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Aortic stenosis post-COVID-19: A mathematical model on waiting lists and mortality

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2
3 **45 Abstract**
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5 46
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7 **47 Objectives**

8 48 To provide estimates for how different treatment pathways for the management of severe
9 49 aortic stenosis (AS) may affect NHS England waiting list duration and associated mortality.
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11

12 50
13 **51 Design**

14 52 We constructed a mathematical model of the excess waiting list and found the closed-form
15 53 analytic solution to that model. From published data, we calculated estimates for how the
16 54 following strategies may affect the time to clear the backlog of patients waiting for treatment
17 55 and the associated waiting list mortality.
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23 56
24 **57 Setting**

25 58 The NHS in England.
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28 59
29 **60 Participants**

30 61 Estimated aortic stenosis patients in England.
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33 62
34 **63 Interventions**

35 64 1) increasing the capacity for the treatment of severe AS, 2) converting proportions of cases
36 65 from surgery to transcatheter aortic valve implantation, and 3) a combination of these two.
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40 66
41 **67 Results**

42 68 In a capacitated system, clearing the backlog by returning to pre-COVID-19 capacity is not
43 69 possible. A conversion rate of 50% would clear the backlog within 666 (95% CI, 533–848)
44 70 days with 1419 (95% CI, 597–2189) deaths whilst waiting during this time. A 20% capacity
45 71 increase would require 535 (95% CI, 434–666) days, with an associated mortality of 1172
46 72 (95% CI, 466–1859). A combination of converting 40% cases and increasing capacity by
47 73 20% would clear the backlog within a year (343 (95% CI, 281–410) days) with 784 (95% CI,
48 74 292–1324) deaths whilst awaiting treatment.
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76 **Conclusion**

77 A strategy change to the management of severe AS is required to reduce the NHS backlog
78 and waiting list deaths during the post-COVID-19 ‘recovery’ period. However, plausible
79 adaptations will still incur a substantial wait and many hundreds dying without treatment.

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3 80 **What is already known on this subject?**
4

5 81 It has been estimated that almost 5000 patients were left untreated for severe aortic stenosis
6 82 in England due to indirect effects of the COVID-19 pandemic up to November 2020.

7
8 83 However, to our knowledge, there has been no published literature examining how to manage
9 84 the extra backlog this will cause on the waiting list for treatment.
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13 85
14 86 **What might this study add?**

15 87 In this study, we found that without significant intervention, the waiting list of patients
16 88 seeking treatment for severe aortic stenosis will not return to pre-pandemic levels for several
17 89 years, resulting in thousands of preventable deaths. This study presents a model for
18 90 evaluating the relative efficacy of different interventions, including adding extra treatment
19 91 capacity and converting a proportion of cases to TAVI from surgery, to clear the backlog and
20 92 minimise mortality of patients waiting for treatment.
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27 93
28 94 **Strengths and limitations of this study**

- 29 95
- 30 96 • This model's greatest strength is that it provides a good basis to begin to solve a time-
31 97 critical problem when data gathering is likely to result in a greater number of deaths.
 - 32 98 • The discussion about how treating some SAVR patients with TAVI instead is a useful
33 99 tool that examines how giving some patients what might be seen by some as sub-
34 100 optimal treatment, results in better overall outcomes for the target population.
 - 35 101 • The assumption that the entire NHS can be modelled as a single entity with a single
36 102 waiting list is a limitation of this study.
 - 37 103 • We also recognise that the waiting numbers we use in our study are likely to be
38 104 flawed as we do not know how many AS patients have died due to catching COVID-
39 105 19.
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106 Introduction

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108 The COVID-19 pandemic has led to the reorganisation of healthcare services to limit the
109 transmission of the virus and deal with the sequelae of infection. This reorganisation had a
110 detrimental effect on cardiovascular services, with reductions in hospitalisations for acute
111 cardiovascular events and the deferral of all but the most urgent interventional procedures
112 and operations.[1, 2]

113

114 Aortic stenosis (AS) is the most common form of valvular heart disease. Once stenosis is
115 severe, symptoms follow and the prognosis is poor, with 50% mortality within two years of
116 symptom onset.[3] Thus, timely treatment is of paramount importance. Surgical aortic valve
117 replacement (SAVR) has historically been the default treatment strategy. However,
118 transcatheter aortic valve implantation (TAVI) has recently emerged as an effective and
119 increasingly utilised option across operative risk strata.[4-8]

120

121 There was a large decline in TAVI and SAVR procedural activity to treat severe AS during
122 the COVID-19 pandemic.[9] Between the period March to November 2020, it is estimated
123 that the decrease in activity accounted for 4989 (95% CI. 4020–5959) patients in England
124 with severe AS left untreated by TAVI or SAVR.[9] As we move into an era of ‘living with’
125 COVID-19, plans must urgently be put in place to best manage the additional waiting list
126 burden for treatment of severe AS.[10]

127

128 In this study, we used mathematical methods to examine the extent to which additional
129 capacity to provide treatment of severe AS should be created to clear the backlog and
130 minimise deaths of people on the waiting list.

131

132

133 Methods

134

135 Study population and assumptions

136 Data from the UK TAVR registry and NICOR (National Institute for Cardiovascular
137 Outcomes Research) National Adult Cardiac Surgery Audit (NACSA) between 2017 and
138 2020 have previously been extracted to estimate an excess waiting list size (W_0) of 4989

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2
3 139 (95% CI, 4020–5959) patients with severe AS left untreated as of November 2020.[9] In the
4
5 140 absence of contemporaneous data on waiting lists and SAVR and TAVI activity, we have
6
7 141 taken this number as the excess backlog on which to model solutions. The incidence of AS
8
9 142 has not increased over recent years.[11] Therefore, we assumed that the system was in a
10
11 143 steady state before the COVID-19 pandemic and without loss of generality defined the
12
13 144 steady-state waiting list to be zero. Additionally, we assumed that the normal rate of flow (f)
14
15 145 of new patients into the waiting list for treatment of severe AS would be maintained upon the
16
17 146 commencement of additional operations. Thus, the extra capacity that we model is to clear
18
19 147 the excess post-COVID-19 backlog.

148

20
21 149 We took one-year mortality (μ) after the onset of symptoms in severe AS to be 36% (95% CI,
22
23 150 12% – 60%).[12] More recent studies have estimated the one-year mortality to be 51%[5] and
24
25 151 55%, but these included cohorts that were considered inappropriate for SAVR, thus, we
26
27 152 considered these estimates unrepresentative of an unselected population with severe AS.[13]
28
29 153 The routine capacity for treatment of severe AS was taken from the pre-pandemic period. In
30
31 154 2018/19, the NHS in England performed 7830 SAVR ($r_S^0 = 7830$) and 5197 TAVI (r_T^0
32
33 155 $= 5197$) procedures, for a total throughput of about 13,000 per year.[14]

156

157 Modelling

34
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36 158 Patients on the waiting list for treatment of severe AS were represented as a dynamical
37
38 159 system (figure 1).

160

40
41 161 To this model, we introduce capacity in surplus to the 2018/19 performance and call this
42
43 162 capacity T_e (further details are provided in supplementary material). We assume that the
44
45 163 typical caseload for which the NHS in England can deal with continues; therefore, the
46
47 164 backlog is only reduced by treating patients with this extra capacity or by patient mortality
48
49 165 before receiving treatment. We also consider patients in the backlog and patients new to the
50
51 166 waiting list indistinguishable. Thus, the waiting list size represents the excess number of
52
53 167 people seeking treatment who are unable to be treated immediately at any one time. We also
54
55 168 assume that other paths out of the waiting list (i.e. patients seeking private treatment) would
56
57 169 be so small in comparison to the uncertainty estimates as to be negligible on the results of our
58
59 170 analysis.

171

1
2
3 172 These assumptions then come together to give an estimated time (see supplementary material
4
5 173 for derivation) to clear the waiting list (t_C)

$$t_C = \frac{\ln\left(1 + \frac{W_0\mu}{T_e}\right)}{\mu} \quad (1)$$

6
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9 174
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11 175 and associated mortality ($m(t_C)$)

$$m(t_C) = W_0 - T_e t_C. \quad (2)$$

12
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15 177
16
17 178 Using equations (1) and (2), we can predict the length of time and associated mortality for
18
19 179 different percentage increases in capacity. We assume any capacity increase to be constant
20
21 180 throughout the entire modelled period. For example, if we increased daily capacity by 5% this
22
23 181 would result in, $T_e = \frac{r_s^0 + r_f^0}{365} * 5\% = 1.785$ extra procedures per day, across the whole of the
24
25 182 NHS in England. We generated 10,000 random values for the one-year mortality rate and
26
27 183 initial waiting list length. We assumed that the uncertainty in both variables was normally
28
29 184 distributed.

30 185

31 186 Interventions and outcomes

32
33 187 We investigated three types of capacity increase: 1) a general increase in the capacity to
34
35 188 provide SAVR and TAVI, which could be facilitated by an increased number of procedures
36
37 189 per list, additional lists, and prioritisation of care pathways and staffing to treat severe AS; 2)
38
39 190 extra capacity created by treating some patients with TAVI who would routinely have SAVR;
40
41 191 3) a combination of a general increase in capacity and the conversion of a proportion of cases
42
43 192 from SAVR to TAVI. During the COVID-19 pandemic, TAVI was performed in patients
44
45 193 usually referred for surgery, with no difference in short term outcomes compared to historical
46
47 194 reference groups.[15, 16]

48 195

49 196 We assumed that the duration of a SAVR would routinely be between 2-4 hours and a TAVI
50
51 197 between 1-2 hours.[17, 18] As such, we assumed within the time for two SAVR operations,
52
53 198 three TAVI could be performed instead.[19] Several clinical factors may favour SAVR over
54
55 199 TAVI (including concomitant severe coronary artery disease, low STS score, bicuspid aortic
56
57 200 valve etc.); therefore, we assumed that, in the short term, no more than 50% of patients could
58
59 201 be converted from SAVR to TAVI.[20] We also assumed that no more than 50% extra

202 capacity could be created by other means (e.g. extra lists, more procedures per list). We
203 simulated two principal outcomes based on the creation of additional capacity (T_e):

- 204 1. Time to clear the backlog (reduce to zero),
- 205 2. Mortality of patients within the excess backlog whilst on the waiting list to be treated.

206
207 We completed additional sensitivity analyses for how the conversion of SAVR to TAVI
208 would affect the principal outcomes, including if three SAVR operations could be routinely
209 completed in a day and four to five TAVI procedures per day (presuming increasing uptake
210 of a minimalist TAVI approach without general anaesthesia enabling more rapid procedure
211 time).[21]

212 213 Patient and public involvement

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

215 216 217 Results

218
219 In the pre-COVID-19 period, the routine capacity for treatment of severe AS was set to cover
220 the normal incident rate. That is, clearing the backlog by returning to pre-COVID-19 capacity
221 is not possible. As a result, mortality on the excess waiting list at one year are estimated to be
222 more than 1500, putting a strong emphasis on the need for change.

223 224 Total additional capacity

225 Figure 2 provides simulations of the time to clear the excess backlog and the mortality of
226 patients on the waiting list based on the amount of total additional capacity, T_e . With a 5%
227 increase in the capacity to provide treatment of severe AS, we estimate it would take 1384
228 (95% CI, 1025–1994) days to clear the excess backlog, with 2526 (95% CI, 1355–3516)
229 deaths. A 20% increase in total capacity would provide a sharp benefit in clearing the excess
230 backlog within 536 (95% CI, 434–666) days, with an estimate of 1173 (95% CI, 466–1859)
231 deaths. As total capacity increases further, there is a diminishing return in clearing the
232 backlog and avoiding associated mortality; the greater the capacity increase, the fewer lives
233 are saved for every extra increase in capacity. Even if it was possible to double capacity, it

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2
3 234 would take 131 (95% CI, 126–137) days to clear the backlog and there would be 313 (95%
4 235 CI, 118–494) deaths on the waiting list.

6 236

8 237 The effect of converting SAVR to TAVI

10 238 The conversion of a proportion of cases from surgery to TAVI provides a modest
11 239 improvement in estimates of time to clear the backlog and mortality on the waiting list. With
12 240 the conversion of 30% of SAVR operations to TAVI procedures, without the creation of
13 241 additional capacity in the system, we estimate it would take 975 (95% CI, 741–1284) days to
14 242 clear the backlog and result in 1914 (95% CI, 923–2809) deaths on the waiting list. Even with
15 243 the conversion of 50% of SAVR operations to TAVI procedures, we estimate the backlog
16 244 would be cleared within 666 (95% CI, 533–848) days with 1419 (95% CI, 597–2189) deaths.

22 245

24 246 Combining conversion of SAVR to TAVI and additional capacity

25 247 Figures 3a and 3b demonstrate the range of possibilities in creating extra capacity. Each line
26 248 demonstrates a range of intervention strategies that provide the same result. For example, to
27 249 reduce mean predicted deaths to 1000 people (red line figure 3b), centres could increase
28 250 capacity to provide an extra 25% procedures per week at the same mix as pre-pandemic, or
29 251 they could convert 50% of SAVR operations to TAVI and increase capacity by 8.7% at that
30 252 mix. Figures 3c and 3d represent how the combinations of interventions to increase capacity
31 253 within the system alongside the conversion of SAVR to TAVI would impact the time to clear
32 254 the backlog and on the associated mortality of waiting. Mortality on the waiting list is less
33 255 responsive to our modelled interventions than the time to clear the backlog (the darker
34 256 coloured regions of figure 3d make up a greater proportion of the estimates than those of
35 257 figure 3c). Increasing capacity within the system alongside converting a proportion of SAVR
36 258 cases to TAVI provides the greatest benefit in clearing the backlog and avoiding associated
37 259 mortality. A combination that would result in the clearance of the backlog within a year
38 260 might be of interest for decision makers. With the conversion of 40% of SAVR operations to
39 261 TAVI and creation of an additional 20% capacity, we estimate the backlog would be cleared
40 262 in just under a year – 343 days (95% CI, 281–410) with 784 (95% CI, 292–1324) deaths
41 263 before treatment. Sensitivity analyses where the number of TAVI procedures that could be
42 264 completed within the same time as SAVR was altered (TAVI to SAVR: 4 to 3, 4 to 2, 5 to 3)
43 265 support these findings (supplementary material figures S1 – S3). Furthermore, sensitivity
44 266 analyses show that with the best-in-class practices (TAVI to SAVR: 4 to 2), even a more

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3 267 modest combination (a conversion of 35% and creation of an additional 10% capacity) would
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5 268 be enough to clear the backlog within a year.

