

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Baseline characteristics per group (with and without postoperative HRT)

	RRS without HRT		RRSO without HRT at three months		P-value	RRS total		RRSO with HRT at three months		P-value
	Mean/N	SD/%	Mean/N	SD/%		Mean/N	SD/%	Mean/N	SD/%	
	n=	368	n=	42		n=	375	n=	97	
Age at first questionnaire	36.6	3.5	38.9	3.1	<0.001	36.6	3.5	38.8	2.9	<0.001
<i>BRCA1</i>	35.3	3.2	37.0	2.0	0.026	35.3	3.2	37.0	2.0	<0.001
<i>BRCA2</i>	37.8	3.4	40.9	2.8	<0.001	37.8	3.4	41.8	1.5	<0.001
Age at first surgery	36.8	3.5	39.0	3.0	<0.001	36.8	3.5	38.8	2.9	<0.001
<i>BRCA1</i>	35.5	3.2	37.0	3.2	0.031	35.5	3.2	37.0	1.9	<0.001
<i>BRCA2</i>	37.9	3.4	41.0	2.8	<0.001	38.0	3.4	41.9	1.5	<0.001
Type of <i>BRCA</i> pathogenic variant					NS					NS
<i>BRCA1</i>	177	48.1%	21	50.0%		180	48.0%	62	63.9%	
<i>BRCA2</i>	191	51.9%	21	50.0%		195	52.0%	35	36.1%	
Time since pathogenic variant detection					NS					NS
< 5 years	181	49.2%	24	57.1%		185	49.3%	49	50.5%	
≥ 5 years	184	50.0%	18	42.9%		188	50.1%	48	49.5%	
Unknown	3	0.8%				2	0.5%		0.0%	
Relationship status					NS					NS
Conjoined	328	89.1%	38	90.5%		335	89.3%	90	92.8%	
Single	38	10.3%	4	9.5%		38	10.1%	7	7.2%	
Unknown	2	0.5%				2	0.5%			
Offspring					NS					NS
No	43	11.7%	6	14.3%		45	12.0%	7	7.2%	
Yes	322	87.5%	36	85.7%		327	87.2%	90	92.8%	
Unknown	3	0.8%				3	0.8%			
Educational level					NS					NS
Low	40	10.9%	6	14.3%		40	10.7%	10	10.3%	
Medium	131	35.6%	20	47.6%		133	35.5%	33	34.0%	
High	195	53.0%	16	38.1%		200	53.3%	54	55.7%	
Unknown	2	0.5%				2	0.5%			
Breast cancer in personal history					<0.001					0.001
No	310	84.2%	25	59.5%		317	84.5%	95	97.9%	
Yes	56	15.2%	17	40.5%		56	14.9%	2	2.1%	
Unknown	2	0.5%				2	0.5%			
Risk reducing mastectomy					NS					NS
No	222	60.3%	24	57.1%		224	59.7%	32	33.0%	
Yes	144	39.1%	18	42.9%		149	39.7%	65	67.0%	
Unknown	2	0.5%				2	0.5%			
First degree family member with breast cancer					NS					NS
No	189	51.4%	23	54.8%		190	50.7%	57	58.8%	
Yes	176	47.8%	19	45.2%		182	48.5%	40	41.2%	
Unknown	3	0.8%				3	0.8%			
First degree family member with ovarian cancer					NS					NS
No	316	85.9%	39	92.9%		323	86.1%	77	79.4%	
Yes	49	13.3%	3	7.1%		49	13.1%	20	20.6%	
unknown						3	0.8%			

Abbreviations: RRS risk-reducing salpingectomy; RRSO risk-reducing salpingo-oophorectomy; N number of patients; SD standard deviation; CFB change from baseline; NS not significant

eTable 2. Overview of hormone replacement therapy at three and twelve months after surgery

