SUPPLEMENTARY MATERIALS

Supplementary Methods

HEBON cohort study

Women are eligible for inclusion in the "HEreditary Breast and Ovarian cancer study, the Netherlands (HEBON cohort study)[1, 2] if they have undergone genetic testing for *BRCA1/2* and *CHEK2* in one of the participating centres (all Dutch academic medical centres and the Netherlands Cancer Institute). The HEBON cohort study collects data from participants via questionnaires and input from the Netherlands Cancer Registry (NCR), the Dutch Pathology Registry (PALGA)[3] and the municipal administration (BRP). The HEBON cohort study is performed in accordance with the declaration of Helsinki.

Data collection

Data entry into the central HEBON database is exclusively performed by trained data managers. Data on the type of mutation (*BRCA1, BRCA2*) and the date of the *BRCA1/2* DNA test were retrieved from the hospitals where screening took place. Data on personal cancer history (based on topographical and morphological codes; ICD-0-3 codes; http://codes.iarc.fr/), date/age/year of cancer diagnosis and treatment history (latter only available for breast cancer (BC) and tubo-ovarian cancer (OC)) were retrieved from the NCR, which registers all cancer diagnoses in the Netherlands and includes other variables such as treatment history. If additional data were found in pathology reports obtained via PALGA (e.g. on treatment history), these were added to the previously mentioned variables. Data on risk-reducing salpingo-oophorectomies (RRSO) and date of RRSO was obtained via PALGA. Data on deaths and date of deaths were obtained via the BRP, supplemented with data from the NCR, pathology reports and information obtained from family members.

For *BRCA1/2* mutation carriers who provided informed consent the most recent data input from the NCR and PALGA was in June and December 2017 (tumour registration/data complete up to January 2016). For all other women (*BRCA1/2* and non-*BRCA1/2* mutation carriers), the most recent NCR and PALGA input dates to April and June 2015, respectively (tumour registration/data complete up to January 2012). The most recent data from the BRP were received in December 2016 for *BRCA1/2* mutation carriers with informed consent, and June 2012 for all other women.

Data handling and missing variables

Four women (*BRCA1/2* mutation carriers, *n*=3/5,980 (0.05%); non-*BRCA1/2* mutation carriers, *n*=1/8,451 (0.1%)) were registered as deceased in the HEBON database while the date/age/year of death was unknown. In these cases, the date of death was considered to be between the last live contact and the end of follow-up.

For 2,896 women (*BRCA1/2* mutation carriers, *n*=1,682/5,980 (28.1%); non-*BRCA1/2* mutation carriers, *n*=1,214/5,980 (14.4%)), the date of the *BRCA1/2* DNA test was unknown. In these cases the date of a *BRCA1/2* DNA test was considered to be 01-01-1995 (date from which *BRCA1/2* DNA testing became regularly available).

The date/age/year of BC diagnosis was unknown for one *BRCA2* mutation carrier. In the subanalyses where BC was added as censoring event, the first occurring censoring event other than date of BC was used for censoring. For the description of baseline characteristics, BC was considered to have occurred during the observation period.

The date/age/year of OC diagnoses was unknown for two non-*BRCA1/2* mutation carriers. For the description of baseline characteristics, OC diagnoses were considered to have occurred during the observation period.

Data on a history of RRSO were manually curated for all women who developed endometrial cancer (including uterine sarcomas; EC) during follow-up, using the pathology reports (if available) retrieved from PALGA.

Data on whether or not women received hormone treatment (HT) for a specific BC was retrieved by the NCR from medical files, and centrally collected by HEBON. This variable was available for the majority of BCs, but the type and duration of HT was not specified. If a women had both a history of HT-treated BC and a tumour with an unknown HT status (*BRCA1/2* mutation carriers *n*=17, non-*BRCA1/2* mutation carriers *n*=8*)*, the date of HT-treated BC was used for all analyses that included HT-status.

Pathology review and histologic and molecular subgrouping

Pathology reports, hematoxylin and eosin (H&E) stained slides and formalin-fixed paraffin-embedded (FFPE) tumour tissue blocks for ECs of HEBON cohort *BRCA1/2* and non-*BRCA1/2* mutation carriers were

collected via PALGA and centrally reviewed by at least one expert gynaecopathologist to confirm histotype and endometrial origin. All specimens were handled in compliance with the Code of Conduct for dealing responsibly with human tissue in the context of health research (2011) drawn up by the Federation of Dutch Medical Scientific Societies.

Assignment of histologic subgroups

Histologic subtype diagnosis for cases that were available for pathology review were based on The World Health Organization (2014) criteria. Pathology review was primarily based on morphology (H&E slides without immunohistochemical stains), with the exception of high-grade EC without defining features (ambiguous EC). All cases with high-grade histology without defining features/for which histotype was difficult to establish ("ambiguous") were reviewed by at least two gynaecopathologists. When both agreed that the case was "ambiguous", *TP53*-mutation status/P53-IHC expression was used for further differentiation. *TP53*-wildtype/p53-wildtype ambiguous carcinomas were considered to be of the "endometrioid" histologic subgroup, and *TP53*-mutant/p53-abnormal ambiguous carcinomas were considered to be of the "serous-like" histologic subgroup. For cases that were not available for revision, histologic subtype and grade were extracted from pathology reports or, if unavailable, from the morphological ICD-0-3.1 code.

After pathology review, ECs were divided in the same histologic subgroups as the comparison group 1: (1) endometrioid (including *TP53*-wildtype/p53-wildtype ambiguous carcinomas), (2) serous-like (including *TP53*-mutant/p53-abnormal ambiguous carcinomas), (3) clear cell carcinoma, (4) sarcoma and (5) other.

Histologic, molecular and clinical characteristics of a subset of ECs in *BRCA1/2* mutation carriers were comprehensively described previously (case-ID; 1-41).[2]

Assignment of molecular subgroups

In the case of the *BRCA1/2* mutation carriers included in the study by de Jonge and colleagues,[2] the UCM-OncoPlus Assay[4] on FFPE-isolated tumour DNA was used for *TP53* mutation analyses. For the ECs in *BRCA1/2* mutation carriers included in this study, but for which mutation analysis failed/was not available (*n=3),* and for the ECs of both *BRCA1/2* mutation carriers (CaseID 42-62) and non-*BRCA1/2* mutation carriers (CaseID 101-140) that were not included in the study by de Jonge and collegues,[2] p53 immunohistochemistry was used as a surrogate marker to determine *TP53* mutation status. This was either performed manually (clone DO-7, 1:2000, DAKO) as described previously[2] or using the Dako Omnis autostainer (Agilent, Santa Clara,

CA). For the Dako Omnis autostainer, slides were deparaffinized and antigen retrieval was achieved on board using EnVision FLEX High pH Target Retrieval Solution for 30 minutes at 97 °C. Slides were then incubated on board at 32 °C with the following primary antibodies: p53, clone DO-7, Ready-To-Use (Dako) for 25 minutes; PMS2, clone EP51.2, ready-to-use for (Dako) for 25 minutes and MSH6 1:400; clone EPR3945 (Abcam) for 20 minutes. For PMS2, this was followed by incubation with a secondary antibody (EnVision FLEX+ rabbit LINKER) for 10 minutes. EnVision FLEX DAB+ was used as chromogen for 5 minutes, followed by counterstaining of the slides for 6 minutes using Mayer's hematoxylin.