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10 271 **Discussion**

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12
13 273 In this study, using dynamical system modelling, we provide estimates for how changes to
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15 274 treatment pathways for severe aortic stenosis may affect the time taken to clear the backlog
16
17 275 and minimise mortality on the waiting list in the NHS of England. Without providing at least
18
19 276 20% total additional capacity for the interventional treatment of AS, we estimated there
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21 277 would be more than 1000 deaths on the waiting list over a period of nearly 1.5 years. A
22
23 278 conversion of cases from SAVR to TAVI would expedite the clearance of the backlog, but
24
25 279 even converting half the cases to TAVI would still result in over 1400 deaths over a period of
26
27 280 almost 2 years. A combination of converting 40% of cases usually planned for SAVR to
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29 281 TAVI and creating 20% additional capacity for procedures (through measures such as extra
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31 282 lists) would clear the excess backlog within one year, with 784 deaths.

32 283

33 284 Our study has several strengths. First, in an urgent situation of many unknowns, our use of
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35 285 novel mathematical models provides plausible estimates on which to base planning and
36
37 286 provides an exemplar that may be used in service delivery in other conditions in the post-
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39 287 pandemic landscape. Given the high event rate amongst this population, waiting for more
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41 288 contemporary data to be collected may well not provide enough time to institute system
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43 289 changes to prevent deaths. Second, we also provide specific estimates for how the conversion
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45 290 of cases to TAVI from surgery may affect waiting lists and associated mortality, which can
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47 291 inform local MDT discussions. Third, our model can act as a basis for a clinical and cost-
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49 292 benefit analysis to evaluate different ways to increase capacity and define the optimal
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51 293 strategy at each centre. For each centre, the most effective combination of converting SAVR
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53 294 to TAVI and provision or prioritisation of treatment of severe AS can be generated.

54 295

55 296 We also recognise the limitations inherent in modelling a complex situation. First, we
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57 297 represent the NHS in England as a single entity. As such, we implicitly assume that
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59 298 population and capacity are distributed evenly throughout the country by treating centre
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299 capacity. If the distribution of waiting list patients deviates significantly from the distribution

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3 300 of treatment centres weighted by capacity, the time it would take to clear the waiting list, and
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5 301 thus the mortality rate would be higher. Second, we have not attempted to calculate how
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7 302 many AS patients may have died in the COVID-19 pandemic. Third, our assumed mortality
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9 303 rate may differ at a centre-level due to prioritising clinically more vulnerable patients on the
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11 304 waiting list. Fourth, a centre-level analysis could account for the different practices in each
12
13 305 treatment centre and identify strategies that work best for each centre. Fifth, our estimates
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15 306 from converting cases from SAVR to TAVI does not include post-procedural factors such as
16
17 307 the requirement for intensive care capacity, hospital stay and further procedures because
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19 308 these rely on multiple centre-specific factors. Finally, it has been shown that rapid growth in
20
21 309 the demand for TAVI can overwhelm current capacity,[22] which may lead to prolonged wait
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23 310 times and subsequent adverse outcomes while patients are on the waitlist. Therefore, a
24
25 311 demand model that captures the changes of demand for TAVI and SAVR would be a helpful
26
27 312 future direction of analysis.

313

27 314 A previous study used a mathematical model to quantify the cumulative cardiac surgical
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29 315 backlog (including coronary artery bypass grafting surgery, valve replacement and
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31 316 transcatheter aortic and mitral valve replacements) in two centres based on the projected
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33 317 pandemic duration in the United States of America (USA).[23] The authors used simple
34
35 318 mathematical models to predict the time required to clear the backlog depending on increased
36
37 319 operating capacity. However, the authors did not consider mortality, which we have as it is of
38
39 320 critical importance to patients and when planning services.

321

41 322 The results of our study highlight concerns pertaining to the deferral of non-emergency
42
43 323 treatment for severe AS during the 'recovery period' of COVID-19. Severe AS is a
44
45 324 progressive condition with valve replacement the only available treatment improving
46
47 325 prognosis.[24] On a local, regional, and national scale, healthcare systems will need to
48
49 326 examine capacity, set priorities, and plan for adequate capacity to manage the backlog of
50
51 327 patients with severe AS. The response will be complicated by prior exhaustion of human
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53 328 resources from the pandemic and competition with other specialities, which will also have
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55 329 backlogs.[25]

330

56 331 Nonetheless, planning should prioritise patients at the highest risk from a deferral of
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58 332 treatment. Mortality on the waiting list for AS has been reported to be as high as 14%.[26]

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3 333 Furthermore, patients awaiting structural procedures deferred due to the pandemic have been
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5 334 found to have significantly higher mortality rates compared to those with stable coronary
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7 335 artery disease.[27] Prioritising capacity for treatment of patients with severe AS may mean
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9 336 reduced capacity for other procedures. This interaction will require collaborative decision-
10
11 337 making on a local level accepting that these are difficult, imperfect times. We also show that
12
13 338 the conversion of a proportion of cases that would usually be managed by SAVR to TAVI
14
15 339 can help expedite treatment and reduce mortality on the waiting list. During the pandemic,
16
17 340 TAVI procedures were performed in patients usually referred for surgery with no apparent
18
19 341 difference in short term outcomes;[15, 16] and data continues to emerge for longer-term
20
21 342 efficacy and safety of TAVI across operative risk strata.[28,29] Recent European guidelines
22
23 343 suggest that TAVI would be a preferable option for patients over 75 years of age compared to
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25 344 SAVR.[20] To help planning, we provide an app ([https://github.com/Christian-P-](https://github.com/Christian-P-Stickels/AS_Waitinglist_data)
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27 345 [Stickels/AS_Waitinglist_data](https://github.com/Christian-P-Stickels/AS_Waitinglist_data)) to explore the impact of alterations in capacity and treatment
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29 346 pathways on waiting lists and mortality related to severe AS at a local, regional and national
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31 347 level (supplementary material).
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350 **Conclusions**

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352 In this study, we identify that without a combination of increased capacity for treatment of
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354 patients with severe aortic stenosis, and consideration of expanding the use of TAVI, there
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356 will be unpalatable rates of mortality in this high-risk group during the post-COVID-19
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358 ‘recovery’ period. These results should inform the planning of cardiac services.

359 **Acknowledgement**

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361
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363
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365
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4
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9 369 Trust.

10 370

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19 375 Newton Institute, but at time of submission, this has not been approved. None of these funding
20
21 376 sources had an impact on the design, data analysis, writing of, or decision to publish this paper.

22 377

23 378 **Competing Interests**

24
25 379 CG acknowledges grants not related to this project from Abbott, the British Heart Foundation,
26
27 380 and Deputy Editorship at EuroHeart. BG acknowledges grants not related to this project from
28
29 381 the David Telling Charitable Trust, and the Biotechnology and Biological Sciences Research
30
31 382 Council, he additionally declared Associate Editorship of Anesthesia Journal, and being the
32
33 383 chair DMSC for the COPIA Trial. All other authors confirm that they have no competing
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35 384 interests to declare.

36 385

37 386 **Data Sharing**

38 387 No additional data available

39 388

40 389 **Contributorship statement**

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42
43 390 MM proposed the initial workshop, MM, CG, RN, BG and JHFR all helped to run said
44
45 391 workshop as clinical experts. All members but KC and FE were involved in conceptualisation
46
47 392 in the initial workshop. CS, HJ, KS, and FE designed the model with clinical guidance from
48
49 393 MM, CG, RN, BG and JHFR. CS performed data analysis. CS, RJ and FE wrote the initial
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51 394 manuscript. All authors helped to improve the final manuscript. All authors approved the
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53 395 final manuscript.

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55 397 **Ethics Statement**

56 398 This paper did not require ethics approval.

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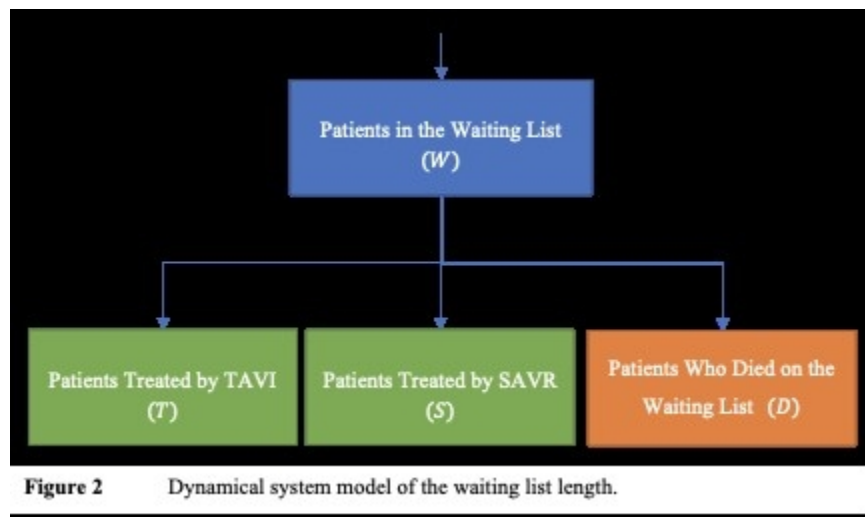


Figure 1: Dynamical system model of the waiting list length

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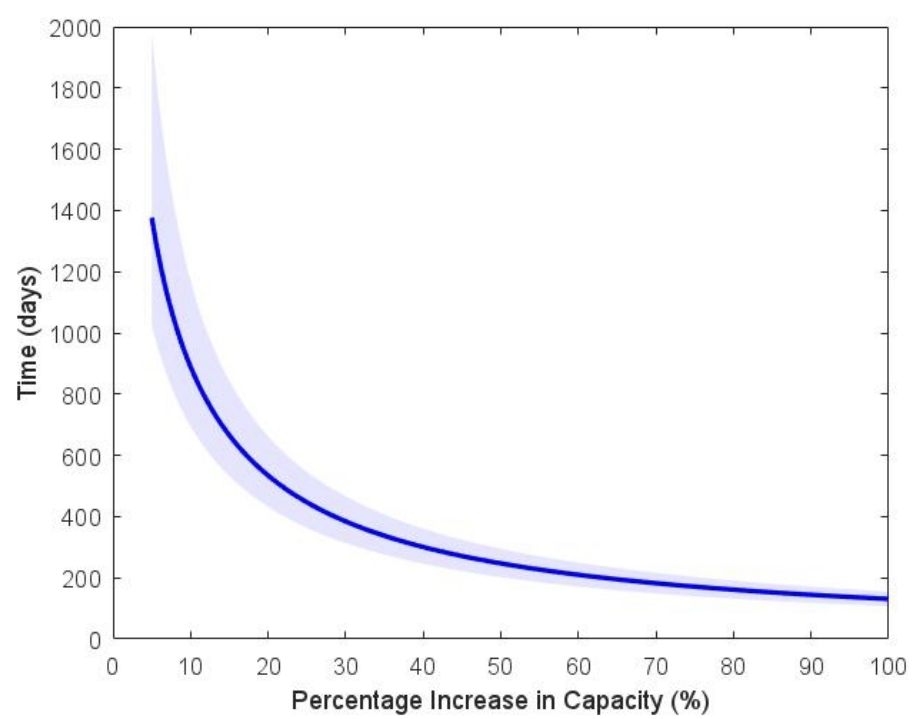


Figure 2a: Time to clear backlog (left) and the resulting deaths (right) with associated 95% confidence intervals as a function of daily percentage increase in capacity, with uncertainty from mortality and the initial waiting list. The x-axis is truncated at 5% for visualisation and clarity.

246x185mm (72 x 72 DPI)

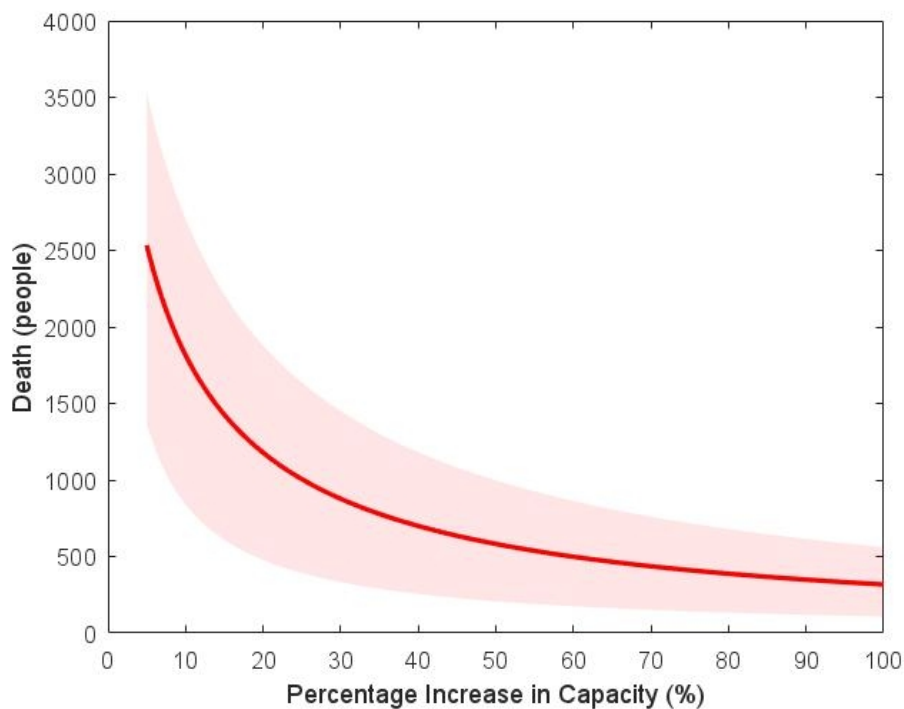


Figure 2b: Time to clear backlog (left) and the resulting deaths (right) with associated 95% confidence intervals as a function of daily percentage increase in capacity, with uncertainty from mortality and the initial waiting list. The x-axis is truncated at 5% for visualisation and clarity.

