SUPPLEMENTARY MATERIAL

APPENDIX I: RULES FOR MISSING DATES AND OUTLIERS

1. Imputation of missing day in the date

   Imputation rules for missing day (given month and year are known):

   a) Set missing day to '16';
   b) Consider adjacent dates in a backwards order (from "Treatment" to "First presentation"). For each pair of such adjacent dates: If dates are not in a logical order (e.g. "Treatment" is before "Diagnosis"), but month and year are the same in both dates, and the day was imputed to '16' in one of the dates:
      - Recode the day imputed earlier to '16' to the day from the adjacent date.

2. Range of Time intervals

   The time intervals (primary care interval, secondary care interval and diagnostic interval) must be in range 0-1 year.

   If > 1 year: set the interval to 365 days.

   If negative: set the interval to 0.

APPENDIX II: SUPPLEMENTARY MATERIAL ON STAGING

The ICBPM4 survey included histologically confirmed stage from either registries, PCPs or CTSs. We prioritised the use of T, N and M data over Dukes' and FIGO stage where both were available, and used an algorithm allowing certain missing stages to be assigned, assuming that additional data enabled categorization (Table 4, applied from Ostenfeld et al. 2012).

Table A1: Algorithm for cancer staging according to classification system

Tumour stage	TNM tumour stage	Dukes	SEER	FIGO
Localised	I + II	A + B	0 + 1	A+B
Regional	III	C	2	C
Distant	IV	D	3	D
Unknown	X	X	X	X

Abbreviation: TNM, tumour, node, metastasis. SEER, Surveillance, Epidemiology and End Results of the National Cancer Institute.

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Ostenfeld EB, Frøslev T, Friis S, Gandrup P, Madsen MR, Søgaard M. Completeness of colon and rectal cancer staging in the Danish Cancer Registry, 2004-2009. *Clin Epidemiol*. 2012;4 (SUPPL.2):33-38.

APPENDIX III: FLOWCHARTS FOR EACH CANCER

Figure A1: Flowchart showing breast cancer patient inclusion
Boxes on the left indicate exclusion of patients, while boxes on the right indicate drop-outs.

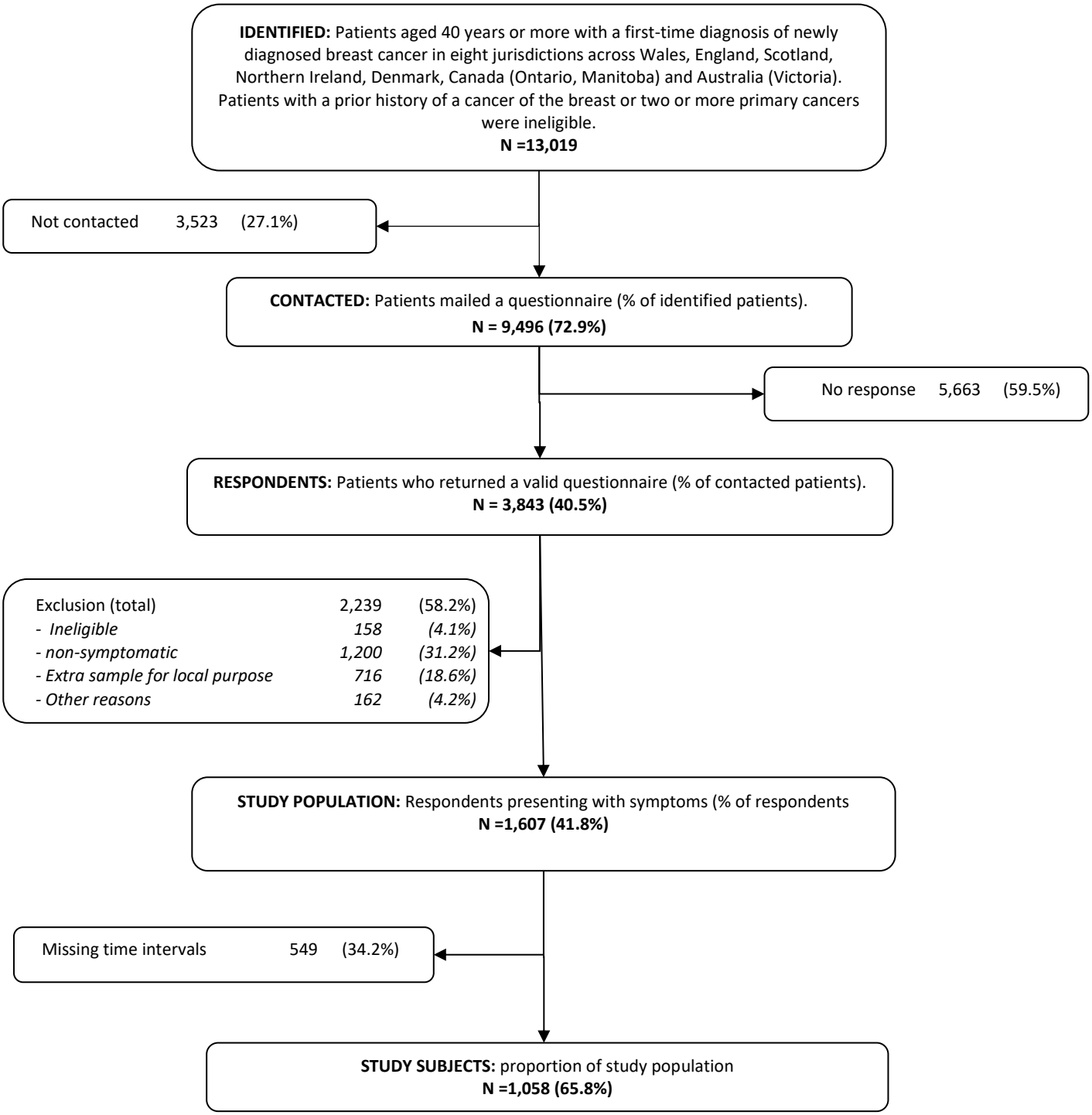


Figure A2: Flowchart showing colorectal cancer patient inclusion
Boxes on the left indicate exclusion of patients, while boxes on the right indicate drop-outs

