APPENDIX

Cost-effectiveness of total hip and knee replacements
for the Australian population with osteoarthritis:
discrete-event simulation model

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1. Epidemiological modelling

1.1. Model outline

The cost-effectiveness analysis of hip and knee replacements employs a discrete-event simulation (DES) model that follows individuals with OA throughout their life courses. The schematic depiction of the model was provided in the Figure 1 of the main text, and hence is not reproduced here. Table A lists all patient attributes and events with the corresponding Sections of this Appendix where the details of the relevant parameters are provided.

Table A: Attributes and events that forme the model

	Parameter description	Section
Patient attributes		
OA grade 2 (asymptomatic)	OA associated with minor DW	1.8
OA grade 2 (symptomatic)	OA associated with moderate DW	1.8
OA grade 3-4 (asymptomatic)	OA associated with moderate DW	1.8
OA grade 3-4 (symptomatic)	OA associated with severe DW	1.8
Well with primary implant	Reduced DW associated with primary implants	1.8
Well with revision implant	Increased DW associated with revised implants	1.8
Death	Includes both deaths from surgery and all other causes	1.6, 1.7
Events		
Entry into the model	All individuals aged 40 and older, with either unilateral or bilateral OA on hips or knees in Australia, 2003	1.2, 1.3
OA progression	Time to progression of OA severity from a grade to the next	1.5
Primary replacement	Time to primary replacement surgery of hips or knees	1.4
Primary implant revision	Time to revision of primary implants due to some failures	1.9
Repeated implant revision	Time to revision of revised implants due to some failures	1.9
Dying from surgery	Probability of dying from hip or knee replacements	1.6
Dying from other causes	Probability of dying from causes other than hip or knee replacements	1.7

OA: osteoarthritis; DW: disability weight

For the purpose of simplifications, the abbreviations provided in Table B are used to describe the OA grades in all parameters appearing in this document.

Table B: Abbreviations for OA severity

<table>
<tr><th>OA grade</th><th colspan="5">Abbreviations</th></tr>
<tr><td>Less than Grade 2</td><td><2A</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Grade 2 (asymptomatic)</td><td>2A</td><td rowspan="4">2A+</td><td></td><td></td><td></td></tr>
<tr><td>Grade 2 (symptomatic)</td><td>2S</td><td rowspan="3">2S+</td><td></td><td rowspan="2">2S3A</td></tr>
<tr><td>Grade 3-4 (asymptomatic)</td><td>3A</td><td rowspan="2">3A+</td></tr>
<tr><td>Grade 3-4 (symptomatic)</td><td>3S</td><td></td></tr>
</table>

1.2. Number of people with hip and knee OA in 2003

The study population was calculated from data available from the Australian Burden of Disease study 2003 [1]. However, the estimated prevalence of people with OA was not divided into hips or knees in the study. In order to derive the number of people with hip OA and knee OA separately with different severities, we first calculated the number of people with OA (hip and knee mixed) with different grades as follows:

$$OAnum_{age}^{2A} = OAprev_{age}^{2A+} \times \left(1 - OAprop_{age}^{3A+}\right) \times \left(1 - OAprop_{age}^{2S}\right) \times Pop_{age}^{2003}$$
$$OAnum_{age}^{2S} = OAprev_{age}^{2A+} \times \left(1 - OAprop_{age}^{3A+}\right) \times OAprop_{age}^{2S} \times Pop_{age}^{2003}$$
$$OAnum_{age}^{3A} = OAprev_{age}^{2A+} \times OAprop_{age}^{3A+} \times \left(1 - OAprop_{age}^{3S}\right) \times Pop_{age}^{2003}$$
$$OAnum_{age}^{3S} = OAprev_{age}^{2A+} \times OAprop_{age}^{3A+} \times OAprop_{age}^{3S} \times Pop_{age}^{2003}$$

where

$OAnum_{age}^{2A/2S/3A/3S}$ is the number of people with OA at each severity and each age-group in 2003;

$OAprev_{age}^{2A+}$ is the OA prevalence rate with grade 2A or higher at each age-group in 2003 (obtained from the Burden of Disease study 2003);

$OAprop_{age}^{3A+/2S/3S}$ is the proportion of people with OA of grade 3A+, and the proportion of for grades 2S and 3S at each age-group derived from Felson and Guccione et al.[2,3]; and

Pop_{age}^{2003} is the age-group specific number of Australian population in 2003.

Second, we calculated the number of hip and knee replacement surgeries due to OA that were conducted in Australia in 2003 [4]:

$$Snum_{age}^{hipOA} = Snum_{age}^{hip} \times SpropOA_{age}^{hip}$$
$$Snum_{age}^{kneeOA} = Snum_{age}^{knee} \times SpropOA_{age}^{knee}$$

where

$Snum_{age}^{hipOA/kneeOA}$ is the number of primary replacement surgeries for hip or knee (total hip and knee, hip resurfacing, unicompartmental knee) in each age-group in 2003 due to OA;

$Snum_{age}^{hip/knee}$ is the number of primary replacement surgeries for hip or knee (total hip & knee, hip resurfacing, unicompartmental knee) in each age-group in 2003 from all causes; and

$SpropOA_{age}^{hip/knee}$ is the proportion of people with OA who underwent primary replacement surgeries for hip or knee (total hip & knee, hip resurfacing, unicompartmental knee) in each age-group in 2003.

Finally, we derived the number of people with hip and knee OA in 2003:

$$OAnum_{age}^{hip2A/2S/3A/3S} = OAnum_{age}^{2A/2S/3A/3S} \times \frac{Snum_{age}^{hipOA}}{Snum_{age}^{hipOA} + Snum_{age}^{kneeOA}}$$
$$OAnum_{age}^{knee2A/2S/3A/3S} = OAnum_{age}^{2A/2S/3A/3S} \times \frac{Snum_{age}^{kneeOA}}{Snum_{age}^{hipOA} + Snum_{age}^{kneeOA}}$$

where

$OAnum_{age}^{hip/knee,2A/2S/3A/3S}$ is the number of hip or knee OA at each grade in each age-group in 2003.

The underlying assumption for the derivation was that the proportion between numbers of hip OA and knee OA is equivalent to the proportion between numbers of hip replacement and knee replacement surgeries conducted for OA in Australia.

Tables C and D provide the estimated number of people with hip and knee OA for grade 2S+ on at least one joint for each age-group in 2003. These people entered the model.

Table C: Number of hip OA in each grade for each age-group in 2003

Age	Male (Total 30,347)			Female (Total 38,562)		
	2S	3A	3S	2S	3A	3S
40-44	201	889	355	90	321	128
45-49	325	1,436	573	199	712	284
50-54	460	2,032	811	330	1,181	471
55-59	385	1,701	679	344	1,228	490
60-64	428	1,888	754	483	1,728	690
65-69	448	1,977	789	641	2,292	915
70-74	518	2,287	913	828	2,962	1,182
75-79	491	2,717	1,085	1,061	3,634	1,451
80-84	358	1,982	791	1,000	3,427	1,368
85-89	237	1,313	524	930	3,187	1,272
90-94	87	481	192	474	1,622	648
95-99	21	118	47	143	488	195
100+	6	34	14	28	96	38
Total	3,965	18,855	7,527	6,551	22,878	9,132

Table D: Number of knee OA in each grade for each age-group in 2003

Age	Male (Total 42,930)			Female (Total 57,728)		
	2S	3A	3S	2S	3A	3S
40-44	201	889	355	82	295	118
45-49	325	1,437	573	183	653	261
50-54	460	2,032	811	303	1,084	433
55-59	561	2,475	988	576	2,057	821
60-64	622	2,748	1,097	810	2,895	1,156
65-69	749	3,308	1,321	1,126	4,024	1,606
70-74	867	3,827	1,528	1,454	5,198	2,075
75-79	837	4,637	1,851	1,871	6,407	2,558
80-84	611	3,384	1,351	1,764	6,042	2,412
85-89	238	1,318	526	965	3,306	1,320
90-94	87	482	193	491	1,683	672
95-99	21	119	47	148	507	202
100+	6	34	14	29	100	40
Total	5,585	26,690	10,655	9,802	34,251	13,674

1.3. Proportion of bilateral hip and knee OA

Once the number of people with hip OA and knee OA were derived with different severities, further modelling was required to estimate the proportion of people with bilateral OA in 2003. This was necessary in order to account for the dual nature of OA and simulate the progression of OA and surgeries between two joints separately. The proportion of bilateral OA was estimated from literature findings by means of weighted average[5-13].