246x185mm (72 x 72 DPI)

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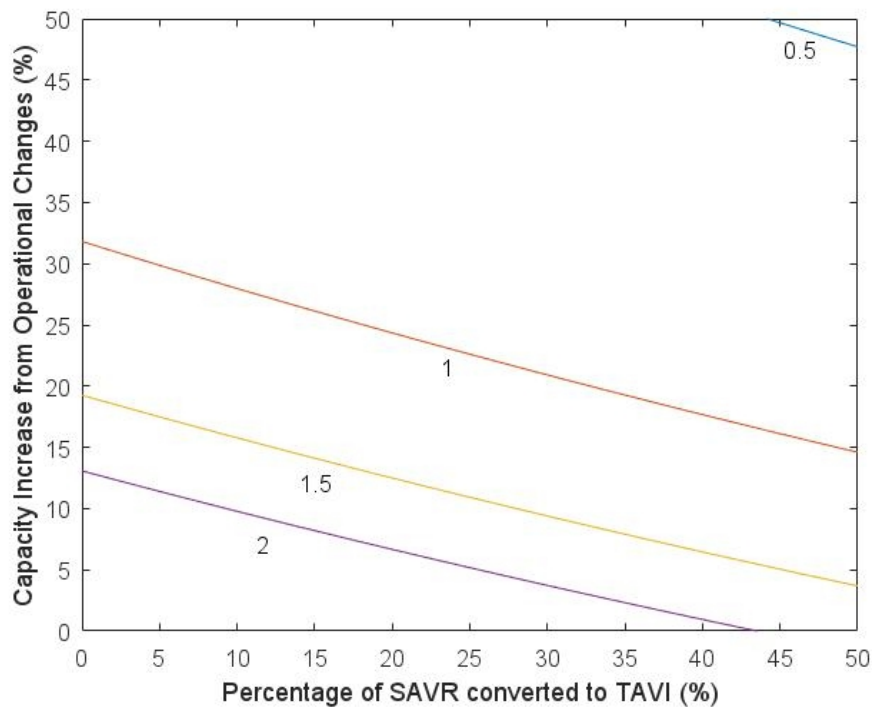


Figure 3a: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis) (Presented in two different forms). A) Isoclines of constant mean clearance-time going from half a year (blue) to 2 years (purple) in half-year increments. B) Isoclines of constant mean mortality after clearing the backlog from 500 people (blue) to 2000 (purple) in 500-person increments. C) Heatmap of different combinations of conversion and daily capacity increases and how long the backlog would take to clear on average, in days. D) Heatmap of different combinations of conversion and daily capacity increases and how many people would die, on average.

246x185mm (72 x 72 DPI)

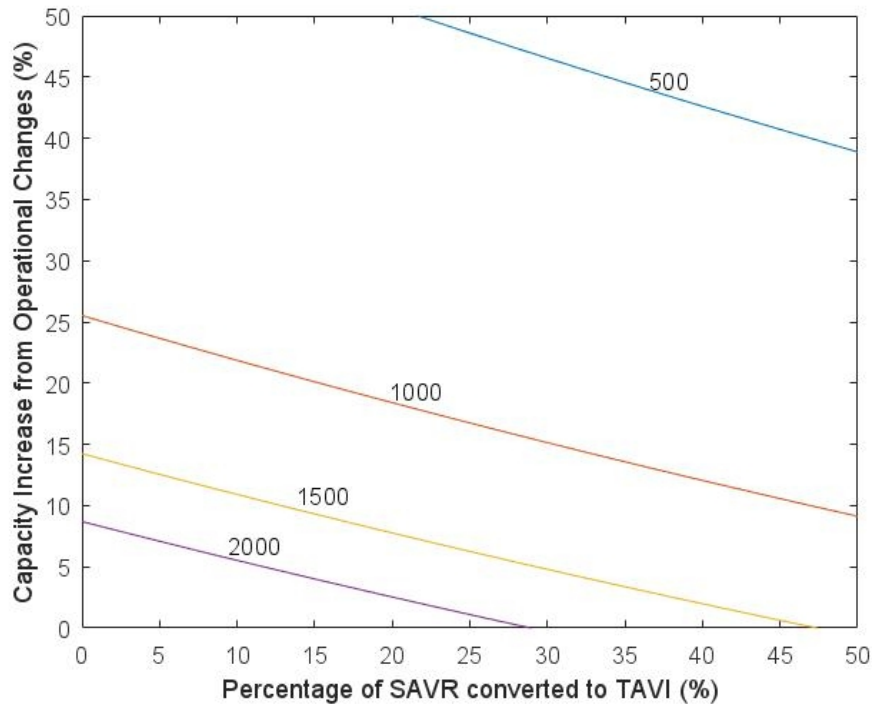


Figure 3b: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis) (Presented in two different forms). A) Isoclines of constant mean clearance-time going from half a year (blue) to 2 years (purple) in half-year increments. B) Isoclines of constant mean mortality after clearing the backlog from 500 people (blue) to 2000 (purple) in 500-person increments. C) Heatmap of different combinations of conversion and daily capacity increases and how long the backlog would take to clear on average, in days. D) Heatmap of different combinations of conversion and daily capacity increases and how many people would die, on average.

246x185mm (72 x 72 DPI)

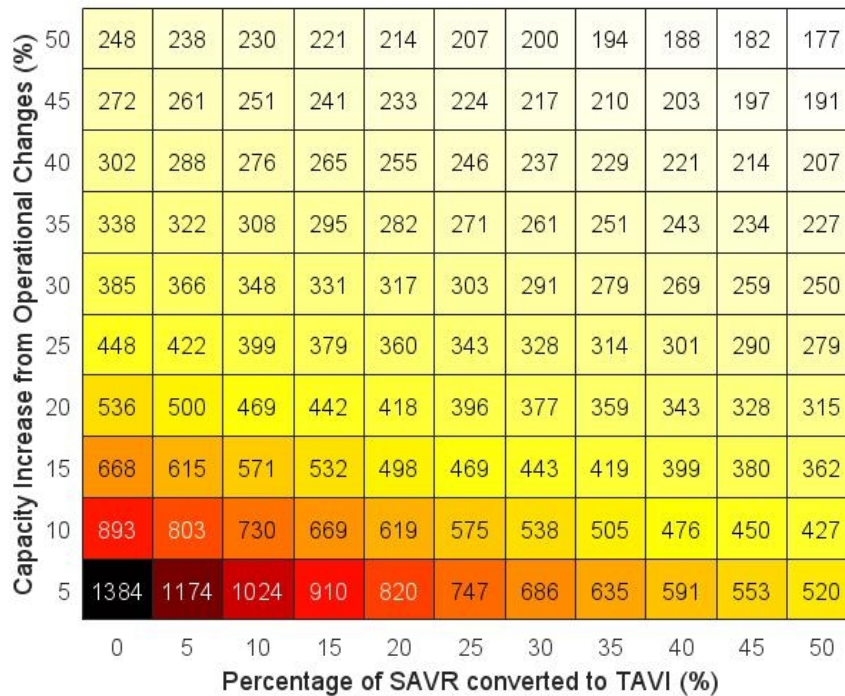


Figure 3c: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis) (Presented in two different forms). A) Isoclines of constant mean clearance-time going from half a year (blue) to 2 years (purple) in half-year increments. B) Isoclines of constant mean mortality after clearing the backlog from 500 people (blue) to 2000 (purple) in 500-person increments. C) Heatmap of different combinations of conversion and daily capacity increases and how long the backlog would take to clear on average, in days. D) Heatmap of different combinations of conversion and daily capacity increases and how many people would die, on average.

246x185mm (72 x 72 DPI)

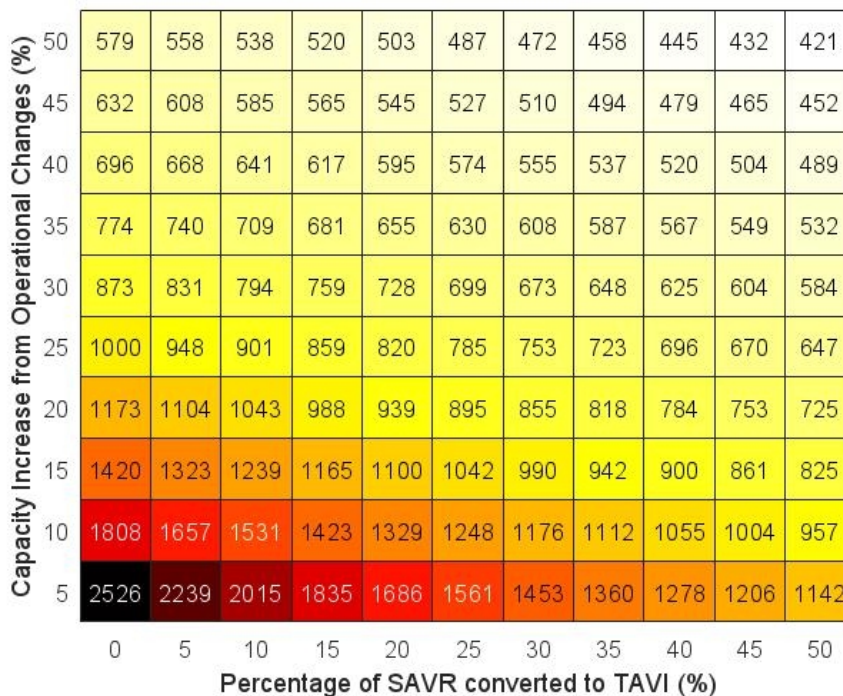


Figure 3d: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis) (Presented in two different forms). A) Isoclines of constant mean clearance-time going from half a year (blue) to 2 years (purple) in half-year increments. B) Isoclines of constant mean mortality after clearing the backlog from 500 people (blue) to 2000 (purple) in 500-person increments. C) Heatmap of different combinations of conversion and daily capacity increases and how long the backlog would take to clear on average, in days. D) Heatmap of different combinations of conversion and daily capacity increases and how many people would die, on average.

246x185mm (72 x 72 DPI)

SUPPLEMENTS

Supplement 1: Mathematical Derivation of the Differential Equation and its Solution

From figure 1, we can write the following equation:

$$\frac{dW}{dt} = f - r_T - r_S - \mu W.$$

We can then re-write and integrate this equation

$$\int_0^{t_c} 1 dt = \int_{W_0}^0 \frac{1}{f - r_T - r_S - \mu W} dW$$

$$t_c = \left[-\frac{1}{\mu} \ln (f - r_T - r_S - \mu W) \right]_{W_0}^0 = \left[\frac{1}{\mu} \ln (f - r_T - r_S - \mu W) \right]_0^{W_0}.$$

We can now define T_e , the extra capacity, as $T_e = r_T + r_S - f$. This is because we claim that under normal conditions, $f = r_T^0 + r_S^0$, such that the waiting list never grows above zero, and that the additional patients are already on the waiting list. The equation for T_e follows the observation that the current rates of TAVI and SAVR treatment are the normal rates plus the additional capacity.

This substitution allows us to write

$$t_c = \frac{1}{\mu} (\ln (-T_e - \mu W_0) - \ln (-T_e)) = \ln \left(1 + \frac{\mu W_0}{T_e} \right) \mu^{-1}.$$

This is the solution we use for calculating the time when the waiting list becomes zero.

We now rely on the assumption that T_e is constant to write

$$m(t_c) = W_0 - T_e t_c.$$

That is, by the time the waiting list is zero, everyone who has not been treated is unfortunately dead.

The assumption of a front-loaded waiting list (i.e., that all additional patients are identified and waiting) is not a strict requirement for this model to be valid. If it is the case that the additional patients are still being identified when the extra capacity is created, then as long as

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3 they are identified at a faster rate than they are treated, the predictions in this model hold. It is
4 only in cases where the identification rate is less than the treatment rate that this assumption
5 becomes invalid. In such cases, T_e can be said to be equal to the identification rate instead.
6
7 This is true because mortality is not tied to being on the waiting list but from the onset of
8 symptoms. In this way, the waiting list in our model can be thought of as the list of all people
9 who need treatment, even if the NHS is unaware of them.
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15 This model can be extended to predict mortality and time to clear a waiting list for non-
16 constant T_e , but we do not expand on that here.
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20 Supplement 2: Data

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22 We calculate the increase in capacity due to conversions and operational changes as follows.
23 Assume that we increase operations by 20% due to operational changes and convert 10% of
24 all SAVR to TAVI. Also assume that for every three SAVR patients five TAVI patients can
25 be processed. If we convert 10% of SAVR cases to TAVI (783 SAVR patients), we can treat
26 an additional 522 patients from the waiting list. From the 20% increase, we get extra 1039
27 TAVI and 1566 SAVR operations per year. If we apply 10% conversion to this extra
28 capacity, 156 SAVR operations can be converted into 260 TAVI operations. In total, the
29 operational changes and conversion create an extra capacity of 3232 operations with which to
30 service the waiting list each year: 1822 (1,039+522+261) TAVI and 1410 (1,566-156) SAVR
31 operations.
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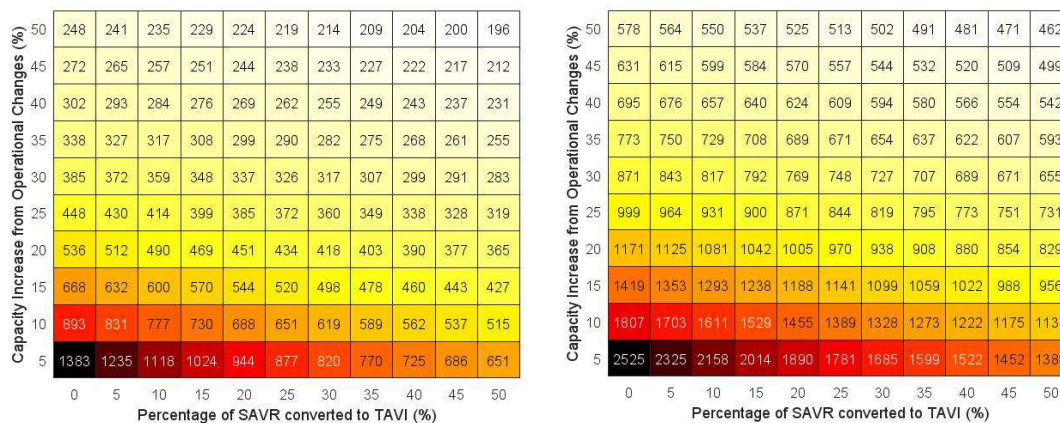
43 N.B. We make no assumptions about who the extra TAVI procedures treat, for example, if in
44 the above example, the additional 626 TAVI procedures we gain from conversion (522 from
45 converting the normal capacity and 104 from converting the additional capacity) treated only
46 SAVR patients, the conversion rate would actually be $\frac{626+783+156}{626+1566+78} = 15.6\%$. Normally, we
47 would expect that the application of this extra TAVI would be in the same proportion as the
48 ratio of SAVR to TAVI, which would give a real-world conversion rate of 13.5%.
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56 Supplement 3: App