	Dosage a day	Three months	One year
Tibolon		58 (60%)	43 (54%)
	2,5 mg	58 (60%)	43 (54%)
Estradiol/dydrogesteron		21 (22%)	22 (28%)
	1 mg / 5 mg	11 (11%)	8 (10%)
	1 mg / 10 mg	2 (2%)	-
	2 mg / 10 mg	-	3 (4%)
	Unknown	8 (8%)	11 (14%)
Transdermal estradiol		6 (6%)	7 (89%)
	50 ugr	2 (2%)	4 (5%)
	75 ugr	1 (1%)	1 (1%)
	Unknown	3 (3%)	2 (3%)
Other		2 (2%)	1 (1%)
Unknown		10 (10%)	6 (8%)

eTable 3. Subscales of the Greene Climacteric Scale in women without hormone replacement therapy.

		RRS			RRSO			RRSO - RRS		
		N	Observed Mean	SD	N	Observed Mean	SD	Adjusted MD	95% CI	P-value
Anxiety <i>range</i> 0-18	Baseline ^a	368	2.0 ^a	1.0;4.0 ^a	42	3.0 ^a	2.0;4.0 ^a	1.8 ^b	1.2;2.4	<0.001
	3 months CFB	368	0.1	2.2	42	2.0	2.7			
	1 year CFB	296	0.2	2.4	40	1.8	2.9			
Depression <i>range</i> 0-15	Baseline ^a	368	2.0 ^a	1.0;4.0 ^a	42	3.0 ^a	2.0;5.0 ^a	1.0 ^b	0.5;1.6	<0.001
	3 months CFB	368	0.2	2.1	42	0.8	2.3			
	1 year CFB	296	0.1	2.4	40	1.0	2.6			
Somatic <i>range</i> 0-21	Baseline ^a	368	1.0 ^a	0.0;3.0 ^a	42	2.0 ^a	1.0;3.3 ^a	1.4 ^b	0.8;2.0	<0.001
	3 months CFB	368	0.3	2.1	42	1.7	2.3			
	1 year CFB	296	0.3	2.3	40	1.8	3.1			
Vasomotor <i>range</i> 0-6	Baseline ^a	368	0.0 ^a	0.0;0.0 ^a	42	0.0 ^a	0.0;0.0 ^a	2.0 ^b	1.8;2.2	<0.001
	3 months CFB	368	0.0	0.7	42	2.1	1.3			
	1 year CFB	296	0.1	0.8	40	2.1	1.3			
Sexual <i>range</i> 0-3	Baseline ^a	368	0.0 ^a	0.0;0.0 ^a	42	1.0 ^a	0.0;1.0 ^a	0.5 ^b	0.3;0.7	<0.001
	3 months CFB	368	-0.3	0.7	42	0.3	0.8			
	1 year CFB	296	0.0	0.8	40	0.7	0.9			

^a median and interquartile range (IQR)

^b Interaction between choice and visit was not statistically significant (p=0.7), thus the adjusted estimated difference is the same for both timepoints

* Baseline value of women with hormone replacement therapy at three months after RRSO; median and interquartile range (IQR)

Abbreviations: RRS risk-reducing salpingectomy; RRSO risk-reducing salpingo-oophorectomy; MD mean difference; SD standard deviation; CFB change from baseline; 95% CI 95% confidence interval; NS not significant

eTable 4. Subscales of the Greene Climacteric Scale in women with hormone replacement therapy after RRSO.

