Introduction/Background* Hereditary BRCA 1-2 mutations are known risk factors for the development of breast and ovarian cancer. Risk-Reducing Salpingo-Oophorectomy (RRSO) and bilateral mastectomy are the only effective risk-reducing strategies for these patients. Commonly these are two step surgical procedures performed separately. The aim of this study was to evaluate the feasibility and the efficacy of RRSO, combined with simultaneous mastectomy and breast reconstruction in BRCA 1-2 mutation carriers.

Methodology We conducted an observational retrospective study on patients with BRCA 1-2 mutation who undergone combined and simultaneous laparoscopic RRSO and mastectomy with breast reconstruction at the Gynaecology Clinic of Padua and Breast Unit of Veneto Institute of Oncology (IOV). Inclusion criteria: patients with BRCA 1-2 mutation, consent to simultaneous surgery. We collected data about age, menopausal status, history of breast carcinoma, pre-operative CA-125 levels, transvaginal-ultrasound features before surgery, operative times, intra and post-operative complications, follow up (FUP) information after RRSO and satisfaction about the simultaneous procedure.

Result(s)* We included 40 patients: baseline characteristics are reported in table 1. RRSO was performed in all patients. 37 women underwent to bilateral mastectomy and 3 to monolateral mastectomy (all with breast reconstruction). The mean operative time was 229.6 ± 50.7 minutes (48 ± 16.9 minutes for the RRSO, 147.1 ± 43.6 for mastectomy and reconstruction with a mean surgical team changing time of 34.4 ± 19.6 minutes). No operative complications were reported for RRSO; concerning breast surgery we reported 4 cases of prosthesis loss and one of breast hematoma with a median FUP of 20 months (6-95). The mean hospitalization days was 3.4 ± 2.3. After one months after surgical procedure all patients expressed high satisfaction about the simultaneous surgery.

Abstract 743 Table 1 Patients general features

	BRCA 1 carriers (n= 23)	BRCA 2 carriers (n= 17)	TOTAL (n= 40)
Mean Age at RRSO*	46.1 ± 6.6	49.7 ± 8.1	47.6 ± 7.3
Brest Cancer before RRSO*	16 (69.5%)	10 (58.8%)	26 (65%)
Negative Preoperative CA-125	23 (100%)	17 (100%)	40 (100%)
Menopausal Status			
Pre-menopausal	15 (65.2%)	5 (29.4%)	20 (50%)
Post-menopausal	8 (34.8%)	12 (70.6%)	20 (50%)
Familiarity			
Ovarian Cancer	12 (52.1%)	7 (41.1%)	19 (47.5%)
Breast Cancer	15 (65.2%)	13 (76.5%)	28 (70%)
Negative	3 (13%)	3 (17.6%)	6 (15%)

Legend: RRSO risk reducing salpingo-oophorectomy

Conclusion* RRSO combined with simultaneous mastectomy and breast reconstruction is feasible, effective and provides an intriguing option for BRCA 1-2 mutation carriers. A single time for anaesthesia, hospitalization and a not increased complication rate lead to high satisfaction of the patients. Nevertheless, patient's selection should be carefully performed and surgical teams have to be properly instructed and coordinated.

756 PROPHYLACTIC SALPINGO-OOPHORECTOMY IN BRCA 1–2 PATIENTS. PROFILE EPIDEMIOLOGICAL

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Introduction/Background* Familial predisposition has been described in 5-10% of women who develop ovarian cancer. Women with germ-line BRCA1/2 mutations have an increased risk of breast and ovarian cancer as compared with the rest of the population. Women with BRCA1 mutation have a 44% lifetime risk of developing ovarian cancer, whereas, BRCA2 mutation has lifetime risks of 17%. These women often undergo bilateral prophylactic oophorectomy to reduce this risk.

The objective of this study was to analyze the epidemiological characteristics of patients with BRCA 1/2 mutation undergoing prophylactic salpingoophorectomy for adnexal high-grade serous epithelial carcinoma.

Methodology We performed a prospective cohort study between January 2013 to January 2021. Patients with BRCA 1/2 mutations who underwent prophylactic bilateral salpingoophorectomy were included. A descriptive study of epidemiological characteristics of these patients was performed. All statistical analysis was performed with Stata/IC 13.0 for Windows.

Result(s)* We analyze the epidemiological characteristics of 115 patients that were included. Of them, 50.4% (58) had BRCA 1 mutation and 49.6% (57) BRCA 2 mutation. Most occult ovarian carcinomas are found in women over 45 years of age. The median age at surgery was 49.2 (standar deviation, SD 5.8) years and 59.1% (68) of patients were posmenopausal.

Fifty (43.5%) of them were the family index case (first case of cancer) and sixty (52.2%) had a previous diagnosis of breast cancer. The most frequent family history was: two cases of breast cancer in their family of 1 or 2 degree whose sum of ages at diagnosis was less than 120 years. The median Ca 125 value prior to surgery was 29.4 u/L. Adnexal findings were described in presurgery ultrasound as normal (104, 90.4%) or bening cyst (11, 17.4%).

Conclusion* Most occult carcinomas are found in women over 45 years of age. Unfortunately, there is no screening test effective in detecting ovarian cancer at early stages. Therefore, the current recommendation is to undergo risk-reducing bilateral salpingo-oophorectomy after completing the gestational desire in carriers of BRCA1/2 mutations. Although, the main negative consequence of this surgery in premenopausal women is premature menopause. However, the risk is balanced by the morbidity and mortality associated with ovarian cancer, and these symptoms can be treated with some drugs.