$$BIprop_{BB}^{hip/knee} = \frac{\sum(BIprop_n^{hip/knee} \times N_n)}{\sum N_n}$$

$$BIprop_{BA}^{hip/knee} = 1 - BIprop_{2S3A\_2S3A}^{hip/knee}$$

$$BIprop_{2S3A\_3S}^{hip/knee} = BIprop_{2S3A\_2S3A}^{hip/knee} \times \frac{OAnum_{all\ age}^{\frac{hip}{knee},2S3A}}{OAnum_{all\ age}^{hip/knee,2S+}}$$

$$BIprop_{3S\_3S}^{hip/knee} = BIprop_{2S3A\_2S3A}^{hip/knee} \times \frac{OAnum_{all\ age}^{\frac{hip}{knee},3S}}{OAnum_{all\ age}^{hip/knee,2S+}}$$

$$BIprop_{3S\_2A}^{hip/knee} = 1 - BIprop_{2S3A\_3S}^{hip/knee} - BIprop_{3S\_3S}^{hip/knee}$$

where

2S3A_2A/2S3A_2S3A /2S3A_3S/3S_2A/3S_3S is an OA state with one hip/knee at state 2S3A or 3S, and the other one at state 2A, 2S3A B or 3S;

$BIprop_{2S3A\_2S3A\ /2S3A\_2A/2S3A\_3S/3S\_2A/3S\_3S}^{hip/knee}$ is the proportion of bilateral OA for each OA state;

$BIprop_n^{hip/knee}$ is the proportion of bilateral OA from the nth literature; and

N_n is the sample size of the study in the nth literature.

The estimated probabilities to have bilateral OA from the above equations are provided in Table E.

Table E: Probability of having bilateral OA

	Male		Female	
Other joint (no.2) / Worse joint (no.1)	2S3A	3S	2S3A	3S
Hip 2S3A	28.3%	-	28.3%	-
Hip 3S	21.3%	7.0%	21.6%	6.7%
Knee 2S3A	61.3%	-	61.3%	-
Knee 3S	46.1%	15.2%	14.5%	46.8%

1.4. Time to primary joint replacement

A person with OA is eligible for hip or knee replacement surgery once the person reached the highest OA severity (3S) and non-surgical therapies are no longer capable in managing the symptoms. However, not all individuals will immediately receive replacements due to waiting time and personal preference. In order to model the time to primary replacement surgery, we first calculated the remission rates (joint replacement rates) for hip and knee OA in 2003 for each age-group based on the information from the Australian burden of disease and injury study as follows [1]:

$$REMnum_{age}^{2A+} = REMrate_{age}^{2A+} \times OAprev_{age}^{2A+} \times Pop_{age}^{2003}$$

$$REMrate_{age}^{hip/knee2S+} = \left[REMnum_{age}^{2A+} \times \frac{Snum_{age}^{hip/kneeOA}}{Snum_{age}^{hipOA} + Snum_{age}^{kneeOA}} \right] \div OAnum_{age}^{hip/knee2S+}$$

$$REMrate_{age}^{hip/knee3S} = \left[REMnum_{age}^{2A+} \times \frac{Snum_{age}^{hip/kneeOA}}{Snum_{age}^{hipOA} + Snum_{age}^{kneeOA}} \right] \div OAnum_{age}^{hip/knee3S}$$

where

$REMnum_{age}^{2A+}$ is the number of OA remissions (hip or knee replacement) in each age-group in 2003;

$REMrate_{age}^{2A+}$ is the remission rate (hip or knee replacement) of hip or knee OA at grade 2A or higher in each age-group obtained from ABOD 2003; and

$REMrate_{age}^{hip/knee2S+,hip/knee3S}$ is the remission rate (hip or knee replacement) of hip or knee OA at grade 2S or higher, or grade 3S estimated for each age-group in 2003.

The derived age-specific remission rates now provide the probability of undergoing replacement surgeries at each age which were given an Empirical distribution to model the time to primary hip or knee replacement in the simulation along the life course of each patient.

1.5. Progression of OA to a higher severity

As mentioned above, only persons with the highest severity of OA (3S) are eligible for the replacement surgery. The severity of OA that were less at the initial stage of the simulation will gradually progress over time until the joint becomes eligible for surgery. In order to model the progression of OA, we utilised information from literature and applied to the following equations:

$$OA_{age}^{2A\ to\ 2S3A} = 1 - e^{-\left(-\frac{\ln[1-\{(Mild0-Mild8)+(None0-None8)\}\div Mild8]}{8years}\right)}$$

$$OA_{age}^{2S3A\ to\ 3S} = \left[\left(OAnum_{age}^{2S3A} + OAnum_{age}^{3S}\right) \times \left(1 - REMrate_{age}^{2S+}\right) \times REMrate_{age}^{2S+} - REMrate_{age}^{3S} \times \left(OAnum_{age}^{3S} - OAnum_{age}^{3S} \times REMrate_{age}^{3S}\right)\right] \div \left(OAnum_{age}^{2S3A} \times REMrate_{age}^{3S}\right)$$

where

$OA_{age}^{2A\ to\ 2S3A;\ 2S3A\ to\ 3S}$ is the probability of a person to progress from OA grade 2A to 2S3A or from grade 2S3A to 3S at each age;

$Mild0/8$ is the number of people with OA (assumed comparable to grade 2A) at the beginning of study or eight years after in Dieppe et al.[14];

$None0/8$ is the number of people with OA (assumed comparable to grade <2A) at the beginning of study or eight years after in Dieppe et al.[14]; and

$8years$ is the length of follow up of people with OA in Dieppe et al.[14]

$OA_{age}^{2S/3A\ to\ 3S}$ was set to satisfy $OAnum_{age}^{2S+} \times REMrate_{age}^{2S+} = OAnum_{age}^{3S} \times REMrate_{age}^{3S}$

1.6. Probability of dying from hip or knee replacement surgeries

Once an OA patient becomes eligible for surgery and selects to undergo replacement, the person receives the operation. However, hip and knee replacement surgeries are not without the risk for mortality. Therefore the probability of surgical death was extrapolated from data obtained from the Canadian joint replacement registry[15], which was adjusted to distinguish the risks between primary and revision surgeries (Table F).

Table F: Probability of dying from surgery

Age	Hip primary	Hip revision	Knee primary	Knee revision
<75	0.00198	0.00368	0.00099	0.00160
75-84	0.00853	0.01581	0.00387	0.00626
85+	0.04174	0.07731	0.00736	0.01189

The model was designed so that a random draw from a value between 0 and 1 is compared with the probability. If the drawn value is greater than the probability, the surgery was deemed success (with or without complications), while a smaller value results in surgical death. The following provides the mathematical background in estimating these probabilities

$$Sdeath_{Prim}{}_{age}^{hip/knee} = \frac{Sdeath_{CA}{}_{age}^{hip/knee}}{PropPrim_{CA}{}_{age}^{hip/knee} + PropRev_{CA}{}_{age}^{hip/knee} \times \frac{DeathRev_{AU}^{hip/knee}}{DeathPrim_{AU}^{hip/knee}}}$$

$$Sdeath_{Rev}{}_{age}^{hip/knee} = Sdeath_{Prim}{}_{age}^{hip/knee} \times \frac{DeathRev_{AU}^{hip/knee}}{DeathPrim_{AU}^{hip/knee}}$$

where

$Sdeath_{CA}{}_{age}^{hip/knee}$ is the surgical death rate in Canada for hip or knee replacement (primary and revision mixed) at each age-group;

$Sdeath_{Prim/Rev}{}_{age}^{hip/knee}$ is the extrapolated surgical death rate in Australia for hip or knee, primary or revision replacements for each age-group;

$PropPrim/Rev_{CA}{}_{age}^{hip/knee}$ is the proportion of primary and revision surgeries conducted for hips or knees in each age-group in 2005-2006, Canada; and

$DeathPrim/Rev_{AU}^{hip/knee}$ is the death rate per person years following hip or knee replacements for primary or revision surgeries between 1999 and 2005 in Australia.

1.7. Probability of dying from non-surgical causes among people with OA

Although OA itself is not a life-threatening disease, its presence increases the risk of overall mortality among the patients [16]. In order to adjust for this excess mortality among OA patients, the probability of dying from non-surgical causes was adjusted as follows:

$$NSdeath_{age}^{OA} = 1 - e^{-\left(\frac{Mort_{age}^{popn}}{OAprev_{age}^{2A+} \times RR + (1 - OAprev_{age}^{2A+}) \times 1}\right)}$$

$$Death_{age}^{popn} = NSdeath_{age}^{OA} \times RR$$

where

$NSdeath_{age}^{OA}$ is the probability of dying among people with OA in each age-group from other causes than hip or knee replacement surgeries;

$Death_{age}^{popn}$ is the probability of dying among people without OA in each age-group;

$Mort_{age}^{popn}$ is the background mortality rate of Australian population for each age-group in 2003; and

RR is the relative risk of dying among people with OA compared to without, which was assumed 1.1 in the Burden of Disease study 2003.

