1 **Title**: Protocol for Project Recovery: Cardiac Surgery - Leveraging Digital

2 Platform for Efficient Collection of Longitudinal Patient-Reported Outcome Data

3 Towards Improving Postoperative Recovery

4

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37

38 **Abstract** (287/300)

39 Introduction

40 Improving postoperative patient recovery after cardiac surgery is a priority,

41 but our current understanding of individual variations in recovery and factors

42 associated with poor recovery is limited. We are using a health-information

43 exchange platform to collect patient-reported outcome measures (PROMs) and

44 wearable device data to phenotype recovery patterns in the 30-day period after

45 cardiac surgery hospital discharge, to identify factors associated with these

46 phenotypes and to investigate phenotype associations with clinical outcomes.

47

48 Methods and analysis

49 We designed a prospective cohort study to enroll 200 patients undergoing

50 valve, coronary artery bypass graft, or aortic surgery at a tertiary center in the

51 U.S. We are enrolling patients postoperatively after the intensive care unit (ICU)

52 discharge, and delivering electronic surveys directly to patients every 3 days for

53 30 days after hospital discharge. We will conduct medical record reviews to

54 collect patient demographics, comorbidity, operative details and hospital course

55 using the Society of Thoracic Surgeons (STS) data definitions. We will use phone

56 interview and medical record review data for adjudication of survival, readmission,

57 and complications. We will apply group-based trajectory modeling to the time-

58 series PROM and device data to classify patients into distinct categories of

59 recovery trajectories. We will evaluate whether certain recovery pattern predicts

60 death or hospital readmissions, as well as whether clinical factors predict a

61   patient having poor recovery trajectories. We will evaluate whether early recovery

62   patterns predict the overall trajectory at the patient-level.

63

64   Ethics and dissemination

65   The Yale Institutional Review Board approved this study. Following the

66   description of the study procedure, we obtain written informed consent from all

67   study participants. The consent form states that all personal information, survey

68   response, and any medical records are confidential, will not be shared, and are

69   stored in an encrypted database.

70

71   **Strengths and limitations of this study**

72   • This study will assess the patient perspective on recovery after cardiac

73   surgery at a high frequency within the 30-day postoperative period with

74   surveys and activity monitoring via a health information platform and

75   wearable devices.

76   • Using longitudinal patient-reported outcomes measure (PROM) data, this

77   study will define recovery patterns and factors associated with different

78   recovery trajectories and guide the development interventions to improve

79   recovery and support expansion of the study to additional sites.

80   • The study is single center and the sample size is limited.

81   Text (4081 words)

82   **Background**

83   Improving postoperative patient recovery is a priority. Readmission rates

84   in the post-operative period are high. Moreover, in the United States, the

85   expansion of episode-based payments and performance measures is increasing

86   interest in the post-acute experience of patients[1,2]. However, we generally lack

87   systematically-collected information on the experience of patients in the post-

88   acute period, as few studies rigorously collecting information using established

89   patient-reported outcomes measures (PROMs). We have, for example, little

90   information about the variation of the trajectories of recovery and the factors most

91   strongly associated with better outcomes[3].

92   The assessment of the patient experience can provide important insights

93   into the process of recovery that is not evident through clinical outcomes or

94   intermittent clinical office visits. PROMs and wearable devices can provide

95   complementary information by providing measurements of how the patient's

96   experience and functional status change over time[4]. Current digital platforms

97   allow us to efficiently collect PROMs and wearable-generated data at high

98   frequencies and with little cost and burden. These automated data collection

99   approaches may minimize the bias introduced by clinician-directed patient

100   interviews[5]. Such a platform is highly suited to obtain repeated measures to

101   characterize a time-dependent process such as recovery[6].

102   Cardiac surgery is an ideal area for the study of recovery. Many patients

103   have good outcomes, but the limited existing evidence suggests a wide variation

104   in the post-operative experience of these patients[7]. However, these patients'

105   experience has been poorly studied, as most studies of recovery simply assess

106   deaths and complications.

107   Characterizing the recovery from the patient perspective is important for

108   many reasons. First, shared decision-making and informed consent should be

109   guided not only by the risk of mortality and complications but also by the recovery

110   experience. Understanding variations in recovery could enable the early

111   identification of people who are struggling and require additional attention.