		RRS			RRSO			RRSO - RRS		P-value
		N	Observed Mean	SD	N	Observed Mean	SD	Adjusted MD	95% CI	
Anxiety <i>range</i> 0-18	Baseline*	375	2.0	1.0;4.0	97	2.0	1.0;4.0			<0.001
	3 months CFB	375	0.2	2.2	97	0.7	2.5	0.9	0.4;1.3	
	1 year CFB	302	0.2	2.4	79	1.1	3.3			
Depression <i>range</i> 0-15	Baseline*	375	2.0	1.0-4.0	97	2.0	1.0-4.0			0.004
	3 months CFB	375	0.8	2.4	97	0.8	2.4	0.6	0.2;1.1	
	1 year CFB	302	1.3	2.1	79	1.1	3.3			
Somatic <i>range</i> 0-21	Baseline*	375	1.0	0.0-3.0	97	1.0	1.0;3.0			<0.001
	3 months CFB	375	0.3	2.1	97	1.0	2.4	0.8	0.4;1.2	
	1 year CFB	302	0.3	2.3	79	1.3	2.1			
Vasomotor <i>range</i> 0-6	Baseline*	375	0.0	0.0-0.0	97	0.0	0.0;1.0			<0.001
	3 months CFB	375	0.0	0.7	97	1.0	1.2	1.0	0.8;1.2	
	1 year CFB	302	0.1	0.8	79	0.9	1.2			
Sexual <i>range</i> 0-3	Baseline*	375	0.0	0.0;1.0	97	0.0	0.0;1.0			0.012
	3 months CFB	375	0.0	0.7	97	0.1	0.9	0.2	0.0;0.3	
	1 year CFB	302	0.0	0.8	79	0.2	1.0			

* Baseline value of women with hormone replacement therapy at three months after RRSO; median and interquartile range (IQR)
 Abbreviations: RRS risk-reducing salpingectomy; RRSO risk-reducing salpingo-oophorectomy; MD mean difference; SD standard deviation; CFB change from baseline; 95% CI 95% confidence interval; NS not significant

eTable 5. Secondary outcome measures

			RRS			RRSO			RRSO - RRS		
			N	Observed Mean	SD	N	Observed Mean	SD	Adjusted MD	95% CI	P-value
Women without HRT											
SF-36	Physical component summary score										
	<i>BRCA1/2</i>	Baseline ^a	368	56.2 ^a	15.2;58.6 ^a	42	53.0 ^a	40.5;57.8 ^a			
		3 months CFB	368	0.0	6.3	42	0.9	6.7	-1.5	-3.3;0.3	NS
		1 year CFB	296	0.1	7.5	40	0.8	12.3	-1.9	-4.2;0.5	NS
	Mental component summary score										
	<i>BRCA1/2</i>	Baseline ^a	368	52.6 ^a	46.4;56.1 ^a	42	46.3 ^a	38.6;55.2 ^a			
	3 months CFB	368	-0.5	7.8	42	0.5	10.1	0.0	-2.7;2.6	NS	
	1 year CFB	296	-5.0	12.6	40	-1.4	13.5	2.4	-1.8;6.6	NS	
FSFI											
<i>Range 2-36</i>	<i>BRCA1/2</i>	Baseline ^a	368	30.5 ^a	24.8;32.6 ^a	42	29.2 ^a	20.0;29.0 ^a			
		3 months CFB	368	0.3	6.9	42	-2.1	8.4	-2.8	-4.9;-0.6	0.011
		1 year CFB	296	0.3	7.1	40	-5.1	8.2	-5.7	-7.9;-3.5	<0.001
FSDS											
<i>Range 2-52</i>	<i>BRCA1/2</i>	Baseline ^a	368	4.0 ^a	0.0;11.0 ^a	42	4.5 ^a	0.0;16.5 ^a			
		3 months CFB	368	0.7	6.8	42	3.7	8.9	3.6	1.4;5.8	0.002
		1 year CFB	296	0.8	7.3	40	6.5	11.0	7.0	4.5;9.5	<0.001
CWS											
<i>Range 8-32</i>	<i>BRCA1/2</i>	Baseline ^a	368	14.0 ^a	12.0;16.0 ^a	42	14.5 ^a	12.0;17.3 ^a			
		3 months CFB	368	-1.5	2.6	42	-1.9	3.6	-0.4	-1.2;0.4	NS
		1 year CFB	296	-1.6	3.1	40	-1.9	4.1	-0.5	-1.5;0.6	NS
DCS											
<i>Range 0-100</i>	<i>BRCA1/2</i>	Baseline ^a	368	30.5 ^a	24.8;32.6 ^a	42	29.2 ^a	20.0;32.0 ^a			NS
DRS											
<i>Range 0-100</i>	<i>BRCA1/2</i>	1 year	296	12.7	15.1	40	16.1	17.6	-0.5	-5.0;6.1	NS
Women with HRT after RRSO^b											
SF-36	Physical component summary score										
	<i>BRCA1/2</i>	Baseline ^c	375	56.1 ^c	51.9;58.7 ^c	97	56.3 ^c	53.4;58.7 ^c			
		3 months CFB	375	0.1	6.4	97	-2.2	7.8	-2.4	-3.8;-1.0	0.001
	1 year CFB	302	0.7	7.4	79	-1.1	7.1	-1.2	-2.9;0.5	NS	

