Sgrinio Cyn Geni Cymru
Antenatal Screening Wales

Screening Handbook for Midwives

8th Edition
June 2021

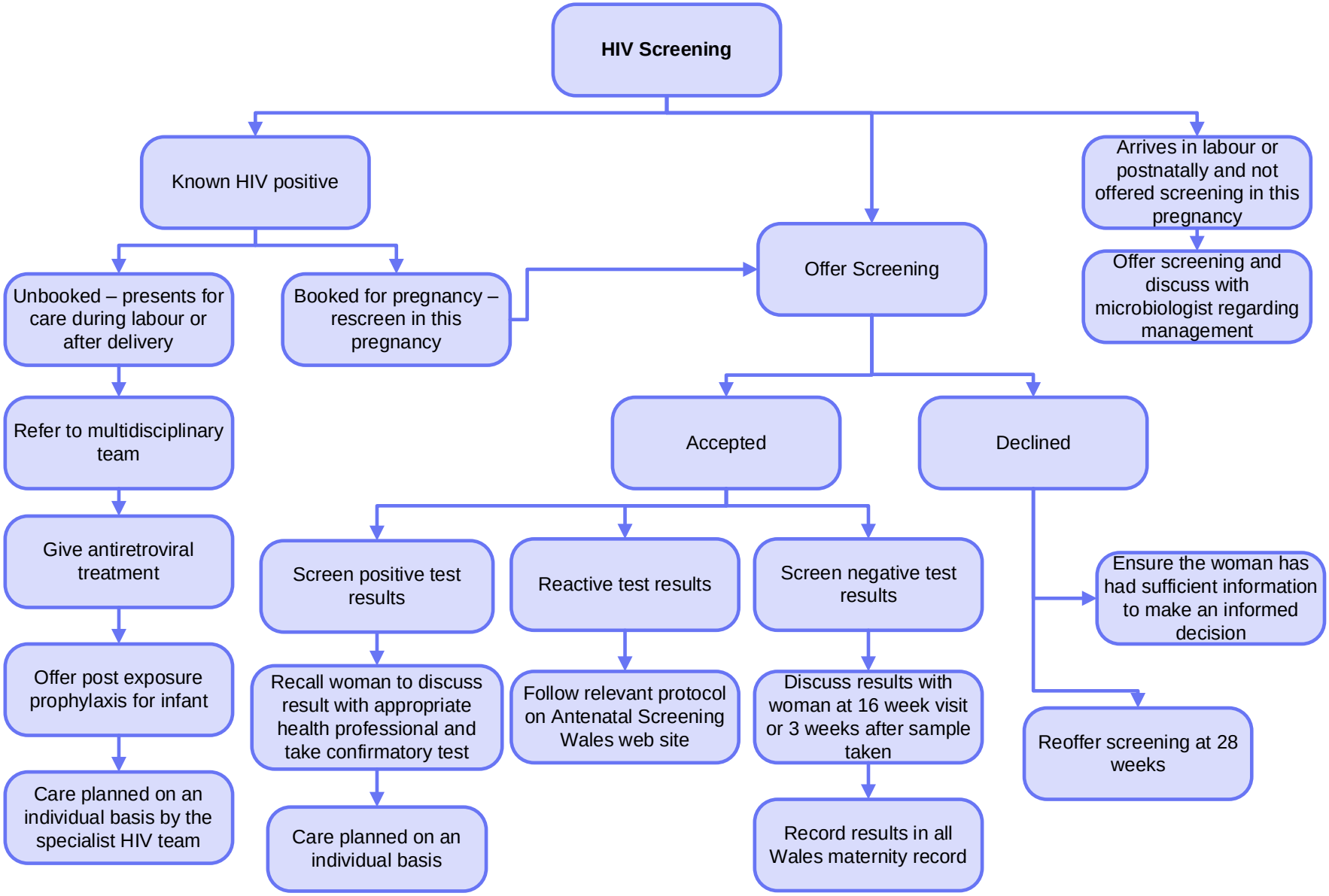
GIG CYMRU NHS WALES
Iechyd Cyhoeddus Cymru
Public Health Wales

Previous changes have been summarised in Appendix 1 (Page 22). New changes for this version of the handbook are summarised here.