57 The app can be accessed at https://github.com/Christian-P-Stickels/AS_Waitinglist_data
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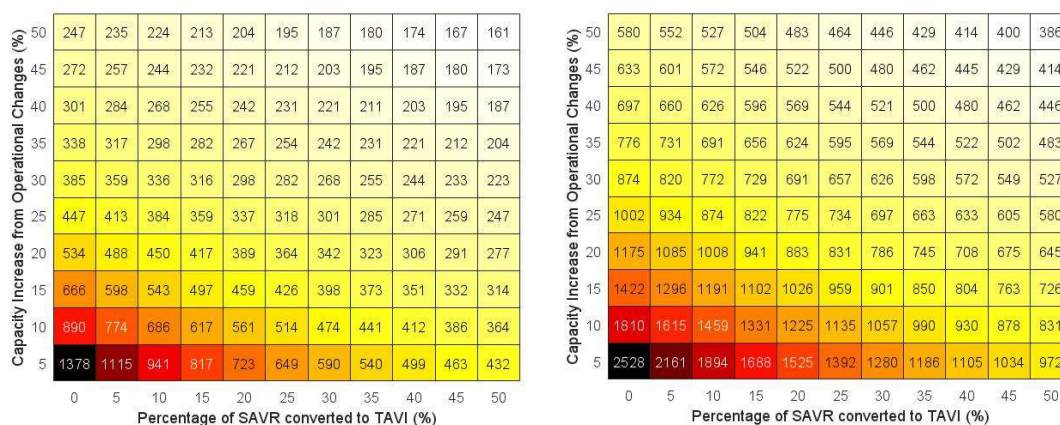
Supplement 4: Additional Results

Supplementary figure S1: Heat map of a three-to-four SAVR-to-TAVI conversion



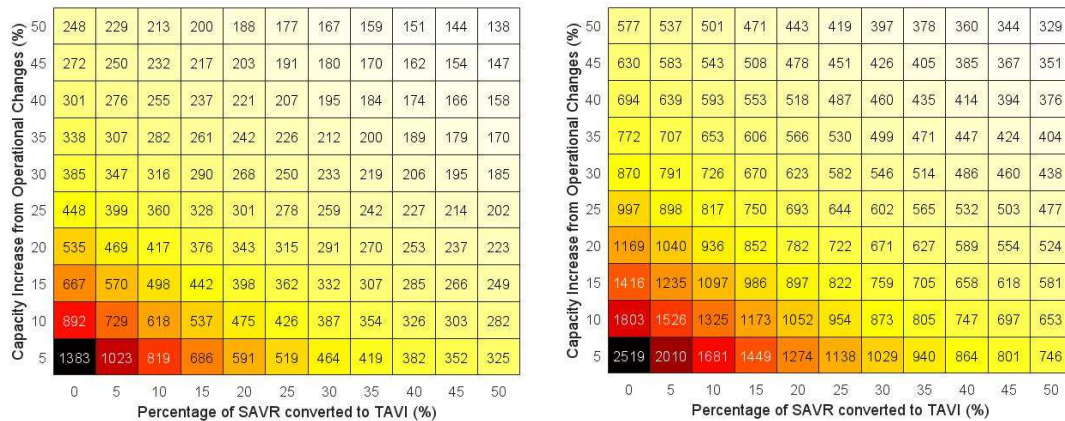
Supplementary Figure S1: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis), assuming that for every three SAVR operations, four TAVI procedures can be performed instead.

Supplementary figure S2: Heat map of a three-to-five SAVR-to-TAVI conversion



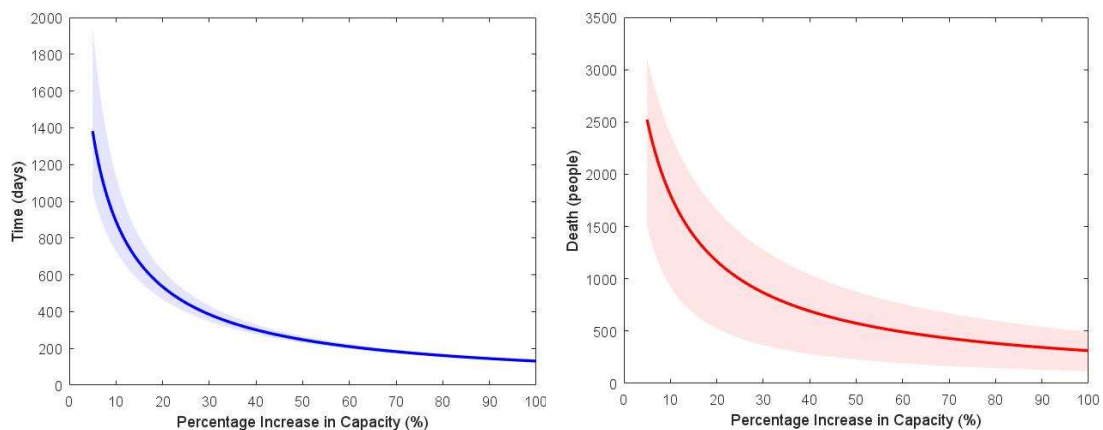
Supplementary Figure S2: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis), assuming that for every three SAVR operations, five TAVI procedures can be performed instead.

Supplementary figure S3: Heat map of a two-to-four SAVR-to-TAVI conversion



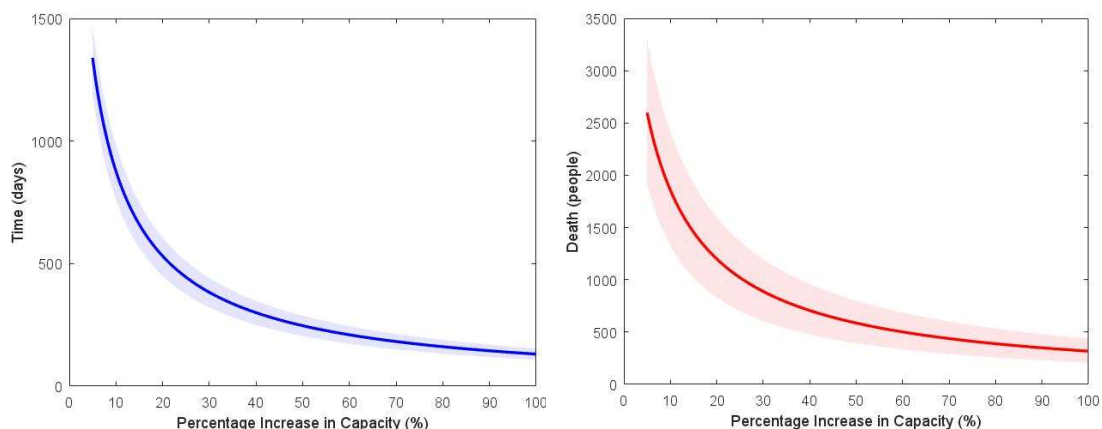
Supplementary Figure S3: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis), assuming that for every two SAVR operations, four TAVI procedures can be performed instead.

Supplementary figure S4: Error from mortality estimates



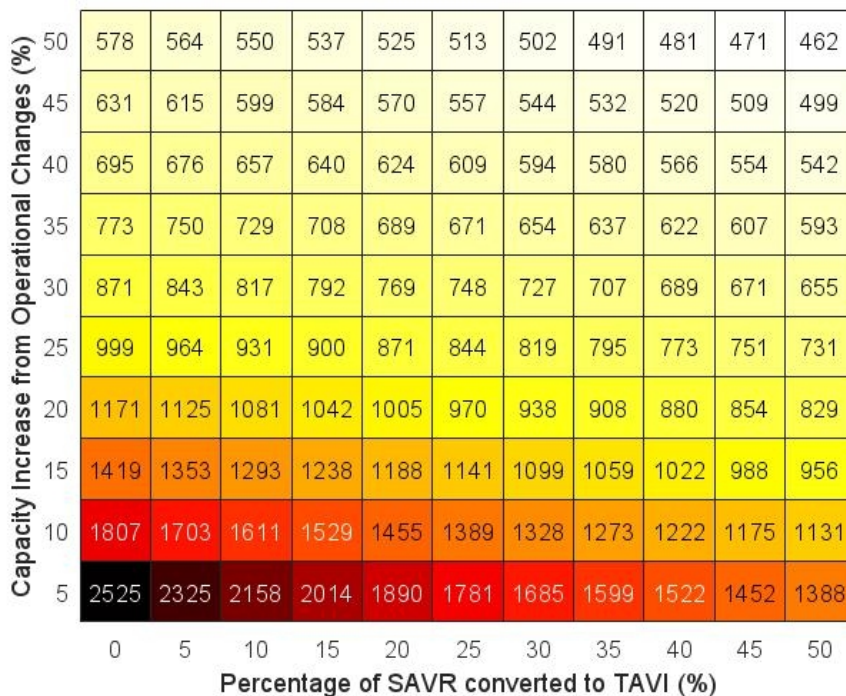
Supplementary figure S4: Time to clear backlog (left) and the resulting deaths (right) with associated 95% confidence intervals as a function of daily percentage increase in capacity, with uncertainty from mortality only. The x-axis is truncated at 5% for visualisation and clarity.

We find that error in the one-year mortality causes higher uncertainty at lower capacity increases, but at higher capacity increases, this uncertainty decreases until it is almost zero with regards to clearance time. This is likely because at higher capacity increases, more of our waiting list clearance comes from treatment, as opposed to death, resulting in less error.

Supplementary figure S5: Error from wait list (W_0) estimates

Supplementary figure S5: Time to clear backlog (left) and the resulting deaths (right) with associated 95% confidence intervals as a function of daily percentage increase in capacity, with uncertainty from initial waiting list estimates only. The x-axis is truncated at 5% for visualisation and clarity.

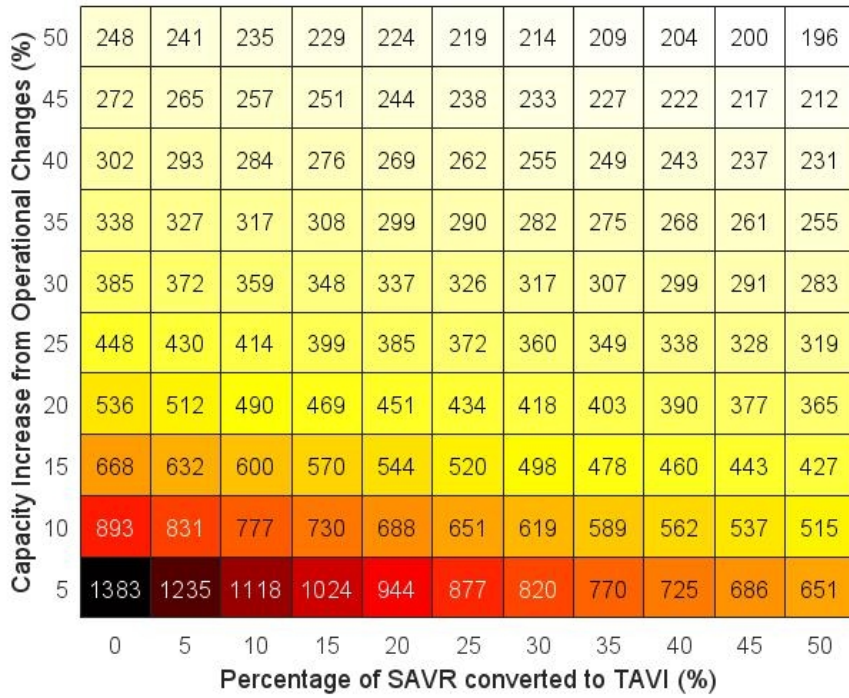
We find that error in the estimate of the wait list length W_0 causes uncertainty that is fairly constant in the time it takes to clear the backlog and in resultant deaths. This is to be expected as we can show that the uncertainty scales with $\ln W_0$. There is a small decrease in uncertainty as we increase capacity, once again because an increase in capacity results in more control of the waiting list reduction.



