



## **Supporting Information**

### **Supplementary methods and results**

**This appendix was part of the submitted manuscript and has been peer reviewed.  
It is posted as supplied by the authors.**

Appendix to: Kou K, Aitken JF, Pyke C, et al. Treatment intervals and survival for women diagnosed with early breast cancer in Queensland: the Breast Cancer Outcomes Study, a population-based cohort study. *Med J Aust* 2023; doi: 10.5694/mja2.52091.

## **Box 1. Levels of evidence and grades of recommendation**

### **Infectious Diseases Society of America–United States Public Health Service Grading System, adapted) (1)**

#### **Levels of evidence**

I Evidence from at least one large randomised, controlled trial of good methodological quality (low potential for bias) or meta-analyses of well-conducted randomised trials without heterogeneity

II Small randomised trials or large randomised trials with a suspicion of bias (lower methodological quality) or meta-analyses of such trials or of trials with demonstrated heterogeneity

III Prospective cohort studies

IV Retrospective cohort studies or case–control studies

V Studies without control group, case reports, expert opinions

#### **Grades of recommendation**

A Strong evidence for efficacy with a substantial clinical benefit, strongly recommended

B Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended

C Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs, etc.), optional

D Moderate evidence against efficacy or for adverse outcome, generally not recommended

E Strong evidence against efficacy or for adverse outcome, never recommended

### **National Health and Medical Research Council (2,3)**

#### **Levels of evidence**

I Evidence obtained from a systematic review of all relevant randomised controlled trials.

II evidence obtained from at least one properly designed randomised controlled trial.

III-1 evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).

III-2 evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case–control studies, or interrupted time series with a control group.

III-3 evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group.

IV evidence obtained from case series, either post-test or pre-test and post-test.

#### **Grades of recommendation**

A Body of evidence can be trusted to guide practice

B Body of evidence can be trusted to guide practice in most situations

C Body of evidence provides some support for recommendation(s) but care should be taken in its application

D Body of evidence is weak and recommendation must be applied with caution

## References

1. Cardoso F, Kyriakides S, Ohno S, et al; ESMO Guidelines Committee. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2019; 30: P1194-P1220.
2. National Health and Medical Research Council. A guide to the development, implementation and evaluation of clinical practice guidelines. 16 Nov 1998.  
[https://www.health.qld.gov.au/\\_\\_data/assets/pdf\\_file/0029/143696/nhmrc\\_clinprgde.pdf](https://www.health.qld.gov.au/__data/assets/pdf_file/0029/143696/nhmrc_clinprgde.pdf) (viewed July 2023).
3. National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Pilot program 2005–2007. Archived:  
[https://web.archive.org/web/20091011190626/http://www.nhmrc.gov.au/guidelines/\\_files/levels\\_grades05.pdf](https://web.archive.org/web/20091011190626/http://www.nhmrc.gov.au/guidelines/_files/levels_grades05.pdf) (viewed July 2023).

## **Box 2. Variables for which data were obtained from linked Queensland Cancer Registry, medical records, and telephone interviews**

- Age at diagnosis<sup>a\*</sup>
- Tumour characteristics<sup>a,b\*</sup> (stage, grade)
- Health characteristics<sup>c\*</sup> (family history of breast or ovarian cancer, other medical conditions)
- Lifestyle factors<sup>c\*</sup> (marital status, alcohol and tobacco use, physical activity levels)
- Individual-level socio-economic information<sup>c\*</sup> (annual income, number of dependents, employment status, highest education level, private health insurance status)
- Area-level socio-economic status<sup>a\*</sup> (Index of Relative Socio-economic Advantage and Disadvantage (1), remoteness of residential address (2), treatment accessibility (3))
- Mode of detection<sup>c</sup> (screening/symptoms)
- Treatment pathway (commencement and completion of mastectomy<sup>b</sup>, breast-conserving surgery<sup>b</sup>, chemotherapy<sup>c</sup>, anti-HER2 therapy<sup>c</sup>, endocrine therapy<sup>c</sup>, radiotherapy<sup>c</sup>)
- Screening facilities<sup>c\*</sup>
- Number (single, multiple) and time of year (February–November, December–January) of treatments<sup>b,c\*</sup>

a: information obtained from Queensland Cancer Register; b: information obtained from medical records; c: information obtained from telephone interview.

\* Factors initially included in statistical analysis of the characteristics of women in the “guideline non-compliance” group.

### **References**

1. Australian Bureau of Statistics. Census of Population and Housing: Socio-Economic Indexes for Areas (SEIFA), 2016 (2033.0.55.001) 27 Mar 2018. <https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/2033.0.55.001~2016~Main%20Features~IRSAD~20> (viewed July 2023).
2. Australian Bureau of Statistics. Australian Statistical Geography Standard (ASGS), volume 5: remoteness structure, July 2016 (1270.0.55.005). 16 Mar 2018. <https://www.abs.gov.au/ausstats/abs@.nsf/mf/1270.0.55.005> (viewed July 2023).
3. Kou K, Dasgupta P, Aitken JF, Baade PD. Impact of area-level socioeconomic status and accessibility to treatment on life expectancy after a cancer diagnosis in Queensland, Australia. *Cancer Epidemiol* 2020; 69: 101803.