Summary of Changes			
Date	Change	Page	Comments
June 2021	HIV (human immunodeficiency virus) Clinical Information	5	Update to HIV statistics
June 2021	Hepatitis B Clinical Information	7	Update to Hep B statistics
June 2021	Sickle Cell and Thalassaemia Clinical Information	13	Prevalence figure updated
June 2021	Down's syndrome, Edwards' syndrome and Patau's syndrome Screening Pathway and Clinical Information	14-15	Addition of the offer of NIPT in twins who have a higher chance result from the combined test

Contents

HIV Screening Pathway



HIV (human immunodeficiency virus) Clinical Information

Aim

Antenatal screening for HIV is to identify women who have an established HIV infection so that treatment and care can be offered to reduce vertical transmission of the virus from mother to baby. The identification and treatment of HIV also has considerable health benefits for the woman.

Clinical Information

HIV is a retrovirus that attacks and destroys T-lymphocytes, resulting in immune-suppression that eventually leads to acquired immune deficiency syndrome (AIDS). Vertical transmission of the virus from mother to fetus or baby can occur during pregnancy, at delivery or postnatally through breastfeeding. Two forms of the virus have been identified: HIV-1 and HIV-2. The commonest and most virulent form is HIV-1.

HIV Infection and Pregnancy

- Infants and young children who acquire HIV have an exceptionally high risk of morbidity and mortality, and half will die before their second birthday if they do not receive treatment.
- Without intervention vertical transmission is 15-25%. Intrauterine infection is extremely rare but the baby can be infected during the birth process.
- With correct treatment the risk of vertical transmission is 0.28%.