112   Recovery data from the patient perspective may enable remote monitoring after

113   the procedure to selectively and preemptively intervene on those at high risk of

114   poor recovery to improve outcomes. Characterization of recovery can also be

115   used to identify patient, surgeon, procedural, and institutional factors that are

116   associated with different patterns. With this information we can identify modifiable

117   risk factors for poor recovery.

118   Thus, at this juncture, there are several notable gaps in knowledge. First,

119   although recovery occurs over time, most studies of recovery included a small

120   number of timepoints, and the recovery trajectory phenotypes remains poorly

121   defined[3]. Cohort-level average of recovery trajectories is a common way of

122   reporting[3] and can indicate how patients recover on average[7], but it obscures

123   individual variation such as rapid early recovery, gradual recovery, or initial

124   recovery followed by a decline. Second, we have limited understanding of how

125   recovery trajectories vary by patient factors, operation types, center or surgeon

126   characteristics, procedural processes, and complications, which limit

127   opportunities to identify high risk patients preemptively and intervene.

128   Accordingly, our overall objective is to characterize short-term trajectories

129   of patient recovery after cardiac surgery using PROMs and wearable data. We

130   are conducting a prospective study to characterize trajectories of postoperative

131   recovery in multiple domains after cardiac surgery. The specific aims of this study

132   are to: 1) leverage a digital data platform to collect PROM and wearable device

133   data to bring forth the variable individual recovery trajectories, 2) describe distinct

134   classes of recovery trajectories and clinical factors associated with the classes,

135   and 3) to evaluate whether early postoperative recovery trajectory predicts later

136   recovery trajectory. In addition, we will investigate optimal ways to manage

137   missing data specific to these time-series data This study is a step toward using

138   this approach to prospectively monitor and preemptively identify patients at risk of

139   poor recovery and facilitate intervention to reduce the risk of adverse events.

140

141   **Methods**

142   *Design Overview*

143   This is a prospective cohort study of patients who are undergoing valve,

144   CABG, or aortic surgery at a tertiary center in the U.S. We chose the operations

145   because they are the most common cardiac operations performed[8]. We are

146   enrolling patients postoperatively after ICU discharge in order to ensure clinical

147   stability, and we electronically delivering surveys directly to patients every 3 days

148   for 30 days after hospital discharge to study patient trajectories in multiple

149   domains characterizing recovery. The closing phone interview after 30 days,

150   electronic medical record review, and linkage to the Society of Thoracic

151   Surgeons database are used to confirm survival, readmission, and complications.

152   The closing interview asks about details of readmissions if they occurred,

153   patients' overall satisfaction with the study, and whether their experience was

154   well captured by the summary of their PROM data. We will apply group-based

155   trajectory modeling to the longitudinal PROM data to identify distinct categories of

156   recovery trajectories in a data-driven fashion. We also identify predictors of

157   protracted recovery trajectory and evaluate whether early recovery patterns (<10

158   days) predict the overall trajectory (30 days) at the patient-level. The Yale

159   Institutional Review Board approved this study.

160

161   *Patient Population*

162   This study began in January 2019 and is ongoing. The study is taking

163   place at Yale-New Haven Hospital, a tertiary center in the United States, where

164   over 1,100 cardiac surgeries are performed annually. Inclusion criteria are

165   patients of age 18 and older who are undergoing coronary artery bypass grafting

166   (CABG), valve replacement or repair, or aortic operations. Exclusion criteria are

167   those who undergo heart transplant, extracorporeal membrane oxygenation

168   (ECMO), adult congenital operations, or ventricular assist device implantation, as

169   these patient populations tend to have a longer course of intensive care unit stay[9],

170   precluding the timely enrollment necessary to capture immediate postoperative

171   recovery. We also excluded those who do not own a smartphone or a tablet or

172   those who do not speak or read English, because the digital platform for PROM

173   data collection relies on patients responding to surveys displayed on web

174   browser via email or text, and the surveys were written in English language. We

175   do not allow proxy for survey response and consequently excluded patients who

176   were not able to respond by themselves as determined by the research assistant.

177

178   *Recruitment*

179   Recruitment takes place postoperatively after the patient has left the

180   intensive care unit (ICU) for the step-down or floor unit (Figure 1). We chose to

181   enroll patients postoperatively, as opposed to preoperatively, because

182   postoperative enrollment allows for enrollment of patients who undergo surgery

183   under non-elective settings. Recruitment after transfer from the ICU setting

184   ensures clinical stability. A research assistant (RA) visits the patient and after

185   confirming the patient is eligible to participate and following the description of the

186   study procedure, obtains written informed consent (Supplementary Material S1)

187   from all study participants. The informed consent form states that all personal

188   information, survey response, and any medical records are confidential, will not

189   be shared, and will be stored in an encrypted database.