1.8. Health gains

Once an OA patient undergoes a hip or knee replacement surgery with success (i.e. survived surgery), the person benefits from an improvement in the quality of life and a reduction in the probability of dying. Such health gains were modelled through the differences in DALYs faced by the people between intervention and comparator by using the DW obtained from the Burden of Disease study 2003. The following sections describe how the health gains were modelled in the simulation.

Reduction of probability of dying

It was assumed that the probability of dying would be reduced to the level of population without OA when none of the hips or knees fell in OA grades 2S, 3A and 3S.

$NSdeath_{age}^{OA} \rightarrow Death_{age}^{popn}$.

However, if one hip or knee was replaced but not the other one, and if the other one was in OA grades 2S, 3A or 3S, then the person was deemed to be subject to the probability of dying of people with OA.

Improvements in quality of life

We first derived the adjusted DW for one hip or knee from the original DW used in the Australian Burden of Disease study 2003. This adjustment was made in order to account for the dual nature of joints so that people with bilateral OA have severer disability than those with unilateral OA. We used the Solver function of Microsoft Excel to calculate the adjusted DW so that it satisfied:

$$(1 - DW_u) \times OAnum_{age}^{hip/knee,2A/2S3A/3S} = (1 - DW_a) \times \left(1 - BIprop_{AA/BB/CC}^{hip/knee}\right) \times OAnum_{all\ age}^{hip/knee,2A/2S3A/3S} + (1 - DW_a)^2 \times BIprop_{AA/BB/CC}^{hip/knee} \times OAnum_{all\ age}^{hip/knee,2A/2S3A/3S}$$

where

DW_u is the original DW of OA obtained from Burden of Disease study 2003 (i.e. per person); and

DW_a is the adjusted DW of OA for one hip or knee (i.e. per joint).

The concept of this equation is to redistribute the total amount of disability of OA experienced by the Australian population in 2003 to the estimated number of affected joints rather than to the number of patients. The total DW for two hips or knees is then calculated:

$$DW_a^{both\ hip/knee} = 1 - (1 - DW_a^{right\ hip/knee}) \times (1 - DW_a^{left\ hip/knee}) .$$

Table G provides the values of both DWs.

Table G: Disability weights

OA severity	Hip		Knee	
	Original DW	Adjusted DW	Original DW	Adjusted DW
2A	0.01	0.00781	0.01	0.00622
2S3A	0.14	0.11190	0.14	0.08989
3S	0.42	0.35523	0.42	0.29309

We used different approaches to calculate the effect sizes and post-surgical DWs for hip and knee replacements.

Hip replacement

To estimate the effect of hip replacement on the DW, we used the regression model from Briggs et al.[17] to estimate the DW for post replacement.

$$Effect_n^{hip,primary/revision} = \frac{1 - EQpost_{age}}{1 - EQpre_{age}}$$

$$DWpost_{age}^{hip,primary/revision} = Effect_n^{hip,primary/revision} \times DW_a$$

where

$Effect_n^{hip,primary/revision}$ is the effect size of hip replacement for primary replacement or revision;

$EQpre/post$ is the calculated EuroQol score of pre/post hip replacement at each age; and

$DWpost_{age}^{hip,primary/revision}$ is the post hip replacement DW for one hip at each age.

The regression coefficients and their correlations are provided in Tables H and I. We used the median value amongst $DWpost_{age}^{hip,primary/revision}$ calculated for ages between 40 and 100 for all ages. The values of effect sizes provided in Table 2 of the main text were obtained by running a Monte Carlo simulation with 5,000 iterations by assuming normal distributions for each regression coefficient in Table H.

Table H: Regression coefficients for EQ-5D index estimation (hip replacement)

Variable	Pre-surgery			Post-surgery		
	Coefficient	Standard error	P-value	Coefficient	Standard error	P-value
Constant	-0.456	0.040	0.000	-1.658	0.077	0.000
Age	-0.001	0.001	0.372	0.001	0.002	0.692
Male	-0.188	0.031	0.000	-0.226	0.058	0.000
Revision	0.042	0.038	0.267	0.503	0.058	0.000

Source: Briggs et al.[17]

Table I: Correlation between coefficients (hip replacement)

Variable	Pre-surgery				Post-surgery			
	Constant	Age	Male	Revision	Constant	Age	Male	Revision
Constant	1				1			
Age	-0.839	1			-0.838	1		
Male	-0.381	0.063	1		-0.351	0.043	1	
Revision	-0.196	0.010	-0.029	1	-0.332	0.032	0.033	1

Source: Briggs et al.[17]

For an example, the pre-surgery score of a 70 years old male patient who undertakes a revision of his hip implant was calculated as:

$$-0.456 - 0.001 \times 70 - 0.188 \times 1 + 0.042 \times 1 = -0.672.$$

Since the regression model underwent a non-liner transformation g(y) = ln(1–y) where y is the EQ-5D score, the estimated value was back transformed to the original EQ-5D score:

$$1 - Exp(-0.672) = 0.489.$$

It should be noted that this example used the point estimates of regression coefficients (without accounting for the standard errors). When running the simulation model with uncertainty, the values drawn from the assumed normal distribution of each regression coefficient are constrained by the correlation coefficients provided in Table I so that they are correlated with each other.

Knee replacement

To estimate the effect of knee replacement on the DW, we used the literature reporting pre and post scores of EQ-5D, HAQ, and SF-36 (converted to a single index by means of TTU method) [18] and estimated the effect size of individual study as:

$$Effect_n^{knee,M/F} = \frac{\left[\left(1 - PYLD_{mean\ age\ n}^{M/F}\right) - Score_n^{post}\right] \div \left(1 - PYLD_{mean\ age\ n}^{M/F}\right)}{\left[\left(1 - PYLD_{mean\ age+1\ n}^{M/F}\right) - Score_n^{pre}\right] \div \left(1 - PYLD_{mean\ age+1\ n}^{M/F}\right)}$$

where

$Effect_n^{knee,M/F}$ is the effect size of knee replacement for male or female derived from the nth literature;

$PYLD_{mean\ age/+1\ n}^{M/F}$ is the prevalent years lived with disability of the Australian males or females obtained from the Burden of Disease study 2003 at the mean age or one year older of the study sample in the nth literature (this was included to account for the age variations of samples between literature); and

$Score_n^{pre/post}$ is the single index reported or converted from EQ-5D, HAQ, and SF-36 of pre/post knee replacement in the nth literature,

and performed a non-parametric bootstrap with 5,000 iterations to obtain the mean values and 95% CI of the effect size (Male: 0.5202, 0.3888–0.6606; Female: 0.5205, 0.3891–0.6580; other values are provided in Table 2 of the main text). The list of literature used for this modelling is provided in Table J.

The DW of post knee replacement was then calculated as:

$$DWpost_{M/F}^{knee,primary} = DW_a^{knee} \times Effect_{M/F}$$

where

$DWpost_{M/F}^{knee,primary}$ is the post primary replacement DW of knee for male or female;

DW_a^{knee} is the pre replacement DW of one knee; and

$Effect_{M/F}$ is the effect size of knee replacement for male or female obtained from bootstrap.

The post surgery DW for knee revision was derived by applying the information of DW for post replacement DW of hip and post revision DW of hip:

$$DWpost_{M/F}^{knee,revision} = DW_a^{knee} - \frac{DW_a^{hip} - DWpost_{M/F}^{hip,revision}}{DW_a^{hip} - DWpost_{M/F}^{hip,primary}} \times (DW_a^{knee} - DWpost_{M/F}^{knee,primary})$$

where

$DWpost_{M/F}^{knee,revision}$ is the post revision replacement DW of knee for male or female;

DW_a^{hip} is the pre replacement DW of one hip; and

$DWpost_{M/F}^{hip,primary/revision}$ is the post primary or revision replacement DW of hip for male or female.

Finally, the DW of a person at each age was calculated as follows:

$$DW_{age}^{person\ hip/knee} = 1 - \left(1 - DW_a^{both\ hip/knee}\right) \times \left(1 - PYLD_{age}\right)$$

where

$DW_{age}^{person\ hip/knee}$ is the DW of a person who originally had hip or knee OA, may or may not have undergone replacement surgeries for each hip or knee, at each age; and

$DW_a^{both\ hip/knee}$ is the DW of both hips or knees of a person who originally had hip or knee OA, may or may not have undergone replacement surgeries for each hip or knee.