Focal, weak and heterogeneous (not subclonal) nuclear p53 staining was considered as p53 "wild-type". Diffuse and strong nuclear staining >90% or completely absent nuclear staining "null pattern" (with positive internal control) was considered as p53-abnormal/mutant. In cases where p53 IHC was inconclusive, molecular analysis using next-generation sequencing was performed to determine final *TP53* mutation status (*n*=1). If a EC showed abnormal p53 expression or a *TP53* mutation, additional staining for MMR proteins (PMS2, MSH6) was performed. Expression of MMR proteins was scored in three categories (retained, loss and subclonal/regional loss of protein expression) as described previously reported by Stelloo and colleagues.[5] Tumours in which at least one of the mismatch repair proteins showed loss of expression were considered MMR-deficient (MMRd).

Using these surrogate markers, tumours were subsequently classified in one of the molecular subgroups as previously described:[6-8] (1) p53-abnormal or (2) other (including *POLE*-mutant: only analysed for cases included in the study by de Jonge and colleagues;[2] mismatch repair (MMR)-deficient and no surrogate marker profile group (NSMP)). In case both a *TP53* mutation/abnormal p53 expression and a MMRd phenotype were present (not considering subclonal/regional loss of MMRd), cases were assigned to the "other" group.[6, 9]

For cases in which no FFPE block was available for p53 analysis, p53 status was based upon histologic subtype and grade. These were used for classification in the molecular subgroups and subsequent analyses: EEC grade1/2, adenocarcinoma NOS grade 1/2, EEC/adenocarcinoma NOS grade not specified and clear cell carcinomas were assigned to the *TP53*-wildtype group.[6, 10, 11] EEC grade 3 and adenocarcinoma NOS grade 3 were considered 50% *TP53* wildtype, 50% *TP53* mutant.[6, 12] Uterine serous carcinomas and carcinosarcomas were considered *TP53* mutant.[6, 13]

Supplementary References

1. Heemskerk-Gerritsen BA, Seynaeve C, van Asperen CJ, et al. Breast cancer risk after salpingo-oophorectomy in healthy BRCA1/2 mutation carriers: revisiting the evidence for risk reduction. *J Natl Cancer Inst* 2015;107(5).

2. de Jonge MM, Ritterhouse LL, de Kroon CD, et al. Germline BRCA-associated Endometrial Carcinoma is a Distinct Clinicopathologic Entity. *Clin Cancer Res* 2019;25(24):7517–7526.

3. Casparie M, Tiebosch AT, Burger G, et al. Pathology databanking and biobanking in The Netherlands, a central role for PALGA, the nationwide histopathology and cytopathology data network and archive. *Cell Oncol* 2007;29(1):19–24.

4. Kadri S, Long BC, Mujacic I, et al. Clinical Validation of a Next-Generation Sequencing Genomic Oncology Panel via Cross-Platform Benchmarking against Established Amplicon Sequencing Assays. *J Mol Diagn* 2017;19(1):43–56.

5. Stelloo E, Jansen AML, Osse EM, et al. Practical guidance for mismatch repair-deficiency testing in endometrial cancer. *Ann Oncol* 2017;28(1):96–102.

6. Kandoth C, Schultz N, Cherniack AD, et al. Integrated genomic characterization of endometrial carcinoma. *Nature.* 2013;497(7447):67–73.

7. Talhouk A, McConechy MK, Leung S, et al. A clinically applicable molecular-based classification for endometrial cancers. *Br J Cancer* 2015;113(2):299–310.

8. Stelloo E, Bosse T, Nout RA, et al. Refining prognosis and identifying targetable pathways for high-risk endometrial cancer; a TransPORTEC initiative. *Mod Pathol* 2015;28(6):836–44.

9. León-Castillo A, de Boer SM, Powell ME et al. Molecular Classification of the PORTEC-3 Trial for High-Risk Endometrial Cancer: Impact on Prognosis and Benefit From Adjuvant Therapy. *J Clin Oncol* 2020;38(29):3388-97.

10. DeLair DF, Burke KA, Selenica P, et al. The genetic landscape of endometrial clear cell carcinomas. *J Pathol* 2017;243(2):230–241.

11. Stelloo E, Nout RA, Osse EM, et al. Improved Risk Assessment by Integrating Molecular and Clinicopathological Factors in Early-stage Endometrial Cancer-Combined Analysis of the PORTEC Cohorts. *Clin Cancer Res* 2016;22(16):4215–24.

12. Bosse T, Nout RA, McAlpine JN, et al. Molecular Classification of Grade 3 Endometrioid Endometrial Cancers Identifies Distinct Prognostic Subgroups. *Am J Surg Pathol* 2018;42(5):561–8.

13. Cherniack AD, Shen H, Walter V, et al. Integrated Molecular Characterization of Uterine Carcinosarcoma. *Cancer cell* 2017;31(3):411–23.

Supplementary Tables

Supplementary Table 1. Previously published cohort studies on endometrial cancer risk in*BRCA1/2* mutation carriers

