Further detail on EAG response to stakeholder comments on monitoring frequency and baseline HFH, and additional EAG results

Point 1: Concerns that monitoring costs are over-stated in the EAG model

Stakeholders raised concerns that the monitoring frequencies used in the economic model are too high, and did not reflect the committee's preferences, which were described as "to calibrate the technology after sensor implantation, then monitor weekly for the weeks 1, 2 and 3, then monitor every 3 months. The monitoring schedule would be repeated from the start if heart failure worsens.", as stated in section 3.18 of the draft guidance.

The EAG updated their base-case in response to a request from NICE to reflect the committee's preferences. However, there was some further clarification between the EAG and NICE on what the committee preferences were, which led to further discussions between the clinical experts on the Committee. Following this, it was agreed with NICE that the EAG would include:

- A single monitoring check during calibration after implantation.
- Monitoring three times per week during the first 3 months (ie 12 checks per month).
- Monthly monitoring thereafter for stable patients, but for those requiring treatment escalation the more frequent monitoring schedule would start again. To model this, we required an estimate of the proportion of patients who would have treatment escalation and re-start the more intensive monitoring each month. Treatment escalation was determined using an average escalation of treatment calculated from the MONITOR-HF and GUIDE HF trials. In MONITOR-HF there was a rate of 0.73 medication changes per patient month, which gives an estimated monthly proportion of medication change of 0.518. In GUIDE-HF there was a rate of 1.031 medication changes per patient month, which gives an estimated monthly proportion of medication change of 0.643. After discussion with the clinical experts on the Committee we agreed to use an average of GUIDE-HF and MONITOR-HF to give a monthly proportion of medication change of 0.5807. The average number of monitoring checks after the first 3 months is therefore estimated to be: 0.5807*12 + 0. 4191*1 = 7.39 checks, which is what we assumed in our updated base-case.

Note that in the request from NICE intensification was stated as being required "if a patient becomes unwell and needs escalation of treatment". This is why the EAG modelled intensification of monitoring following medication changes. The EAG acknowledges that data on medication changes may not just include treatment escalation. To explore the impact of this, we have now run an additional scenario where monitoring is only intensified following a hospitalisation (see scenario analyses provided below).

In addition, we changed the band 5 nurse/cardiac physiologist (costed at £44 per hour) to a band 7 nurse who could prescribe (£67 per hour) in the calculation of the costs, in line with the

Committee's preferences. We also updated the unit cost of a consultant's time in line with the corrected Unit Costs of Health and Social Care 2024 value (£121 per hour).

The updated EAG model was therefore designed to reflect the Committee's preferences, but based on further discussions and clarifications between NICE and the expert clinical members of the Committee following the issuing of the draft guidance.

We recognise that the model is very sensitive to monitoring frequency. To investigate the validity of our assumptions, we extracted reported monitoring frequencies (or monthly minutes of nurse time) from studies identified during the systematic reviews of studies evaluating CardioMEMS and Cordella devices and economic models of PAP monitoring technologies (Table 1 below). We excluded studies reporting only a cost without reporting the frequencies and studies which based their estimates on another study already reported. The frequency of monitoring the PAP device varied from daily to once every two weeks. Furthermore, Abbott's response to our request to supply their recommended monitoring frequency was that "Clinicians are advised that during a period when they are modifying medications they should be reviewing the data from a patient twice-weekly. Once a patient is stable, clinicians are encouraged to set thresholds around the optimal pressure for a patient and enable Merlin to inform them should a patient's pressures deviate from their optimal state. Clinicians are encouraged to proactively review these patients at least once a month."

We note that this Company statement reflects a higher monitoring frequency than the monitoring frequency stated as the Committee's preference in the draft guidance, and used in Abbott's updated modelling.

Finally, we note that the estimates of efficacy of CardioMEMS were based on the monitoring schedules used in the RCTs. Whilst lower monitoring schedules may be used in practice, this may come with a reduction in the effectiveness of the device, although empirical evidence would be required to explore the impact of this.

