Information for Clinicians

Gynaecology Department

Amendment History

Issue	Status	Date	Reason for Change	Authorised
1	New document	05/06/2025	New document	10/7/2025

The Management of Patients with Elevated Ca 125 Levels in the Presence of a Normal Pelvic Ultrasound Scan

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Background

Serum Ca125 levels are increasing checked in women of all ages as part of primary care investigations based on NICE guidance (CG 122)[1]. NICE recommends considering performing a Ca125 level in women of all ages (especially over the age of 50) who present with signs or symptoms which may suggest ovarian cancer, including:

- persistent abdominal distension (bloating)
- feeling full (early satiety) or loss of appetite
- pelvic or abdominal pain
- increased urinary urgency or frequency

Risk factors for ovarian cancer include:

- Increasing age
- Genetic factors - mutations e.g. BRCA1 and BRCA2, Lynch syndrome
- Reproductive factors – nulliparity, early menarche, late menopause.
- Medical conditions – personal history of breast or bowel cancer; endometriosis, diabetes
- Lifestyle factors – smoking, obesity, occupational exposure to asbestos

Women who have a raised Ca125 (determined as > 35 IU/ml) are recommended to have a pelvic ultrasound scan. Women with a pelvic ultrasound scan concerning for ovarian cancer are then recommended to be referred urgently for assessment. Women with a normal pelvic ultrasound who have a raised Ca125, or those with persistent symptoms and a normal serum Ca125, are advised to be reviewed for any other cause of symptoms, and safety netted to return to see their

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general practitioner if new or ongoing concerns. There is a lack of clear national guidance as to whether Ca125 levels need ongoing investigation or monitoring in the context of a normal ultrasound scan.

Unfortunately, serum Ca125 levels are neither sensitive nor specific for gynaecological cancer, especially in pre-menopausal women. Levels can be elevated for physiological reasons, in benign gynaecological conditions including menstruation, as well as in non-gynaecological pathology causing peritoneal irritation (see Figure 1)[2].