Table J: Literature and indexes included for bootstrap (knee replacement)

Literature	Sample size	Index	Transformed index	
			Pre-surgery	Post-surgery
Brazier et al.[19]	109	EQ-5D	0.45[a]	0.54[a]
	109	HAQ	0.37[a]	0.43[a]
	109	SF-36	0.39	0.50
van Essen GJ et al.[20]	73	SF-36	0.47	0.56
Bennett KJ et al.[21]	41	SF-36	0.42	0.46
Dawson J et al.[22]	117	SF-36	0.40	0.59
Heck DA et al.[23]	291	SF-36	0.45	0.65
Kiebzak GM et al.[24]	78	SF-36	0.46	0.55
Shields RK et al.[25]	24	SF-36	0.53	0.73
Jones CA et al.[26]	276	SF-36	0.39	0.58
Jones CA et al.[27]	222	SF-36	0.39	0.60
	35	SF-36	0.37	0.54
Bachmeier CJ et al.[28]	108	SF-36	0.43	0.63
Bayley KB et al.[29]	117	SF-36	0.50	0.65
Hozack WJ et al.[30]	149	SF-36	0.50	0.65
Kiebzak GM et al.[31]	235	SF-36	0.45	0.60

[a] These indexes are original values

1.9. Time to revision of hip and knee implants

Once an OA patient has undergone a jip or knee primary replacement, the next issue is on the durability of implants before they need to be revised. Such time to failure of implants was assumed to be caused either by short-run or long-run causes. We assumed separate Weibull distributions for each cause and derived two cumulative density curves. The time to revision was modelled as the weighted and normalised sum of these two curves by fitting the estimated values to the observed values from literature (see main text for reference) by means of weighted least square. The Solver function of Microsoft Excel was used for the calculation.

$$TTFcomb_{age} = TTFshort_{age} \times WTshort_{age} + TTFlong_{age} \times (1 - WTshort_{age})$$

where $TTFshort/long/comb_{age}$ is the probability density of time to failure of hip or knee implants at short-term, long-term, or both combined, for primary/revision for hip/knee in each age-group, and $WTshort_{age}$ is the weight of short-term cause of failure of hip or knee implants for primary/revision surgeries in each age-group. We defined the "weight" as the probability of a failure being attributed to short-term cause over long-term, and so the weight of long-term cause is calculated as 1 – (weight of short-term cause). These weights were simultaneously estimated by the Solver function so that the combined mixture distribution would best fit to the observed values. Table K provides the sources of data used in modelling the time to failure/revision of hip and knee implants.

Table K: Data used to model the time to failure of joint implants

	Hip implant	Knee implant
Short-term		
Primary	Australian joint replacement registry 2008[32]	Australian joint replacement registry 2008[32]
Revision	ditto	ditto
Long-term		
Primary	Schulte et al.,[33] Madey et al.,[34] Callaghan et al.,[35] Callaghan et al.[36]	Rand et al.[37]
Revision	Schreurs et al.[38]	Rand & Ilstrup.[39]

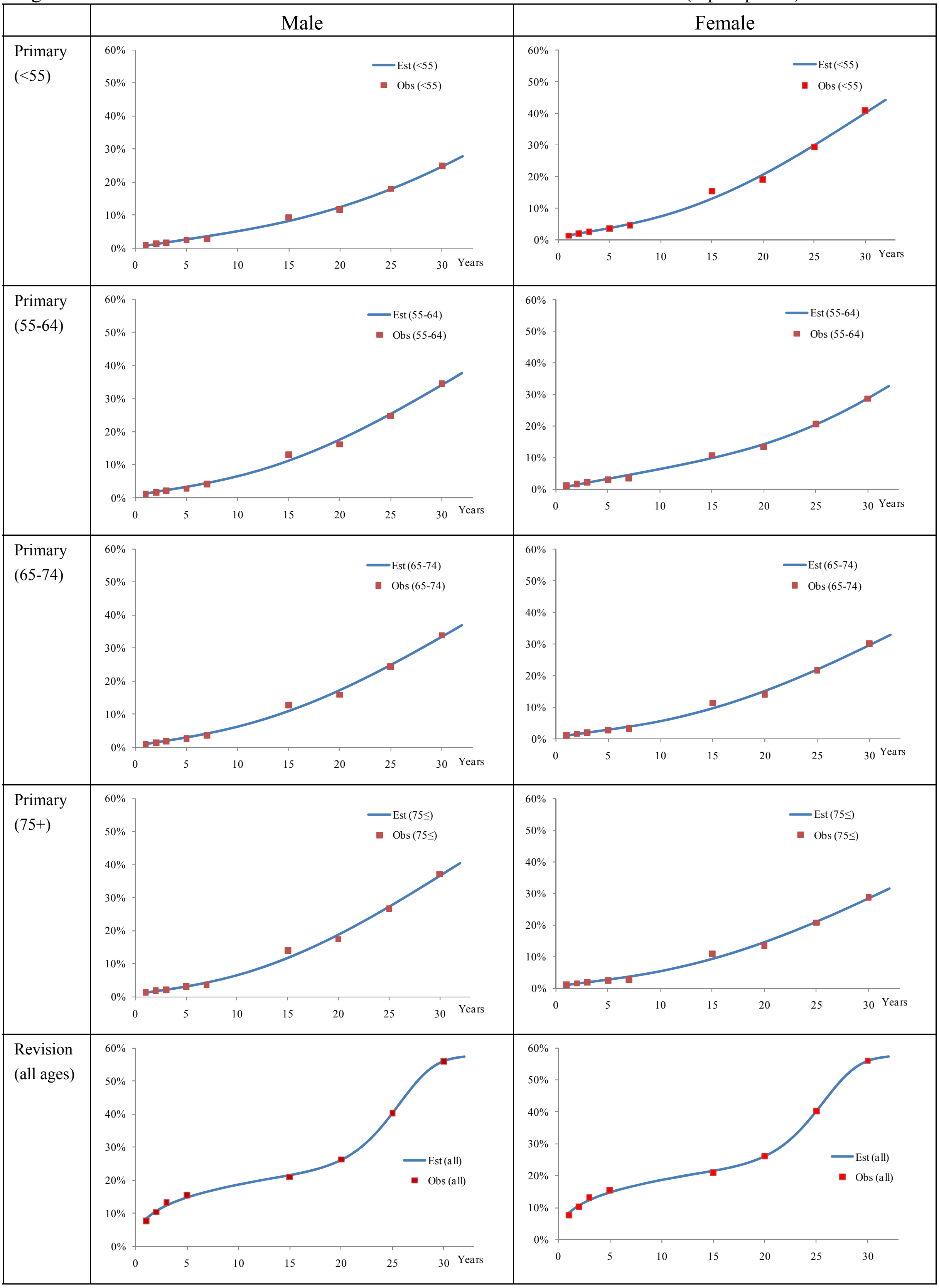
The Weibull parameters estimated to model the time to failure/revision are provided in Table L. Alpha represents the scale parameter and Beta the shape parameter.

Table L Weibull parameters for time to failure of hip or knee implants

Type	Term	Age	Male			Female		
			Alpha	Beta	Weight	Alpha	Beta	Weight
Hip								
Primary	Short	<55	0.87	45.51	0.18	0.56	152.96	0.23
		55-64	0.57	240.21	0.27	0.99	101.56	0.64
		65-74	0.66	172.30	0.26	0.57	397.46	0.31
		75+	0.43	274.13	0.15	0.58	412.47	0.30
	Long	<55	2.84	51.90	0.82	2.43	38.32	0.77
		55-64	2.38	41.67	0.73	4.25	36.90	0.36
		65-74	2.34	42.67	0.74	2.39	43.38	0.69
		75+	2.24	42.11	0.85	2.34	44.92	0.70
Revision	Short	All	0.39	200.36	0.70	0.39	200.36	0.70
	Long	All	8.92	26.05	0.30	8.92	26.05	0.30
Knee								
Primary	Short	<55	0.55	131.27	0.50	0.66	149.67	0.68
		55-64	0.32	241.20	0.10	0.69	409.25	0.13
		65-74	0.71	846.51	0.39	0.70	947.36	0.37
		75+	1.58	658.23	0.28	1.69	559.00	0.28
	Long	<55	2.98	29.88	0.50	3.64	27.20	0.32
		55-64	1.62	40.83	0.90	1.60	45.15	0.87
		65-74	1.66	28.66	0.61	1.61	34.31	0.63
		75+	1.62	31.54	0.72	1.62	32.46	0.72
Revision	Short	All	1.44	1.91	0.17	1.44	1.91	0.17
	Long	All	2.48	21.13	0.83	2.48	21.13	0.83