190   We iteratively refined the enrollment process to minimize the onboarding

191   time, which includes obtaining informed consent and signup process directed by

192   the RA on a tablet device to enter patient name and email address or phone

193   number and takes approximately 10-15 minutes.

194

195   *PROM instrument and administration*

196   We use 24-item quality of recovery (QoR-24) to characterize patients'

197   postoperative recovery in various domains. The questionnaire consists of 24

198   items that were developed and validated in inpatient and outpatient surgical

199   populations[10-13]. The instrument was previously adapted into a mobile format and

200   was successfully used to administer the survey daily for 14 days[11, 12]. We added

201   3 items to QoR-24 to capture the self-reported time patients went to sleep, the

202   time they awakened, and their global perception of how much they have

203   'recovered' in a 0-100% scale. The resulting 27-item questionnaire takes 2-4

204   minutes to complete, making its frequent administration feasible (Supplementary

205   Material S2). Among the published studies in cardiac surgery, this study will have

206   the highest number of PROM data points collected in the first postoperative

207   month[3].

208

209   *Digital data platform*

210   We are delivering surveys on the day of enrollment and every 3 days for

211   30 days. This method provides detailed longitudinal data across multiple domains

212   of recovery (Figure 2). To facilitate data organization and scheduled survey

213   delivery, we use Hugo (Me2Health, LLC, Guilford CT, USA) a patient-centered

214   health data sharing platform, which has a customizable survey delivery function

215   and reminder feature to facilitate data collection. Hugo platform allows for

216   automated delivery of surveys without researchers having to directly contact

217   patients, which facilitates high-frequency data collection. Additionally, it imports

11

218   data from connected wearable devices to facilitate centralization of patient health

219   data. The patients retain access to their own data in a cloud-based account.

220

221   *Identifying common reasons for low response rate*

222   Recognizing that the survey response will be incomplete for some

223   participants, we have conducted a phone interview with the first 22 patients to

224   learn reasons for low responses and identify strategies to minimize the barriers

225   toward survey response for subsequent participants. In the first 22 patients, we

226   identified 5 with response rate of <50% and conducted recorded phone

227   interviews. Our interview guide (Supplementary Material S3) contained questions

228   to elucidate technical barriers, differential preferences for engagement, and or

229   any other issues precluding survey completion. We also asked whether the

230   length of the questionnaire or types of questions asked made it difficult to

231   complete the survey. Two members of the research team (CB and MM)

232   evaluated the interview recordings to identify common reasons for low response

233   rate. This suggested the potential importance of reminder to maintain patient

234   engagement. We modified the protocol to contact all participants approximately

235   10 days after enrollment.

236

237

238   *Additional clinical data and adjudication of hospitalization and survival*

239   Additionally, we are using the Society of Thoracic Surgeons (STS) Adult

240   Cardiac Surgery Database data specifications to retrospectively collect clinically

241   relevant data in this patient population. Pre-specified candidate predictors in this

242   database will be used to identify clinical predictors of recovery trajectories (Table

243   1). The STS database contains patient demographics, comorbidities, presenting

244   clinical status, operative details, and postoperative mortality and morbidity up to

245   30 days after the time of operation[14]. These data are routinely collected at Yale

246   New Haven Hospital.

247   We will determine mortality and hospital readmissions by several

248   approaches: review of hospital records, review of cardiac surgery clinic notes,

249   and conducting closing phone interviews with the patient or contact person

250   previously identified.

251

252   *Patient Involvement*

253   Prior to launching the study, we interviewed 5 patients both in pre and

254   postoperative settings to evaluate whether the frequency of survey delivery and

255   PROM instrument were likely to adequately capture their experience of recovery.

256   All patients agreed that the frequency of questionnaire administration and the

257   length of the PROM instrument were reasonable and provided face validity that

258   the questionnaire captured aspects of recovery that were important to the

259   patients. Additionally, this article is authored with a patient (LG) who participated

260   in the study to reflect his perspective on the study design and experience in

261   responding to the surveys.