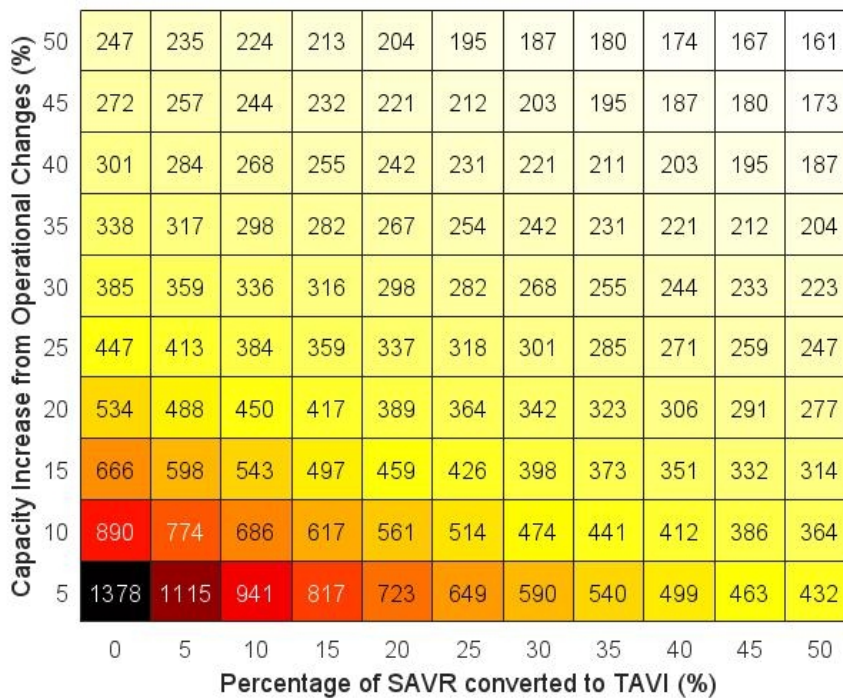
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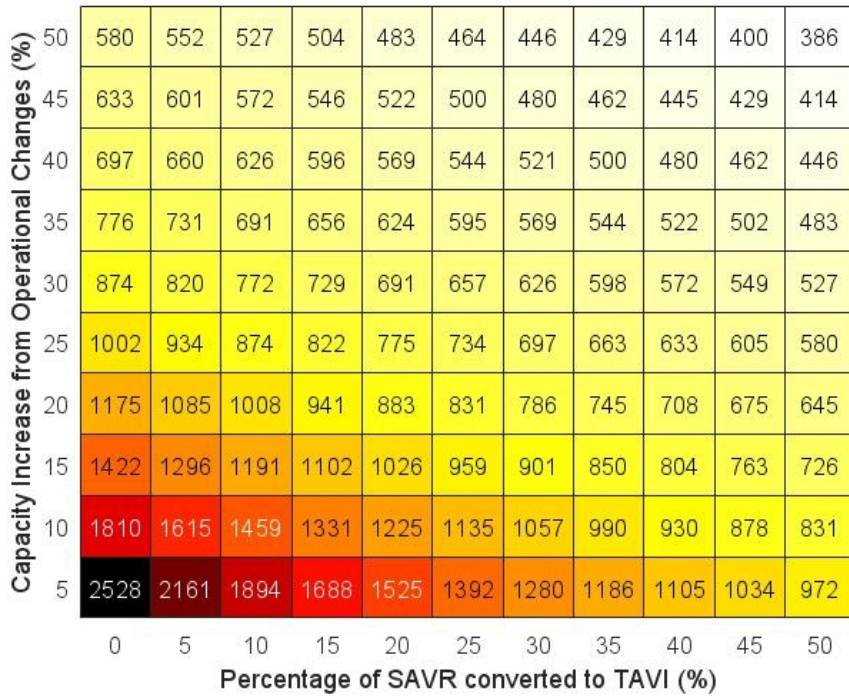
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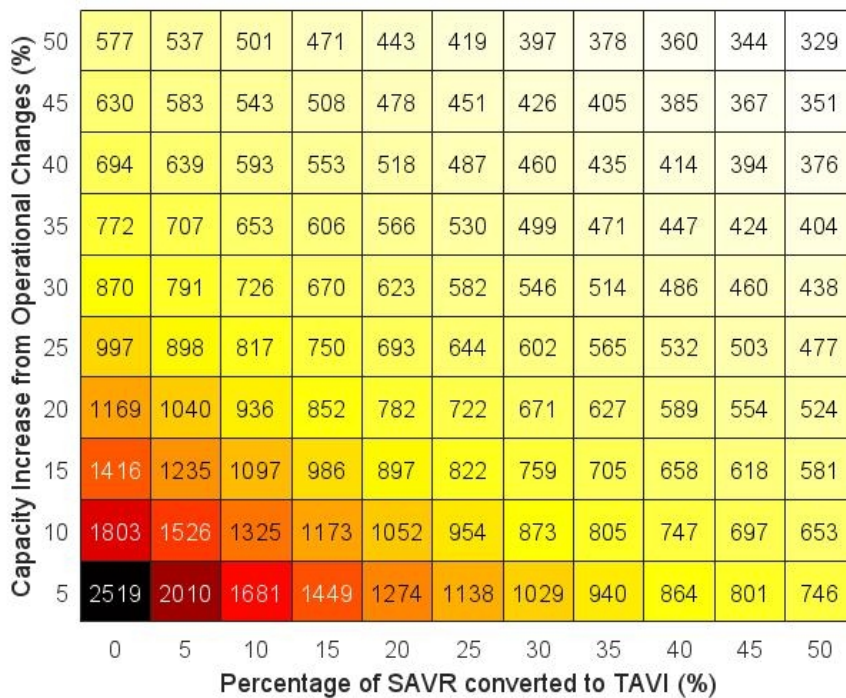
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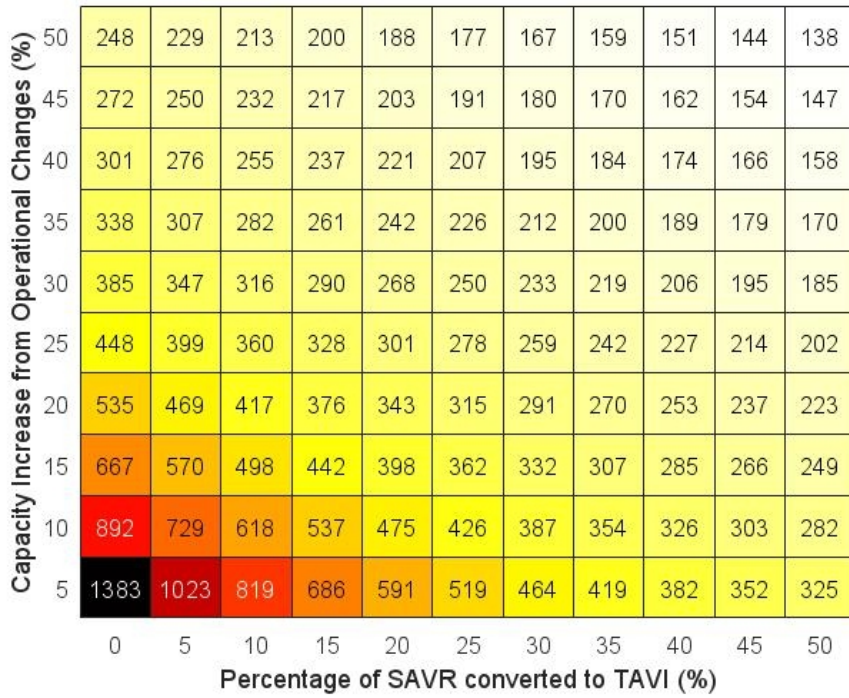


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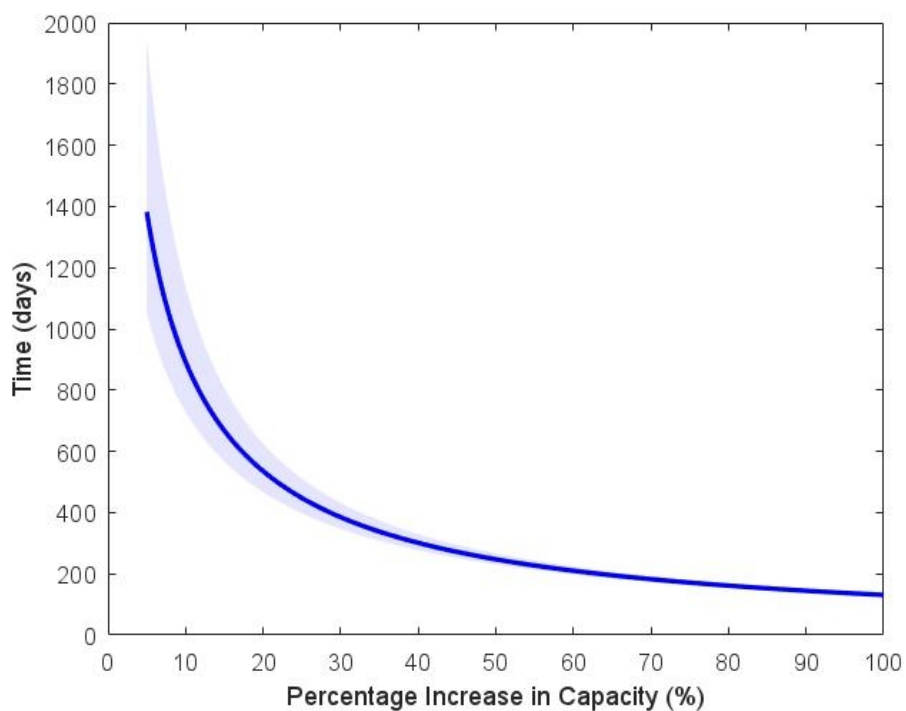


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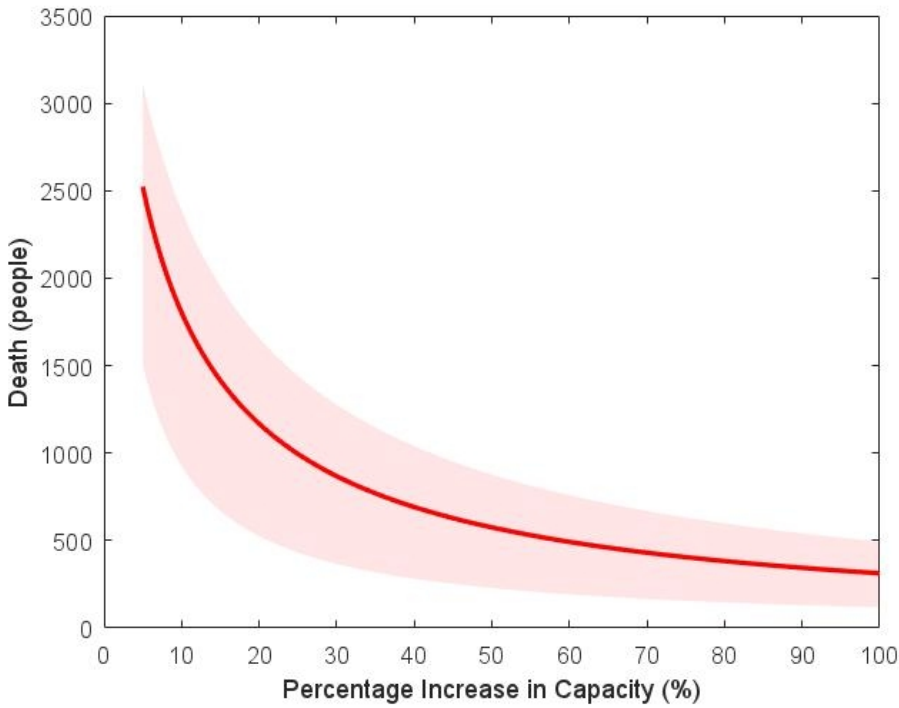
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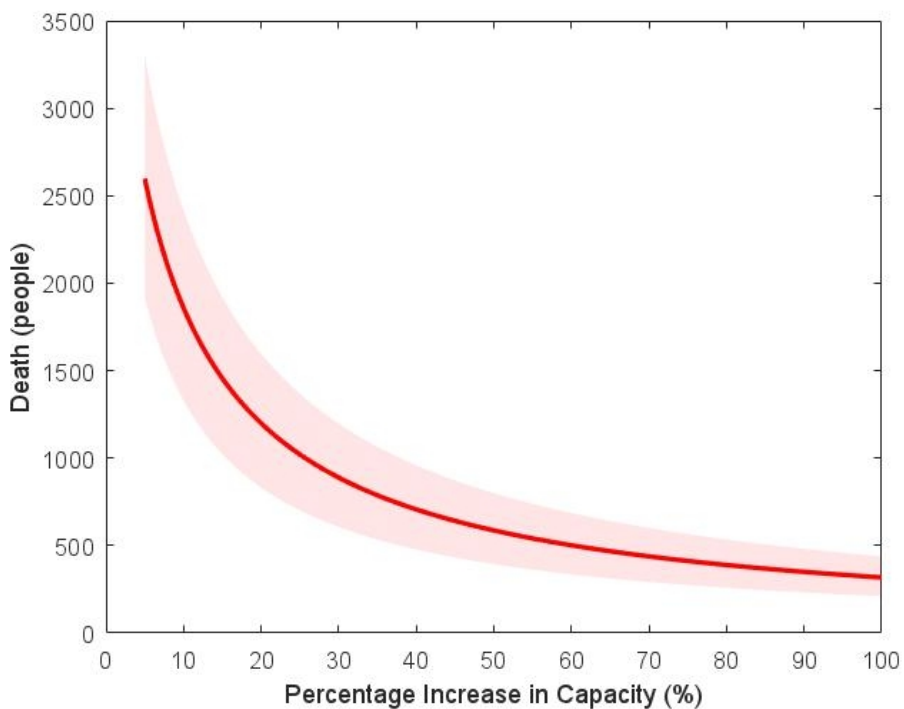
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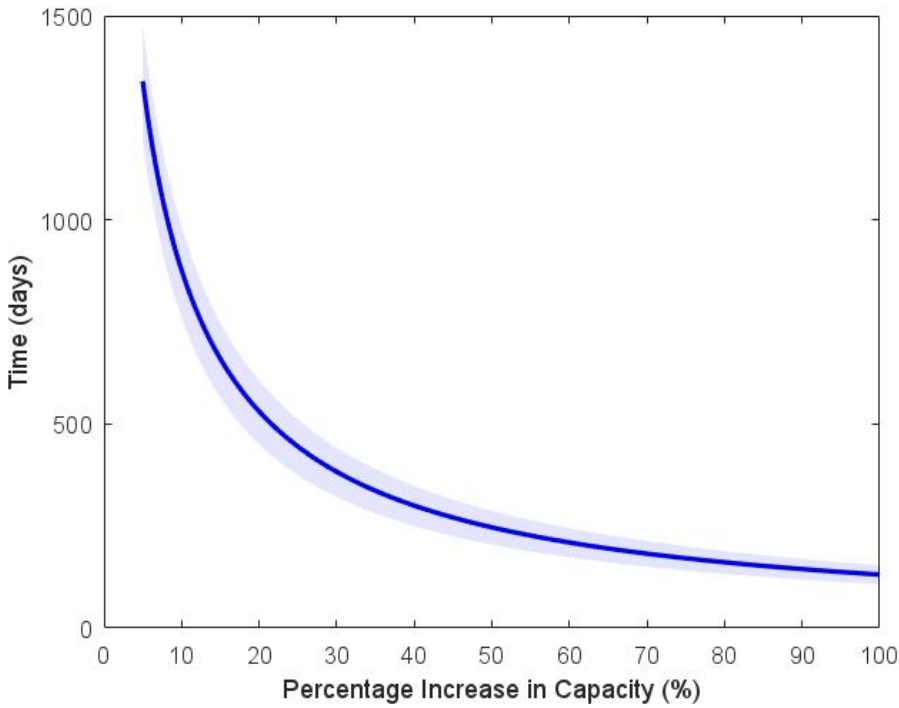
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Aortic stenosis post-COVID-19: A mathematical model on waiting lists and mortality