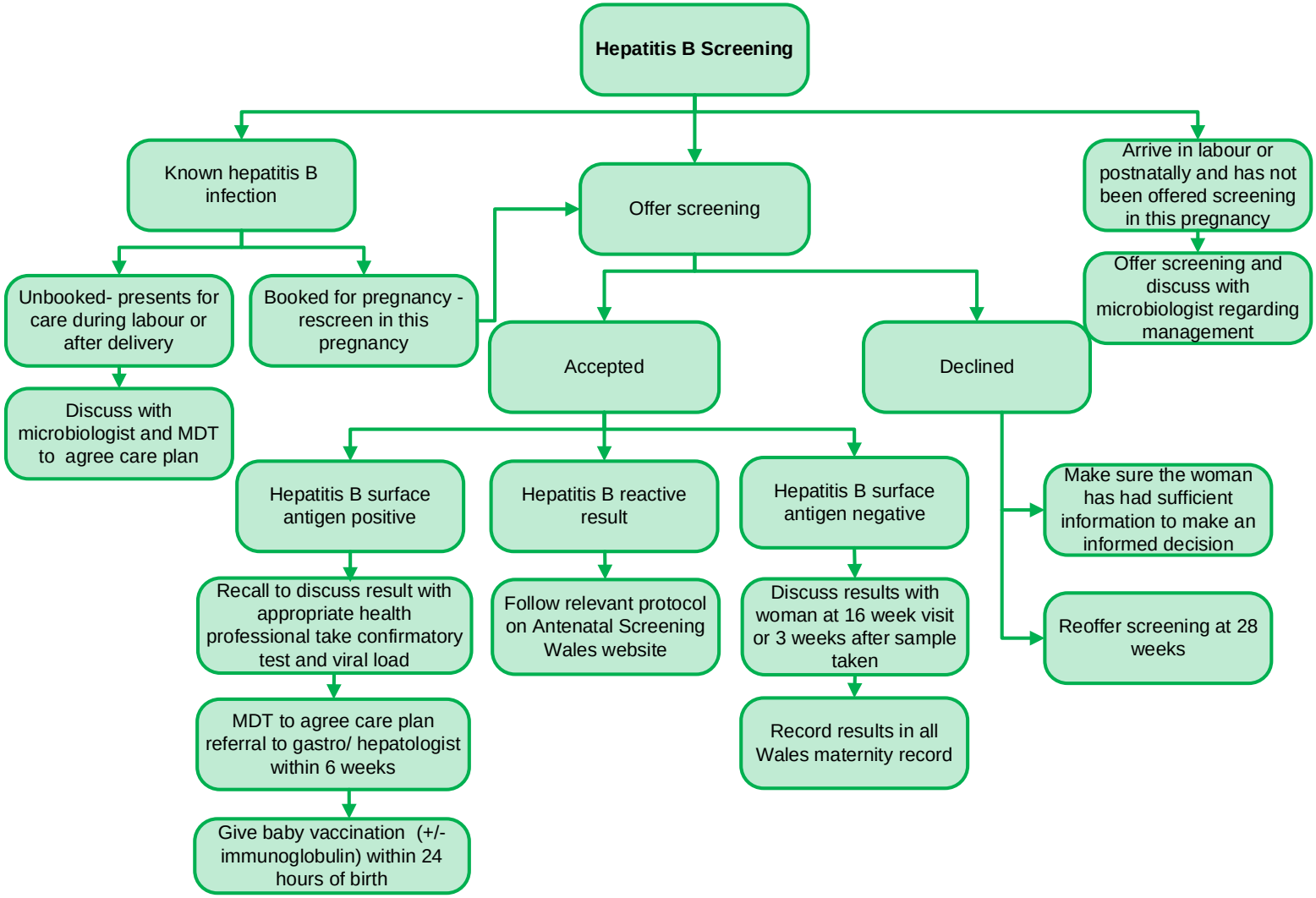
Global Incidence and Prevalence

- Globally around 38.0 million people were living with HIV in 2019.
- Vertical transmission accounts for 9% of new infections of HIV globally.
- In 2019 an estimated 150 000 children were newly infected with HIV, and an estimated 1.8 million children were living with HIV globally. Globally there are 26.0 million people accessing antiretroviral therapy.

UK/ Wales

- There are around 35,000 women living with HIV in the UK and around 1200 become pregnant each year
- Over 99% of births are to women on antiretroviral therapy (ART)
- 70% of births are to women who were taking ART at conception
- 88% were aware of their diagnosis before becoming pregnant
- 93% have undetectable virus when they deliver
- Vertical transmission of HIV was diagnosed in 118 children born in the UK between 2006 and 2013 (67 were born to mothers undiagnosed during pregnancy).
- Between 1st April 2015 - 31st March 2016 there were just 4 confirmed vertical transmissions among 1,438 babies born to diagnosed women living with HIV, corresponding to a rate of 0.28%.

Hepatitis B Screening Pathway



Hepatitis B Clinical Information

Aim

Antenatal screening for hepatitis B is to enable the identification of women who are infected with hepatitis B whose infants will be at significant risk of contracting hepatitis B at or around the time of delivery. This will enable the offer of post-exposure prophylaxis to the neonate.

Hepatitis B is an infectious disease of the liver caused by the hepatitis B virus and can be detected in blood, saliva and semen and transmitted:

- vertically from mother to baby
- through contact with contaminated blood
- through sexual contact.

Possible Outcome from a Hepatitis B Infection

- Recovery and immunity.
- Persistently infected or chronic carrier state. Between 20-25% percent of individuals with chronic hepatitis B infection have progressive liver disease, leading to cirrhosis in some patients.
- Fulminant hepatitis (less than1% of symptomatic cases).

Neonatal Implications

- Vertical transmission (mother to infant) of infection occurs in ninety percent of pregnancies where the mother is hepatitis B e antigen positive and in about ten percent of surface antigen positive, e antigen negative mothers.
- Most (>90%) of infected infants become chronic carriers.
- The risk of vertical transmission can be reduced by ninety percent by vaccinating the infant appropriately.

Prevalence

Hepatitis B is endemic worldwide, apart from isolated communities, with very high carriage rates (up to 20%) particularly in South and East Asia, but also in Southern Europe, Central and South America, Africa and Eastern Europe.

