Recurrent pregnancy loss care pathway for Northern Ireland

Review 2021

HSC Public Health Agency

Contents

Section 1 – Recurrent pregnancy loss

1.1 Pregnancy loss is defined as the spontaneous loss of a pregnancy before the foetus reaches viability. It therefore includes all pregnancy losses from the time of conception until 24 weeks of gestation.[1]

1.2 Defining recurrent pregnancy loss (RPL) is complex, as illustrated by the variation in definitions utilised by various guidelines across different countries, and is limited by pathophysiological evidence to support the definition being extended or constricted. The RCOG guidance defines recurrent pregnancy loss as **'the loss of three or more consecutive pregnancies'.** The more recently published ESHRE guidance has highlighted the need for further research in this area and the guideline development group did not reach consensus on a definition. The definition offered by this guideline is **'A diagnosis of Recurrent Pregnancy Loss (RPL) could be considered after the loss of two or more pregnancies'**.[2] The tentative wording underscores the uncertainty. It also makes reference to the need to consult with couples as to when investigations should be conducted, as well as considering available resources.

1.3 In June 2016 as part of a regional process on gynaecology outpatient reform, advice pages were developed to aid GPs in referring patients to secondary care gynaecology services. An advice page was developed for recurrent pregnancy loss by this group and is currently in use on the Clinical Communication Gateway (CCG). This advises GPs that the following patients can be considered for referral:

- All women with 3 or more consecutive pregnancy losses
- All women with 1 or more second trimester pregnancy losses
- All women with a history of pregnancy loss and an associated condition such as antiphospholipid syndrome, PCOS, chronic medical disorder
- All women over 35 years old with 2 or more pregnancy losses

[1] Royal College Obstetricians and Gynaecologists. The Investigation and Treatment of Couples with Recurrent First-trimester and Second-trimester Miscarriage. Green-top Guideline No.17, April 2011.
[2] European Society of Human Reproduction and Embryology (ESHRE). Recurrent Pregnancy Loss Guidelines. November 2017.

1.4 This represents elements of both an academic definition and also service inclusion criteria eg the accommodation of patients over 35 years of age.

1.5 This pathway recommends that the criteria above, already agreed and in use in Northern Ireland, are utilised in this pathway in defining which patients should be considered for referral to Health and Social Care Trusts (HSCTs) for investigation and management of recurrent pregnancy loss

1.6 The calculation of a population estimate of those affected by recurrent pregnancy loss is challenging due to the lack of available data and the existence of multiple definitions.

1.7 Based on available data from the literature it is estimated that there may be between 262 and 786 women affected in Northern Ireland each year, equating to approximately 52–157 patients per Trust per year.[3]

This is based on NISRA live birth data in 2017, a population-based study in Denmark reporting an overall risk of pregnancy loss of 13.5%, and assuming an incidence of recurrent pregnancy loss of either 1% or 3% in those trying to conceive, when recurrent pregnancy loss is defined as the loss of 3 consecutive pregnancies.

This is an approximate estimate with numerous assumptions. Therefore, future monitoring or data collection will be important to understand the population.

Section 2 – Purpose and aims of the care pathway

2.1 The purpose of this care pathway is to make clear to patients, partners and professionals what care should be provided at each stage in the process of investigating and managing a couple experiencing recurrent pregnancy loss

[3] Based on 23076 registered live births in 2017 (NISRA) and overall risk of pregnancy loss within population-based study of 13.5% (Source: Anne-Marie Nybo Andersen, Jan Wohlfahrt, Peter Christens, Jørn Olsen, Mads Melbye. Maternal age and fetal loss: population based register linkage study. BMA 2000;320:1708–12). Assumptions include that all women trying to conceive will achieve pregnancy and that the risk of foetal loss noted in the literature is generalizable to the Northern Irish population. Foetal loss referred to within this study includes stillbirth, miscarriage, termination of pregnancy, ectopic pregnancy and hydatidiform mole.

2.2 The aims of the pathway are to:

- promote consistency and reduce variation of care irrespective of where patients access care
- enhance understanding for couples as to what care they can expect at each stage of their journey
- facilitate open and constructive conversations and joint decision making between couples and healthcare professionals, enabling joint care planning and better understanding for couples of the issues and prognosis associated with recurrent pregnancy loss.