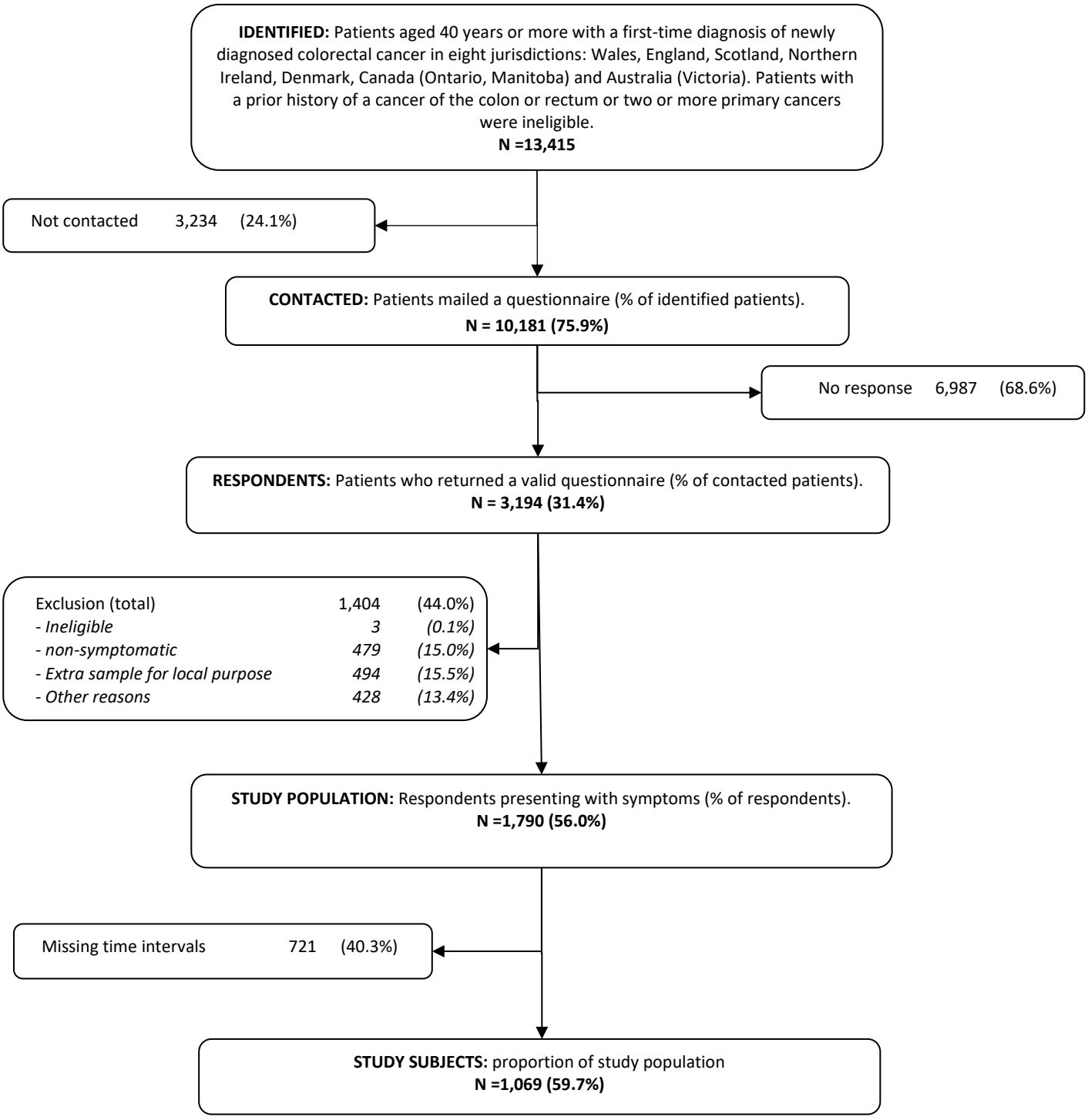


Figure A3: Flowchart showing lung cancer patient inclusion. Boxes on the left indicate exclusion of patients, while boxes on the right indicate drop-outs

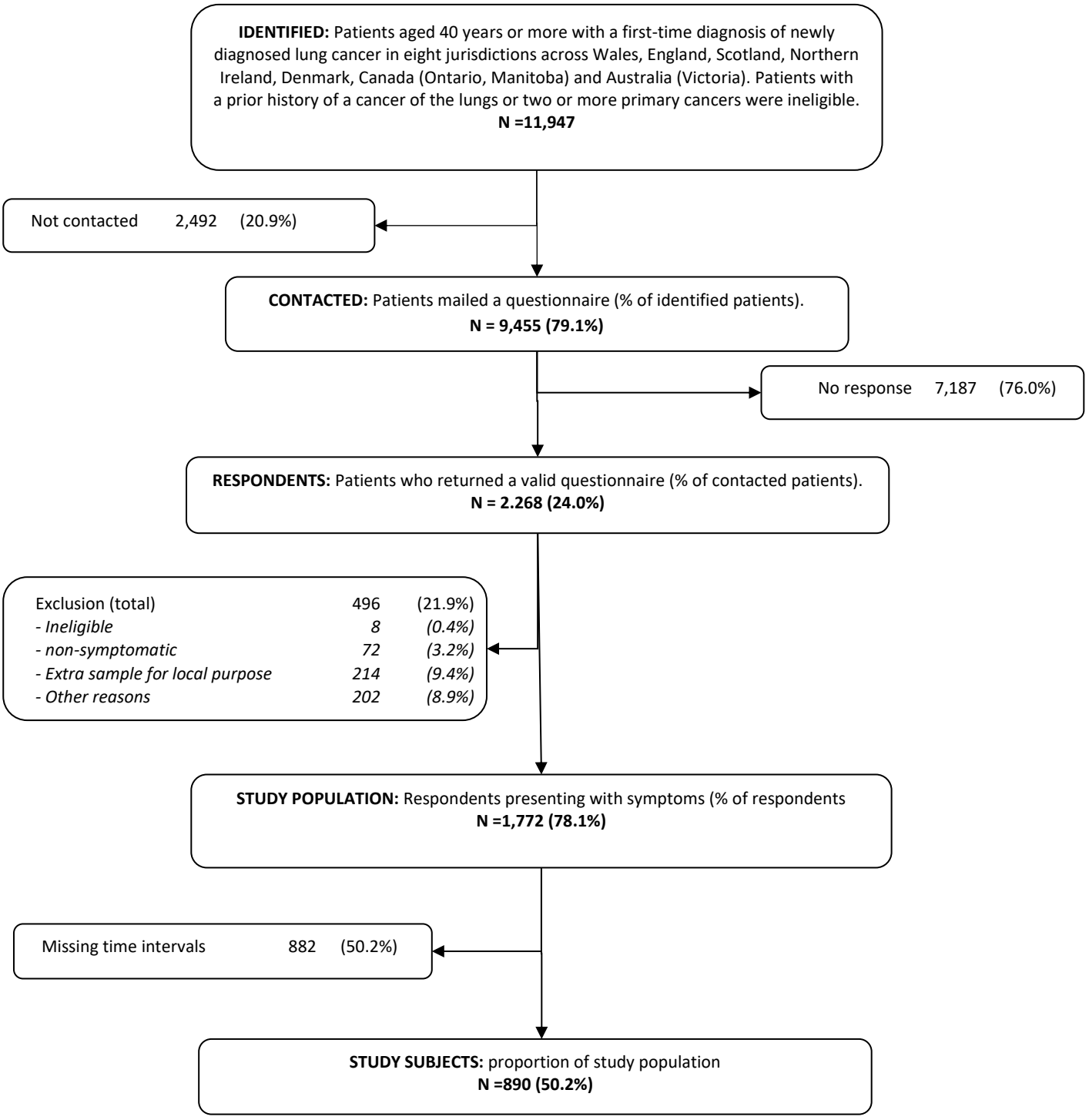
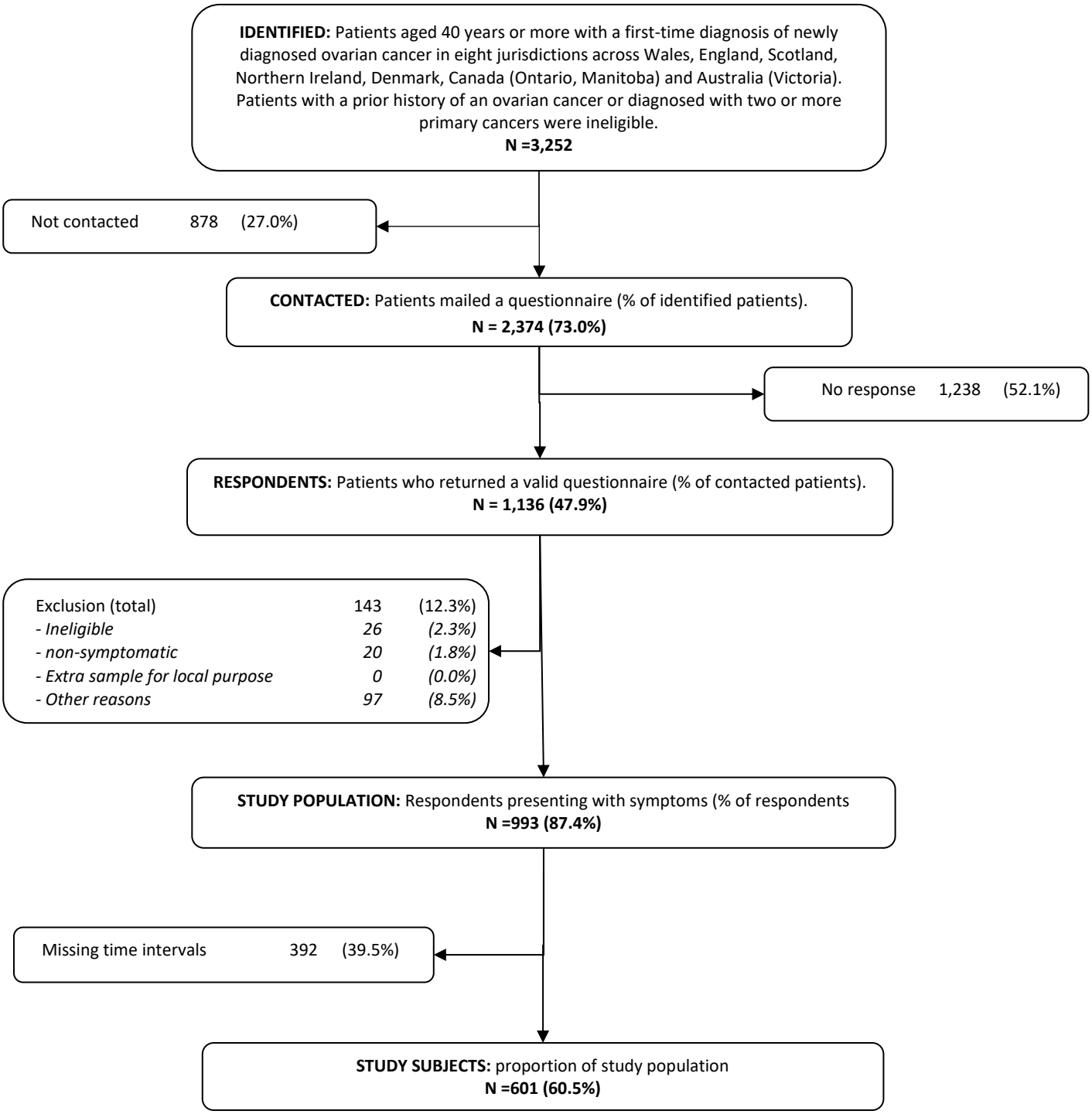