262

263   *Sample size*

264   The study sample target is 200 patients. Adequate sample size for studies

265   using group-based trajectory modeling depends on the dataset's

266   representativeness of the population of interest[15]. Therefore, the concept of

267   statistical power traditionally used for sample size calculation does not apply to

268   latent class analyses. We may generate a larger simulation dataset from the

269   measured patient trajectory data to perform a split-sample testing, evaluating

270   whether trajectories generated from the derivation sample would allow for

271   satisfactory categorization of the testing dataset. Additionally, the study setting is

272   scalable to increase the sample size by increasing the enrollment period, should

273   a larger sample size become necessary.

274

275   *Analytical approach – group-based trajectory modeling*

276   The resulting dataset is a complex time-series data, with each patient

277   having 10 data points (one every three days) at different postoperative times for

278   each item. A practical approach to dimension reduction is group-based trajectory

279   modeling, which is a type of latent class analysis that groups similar patient

280   trajectories according to a number of features derived from the time-series data[16,

281   17]. This approach allows for dimension reduction of the complex time-series data

282   into several distinct classes of recovery trajectories. These trajectories can be

283   labeled according to the observed clinical phenotype of trajectories, for example

284   'fast recovery,' 'average recovery,' or 'protracted recovery,'. This data-driven

285   categorization enables additional regression modeling to identify predictors of

286   patients belonging to a certain class of recovery path.

287   The dataset will be classified into distinct categories of trajectories at

288   domain level, using group-based trajectory modeling[16, 17]. Traj package on R[18] or

289   Proc Traj package on SAS[15], performs trajectory modeling by first extracting 24

290   features of patient-level trajectory, selecting a subset of features that describes

291   the overall trajectory, and identifying optimal number of classes to group the

292   trajectories based on the longitudinal k-means method. The 24 features include

293   range, mean change per unit time, and slope of the linear model (Table 2), which

294   have been demonstrated to discriminate between stable-unstable, increasing-

295   decreasing, linear-nonlinear, and monotonic-nonmonotonic patterns of

296   trajectories[18]. K-means method partitions the time-series data into k groups such

297   that the mean squared error distance of each data point from the assigned

298   cluster is minimized[19]. The optimal number of clusters is determined by the

299   minimization of Bayesian information criterion, which signifies the balance

300   between model's complexity and the ability to describe the dataset. This process

301   yields distinct classes of patient trajectories in a data-driven fashion. Trajectories

302   will be identified separately for the 5 domains and 1 global recovery measure.

303

304   *Analytical approach – missing data*

305   Because missing data are inevitable in longitudinal PROMs, there is a

306   need employ an appropriate handling of missing data. Multiple imputation prior to

307   latent class analysis may yield a less biased estimate of the resulting trajectories.

308   An alternative approach used in group-based trajectory models assumes the data

309   are missing at random (MAR) and generates the maximum likelihood of the

310   model parameters[20]. MAR is valid when the response attrition is independent of

311   the group membership. However, patient attrition is oftentimes dependent on

312   clinical characteristics and likely related to the class of trajectory itself. An

313   extension of the model allows for modeling of attrition across trajectory groups[21],

314   permitting dropout probability to vary as a function of covariates or observed

315   outcomes prior to dropout and yields a more robust estimate of the probability of

316   group membership. As such, we will perform sensitivity analysis to compare the

317   trajectories generated via raw data vs. data preprocessed with multiple

318   imputation vs. trajectories generated via trajectory model accounting for response

319   attrition.

320

321   **Results**

322   Between January and May 2019, we have enrolled 22 patients who

323   completed the 30-day follow-up. In this cohort, median age was 58.5 years

324   (interquartile range 53.5-67.0) and 7 (32%) were women. There were 9 (41%)

325   mitral valve repair cases and 6 isolated or concomitant CABG (27%).

326

327   *Barriers to completing surveys*

328   Of the 22 patients enrolled, 3 (14%) did not complete any surveys, 19

329   (86%) completed at least 3 surveys, and 17 patients (77%) completed at least 6

330   of 11 delivered surveys (>50% of delivered surveys). Of the 5 patients who

331   completed less than half of the surveys, we successfully contacted 4, and 1 could

332   not be reached after 5 attempts. All 4 reported that the major barriers precluding

333   survey completion were their clinical conditions: 2 described readmissions as an

334   overwhelming event that made them feel continuing survey participation

335   challenging, and 2 described not feeling well in general, which precluded

336   participation. All 4 patients noted that text or email reminders might have been

337   helpful to sustain participation. Based on these responses, we modified the

338   protocol to contact all participants approximately 10 days after enrollment to

339   improve engagement and resolve any patient-specific issues in completing the

340   surveys.