Section 3 – Care pathway principles

3.1 **Evidenced-based** – This care pathway has been based on best evidence where available, to guide effective and cost-effective provision of care. It recognises that the evidence base for treatment for recurrent pregnancy loss is still developing and promotes access to clinical trials where appropriate.

3.2 **Co-ordinated** – The care pathway has made use of existing pathways and guidance already in use and agreed for Northern Ireland, to promote co-ordinated and consistent care. Relevant links and information are provided as relevant.

3.3. **Patient-centred** – The care recommended in this pathway is based on evidenced recommendations from recognised authoritative bodies, and should be applied in a standard approach. However, all couples have different needs and this should be recognised in joint care planning with professionals. Reactions and approaches to dealing with recurrent pregnancy loss will vary; in particular the emotional support required and availed of will be decided on an individual basis by couples and this should be recognised and supported by professionals.

Section 4 – Overview of the care pathway

Structure of the care pathway

4.1 The care pathway has a number of steps, reflecting the steps in the patient journey:

- the care pathway ‘at a glance’
- pre-referral to recurrent pregnancy loss clinic (see page 10)
- recurrent pregnancy loss clinic
- onward referral and clinical trials
- emotional support for couples with recurrent pregnancy loss.

It should be noted that the section on emotional support should underpin each step in the pathway and be a consistent element at each step.

4.2 The following products have been developed to be used alongside the care pathway:

- a regional information leaflet
- a summary of resources available to provide emotional support for patients experiencing recurrent pregnancy loss.

How the care pathway should be used

4.3 The principles of the regional care pathway should be incorporated into local services by each Health and Social Care Trust.

4.4 This care pathway should be provided to women and couples to inform them of the likely steps in their journey once a diagnosis of recurrent pregnancy loss has been considered or confirmed. This can be provided to patients by GPs, the early pregnancy clinic or gynaecology services.

4.5 Healthcare professionals should use the care pathway and the associated documents to support and facilitate conversations with couples on the likely steps through the patient journey and to inform and manage a couple’s expectations of their pathway through the Trust service.

Section 5 – The care pathway

Enquire at each step in the pathway about emotional wellbeing, signpost to relevant support and provide information leaflet including the summary of support organisations

Pre-referral

- Assess whether patient requires referral to recurrent pregnancy loss clinic
- Provide regional information leaflet and details of available support services

Recurrent pregnancy loss clinic

Assessment

- Information and support
- History and assessment
- Investigations

Management

- Supportive care
- Specific management

Onward referral and clinical trials

- Consider ECR in exceptional clinical circumstances
- Discuss referral for inclusion in a clinical trial where appropriate

Pre-referral

If patient experiences vaginal bleeding in early pregnancy:

1. **Refer to regional pathway for referral to early pregnancy services (See page 7)**

2. **Consider whether patient experiencing pregnancy loss meets the referral criteria for recurrent pregnancy loss as per criteria for GP referrals to secondary care services (see page 9)**

Patient diagnosed with recurrent pregnancy loss by GP, early pregnancy service or gynaecology service and/or meets the proposed referral criteria