Figure A4: Flowchart showing ovarian cancer patient inclusion. Boxes on the left indicate exclusion of patients, while boxes on the right indicate drop-outs



APPENDIX IV: PATIENT CHARACTERISTICS FOR EACH CANCER

Table A1. The characteristics of symptomatic patients aged 40 or over with the first diagnosis of cancer included in the analyses for each cancer and each jurisdiction (n and % if nothing else stated)

	Wales	England	Scotland	N Ireland	Denmark	Ontario	Manitoba	Victoria
Breast cancer	**(N=97)**	**(N=167)**	**(N=160)**	**(N=172)**	**(N=141)**	**(N=70)**	**(N=109)**	**(N=142)**
Age (years), Median (IQI)	65 (50,78)	62 (51,74)	61 (52,75)	59 (49,70)	67 (51,77)	59 (51,68)	59 (50,69)	57 (49,69)
Comorbidity[1]								
None	64 (66)	117 (70)	111 (69)	131 (76)	78 (55)	48 (69)	77 (71)	103 (73)
Medium	32 (33)	47 (28)	46 (29)	39 (23)	61 (43)	20 (29)	30 (28)	39 (27)
High	1 (1)	2 (1)	2 (1)	2 (1)	1 (1)	0 (0)	2 (2)	0 (0)
Missing	0 (0)	1 (1)	1 (1)	0 (0)	1 (1)	2 (3)	0 (0)	0 (0)
Tumour stage – TNM								
I	27 (28)	60 (36)	53 (33)	62 (36)	43 (31)	21 (30)	38 (35)	49 (35)
II	52 (54)	70 (42)	77 (48)	71 (41)	57 (40)	36 (51)	57 (52)	69 (49)
III	10 (10)	17 (10)	14 (9)	33 (19)	18 (13)	12 (17)	10 (9)	21 (15)
IV	1 (1)	6 (4)	10 (6)	5 (3)	8 (6)	1 (1)	3 (3)	1 (1)
Missing	7 (7)	14 (8)	6 (4)	1 (1)	15 (11)	0 (0)	1 (1)	2 (1)
Time interval, Median (IQI) days								
Primary care interval	0 (0,0)	0 (0,0)	0 (0,1)	0 (0,0)	0 (0,0)	20 (7,37)	17 (7,30)	7 (4,15)
Secondary care interval	29 (20,52)	11 (8,14)	17 (13,30)	14 (10,18)	7 (2,17)	0 (0,17)	10 (0,17)	5 (0,10)
Diagnostic interval	29 (20,54)	12 (8,17)	19 (14,34)	14 (9,20)	8 (3,21)	27 (14,48)	27 (16,41)	13 (7,22)
CRC	**(N=157)**	**(N=152)**	**(N=127)**	**(N=160)**	**(N=207)**	**(N=77)**	**(N=72)**	**(N=117)**
Age (years), Median (IQI)	72 (64,80)	73 (64,80)	73 (60,80)	66 (59,74)	71 (65,77)	67 (57,76)	74 (66,81)	65 (54,75)
Gender, Male	92 (59)	84 (52)	68 (54)	97 (61)	120 (58)	44 (57)	36 (50)	70 (60)
Comorbidity[1]								
None	75 (48)	82 (54)	73 (57)	89 (56)	102 (50)	46 (60)	43 (60)	67 (57)
Medium	79 (50)	63 (41)	54 (43)	68 (43)	98 (47)	28 (36)	27 (38)	46 (39)
High	3 (2)	7 (5)	0 (0)	3 (2)	6 (3)	3 (4)	2 (3)	3 (3)
Missing	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)	0 (0)	1 (1)
Tumour stage – TNM or Dukes								
I	28 (18)	28 (18)	12 (9)	20 (13)	42 (20)	15 (19)	12 (17)	22 (19)
II	39 (25)	45 (30)	49 (39)	50 (31)	74 (36)	24 (31)	23 (32)	45 (39)
III	61 (39)	46 (30)	45 (35)	66 (41)	51 (25)	25 (32)	28 (39)	35 (30)
IV	21 (13)	25 (16)	20 (16)	23 (14)	29 (14)	7 (9)	8 (11)	13 (11)
Missing	8 (5)	8 (5)	1 (1)	1 (1)	11 (5)	6 (8)	1 (1)	2 (2)
Time interval, Median (IQI) days								
Primary care interval	3 (0,20)	2 (0,21)	4 (0,28)	0 (0,14)	1 (0,10)	1 (0,23)	4 (0,30)	9 (0,32)
Secondary care interval	40 (21,104)	34 (18,60)	21 (10,53)	49 (23,91)	20 (11,42)	47 (16,97)	56 (20,117)	13 (0,33)
Diagnostic interval	60 (29,153)	45 (23,83)	38 (21,92)	63 (28,105)	27 (13,64)	55 (27,133)	80 (40,171)	29 (12,66)
Lung cancer	**(N=109)**	**(N=143)**	**(N=118)**	**(N=123)**	**(N=154)**	**(N=74)**	**(N=80)**	**(N=89)**