Table 1: Monitoring frequencies reported for CardioMEMS

Source	Monitoring frequency	Minimum frequency	Nature of estimate
COAST-UK	"Initially, thresholds will be set automatically at the acceptable range. The physician can adjust the thresholds specifically for each patient. These threshold notifications are intended to guide the physician to review the Merlin.net website. Every attempt should be made to keep the pulmonary artery pressures within the specified pulmonary artery pressure ranges utilizing the guidelines. In order to clinically manage patient's PA pressures, the physician must review the PA pressure measurements on a frequent basis, for example, some patients may require a daily review of their PA pressure	Weekly	Recommended

	measurements, while some patients may need a weekly review. The physician or designee has unlimited access to the Merlin.net website." Acceptable PA pressure (optivolaemic) – weekly Elevated PA pressure – at least 2-3 times a week until optivolaemic Low PA pressure – at least 2-3 times a week Medication modifications – at least 2-3 times a week until pressure stabilises Significant deviations in trend data – at least 2-3 times a week until pressure stabilises		
MEMS-HF	"Uploaded PAP information was reviewed at least weekly by local study personnel" "Caregiver adherence to weekly review of PAP data was 89.8 ± 18.7% [100%(87.4–92.2%)]." "Additional PAP reviews were triggered by email notifications of PAP excursions outside the user-defined thresholds automatically issued by the Merlin.net™ system." Frequency of triggers unknown.	Weekly	Reported
CARDIO-MEMS PAS	"Clinicians reviewed PAP at least weekly and used PA pressure goals to guide therapy, even in the absence of change in weight or symptoms."	Weekly	Reported
CHAMPION	"In the treatment group, review of pressure data was done at least once a week and more frequently, if changes occurred in treatment."	Weekly	Reported
MONITOR-HF (Mokri model, Supplementary information)	"The first phase takes place in weeks one and two after implantation (14 days); in these week patients are monitored twice weekly, for a duration of three minutes per patient per monitor. The second phase is from week three to three months after implantation (70 days). In this phase, patient monitoring occurs once a week for three minutes per patient. The third phase runs from 4 to 12 months after implantation (274 days) and involves monitoring the patient once every two weeks, which takes two minutes per patient." "Monitoring costs (PA uploads Merlin.net) were derived from the trial recommendations and multiple clinical experts and nurses who participated in the MONITOR-HF trial	Every 2 weeks	Estimate based on expert clinical opinion of trial participants

	regarding the duration and frequency of the monitoring sessions."		
Dauw et al[a]	"Monitoring cost was estimated at € 25 per patient per month, based upon staffing costs for daily monitoring (1 min/patient/day) and contacting patients (2 min/patient/week) at a rate of € 50/h. The time management estimates were based upon 3 months of daily time registration by monitoring nurses at Ziekenhuis Oost-Limburg."	Daily	Estimate based on reported data
Codina et al	"Monitoring costs were accounted for as a nurse's 30 min salary, which is the daily time a nurse needs to consult the pulmonary pressures of CardioMEMS patients (this process is repeated 5 days a week). Such cost is accounted as €63 per patient per year, given the fact that all patients are covered under that time."	Daily	Not clear how cost was calculated. Implication is that monitoring occurred daily.
Cowie et al (2017)	"A scenario analysis was also performed including the time spent on monitoring patients by a nurse (23–70 min per month). The lower bound of this range is from data collected by L.K. on CardioMEMS patients at his centre, and the upper bound is from a previous telemonitoring study using different technology. Physician time was included at 7 min per month, again from early real-world data collected by L.K. at the University of California, San Francisco, Medical Centre."	23 minutes per month (approx. twice per month[b])	Unpublished data
Cowie et al (2023)	"Monitoring costs were included in the base case analyses and sourced from literature related to CardioMEMS. The cost of remote monitoring was estimated to be £37.60 (~€44) per month based on 40 min of nurse (band 5) and 5 min of physician time, with hourly costs of £41 and £123, respectively (Table 1)."	40 minutes per month (approx. weekly[b])	

[a] Study identified via our systematic reviews but excluded at full-text. [b] Based on 10mins per monitoring check.

Point 2: Model baseline is not reflective of the PAP monitoring patient cohort

Stakeholders state that the use of the Lahoz study under-estimates baseline HFH rates because the UK Clinical Practice Research Datalink (CPRD) population is heterogeneous and less sick/symptomatic than the NYHA Class III population eligible for CardioMEMS.