### **Box 3. Optimal cut-point analysis**

The optimal cut-points for intervals 3 to 6 were estimated from the survival and hazard ratio curves, using the minimum  $P$  value method (1).

The cubic splines curves of cause-specific survival and hazard ratio at eight years from diagnosis by the number of interval days were predicted using flexible parametric survival models. The optimal number of knots for the cubic splines were determined using the Akaike information criterion, the Bayes information criterion, and the likelihood ratio test statistic (2). The reference hazards of the hazard ratio curves were selected as the hazard of interval days with the most observations. The curves were generated using “stpm2” and “standsurv” function in Stata (3).

For each interval, a number of cut-points candidates ( $N$ ) were initially selected between the inflection points of the hazard ratio or survival curves (1). The outer 5% of the number of interval days were excluded to avoid small numbers in one of the groups following dichotomization (4). The number of interval days was dichotomised by each candidate cut-point and included in a survival model.  $P$ -values of the dichotomized variable were extracted from the model results. For each interval, the analysis was conducted  $N$  times based on  $N$  candidate cut-points. Thus, the  $p$ -values were multiplied by  $N$  based on the Bonferroni correction to avoid type I error (5). Candidate cut-points with the smallest  $p$  value and having a Bonferroni adjusted  $p$ -value less than 0.2 were selected as the optimal cut-points.