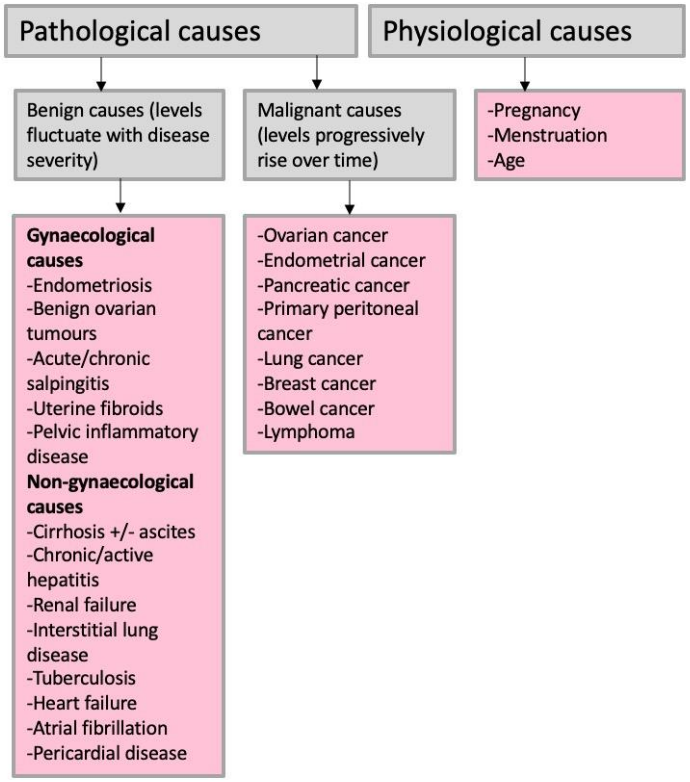
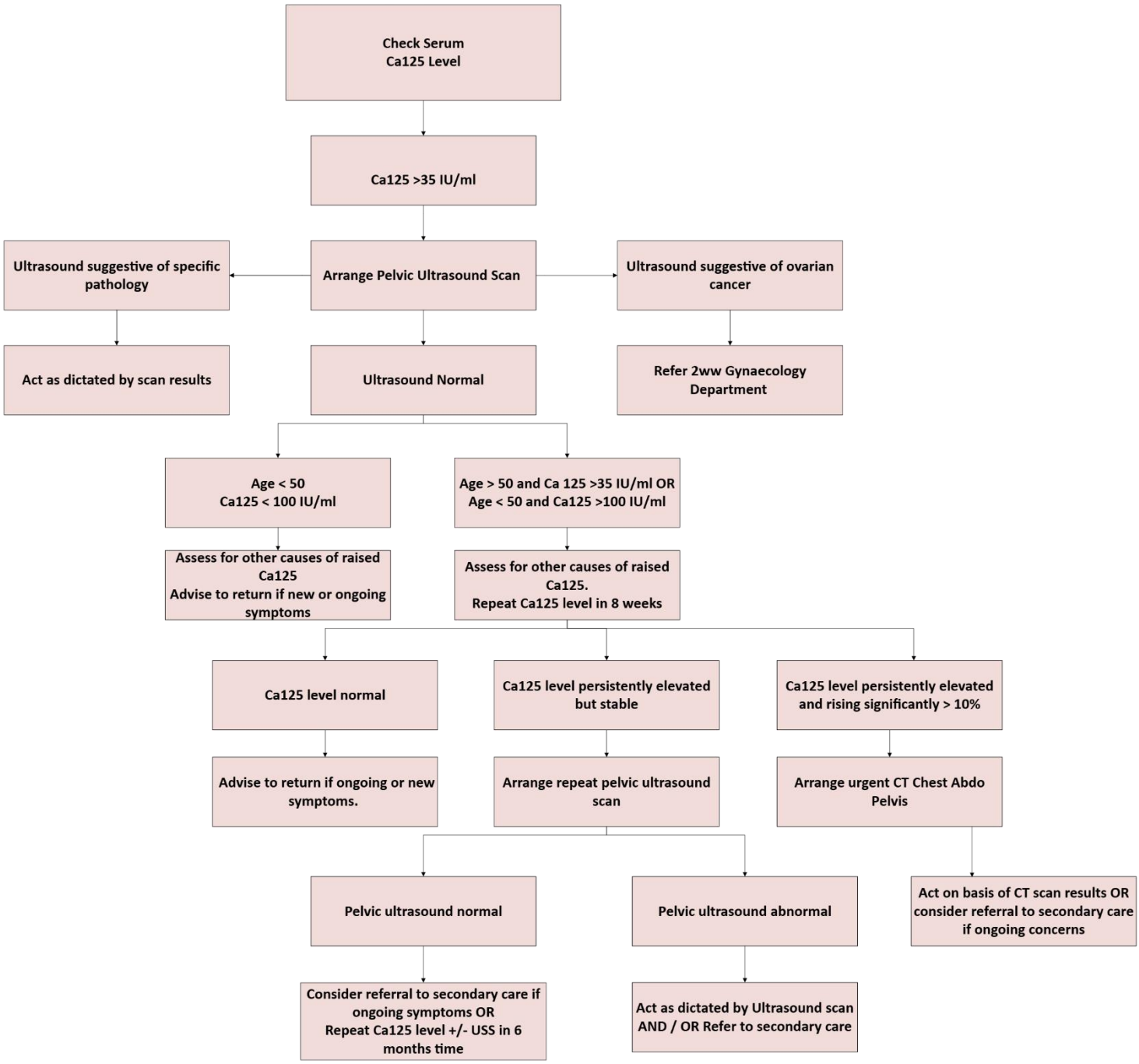


Figure 1: Potential Causes of an Elevated Ca125 level

As Ca125 levels can be elevated in women with pre-menopausal conditions, such as endometriosis and fibroids, clinicians should be more cautious in interpreting raised Ca125 levels in this patient group. Furthermore, there is evidence that the probability of a raised Ca125 level being associated with ovarian cancer varies with age. NICE use a 3% probability of ovarian cancer as a recommendation for further investigation. A study of over 50,000 women showed that the Ca125 level equating to a 3% prediction of ovarian cancer was 104 IU/ml in women aged under 40, compared to 32 IU/ml in women over 70 years of age[3].

The below flowchart gives guidance for the management of pre and post-menopausal women with a raised Ca125 level and a normal ultrasound scan. For each individual patient clinical acumen should be used and gynaecological advice sought if there are going concerns in the community.