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2
3 45 **Abstract**
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7 47 **Objectives**

8 48 To provide estimates for how different treatment pathways for the management of severe
9 49 aortic stenosis (AS) may affect NHS England waiting list duration and associated mortality.
10
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12 50

13 51 **Design**

14
15 52 We constructed a mathematical model of the excess waiting list and found the closed-form
16 53 analytic solution to that model. From published data, we calculated estimates for how the
17 54 following strategies may affect the time to clear the backlog of patients waiting for treatment
18 55 and the associated waiting list mortality.
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24 57 **Setting**

25 58 The NHS in England.
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29 60 **Participants**

30 61 Estimated aortic stenosis patients in England.
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34 63 **Interventions**

35
36 64 1) Increasing the capacity for the treatment of severe AS, 2) converting proportions of cases
37 65 from surgery to transcatheter aortic valve implantation, and 3) a combination of these two.
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40 66

41 67 **Results**

42 68 In a capacitated system, clearing the backlog by returning to pre-COVID-19 capacity is not
43 69 possible. A conversion rate of 50% would clear the backlog within 666 (533–848) days with
44 70 1419 (597–2189) deaths whilst waiting during this time. A 20% capacity increase would
45 71 require 535 (434–666) days, with an associated mortality of 1172 (466–1859). A combination
46 72 of converting 40% cases and increasing capacity by 20% would clear the backlog within a
47 73 year (343 (281–410) days) with 784 (292–1324) deaths whilst awaiting treatment.
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3 75 **Conclusion**
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5 76 A strategy change to the management of severe AS is required to reduce the NHS backlog
6
7 77 and waiting list deaths during the post-COVID-19 'recovery' period. However, plausible
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9 78 adaptations will still incur a substantial wait to treatment and many hundreds dying whilst
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11 79 waiting.
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80 **Strengths and limitations of this study**

81

82 • Our model provides a good basis from which to alleviate a time-critical health system
83 problem when data gathering is likely to result in a greater number of deaths.

84 • Offering TAVI to some SAVR patients in what might be considered sub-optimal per-
85 patient treatment in ideal conditions, could result in better target population-based
86 outcomes.

87 • The assumption that the entire NHS can be modelled as a single entity with a single
88 waiting list is a limitation of this study.

89 • We recognise that the waiting numbers used in our study are only estimates because
90 we do not know how many patients with AS died due to COVID-19 infection.

91

92 Introduction

93

94 The COVID-19 pandemic has led to the reorganisation of healthcare services to limit the
95 transmission of the virus and deal with the sequelae of infection. This reorganisation had a
96 detrimental effect on cardiovascular services, with reductions in hospitalisations for acute
97 cardiovascular events and the deferral of all but the most urgent interventional procedures
98 and operations.[1, 2]

99

100 Aortic stenosis (AS) is the most common form of valvular heart disease. Once stenosis is
101 severe, symptoms follow and the prognosis is poor, with 50% mortality within two years of
102 symptom onset.[3] Thus, timely treatment is of paramount importance. Surgical aortic valve
103 replacement (SAVR) has historically been the default treatment strategy. However,
104 transcatheter aortic valve implantation (TAVI) has recently emerged as an effective and
105 increasingly utilised option across operative risk strata.[4-8]

106

107 There was a large decline in TAVI and SAVR procedural activity to treat severe AS during
108 the COVID-19 pandemic.[9] Between the period March to November 2020, it is estimated
109 that the decrease in activity accounted for 4989 (95% CI. 4020–5959) patients in England
110 with severe AS left untreated by TAVI or SAVR.[9] As we move into an era of ‘living with’
111 COVID-19, plans must urgently be put in place to best manage the additional waiting list
112 burden for treatment of severe AS.[10]

113

114 In this study, we used mathematical methods to examine the extent to which additional
115 capacity to provide treatment of severe AS should be created to clear the backlog and
116 minimise deaths of people on the waiting list.

117

118

119 Methods

120

121 Study population and assumptions

122 Data from the UK TAVR registry and NICOR (National Institute for Cardiovascular
123 Outcomes Research) National Adult Cardiac Surgery Audit (NACSA) between 2017 and
124 2020 have previously been extracted to estimate an excess waiting list size (W_0) of 4989

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3 125 (95% CI, 4020–5959) patients with severe AS left untreated as of November 2020.[9] In the
4
5 126 absence of contemporaneous data on waiting lists and SAVR and TAVI activity, we have
6
7 127 taken this number as the excess backlog on which to model solutions. The incidence of AS
8
9 128 has not increased over recent years.[11] Therefore, we assumed that the system was in a
10
11 129 steady state before the COVID-19 pandemic and without loss of generality defined the
12
13 130 steady-state waiting list to be zero. Additionally, we assumed that the normal rate of flow (f)
14
15 131 of new patients into the waiting list for treatment of severe AS would be maintained upon the
16
17 132 commencement of additional operations. Thus, the extra capacity that we model is to clear
18
19 133 the excess post-COVID-19 backlog.

134

20
21 135 We took one-year mortality (μ) after the onset of symptoms in severe AS to be 36% (95% CI,
22
23 136 12% – 60%).[12] More recent studies have estimated the one-year mortality to be 51%[5] and
24
25 137 55%, but these included cohorts that were considered inappropriate for SAVR, thus, we
26
27 138 considered these estimates unrepresentative of an unselected population with severe AS.[13]
28
29 139 The routine capacity for treatment of severe AS was taken from the pre-pandemic period. In
30
31 140 2018/19, the NHS in England performed 7830 SAVR ($r_S^0 = 7830$) and 5197 TAVI (r_T^0
32
33 141 $= 5197$) procedures, for a total throughput of about 13,000 per year.[14]

142

143 Modelling

34
35
36 144 Patients on the waiting list for treatment of severe AS were represented as a dynamical
37
38 145 system (figure 1).

146

41
42 147 To this model, we introduced capacity in surplus to the 2018/19 performance and called this
43
44 148 capacity T_e (further details are provided in supplementary material). We assumed that the
45
46 149 typical caseload for which the NHS in England can deal with continues; i.e., we assumed that
47
48 150 the system will return to pre-pandemic levels first using its baseline capabilities. The backlog
49
50 151 accumulated during the pandemic is only reduced by treating patients with this extra capacity
51
52 152 or by patient mortality before receiving treatment. We also considered patients in the backlog
53
54 153 and patients new to the waiting list indistinguishable. Accordingly, the waiting list size
55
56 154 represents the excess number of people seeking treatment who are unable to be treated
57
58 155 immediately at any one time. We also assumed that other paths out of the waiting list (i.e.
59
60 156 patients seeking private treatment) would be so small in comparison to the uncertainty
157
158 estimates as to be negligible on the results of our analysis.

158

159 These assumptions were brought together to give an estimated time (see supplementary
160 material for derivation) to clear the waiting list (t_c)

$$t_c = \frac{\ln\left(1 + \frac{W_0\mu}{T_e}\right)}{\mu} \quad (1)$$

162 and associated mortality ($m(t_c)$)

$$m(t_c) = W_0 - T_e t_c. \quad (2)$$

164

165 Using equations (1) and (2), we predicted the length of time and associated mortality for
166 different percentage increases in capacity. We assumed any capacity increase to be constant
167 throughout the entire modelled period. For example, if we increased daily capacity by 5% this
168 would result in, $T_e = \frac{r_s^0 + r_t^0}{365} * 5\% = 1.785$ extra procedures per day, across the whole of the
169 NHS in England. We generated 10,000 random values for the one-year mortality rate and
170 initial waiting list length. We assumed that the uncertainty in both variables was normally
171 distributed. For every T_e , we present the mean and the 2.5 and 97.5 percentiles of the 10,000
172 simulations for time to clear the waiting list and the associated mortality. That is, we present
173 the 95% reference range.[15]

174

175 Interventions and outcomes

176 We investigated three types of capacity increase: 1) a general increase in the capacity to
177 provide SAVR and TAVI, which could be facilitated by an increased number of procedures
178 per list, additional lists, and prioritisation of care pathways and staffing to treat severe AS; 2)
179 extra capacity created by treating some patients with TAVI who would routinely have SAVR;
180 3) a combination of a general increase in capacity and the conversion of a proportion of cases
181 from SAVR to TAVI. During the COVID-19 pandemic, TAVI was performed in patients
182 usually referred for surgery, with no difference in short term outcomes compared to historical
183 reference groups.[16, 17]

184

185 We assumed that the duration of a SAVR would routinely be between 2-4 hours and a TAVI
186 between 1-2 hours.[18, 19] As such, we assumed within the time for two SAVR operations,
187 three TAVI could be performed instead.[20] Several clinical factors may favour SAVR over
188 TAVI (including concomitant severe coronary artery disease, low STS score, bicuspid aortic

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3 189 valve etc.); therefore, we assumed that, in the short term, no more than 50% of patients could
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5 190 be converted from SAVR to TAVI.[21] We also assumed that no more than 50% extra
6
7 191 capacity could be created by other means (e.g. extra lists, more procedures per list). We
8
9 192 simulated two principal outcomes based on the creation of additional capacity (T_e): the time
10
11 193 to clear the backlog (reduce to zero), and the mortality of patients within the excess backlog
12
13 194 whilst on the waiting list to be treated.
14

195

15 196 We completed additional sensitivity analyses for how the conversion of SAVR to TAVI
16
17 197 could affect the principal outcomes, including if three SAVR operations could be routinely
18
19 198 completed in a day and four to five TAVI procedures per day (presuming increasing uptake
20
21 199 of a minimalist TAVI approach without general anaesthesia enabling more rapid procedure
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23 200 time).[22]
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202 Patient and public involvement

203 Patients and the public were not involved in the conduct of this study.
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206 Results

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208 In the pre-COVID-19 period, the routine capacity for treatment of severe AS was set to cover
209
210 the normal incident rate. That is, clearing the backlog by returning to pre-COVID-19 capacity
211
212 is not possible. As a result, mortality on the excess waiting list at one year are estimated to be
213
214 more than 1500, putting a strong emphasis on the need for change.
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213 Total additional capacity

214 Figure 2 provides simulations of the time to clear the excess backlog and the mortality of
215
216 patients on the waiting list based on the amount of total additional capacity, T_e . With a 5%
217
218 increase in the capacity to provide treatment of severe AS, we estimate it would take 1384
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220 (1025–1994) days to clear the excess backlog, with 2526 (1355–3516) deaths. A 20%
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222 increase in total capacity would provide a benefit in clearing the excess backlog within 536
(434–666) days, with an estimate of 1173 (466–1859) deaths. As total capacity increased
further, there was a diminishing return in clearing the backlog and avoiding associated
mortality; the greater the capacity increase, the fewer lives are saved for every extra increase

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3 222 in capacity. Even if it was possible to double capacity, it was estimated that it may take 131
4 223 (126–137) days to clear the backlog and there would be 313 (118–494) deaths on the waiting
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6 224 list.
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10 226 The effect of converting SAVR to TAVI

11 227 The conversion of a proportion of cases from surgery to TAVI provides a modest
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13 228 improvement in estimates of time to clear the backlog and mortality on the waiting list. With
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15 229 the conversion of 30% of SAVR operations to TAVI procedures, without the creation of
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17 230 additional capacity in the system, we estimated that it would take 975 (741–1284) days to
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19 231 clear the backlog and there would be 1914 (923–2809) deaths on the waiting list. Even with a
20
21 232 conversion of 50% of SAVR operations to TAVI procedures, the estimated backlog would be
22
23 233 cleared within 666 (533–848) days with 1419 (597–2189) deaths. For the highest conversion
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25 234 ratio that we considered (2:4), at a 50% rate of conversion, we estimated the backlog to be
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27 235 cleared in 384 (330–462) days with 871 (314–1426) deaths. Whilst this result is improved,
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29 236 we consider a 2:4 conversion ratio the highest reasonable ratio in the short-term, and is
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31 237 unlikely to be achieved at every centre immediately. It is also worth noting that even if this
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33 238 was achieved, the backlog would still take over a year to clear.