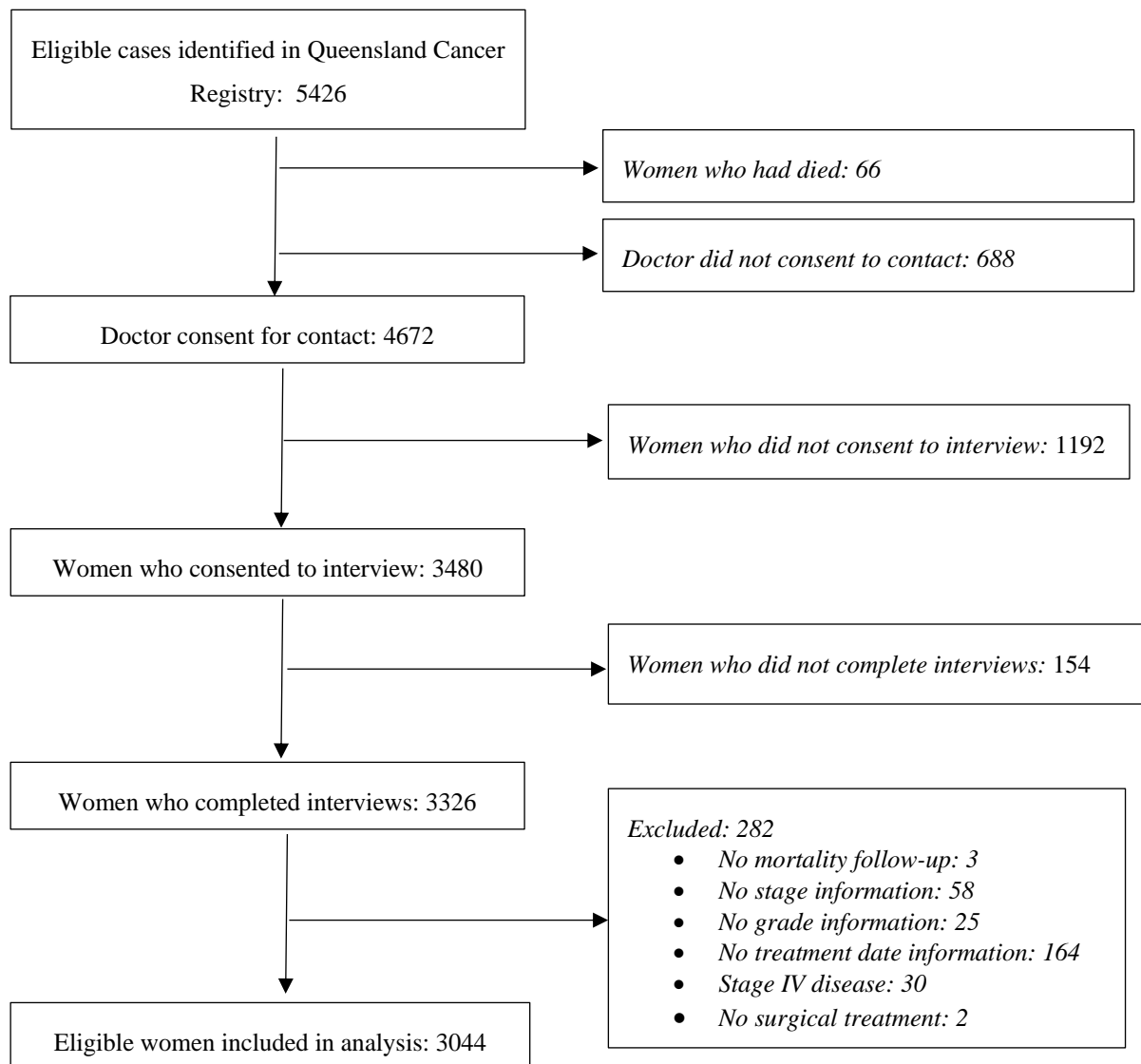
### **References**

1. Williams BA, Mandrekar JN, Mandrekar SJ, et al. Finding optimal cutpoints for continuous covariates with binary and time-to-event outcomes (Technical report series #79). Department of Health Sciences Research; June 2006. <https://www.mayo.edu/research/documents/biostat-79pdf/doc-10027230> (viewed July 2023).
2. Schwarz G. Estimating the dimension of a model. *Ann Stat* 1978; 6: 461-464.
3. Lambert PC, Royston P. Further development of flexible parametric models for survival analysis. *Stata J* 2009; 9: 265-290.
4. Mazumdar M, Glassman JR. Categorizing a prognostic variable: review of methods, code for easy implementation and applications to decision-making about cancer treatments. *Stat Med* 2000; 19: 113-132.
5. Armstrong RA. When to use the Bonferroni correction. *Ophthalmic Physiol Opt* 2014; 34: 502-508.

**Table 1. Missing data, by variable**

Variables with missing data	Number of missing	Proportion
Family history of breast or ovarian cancer	169	5.6%
Comorbidities	3	0.1%
Drinking	3	0.1%
Smoking	5	0.2%
Physical activities	44	1.4%
Annual income	333	10.9%
Number of dependent	1	0.0%
Employment status	17	0.6%
Insurance status	1	0.0%
At least one missing	528	17.4%

**Figure 1. Flow diagram of recruitment and participation**



**Table 2. Guideline non-adherence, overall and by treatment interval, by women's characteristics\***

Characteristics	Overall		3. <i>Diagnosis to surgery</i>		4. <i>Surgery to chemotherapy</i>		5. <i>Surgery to radiotherapy</i>		6. <i>Chemotherapy to radiotherapy</i>	
	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence
<b>Overall</b>	<b>3044</b>	<b>1375 (45%)</b>	<b>2972</b>	<b>135 (5%)</b>	<b>1574</b>	<b>464 (29%)</b>	<b>1071</b>	<b>525 (49%)</b>	<b>1156</b>	<b>443 (38%)</b>
Age at diagnosis (years)										
<50	803	373 (46%)	775	27 (3%)	605	162 (27%)	142	68 (48%)	451	173 (38%)
50-59	865	409 (47%)	843	37 (4%)	503	154 (31%)	283	138 (49%)	383	143 (37%)
60-69	959	413 (43%)	941	49 (5%)	374	112 (30%)	436	213 (49%)	264	97 (37%)
70-79	417	180 (43%)	413	22 (5%)	92	36 (39%)	210	106 (50%)	58	30 (52%)
<b><i>Clinical variables</i></b>										
Type of screening facility/mode of detection										
Private screening facility	391	126 (32%)	389	8 (2%)	146	30 (21%)	175	66 (38%)	98	34 (35%)
Public screening facility	1180	567 (48%)	1176	59 (5%)	426	143 (34%)	583	311 (53%)	312	130 (42%)
Symptom-based	1473	682 (46%)	1407	68 (5%)	1002	291 (29%)	313	148 (47%)	746	279 (37%)
Tumour stage										
I	1550	656 (42%)	1540	68 (4%)	392	114 (29%)	887	428 (48%)	273	104 (38%)
II	1196	573 (48%)	1165	53 (5%)	935	288 (31%)	152	87 (57%)	667	258 (39%)
III	298	146 (49%)	267	14 (5%)	247	62 (25%)	32	10 (31%)	216	81 (38%)
Tumour grade										
1	603	248 (41%)	594	26 (4%)	106	39 (37%)	376	182 (48%)	77	27 (35%)
2	1487	666 (45%)	1447	67 (5%)	687	221 (32%)	590	286 (48%)	491	183 (37%)
3	954	461 (48%)	931	42 (5%)	781	204 (26%)	105	57 (54%)	588	233 (40%)
Number of treatments										
One	286	29 (10%)	286	29 (10%)	0	0	0	0	0	0
More than one	2758	1346 (49%)	2686	106 (4%)	1574	464 (29%)	1071	525 (49%)	1156	443 (38%)
Time of treatment <sup>†</sup>										
February-November	1864	699 (38%)	2384	102 (4%)	1177	309 (26%)	798	363 (45%)	874	302 (35%)
December-January	1180	676 (57%)	588	33 (6%)	397	155 (39%)	273	162 (59%)	282	141 (50%)
<b><i>Health status</i></b>										
Family history of breast or ovarian cancer										
No	1566	739 (47%)	1520	70 (5%)	808	253 (31%)	558	279 (50%)	618	243 (39%)
Yes	1309	548 (42%)	1285	57 (4%)	680	182 (27%)	446	207 (46%)	473	172 (36%)