Age (years), Median (IQI)	69 (64,75)	70 (64,76)	68 (64,76)	70 (63,75)	68 (62,74)	70 (65,74)	70 (64,77)	69 (63,74)
Gender, Male	65 (60)	73 (51)	63 (53)	64 (52)	80 (52)	39 (53)	34 (43)	52 (58)
Comorbidity[1]								
None	45 (41)	68 (48)	50 (42)	51 (41)	54 (35)	22 (30)	34 (43)	33 (37)
Medium	60 (55)	69 (48)	61 (52)	63 (51)	93 (60)	44 (59)	43 (54)	52 (58)
High	4 (4)	6 (4)	7 (6)	9 (7)	7 (5)	8 (11)	3 (4)	4 (4)
Tumour stage – TNM								
I	11 (10)	26 (18)	24 (20)	26 (21)	31 (20)	30 (41)	29 (36)	41 (46)
II	15 (14)	25 (17)	21 (18)	20 (16)	9 (6)	9 (12)	11 (14)	28 (31)
III	40 (37)	42 (29)	34 (29)	37 (30)	54 (35)	17 (23)	16 (20)	9 (10)
IV	33 (30)	43 (30)	31 (26)	39 (32)	56 (36)	16 (22)	22 (28)	8 (9)
Missing	10 (9)	7 (5)	8 (7)	1 (1)	4 (3)	2 (3)	2 (3)	3 (3)
Time interval, Median (IQI) days								
Primary care interval	20 (6,43)	11 (3,30)	17 (5,35)	13 (1,50)	7 (1,20)	32 (9,79)	30 (10,75)	10 (4,36)
Secondary care interval	19 (11,55)	31 (16,58)	18 (7,39)	32 (15,64)	21 (15,35)	34 (13,55)	45 (19,92)	29 (9,72)
Diagnostic interval	50 (23,116)	51 (29,93)	42 (21,90)	64 (27,117)	35 (22,69)	64 (37,171)	96 (43,136)	58 (23,107)
Ovarian cancer	**(N=52)**	**(N=153)**	**(N=60)**	**(N=57)**	**(N=160)**	**(N=24)**	**(N=31)**	**(N=64)**
Age (years), Median (IQI)	64 (58,72)	64 (56,71)	64 (54,72)	63 (56,70)	67 (58,74)	60 (53,67)	59 (56,70)	61 (54,68)
Comorbidity[1]								
None	32 (62)	110 (72)	46 (77)	47 (82)	107 (67)	14 (58)	18 (58)	47 (73)
Medium	20 (38)	42 (27)	12 (20)	10 (18)	53 (33)	9 (38)	12 (39)	17 (27)
High	0 (0)	1 (1)	2 (3)	0 (0)	0 (0)	1 (4)	1 (3)	0 (0)
Tumour stage – TNM or Figo								
I	21 (40)	20 (33)	29 (31)	13 (23)	42 (26)	6 (25)	6 (19)	16 (25)
II	4 (8)	7 (12)	13 (14)	3 (5)	7 (4)	0 (0)	3 (10)	12 (19)
III	16 (31)	22 (37)	34 (36)	36 (63)	60 (38)	11 (46)	14 (45)	33 (52)
IV	6 (12)	8 (13)	13 (14)	4 (7)	32 (20)	2 (8)	5 (16)	3 (5)
Missing	5 (10)	3 (5)	5 (5)	1 (2)	19 (12)	5 (21)	3 (10)	0 (0)
Time interval, Median (IQI) days								
Primary care interval	8 (0,37)	7 (0,24)	13 (3,32)	7 (0,24)	1 (0,11)	13 (7,64)	18 (1,50)	6 (2,22)
Secondary care interval	43 (24,61)	35 (18,58)	12 (4,36)	54 (23,91)	42 (25,101)	43 (35, 57)	17 (0,48)	13 (5,26)
Diagnostic interval	64 (36,106)	51 (32,80)	31 (14,59)	68 (33,118)	51 (29,111)	61 (42,137)	46 (20,119)	25 (14,43)

[1] Comorbidity coded as none=none reported, medium=1-2 reported and high=3+ reported;

IQI: inter-quartile interval

Table A2. Clinical features for excluded and included patients

	Excluded due to missing time intervals (N=2,544)		**Included** (N=3,618)	
Age (years), Median (IQI)	68	**(59,76)**	67	(58,75)
Gender, Male, among CRC and Lung cancer patients	850	(53)	1,081	(55)
Comorbidity				
None	1539	**(61)**	2,084	(58)
Medium	864	**(34)**	1,437	(40)
High	37	**(1)**	90	(2)
Missing	104	**(4)**	7	(1)
Tumour stage				
I	788	**(31)**	914	(25)
II	597	**(23)**	1,028	(28)
III	648	**(25)**	1,002	(28)
IV	341	**(13)**	511	(14)
Missing	170	**(7)**	163	(5)

Bold numbers indicate statistically significant result at p<0.05 or less.
N and % if nothing else is stated.

APPENDIX V: CRUDE AND ADJUSTED ESTIMATES

These figures show the crude (grey dashed) and adjusted odds ratios of being diagnosed at advanced tumour stage (III-IV) vs early tumour stage (I-II) as a function of length of the care interval calculated for each type of cancer and adjusted for jurisdiction, age, comorbidity and gender (lung, colorectal). The time interval was treated as a continuous variable using restricted cubic splines with three knots and 30 days as a reference point. Odds ratios are shown on a log scale, time intervals are shown on a squared scale. The solid curve indicates adjusted estimates with 95% confidence limits as dashed lines. The brown spikes show the distribution of the time interval.