341

342   *Clinical outcomes*

343   There were no deaths during follow-up. Two (9%) patients experienced at

344   least 1 hospital readmission. Figure 2 depicts the breadth in recovery trajectories

345   in pain, sleep, ability to take care of own hygiene, and perception of overall

346   recovery in five patients with complete response.

347

348   *Patient perspective*

349   An author (LG) participated in this study as he underwent cardiac surgery.

350   He noted that the length and frequency of the questionnaire was reasonable and

351   helped him to be more aware of the recovery process because responding to the

352   questions facilitated introspection on his progress across different domains. He

353   recommended that the study platform feedback the data to study participants,

354   such as a visual summary of the trajectory or response for patients to better

355   gauge their progress. Additionally, he noted that responses may differ across the

356   time of the day, as he was able to better function physically in the afternoon

357   compared with in the morning. Finally, he suggested the potential value of

358   reviewing the questionnaire during preoperative counseling to highlight important

359   aspects of recovery to provide better patient and family expectations.

360   Investigators plan on providing a brochure to the clinic that contains this

361   information.

362

363   **Discussion**

364   This study will provide time-series data on short-term recovery after

365   cardiac surgery using PROM instruments complemented by clinical records

366   obtained via the STS database and electronic health records. This study will

367   provide one of the highest density of postoperative PROM data in existing

368   cardiac surgery literature[3], and it will characterize the variability in individual

369   recovery processes with a high temporal resolution. This study will be important

370   in closing knowledge gaps around patient-level variations in trajectories because

371   prior studies have mostly focused on changes in PROM scores at a limited

372   number of time points[3] or reporting group-level aggregate of longitudinal recovery

373   data[7, 22]. Because recovery is an individual, variable, and time-dependent

374   process, we designed our data collection and analytical approach to capture such

375   features important to recovery.

376   This study has the potential to make a variety of contributions toward

377   improving post-acute phase of care. First, we will be able to develop a

378   preliminary nomogram of postoperative recovery for each domain and overall

379   perception of recovery, which would be instrumental for patients and clinicians to

380   gauge the breadth of possible recovery trajectories to facilitate informed shared

381   decision-making. Second, identifying predictors of accelerated or protracted

382   recovery, as classified by group-based trajectory model, may allow for

383   individualized prediction of the postoperative recovery course to better inform the

384   patients and family members. Third, early detection of recovery signals related to

385   adverse events, such as mortality and readmission, may eventually facilitate

386   preemptive intervention and focused monitoring of patients at an elevated risk for

387   such events. Our design of the longitudinal PROM data collection allows for

388   incremental update of such prediction as patients progress through the phase of

389   recovery.

390   There are many challenges to the successful acquisition of patient

391   measurements during recovery: efficient administration of PROMs in a way that

392   does not require prohibitive amount of resources, minimizing selection bias

393   originating from barriers to survey completion, handling of missing data that

394   inevitably occurs in PROMs, and summarizing the complex data in a way that is

395   interpretable to surgeons and patients[23]. Additionally, the use of wearables and

396   device data require active patient participation in periodically charging the device,

397   wearing them correctly, and reliably syncing the device to the server for data

398   uploads. Moreover, there is a need to provide value to the patients for providing

399   their recovery profile, such as giving them access to their health data in a

400   meaningful way.

401   The resulting data collection, analytical, and output platforms have the

402   potential of being implemented in the clinical setting where an integration of

403   incrementally increasing PROM and clinical data provides the near-real time

404   estimate of individual patient risk of adverse post-operative events. Such a model

405   may allow for triggering of preemptive clinical intervention. An output may

406   assimilate a form of clinical dashboard within the electronic health record system,

407   which may be monitored at a centralized location where a trained clinician

408   reviews high-risk cases filtered by the algorithm to further evaluate whether the

409   patient condition warrants an intervention. Together, this workflow has a

410   tremendous potential to improve post-acute phase of care following surgery.

411

412   *Lessons Learned from the initial experience*

413   Through this first group of enrolled patients, we learned that most of the

414   patients approached were willing to participate and consented to the study. By

415   streamlining the enrollment process, the enrollment time shortened from over 1

416   hour on the first patient to approximately 10-15 minutes for the current enrollment.