Study	Cohort size	Total years at risk	Mean/median age at enrolment	Mean/median follow-up years	Path review	Observed (of which tamoxifen exposed)	Expected	SIR (95% CI, *p*-value)	EC distribution by *BRCA*-mutation	Countrie(s) from which the study population was retrieved
Beiner et al., 2007	All: 857 *BRCA1;* 619 *BRCA2;* 236 both; 2	2787	54.4 (range: 45-70)	3.3 (range: 0.01-9.6)	No	6 (4) EC *6* (4) *endometrioid*	1.13 n.a	5.3 (n.a, *p*=0.0011)[a]	4x *BRCA1* 2x *BRCA2*	North America, Europe, and Israel
Segev et al., 2013	All: 4456 *BRCA1;* 3536 *BRCA2;* 920	25322	42.7 (range: n.a.)	5.7 (range: n.a.)	No	17 (8) EC	9.06	1.87 (1.13-2.94, *p*=0.01)[b]	13x *BRCA1* 4x *BRCA2*	Canada, Italy, USA, Austria, Poland, Norway
Reitsma et al., 2013	All: 315 *BRCA1;* 201 *BRCA2;* 114	2062	43 (range: 30–71)	6 (range: 0-27)	No	2 (0) EC *2 (0) endometrioid*	0.94 *n.a*	2.13 (0.24-7.69, *p*=0.27)	1x *BRCA1* 1x *BRCA2*	The Netherlands
Shu et al., 2016	All: 1083 *BRCA1;* 627 *BRCA2;* 453 both; 3	6377	45.6 (IQR: 40.9-52.5)	5.1 (IQR: 3.0-8.4)	Partly	8 (5) EC *2 (2) endometrioid* *5 (3) serous(-like)* *1 (0) sarcoma*	4.30 3.62 0.34 0.14	1.9 (0.8-3.7, *p*=0.09) *0.6 (0.1-2.0, p=0.88)* *14.8 (4.8-34.6, p<0.001)*[c] *7.1 (0.2-39.4, p=0.13)*	5x *BRCA1* 3x *BRCA2*	USA and United Kingdom
Lee et al., 2017	All: 828 *BRCA1;* 438 *BRCA2;* 390	*n.a.*	43 (IQR: 34-52)	9 (IQR: n.a.)	No	5 (3) EC *5 (3) endometrioid*	2.04 *n.a*	2.45 (0.80-5.72, *p*=0.11)	3x *BRCA1* 2x *BRCA2*	Australia and New Zealand
Saule et al., 2018	All: 369 *BRCA1;* 238 *BRCA2;* 131	1779	*BRCA1:*47.22 (IQ: 1.29) *BRCA2:* 52.75 (IQ: 6.83)	*n.a.*[d] *n.a.*[d]	Yes	2 (0) EC *2 (0) serous*	0.62 0.062	"not increased", *p*=0.26 *32.2 (11.5-116.4, p<0.001)*	2x *BRCA1* 0x *BRCA2*	France
Laitman et al., 2019	All: 2627 *BRCA1;* 1463 *BRCA2;* 1154 both; 10	32774	*n.a.*	*n.a.*	No	14 (2[e]) EC *5* ([e]) *endometrioid* *5 (1) serous(-like)* *4 (1) sarcoma*	3.52 *n.a* 0.35 0.106	3.98 (2.174-6.673, *p<0.001*) *n.a.* *14.29 (4.639-33.34, p<0.001)* *37.74 (10.28-96.62, p<0.001)*	10x *BRCA1* *4x BRCA2*	Israel, mainly includes founder mutations; (*BRCA1*; 185delAG & 5382insC, *BRCA2*; 6174delT)
Kitson et al., 2020	All: 2609 *BRCA1;* 1350 *BRCA2;* 1259	59199	20.0 (IQR: 20.0-31.6)	23.8 (IQR: n.a.)	Partly	14 (3[f]) EC *7 (2[f]) endometrioid* *3 (1[f]) serous-like* *4 (0[f]) unknown*	8.22 *n.a.* 0.82 *n.a.*	1.70 (0.74-3.33, *p=n.a.*) *n.a.* *3.66 (0.01-23.41, p=n.a.)* *n.a.*	7x *BRCA1* 7x *BRCA2*	United Kingdom
de Jonge et al., current study	**All: 5980** *BRCA1;* 3788 *BRCA2;* 2151 both; 41	119296	27.4 (IQR: 25.0-37.8)	22.5 (IQR: 15.2-27.0)	Partly	58 (8[g]) EC *35 (3[g]) endometrioid* *19 (5[g]) serous(-like)* *3 (0) sarcoma* *1 (0) clear cell*	20.53 16.85 1.95 1.3 0.29	2.83 (2.2-3.7), p<0.001[h] *2.07 (1.5-2.9), p<0.001*[h] *9.77 (6.2-15.3), p<0.001*[h] *2.30 (0.7-7.1), p=0.14* *3.40 (0.5-24.1), p=0.25*	44x *BRCA1* 14x *BRCA2*	The Netherlands

[a]SIR only including non-tamoxifen exposed women; 2.7 (95% CI: n.a., *p*=0.17). [b]SIR only including non-tamoxifen exposed women; 1.67 (95% CI: 0.81-3.07, p=0.1). [c]SIR (serous-like) only including non-tamoxifen exposed women; 11.3 (95% CI: 1.4-40.8, *p*=0.01). [d]Age at end follow-up was given instead of follow-up years; *BRCA1*: 52.75 (IQR: 6.83), *BRCA2*: 56.51 (IQR: 0.8). [e]For 2/5 endometrioid EC, tamoxifen-exposure status was unknown, [f]History of tamoxifen-use was unknown for 4 cases; 1 with endometrioid histology, 2 with serous-like histology and 1 with unknown histology [g]Type and duration of hormone treatment not available. [h]For hazard ratios when additionally censoring for hormone-treated breast cancer, see Table 4.

Supplementary Table 2. Description of morphological ICD-0-3.1 codes assigned to the different histologic subgroups

Endometrioid (includes mucinous)	ICD-0 code	Serous/serous-like	ICD-0 code	Clear cell	ICD-0 code	Sarcoma	ICD-0 code	Other	ICD-0 code
Endometrioid adenocarcinoma, NOS	8380	Serous cystadenocarcinoma, NOS	8441	Clear cell adenocarcinoma, NOS	8310	Endometrial stromal sarcoma, NOS	8930	Neoplasm, malignant	8000
Endometrioid adenocarcinoma, secretory variant	8382	Papillary adenocarcinoma, NOS	8260			Endometrial stromal sarcoma, low grade	8931	Tumour cells, malignant	8001
Endometrioid adenocarcinoma, ciliated cell variant	8383	Serous surface papillary carcinoma	8461			Leiomyosarcoma, NOS	8890	Carcinoma, undifferentiated, NOS	8020
Adenocarcinoma with squamous metaplasia	8570	Papillary serous cystadenocarcinoma	8460			Epithelioid leiomyosarcoma	8891	Large cell carcinoma, NOS	8012
Adenosquamous carcinoma	8560	Cystadenocarcinoma	8440			Myxoid leiomyosarcoma	8896	Large cell neuroendocrine carcinoma	8013
Adenocarcinoma with spindle cell metaplasia	8572	Mesodermal mixed tumour	8951			Rhabdomyosarcoma, NOS	8900	Large cell carcinoma with rhabdoid phenotype	8014
Adenocarcinoma with apocrine metaplasia	8573	Carcinosarcoma, NOS	8980			Myosarcoma	8895	Glassy cell carcinoma	8015
Mucin-producing adenocarcinoma	8481	Mullerian mixed tumour	8950			Pleomorphic rhabdomyosarcoma, adult type	8901	Giant cell carcinoma	8031
Villous adenocarcinoma	8262	Metaplastic carcinoma, NOS	8575			Mixed type rhabdomyosarcoma	8902	Pseudosarcomatous carcinoma	8033
Adenocarcinoma, NOS	8140	Carcinofibroma	8934			Embryonal rhabdomyosarcoma, NOS	8910	Small cell carcinoma, NOS	8041
Carcinoma, NOS	8010	Adenocarcinoma with mixed subtypes	8255			Alveolar rhabdomyosarcoma	8920	Combined small cell carcinoma	8045
Solid carcinoma, NOS	8230	Mixed cell adenocarcinoma	8323			Sarcoma, NOS	8800	Non-small cell carcinoma	8046
Adenocarcinoma in adenomatous polyp	8210					Spindle cell sarcoma	8801	Squamous cell carcinoma, NOS	8070
Adenocarcinoma in villous adenoma	8261					Giant cell sarcoma (except of bone M-9250/3)	8802	Squamous cell carcinoma, keratinizing, NOS	8071
Adenocarcinoma in tubolovillous adenoma	8263					Small cell sarcoma	8803	Squamous cell carcinoma, large cell, nonkeratinizing, NOS	8072
Endometrioid adenofibroma, malignant	8381					Undifferentiated sarcoma	8805	Squamous cell carcinoma, spindle cell	8074
Mucinous adenocarcinoma	8480					Fibrosarcoma, NOS	8810	Basaloid squamous cell carcinoma	8083
						Malignant fibrous histiocytoma	8830	Squamous cell carcinoma, clear cell type	8084
						Malignant perivascular epitheliod cell tumour	8714	Transitional cell carcinoma	8120
						Adenosarcoma	8933	Scirrhous adenocarcinoma	8141
						Stromal sarcoma, NOS	8935	Superficial spreading adenocarcinoma	8143
						Mesenchymoma, malignant	8990	Adenoid cystic carcinoma	8200
						Synovial sarcoma, NOS	9040	Cribriform carcinoma, NOS	8201
						Haemangiosarcoma	9120	Tubular adenocarcinoma	8211
						Chondrosarcoma, NOS	9220	Carcinoid tumour, NOS	8240
						Ewing sarcoma	9260	Mixed adenoneuroendocrine carcinoma	8244
								Neuroendocrine carcinoma, NOS	8246
								Acidophil carcinoma	8280
								Clear cell adenocarcinofibroma	8313