eTable 5. Secondary outcome measures - continued

			RRS			RRSO			RRSO-RRS		
			N	Observed Mean	SD	N	Observed Mean	SD	Adjusted MD	95%-CI	P-value
SF-36	Mental component summary score										
	<i>BRCA1/2</i>	Baseline ^c	375	52.6 ^c	46.2;56.0 ^c	97	52.4 ^c	47.1;56.0 ^c			
		3 months CFB	375	-0.5	7.8	97	-2.0	9.7	-1.2	-3.1;0.7	NS
		1 year CFB	302	-5.0	12.6	79	-8.0	12.7	-2.8	-6.0;0.4	NS
FSFI											
<i>Range</i>	<i>BRCA1/2</i>	Baseline ^c	375	30.5 ^c	24.4;32.7 ^c	97	28.5 ^c	21.9;31.7 ^c			
2-36		3 months CFB	375	0.4	6.9	97	0.2	8.2	-0.6	-2.1;1.0	NS
		1 year CFB	302	0.3	7.0	79	-1.2	10.7	-2.0	-3.8;-0.2	0.033
FSDS											
<i>Range</i>	<i>BRCA1/2</i>	Baseline ^c	375	4.0 ^c	0.0;11.0 ^c	97	6.0 ^c	0.0;13.5 ^c			
2-52		3 months CFB	375	0.7	6.8	97	0.1	9.5	-0.2	-1.8;1.5	NS
		1 year CFB	302	0.8	7.2	79	1.4	11.0	1.4	-0.5;3.3	NS
CWS											
<i>Range</i>	<i>BRCA1/2</i>	Baseline ^c	375	14.0 ^c	12.0;16.0 ^c	97	14.0 ^c	12.0;17.0 ^c			
8-32		3 months CFB	375	-1.5	2.7	97	-1.9	2.5	-0.4	-1.0;0.2	NS
		1 year CFB	302			79	-2.3	3.8	-0.5	-1.2;0.3	NS
DCS											
<i>Range</i>	<i>BRCA1/2</i>	Baseline ^c	375	30.5 ^c	24.4;32.7 ^c	97	28.5 ^c	21.9;31.7 ^c			NS
0-100											
DRS											
<i>Range</i>	<i>BRCA1/2</i>	1 year	302	12.7	15.0	79	11.5	13.7	-2.8	-6.6;1.0	NS
0-100											

^a Baseline value of women without hormone replacement therapy at three months; median and interquartile range (IQR)
^b All women after RRS (with and without HRT) and only the women using HRT after RRSO are included
^c Baseline value of women with hormone replacement therapy at three months after RRSO; median and interquartile range (IQR)
Abbreviations: RRS risk-reducing salpingectomy; RRSO risk-reducing salpingo-oophorectomy; MD mean difference; SD standard deviation; CFB change from baseline; 95% CI 95% confidence interval; SF-36 Short Form 36; FSDS Female Sexual Distress Scale; FSFI Female Sexual Functioning Index; CWS Cancer Worry Scale; DCS Decisional Conflict Scale; DRS Decision Regret Scale

eTable 6. Surgical complications and serious adverse events (SAE)