Characteristics	Overall		3. Diagnosis to surgery		4. Surgery to chemotherapy		5. Surgery to radiotherapy		6. Chemotherapy to radiotherapy	
	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence
Unknown	169	88 (52%)	167	8 (5%)	86	29 (34%)	67	39 (58%)	65	28 (43%)
Other medical conditions										
None	680	303 (45%)	654	25 (4%)	428	110 (26%)	193	92 (48%)	316	113 (36%)
1 or 2	1359	603 (44%)	1326	48 (4%)	704	205 (29%)	501	229 (46%)	527	199 (38%)
More than 2	1002	467 (47%)	989	62 (6%)	440	148 (34%)	376	203 (54%)	311	130 (42%)
Unknown	3	2 (67%)	3	0	2	1 (50%)	1	1 (100%)	2	1 (50%)
<b><i>Lifestyle before diagnosis</i></b>										
Marital status										
Married	2243	976 (44%)	2197	82 (4%)	1214	339 (28%)	766	358 (47%)	901	335 (37%)
Not married	801	399 (50%)	775	53 (7%)	360	125 (35%)	305	167 (55%)	255	108 (42%)
Drinking (per month)										
Less than once	1158	526 (45%)	1131	58 (5%)	579	181 (31%)	395	203 (51%)	408	168 (41%)
At least once	1883	847 (45%)	1838	77 (4%)	993	282 (28%)	675	321 (48%)	746	274 (37%)
Unknown	3	2 (67%)	3	0	2	1 (50%)	1	1 (100%)	2	1 (50%)
Smoking										
Never smoked	1735	742 (43%)	1688	58 (3%)	893	244 (27%)	614	299 (49%)	648	239 (37%)
Former smoker	1062	492 (46%)	1041	55 (5%)	546	160 (29%)	376	184 (49%)	411	153 (37%)
Current smoker	242	137 (57%)	238	22 (9%)	132	59 (45%)	79	40 (51%)	94	49 (52%)
Unknown	5	4 (80%)	5	0	3	1 (33%)	2	2 (100%)	3	2 (67%)
Physical activity <sup>‡</sup>										
Sufficient	1689	747 (44%)	1651	65 (4%)	917	260 (28%)	571	272 (48%)	667	246 (37%)
Insufficient	727	341 (47%)	717	39 (5%)	360	106 (29%)	274	148 (54%)	268	102 (38%)
Sedentary	584	264 (45%)	566	29 (5%)	283	90 (32%)	204	96 (47%)	212	89 (42%)
Unknown	44	23 (52%)	38	2 (5%)	14	8 (57%)	22	9 (41%)	9	6 (67%)
<b><i>Individual socio-economic factors before diagnosis</i></b>										
Household annual income										
>\$130k	434	165 (38%)	426	8 (2%)	285	53 (19%)	114	49 (43%)	212	71 (33%)
\$52k-\$130k	1162	509 (44%)	1132	37 (3%)	692	197 (28%)	359	160 (45%)	521	192 (37%)
<\$52k	1115	566 (51%)	1088	79 (7%)	455	174 (38%)	463	250 (54%)	325	145 (45%)
Unknown	333	135 (41%)	326	11 (3%)	142	40 (28%)	135	66 (49%)	98	35 (36%)
Number of dependents										
None	2002	912 (46%)	1953	89 (5%)	898	292 (33%)	806	405 (50%)	649	243 (37%)
1 or 2	1041	462 (44%)	1018	46 (5%)	675	171 (25%)	265	120 (45%)	506	199 (39%)