	Granular cell carcinoma	8320
	Follicular adenocarcinoma, NOS (C73.9)	8330
	Adenocarcinoma, endocervical type	8384
	Papillary cystadenocarcinoma, NOS	8450
	Papillary mucinous cystadenocarcinoma	8471
	Mucinous adenocarcinoma, endocervical type	8482
	Signet ring cell carcinoma	8490
	Adenocarcinoma with neuroendocrine differentiation	8574
	Mesonephroma, malignant	9110
	Peripheral neuroectodermal tumour	9364
	Malignant peripheral nerve sheath tumour	9540
	No microscopic confirmation	9990

Supplementary Table 3. Number of person-years at risk and number of events per 5-year age category for*BRCA1/2* mutation carriers and non-*BRCA1/2* mutation carriers

	***BRCA1/2* carriers**					**non-*gBRCA1/2* carriers**			
Age category	**Person-years at risk, No. (%)**	**All ECs[a], No (%)**	**Endometrioid**	**Serous-like**	**Sarcoma**	**Person-years at risk, No. (%)**	**All ECs[b], No. (%)**	**Endometrioid**	**Serous-like No. (%)**
25-29	14643 (12.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	19663 (12.2)	1 (3.0)	1 (3.3)	0 (0.0)
30-34	17091 (14.3)	2 (3.4)	1 (2.9)	0 (0.0)	1 (33.3)	23376 (14.5)	0 (0.0)	0 (0.0)	0 (0.0)
35-39	17990 (15.1)	2 (3.4)	2 (5.7)	0 (0.0)	0 (0.0)	24984 (15.5)	1 (3.0)	1 (3.3)	0 (0.0)
40-44	17408 (14.6)	2 (3.4)	2 (5.7)	0 (0.0)	0 (0.0)	24303 (15.1)	0 (0.0)	0 (0.0)	0 (0.0)
45-49	15435 (12.9)	7 (12.1)	4 (11.4)	3 (15.8)	0 (0.0)	21314 (13.3)	4 (12.1)	4 (1.3)	0 (0.0)
50-54	12578 (10.5)	7 (12.1)	5 (14.2)	0 (0.0)	2 (66.7)	16704 (10.4)	9 (27.3)	8 (26.7)	1 (33.3)
55-59	9306 (7.8)	9 (15.5)	5 (14.2)	3 (15.8)	0 (0.0)	12133 (7.5)	5 (15.2)	5 (16.7)	0 (0.0)
60-64	6377 (5.3)	11 (19.0)	6 (14.2)	5 (26.3)	0 (0.0)	8124 (5.1)	6 (18.2)	6 (0.2)	0 (0.0)
65-69	4052 (3.4)	14 (24.1)	7 (20.0)	7 (36.8)	0 (0.0)	4580 (2.8)	3 (9.1)	3 (10.0)	0 (0.0)
70-74	2355 (2.0)	3 (5.2)	2 (5.7)	1 (5.3)	0 (0.0)	2709 (1.7)	3 (9.1)	2 (6.7)	1 (33.)
75-79	1225 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1593 (1.0)	1 (3.0)	0 (0.0)	1 (33.3)
80-84	558 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	826 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
85-89	219 (0.2)	1 (1.7)	1 (2.9)	0 (0.0)	0 (0.0)	382 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
90-94	42 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	121 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)
95+	16 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	27 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

[a]One clear cell carcinoma occurred at age 59 years, this tumour is not separately mentioned in the columns. [b]None of the non-*BRCA1/2* mutation carriers developed a sarcoma or clear cell carcinoma during follow-up.
Abbreviations; EC: Endometrial Cancer

Supplementary Table 4. Details on the included endometrial cancers in the cohort

	***BRCA* carriers**	**Non-*BRCA* carriers**	***p* value**[a]
Endometrial cancer, No. (%)	58 (100)	33 (100)	
Median age at diagnoses, yrs (range)	60.2 (33.1-85.4)	57.4 (29.7-79.8)	0.49
Histotype (after review)			
Endometrioid			
grade 1, No. (%)	18 (31.0)	14 (42.4)	
grade 2, No. (%)	3 (5.2)	2 (6.1)	
grade 3, No. (%)	6 (10.3)	1 (3.0)	
Mucinous, No. (%)	1 (1.7)	0 (0)	
Serous, No. (%)	9 (15.5)	1 (3.0)	
Carcinosarcoma, No. (%)	4 (6.9)	2 (6.1)	
Ambiguous, No. (%)	6 (10.3)	0 (0)	
Low grade endometrial stromal sarcoma, No. (%)	1 (1.7)	0 (0)	
Leiomyosarcoma, No. (%)	1 (1.7)	0 (0)	
Adenosarcoma, No. (%)	1 (1.7)	0 (0)	
Not reviewed, No. (%)	8 (13.8)	13 (39.4)	
Histologic groups			0.02
Endometrioid, No. (%)	35 (60.3)	30 (90.9)	
Serous/Serous-like[b], No. (%)	19 (32.8)	3 (9.1)	
Sarcoma, No. (%)	3 (5.2)	0 (0)	
Clear cell, No. (%)	1 (1.7)	0 (0)	
Other, No. (%)	0 (0)	0 (0)	
Occurrence EC			
After *BRCA1/2* DNA test, No. (%)	28 (48.3)	7 (21.2)	
Before *BRCA1/2* DNA test, No. (%)	20 (34.5)	22 (66.7)	
Date *BRCA1/2* DNA test unknown, No. (%)	10 (17.2)	4 (12.1)	
Pathology review			0.01
Available, No. (%)	50 (86.2)	20 (60.6)	
Not available, No. (%)	8 (13.8)	13 (39.4)	
Histologic group change after review			0.0102
Yes, No. (%)	11 (19.0)	0 (0.0)	
No, No. (%)	39 (67.2)	20 (60.6)	
Not reviewed, No. (%)	8 (13.8)	13 (39.4)	
p53-abnormal, including cases not available for review			<0.001
Yes, No. (%)	27 (46.6)	3 (9.1)	
No, No. (%)	31 (53.4)	30 (90.9)	
P53-abnormal, excluding cases not available for review			<0.001
Yes, No. (%)	27 (46.6)	2 (6.1)	
No, No. (%)	23 (39.7)	17 (51.5)	
Not available, No. (%)	8 (13.8)	14 (42.4)	
P53-status based on;			<0.001
Mutation analyses, No. (%)	37 (63.8)	0 (0.0)	
IHC, No. (%)	13 (22.4)	19 (57.6)	
Histotype, No. (%)	8 (13.8)	14 (42.4)	

Abbreviations: EC: Endometrial cancer, IHC: immunohistochemistry
[a]*p* values were calculated using the Chi-square test (categorical variables) and the Mann-Whitney U-test (numerical variables). [b]Includes six carcinomas of ambiguous morphology that were classified as serous-like based on p53-status.

