Clinical Commissioning Policy: Genetic testing for BRCA1 and BRCA2 mutations – a response from Target Ovarian Cancer
April 2015

Target Ovarian Cancer is the national ovarian cancer charity working to save lives and help women diagnosed live their lives to the full, wherever they are in the UK. We do this by improving early diagnosis, finding new treatments and providing support for women.

We welcome the recognition that there is currently variance in access to genetic testing for women with ovarian cancer. The new Clinical Commissioning Policy will serve as an addendum to the Medical Genetics Service Specification (E01/S/a) and help ensure all women with ovarian cancer are able to access testing for the BRCA 1 or BRCA 2 gene mutation.

Do you support the draft policy statement?
Target Ovarian Cancer welcomes the fact that this Clinical Commissioning Policy will bring NHS England commissioning in line with NICE guidance. By lowering the threshold for genetic testing to ten per cent this policy will help address regional variation and ensure that all women with ovarian cancer are eligible for genetic testing.

What further changes, if any do you think need to be made to this document?
It is important that the Clinical Commissioning Policy recognises that all women with non-mucinous epithelial ovarian cancer will now be able to access genetic testing. Women with breast cancer carry a five to ten per cent risk of having a BRCA 1 or BRCA 2 mutation which means that eligibility for genetic testing depends on their family history. In contrast, women with ovarian cancer have a 15 per cent risk of having a BRCA 1 or BRCA 2 gene mutation and no further family history is required. We recommend amending the "Introduction", "Epidemiology and needs assessment" and "Criteria for Commissioning" sections to reflect this and have proposed suitable changes in our submission below.

Introduction
To avoid any confusion over the eligibility of women with ovarian cancer for genetic testing, we propose amending the opening sentence on paragraph four, page six to remove "Up to" so this reads "1 in 6 (15 per cent) of people diagnosed with ovarian cancers may have inherited a harmful BRCA mutation." To then clarify that this means all women with ovarian cancer are eligible for genetic testing, we suggest further inserting the following sentence, "As a consequence, all women with a diagnosis of non-mucinous epithelial ovarian cancer will be eligible for genetic testing."

The current Clinical Commissioning Policy also currently provides two different prevalences for BRCA 1 and BRCA 2 gene mutations in women with ovarian cancer

(page six – "1 in 6 (15 per cent)", page ten – "10 per cent"). Furthermore, the studies cited on page six are all 15 years or more old and those relevant to prevalence among women with ovarian cancer on page ten are equally outdated. More recent research, for example, by Zhang et al, gives a 13 per cent estimate. We therefore recommend updating the references and using the 13 per cent figure on pages six and ten.[1] (Zhang, S., Royer, R., Li, S., McLaughlin, L. R., Rosen, B., Risch, H. A., Fan, I., Bradley, L., Shaw, P. A., and Narod, S. A. (2011) Frequencies of BRCA1 and BRCA2 mutations among 1,342 unselected patients with invasive ovarian cancer. Gynecologic Oncology, 121(2):353-357)

Epidemiology and needs assessment

Prevalence numbers for "Table 3" on page 11 need updating to reflect that all women with ovarian cancer will be eligible for testing under the new Clinical Commissioning Policy. It currently gives the number of affected people expected to be eligible for BRCA 1 and BRCA 2 testing as 3,863. However, as all women with ovarian cancer will now be eligible for BRCA 1 and BRCA 2 testing, this alone accounts for almost 6,000 potential cases a year suggesting these figures need revising. (Cancer Research UK. Available at www.cancerresearchuk.org/cancer-info/cancerstats/types/ovary/incidence/#By [Accessed: 14/4/15])

Criteria for Commissioning

Within this section, the third subsection, "Persons with breast or ovarian cancer" states "Genetic testing will be offered in specialist genetic clinics to a person with breast or ovarian cancer if their combined *BRCA1* and *BRCA 2* mutation carrier probability is 10% or more." We propose adding a further sentence "This will include all women with non-mucinous epithelial ovarian cancer." We appreciate this differs from the NICE guidance, but we feel it is important that a distinction is drawn between women with breast cancer, where a family history may be required, and women with ovarian cancer, who already pass the ten per cent threshold for risk of a BRCA 1 or BRCA 2 gene mutation. This is particularly important if commissioners are to ensure there are adequate services to meet demand.