Figure A5: Advanced colorectal cancer as a function of primary care interval

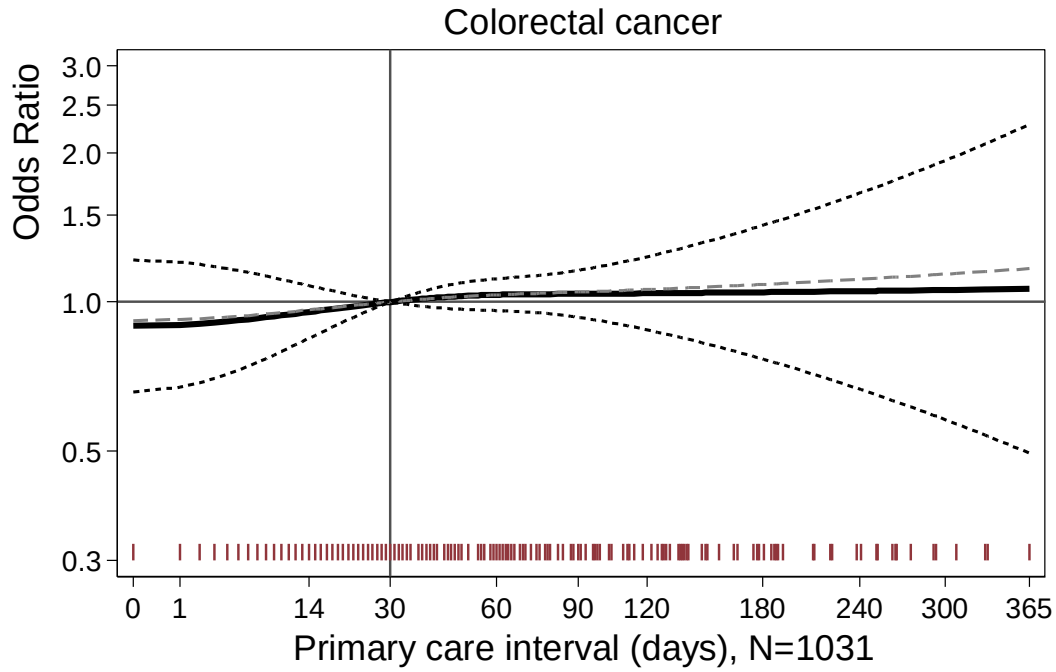


Figure A6: Advanced lung cancer as a function of primary care interval

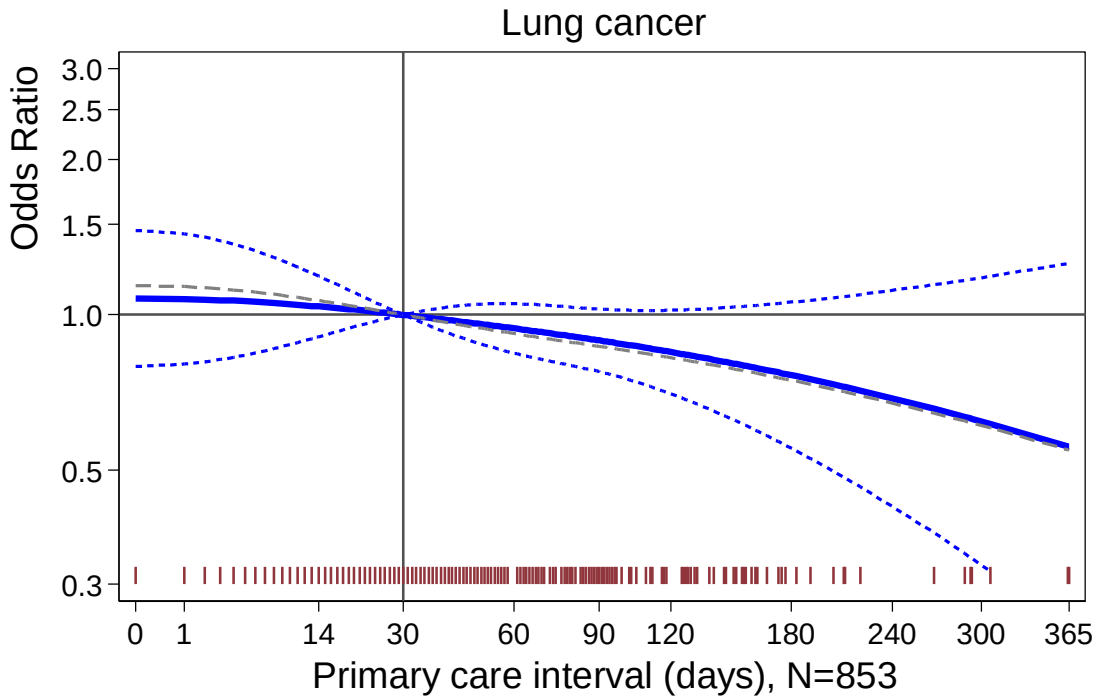


Figure A7: Advanced ovarian cancer as a function of primary care interval

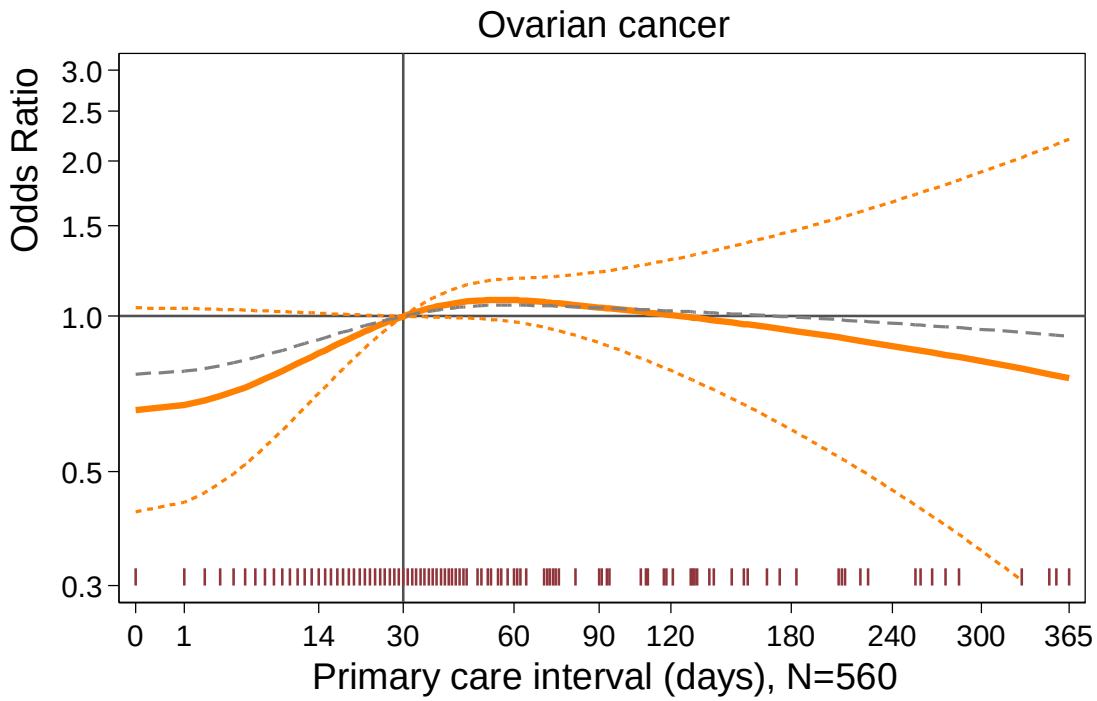


Figure A8: Advanced breast cancer as a function of secondary care interval

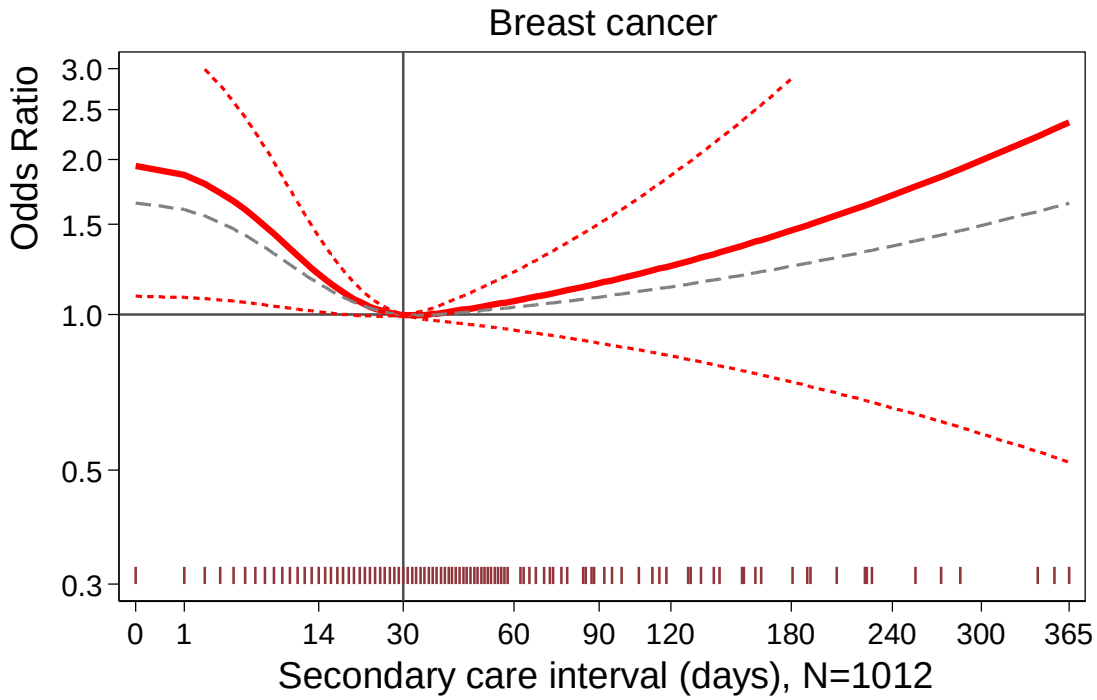


Figure A9: Advanced colorectal cancer as a function of secondary care interval