Supplementary Table 5. Characteristics of endometrial cancers that occurred in the *BRCA1/2* mutation carrier cohort

Case ID[a]	Final histological subgroup[b]	BRCA mutation	Year	Age	Original Diagnoses	Diagnoses after pathology review	P53-status[c]	Category change histologic subgroup after review	Molecular subgroup	RRSO, years in between RRSO-EC	Adnexal involvement/ (history of) ovarian malignancy	Adnexal specimens available for revision	Hysterectomy with/without adnexae
Included as endometrial cancer in main analyses													
1	endometrioid	BRCA1	2011	63	EEC gr1	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy, adnexae removed shortly before (RRSO with EC diagnoses in concurrently performed curettage)
2	endometrioid	BRCA1	2005	55	EEC gr2	EEC gr1	wildtype[d]	No	Other	Yes, 5.1	No	No	Hysterectomy without adnexae (history RRSO)
3	endometrioid	BRCA1	2013	70	EEC gr3	EEC gr3	mutant[d]	No	p53-abnormal	Yes, 15.6	No	Yes	Hysterectomy without adnexae (history RRSO)
11	endometrioid	BRCA1	2004	63	adenocarcinoma NOS, gr1	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy with adnexae
13	endometrioid	BRCA1	2004	50	EEC gr1	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy with adnexae
15	endometrioid	BRCA1	2009	74	EEC gr3	EEC gr3	mutant[d]	No	p53-abnormal	No	No	No, not removed	Hysterectomy without adnexae
17	endometrioid	BRCA1	2013	65	EEC gr3	EEC gr3	mutant[d]	No	p53-abnormal	Yes, 9.0	No	Yes	Hysterectomy without adnexae (history RRSO)
18	endometrioid	BRCA1	2005	59	EEC gr1	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy with adnexae
19	endometrioid	BRCA1	1997	46	EEC gr2	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy, adnexae removed shortly before
20	endometrioid	BRCA1	2011	49	EEC gr2	EEC gr3	mutant[d]	No	p53-abnormal	Yes, 9.5	No	Yes	Hysterectomy without adnexae (history RRSO)
21	endometrioid	BRCA1	2013	65	EEC gr2	EEC gr2	mutant[d]	No	p53-abnormal	Yes, 11.6	No	Yes	Hysterectomy without adnexae (history RRSO)
23	endometrioid	BRCA1	2011	53	mucinous	mucinous	wildtype[d]	No	Other	Yes, 6.1	No	Yes	Hysterectomy without adnexae (history RRSO)
28	endometrioid	BRCA1	2002	44	EEC gr1	EEC gr1	wildtype[d]	No	Other	Yes, 0.4	No	Yes	Hysterectomy without adnexae (history RRSO)
30	endometrioid	BRCA1	2012	39	EEC gr2	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	No	No	No, unknown if removed	Unknown
33	endometrioid	BRCA1	2000	49	EEC gr2	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy with adnexae
34	endometrioid	BRCA1	2005	54	adenocarcinoma NOS, gr2	EEC gr2	mutant[d]	No	p53-abnormal	No[g]	No	Yes	Hysterectomy with fallopian tubes
35	endometrioid	BRCA1	2000	49	EEC gr1	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy with adnexae
37	endometrioid	BRCA1	2014	33	EEC gr2-3	EEC gr2	mutant[d]	No	p53-abnormal	Yes, 5.1	No	Yes	Hysterectomy without adnexae (history RRSO)
38	endometrioid	BRCA1	2010	56	EEC gr1	EEC gr1	wildtype[d]	No	Other	Yes[h], 4.8	History ovarian clear cell carcinoma	Yes	Hysterectomy without adnexae (history ovariectomy)
41	endometrioid	BRCA1	2007	50	EEC gr2	EEC gr1	wildtype[d]	No	Other	Yes, 0.6	No	Yes	Hysterectomy without adnexae (history RRSO)
47	endometrioid	BRCA1	1999	58	adenocarcinoma NOS, gr1-2	EEC gr1	wildtype	No	Other	No	Simultaneous bilateral HGSOC	Yes	Hysterectomy with adnexae

50	endometrioid	BRCA1	2006	85	EEC gr3	EEC gr3	mutant[d]	No	p53-abnormal	No	No	No	Hysterectomy with adnexae
51	endometrioid	BRCA1	1996	69	EEC gr3	EEC gr3	mutant	No	p53-abnormal	No	No	Yes	Hysterectomy with adnexae
56	endometrioid	BRCA1	2007	63	EEC gr1	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	No	Simultaneous HGSOC left side, right side not reported	No	Hysterectomy with adnexae
60	endometrioid	BRCA1	1994	57	adenocarcinoma NOS gr1	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	No	No	No, unknown if removed	Unknown
61	endometrioid	BRCA1	2006	68	EEC, gr not specified	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	No	Simultaneous HGSOC right side, left side not involved	No	Hysterectomy with adnexae
62	endometrioid	BRCA1	2008	40	EEC gr1	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	No	No	No	Hysterectomy with adnexae
4	endometrioid	BRCA2	2015	64	EEC gr1	EEC gr1	mutant[d]	No	Other[f]	Yes, 6.9	No	Yes	Hysterectomy without adnexae (history RRSO)
12	endometrioid	BRCA2	2004	62	EEC gr2	EEC gr1	wildtype[d]	No	Other	Yes, 1.0	No	Yes	Hysterectomy without adnexae (history RRSO)
24	endometrioid	BRCA2	2011	67	EEC gr2	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy with adnexae
27	endometrioid	BRCA2	2009	61	EEC gr1	EEC gr1	wildtype[d]	No	Other	No	No	Yes	Hysterectomy with adnexae
31	endometrioid	BRCA2	2011	50	EEC gr2	EEC gr1	wildtype[d]	No	Other	No	Simultaneous bilateral EOC	Yes	Hysterectomy, adnexae removed shortly before
45	endometrioid	BRCA2	1989	65	adenocarcinoma NOS, gr1	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	No	No	No	Hysterectomy with adnexae
52	endometrioid	BRCA2	2001	67	EEC gr2	EEC gr1	wildtype	No	Other	No	No	Yes	Hysterectomy with adnexae
58	endometrioid	BRCA2	2009	38	EEC gr1	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	yes, 5.0	No	No, unknown if removed	Unknown
5	serous-like	BRCA1	2015	68	serous	ambiguous	mutant[d]	No	p53-abnormal	Yes, 9.4	No	Yes	Hysterectomy without adnexae (history RRSO)
6	serous-like	BRCA1	2008	64	EEC gr3	serous	mutant[d]	Yes	p53-abnormal	No	No	Yes	Hysterectomy with adnexae
7	serous-like	BRCA1	2010	65	EEC gr1	ambiguous	mutant[d]	Yes	p53-abnormal	Yes, 11.7	No	Yes	Hysterectomy without adnexae (history RRSO)
8	serous-like	BRCA1	2009	65	EEC gr3	ambiguous	mutant[d]	Yes	p53-abnormal	Yes, 7.4	No	Yes	Hysterectomy without adnexae (history RRSO)
14	serous-like	BRCA1	2000	49	carcinosarcoma	carcinosarcoma, serous	mutant[d]	No	p53-abnormal	No	No	Yes	Hysterectomy with adnexae
16	serous-like	BRCA1	1996	59	adenocarcinoma NOS, gr2-3	sereus	mutant[d]	Yes	p53-abnormal	No	No	Yes	Hysterectomy with adnexae
22	serous-like	BRCA1	2015	63	carcinosarcoma, serous	carcinosarcoma, ambiguous	mutant[d]	No	Other[f]	Yes, 4.7	No	Yes	Hysterectomy without adnexae (history RRSO)
26	serous-like	BRCA1	2012	49	EEC gr3	carcinosarcoma, ambiguous	mutant[d]	Yes	p53-abnormal	Yes, 4.0	No	Yes	Hysterectomy without adnexae (history RRSO)
39	serous-like	BRCA1	2003	65	EEC gr2	ambiguous	mutant[d]	Yes	p53-abnormal	Yes	No	Yes	Hysterectomy without adnexae (history RRSO)
40	serous-like	BRCA1	2006	58	EEC gr3	serous	mutant[d]	Yes	p53-abnormal	Yes, 6.8	No	Yes	Hysterectomy without adnexae (history RRSO)
43	serous-like	BRCA1	2006	60	serous	serous	mutant	No	p53-abnormal	No	No	Yes	Hysterectomy with adnexae