↓

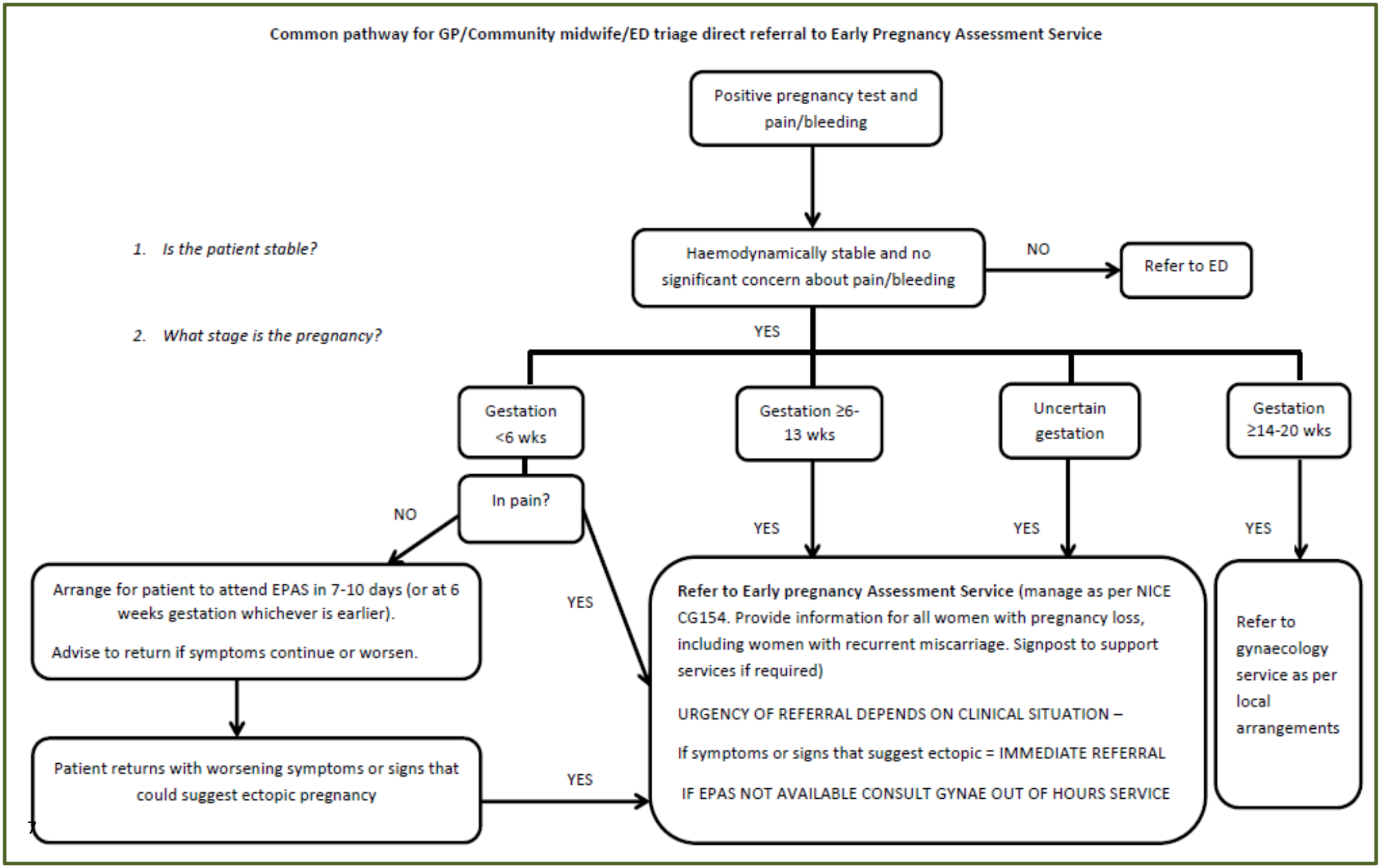
Patient offered referral to recurrent pregnancy loss clinic (investigations for recurrent pregnancy loss should be undertaken only in secondary care)

↓

Patient given pre-conceptual advice to include:

- ✓ Folic acid and vitamin D supplementation (see regional guidance for health professionals, available at: www.publichealth.hscni.net/publications/folic-acid-and-vitamin-d-guidelines-health-professionals)
- ✓ Assessment of smoking status and signposting and referral to smoking cessation services as required (see www.stopsmokingni.info)
- ✓ Assessment of alcohol and drug consumption and signposting and onward referral as required (see https://drugsandalcoholni.info/)
- ✓ Assessment of BMI and signposting and referral as required (see www.choosetolivebetter.com) For further information, refer to National Institute for Health and Care Excellence (NICE) Public Health Guideline PH 27.

Regional pathway for referral to early pregnancy services



Criteria for GP referrals to secondary care services

Gynaecology (recurrent pregnancy loss)

Criteria for referral:	• All women with three or more consecutive pregnancy losses • All women with one or more second trimester pregnancy losses • All women with a history of pregnancy loss and an associated condition such as antiphospholipid syndrome, PCOS, chronic medical disorder • All women over 35 years old with two or more pregnancy losses
Information to be provided on referral:	• Details of full obstetric history (include pregnancy losses/ TOPs/ectopic pregnancies) • Whether any previous treatment to cervix (if so, please include date of last smear and result) • Relevant past medical/surgical history • Current regular medication

Recurrent pregnancy loss clinic

Patients with recurrent pregnancy loss will be referred to their local HSC Trust's gynaecology service. It is recommended that patients be seen within a specific clinic with a lead consultant. This may be exclusively for patients with recurrent pregnancy loss or also include other patients. The important aspect is that it will be the same team of healthcare professionals looking after this group of patients.