Characteristics	Overall		3. Diagnosis to surgery		4. Surgery to chemotherapy		5. Surgery to radiotherapy		6. Chemotherapy to radiotherapy	
	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence	Eligible women	Non-adherence
Unknown	1	1 (100%)	1	0	1	1 (100%)	0	0	1	1 (100%)
Employment status										
Employed	1768	797 (45%)	1724	61 (4%)	1096	314 (29%)	504	246 (49%)	810	301 (37%)
Unemployed	1259	568 (45%)	1232	74 (6%)	472	146 (31%)	558	273 (49%)	342	140 (41%)
Unknown	17	10 (59%)	16	0	6	4 (67%)	9	6 (67%)	4	2 (50%)
Education										
≥Diploma	1131	482 (43%)	1101	33 (3%)	632	154 (24%)	374	183 (49%)	463	168 (36%)
High school	1012	454 (45%)	989	41 (4%)	553	165 (30%)	329	157 (48%)	413	163 (39%)
< High school	901	439 (49%)	882	61 (7%)	389	145 (37%)	368	185 (50%)	280	112 (40%)
Private health insurance status										
Full cover	1947	762 (39%)	1906	22 (1%)	992	217 (22%)	731	316 (43%)	741	271 (37%)
None/partial cover <sup>§</sup>	1096	613 (56%)	1065	113 (11%)	582	247 (42%)	339	209 (62%)	415	172 (41%)
Unknown	1	0	1	0	0	0	1	0	0	0
<b>Area-level socio-economic status</b>										
Area disadvantage <sup>¶</sup>										
Least disadvantaged	689	261 (38%)	677	10 (1%)	362	66 (18%)	259	123 (47%)	275	89 (32%)
Middle	1829	840 (46%)	1782	91 (5%)	940	286 (30%)	640	312 (49%)	685	274 (40%)
Most disadvantaged	526	274 (52%)	513	34 (7%)	272	112 (41%)	172	90 (52%)	196	80 (41%)
Remoteness <sup>**</sup>										
Major Cities	1810	760 (42%)	1773	58 (3%)	953	240 (25%)	652	305 (47%)	714	248 (35%)
Regional/remote/very remote	1234	615 (50%)	1199	77 (6%)	621	224 (36%)	419	220 (53%)	442	195 (44%)
Accessibility to treatment <sup>††</sup>										
High	2388	1046 (44%)	2332	91 (4%)	1241	326 (26%)	863	416 (48%)	918	345 (38%)
Low	656	329 (50%)	640	44 (7%)	333	138 (41%)	208	109 (52%)	238	98 (41%)

\* Information for intervals 1 and 2 omitted because of small cell numbers.

† The completion date for the former treatment and the starting date of the later treatment for each treatment interval.

‡ Level of physical activity was calculated based on the score of weekly activity before diagnosis; score=minute of walk per week+ minute of moderate activity per week+ 2\*minute of vigorous activity per week; 0-Sedentary; 1~149-Insufficient; ≥150 Sufficient.

§ Partial cover includes women with basic hospital cover only, or extras only, or DVA cover.

¶ Socio-economic status based on Index of Relative Socio-economic Advantage and Disadvantage (1); Q1-Least disadvantaged; Q2-Q4-Middle; Q5-Most disadvantaged.

\*\* Remoteness based on Australian Statistical Geography Standard (2).

†† Accessibility to treatment based on the road travel time from the residential SA2 to the closest radiation facility (high: <1 h, low ≥ 1 h).

## References

1. Australian Bureau of Statistics. Census of Population and Housing: Socio-Economic Indexes for Areas (SEIFA), 2016 (2033.0.55.001) 27 Mar 2018. <https://www.abs.gov.au/ausstats/abs@.nsf/Lookup/by%20Subject/2033.0.55.001~2016~Main%20Features~IRSAD~20> (viewed July 2023).
2. Australian Bureau of Statistics. Australian Statistical Geography Standard (ASGS), volume 5: remoteness structure, July 2016 (1270.0.55.005). 16 Mar 2018. <https://www.abs.gov.au/ausstats/abs@.nsf/mf/1270.0.55.005> (viewed July 2023).

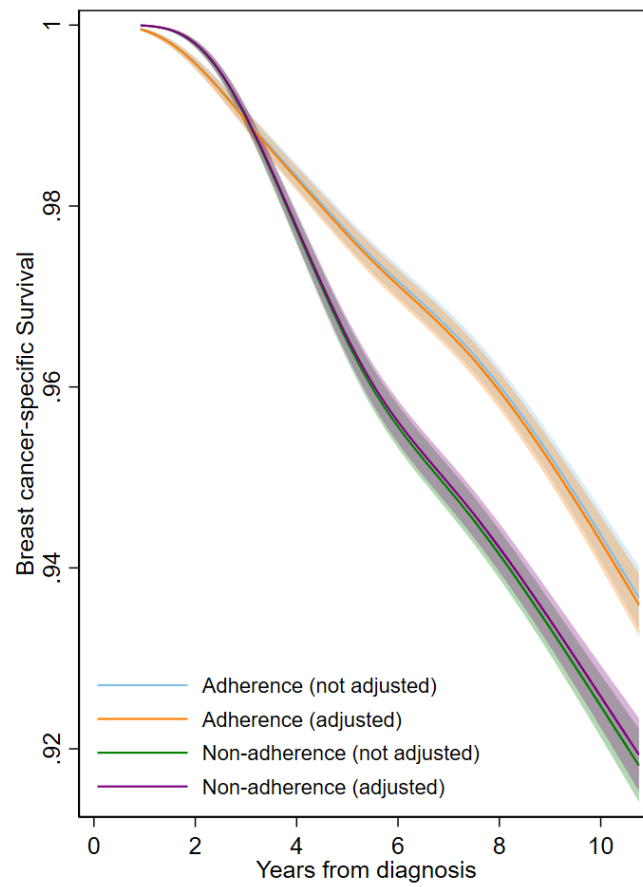
**Table 3. Hazard ratios (with 95% confidence intervals) of breast cancer specific death by guideline compliance status for overall timeframe guideline and six individual guidelines**