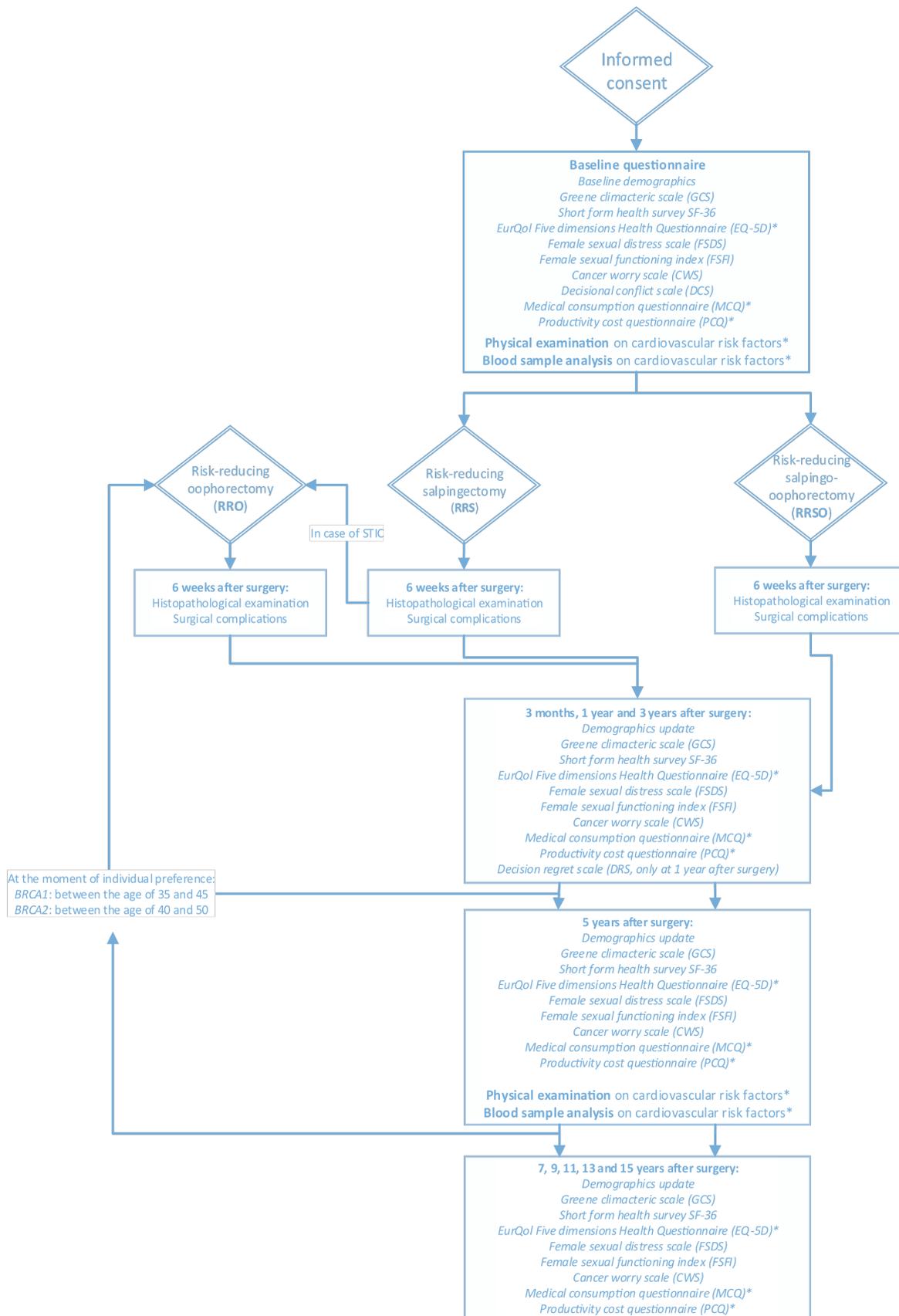
	Age	BRCA- PV	(S)AE	Time since RRS/RRSO	Treatment	Relation to study intervention	
RRS	Surgical complications within 6 weeks						
	36	BRCA2	Bilateral luxation of jaw at intubation	During	Reposition	Definite	
	43	BRCA2	Perforation of the uterus by uterine manipulator	During	Antibiotics	Definite	
	32	BRCA1	Perforation of the uterus by uterine manipulator	During	Antibiotics	Definite	
	37	BRCA2	Perforation of the uterus by uterine manipulator	During	Antibiotics	Definite	
	40	BRCA2	Subcutaneous emphysema neck and upper half thorax	During	Expectative	Definite	
	37	BRCA1	Subcutaneous hematoma	During	Expectative	Definite	
	39	BRCA1	Perforation of the bladder	During	Cystoscopy, transurethral catheter 7 days, antibiotics	Definite	
	32	BRCA2	Pneumonia and abscess with necrosis of m. rectus abdominis	+3 days	Antibiotics and necrotectomy	Definite	
	32	BRCA1	Subcutaneous hematoma	+1 week	Expectative	Definite	
	32	BRCA1	Wound infection	+1 week	Antibiotics	Definite	
	38	BRCA2	Wound infection	16 days	Antibiotics	Definite	
	44	BRCA2	Wound infection	+4 days	Expectative	Definite	
	38	BRCA2	Wound infection	+1 week	Expectative	Definite	
	40	BRCA1	Wound infection	+13 days	Expectative	Definite	
	36	BRCA1	Wound infection	<2 weeks	Expectative	Definite	
	40	BRCA1	Wound infection	+16 days	Expectative	Definite	
	38	BRCA2	Phlebitis	+0 days	Expectative	Definite	
	38	BRCA2	Neuropathy ulnar nerve	+0 days	Expectative	Probable	
	39	BRCA2	Urinary tract infection	+13 days	Antibiotics	Probable	
	35	BRCA1	Wound infection	+4 days	Antibiotics	Probable	
			Postprocedural cervical hemorrhage cervix after concomitant LLETZ	+2 weeks	Cauterization	Unrelated*	
	30	BRCA1	Postprocedural cervical hemorrhage cervix after concomitant LLETZ	+12 days	Unknown	Unrelated*	
	41	BRCA2	Wound infection breast after concomitant risk-reducing mastectomy	+12 days	Antibiotics and surgery	Unrelated	
		Miscellaneous serious adverse events					
	35	BRCA1	Deep venous thrombosis left subclavian vein	+3 months	Anticoagulants	Possible	
	38	BRCA1	Breast cancer	+8 months	Surgery, CT	Unlikely	
40	BRCA2	Breast cancer recurrence (bone metastases and pleuritis carcinomatosis)	+10 months	CT	Unlikely		
39	BRCA1	Breast cancer	+6 months	Surgery, CT	Unlikely		
39	BRCA2	Breast cancer	+11 months	Surgery, HT	Unlikely		