Flowchart Guidance for Raised Ca125 Levels in the Context of a Normal Ultrasound Scan


Check Serum Ca125 Level
Ca125 >35 IU/ml
Ultrasound suggestive of specific pathology
Arrange Pelvic Ultrasound Scan
Ultrasound suggestive of ovarian cancer
Act as dictated by scan results
Ultrasound Normal
Refer 2ww Gynaecology Department
Age < 50 Ca125 < 100 IU/ml
Age > 50 and Ca 125 >35 IU/ml OR Age < 50 and Ca125 >100 IU/ml
Assess for other causes of raised Ca125 Advise to return if new or ongoing symptoms
Assess for other causes of raised Ca125. Repeat Ca125 level in 8 weeks
Ca125 level normal
Ca125 level persistently elevated but stable
Ca125 level persistently elevated and rising significantly > 10%
Advise to return if ongoing or new symptoms.
Arrange repeat pelvic ultrasound scan
Arrange urgent CT Chest Abdo Pelvis
Pelvic ultrasound normal
Pelvic ultrasound abnormal
Act on basis of CT scan results OR consider referral to secondary care if ongoing concerns
Consider referral to secondary care if ongoing symptoms OR Repeat Ca125 level +/- USS in 6 months time
Act as dictated by Ultrasound scan AND / OR Refer to secondary care

References

1. National Institute for Health and Care Excellence (NICE) (2023) *Ovarian cancer: recognition and initial management*. [online] Available from: Recommendations | Ovarian cancer: recognition and initial management | Guidance | NICE Accessed 05/06/02025
2. Howe T, Sokolovsky N, Sayasneh A, Omar K, Tahmasebi F. Raised CA125 – what we actually know… *The Obstetrician & Gynaecologist* 2021; 23: 21–27. **https://doi.org/10.1111/tog.12704**
3. Funston G, Hamilton W, Abel G, Crosbie EJ, Rous B, Walter FM. The diagnostic performance of CA125 for the detection of ovarian and non-ovarian cancer in primary care: A population-based cohort study. PLoS Med. 2020 Oct 28;17(10):e1003295. doi: 10.1371/journal.pmed.1003295. PMID: 33112854; PMCID: PMC7592785.

Document Control Information

Consultation Schedule

Name and Title of Individual	Date Consulted
Jo Ficquet Obstetric & Gynaecology Consultant	10/7/25
Jonathan Frost Gynaeoncology Consultant	4/7/25
Ellen Nelissen Gynaeoncology Consultant	4/7/25
Alison Montgomery Gynaeoncology Consultant	4/7/25
Laura Atherton Obstetric & Gynaecology Consultant	4/7/25
Amy Keightley Gynaeoncology Consultant	4/7/25
Rebecca Palmer Gynaecology Advanced Clinical Practitioner	4/7/25

The following people have submitted responses to the consultation process:

Name and Title of Individual	Date Responded
Jo Ficquet Obstetric & Gynaecology Consultant	10/7/25
Jonathan Frost Gynaeoncology Consultant	4/7/25
Ellen Nelissen Gynaeoncology Consultant	4/7/25
Alison Montgomery Gynaeoncology Consultant	4/7/25
Laura Atherton Obstetric & Gynaecology Consultant	4/7/25
Amy Keightley Gynaeoncology Consultant	4/7/25
Rebecca Palmer Gynaecology Advanced Clinical Practitioner	4/7/25

Name of Committee/s (if applicable)	Date of Committee

Ratification Assurance Statement

Dear Mrs Jo Ficquet

Please review the following information to support the ratification of the below named document.

Name of Guideline:	Ca125 with Normal Ultrasound
Name of author:	Dr Aileen Mohan
Job Title:	ST6 Obstetrics & Gynaecology Registrar

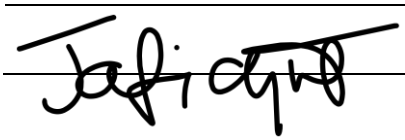
I, the above named author, confirm that:

- The Guideline presented for ratification describes best practise known to me at the time of the development of the guideline.
- I will bring to the attention of my clinical director or line manger any information which may affect the validity of this Guideline as soon as this becomes known to me;
- I have undertaken appropriate consultation on this Guideline and have considered all responses.
- I acknowledge that the policy will be kept under review, and that I may be asked to refine the guideline. If no interim changes are required it will then be formally reviewed on its documented review date.

Signature of Author:  **Date:** 10/7/25

Name of Person Ratifying this Guideline: Mrs Jo Ficquet

Job Title: Consultant Obstetrician and Gynaecologist

Signature:  **Date:** 10/7/25

To the person approving this Guideline:

Please ensure this page has been completed correctly, then print, sign and **post this page only** to: Director's Office, Wolfson Centre (D1), Royal United Hospital

The **whole guideline** must be sent electronically to: ruh-tr.policies@nhs.net