More broadly, we understand that the Clinical Commissioning Policy reflects the latest NICE guidance, which focuses on breast cancer, hence the enhanced requirements under Criteria for Commissioning in relation to breast cancer, but are concerned this risks creating a two tier service, particularly in relation to the "Genetic testing for *BRCA 1/2* mutations within 4 weeks of diagnosis of breast cancer" subsection.

This section has already been amended (dropping references to a multidisciplinary approach to care in 1.5.16 of NICE CG164). We would therefore recommend further amendments to ensure parity in service provision between breast and ovarian cancer and to reflect the division within the clinical community over the role of four

[1] Amended 19 May 2015. Previously gave figure of 15 per cent for Zhang research. Actual figure is 13 per cent.

week testing (the NICE guidance on which the Clinical Commissioning Policy is based stresses division within the clinical community over its merits (CG 164:2.2)).

We propose removing the subheading "Genetic testing for *BRCA 1/2* mutations within 4 weeks of diagnosis of breast cancer" altogether and moving the contents of this section up to join "Persons with breast or ovarian cancer". The whole section would thus appear as:

Persons with breast or ovarian cancer

- Genetic testing will be offered in specialist genetic clinics to a person with breast or ovarian cancer if their combined *BRCA1* and *BRCA 2* mutation carrier probability is 10% or more. This will include all women with non-mucinous epithelial ovarian cancer.
- Offer those people that are eligible for referral to a specialist genetic clinic (based on their risk) a choice of accessing genetic testing during initial management or at any time thereafter.
- For patients having fast-track genetic testing (within 4 weeks of a diagnosis of breast cancer) offer recruitment to a clinical trial, if one is available.
- Offer detailed consultation with a clinical geneticist or genetics counsellor to all those with breast [or ovarian] cancer who are offered genetic testing, regardless of the timeframe for testing.

While we believe that services should be provided equally to all women, regardless of whether they have breast or ovarian cancer, if, after merging these two subsections, it was necessary to distinguish any bullets which apply only to patients with breast cancer, these could be qualified as follows:

"For patients having fast-track genetic testing (within four weeks of a diagnosis of breast cancer) offer recruitment to a clinical trial, if one is available. [breast cancer only]"

These changes would simplify the Criteria for Commissioning by grouping all services for women with a diagnosis of breast or ovarian cancer together under one heading, and help ensure an equitable service for both women with breast cancer and women with ovarian cancer.

[Although unrelated to services for women with ovarian cancer, we note an inconsistency between the second bullet under the current genetic testing section ("For patients having fast-track genetic testing (within 4 weeks of a diagnosis of breast cancer) offer recruitment to a clinical trial, if one is available.") and NICE guidance (CG 164:1.5.15) with the latter qualifying that fast-track testing was available only for women on clinical trials in contrast to the Clinical Commissioning Policy which does not make this clarification.]

Are there any other considerations not reflected in the document that you wish to draw our attention to?

N/A

Final comments

It is important that the commissioning of genetic testing continues to be informed by the evidence base. Currently, there is no evidential support for any approach other than testing through genetic services where women are provided full counselling and support. There are currently trials and programmes underway looking at alternatives, including providing genetic testing directly through oncology services or partnership arrangements with genetic services, but until these report and either the evidence base or NICE guidance changes, testing needs to continue to be conducted through genetic services.

In the future, whether or not a woman with ovarian cancer has a BRCA 1 or BRCA 2 gene mutation is likely to affect her treatment, with the introduction of a targeted second-line treatment widely anticipated. However, as this will be a second-line treatment, there will still be adequate time for women to undergo testing with the current four week turnaround time (E01/S/a) and the full support of genetic services.