44	serous-like	BRCA1	2001	73	adenocarcinoma NOS, gr3	serous	mutant	Yes	p53-abnormal	No	Unknown	No, no hysterectomy/ adnexextirpation	No hysterectomy/adnexextirpation performed, diagnosis based on cervical biopsy, vagina wand biopsy and curretage
48	serous-like	BRCA1	1989	47	adenocarcinoma NOS, gr1	serous	mutant	Yes	p53-abnormal	No	No	No, not removed	Hysterectomy without adnexae
49	serous-like	BRCA1	1997	65	EEC gr3	ambiguous	mutant	Yes	p53-abnormal	No	Unknown	No	Hysterectomy with adnexae
53	serous-like	BRCA1	2001	65	carcinosarcoma, unspecified	carcinosacoma, serous	mutant	No	p53-abnormal	No	No	Yes	Hysterectomy with adnexae
25	serous-like	BRCA2	2015	64	serous	serous	mutant[d]	No	p53-abnormal	Yes, 4.5	No	Yes	Hysterectomy without adnexae (history RRSO)
29	serous-like	BRCA2	2006	57	serous	serous	mutant[d]	No	p53-abnormal	Yes, 6.1	No	Yes	Hysterectomy without adnexae (history RRSO)
32	serous-like	BRCA2	2009	62	serous	serous	mutant[d]	No	p53-abnormal	No	No	Yes	Hysterectomy with adnexae
55	serous-like	BRCA2	2009	68	large cell carcinoma NOS	ambiguous	mutant	Yes	p53-abnormal	No	Unknown	No, no hysterectomy/ adnexextirpation	No hysterectomy/adnexextirpation performed, diagnoses based on vaginal and cervical biopsy
36	sarcoma	BRCA1	2007	33	low-grade ESS	low-grade ESS	wildtype	No	Other	No	No	Yes	Hysterectomy without adnexae, fallopian tubes were removed shortly prior to hysterectomy during uterine biopsy
42	sarcoma	BRCA2	1995	53	leiomyosarcoma	leiomyosarcoma	wildtype	No	Other	No	No	No, not removed	Hysterectomy without adnexae
46	sarcoma	BRCA2	2001	54	adenosarcoma	adenosarcoma	wildtype	No	Other	No	No	No, not removed	Hysterectomy without adnexae
59	clear cell	BRCA1	2003	59	clear cell carcinoma	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	No	No	No	Unknown
Endometrial cancer outside observation period main analyses													
10	serous-like	BRCA2	2016	49	EEC gr1	carcinosarcoma, serous	mutant[d]	Yes	p53-abnormal	Yes, 4.3	No	Yes	Hysterectomy without adnexae (history RRSO)
54	serous-like	BRCA1	1988	62	adenocarcinoma NOS, gr3	serous	mutant	Yes	p53-abnormal	No	No	Yes, only left side resected	Hysterectomy and left adnex
57	endometrioid	BRCA2	2012	65	EEC gr2	n.a.	n.a., considered *TP53* wildtype	n.a.	Other[e]	yes, 12.1	No	No	Hysterectomy without adnexae (history RRSO)
Not considered endometrial cancer after revision, outside observation period													
9	No EC	BRCA1	1983	45	endocervical adenocarcinoma	n.a.	n.a.	n.a.		Yes, no EC after revision	No	No	Unknown, RRSO one month before resection

Abbreviations: EEC: Endometrioid endometrial carcinoma, n.a.: not available, NOS: Not otherwise specified, RRSO: Risk-reducing salpingo-oophorectomy, EC: Endometrial cancer [a]CaseIDs number 1-41 correspond with CaseIDs from our previous publication; De Jonge and colleagues, CCR 2019. [b]Based on diagnoses after pathology review when available. [c]P53-status based on IHC, molecular analyses or most common pattern based on literature in case no FFPE blocks were available. "Mutant" includes both overexpression pattern and null-pattern. [d]P53-status based on mutational analyses (see de Jonge and colleagues, CCR 2019). [e]Molecular subgroup based on most prevalent p53 status for the histologic subtype, no FFPE-tumour tissue block was available for determining p53-status. [f]Tumour was also mismatch repair deficient and therefore considered as "other" molecular subgroup. [g]Ovaries were previously removed (without fallopian tubes); this was not considered as RRSO. [h]History of therapeutic ovariectomy because of ovarian clear cell carcinoma.

Supplementary Table 6. Characteristics of endometrial cancers that occurred in the non-*BRCA1/2* mutation carrier cohort