824 DOUBLE HETEROZYGOTES FOR HIGH PENETRANCE SUSCEPTIBILITY GENES ARE NOT RARE AND REQUIRE SPECIAL CARE

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Introduction/Background* Implementation of NGS panel sequencing (instead of single/double gene/s sequencing) into standard genetic testing for cancer susceptibility generates new and unexpected data on spectrum, proportion and combination of susceptibility genes´ mutations.
Methodology We analyzed results of genetic testing in healthy patients referred to our survailance office, their pedigrees and clinical manifestations to identify and describe clinical meaning of combined heterozygosity in different cancer suceptibility genes. We also discusse prophylactic measures in these double heterozygotes.
Result(s)* In the group of 455 individuals who underwent genetic testing for known or suspicious genetic susceptibility to cancer, we identify 11 (2.4%) double heterozygotes, i.e. individual harbouring germ-line pathologic mutations in two high penetrance susceptiblity genes. 8 of them have mutations in either BRCA1/2 genes and mismatch-repair genes (MLH1 or MSH2), 3 remaining have combination of BRCA1 mutation and RAD51, VHL and CHEK2, respectivelly. 3 out of 11 double heterozygotes developer cancer through median follow-up of 34 moths, 2 breast cancer, 1 colorectal cancer. Pedigree analysis does not allow for individualisation of risk calculation.
Conclusion* Double heterozygotes are known from literature, till the era of NGS panel sequencing, they wer thought to be extremelly rare. These individuals, however, represent a substantional proportion of our patients and need individualised scenario of survailance with respect to different spectrum of risks compared to single mutation carriers.

874 UPTAKE OF POPULATION BASED BRCA-TESTING ACROSS JEWISH DENOMINATIONS AND AFFECT OF CULTURAL AND RELIGIOUS FACTORS: A COHORT STUDY

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Introduction/Background* Population-based *BRCA*-testing in the Ashkenazi Jewish (AJ) population is feasible, acceptable, reduces anxiety, identifies more *BRCA*-carriers and is cost-effective. The Jewish population is the first population for whom unselected population testing is now being implemented with Israel recently adopted this into national policy. Guideline change is being advocated in the UK and by others too. It is unknown whether *BRCA*-testing differs across Jewish denominational affiliations and religious or cultural outlook. We evaluate the association of Jewish cultural and religious identity and denominational affiliation with interest-in, intention-to undertake and uptake-of population-based BRCA-testing
Methodology
Design Cohort-study set within recruitment to GCaPPS-trial (ISRCTN73338115).

AJ men and women, >18years, from London, self-referred, and attended recruitment clinics(clusters) for pre-test counselling. Subsequently consenting individuals underwent BRCA-testing. Mina oucome measures were: Interest, intention, uptake-of BRCA-testing. Participants self-identified to one Jewish denomination: Conservative/Liberal/Reform/Traditional/Orthodox/Unaffiliated. Validated scales measured Jewish Cultural-Identity (JI) and Jewish Religious-identity (JR). 4-item Likert-scales analysed initial 'interest' and 'intention-to-test' pre-counselling. Item-Response-Theory and graded-response-models, modelled responses to JI and JR scales. Ordered/multinomial logistic regression modelling evaluated association of JI-scale, JR-scale and Jewish Denominational affiliation on interest, intention and uptake-of BRCA-testing.
Result(s)* 935 AJ women/men of mean-age=53.8 (S.D=15.02) years, received pre-test education and counselling through 256 recruitment clinic clusters (mean cluster size=3.64). Denominational affiliations included Conservative/Masorti=91(10.2%); Liberal=82(9.2%), Reform=135(15.1%), Traditional=212 (23.7%), Orthodox=239(26.7%); and Unaffiliated/Non-practising=135(15.1%). Overall BRCA-testing uptake was 88%. Pre-counselling 96% expressed interest and 60% intention-to test. JI and JR scores were highest for Orthodox, followed by Conservative/Masorti, Traditional, Reform, Liberal and Unaffiliated Jewish denominations. Regression modelling showed no significant association between overall Jewish Cultural or Religious Identity with either interest, intention or uptake-of BRCA-testing. Interest, intention and uptake of BRCA-testing was not significantly associated with denominational affiliation.
Conclusion* Jewish religious/cultural identity and denominational affiliation do not appear to influence interest, intention or uptake of population-based BRCA-testing. BRCA-testing was robust across all Jewish denominations.

943 RISK-REDUCING SURGERY IN BRCA MUTATION: A MULTICENTRIC PROSPECTIVE STUDY

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Introduction/Background* BRCA1/2 are tumour-suppressor genes involved in DNA homologous recombination and ovarian cancer development.
Methodology Risk-reducing surgery (RRS) was performed in 148 patients carrying BRCA1 (aged between 30-73 years, median age was 51 years) and BRCA 2 mutation (aged between 36-70 years, median age was 53 years). Seventy-nine patients had previous history of breast cancer.
Result(s)* Between the all patients, 131 women underwent risk-reducing salpingo-oophorectomy (RRSO) through a laparoscopic minimally invasive approach, 11 (7,4%) underwent laparoscopic RRSO and contextual hysterectomy, 2 woman (1,3%) underwent RRSO through a laparotomic approach and 12 women (8,1%) laparotomic RRSO and hysterectomy. During 7 (4,7%) laparoscopic RRSO, prophylactic bilateral mastectomy was also performed.
Conclusion* RRSO is safe and feasible in BRCA mutation carriers. The procedure is effective for genetic prevention of ovarian cancer.