It is important to note that the EAG model distinguishes between the number of previous HFHs a patient has had, and so the baseline HFH rate that is used reflects those who have had no recurrent HFH (after their index HFH). The Lahoz study was used to inform the **hazard ratios** for those with 1, 2, or 3 previous recurrent HFHs **relative to** the hazard ratio for HFH for those with no recurrent HFH (ie those in state Stable HF1). It was not used directly to inform the baseline HFH rate in Stable HF1. Instead the COAST UK population was used to inform the baseline HFH rate for those with no recurrent HFHs. However, COAST UK enrolled NYHA Class III patients with **at least 1 HFH** in the previous 12 months. COAST UK estimated a rate of 1.52 HFHs, however this would include those with a first recurrent HFH, those with a second recurrent HFH, those with a 3rd recurrent HFH etc, whereas the EAG model needed an estimate for those with 1 prior HFHs for state Stable HF1. We know from Lahoz et al (and other sources) that the risk of HFH increases with the number of previous HFHs a patient has had. 1.52 is therefore an over-estimate of the rate that would be expected in patients in state Stable HF1 (ie those with no previous recurrent HFHs), in order for the weighted average across all Stable HF states in COAST UK to be 1.52. This is why we made an adjustment. Note that in the EAG model the HFH rate in the Stable HF2, Stable HF3, and Stable HF4 states is higher than that in Stable HF1, so that the average across these states is higher than the rate in the Stable HF1 state.

To make the adjustment we used the Lahoz study estimates of the proportions of patients with 0, 1, 2, 3+ previous recurrent HFHs, and the hazard ratios for those with 1, 2, or 3 previous recurrent HFHs **relative to** the HR for HFH for those with no recurrent HFH. We work out the fraction of the total hazard attributable to those with no previous recurrent HFHs, and then apply that to the total hazard from COAST UK to get an estimate of the hazard for those in state Stable HF1. **However**, we have checked our calculation for the adjustment and found an error. We had calculated the weighted hazard rather than the hazard itself. The corrected calculation is to solve:

$$\left(p_0 \times 1 + p_1 HR_{1vs0} + p_2 HR_{2vs0} + p_{3+} HR_{3+vs0}\right) \times Haz_1 = 1.52$$

$$So,$$

$$Haz_1 = \frac{1.52}{\left(p_0 \times 1 + p_1 HR_{1vs0} + p_2 HR_{2vs0} + p_{3+} HR_{3+vs0}\right)}$$

$$Haz_1 = \frac{1.52}{\left(0.7158 \times 1 + 0.182 \times 1.7 + 0.0602 \times 1.86 + 0.042 \times 3.11\right)} = 1.199$$

The resulting estimate is 1.199 with 95%CI (1.022, 1.326), which is modelled on the log-scale with a Normal distribution with mean 0.181 and standard error 0.080.

The same computation error was made in the computation of the mortality rates in Stable HF1 under standard care. The corrected estimates are:

Age-range	Monthly mortality probability	Monthly mortality rate	Corrected adjusted monthly mortality rate	Corrected adjusted monthly mortality probability

60-65	0.0046	0.004611	0.003366	0.003361
65-70	0.00698	0.007004	0.005114	0.005101
70-75	0.01044	0.010495	0.007663	0.007634
75-80	0.01566	0.015784	0.011525	0.011459
80-85	0.02136	0.021591	0.015765	0.015642
85-90	0.02301	0.023279	0.016997	0.016854
90+	0.01864	0.018816	0.013739	0.013645

We have corrected these errors in the EAG updated base-case model (results provided below).

The stakeholders make the valid point that the Lahoz study may provide an underestimate of the HFH rate since the population is likely to be heterogeneous and less sick/symptomatic than a NYHA class II population. If that were the case then the proportions of patients having more previous recurrent HFHs would be lower than in the COAST UK cohort. To adjust for this we would need to increase these proportions in the formula above, which would lead to a **lower** adjusted hazard for Stable HF1 from COAST UK. In other words the company's argument would imply that our (corrected) adjusted baseline hazard rate is in fact too high, rather than too low.

The EAG model does however assume that all patients start in state Stable HF1, ie that patients are implanted when they are NYHA Class III following an index HFH. If there is a mix of previous HFH history in the decision population, then the model would need to be run with a mix of initial starting states, which would give a higher overall HFH rate. To give an indication of the impact of this we have also provided results using the raw HFH rate of 1.52 from COAST UK for comparison. To demonstrate the implications of the assumptions for Stable HF1, we have plotted the implied annualised HFH rate for all patients alive under routine monitoring calculated in the model when we use 1.19 and 1.52 for Stable HF1 respectively (Figure 3). This shows that by 12 months the annualised hazard from the EAG base-case model is aligned with the rate from COAST-UK. The rate increases over time as patients progress to model states with higher HFH rates. When using the raw rate of 1.52 from COAST-UK the HFH rates are much higher.