eTable 6. Surgical complications and serious adverse events (SAE) - continued

	Age	BRCA-PV	(S)AE	Time since RRS/RRSO	Treatment	Relation to study intervention
	42	BRCA2	Breast cancer	RRS +4 yr	Surgery	Unlikely
	36	BRCA2	Breast cancer detected in risk-reducing mastectomy specimen	RRO +3 yr	HT	Unlikely
	37	BRCA1	Breast cancer recurrence (even after bilateral mastectomy) (RRO because of STIC at RRS)	+1 yr	Surgery, CT, RT	Unlikely
	43	BRCA1	Breast cancer detected in risk-reducing mastectomy specimen	+3 yr	CT	Unlikely
	40	BRCA1	Osteoarthritis knee (arthroscopy already planned before RRS)	+2 months	Surgery	Unrelated
	43	BRCA2	Knee injury due to fall from bike	+2 yr	Surgery	Unrelated
	44	BRCA2	Appendicitis	+3 yr	Surgery	Unrelated
	31	BRCA1	Symptomatic gall stones	+3 months	Surgery	Unrelated
	36	BRCA1	Cervical cancer FIGO stage Ia1	Before	Surgery	Unrelated
			Vaginal vault dehiscence after concomitant hysterectomy	+6 weeks	Surgery	Unrelated*
	38	BRCA1	Stress fracture of the hip	+6 months	Surgery	Unrelated
	40	BRCA2	Wound infection after breast surgery	<1 yr	Surgery	Unrelated
	42	BRCA2	Death due to fall from stairs	+4 yr	N/A	Unrelated
	34	BRCA1	Wound infections after risk-reducing breast surgery	+7 months	Surgery, antibiotics	Unrelated