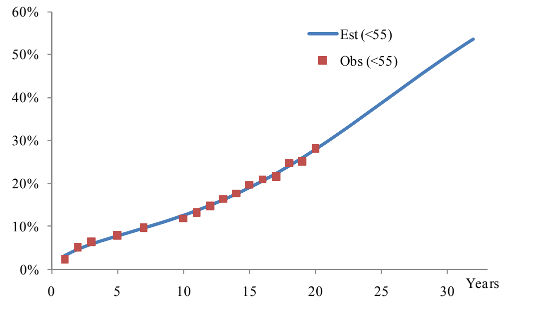
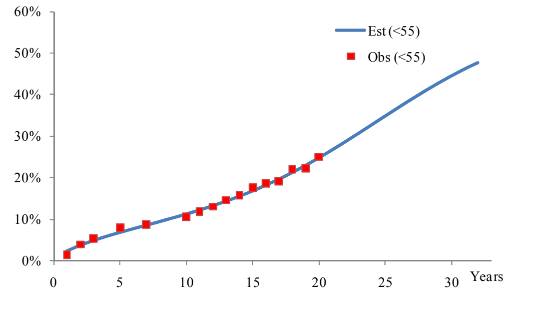
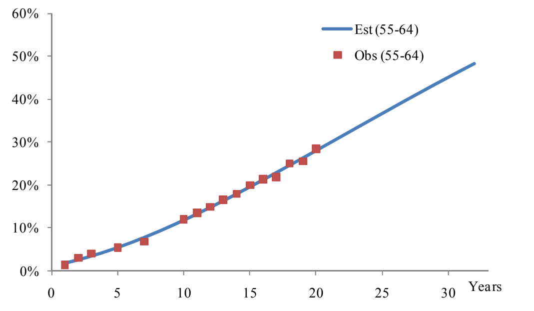
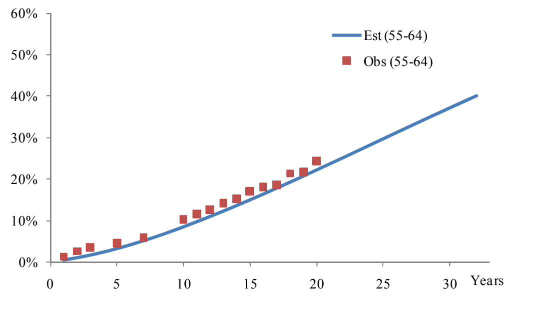
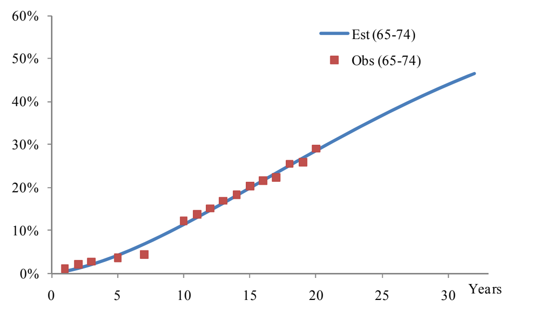
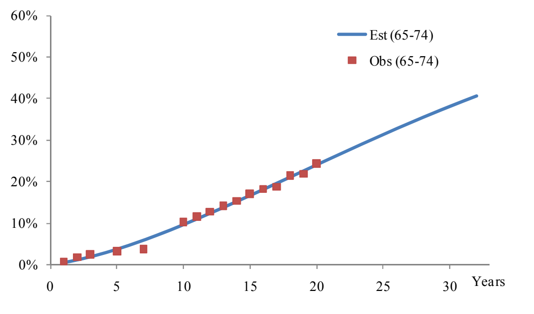
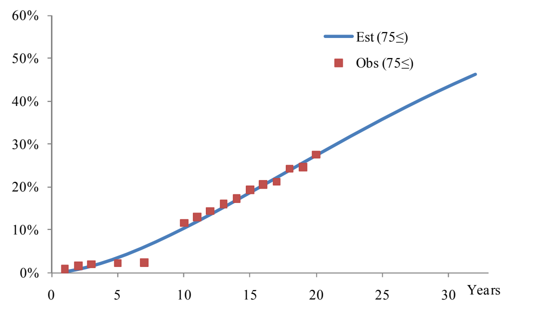
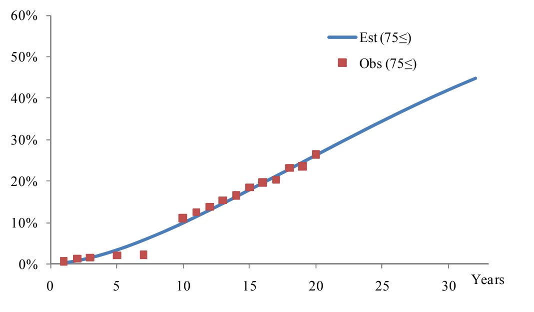
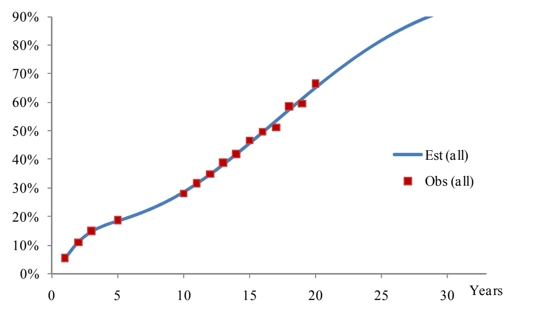
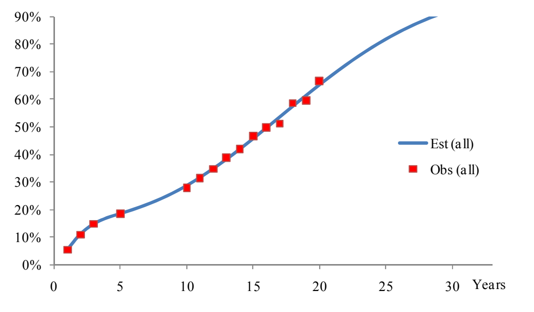
Based on these parameters and the above equation, we derived the probability density curve and cumulative distribution curve to simulate the time to failure of joint implants. Figures A and B provide the cumulative distribution curves, where the red dots represent the observed cumulative implant failure rates from the literature (Table K) and the blue line the estimated values.

Figure A: Cumulative distribution curve of time to revision with observed values (hip implants)



Est: estimated curve; Obs: observed values

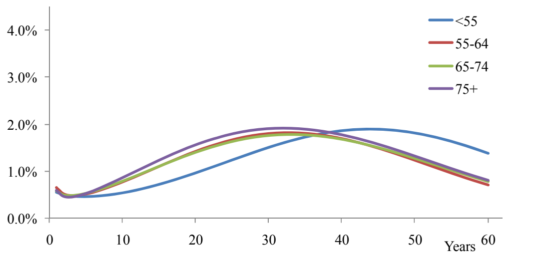
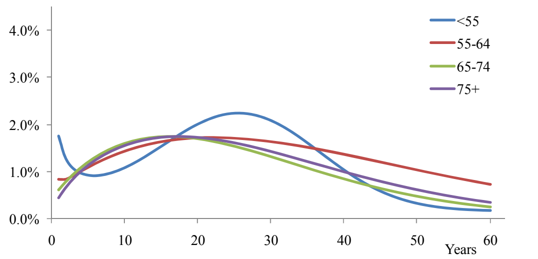
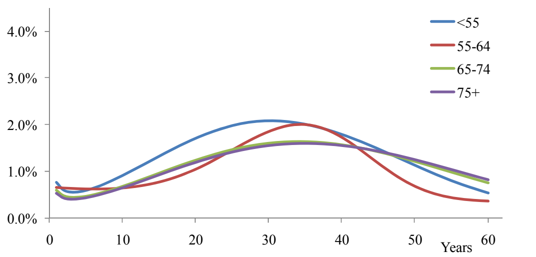
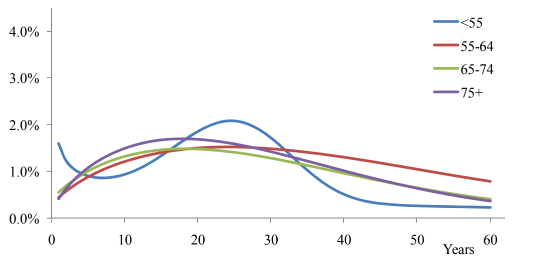
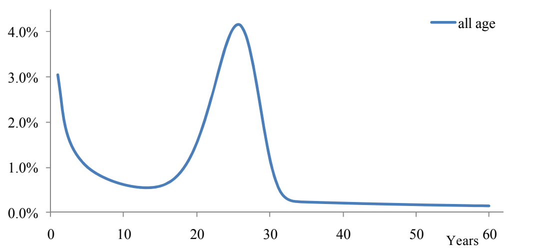
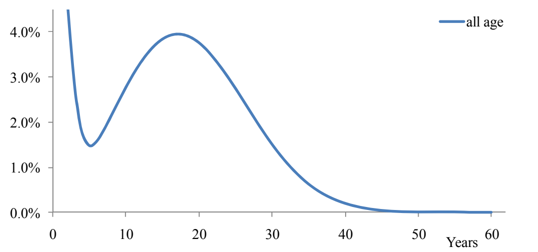
Figure B: Cumulative distribution curve of time to revision with observed values (knee implants)

	Male	Female
Primary (<55)		
Primary (55-64)		
Primary (65-74)		
Primary (75+)		
Revision (all ages)		

Est: estimated curve; Obs: observed values

Similarly, Figure C provides the probability density curve modelled from the estimated parameters.