We acknowledge that we also assume the hazard ratios for those with 1, 2, or 3 previous recurrent HFHs **relative to** the HR for HFH for those with no recurrent HFH (ie those in state Stable HF1) from Lahoz in a general HF population would also apply to a NHYA class III population which may not hold. We are not aware of any other UK based sources which are specific to NHYA class III patients, and so do not have any alternative data sources on which to base these estimates.

Additional results produced by the EAG

After DACM1 NICE requested the EAG to update their model in line with committee preferences. Following clarification with NICE and discussion between the clinical experts on the committee, the EAG made the following assumptions in their base-case model:

1. Adopting the assumptions from Scenario 6c for utilities. This includes using utilities from MONITOR HF for the first 12 months, then applying the state base utilities thereafter.

2. Changing the monitoring schedule to include:
    - A single monitoring check during calibration after implantation.
    - Monitoring three times per week during the first 3 months (ie 12 checks per month).
    - Monthly monitoring thereafter for stable patients, but for those requiring treatment escalation the more frequent monitoring schedule would start again. After discussion with the clinical experts on the Committee we agreed to use an average of GUIDE-HF and MONITOR-HF to give a monthly proportion of medication change of 0.5807. The average number of monitoring checks after the first 3 months is therefore estimated to be: 0.5807*12 + 0. 4191*1 = 7.39 checks, which is what we assumed in our updated base-case.
3. The cost of the professional doing the monitoring was changed from a band 5 nurse/cardiac physiologist (costed at £44 per hour) to a band 7 nurse who could prescribe (£67 per hour) in the calculation of the costs, in line with the Committee's preferences.

In addition, we corrected the EAGs error in the baseline HFH and mortality rates in the Stable HF1 state (as described in Issue 2 above) and also updated the unit cost of a consultant's time in line with the corrected Unit Costs of Health and Social Care 2024 value (£121 per hour), as the EAG were informed by the authors of the unit costs of health and social care 2024 manual that there was an error in the 2024 estimate of the cost per working hour of a medical consultant. These corrections were applied for all scenarios reported in this document.

The corrected updated EAG probabilistic base-case is presented below in Table 2, **Error! Reference source not found.**, and Figure 2, and the deterministic results are labelled as CS1 in Table 3.

In scenarios we explored the impact of using the proportion with medication changes per month from MONITOR-HF (CS2) and GUIDE-HF (CS3) and respectively in the calculation of the monthly proportion with intensive monitoring. We provide a scenario using the lower monitoring frequency in line with that stated as the committee's preference in the draft guidance (CS4), and provide a scenario where intensification of monitoring occurs following HFH (CS5). Finally we provide a scenario where a rate of 1.52 (log-rate 0.419 with standard error 0.08) is used for the baseline HFH for the Stable HF1 state using the unadjusted rate from COAST UK.

Table 2 Probabilistic results of the corrected updated EAG model – using and average of GUIDE-HF/MONITOR HF to estimate treatment escalations (CS1) (10,000 iterations)

	Total costs	Total LYs	Total QALYs	Incremental costs	Incremental QALYs	ICER vs standard care
CardioMEMS	£45,677	4.902	3.057	£7,657	0.243	£31,478
Standard care	£38,020	4.636	2.814	-	-	-

Figure 1 Cost-effectiveness plane for CardioMEMS using the corrected updated EAG model – using and average of GUIDE-HF/MONITOR HF to estimate treatment escalations (CS1)