417   The overall response rate is acceptable, with 77% of the participants completing

418   more than half of the delivered surveys independently without any intervention by

419   researchers. Challenging recovery course, including readmissions may have

420   interfered with patient engagement. While this would have resulted in an

421   underrepresentation of those with protracted recovery or with complications, our

422   preliminary data show we were able to capture variations in the trajectories of

423   recovery.

424   To sustain patient engagement through challenging recovery course, we

425   implemented a protocol for a research assistant to call the patient around 10

426   days after enrollment to troubleshoot any issues and reemphasize the

427   importance of their participation. We believe that once the survey becomes part

428   of clinical workflow with clinicians monitoring and responding to the PROM

429   response, patient response rate would improve further.

430   We modified the enrollment protocol to reduce the enrollment time,

431   because to some patients, the complexity and prolonged time spent for

432   enrollment discouraged signups. Initial protocol for enrollment required patients

433   to download an app and register. This resulted in a wide range of time spent for

434   enrollment between 15 minutes and 90 minutes, with longer enrollment owing to

435   technical challenges. These challenges include patients forgetting the password

436   for app download, having to reset the password, and not having immediate email

437   access to check account confirmation emails. Because our cardiac surgery

438   patient population tended to be older, these technical challenges may have been

439   pronounced. By not including the app download and allowing for the research

440   assistant to enroll the patient via an online form with their permission, the

441   enrollment time shortened significantly to 10-15 minutes.

442   Examining the initial individual data on recovery, there were wide

443   variations in the trajectories of recovery even among only 5 patients. The

444   variation suggests that the instrument we used was sensitive to capturing such

445   differences. We also noted variations in improvement over time across different

446   domains of recovery, where overall perception of recovery seemed to have a

447   steady improvement pattern, while pain varied between consecutive

448   measurements in some patients.

449

450   *Limitations*

451   There are several limitations to this study. First, the single-center tertiary

452   care setting limits the sample size and applicability of the findings to patients

453   cared for in different settings. A multi-center study following the current study

454   would address this limitation and evaluate whether the findings at our center are

455   comparable to findings in other centers. Additionally, group-based trajectory

456   modeling will classify patients into distinct trajectories based on similar recovery

457   patterns, and this analytical approach may allow for generalization of the

458   variations in the trajectories as long as our sample represents the breadth of the

459   possible variation in recovery.

460   Another limitation is the exclusion of patients who cannot participate for

461   various reasons. The use of digital platform is advantageous in reducing the

462   resource intensity for data collection, but leads to exclusion of patients who do

463   not own mobile devices, which likely affects older patients disproportionately. As

464   the number of adults using mobile devices is increasing[24], we believe this will

465   become less of a limitation over time. Initiating this study now despite this

466   limitation is important to establish a platform that may become the standard of

467   postoperative care when the vast majority of patient population own digital

468   devices in a predictably near future. Those who cannot participate due to lack of

469   interest represent an important population that may be distinct in characteristics

470   and risk profiles. We plan on minimizing the non-participation for the lack of

471   interest by intermittent phone check-ins to sustain interests and identify barriers

472   to inform strategies to increase engagement. In following studies, we may

473   consider other forms of incentives to participate, if this population is indeed

474   distinct and large in proportion. Additionally, when the PROM data are integrated

475   into routine clinical care, patient engagement will likely increase substantially

476   because they will be more inspired to share these data if they are used by their

477   clinicians.

478   Finally, postoperative enrollment and retrospective assessment of

479   preoperative health status, as opposed to preoperative enrollment, may introduce

480   recall bias. We decided on postoperative enrollment, because preoperative

481   enrollment precluded standardized enrollment of patients operated on under non-

482   elective settings. Given the retrospective assessment of baseline health status

483   takes place on the first postoperative survey, we believe the recall bias is

484   minimized owing to the temporal proximity.

485

486   **Conclusion**

487   This study will generate highly granular, longitudinal PROM data to

488   characterize individual trajectories of patient recovery after cardiac surgery.

489   Digital data sharing platforms promise to minimize the patient and researcher

490   burden in administering and completing PROMs, allowing for characterization of

491   granular progression of patients' state of health over time in the postoperative

492   period. Implementation of such study is complex but feasible, and it will serve as

493   an important platform to facilitate clinical use of PROM data to improve the

494   overall patient recovery.