There should be a discussion to identify each individual's preference of language to be used in any discussions, eg recurrent pregnancy loss, recurrent miscarriage or alternative terminology.

The location of the clinic should be considered by each Trust, with attempts made to separate from maternity services where possible.

It is important to note that the recommended investigation and management options are available in Northern Ireland. Whilst recurrent pregnancy loss is a growing area of research, experimental tests or treatments are not recommended outside of research settings. Suitable research options available elsewhere should be considered where appropriate. Details regarding research and extra-contractual referrals (ECRs) to services outside Northern Ireland) are discussed in the next section (page 14).

Information and support

- Provide regional information leaflet.
- Highlight the sources of emotional support within the Trust and voluntary organisations.
- Explore which sources of support may be best for the woman/couple using the regional summary.

History and assessment

- Collect information on medical and obstetric history and relevant lifestyle factors for both members of the affected couple.

Investigations

Details obtained during history and assessment should be used to tailor investigations performed.

- For women with a history of three consecutive pregnancy losses (or following two pregnancy losses where a diagnosis of recurrent pregnancy loss is being

considered), perform antiphospholipid screen at least six weeks following pregnancy loss (Lupus anticoagulant + Anticardiolipin antibodies)
    - If the first result is positive, then repeat the test 12 weeks later
    - If second test is indicated, patients should be advised not to become pregnant before second blood sample has been taken at 12 weeks as this will affect interpretation

- Thyroid function tests, including thyroid peroxidase (TPO) antibodies. Women with abnormal thyroid-stimulating hormone (TSH) and thyroid peroxidase (TPO) antibodies should be followed up with thyroxine (T4) testing.

- Rubella IgG

- Assess uterine anatomy

- Additional investigations may be appropriate based on individual risk assessment (including medical and family history of individuals):

    - It is recommended that screening for hereditary thrombophilia is only undertaken in the context of research, or in those with additional risk factors for thrombophilia (such as a family history of hereditary thrombophilia or a history of venous thromboembolism).

    - A ‘day 2–5’ hormone profile (FSH, oestradiol, FSH/LH ratio) may be considered based on individual assessment. Such tests are not routinely recommended for all women.
    - Parental karyotyping may be considered based on individual assessment.

- Consider the following investigations for explanatory purposes, ie the results may identify an association or assist prognosis but will not influence management:

    - Genetics of pregnancy tissue

    - Antinuclear antibodies

- Each individual and/or couple should have a tailored investigation plan which is explained to them, including details about expected timeframes where known

Management – supportive care

- Supportive care should be tailored to each individual.
- Provide information and explanation about recurrent pregnancy loss, the challenge in identifying a cause, the lack of evidence-based treatments and the excellent prognosis for future pregnancy outcome without pharmacological intervention if offered supportive care alone in the setting of a dedicated early pregnancy assessment unit.
- Provide prognostic information based on recognised prognostic tools such as Lund, Brigham (Further information available in *Part E: Prognosis and Treatment* of *ESHRE Recurrent Pregnancy Loss Guidelines 2017, page 85*. Available at www.eshre.eu/Guidelines-and-Legal/Guidelines/Recurrent-pregnancy-loss.aspx).
- Advise women and couples regarding changes to lifestyle factors as relevant, including; smoking cessation, weight management, healthy eating and physical activity, reducing alcohol and drug consumption.
- Acknowledge the emotional impact of pregnancy loss and recurrent pregnancy loss in particular, for both partners. Highlight that support is available in different forms and locations to suit individual needs and preferences.
- Refer/signpost patient as required to Trust bereavement midwife and bereavement services, voluntary organisations, GP for further assessment as per the regional information resource and the patient's/couple's preferences (See Section 6 on page 15).
- Provide access and contact details of local early pregnancy clinic and advise of any specific arrangements for early review in next pregnancy (including ultrasound scanning arrangements).
- It is noted that women with a history of recurrent pregnancy loss may have a higher risk of complications in future pregnancies and therefore a tailored antenatal plan should be developed at antenatal booking appointments.[4]

[4] Bhattacharya S, Bhattacharya S. Effect of miscarriage on future pregnancies. Women's Health 2009: 5(1);5-8.