	Overall	1. Diagnosis to neoadjuvant therapy	2. Neoadjuvant therapy to surgery	3. Diagnosis to surgery	4. Surgery to chemotherapy	5. Surgery to radiotherapy	6. Chemotherapy to radiotherapy
<b>Eligible women</b>	<b>3044</b>	<b>67</b>	<b>67</b>	<b>2972</b>	<b>1574</b>	<b>1071</b>	<b>1156</b>
<b>Guideline adherence</b>							
Adherence	1	1	1	1	1	1	1
Non-adherence	<b>1.43 (1.03–1.96)</b>	1.45 (0.39–5.38)	3.89 (0.89–17.0)	<b>2.14 (1.18–3.89)</b>	1.39 (0.94–2.05)	0.95 (0.43–2.11)	<b>1.62 (1.06–2.47)</b>
<b>Number of treatments*</b>							
Multiple treatment	1	–	–	–	–	–	–
Single treatment	<b>2.30 (1.33–3.99)</b>	–	–	–	–	–	–
<b>Age at diagnosis</b>							
<50	1	1	1	1	1	1	1
50-59	1.08 (0.71–1.64)	1.76 (0.39–7.98)	2.37 (0.50–11.3)	0.99 (0.64–1.54)	0.93 (0.59–1.48)	1.95 (0.48–7.84)	0.97 (0.58–1.62)
60-69	1.35 (0.89–2.04)	3.59 (0.84–15.3)	<b>5.28 (1.13–24.7)</b>	1.22 (0.79–1.90)	1.16 (0.72–1.87)	2.52 (0.68–9.27)	1.11 (0.64–1.95)
70-79	1.59 (0.99–2.56)	<b>15.8 (2.08–120)</b>	<b>12.98 (1.59–106)</b>	<b>1.74 (1.09–2.78)</b>	1.32 (0.68–2.56)	<b>3.80 (1.02–14.1)</b>	0.84 (0.33–2.14)
<b>Tumour stage</b>							
I	1	–†	–†	1	1	1	1
II	<b>2.60 (1.62–4.19)</b>	–	–	<b>2.42 (1.50–3.90)*</b>	<b>2.25 (1.17–4.32)</b>	1.25 (0.41–3.80)	1.93 (0.89–4.16)
III	<b>9.51 (5.79–15.6)</b>	–	–	<b>7.73 (4.65–12.8)*</b>	<b>6.72 (3.43–13.2)</b>	<b>14.3 (5.91–34.5)</b>	<b>6.12 (2.82–13.3)</b>
<b>Tumour grade</b>							
1	1	1	1	1	1	1	1
2	2.04 (0.97–4.23)	0.71 (0.13–3.88)	0.73 (0.14–3.79)	2.33 (0.99–5.46)	1.33 (0.47–3.75)	2.41 (0.69–8.36)	1.27 (0.38–4.22)
3	<b>3.80 (1.81–7.96)</b>	0.40 (0.06–2.73)	0.46 (0.06–3.34)	<b>4.78 (2.05–11.1)*</b>	2.50 (0.91–6.88)	<b>4.92 (1.31–18.5)</b>	2.19 (0.68–7.06)
<b>Mode of detection</b>							
Screening	1	1	1	1	1	1	1
Symptoms	<b>2.36 (1.55–3.58)</b>	0.93 (0.11–7.83)	0.84 (0.10–7.02)	<b>2.23 (1.45–3.43)*</b>	<b>1.77 (1.09–2.88)</b>	<b>8.51 (2.73–26.5)</b>	<b>1.79 (1.02–3.16)</b>

\* Included only in model for overall guideline adherence.

† Excluded from model because of small numbers for some levels.