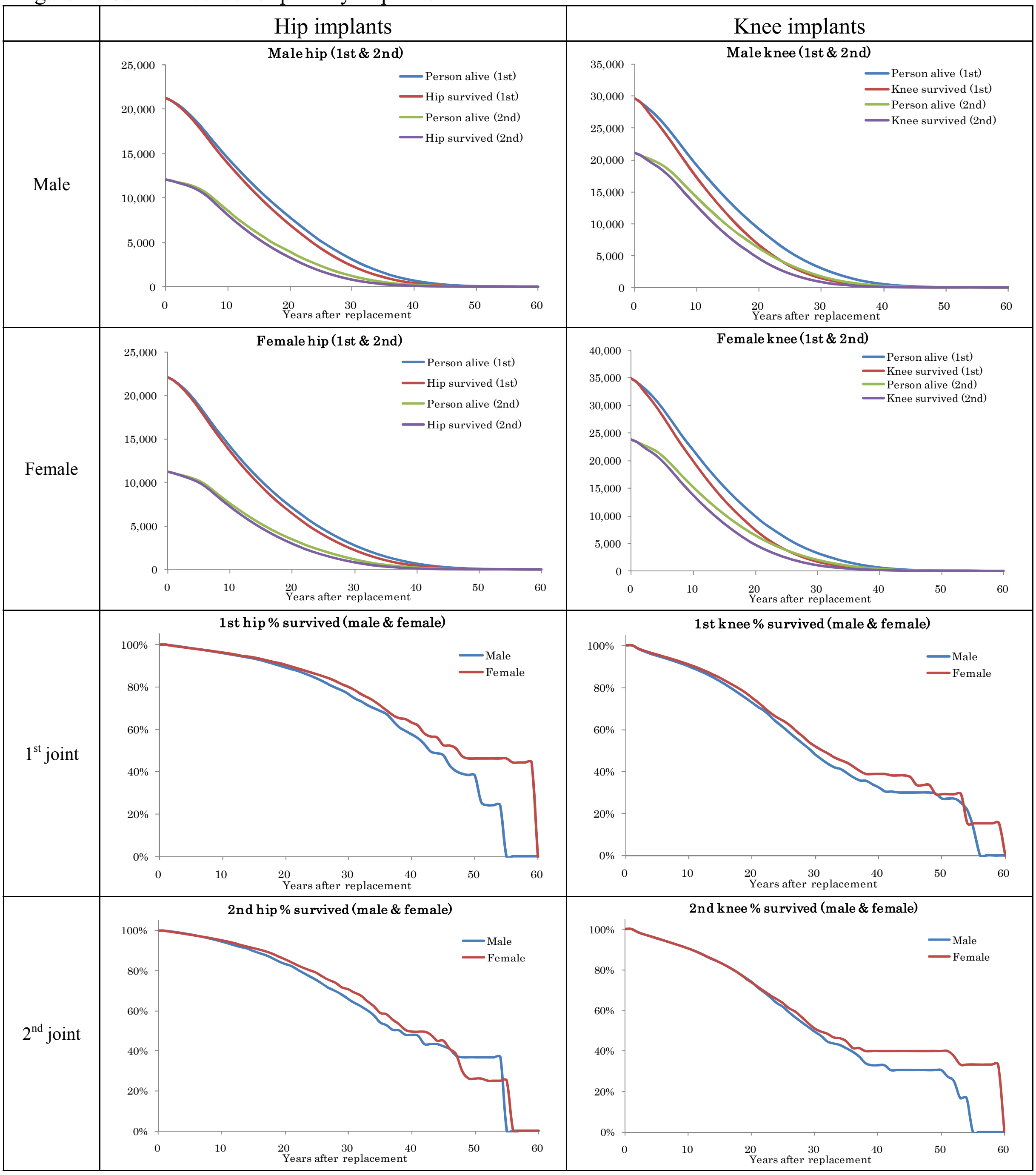
Figure C: Probability density curve of time to revision

<table>
<tr><th></th><th>Hip implants</th><th>Knee implants</th></tr>
<tr><td>Male</td><td></td><td></td></tr>
<tr><td>Female</td><td></td><td></td></tr>
<tr><td>Revision (male & female)</td><td></td><td></td></tr>
</table>

1.10. Survival curve of implants (primary joint replacement)

Sections 1.1–1.9 provided all details of the mathematical backgrounds and assumptions made to derive the epidemiological parameters. Before proceeding to the estimation of costs, we ran the simulation to derive the survival curves of patients who underwent primary replacement and the primary implants. The results are provided in Figure D.

Figure D: Survival curve for primary implants



Person alive(1^{st}): number of people who are alive X years after primary replacement of the 1^{st} joints
Person alive (2^{nd}): number of people who are alive Y years after primary replacement of the 2^{nd} joints

2. Costs

2.1. Costs of hip and knee replacement surgeries

The information on costs for hip and knee surgeries were obtained from the Australian Hospital Statistics 2003-04 and the National Hospital Cost Data Collection 2003-04[40,41]. Although the reported costs from these sources were most accurate, they did not provide as detailed information as was necessary for our study. Therefore, we made some assumptions in separating the cost information to be able to be used in the analysis. Table M provides the original cost information for each item that was available from the above sources.

Table M: Costs of hip and knee replacements

DRG	Item	No. of separations	Average cost per DRG	Average length of stay
I03A	Hip Revision + Cscc[a]	558	30,648	19.01
I03B	Hip Replac+Cscc/Hip Revsn-Cscc	5,222	16,744	12.77
I03C	Hip Replacement - Cscc	6,687	13,648	7.52
I04A	Knee Replacemt & Reattach+Cscc	856	19,620	14.17
I04B	Knee Replacemt & Reattach-Cscc	8,318	13,640	7.08

a Catastrophic or severe complications and comorbidities

The issues in using these data were two-fold. First, the probability of having a complication in the surgery had to be estimated for both primary replacement and revisions as input parameters to the model. However, item I03B included both hip replacements with complications and hip revisions without complications that had to be separated to estimate the probability of complications. Second, no information was provided for the number and average costs of knee revisions. Therefore, we made the following assumptions and derived the necessary information.

Probability of having complications

First the number of hip replacement + Cscc and hip revision – Cscc were separated assuming that the overall proportion between primary hips and revision hips should be the same as the proportion reported in the Australian National Joint Replacement Registry. The Solver function was used to calculate the number of each case by satisfying the following equation:

$$\frac{NOS^{hip}_{rev\ \pm Cscc}}{NOS^{hip}_{prim\ \pm Cscc}} = \frac{NOS^{hip}_{rev\ JRR}}{NOS^{hip}_{prim\ JRR}}$$

where

$NOS^{hip}_{prim/rev,+Cscc/-Cscc}$ is the number of hip surgeries conducted for primary/revision replacement for Cscc/non-Cscc cases for each DRG code

NOS^{hip}_{JRR} is the number of hip surgeries recorded for 2003 in the Australian National Joint Replacement Registry for primary/revision hip surgeries.

Second, the probabilities of having complications for hip and knee replacements were calculated as:

$$Prob^{hip}_{prim/rev,+Cscc} = \frac{NOS^{hip}_{prim/rev+Cscc}}{NOS^{hip}_{prim/rev-Cscc} + NOS^{hip}_{prim/rev+Cscc}}$$

$$Prob^{knee}_{prim+Cscc} = \frac{NOS_{I04A}}{NOS_{I04A} + NOS_{I04B}}$$

$$Prob^{knee}_{rev+Cscc} = Prob^{knee}_{prim+Cscc} \times \frac{Prob^{hip}_{rev+Cscc}}{Prob^{hip}_{prim+Cscc}}$$

where

$NOS_{I04A/I04B}$ is the number of separations for each DRG code

$Prob^{hip/knee}_{prim/rev,+Cscc}$ is the proportion of Cscc cases for primary /revision hip surgeries for hip or knee.

In estimating the probability of complications for knee revisions, we assumed that the proportional probability difference between + Cscc and – Cscc for hip surgeries applies to knee surgeries as well.

The derived probabilities of complications are provided in Table N.