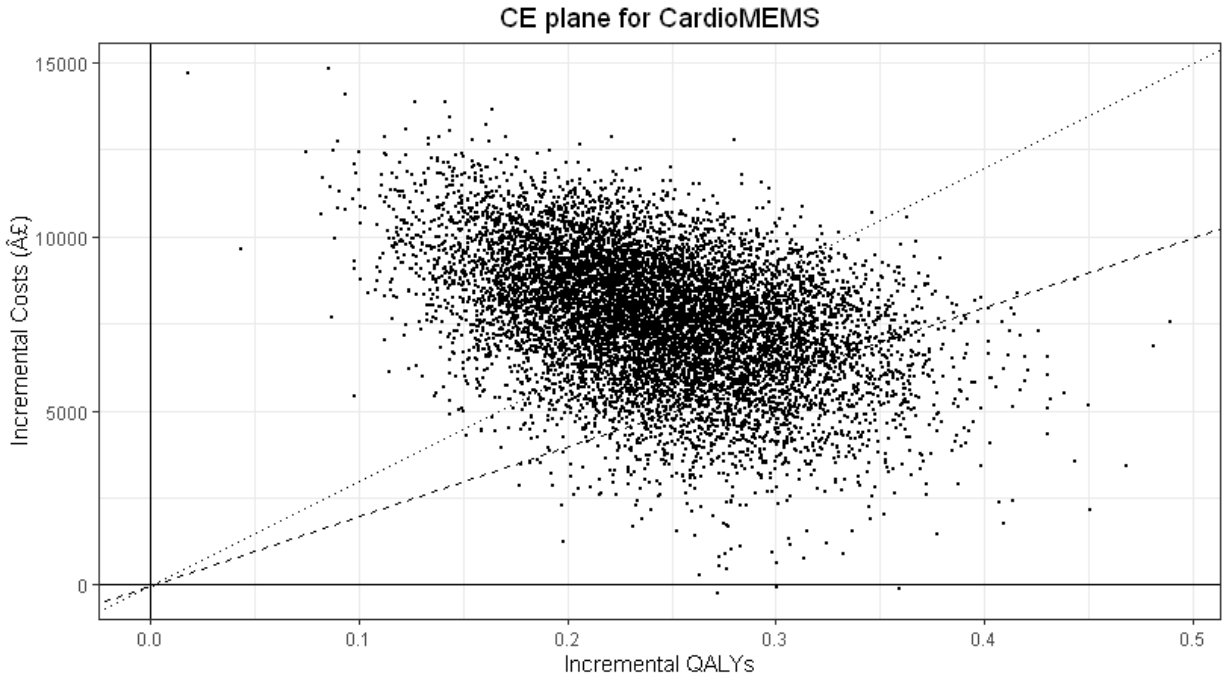


Figure 2 Pairwise cost-effectiveness acceptability curve for CardioMEMS vs standard care using the corrected updated EAG model – using and average of GUIDE-HF/MONITOR HF to estimate treatment escalations (CS1)

