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Supplementary Table 2A Impact of variation in RR with age on cumulative risk estimates; ATM as an example

Age begin (years)	Age end (years)	Population incidence	Population incidence in interval	Population cumulative risk (%)	*ATM* incidence (RR 2.8-Constant)	*ATM* incidence in interval	*ATM* cumulative risk
20	25	0.0000	0.01%	0.0%	0.0000	0.02%	0.0%
25	30	0.0001	0.04%	0.1%	0.0002	0.12%	0.1%
30	35	0.0003	0.14%	0.2%	0.0008	0.38%	0.5%
35	40	0.0006	0.30%	0.5%	0.0017	0.84%	1.4%
40	45	0.0012	0.61%	1.1%	0.0034	1.70%	3.0%
45	50	0.0019	0.94%	2.0%	0.0053	2.64%	5.6%
50	55	0.0022	1.12%	3.1%	0.0063	3.14%	8.5%
55	60	0.0027	1.33%	4.4%	0.0074	3.71%	11.8%
60	65	0.0034	1.72%	6.0%	0.0096	4.81%	16.0%
65	70	0.0042	2.11%	8.0%	0.0118	5.92%	20.8%
70	75	0.0044	2.20%	10.0%	0.0123	6.17%	25.5%
75	80	0.0045	2.24%	12.0%	0.0125	6.26%	30.0%

Age begin (years)	Age end (years)	Population incidence	Population incidence in interval	Population cumulative risk (%)	*ATM* incidence (RR 5 to 50, then 2)	*ATM* incidence in interval	*ATM* cumulative risk
20	25	0.0000	0.01%	0.0%	0.0001	0.04%	0.0%
25	30	0.0001	0.04%	0.1%	0.0004	0.22%	0.3%
30	35	0.0003	0.14%	0.2%	0.0014	0.68%	0.9%
35	40	0.0006	0.30%	0.5%	0.0030	1.51%	2.4%
40	45	0.0012	0.61%	1.1%	0.0061	3.04%	5.3%
45	50	0.0019	0.94%	2.0%	0.0094	4.72%	9.7%
50	55	0.0022	1.12%	3.1%	0.0045	2.24%	11.7%
55	60	0.0027	1.33%	4.4%	0.0053	2.65%	14.0%
60	65	0.0034	1.72%	6.0%	0.0069	3.44%	16.9%
65	70	0.0042	2.11%	8.0%	0.0085	4.23%	20.4%
70	75	0.0044	2.20%	10.0%	0.0088	4.41%	23.8%
75	80	0.0045	2.24%	12.0%	0.0089	4.47%	27.1%

Population incidences are from SEER 2008-2012, all races. ATM RR of 2.8 from Easton et al systematic analysis.[1]
Variable RR estimate for ATM from Thompson et al.[2]

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Supplementary Table 2B Impact of variation in RR with age on cumulative risk estimates; *CHEK2* as an example

Age begin (years)	Age end (years)	Population incidence	Population incidence in interval (%)	Population cumulative risk (%)	*CHEK2* incidence (RR 3.0- constant)	*CHEK2* incidence in interval (%)	*CHEK2* cumulative risk (%)
20	25	0.0000	0.01%	0.0%	0.000042	0.02%	0.0%
25	30	0.0001	0.04%	0.1%	0.000264	0.13%	0.2%
30	35	0.0003	0.14%	0.2%	0.000816	0.41%	0.6%
35	40	0.0006	0.30%	0.5%	0.001806	0.90%	1.5%
40	45	0.0012	0.61%	1.1%	0.003651	1.83%	3.2%
45	50	0.0019	0.94%	2.0%	0.005658	2.83%	5.9%
50	55	0.0022	1.12%	3.1%	0.006729	3.36%	9.0%
55	60	0.0027	1.33%	4.4%	0.007956	3.98%	12.6%
60	65	0.0034	1.72%	6.0%	0.010308	5.15%	17.0%
65	70	0.0042	2.11%	8.0%	0.012678	6.34%	22.1%
70	75	0.0044	2.20%	10.0%	0.013218	6.61%	27.1%
75	80	0.0045	2.24%	12.0%	0.013413	6.71%	31.8%

Age begin (years)	Age end (years)	Population incidence	Population incidence in interval	Population cumulative risk (%)	*CHEK2* incidence (declining RR)	*CHEK2* incidence in interval	*CHEK2* cumulative risk
20	25	0.0000	0.01%	0.0%	0.0001	0.1%	0.1%
25	30	0.0001	0.04%	0.1%	0.0007	0.3%	0.4%
30	35	0.0003	0.14%	0.2%	0.0007	0.4%	0.8%
35	40	0.0006	0.30%	0.5%	0.0016	0.8%	1.6%
40	45	0.0012	0.61%	1.1%	0.0034	1.7%	3.2%
45	50	0.0019	0.94%	2.0%	0.0053	2.6%	5.7%
50	55	0.0022	1.12%	3.1%	0.0048	2.4%	8.0%
55	60	0.0027	1.33%	4.4%	0.0056	2.8%	10.5%
60	65	0.0034	1.72%	6.0%	0.0067	3.4%	13.5%
65	70	0.0042	2.11%	8.0%	0.0082	4.1%	17.0%
70	75	0.0044	2.20%	10.0%	0.0080	4.0%	20.2%
75	80	0.0045	2.24%	12.0%	0.0081	4.1%	23.4%

Population incidences are from SEER 2008-2012, all races.[3] CHEK2 RR of 3.0 (for truncating mutations) from Easton et al systematic analysis.[1] Variable RR estimate for CHEK2 from CHEK2 Breast Cancer Case-Control Consortium (OR 7.91 age <30 years, 2.65 ages 30–39 years, 2.80 ages 40–49 years, 2.13 ages 50–59 years, 1.95 ages 60–69 years, and 1.82 age 70+ years).[4]

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Supplementary Table 2C Impact of variation in RR with family history on cumulative risk estimates; *CHEK2* as an example

Age begin (years)	Age end (years)	Population incidence in interval	*CHEK2* incidence in interval (Constant RR 3)	*CHEK2* incidence in interval (1 FDR, RR 3.12)	CHEK2 incidence in interval (2 FDR, RR 4.17)	CHEK2 incidence in interval ('Familial', RR 4.8)
25	30	0.04%	0.13%	0.13%	0.18%	0.20%
30	35	0.14%	0.41%	0.41%	0.55%	0.64%
35	40	0.30%	0.90%	0.93%	1.24%	1.43%
40	45	0.61%	1.83%	1.90%	2.54%	2.93%
45	50	0.94%	2.83%	2.99%	4%	4.60%
50	55	1.12%	3.36%	3.54%	4.74%	5.45%
55	60	1.33%	3.98%	4.19%	5.60%	6.45%
60	65	1.72%	5.15%	5.52%	7.37%	8.49%
65	70	2.11%	6.34%	6.83%	9.13%	10.51%
70	75	2.20%	6.61%	7.18%	9.59%	11.04%

In format provided by Tung *et al.* (doi:10.1038/nrclinonc.2016.90)

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