**Supplementary material-1: Surgical Protocol for Risk Reducing Surgery for Ovarian Cancer Prevention in Women at Increased Risk**

1. While a minimal access (laparoscopic/robotic) approach is preferable, this is not mandatory for the study.

2. Inspection of abdomino-pelvic cavity is required and this is best done laparoscopically.

3. Peritoneal washings for cytology are mandatory as malignant cells have also been reported – even in the absence of an identifiable ovarian/tubal cancer.

4. In women having a vaginal hysterectomy for benign pathology, the ovaries, tubes and the pelvic cavity should be inspected laparoscopically at the start of the procedure.

5. If there are adhesions between the adnexa and adjacent structures, careful dissection should be performed to ensure complete removal of the ovaries and fallopian tubes.

6. Peritoneal/ Omental biopsies should be taken if indicated.

7. Routine curettage of the uterus is less evidence based, and is advisable in all women on Tamoxifen.

1.1 Hysterectomy is not usually advocated unless there are other indications. If the woman is taking Tamoxifen it is important to ensure that the risk of endometrial cancer has been discussed as the woman may wish to opt for a hysterectomy, although the standard recommendation is that this is not required.

8. Damage to the fimbrio-ampullary end of the tubes by electrosurgery or crushing should be avoided as this can cause artefacts which make diagnosing occult cancer/carcinoma insitu and dysplasia difficult. Monopolar diathermy should be avoided. Use of low power settings and short application times is advisable to reduce inadvertent thermal tissue injury.

9. In women undergoing risk reducing salpingo-oophorectomy or delayed oophorectomy, the infundibulopelvic ligament should ideally be ligated 2cm from the ovarian hilum to reduce the risk of remnant ovarian syndrome.

10. It is important to avoid fragmentation or morcellation of the specimen as this makes systematic histopathological evaluation difficult.

11. Right and left sided specimens should be sent in separate containers/pots. In case of multiple fragments, care should be taken to avoid mixing of right and left sided fragments.

**Supplementary material-2: Protocol for Histopathological processing**

Both tubes/ovaries are entirely embedded and microscopically examined following serial transverse sectioning at 2 mm intervals.

**Ovaries:**

1. After standard recording of size and macroscopic appearance, each ovary should be serially sectioned transversely at 2 mm intervals perpendicular to longest axis and processed in toto. If the ovary is enlarged by 'benign disease', sampling should follow recommended protocols of a minimum of one section per centimetre of maximum diameter.

**Fallopian tubes:**

2. The overall length (including the fimbrial end) and macroscopic appearance of each fallopian tube should be stated.
3. The distal 15 mm (approximately), including the infundibulum and fimbrial end of the tube, is sliced *longitudinally* at 2 mm intervals to maximise exposure and histological examination of the tubal epithelium in this region. If possible this should be processed in 1-2 cassettes to reduce laboratory effort if serial sectioning and/or immunohistochemistry are required; however the cassette(s) must not be overcrowded.
4. The proximal portions of the tube, i.e. isthmus and ampulla, are *transversely* sliced in serial sections at 2 mm intervals. The mid and proximal portions can be processed in separate cassettes with multiple slices in one cassette, avoiding overcrowding.
5. Overall the entire tube can be sampled in 3 or 4 cassettes including any mesosalpinx.
6. Immunohistochemistry (IHC) is only required if there are atypical or abnormal H+E findings and the appropriate block should be selected. All IHC findings must be reported. In general, if STIC or any other atypical tubal mucosal lesion is identified, immunohistochemistry for p53 and the proliferation marker Ki67/ MIB1 should be performed. Other markers, for example WT1, can be performed at the pathologist's discretion.
7. A single level of each tissue block is sufficient, although additional levels can be undertaken at the discretion of the pathologist.
8. When reporting an invasive tumour of STIC, it must be made clear whether lesions are unifocal or multifocal. The largest diameter of STIC/invasion must be reported.
9. Lesions less than STIC may also be reported. However, if reported, the pathologist must state on the issued report that these lesions have no clinical significance.