Management – specific issues

- Each individual/couple should have a tailored management plan.
- **Antiphospholipid syndrome** – if laboratory and clinical criteria are fulfilled, consider referral to local haematology service and discuss potential for treatment with low dose aspirin and heparin in next pregnancy.[5]
- **Thyroid conditions:**[5]
    - **Overt hypothyroidism** – Overt hypothyroidism arising before conception or during early gestation should be treated with levothyroxine in women with RPL. Refer to endocrinology as appropriate.
    - **Subclinical hypothyroidism** – There is conflicting evidence regarding treatment effect of levothyroxine for women with subclinical hypothyroidism and RPL. Treatment of women with subclinical hypothyroidism may reduce the risk of miscarriage, but the potential benefit of treatment should be balanced against the risks. Consider referral to endocrinology.

      Women with a history of RPL and subclinical hypothyroidism who subsequently become pregnant should have their TSH level checked in early gestation (7–9 weeks), and hypothyroidism should be treated with levothyroxine.
    - **Thyroid autoimmunity** – Women with a history of RPL and thyroid autoimmunity who subsequently become pregnant should have their TSH level checked in early gestation (7–9 weeks), and hypothyroidism should be treated with levothyroxine.
    - **Euthyroid women with thyroid antibodies** – There is insufficient evidence to support treatment with levothyroxine in euthyroid women with thyroid antibodies and RPL outside a clinical trial.
- **Genetic abnormalities** – All individuals and couples with an abnormal foetal or parental karyotype result should be offered genetic counselling and consider discussion of possible treatment options relevant to their individual situation.[6]
- **Hyperprolactinaemia** – Bromocriptine treatment may be considered.[6]
- Women with a history of second trimester losses and **suspected cervical weakness** should be offered serial cervical sonographic surveillance.[6]

[5] ESHRE Recurrent Pregnancy Loss Guidelines, 2017
[6] ESHRE Recurrent Pregnancy Loss Guidelines, 2017

- If women ask about multivitamin supplements advice should be given on formulations that are safe in pregnancy.[6]
- Treatment with progesterone may be considered for women with three or more pregnancy losses.[7] [8]

Onward referral and clinical trials

Extra-contractual referrals (ECRs)

- On occasion an ECR to a centre outside of Northern Ireland may be submitted for patients with exceptional clinical circumstances.
- An ECR would be expected to be a referral for specialist opinion and not to be a referral for treatments which are not commissioned locally, unless clinical exceptionality can be demonstrated.
- Regional discussion of cases including consideration of an ECR is encouraged.

Clinical trials

- Patients should be informed about clinical trials for which they may be eligible and additional information provided if the patient/couple are interested in pursuing assessment for eligibility.
- An ECR application can be submitted to request funding for travel costs for consideration of eligibility for a trial. However, once accepted the expectation is that any further costs associated with partaking will be met by the trial.

[7] Coomarasamy A, Devall AJ, Cheed V et al. A Randomised Trial of Progesterone in Women with Bleeding in Early Pregnancy. *The New England Journal of Medicine* 2019; 380: 1815-24.

[8] Haas DM,Hathaway TJ, Ramsey PS. Progestogen for preventing miscarriage in women with recurrent miscarriage of unclear etiology. *Cochrane Database of Systematic Reviews* 2018, Issue 10. Art. No.: CD003511. DOI: 10.1002/14651858.CD003511.pub4.