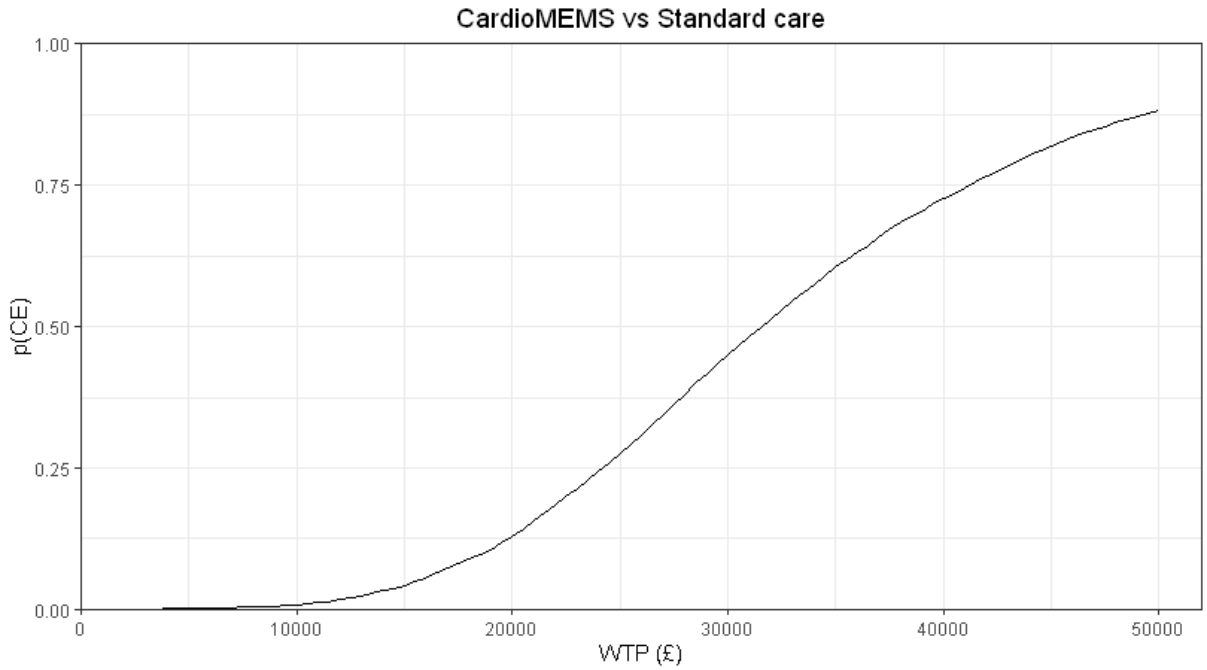
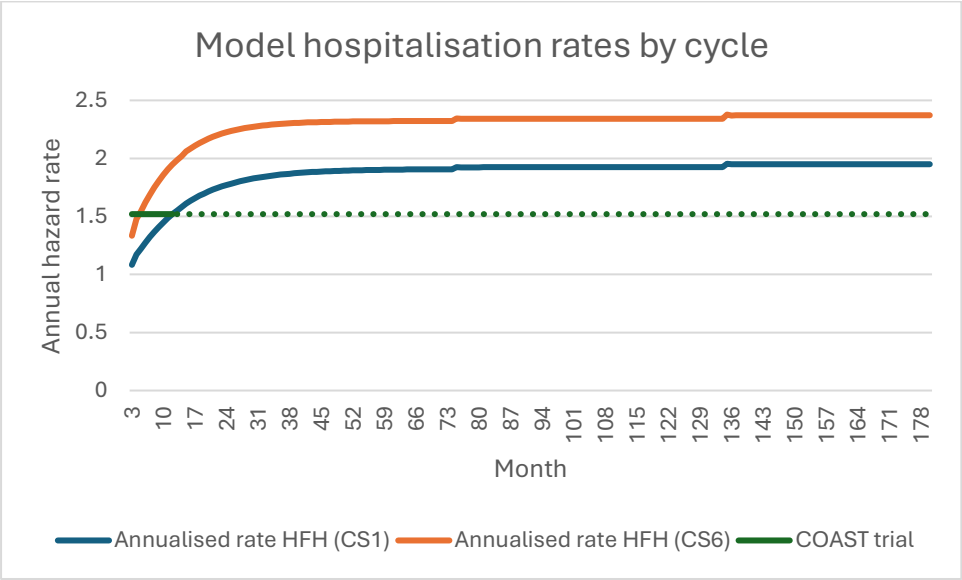


Table 3 Deterministic results of the corrected updated EAG model – using and average of GUIDE-HF/MONITOR HF to estimate treatment escalations (CS1), and various scenarios

	CardioMEMS		**Standard care**		**Incremental**		
Scenario	**Total Costs (£)**	**Total QALYs**	**Total costs (£)**	**Total QALYS**	**Incremental costs (vs SC) (£)**	**Incremental QALYs (vs SC) (£)**	**ICER vs SC (£)**
CS1. Corrected updated EAG base-case – Using GUIDE HF/MONITOR average for treatment escalations	45,395	3.049	37,792	2.806	7,603	0.243	31,264
CS2.As for CS1, but using MONITOR HF for treatment escalations	44,965	3.049	37,792	2.806	7,173	0.243	29,496
CS3.As for CS1, but using GUIDE HF for treatment escalations	49,291	3.049	37,792	2.806	8,029	0.243	33,017
CS4. As for CS1, but using the monitoring schedule stated as the Committee preference in the draft guidance.	41,206	3.049	37,792	2.806	3,413	0.243	14,037

	CardioMEMS		Standard care		Incremental		
Scenario	**Total Costs (£)**	**Total QALYs**	**Total costs (£)**	**Total QALYS**	**Incremental costs (vs SC) (£)**	**Incremental QALYs (vs SC) (£)**	**ICER vs SC (£)**
CS5. As for CS1, but using hospitalisations for monitoring intensification	45,218	3.049	37,792	2.806	4,289	0.243	25,865
CS6. As for CS1, but using a rate of 1.52 for the baseline HFH for state Stable HF1	50,162	2.929	44,176	2.718	5,986	0.212	28,271

Figure 3 Annualised hospitalisation rates over from the corrected updated EAG model (CS1) and under scenario CS6 using the raw COAST-UK baseline HFH rate for Stable HF1 under routine monitoring.



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