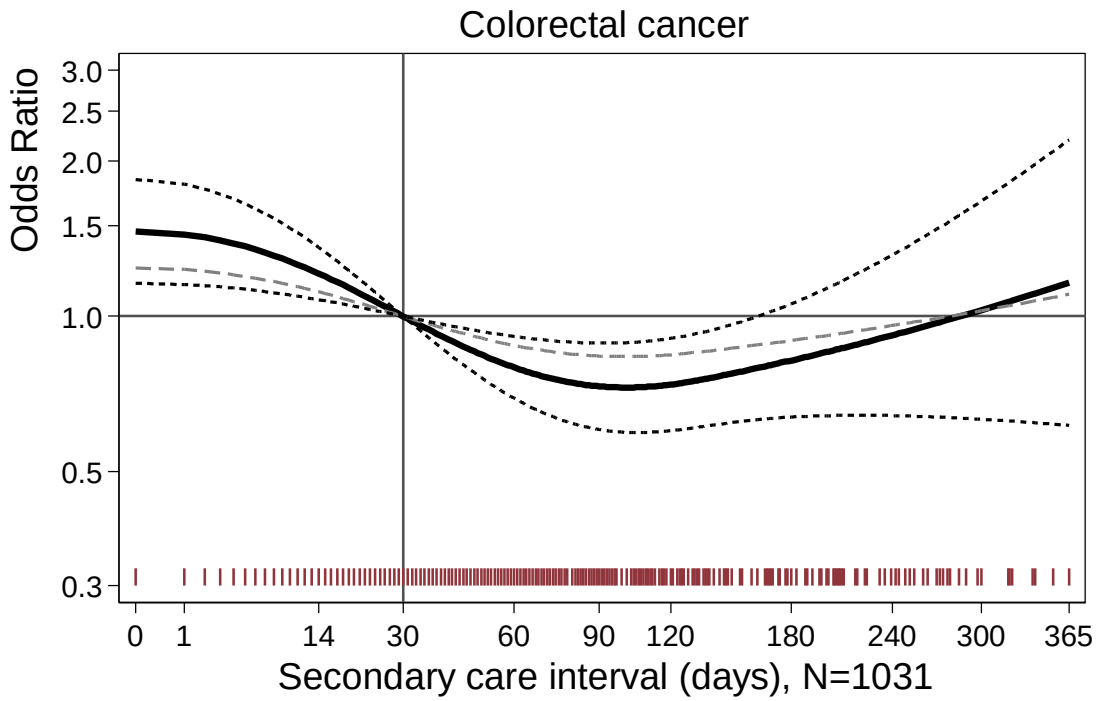


Figure A10: Advanced lung cancer as a function of secondary care interval

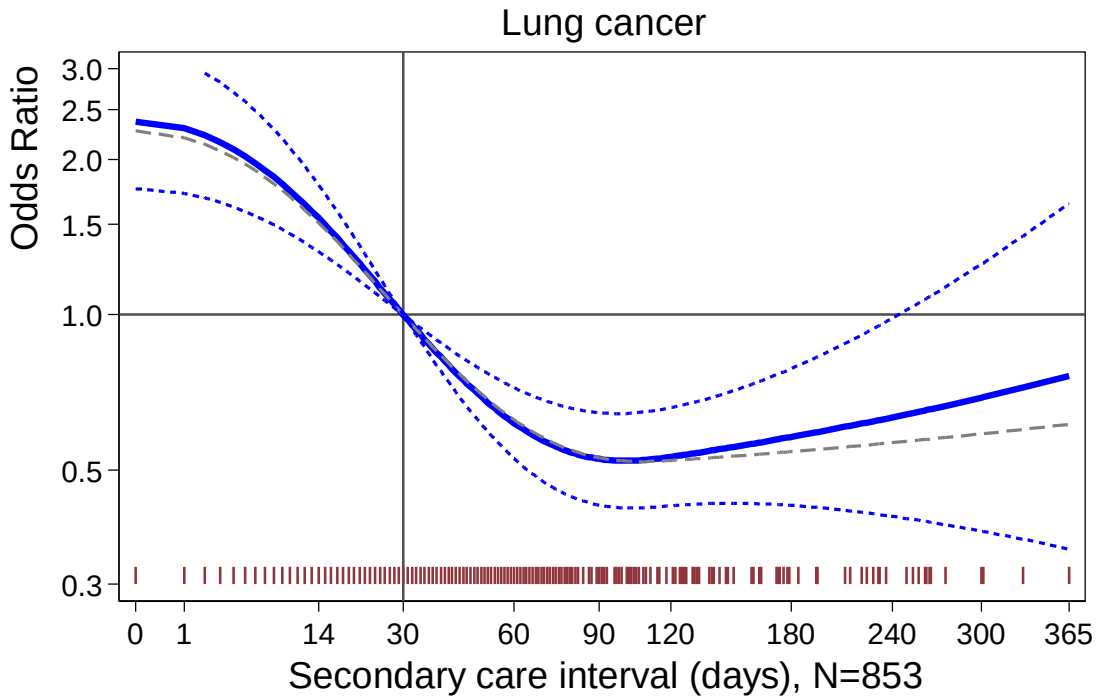


Figure A11: Advanced ovarian cancer as a function of secondary care interval

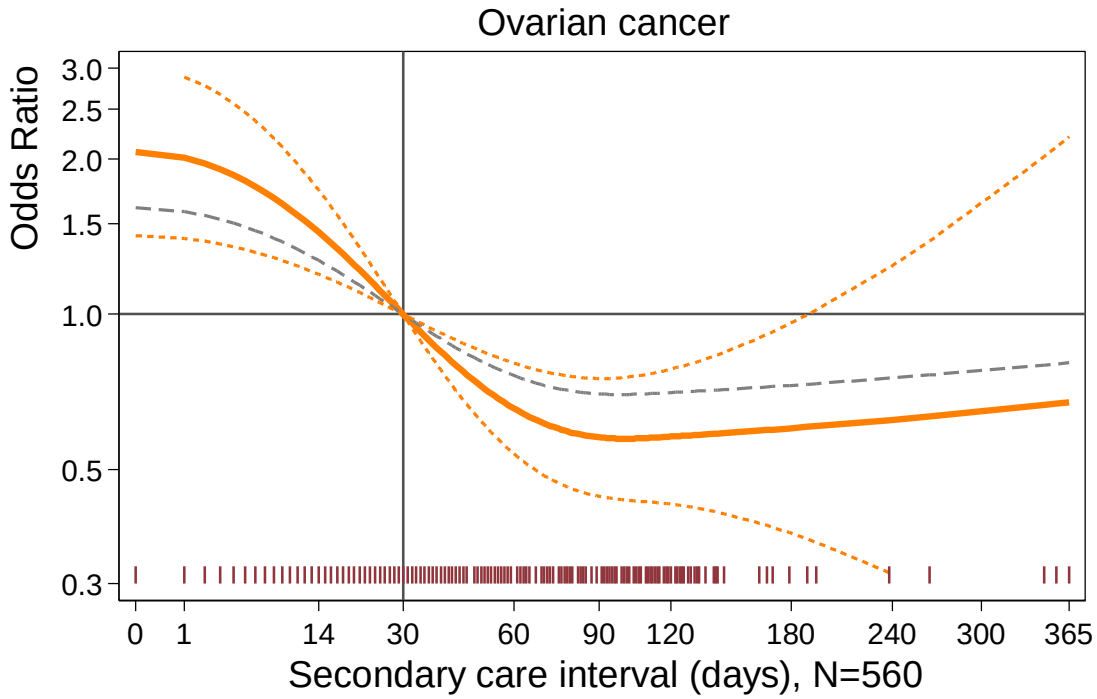
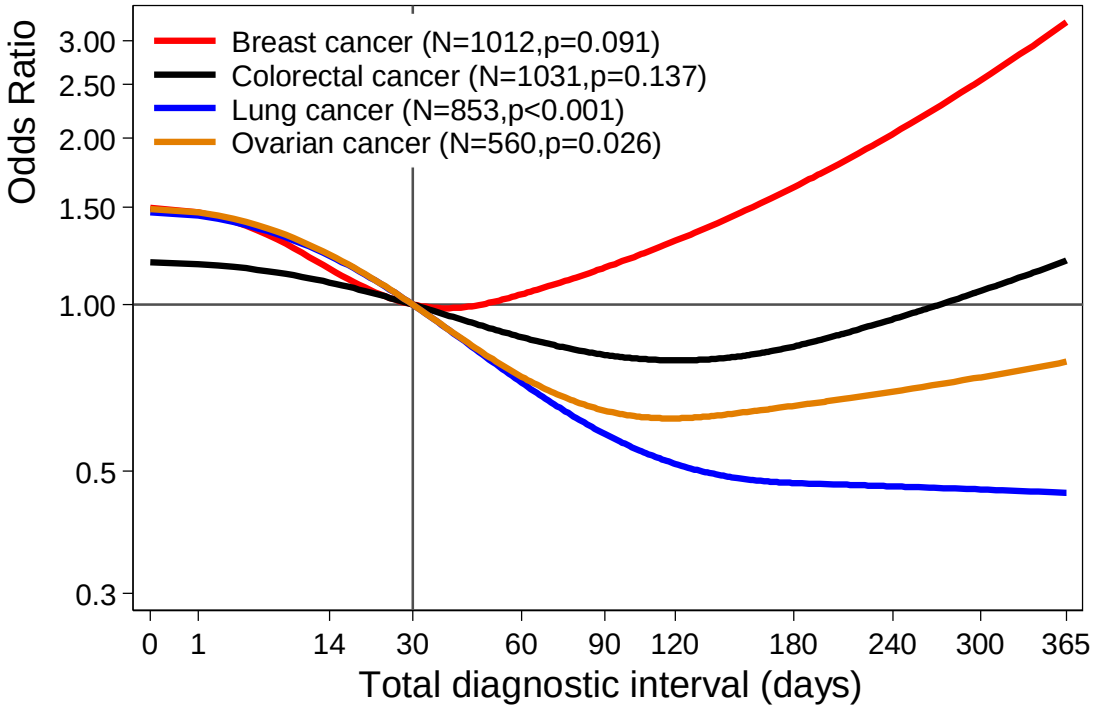


Figure A12: Advanced cancer as a function of diagnostic interval (time from first presentation to diagnosis) This figure show the adjusted (coloured) odds ratios of being diagnosed at advanced tumour stage (III-IV) vs early tumour stage (I-II) as a function of length of the diagnostic interval calculated for each type of cancer and adjusted for jurisdiction, age, comorbidity and gender (lung, colorectal). The time interval was treated as a continuous variable using restricted cubic splines with three knots and 30 days as a reference point. Odds ratios are shown on a log scale, time intervals are shown on a squared scale. The solid curve indicates adjusted estimates with 95% confidence limits as dashed lines.