Table N: Probability of having Cscc

	Primary	Revision
Hip	0.36	0.27
Knee	0.09	0.07

Intervention costs for each item

The costs of hip and knee replacement surgeries were calculated as follows:

$$Cost^{hip}_{prim-Cscc} = CDRG_{I03C}$$
$$Cost^{hip}_{prim+Cscc} = CDRG_{I03B}$$
$$Cost^{hip}_{rev-Cscc} = CDRG_{I03B}$$
$$Cost^{hip}_{rev+Cscc} = CDRG_{I03A}$$
$$Cost^{knee}_{prim-Cscc} = CDRG_{I04B}$$
$$Cost^{knee}_{prim+Cscc} = CDRG_{I04A}$$
$$Cost^{knee}_{rev-Cscc} = CDRG_{I04A}$$
$$Cost^{knee}_{rev+Cscc} = Cost^{knee}_{rev-Cscc} \times \frac{CDRG_{I03A}}{CDRG_{I03B}}$$

where

$Cost^{hip,/knee}_{prim/rev,+Cscc/-Cscc}$ is the cost per primary or revision surgery for hip or knee with or without Cscc

$CDRG_{I03A/I03B/I03C/I04A/I04B}$ is the unit cost for each AR-DRG code

It was assumed that the proportional cost difference between hip revision + Cscc and hip revision – Cscc applies to knee surgeries as well.

2.2. Average length of stay

The average length of stay for each surgical pattern was calculated from Table M following the same logic as the costs for hip and knee replacements.

2.3. Surgery-related costs

Apart from the costs that are directly associated with hip and knee replacement surgeries, OA patients visit the hospitals pre- and post-surgeries that do not involve admissions (e.g. pre-surgical consultations, pathology tests etc.). Such costs are deemed surgery-related costs, and were estimated from the Disease Costs and Impact Study 2000-01(DCIS 2000-01)[42] as follows:

$$Cost_{surg-related} = \frac{Cost_{2000-01}^{Non-admit} + Cost_{2000-01}^{Pathology}}{No_{2000-01}^{OA\ surgery}} \times \frac{Def_{2003}}{Def_{2001}}$$

where

$Cost_{surg-related}$ is the surgery-related cost to the government other than $Cost_{primary,revision}^{hip,knee}$

$Cost_{2000-01}^{Non-admit,pathology}$ is the costs for hospital non-admitted cases and pathology for males and females from DCIS 2000-01

$Cost_{2000-01}^{OA\ surgery}$ is the number of all types of hip and knee replacements conducted for OA patients in 2000-01 for males and females (obtained from the Joint Replacement Registry)[4]

$Def_{2001,2003}$ is the health price deflator for 2001 and 2003[43].

The assumptions set here included:

- Sum of the costs of hospital non-admitted cases and pathology would well approximate the pre/post surgery-related costs to the government;
- The amount does not differ between, hip and knee, primary and revision surgeries, males and females at all ages;
- DCIS only includes government's cost; and
- There is no sampling error (since the data covers the entire country) and so there is no uncertainty distribution given.

2.4. Patient's out-of-pocket costs

Although direct costs associated with hip and knee replacement surgery are deemed to be borne solely by the government, there are other costs associated with pre- and post-surgery that are borne by the patients. This may include co-payment for non-admitted hospital visits, medications, travel costs, etc. Such patient's out-of pocket costs for hip and knee replacements were calculated from March et al.[44] as:

$$Cost_{OOP\ med}^{hip,knee} = Cost_{literature}^{hip,knee} \times \frac{Def_{2003}}{Def_{1995}}$$

$$Cost_{OOP\ fuel}^{hip,knee} = Price_{2003}^{fuel} \times Dist \times 2 \times Visits_{pre\&post}$$

where

$Cost_{OOP\ med}^{hip,knee}$ is the out-of-pocket payment for medical services for a patients undergoing hip or knee replacements surgeries

$Cost_{literature}^{hip,knee}$ is the out of pocket payment of a patient for three months pre/post hip or knee replacements surgeries from the literature

$Cost_{OOP\ fuel}^{hip,knee}$ is the average fuel costs for pre- and post- surgeries medical visits

$Price_{2003}^{fuel}$ is the average fuel price per km in 2003 (assumed to be AUD 0.58per km)

$Dist$ is the average distance between residence and destinations (assumed to be 6.4km)

$Visits_{pre/post}$ is the average number of visits pre- and post surgery from March et al.[44]

The assumptions set here included:

- The out-of-pocket payment of patients during three month prior and post surgery are all related to hip or knee replacement surgeries;
- The amount is the same between primary and revision surgeries, between males and females at all ages; and
- Gamma distribution is assumed for uncertainties.

2.5. Patient's time costs for surgery and recuperation

While there is no out-of-pocket costs falling on the patients during hospital admissions and surgeries, there is an opportunity costs associated with the time of patients in the hospital. Suche patient's time costs for surgery and recuperation were estimated from the Average Weekly Earnings 2003[45] and Labour Force Statistics 2003[46] as follows:

$$Earn_{M,F}^{hour} = Earn_{M,F}^{week}$$

$$Leisure_{M,F}^{hour} = Leisure_{M,F}^{week}$$

$$Timecost_{M,F}^{day} = \left(Earn_{M,F}^{hour} \times \frac{Civ_{M,F}^{working}}{Civ_{M,F}^{total}} + Leisure_{M,F}^{hour} \times \frac{Civ_{M,F}^{not\ working}}{Civ_{M,F}^{total}} \right) \times 7.25hrs)$$

$$Timecost_{M,F}^{hip,knee} = Timecost_{M,F}^{day} \times ALOS^{hip.knee/\ primary,revision} \times 2$$

where

$Earn_{M,F}^{hour,day,week}$ is the hourly/daily/weekly earnings of males and females who are working
$Leisure_{M,F}^{hour,day,week}$ is the hourly/daily/weekly time cost of males and females who are not working
$Timecost_{M,F}^{day}$ is the average daily time cost of males and females
$Civ_{M,F}^{working,not\ working,total}$ is the number of male and female civilians who are working/not working/total within the age range of 15-69
$Timecost_{M,F}^{hip/knee}$ is the time cost of males and females associated with hip or knee replacement surgeries and recuperation
$ALOS_{M,F}^{hip/knee,primary/revision}$ is the average length of stay obtained from the Australian Hospital Statistics 2003-04[40] depending on hip or knee and primary or revision surgeries.

The assumptions set here included:

- The time cost for those not working is 25% of those who are working;
- The recuperation time is same as the length of stay;
- The time cost has a Triangular distribution; and
- The length of stay has a Gamma distribution.

2.6. Patient's time costs for pre-surgery medical visits

Similarly to the time costs associated with hospital admissions and surgeries, the non-admitted hospital visits also take time off the patients and hence there is an opportunity cost. The patient's time costs for pre-surgery medical visits were estimated from March et al.[44] as:

$$Timevisits_{M,F}^{hip/knee} = Timecost_{M,F}^{day}/7.25 \times Time \times Vists_{pre}$$

where

$Timevisits_{M,F}^{hip/knee}$ is the time cost of males and females associated with pre-surgery visits for hip and knee replacements

$Time$ is the total time for travel, waiting, and consultation (assumed to be: 0.25 hours for one way travel; 0.5 hours for waiting; and 0.25 hours for consultation).

2.7. Cost offsets (non-surgical therapies for OA)

The costs for non-surgical therapies for OA management are deemed to be offset once the person undergoes hip or knee replacement surgery. The costs for OA management were obtained from DCIS 2000-01[42]. First, we estimated the annual health expenditure consumed by a person with OA. Whilst it is possible to simply divide the total annual expenditure on OA by the total number of people with OA to derive the average cost per OA patient, it is unlikely that the people with mild OA and severe OA are consuming the same amount. Therefore, we analysed each cost category (e.g. hospital attendance, pharmaceutical with and without prescription etc.) and assigned each item to the relevant OA grades proportionally to the number of people in each grade. The sum of the health expenditure assigned to each OA grade was divided by the number of people in each grade to derive the grade specific health spending per person per year. These costs were assumed to be offset after successful interventions. The costs for each severity of OA are provided in Table O.