Section 6 – Emotional support

The importance of emotional support in recurrent pregnancy loss

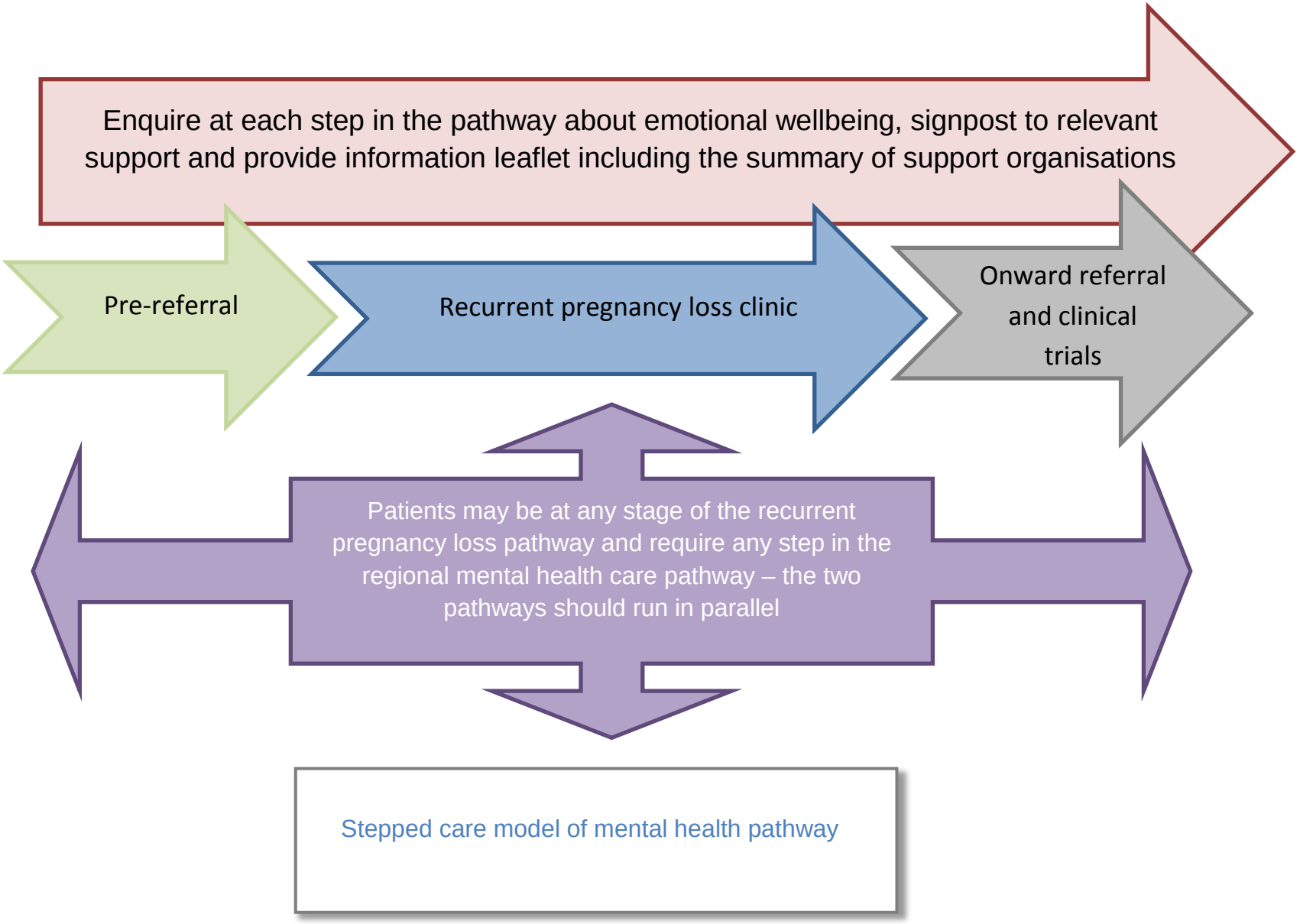
- Recurrent pregnancy loss has a significant emotional impact on women and their partners, as for many women and their partners pregnancy loss represents the loss of a baby and the hopes and plans invested in that child. [*ESHRE Recurrent Pregnancy Loss Guidelines 2017*, pg 17]
- Pregnancy loss is a significant negative life event [*ESHRE Recurrent Pregnancy Loss Guidelines 2017*, pg 18]
- Emotional impacts will vary for each individual, however such circumstances may result in psychological distress including anxiety, depression and trauma.
- It is imperative to recognise the emotional impact of recurrent pregnancy loss on women and their partner, and to acknowledge this at every step in the patient's care.
- The support provided for each individual needs to vary because every person reacts differently. Equally a patient may not require support until some time after initial engagement with services. It is therefore paramount that patients are provided with appropriate information to ensure they are aware that services do exist to support them.
- Options of emotional support available include:
    - Information provision about Recurrent Pregnancy Loss including the potential emotional and psychological impact
    - Bereavement Support Midwife/Childbirth and Loss Specialist Midwife support
    - Trusts Bereavement Services support
    - Trust chaplaincy support
    - Other Trust support, for example a local Trust support group if available
    - Information about support organisations including online support and local support groups

- Primary care support: provision of information, assessment and/or management as indicated; counselling may be available through GP surgery.