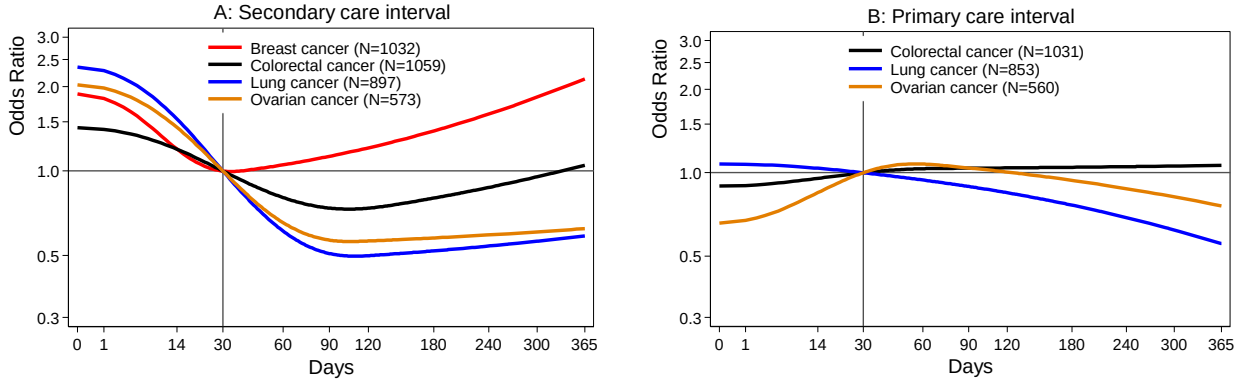
APPENDIX VI: SUPPLEMENTARY SENSITIVITY ANALYSES

We performed four sensitivity analyses testing the robustness of the basic model presented in Figure X. Each set of two figures below shows estimated odds ratios of being diagnosed with advanced cancer as a function of the length of the secondary care interval (figure A) and the primary care interval (figure B) analysed for cancer. The models are adjusted for jurisdiction, age, comorbidity and gender (lung, colorectal).

1. We investigate implications of including all patients from study population (also those for whom not all 3 time intervals were known)
2. We estimated the odds of distant vs. regional or localised cancer (i.e. *stage IV vs. stages I-II-III*) to test a measure which may approximate better to the relative risk.
3. We excluded patients with zero days from presentation to referral and from referral to diagnosis.
4. We investigate the implications of using only PCP data.

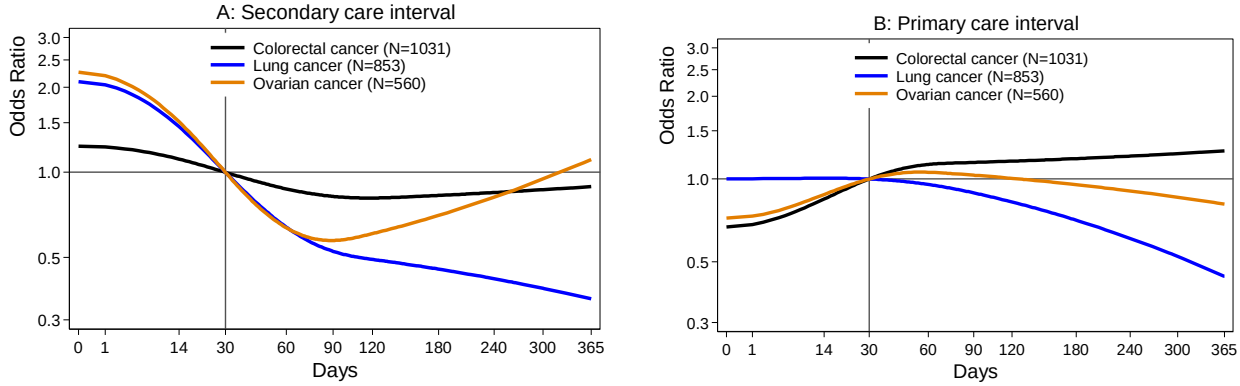
Sensitivity analyses 1: Including excluded patients

Including all patients from study population (also those for whom not all 3 time intervals were known). The splines analysis was not applied to the primary care interval in breast cancer patients due to more than 50% of intervals of zero days.



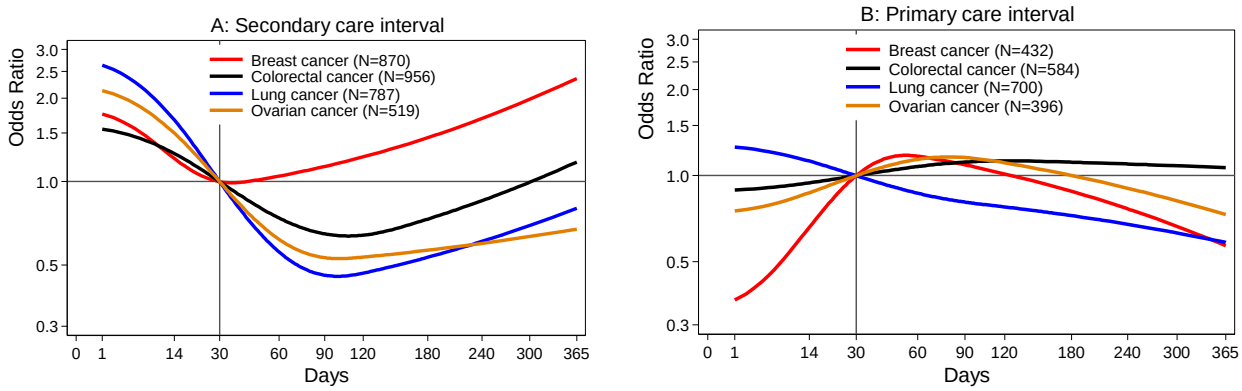
Sensitivity analysis 2: The odds of stage I tumour

The odds ratio of stage IV vs stage I-II-III. Breast cancer patients were excluded due to very small proportion of stage IV (3%).



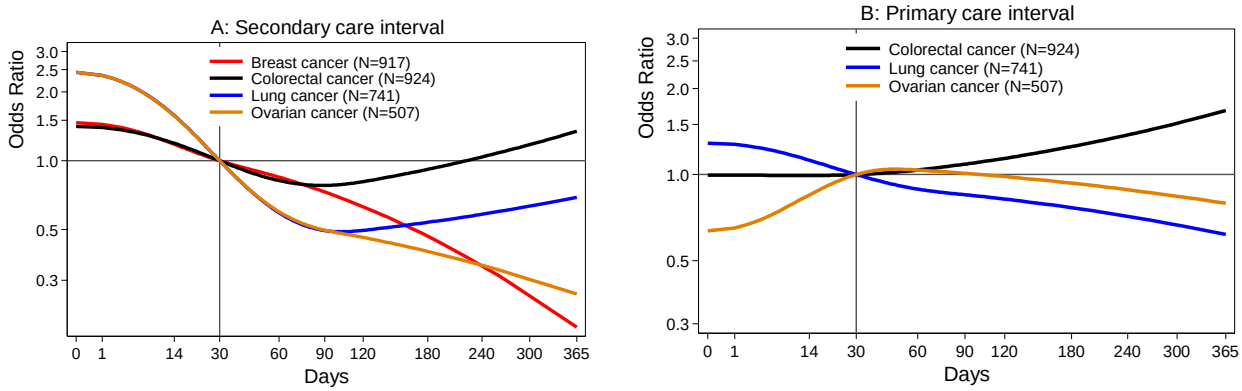
Sensitivity analysis 3: Excluding patients with no delay

Excluding patients with zero days from presentation to referral and from referral to diagnosis.



Sensitivity analysis 4: Using only PCP data

The splines analysis was not applied to the primary care interval in breast cancer patients due to more than 50% of intervals of zero days.



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