495

496   **Authors' contributions**

497   MM, HMK, SD, and AG developed the study and research question. MM and
498   HMK developed analytical strategy with inputs from BJM, GCL, and YZ. SIC and
499   ES guided refining the enrollment strategy and interpretation of the phone
500   interview responses. LAG provided patient perspective on the study protocol and
501   interpretation of the preliminary results. All authors developed and approved the
502   final manuscript before submission.
503

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510   **Competing interest statement**

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515   and 1R21EB028486-01 from the National Institute for Biomedical Imaging and
516   Bioengineering (NIBIB) for work employing machine learning on health data. Dr.
517   Mortazavi reported having a patent US10201746B1 approved for "Near-realistic
518   sports motion analysis and activity monitoring" and a patent to
519   US20180315507A1 is pending.
520   Dr. Krumholz works under contract with the Centers for Medicare & Medicaid
521   Services to support quality measurement programs; was a recipient of a research
522   grant, through Yale, from Medtronic and the U.S. Food and Drug Administration to
523   develop methods for post-market surveillance of medical devices; was a recipient of
524   a research grant with Medtronic and is the recipient of a research grant from Johnson
525   & Johnson, through Yale University, to support clinical trial data sharing; was a
526   recipient of a research agreement, through Yale University, from the Shenzhen
527   Center for Health Information for work to advance intelligent disease prevention and
528   health promotion; collaborates with the National Center for Cardiovascular Diseases
529   in Beijing; receives payment from the Arnold & Porter Law Firm for work related to
530   the Sanofi clopidogrel litigation, from the Ben C. Martin Law Firm for work related to
531   the Cook Celect IVC filter litigation, and from the Siegfried and Jensen Law Firm for

532 work related to Vioxx litigation; chairs a Cardiac Scientific Advisory Board for
533 UnitedHealth; was a participant/participant representative of the IBM Watson Health
534 Life Sciences Board; is a member of the Advisory Board for Element Science, the
535 Advisory Board for Facebook, and the Physician Advisory Board for Aetna; and is the
536 co-founder of HugoHealth, a personal health information platform, and co-founder of
537 Refactor Health, an enterprise healthcare AI-augmented data management company.
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625 **Tables and Figures**

626 Table 1: Candidate predictors of recovery trajectory

Demographic	Comorbidity	Operative factors	Postoperative factors
Age	Diabetes	Cardiopulmonary bypass time	Length of ICU stay
Sex	Prior stroke	Cross clamp time	Length of hospital stay
Race	Congestive heart failure	Operation type	Surgical site infection
Insurance status	Chronic kidney disease	Non-elective status	Prolonged ventilation
BMI	Dialysis	Transfusion requirement	Transfusion requirement
	Prior MI	Minimally invasive approach	Stroke
	Prior cardiac surgery		Reoperation for any reasons
	Ejection fraction		Death
	Arrhythmias		Readmission
	Prior PCI		Pneumonia
	Cardiogenic shock		
	Hypertension		
	Dyslipidemia		
	Smoking status		
	Chronic lung disease		
	Endocarditis		
	Pneumonia		
	Peripheral artery disease		
	Immunocompromised		
	Mechanical circulatory support use		
	Valvular disease severity		

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629   Table 2: 24 features of trajectory used in group-based trajectory model

| N	Features
1	Range
2	Mean-over-time
3	Standard deviation (SD)
4	Coefficient of variation (CV)
5	Change
6	Mean change per unit time
7	Change relative to the first score
8	Change relative to the mean over time
9	Slope of the linear model
10	Proportion of variance explained by the linear model
11	Maximum of the first differences
12	SD of the first differences
13	SD of the first differences per time unit
14	Mean of the absolute first differences
15	Maximum of the absolute first differences
16	Ratio of the maximum absolute difference to the mean-over-time
17	Ratio of the maximum absolute first difference to the slope
18	Ratio of the SD of the first differences to the slope
19	Mean of the second differences
20	Mean of the absolute second differences
21	Maximum of the absolute second differences
22	Ration of the maximum absolute second difference to the mean-over-time
23	Ratio of the maximum absolute second difference to mean absolute first difference
24	Ratio of the mean absolute second difference to the mean absolute first difference

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631   Figure 1: Timing of patient enrollment and PROM administration