Case ID	Final histological subgroup[a]	Year	Age	Original Diagnoses	Diagnoses after pathology review	P53 status[b]	Molecular subgroup	Category change histologic subgroup after review	RRSO, years in between RRSO-EC	Adnexal involvement/ (history of) ovarian malignancy	Adnexal specimens available for revision	Hysterectomy with/without adenxae
Included as endometrial cancer in main analyses												
101	Endometrioid	1990	46	adenocarcinoma NOS, gr3	n.a.	n.a., considered *TP53* mutant	p53-abnormal[c]	n.a.	No	No	No	Hysterectomy with adnexae
102	Endometrioid	2010	53	EEC gr1	EEC gr1	wildtype	other	No	No	No	No	Hysterectomy with adnexae
104	Endometrioid	2004	54	EEC gr2	EEC gr1	wildtype	other	No	No	Simultaneous EOC gr1 right side, considered as second primary	Yes	Hysterectomy with adnexae
105	Endometrioid	2000	54	EEC, gr not specified	EEC gr1	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
106	Endometrioid	1998	65	Adenocarcinoma NOS gr2	EEC gr2	wildtype	other	No	No	No	No	Hysterectomy with adnexae
108	Endometrioid	2009	58	EEC gr1	EEC gr1	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
110	Endometrioid	2005	60	adenocarcinoma NOS gr1	EEC gr1	n.a., considered *TP53* wildtype	other[c]	No	No	No	Yes	Hysterectomy with adnexae
111	Endometrioid	2003	37	adenocarcinoma NOS gr1	EEC gr1	wildtype	other	No	Unknown	No	No, not removed	Hysterectomy without adnexae
112	Endometrioid	2007	49	adenocarcinoma NOS gr1	EEC gr1	wildtype	other	No	No	Simultaneous EOC right side, considered as second primary	Yes, left side not removed	Hysterectomy with right adnex
113	Endometrioid	1997	48	EEC gr1	EEC gr1	wildtype	other	No	No	No	yes	Hysterectomy with adnexae
114	Endometrioid	2008	57	EEC gr 2	EEC gr3	wildtype	other	No	No	No	yes	Hysterectomy with adnexae
115	Endometrioid	2007	67	EEC gr1	EEC gr1	wildtype	other	No	No	No	yes	Hysterectomy with adnexae
116	Endometrioid	2002	66	adenocarcinoma NOS gr2	EEC gr1	wildtype	other	No	No	Simultaneous bilateral serous borderline tumour/low-grade serous carcinoma.	yes	Hysterectomy with adnexae
117	Endometrioid	1999	53	adenocarcinoma NOS gr2	EEC gr2	wildtype	other	No	No	No	No	Hysterectomy with adnexae
118	Endometrioid	2002	62	EIN/ adenocarcioma NOS gr1	EEC gr1	wildtype	other	No	No	No	No	Hysterectomy with adnexae
121	Endometrioid	2011	60	EEC gr1	EEC gr1	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
124	Endometrioid	1999	56	adenocarcinoma NOS, gr1-2	EEC gr1	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
126	Endometrioid	2004	52	adenocarcinoma NOS gr1	EEC gr1	wiltype	other	No	No	No	No, not removed	Hysterectomy without adnexae
129	Endometrioid	2011	64	EEC gr3	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No	Hysterectomy with adnexae
130	Endometrioid	2000	57	EEC gr1	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	Unknown	No	No, unknown if removed	Unknown
131	Endometrioid	2002	63	EEC gr2	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No, unknown if removed	Unknown

132	Endometrioid	2010	74	EEC gr2	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No	Hysterectomy with adnexae
133	Endometrioid	2010	53	EEC gr2	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	Yes, 2.7[d]	No	No	Unknown
134	Endometrioid	2008	58	EEC gr2	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No, unknown if removed	Unknown
135	Endometrioid	2002	49	EEC gr1	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No	hysterectomy with right adnex
136	Endometrioid	2007	72	EEC gr1	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No	hysterectomy with right adnex
137	Endometrioid	2011	29	EEC gr1	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	Simultaneous bilateral serous borderline tumour	No	Hysterectomy with adnexae
138	Endometrioid	1999	60	adenocarcinoma NOS gr2	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No, unknown if removed	Unknown
139	Endometrioid	1999	51	adenocarcinoma NOS gr unspecified	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No	Hysterectomy with adnexae
140	Endometrioid	2007	53	EEC gr 1	n.a.	n.a., considered *TP53* wildtype	other[c]	n.a.	No	No	No, unknown if removed	Unknown
103	Serous-like	1997	53	carsinocarcoma, unspecified	carcinosarcoma, endometrioid	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
123	Serous-like	2007	72	carcinosarcoma, endometrioid	carcinosarcoma, serous	mutant	other	No	No	Simultaneous bilateral serous adenocarcinoma	No	Hysterectomy with adnexae
128	Serous-like	2009	79	serous	serous	mutant	p53-abnormal	No	No	No	Yes	Hysterectomy with adnexae
Endometrial cancer outside follow-up window main analyses												
107	Endometrioid	2012	55	EEC gr1	EEC gr1	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
109	Endometrioid	2013	69	EEC gr1	EEC gr1	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
119	Endometrioid	2012	56	undifferentiated/ dedifferentiated carcinoma	dedifferentiated carcinoma	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
120	Endometrioid	2014	71	EEC gr1	EEC gr2	wildtype	other	No	No	No	Yes	Hysterectomy with adnexae
127	Serous-like	2012	65	carcinosarcoma, unspecified	carcinosarcoma, serous	mutant	p53-abnormal	No	No	No	No	No hysterectomy/adnex extirpation performed (diagnosis based on endometrial curretage)
Not considered endometrial cancer after revision												
122	No EC	1990	59	adenosquamous EC	adenosquamous carcinoma	mutant	No EC	No EC	Unknown	No	No, not removed	Hysterectomy without adnexae
125	No EC	2003	60	EEC gr2	HGSOC	mutant	No EC	No EC	No	Bilateral HGSOC with endometrial involvement	Yes	Hysterectomy with adnexae

Abbreviations: EEC: Endometrioid endometrial carcinoma, EIN: Endometrioid intra-epithelial neoplasia, n.a.: not available, NOS: Not otherwise specified, RRSO: Risk-reducing salpingo-oophorectomy, EC: Endometrial cancer [a]Based on diagnoses after pathology review when available. [b]P53-status based on IHC, molecular analyses or most common pattern based on literature in case no FFPE blocks were available. "Mutant" includes both overexpression pattern and null-pattern. [c]Molecular subgroup based on most prevalent p53 status for the histologic subtype, no FFPE-tumour tissue block was available for determining p53 status. [d]One ovary previously removed.

Supplementary Table 7. Additional sensitivity analyses endometrial cancer risks *BRCA1/2* mutation carriers versus non-*BRCA1/2* mutation carriers

	***BRCA1/2* carriers**			**non-*BRCA1/2* carriers**				
Subgroups	**Total (No.)**	**Events (No.)**	**Person-years at risk**	**Total (No.)**	**Events (No.)**	**Person-years at risk (No.)**	**Hazard Ratio (95% CI)[a]**	***p* value[b]**
Start follow-up from date *BRCA* DNA test, excluding cases for which date of*gBRCA1/2* DNA test was unknown								
All histotypes	4104	28	29821	6885	7	30055	3.79 (1.61-8.91)	0.002
Endometrioid	4104	17	29821	6885	6	30055	3.76 (1.41-9.97)	0.01
Serous-like	4104	10	29821	6885	1	30055	12.39 (1.49-103.29)	0.02
p53-abnormal[c]	4104	16	29821	6885	1	30055	20.06 (2.56-157.22)	0.004
BRCA1, all histotypes[d]	2493	22	18744	6885	7	30055	7.26 (2.96-17.82)	<0.001
BRCA2, all histotypes[d]	1640	6	11298	6885	7	30055	2.46 (0.72-8.44)	0.15
End follow-up 01-01-2012 for all included women								
All	5936	48	105609	8451	33	160841	2.37 (1.52-3.69)	<0.001
Endometrioid	5936	29	105609	8451	30	160841	1.51 (0.91-2.52)	0.11
Serous-like	5936	15	105609	8451	3	160841	8.16 (2.36-28.22)	0.001
p53-abnormal[c]	5936	20	105609	8451	3	160841	10.95 (3.25-36.87)	<0.001
BRCA1, all histotypes[d]	3796	36	66700	8451	33	160841	2.78 (1.73-4.46)	<0.001
BRCA2, all histotypes[d]	2181	12	39704	8451	33	160841	1.45 (0.75-2.81)	0.27
Additional censoring BC[e]								
All	5689	32	88493	8311	21	139488	2.83 (1.62-4.95)	<0.001
Endometrioid	5689	22	88493	8311	20	139488	1.75 (0.95-3.24)	0.07
Serous-like	5689	6	88493	8311	1	139488	8.90 (1.04-76.54)	0.05
p53-abnormal[c]	5689	9	88493	8311	1	139488	14.25 (1.77-114.22)	0.01
BRCA1, all histotypes[d]	3610	22	53898	8311	21	139488	2.61 (1.41-4.84)	0.002
BRCA2, all histotypes[d]	2115	10	35239	8311	21	139488	1.97 (0.93-4.19)	0.08
Additional censoring HT-BC including cases for which HT was unknown[e]								
All histotypes	5895	49	110215	8407	30	153443	2.30 (1.44-3.68)	<0.001