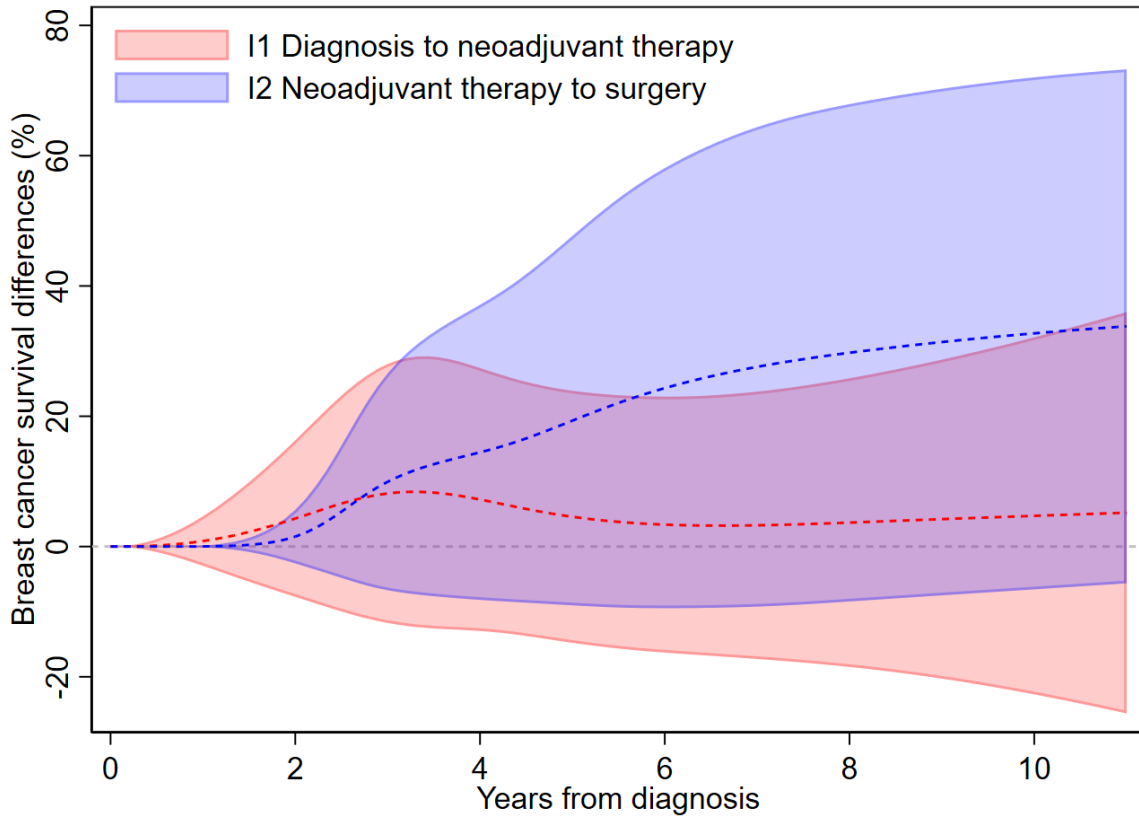
**Figure 2. Survival curves (with 95% confidence intervals) for major analysis survival model\* and after adjustment for further socio-demographic factors†**



\* Adjusted for guideline adherence, number of treatments, age at diagnosis, tumour stage, tumour grade, mode of detection (table 2).

† Adjusted for same variables as main model, and also for family history of breast or ovarian cancer, smoking status, marital status, annual income, private health insurance status, and remoteness.

**Figure 3. Comparison of outcomes for women in the overall non-adherence and adherence groups: survival differences, by treatment interval (intervals 1 and 2)\***



\* The survival differences were not statistically significant for either interval at any time point. Survival differences: survival for women “guideline compliance” minus “non-compliance” group