**Peritoneal /Omental biopsies:**

10. If submitted, these should be processed in their entirety.

**Peritoneal Washings:**

11. Cytological examination of fluid obtained after instillation of normal saline into the peritoneal cavity.

**Criteria for diagnosis of 'Serous Tubal Intraepithelial Carcinoma' (STIC), Serous tubal intraepithelial lesion (STIL), p53 signature**

1. **Serous tubal intraepithelial carcinoma (STIC).** The histologic diagnosis of STIC is based on a combination of features, including variably stratified epithelium with increased nuclear to cytoplasmic ratio, nuclear enlargement, prominent nucleoli, loss of cell polarity, mitotic activity and loss of cilia. Immunohistochemically, these areas exhibit abnormal mutation-type staining with p53 (either diffuse intense nuclear positivity in more than 80% of the lesional cells or completely negative staining in all lesional cells) and expression of the proliferation marker Ki67/ MIB1 in greater than 10% of the cells. STIC most commonly involves the fimbria but may also have a non-fimbrial location.
2. **Serous tubal intraepithelial lesion (STIL).** Lesions less than STIC may also be reported. However, if reported, the pathologist should state on the report that these lesions have no established clinical significance. The preferred designation for these lesions is STIL. This diagnosis should be made sparingly and the criteria are variable but include cases where
    - the morphological features are in keeping with STIC but p53 staining is wild-type and/ or Ki67/ MIB1 is less than 10%,
    - cases where the morphology is suspicious of STIC but p53 staining is wild-type or Ki67/ MIB1 is less than 10%,
    - cases where the morphology is atypical but not considered suspicious of STIC but p53 exhibits mutation-type staining and Ki67/ MIB1 is greater than 10%.
3. **p53 signatures.** These are stretches of morphologically normal non-ciliated/ secretory tubal epithelium exhibiting mutation-type staining with p53. They will only be picked up if p53 staining is undertaken. They are commonly seen in the fallopian tubes and are of no clinical significance. They should not be reported.

**Supplementary material-3: PROTECTOR collaborators and participating centres**

Katie Snape, St George's University Hospitals NHS Foundation Trust

Sadaf Ghaem-Maghami, Imperial College Healthcare NHS Trust

Gautam Mehra, Guy's and St Thomas' NHS Foundation Trust

Angela Brady, London North West Healthcare NHS Trust

Adam Rosenthal, University College London Hospitals NHS Foundation Trust

Michelle MacKintosh, Manchester University NHS Foundation Trust

Ian Harley, Belfast Health & Social Care Trust

Sudha Sundar, Sandwell and West Birmingham Hospitals NHS Trust

Claire Newton, University Hospitals Bristol NHS Foundation Trust

Omer Devaja, Maidstone and Tunbridge Wells NHS Trust

Tim Duncan, Norfolk and Norwich University Hospitals NHS Foundation Trust

Supratik Chattopadhyay, University Hospitals of Leicester NHS Trust

Natalia Povolotskaya, Portsmouth Hospitals NHS Trust

Rema Iyer, East Kent Hospitals University NHS Trust

Lucy Side, University Hospital Southampton NHS Foundation Trust

Anil Tailor, Royal Surrey County Hospital Foundation Trust

Manon van Seters, Worcestershire Acute Hospital Trust

Suma Kodiathodi, North Tees and Hartlepool NHS Foundation Trust

Partha Sengupta, County Durham and Darlington NHS Foundation Trust

Iain Cameron, Gateshead Health NHS Foundation Trust

Sonali Kaushik, Brighton and Sussex University Hospitals NHS Trust

Karin Williamson, Nottingham University Hospitals NHS Trust

Katherine Edey, Royal Devon & Exeter NHS Foundation Trust

Sian Taylor, Liverpool Women's Hospital NHS Foundation Trust

Andrew Phillips, University Hospitals of Derby and Burton NHS Foundation Trust

Mark Willett, East Lancashire Hospitals NHS Trust

Tony Chalhoub, The Newcastle upon Tyne Hospitals NHS Foundation Trust

Sanjay Rao, South Tees Hospitals NHS Foundation Trust

Nicholas Matthews, South Tyneside and Sunderland NHS Foundation Trust

Aarti Sharma, Cardiff and Vale UHB

Scott Fegan, NHS Lothian

Mahalakshmi Gurumurthy, NHS Grampian

Kalpana Ragupathy, NHS Tayside

Beena Abdul, Northampton General Hospitals NHS Trust

Ibraheem Hamoodi, Northumbria Healthcare NHS Foundation Trust

Claire Park, Royal United Hospitals Bath NHS Foundation Trust

Jane Borley, Royal Cornwall Hospitals NHS Trust

Thumuluru Kavitha Madhuri, Royal Surrey County Hospital Foundation Trust

Richard Hutson, Leeds Teaching Hospitals NHS Trust

Kerryn Lutchman-Singh, Swansea Bay University Health Board

Richard Peevor, Betsi Cadwaladr University Health Board