baseline and labour market affiliation when adjusting for potential
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19 confounding factors (e.g. response date, sex, co-morbidity).
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24 Objective 2c: For each diagnostic group, the crude associations between patient reported
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26 outcomes measures at hospital discharge and health care utilization (hospitalizations,
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28 contact with general practitioner, medical specialist, and physiotherapist) after one year,
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30 will be described and assessed using the ANOVA tests for continuous variables and chi-
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32 squared tests for categorical variables. Multivariate Cox proportional hazards regression
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34 models, with age as the time scale, will be used to analyse the association between
35
36 patient reported outcome measures at baseline and health care utilization when adjusting
37
38 for potential confounding variables (e.g. response date, sex, co-morbidity).
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40 *Weighting*

41 It is possible to link both respondents and non-respondents in the survey on an individual
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43 level to different administrative registers. Thus, non-response weights will be computed
44
45 based on register information (e.g. sex and age) in order to reduce non-response bias.
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47 Patients with a low probability of response will be given a higher weight in the analyses to
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49 represent the larger number of non-respondents with similar characteristics. Accordingly,
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51 patients more likely to respond will be given a lower weight.
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Spin-off projects

Several spin-off analyses will be prepared, ~~and conducted, e.g. a three year follow up analysis on the primary outcomes, the association between patient reported outcomes at discharge and cardiac events over time, patient reported outcomes and medication compliance and patient reported outcomes as a screening tool in clinical practice. A follow up survey after two to five years is being considered.~~

Ethics and dissemination

The study is conducted in accordance with the Declaration of Helsinki. According to Danish legislation, surveys should not be approved by an ethics committee system but only by the Danish Data Protection Agency, no. 2007-58-0015/30-0937. The DenHeart survey is approved by the Institutional Boards of the Heart Centres and registered at ClinicalTrials.gov (NCT01926145). [Patients sign informed consent stating that participation is voluntary and that further information from patient records may be obtained.](#)

The National Institute of Public Health stores data from the DenHeart survey. Access to data can only be provided to investigators after approval from the Publication Committee.

All study results will be published in ~~international~~[international](#) research journals and conference presentations.

Discussion

Study population

The five Heart Centres treat the most critically ill cardiac patients in Denmark. Approximately 47 regional or local hospitals treat cardiac patients medically and care for terminally ill cardiac patients. These patients are underrepresented in the DenHeart study.

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8 The patients in this study represent the patients with diagnoses where medical, invasive or
9 surgical treatment is possible, and patients with rare conditions such as heart transplant
10 and congenital heart disease. Furthermore, four of the five Heart Centres have a local
11 hospital function treating all cardiac diagnoses. One surgical unit did not wish to participate
12 in the study.
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18 Patients who are hospitalised several times in the project period will be asked to fill out the
19 questionnaire each time. Repeated measures will only be used in sub-analyses. For
20 reporting of primary outcomes, patients will only be counted once (the first questionnaire
21 returned).
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25 26 *Variables* 27

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29 The majority of the outcome measures included in the questionnaire is comprised of
30 validated and standardised instruments to assess patient reported outcomes, which
31 enhances the validity of the questionnaire. However, in the interpretation of the results, it
32 must be taken into account that patients with different cardiac conditions differ regarding
33 how much their health status has changed prior to admission to hospital, and that some of
34 the instruments have long recall.
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41 *Confounding factors* 42

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44 From previous national health surveys, we know that age and socioeconomic position play
45 a significant role for non-response. Also, regional differences of about 15 % in response
46 rates have been documented.^{29, 30} The patients treated at the Heart Centres are often aged
47 and severely ill, which may be reflected in the response rates. This will be accounted for
48 by reporting both actual responses as well as weighted data for the underrepresented
49 groups in the analyses. However, several different initiatives are being conducted by the
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8 centres to optimize response rates. Nurses are reminded to hand out the questionnaires at
9 local meetings, by posters in the ward and logo-pens, and response rates are continuously
10 shared with the ward nurses in order to secure motivation among the approximately 800
11 nurses involved in the distribution of questionnaires. Letters are sent to the local hospitals
12 that receive patients from the Heart Centres asking to remind the patients to fill out the
13 questionnaire at discharge to home. Some centres are mailing questionnaires to patients
14 after discharge when they are not handed out in hospital. [Mailed questionnaires are sent](#)
15 [with overnight post service allowing the questionnaire to be filled out within the 3 days.](#) As
16 this is a national multicentre study, regional differences in ways to enhance the response
17 rates may occur. All of these different strategies fall within the frame of the DenHeart study
18 and timeframe for responding.
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29 **Contributorship**

30 SKB conceived the study. SKB, AVC, MH, LT, BB, JS, AM, AL, AIC, KJ and OE initiated
31 the study design and implementation. KJ, AIC and OE provided statistical expertise in the
32 clinical trial design. All contributed to the refinement of the study protocol.
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39 **Funding**

40 This work was supported by the five participating Heart Centres in Denmark. Further
41 funding will be applied for from external funds.
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46 **Competing interest**

47 No competing interests have been declared by the authors.
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