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34 240 Combining conversion of SAVR to TAVI and additional capacity

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36 241 Figures 3a and 3b demonstrate the range of possibilities in creating extra capacity. Each line
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38 242 demonstrates a range of intervention strategies that provide the same result. For example, to
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40 243 reduce the mean predicted deaths to 1000 (red line figure 3b), centres could increase capacity
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42 244 to provide an extra 25% procedures per week at the same mix as pre-pandemic, or they could
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44 245 convert 50% of SAVR operations to TAVI and increase their capacity by 8.7% at that mix.
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46 246 Figures 3c and 3d represent how the combinations of interventions to increase capacity
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48 247 within the system alongside the conversion of SAVR to TAVI would impact the time to clear
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50 248 the backlog and on the associated mortality of waiting. Mortality on the waiting list is less
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52 249 responsive to our modelled interventions than the time to clear the backlog (the darker
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54 250 coloured regions of figure 3d make up a greater proportion of the estimates than those of
55
56 251 figure 3c). Increasing capacity within the system alongside converting a proportion of SAVR
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58 252 cases to TAVI provides the greatest estimated benefit in clearing the backlog and avoiding
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60 253 associated mortality. A combination that would result in the clearance of the backlog within a
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255 254 year might be of interest for decision makers. With the conversion of 40% of SAVR

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3 255 operations to TAVI and the creation of an additional 20% capacity, we estimated that the
4 256 backlog would be cleared in just under a year – 343 days (281–410) with 784 (292–1324)
5 257 deaths before treatment.
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10 259 Sensitivity analyses where the number of TAVI procedures that could be completed within
11 260 the same time as SAVR was altered (TAVI to SAVR: 4 to 3, 4 to 2, 5 to 3) support these
12 261 findings (supplementary material figures S1 – S3). Furthermore, sensitivity analyses show
13 262 that with the best-in-class practices (TAVI to SAVR: 4 to 2), even a more modest
14 263 combination (a conversion of 35% and creation of an additional 10% capacity) may be
15 264 enough to clear the backlog within a year.
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24 267 **Discussion**

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27 269 In this study, using dynamical system modelling, we provide estimates for how changes to
28 270 treatment pathways for patients with severe aortic stenosis may affect the time taken to clear
29 271 the backlog and minimise mortality on the waiting list in the NHS of England. Without
30 272 providing at least 20% total additional capacity for the interventional treatment of AS, we
31 273 estimated there would be more than 1000 deaths on the waiting list over a period of nearly
32 274 1.5 years. A conversion of cases from SAVR to TAVI would expedite the clearance of the
33 275 backlog, but even converting half the cases to TAVI would still result in over 1400 deaths
34 276 over a period of almost 2 years. A combination of converting 40% of cases usually planned
35 277 for SAVR to TAVI and creating 20% additional capacity for procedures (through measures
36 278 such as extra lists) would clear the excess backlog within one year, with 784 deaths.
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46 280 Our study has several strengths. First, in a time-critical clinical situation of many unknowns,
47 281 our use of novel mathematical models provides plausible estimates on which to base health
48 282 services planning, and provides an exemplar that may be used in service delivery in other
49 283 conditions in the post-pandemic landscape. Given the high event rate amongst this
50 284 population, waiting for more contemporary data to be collected may well not provide enough
51 285 time to institute system changes to prevent deaths. Second, we also provide specific estimates
52 286 for how the conversion of cases to TAVI from surgery may affect waiting lists and associated
53 287 mortality, which can inform local MDT discussions. Third, our model can act as a basis for a
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3 288 clinical and cost-benefit analysis to evaluate different ways to increase capacity and define
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5 289 the optimal strategy at each centre. For each centre, the most effective combination of
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7 290 converting SAVR to TAVI and provision or prioritisation of treatment of severe AS can be
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9 291 generated.

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11 293 We recognise the limitations inherent in modelling a complex situation. First, we represent
12 294 the NHS in England as a single entity. As such, we implicitly assume that population and
13 295 capacity are distributed evenly throughout the country by treating centre capacity. If the
14 296 distribution of waiting list patients deviates significantly from the distribution of treatment
15 297 centres weighted by capacity, the time it would take to clear the waiting list, and thus the
16 298 mortality rate would be higher. Second, we have not attempted to calculate how many
17 299 patients with AS may have died in the COVID-19 pandemic, which could have reduced the
18 300 numbers of deaths on the waiting list and the duration of the waiting list because of an
19 301 underestimation of ‘abandonment’ from the model. Third, our assumed mortality rate may
20 302 differ at a centre-level due to prioritising clinically more vulnerable patients on the waiting
21 303 list. Fourth, a centre-level analysis could account for the different practices in each treatment
22 304 centre and identify strategies that work best for each centre. Fifth, our estimates from
23 305 converting cases from SAVR to TAVI do not include post-procedural factors such as the
24 306 requirement for intensive care capacity, hospital stay and further procedures because these
25 307 rely on multiple centre-specific factors. Finally, it has been shown that rapid growth in the
26 308 demand for TAVI can overwhelm current capacity,[23] which may lead to prolonged wait
27 309 times and subsequent adverse outcomes while patients are on the waitlist. Therefore, a
28 310 demand model that captures the changes of demand for TAVI and SAVR would be a helpful
29 311 future direction of analysis.

30 312
31 313 A previous study used a mathematical model to quantify the cumulative cardiac surgical
32 314 backlog (including coronary artery bypass grafting surgery, valve replacement and
33 315 transcatheter aortic and mitral valve replacements) in two centres based on the projected
34 316 pandemic duration in the United States of America (USA).[24] The authors used simple
35 317 mathematical models to predict the time required to clear the backlog depending on increased
36 318 operating capacity. However, the authors did not consider mortality, which we have as it is of
37 319 critical importance to patients and when planning services.

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3 321 The results of our study highlight concerns pertaining to the deferral of non-emergency
4 322 treatment for severe AS during the ‘recovery period’ of COVID-19. Severe AS is a
5 323 progressive condition with valve replacement the only available treatment improving
6 324 prognosis.[25] On a local, regional, and national scale, healthcare systems will need to
7 325 examine capacity, set priorities, and plan for adequate capacity to manage the backlog of
8 326 patients with severe AS. The response will be complicated by prior exhaustion of human
9 327 resources from the pandemic and competition with other specialities, which will also have
10 328 backlogs.[26]

11 329
12 330 Nonetheless, planning should prioritise patients at the highest risk from a deferral of
13 331 treatment. Mortality on the waiting list for AS has been reported to be as high as 14%.[27]
14 332 Furthermore, patients awaiting structural procedures deferred due to the pandemic have been
15 333 found to have significantly higher mortality rates compared to those with stable coronary
16 334 artery disease.[28] Prioritising capacity for treatment of patients with severe AS may mean
17 335 reduced capacity for other procedures. Providing 20% extra capacity for TAVI and SAVR
18 336 may only require the addition of one extra list per week at the expense of other procedures, as
19 337 many centres only conduct TAVI procedures on between two and three days per week.[22]
20 338 This interaction will require collaborative decision-making on a local level accepting that
21 339 these are difficult, imperfect times. We also show that the conversion of a proportion of cases
22 340 that would usually be managed by SAVR to TAVI can help expedite treatment and reduce
23 341 mortality on the waiting list. During the pandemic, TAVI procedures were performed in
24 342 patients usually referred for surgery with no apparent difference in short term outcomes;[16,
25 343 17] and data continues to emerge for longer-term efficacy and safety of TAVI across
26 344 operative risk strata.[29,30] Recent European guidelines suggest that TAVI would be a
27 345 preferable option for patients over 75 years of age compared to SAVR.[21]

28 346
29 347 To help planning, we provide an app ([https://github.com/Christian-P-](https://github.com/Christian-P-Stickels/AS_Waitinglist_data)
30 348 [Stickels/AS_Waitinglist_data](https://github.com/Christian-P-Stickels/AS_Waitinglist_data)) to explore the impact of alterations in capacity and treatment
31 349 pathways on waiting lists and mortality related to severe AS at a local, regional and national
32 350 level (supplementary material).

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35 353 **Conclusions**

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5 355 In this study, we found that without a combination of increased capacity for treatment of
6 356 patients with severe aortic stenosis and an expansion in the use of TAVI, there would be
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8 357 many potentially avoidable deaths during the post-COVID-19 recovery period. Our study
9 358 findings and accompanying app may help inform the planning of cardiac services.
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15 361 **Acknowledgement**

16 362

17
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42 378 the design, data analysis, writing of or decision to publish this paper.
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48 380 **Competing Interests**

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51 383 Associate Editorship of Anesthesia Journal, and being the chair DMSC for the COPIA Trial.
52 384 All other authors confirm that they have no competing interests to declare.
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58 386 **Data Sharing**

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3 387 No additional data available

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6 389 **Contributorship statement**

7
8 390 MAM proposed the initial workshop and designed the research question, MAM, CPG, RN,
9 391 BG and JHFR all helped to run said workshop as clinical experts. All members but KC and
10 392 FE were involved in conceptualisation in the initial workshop. CS, HJ, KS, and FE designed
11 393 the model with clinical guidance from MAM, CPG, RN, BG and JHFR. CS performed data
12 394 analysis. CS, RN and FE drafted the initial manuscript. MAM, CPG, BG, JHFR, NH, SL,
13 395 LaSc, MS, LoSu, JWM, KC provided critical interpretation and revision of the manuscript.
14 396 All authors approved the final manuscript.
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21 398 **Ethics Statement**

22 399 This paper did not require ethics approval.
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27 401 **References**

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15 520 **Legends and Captions**

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17 521 Figure 1: Dynamical system model of the waiting list length.
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20 523 Figure 2: Time to clear backlog (left) and the resulting deaths (right) with associated 95%
21 524 confidence intervals as a function of daily percentage increase in capacity, with uncertainty
22 525 from mortality and the initial waiting list. The x-axis is truncated at 5% for visualisation and
23 526 clarity.
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29 528 Figure 3: Mean time to clear backlog (left) and the resulting deaths (right) as a function of
30 529 daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI
31 530 (x-axis) (Presented in two different forms). A) Isoclines of constant mean clearance-time
32 531 going from half a year (blue) to 2 years (purple) in half-year increments. B) Isoclines of
33 532 constant mean mortality after clearing the backlog from 500 people (blue) to 2000 (purple) in
34 533 500-person increments. C) Heatmap of different combinations of conversion and daily
35 534 capacity increases and how long the backlog would take to clear on average, in days. D)
36 535 Heatmap of different combinations of conversion and daily capacity increases and how many
37 536 people would die, on average.
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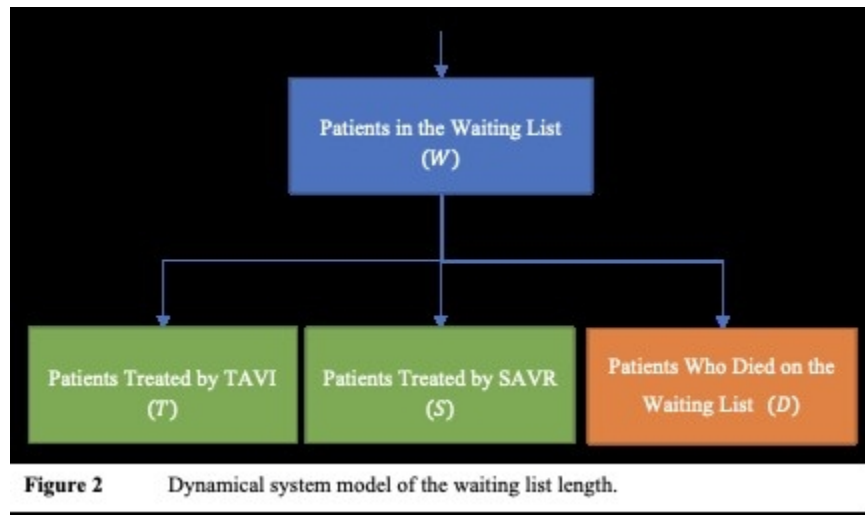


Figure 1: Dynamical system model of the waiting list length

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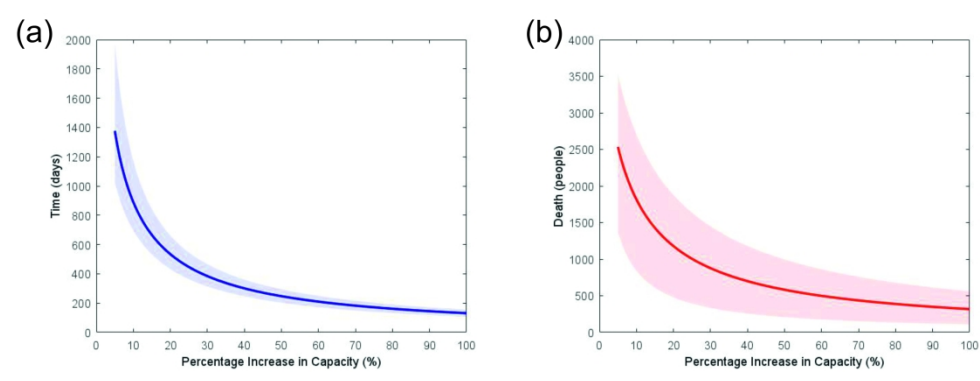


Figure 2: Time to clear backlog (left) and the resulting deaths (right) with associated 95% confidence intervals as a function of daily percentage increase in capacity, with uncertainty from mortality and the initial waiting list. The x-axis is truncated at 5% for visualisation and clarity.

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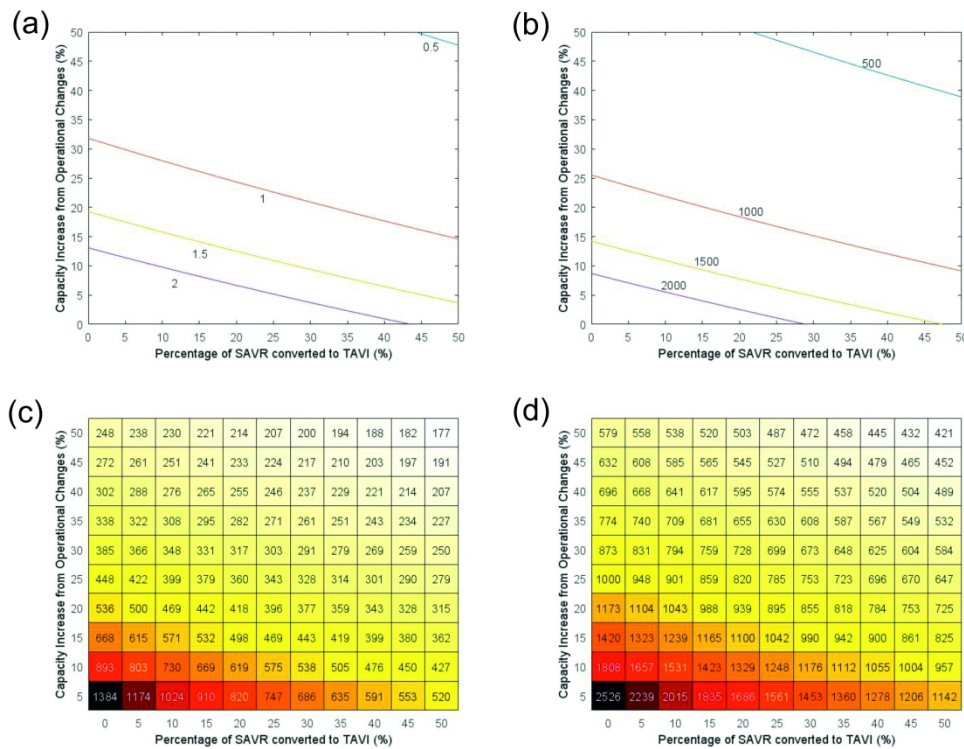


Figure 3: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis) (Presented in two different forms). A) Isoclines of constant mean clearance-time going from half a year (blue) to 2 years (purple) in half-year increments. B) Isoclines of constant mean mortality after clearing the backlog from 500 people (blue) to 2000 (purple) in 500-person increments. C) Heatmap of different combinations of conversion and daily capacity increases and how long the backlog would take to clear on average, in days. D) Heatmap of different combinations of conversion and daily capacity increases and how many people would die, on average.