	37	BRCA1	Infected breast implant	+8 months	Admission, antibiotics	Unrelated
RRSO	Surgical complications within 6 weeks					
	38	BRCA1	Nausea and vomiting caused by incisional herniation of small intestine	+3 days	Surgery	Definite
	44	BRCA2	Collapse after hospital discharge	+0 days	Readmission	Definite
	39	BRCA1	Wound infection	+9 days	Antibiotics	Definite
	35	BRCA1	Wound infection	+15 days	Expectative	Definite
	37	BRCA1	Vasovagal reaction to insertion of intravenous canule, including asystole	During	Chest compressions	Probable
	42	BRCA2	Urinary tract infection	+1 week	Antibiotics	Probable
	43	BRCA2	Collapse at home	+1 day	Expectative	Possible
	42	BRCA2	Ureter injury during concomitant hysterectomy at cleavage of uterine artery next to uterine cervix	During	Conversion, reimplantation	Unrelated*
	Miscellaneous serious adverse events					
	40	BRCA2	Ablation for atrial fibrillation (pre-existent condition at inclusion)	+1 yr	Cardial ablation	Unlikely
			Wound infection after breast surgery	+1 yr	Surgery	Unrelated
	33	BRCA2	Problems with pre-existent ureteric stents	+6 weeks	Admission, nephrostomy catheter	Unrelated

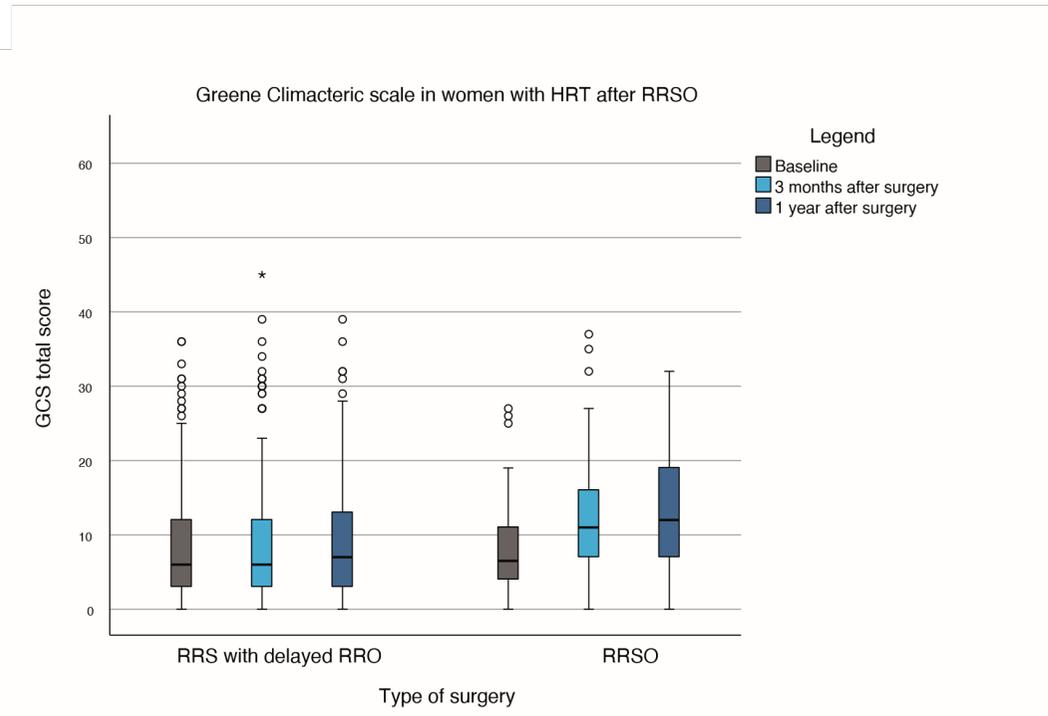
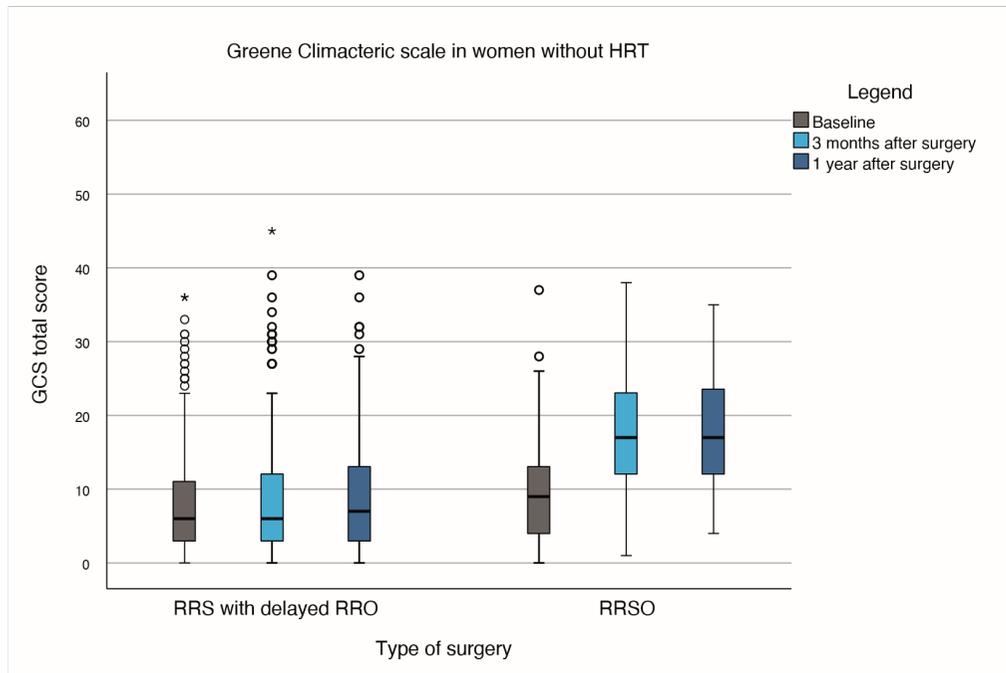
eTable 6. Surgical complications and serious adverse events (SAE) - *continued*