Abbreviations: BC: Breast Cancer, HT: Hormone Treatment

[a]Hazard ratios were adjusted for age.

[b]The P values assessing the null hypothesis of HR=1.00.

[c]Includes cases for which p53-status was unknown (no FFPE tumour block available) and for which p53-status was based on the most common p53-status for the histotype.

[d]Women with both a *BRCA1* and a *BRCA2* mutation were included in both analyses stratified for *gBRCA1/2*-mutation status.

[e]DCIS was considered as BC.

Supplementary Table 8. Observed and expected endometrial cancer rates in non*BRCA1/2* mutation carriers, compared to the Dutch country-specific incidence rates

	non-*BRCA1/2* carriers	Dutch population		
EC subtype	**Observed**	**Expected**	**SIR (95% CI)**	***P* value[a]**
All endometrial cancers	33	26.81	1.23 (0.88-1.73)	0.14
Histologic groups				
Endometrioid	30	22.14	1.35 (0.95-1.94)	0.06
Serous-like	3	2.39	1.26 (0.40-3.89)	0.43
Sarcoma	0	1.73	NA	NA
Clear cell	0	0.36	NA	NA

Abbreviations: SIR: Standardized Incidence Ratio, CI: Confidence Interval. NA: not applicable

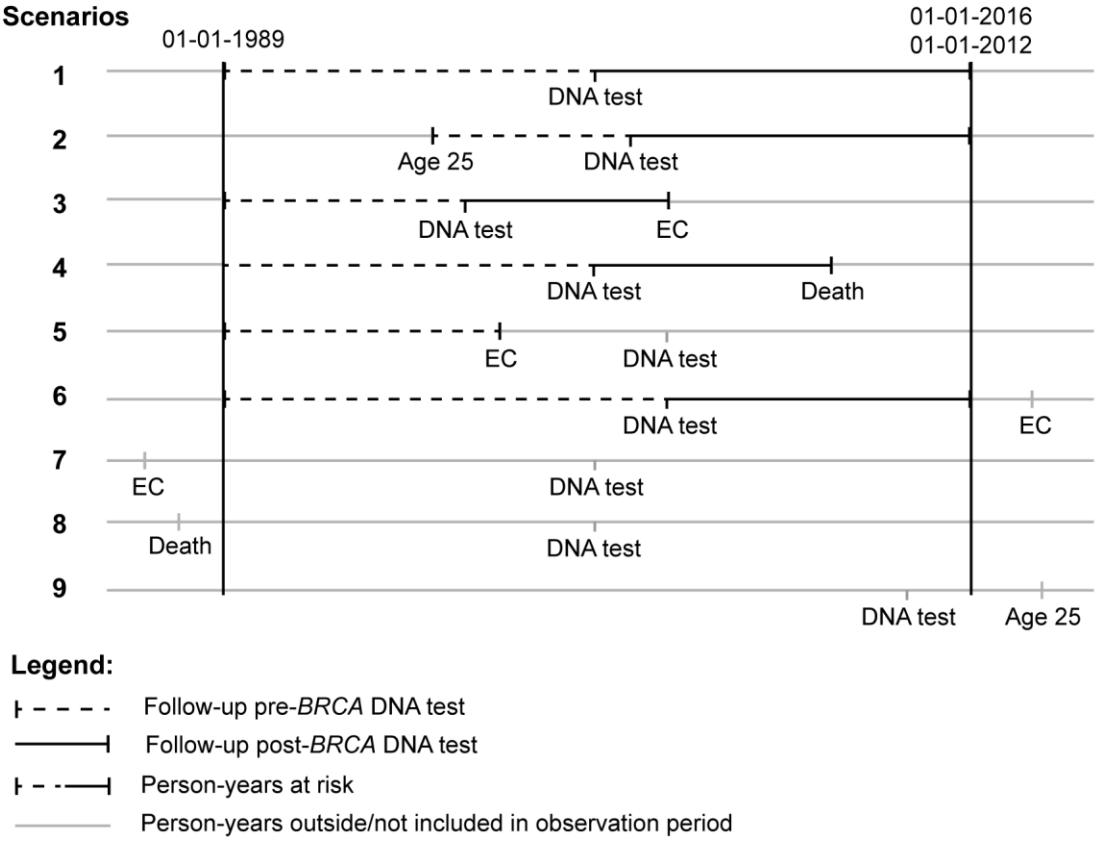
[a]*p* values were estimated assuming a Poisson distribution.

Supplementary Table 9. Cumulative endometrial cancer risks for *BRCA1/2* mutation carriers by the age of 75 years

EC subtype	Cumulative risk (%, 95% CI)
All Endometrial cancers	**2.97 (2.20-3.91)**
BRCA1	3.49 (2.46-4.81)
BRCA2	1.97 (1.09-3.30)
Histologic groups	
Serous-like	**1.14 (0.69-1.80)**
BRCA1	1.42 (0.79-2.37)
BRCA2	0.64 (0.21-1.60)
Endometrioid	**1.70 (1.14-2.44)**
BRCA1	1.97 (1.23-3.01)

Abbreviations, CI: confidence interval

Supplementary Figure 1.



Supplementary Figure 1. Schematic overview of the composition of different observation period scenarios. Follow-up started on the date of nationwide PALGA coverage (01-01-1989) or on the date of attaining 25 years of age (whichever was later). Follow-up ended at date of endometrial cancer diagnosis, date of death, or date of end of follow-up (01-01-2016 for *BRCA1/2* mutation carriers who provided informed consent, 01-01-2012 for all others). The observation period comprised both person-years at risk before *BRCA* DNA testing (dashed line) and person-years at risk after *BRCA* DNA testing (continuous line). Scenario 1 displays the maximum possible observation period. In case endometrial cancer or death occurred before the start of follow-up (scenarios 7 and 8), or age 25 was reached after end of follow-up (scenario 9), cases were excluded. Endometrial cancers that occurred after end of follow-up (scenario 6) were not included as events in the study. Abbreviations; EC: Endometrial cancer