**Table 4. Candidate cut-points for interval 3 to 6\***

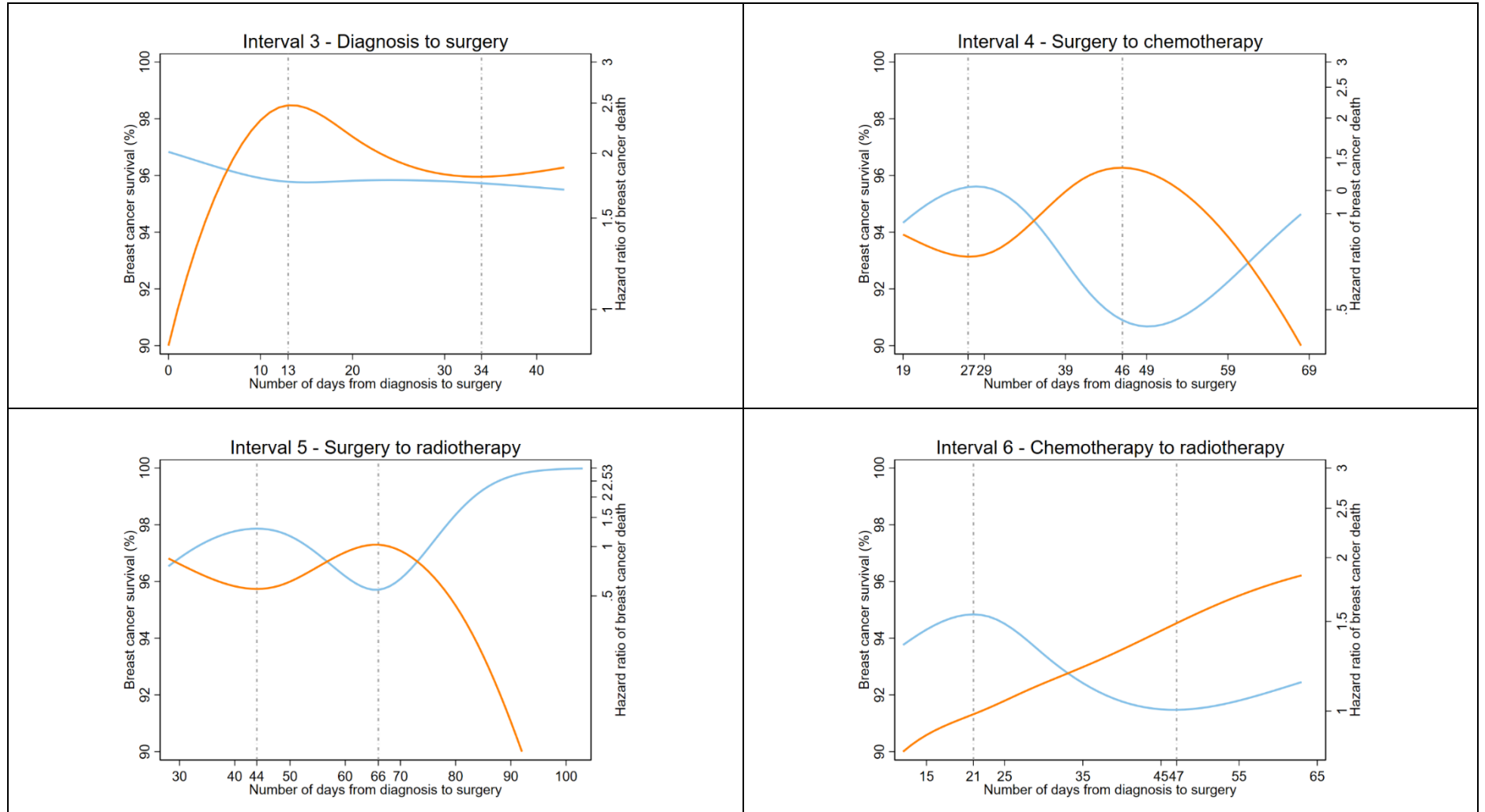
Candidate cut-points	<i>P</i>	Bonferroni-adjusted <i>P</i> <sup>†</sup>
<b>Interval 3</b>		
29	0.0042	0.0921
28	0.0155	0.3401
31	0.0181	0.3992
32	0.0186	0.4097
33	0.0212	0.4658
30	0.0319	0.7014
34	0.0393	0.8636
27	0.0726	1
14	0.0757	1
24	0.0866	1
25	0.1133	1
13	0.1219	1
15	0.1385	1
23	0.1399	1
26	0.1538	1
22	0.2098	1
16	0.2954	1
18	0.3746	1
20	0.4285	1
17	0.4496	1
21	0.4894	1
19	0.5246	1
<b>Interval 4</b>		
36	0.0095	0.1890
34	0.0134	0.2683
35	0.0153	0.3061
37	0.0206	0.4124
40	0.0241	0.4820
38	0.0474	0.9481
29	0.0520	1
32	0.0562	1
33	0.0590	1
44	0.0889	1
31	0.0897	1
41	0.0939	1
42	0.1016	1
30	0.1026	1
39	0.1046	1
46	0.1674	1
43	0.1791	1
45	0.1855	1
27	0.2303	1
28	0.2436	1
<b>Interval 5</b>		
49	0.1475	1
52	0.3647	1
51	0.4362	1
50	0.4482	1
61	0.4731	1
54	0.4796	1
45	0.5117	1
48	0.5213	1
44	0.5883	1
62	0.6180	1
55	0.6187	1
47	0.6455	1
46	0.7164	1
59	0.8295	1
53	0.8397	1
60	0.8472	1
63	0.8495	1
58	0.9382	1
64	0.9485	1
65	0.9539	1
56	0.9571	1
66	0.9802	1
57	0.9920	1

Candidate cut-points	<i>P</i>	Bonferroni-adjusted <i>P</i> <sup>†</sup>
<b>Interval 6</b>		
31	0.0054	0.1470
29	0.0109	0.2948
32	0.0122	0.3303
30	0.0157	0.4241
28	0.0254	0.6865
33	0.0385	1
47	0.0609	1
38	0.0633	1
36	0.0726	1
46	0.0778	1
37	0.0892	1
44	0.0950	1
35	0.0950	1
40	0.0998	1
27	0.1037	1
34	0.1093	1
39	0.1309	1
45	0.1338	1
43	0.1513	1
41	0.1595	1
42	0.2997	1
26	0.3871	1
23	0.4982	1
25	0.5439	1
22	0.7223	1
21	0.8080	1

\* Extracted from flexible parametric survival models, adjusted for age at diagnosis, tumour stage and grade, and mode of detection.

† Bonferroni-adjusted *P* values were truncated to 1.

**Figure 4. Survival (blue) and hazard ratio (orange) curves\* eight years from diagnosis,† by interval and time (days) since diagnosis**



\* Reference for hazard ratios was the day with most observations (number of women): day 1 for interval 3; day 36 for interval 4; day 63 interval 5; day 22 for interval 6. Days between the dashed lines were selected as cut-point candidates.

† All women with uncensored data were followed for at least 7.5 years (1 June 2013 – 31 December 2020).