	Age	BRCA- PV	(S)AE	Time since RRS/RRSO	Treatment	Relation to study intervention
	35	<i>BRCA1</i>	Unexplained transient neurological symptoms (headache, muscle ache and backpain)	+3 months	Hospital admission	Unrelated
	42	<i>BRCA2</i>	Bartholinic cyst	+5 months	Surgery	Unrelated
	38	<i>BRCA1</i>	Breast cancer	+1 yr	Surgery, CT, RT	Unrelated
	44	<i>BRCA2</i>	Breast cancer	+3 yr	Surgery	Unrelated
<p>*(S)AE related to intervention other than study intervention (RRS, RRSO or RRO) Abbreviations: (S)AE (serious) adverse event; RRS risk-reducing salpingectomy; CT chemotherapy; LLETZ Large Loop Excision of the Transformation Zone; HT hormone therapy; RT radiotherapy; N/A not applicable; RRSO risk-reducing salpingo-oophorectomy; RRO risk-reducing oophorectomy; The following events were not included as serious adverse events according to the study protocol: elective hospital admissions, elective (risk-reducing) surgeries</p>						



eFigure 1: A schematic overview of data collection and timing of questionnaires

* Secondary outcome measures for which follow-up has not been completed yet, they are not included in this report (evaluation planned at five and eight years after surgery)



eFigure 2. Box plots of the Greene climacteric scale

Abbreviations: HRT hormone replacement therapy; GCS Greene Climacteric scale; RRS risk-reducing salpingectomy; RRO risk-reducing oophorectomy; RRSO risk-reducing salpingo-oophorectomy