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SUPPLEMENTS

Supplement 1: Mathematical Derivation of the Differential Equation and its Solution

From figure 1, we can write the following equation:

$$\frac{dW}{dt} = f - r_T - r_S - \mu W.$$

We can then re-write and integrate this equation

$$\int_0^{t_c} 1 dt = \int_{W_0}^0 \frac{1}{f - r_T - r_S - \mu W} dW$$

$$t_c = \left[-\frac{1}{\mu} \ln (f - r_T - r_S - \mu W) \right]_{W_0}^0 = \left[\frac{1}{\mu} \ln (f - r_T - r_S - \mu W) \right]_0^{W_0}.$$

We can now define T_e , the extra capacity, as $T_e = r_T + r_S - f$. This is because we claim that under normal conditions, $f = r_T^0 + r_S^0$, such that the waiting list never grows above zero, and that the additional patients are already on the waiting list. The equation for T_e follows the observation that the current rates of TAVI and SAVR treatment are the normal rates plus the additional capacity.

This substitution allows us to write

$$t_c = \frac{1}{\mu} (\ln (-T_e - \mu W_0) - \ln (-T_e)) = \ln \left(1 + \frac{\mu W_0}{T_e} \right) \mu^{-1}.$$

This is the solution we use for calculating the time when the waiting list becomes zero.

We now rely on the assumption that T_e is constant to write

$$m(t_c) = W_0 - T_e t_c.$$

That is, by the time the waiting list is zero, everyone who has not been treated is unfortunately dead.

The assumption of a front-loaded waiting list (i.e., that all additional patients are identified and waiting) is not a strict requirement for this model to be valid. If it is the case that the additional patients are still being identified when the extra capacity is created, then as long as

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2
3 they are identified at a faster rate than they are treated, the predictions in this model hold. It is
4 only in cases where the identification rate is less than the treatment rate that this assumption
5 becomes invalid. In such cases, T_e can be said to be equal to the identification rate instead.
6
7 This is true because mortality is not tied to being on the waiting list but from the onset of
8 symptoms. In this way, the waiting list in our model can be thought of as the list of all people
9 who need treatment, even if the NHS is unaware of them.
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15 This model can be extended to predict mortality and time to clear a waiting list for non-
16 constant T_e , but we do not expand on that here.
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20 Supplement 2: Data

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23 We calculate the increase in capacity due to conversions and operational changes as follows.
24 Assume that we increase operations by 20% due to operational changes and convert 10% of
25 all SAVR to TAVI. Also assume that for every three SAVR patients five TAVI patients can
26 be processed. If we convert 10% of SAVR cases to TAVI (783 SAVR patients), we can treat
27 an additional 522 patients from the waiting list. From the 20% increase, we get extra 1039
28 TAVI and 1566 SAVR operations per year. If we apply 10% conversion to this extra
29 capacity, 156 SAVR operations can be converted into 260 TAVI operations. In total, the
30 operational changes and conversion create an extra capacity of 3232 operations with which to
31 service the waiting list each year: 1822 (1,039+522+261) TAVI and 1410 (1,566-156) SAVR
32 operations.
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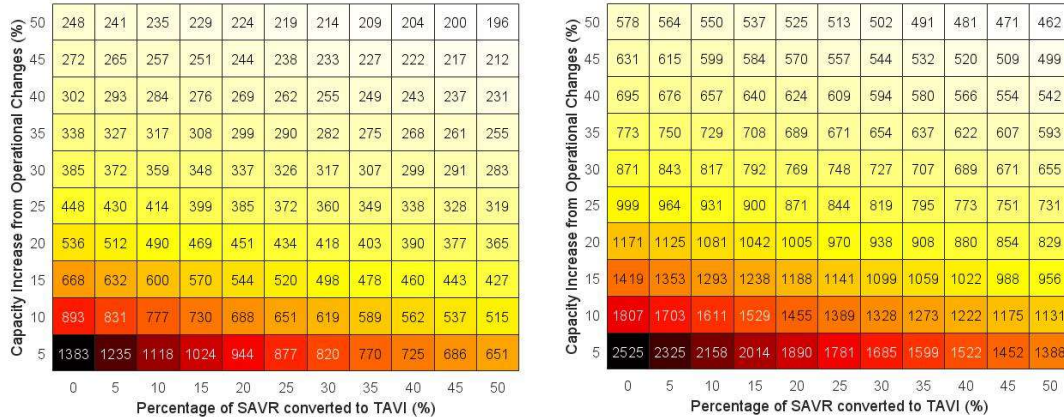
43 N.B. We make no assumptions about who the extra TAVI procedures treat, for example, if in
44 the above example, the additional 626 TAVI procedures we gain from conversion (522 from
45 converting the normal capacity and 104 from converting the additional capacity) treated only
46 SAVR patients, the conversion rate would actually be $\frac{626+783+156}{626+1566+7830} = 15.6\%$. Normally, we
47 would expect that the application of this extra TAVI would be in the same proportion as the
48 ratio of SAVR to TAVI, which would give a real-world conversion rate of 13.5%.
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56 Supplement 3: App

57 The app can be accessed at https://github.com/Christian-P-Stickels/AS_Waitinglist_data
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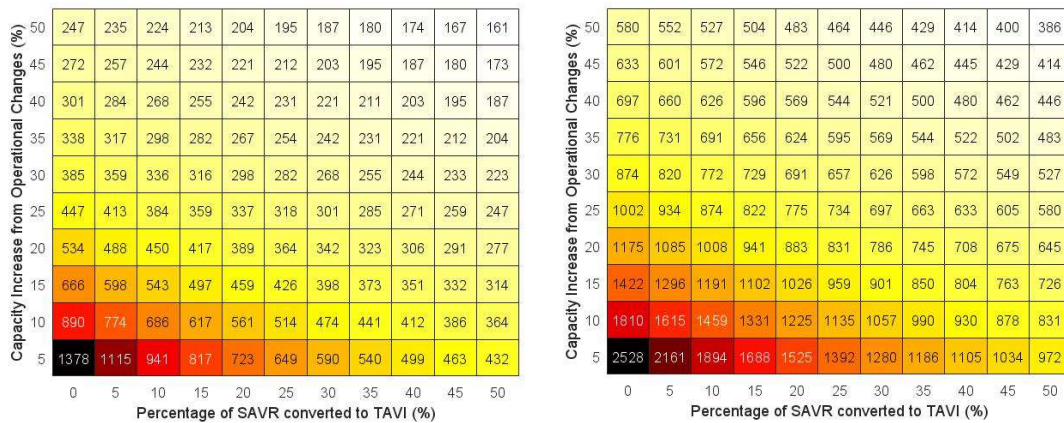
Supplement 4: Additional Results

Supplementary figure S1: Heat map of a three-to-four SAVR-to-TAVI conversion



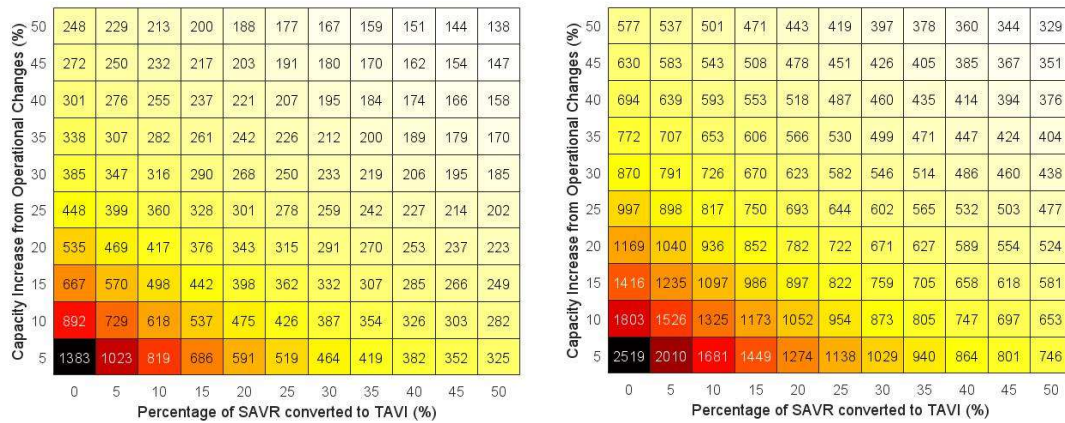
Supplementary Figure S1: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis), assuming that for every three SAVR operations, four TAVI procedures can be performed instead.

Supplementary figure S2: Heat map of a three-to-five SAVR-to-TAVI conversion



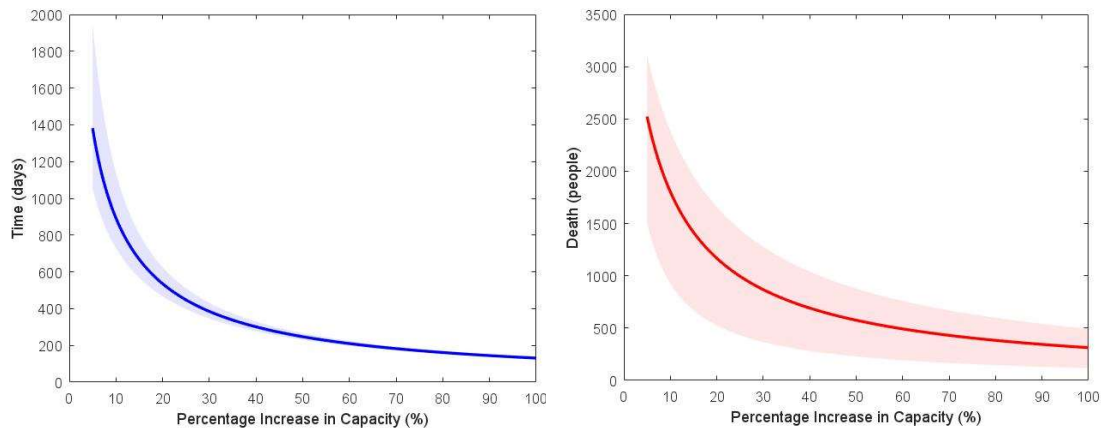
Supplementary Figure S2: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis), assuming that for every three SAVR operations, five TAVI procedures can be performed instead.

Supplementary figure S3: Heat map of a two-to-four SAVR-to-TAVI conversion



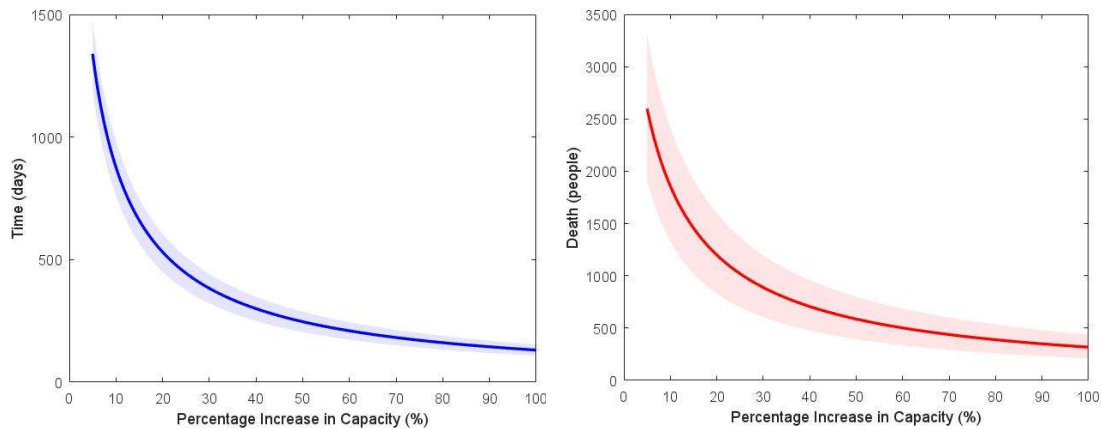
Supplementary Figure S3: Mean time to clear backlog (left) and the resulting deaths (right) as a function of daily percentage increase in capacity (y-axis) and percentage of SAVR converted to TAVI (x-axis), assuming that for every two SAVR operations, four TAVI procedures can be performed instead.

Supplementary figure S4: Error from mortality estimates



Supplementary figure S4: Time to clear backlog (left) and the resulting deaths (right) with associated 95% reference ranges as a function of daily percentage increase in capacity, with uncertainty from mortality only. The x-axis is truncated at 5% for visualisation and clarity.

We find that error in the one-year mortality causes higher uncertainty at lower capacity increases, but at higher capacity increases, this uncertainty decreases until it is almost zero with regards to clearance time. This is likely because at higher capacity increases, more of our waiting list clearance comes from treatment, as opposed to death, resulting in less error.

Supplementary figure S5: Error from wait list (W_0) estimates

Supplementary figure S5: Time to clear backlog (left) and the resulting deaths (right) with associated 95% reference ranges as a function of daily percentage increase in capacity, with uncertainty from initial waiting list estimates only. The x-axis is truncated at 5% for visualisation and clarity.

We find that error in the estimate of the wait list length W_0 causes uncertainty that is fairly constant in the time it takes to clear the backlog and in resultant deaths. This is to be expected as we can show that the uncertainty scales with $\ln W_0$. There is a small decrease in uncertainty as we increase capacity, once again because an increase in capacity results in more control of the waiting list reduction.