Table O: Annual cost per individuals with OA for conservative therapy (to be offset) (Unit: AUD)

Age	Male				Female			
	<2A	2A	2S3A	3S	<2A	2A	2S3A	3S
40–44	144	473	911	1,785	63	844	2,005	4,328
45–54	63	389	844	1,753	66	1,093	2,165	4,309
55–64	72	497	1,013	2,045	81	750	1,681	3,542
65–74	132	489	1,040	2,141	79	529	1,169	2,450
75–84	96	322	693	1,434	139	372	792	1,631
85+	40	163	446	1,013	74	176	419	904

A: asymptomatic; S: symptomatic

The following describe how each cost for different severities of OA was estimated:

$$Cost_{M,F}^{<2A} = \left(Exp_{M,F}^{Unref} + Exp_{M,F}^{Prof}\right) \times \frac{Num_{M,F}^{<2A}}{Num_{M,F}^{OAall}} \div Num_{M,F}^{<2A} \times \frac{Def_{2003}}{Def_{2001}}$$

$$Cost_{M,F}^{2A} = \left[\left(Exp_{M,F}^{Unref} + Exp_{M,F}^{Prof}\right) \times \frac{Num_{M,F}^{2A}}{Num_{M,F}^{OAall}} + \left(Exp_{M,F}^{image} + Exp_{M,F}^{pharmOTC}\right) \times \frac{Num_{M,F}^{2A}}{Num_{M,F}^{2A+}}\right] \div Num_{M,F}^{2A} \times \frac{Def_{2003}}{Def_{2001}}$$

$$Cost_{M,F}^{2S3A} = \Bigg[\left(Exp_{M,F}^{Unref} + Exp_{M,F}^{Prof}\right) \times \frac{Num_{M,F}^{2S3A}}{Num_{M,F}^{OAall}} + \left(Exp_{M,F}^{image} + Exp_{M,F}^{pharmOTC}\right) \times \frac{Num_{M,F}^{2S3A}}{Num_{M,F}^{2A+}}$$

$$+ \left(Exp_{M,F}^{med} + Exp_{M,F}^{pharmPr}\right) \times \frac{Num_{M,F}^{2S3A}}{Num_{M,F}^{2S3A} + Num_{M,F}^{3S} \times DW^{3S}/DW^{2S3A}}\Bigg]$$

$$\div Num_{M,F}^{2S3A} \times \frac{Def_{2003}}{Def_{2001}}$$

$$Cost_{M,F}^{3S} = \Bigg[\left(Exp_{M,F}^{Unref} + Exp_{M,F}^{Prof}\right) \times \frac{Num_{M,F}^{3S}}{Num_{M,F}^{OAall}} + \left(Exp_{M,F}^{image} + Exp_{M,F}^{pharmOTC}\right) \times \frac{Num_{M,F}^{3S}}{Num_{M,F}^{2A+}}$$

$$+ \left(Exp_{M,F}^{med} + Exp_{M,F}^{pharmPr}\right) \times \frac{Num_{M,F}^{3S}}{Num_{M,F}^{2S3A} + Num_{M,F}^{3S} \times DW^{3S}/DW^{2S3A}} \times \frac{DW^{3S}}{DW^{2S3A}}\Bigg]$$

$$\div Num_{M,F}^{2S3A} \times \frac{Def_{2003}}{Def_{2001}}$$

where

$Cost_{M,F}^{2A,2S3A,3S}$ is the annual cost for OA management per person for each severity

$Exp_{M,F}^{unref,prof,image,pharmOTC,pharmPr,med}$ is the expenditure for each cost category in 2000-01 (unreferred attendances, other professionals, imaging, pharmaceuticals over the counter, pharmaceuticals requiring prescriptions, and other medical services)

$Num_{M,F}^{<2A,2A,2S\&3A,3S,2A-3S,OAall}$ is the number of population with different OA severity.

These costs were added to the comparator in the analysis to account for the cost that would be saved from hip and knee replacements.

NB: There would still be some recurrent costs after replacement surgeries to follow-up hip or knee implants. We treated such costs to be part of non-surgical therapies which would not be offset by the intervention (rather than part of the intervention costs). We assumed that such recurrent costs are equivalent to the costs of non-surgical therapies required for OA grade 2A at three years intervals (this grade was selected since it includes imaging which would be the main service to be provided for follow-up), and deducted from the amount of cost offset. Under this assumption, such recurrent costs were not included in the "without cost offset" scenario.

The assumptions set here included:
- The assumption set above;
- <2A patients only utilise unreferred attendances and other professionals;
- 2A patients utilise <2A costs + imaging and pharmaceuticals over the counter;
- 2S & 3-4A and 3-4S patients utilise 2A costs + pharmaceuticals requiring prescriptions and other medical services which are weighted by the proportion of DWs of 2S&3-4A and 3-4S;
- Costs for hospital admissions are not used for non-surgical therapies;
- Costs for aged care homes and research are not offset by the intervention; and
- There is no sampling error (since the data covers the entire country) and so there is no uncertainty distribution given.

3. Additional results

3.1. Sex-specific results

Table P provides the sex-specific cost-effectiveness ratios for hip and knee replacements.

Table P: Incremental cost-effectiveness ratio (sex-specific)

Scenario	Hip (AUD/DALY averted)		Knee (AUD/DALY averted)	
	Mean	95%UI	Mean	95%UI
With cost offset				
Without time cost (M)	4,100	3,600−4,900	11,000	8,500−14,000
Without time cost (F)	3,100	2,700−3,600	9,000	7,400−12,000
With time costs (M)	5,800	4,800−7,100	14,000	10,000−18,000
With time costs (F)	4,300	3,600−5,300	12,000	8,900−15,000
Without cost offset				
Without time cost (M)	9,900	8,700−12,000	19,000	15,000−25,000
Without time cost (F)	10,000	9,200−12,000	19,000	15,000−25,000
With time costs (M)	12,000	10,000−14,000	22,000	17,000−28,000
With time costs (F)	11,000	10,000−13,000	21,000	16.000−28,000

NB: The values are rounded to two digits of significance

3.2. Age-group specific results

Table Q provides the age-group specific results of the analysis (uncertainties are not included).

Table Q: Incremental cost-effectiveness ratio (age-group specific)

Scenario	Hip (AUD/DALY averted)		Knee (AUD/DALY averted)	
	Without time cost	With time cost	Without time cost	With time cost
With cost offset				
40-49	Dominant*	770	2,900	5,000
50-59	1,000	2,200	4,200	6,200
60-69	3,300	4,700	8,800	11,000
70-79	8,700	11,000	16,000	19,000
80-90	17,000	19,000	25,000	29,000
90+	32,000	37,000	47,000	53,000
Without cost offset				
40-49	7,100	8,200	14,000	16,000
50-59	8,200	9,500	15,000	17,000
60-69	9,700	11,000	18,000	20,000
70-79	14,000	16,000	22,000	25,000
80-90	21,000	23,000	30,000	34,000
90+	36,000	41,000	52,000	58,000

* Dominant refers to health gain with net-cost saving.

3.3. Results from sensitivity analyses

Table R provides the results by assuming an extreme correlation between the left and right joints disease progression.

Table R Incremental cost-effectiveness ratio

Scenario	Original (AUD/DALY averted)*		**±0.99 correlation** (AUD/DALY averted)	
	Hip	Knee	Hip	Knee
With cost offset				
Without time cost	3,600	10,000	3,700	10,000
With time costs	5,100	12,000	5,100	13,000
Without cost offset				
Without time cost	10,000	19,000	10,000	19,000
With time costs	12,000	21,000	12,000	21,000

* In mean values.

Table S provides the results by assuming that only one joint is affected by OA through out the life.

Table S: Incremental cost-effectiveness ratio

Scenario	Original (AUD/DALY averted)*		**One joint** (AUD/DALY averted)	
	Hip	Knee	Hip	Knee
With cost offset				
Without time cost	3,600	10,000	Dominant**	1,700
With time costs	5,100	12,000	800	3,000
Without cost offset				
Without time cost	10,000	19,000	6,900	11,000
With time costs	12,000	21,000	7,900	12,000

* In mean values.

** Dominants refers to more health gains at lower cost.

Table T provides the results of hip replacement by using EQ-5D as the outcome measure.

Table T: Incremental cost-effectiveness ratio (hip)

Scenario	Original (AUD/DALY averted)*		**EQ-5D** (AUD/QALY averted)	
	Hip (2 joints)	Hip (1 joint)	Hip (2 joints)	Hip (1 joint)
With cost offset				
Without time cost	3,600	Dominant**	3,900	Dominant**
With time costs	5,100	800	5,400	780
Without cost offset				
Without time cost	10,000	6,900	11,000	6,500
With time costs	12,000	7,900	12,000	7,400

* In mean values.

** Dominants refers to more health gains at lower cost.

3.4. Testing for internal consistency

In order to test the internal consistency of the model, the model was verified by comparing the proportions of total joint replacements occurring in each sex/age-group for a given year between the joint registry and our simulation. Table U provides the comparisons.

Table U: Comparison of observed vs. simulated proportions of sex/age-specific joint replacements per year

Group	Hip		Knee	
	Observed	Simulated	Observed	Simulated
Male <55	5%	9%	3%	4%
Male 55–64	10%	11%	10%	11%
Male 65–74	15%	14%	16%	15%
Male75–84	12%	10%	13%	11%
Male 85+	2%	2%	1%	2%
Female <55	7%	7%	4%	4%
Female 55–64	12%	11%	13%	12%
Female 65–74	20%	17%	22%	20%
Female75–84	15%	16%	17%	18%
Female 85+	3%	5%	2%	4%
Total	100%	100%	100%	100%

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