632
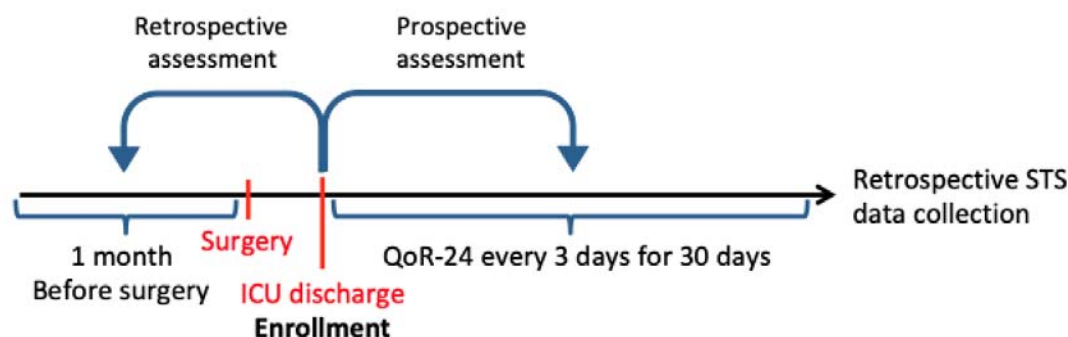
633   The figure shows the timing of patient enrollment and PROM administration over

634   the clinical course. Baseline function is assessed by retrospectively asking the

635   patient about their state of health during 1 month prior to the operation. 24-item

636   Quality of Recovery questionnaire is administered every 3 days for 30 days

637   following discharge from the intensive care unit.

638

639   Figure 2: Sample trajectories of recovery in 5 patients

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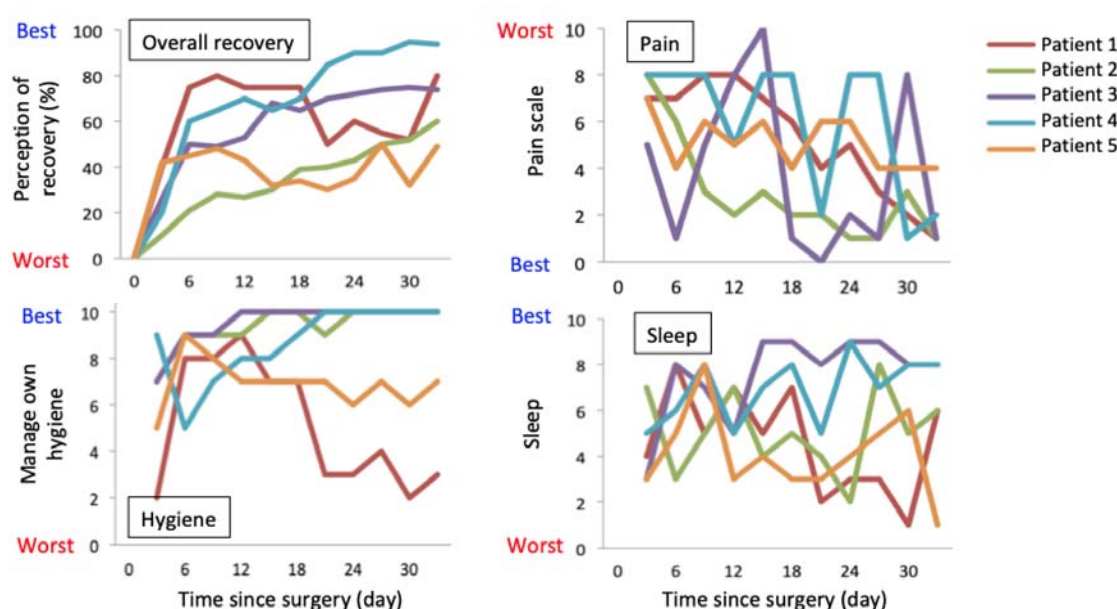
641   The figures display trajectories of recovery in different domains in 5 patients.

642   Each color corresponds to the same patient. Overall recovery is the patient's

643   perception of overall recovery in 0 to 100% scale. Pain in surgical site is reported

644   in 0 to 10 point scale, with 10 representing the worst pain. Being able to take care

645   of own hygiene is reported in 0 to 10 point scale, with 10 representing complete

646   independence in managing own hygiene. Patient's perception of sleep quality is

647   reported in 0 to 10 point scale, with 10 being the best sleep.