A model for providing emotional support for women and their partners throughout the regional pathway for recurrent pregnancy loss

- As represented in the schematic on page 18 the provision of emotional support should be delivered as a continuum throughout the care pathway rather than at a particular point or step.
- The model for providing emotional support to women and their partners has been represented overleaf in relation to the regional mental health pathway.

Schematic of emotional support



Overview of stepped care model of mental health pathway

Stepped Care Model - how services are organised

Principles of the approach to the provision of emotional support during the recurrent pregnancy loss pathway

- Emotional support services, whilst referred to within this document for those experiencing recurrent pregnancy losses, are also applicable to all those experiencing pregnancy loss.

- Trusts and community and voluntary services treating women or couples experiencing recurrent pregnancy loss should ensure that at all times the following are features of that care:
    - sensitivity to emotions of all affected
    - respect
    - empathy
    - clear and sensitive language
    - honesty
    - acknowledgement of loss.

- All women and couples should receive the regional information leaflet and the summary of sources of support at an early stage in the pathway. This will facilitate repeated discussion as appropriate.

- All women and couples should be asked about their emotional support needs at every clinic appointment.

- Emotional support should be tailored to each woman and couple.

- The first step for most women and couples will approximate to **Step 1 of the Regional Mental Health Pathway** – Self-directed help and health and wellbeing services, ie low impact on personal functioning.

- On further enquiry with the woman/couple and based on responses, the following options of support should be highlighted to the woman/couple supported by the summary of sources of support:
    - Bereavement services to include, where available, Bereavement Support Midwife/Childbirth and Pregnancy Loss Specialist Midwife
    - Health and Social Care Trust (HSCT) and Community and Voluntary Sector (CVS) resources, eg websites, online forums, support groups
    - Trust bereavement services (eg book of remembrance/services of remembrance)

- If women or their partner indicate that they are experiencing an impact on personal functioning partially or fully as a result of the emotional impact of recurrent pregnancy loss, encourage the woman and or her partner to seek assessment and help from GP services. This will allow:
    - an assessment by a GP as to the extent of the morbidity
    - further management within primary care as appropriate, ie **Step 2 of the Regional Mental Health Pathway**
    - onward referral to mental health services if indicated by moderate to high impact on personal functioning, ie **Step 3 of the Regional Mental Health Pathway**

- It is important to identify those affected by recurrent pregnancy loss and offer them additional emotional support in any future pregnancies. This should be identified as part of the management plan.

Pathway development

This pathway was developed in conjunction with healthcare professionals, HSC Trust management and service users. These stakeholders were brought together in a working group over a period of 18 months to develop this pathway, an information leaflet and a summary of available support organisations. In addition to the working group members listed below, service users also influenced the development of this pathway via a service user event and an online survey conducted at the end of 2018.

Name	Role	Organisation
Gary Benson	Consultant Haematologist	Belfast Health and Social Care Trust
Denise Boulter	Consultant midwife	Public Health Agency
Caroline Bryson	Consultant Obstetrics and Gynaecology	South Eastern Health and Social Care Trust
Catherine Coyle (Chair)	Public Health Consultant	Public Health Agency
Melissa Crockett	Bereavement Midwife	Western Health and Social Care Trust
Tracey Cruickshanks	GP	Northern Local Commissioning Group
Susanna Finnegan	Specialty Doctor, Obstetrics and Gynaecology	Southern Health and Social Care Trust
Barbara Gergett	Bereavement Midwife	Belfast Health and Social Care Trust
Bride Harkin	Assistant Director of Commissioning	Health and Social Care Board
David Hunter	Consultant Obstetrics and Gynaecology	Belfast Health and Social Care Trust
Sarah Meekin	Clinical Psychology Services Lead	Belfast Health and Social Care Trust
Kathy McCandless	Midwifery Sister	Belfast Health and Social Care Trust
Paul McCarthy	Service Manager, Gynaecology	Belfast Health and Social Care Trust
Catherine McEvoy		Service User
Christine McKee	Public Health Registrar	Public Health Agency
Jackie McNeill	Involvement Services Programme Manager	Patient Client Council
Catriona O'Kane	Consultant, Obstetrics and Gynaecology	Northern Health and Social Care Trust
Hilary Patterson	Bereavement Midwife	South Eastern Health and Social Care Trust
Jane Reilly	Personal and Public Involvement Officer	Patient Client Council
Sharon Watt	Early Pregnancy Clinic Manager	South Eastern Health and Social Care Trust