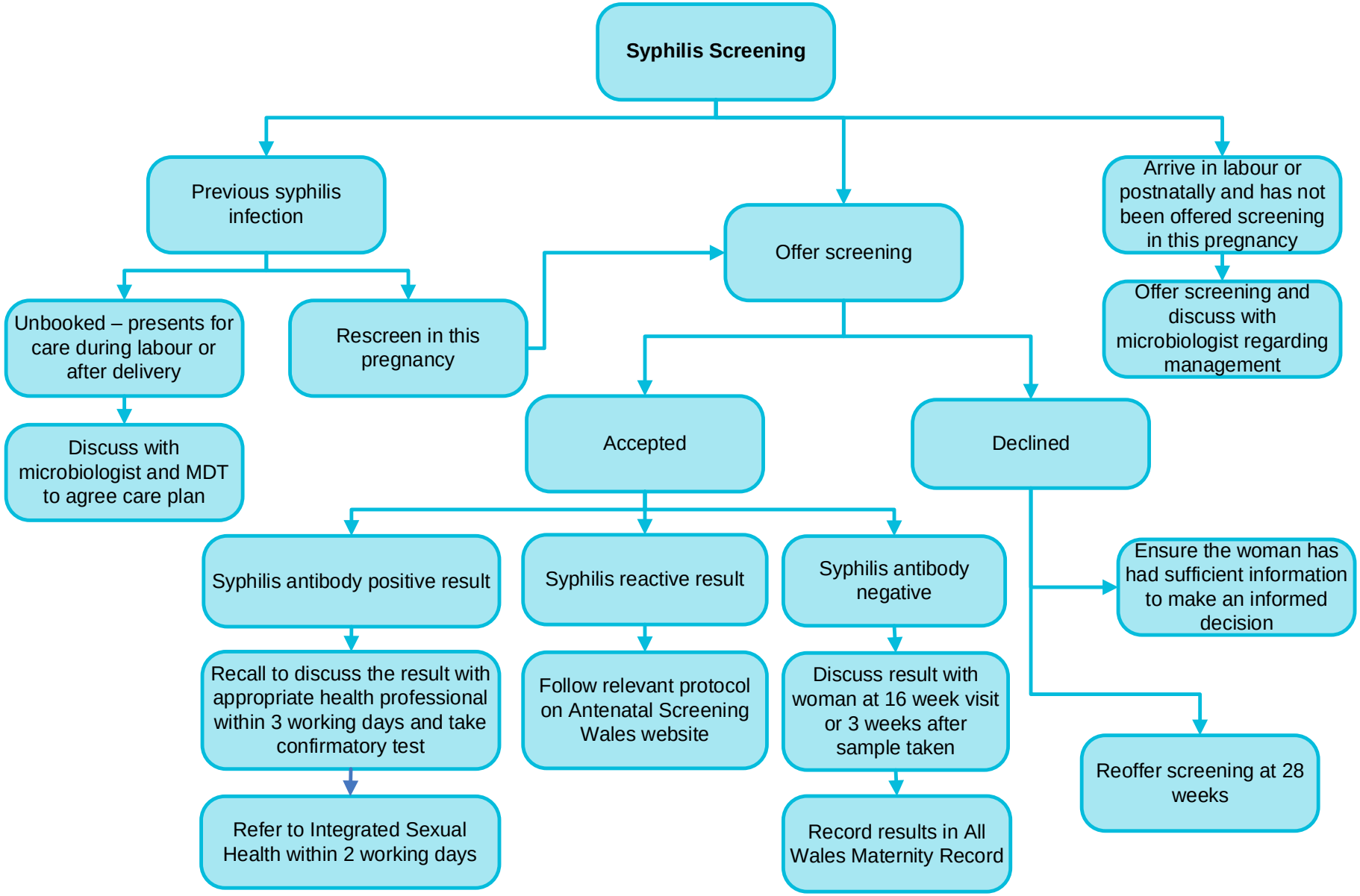
Worldwide, there are an estimated 257 million chronically infected persons.

UK/ Wales Incidence in Pregnant Women

This varies across ethnic groups and is higher from women born in countries where disease is endemic (e.g. 67% of carriers are women born in Africa, China or South Asia) but overall the incidence of hepatitis B infection in pregnant women in the UK is 0.15% (1 - 2 per 1000 women).

In 2018 there were 55 babies born to mothers chronically infected with hepatitis B (hepatitis b surface antigen (HBsAg) positive), one less than in 2017.

Syphilis Screening Pathway



Syphilis Clinical Information

Aim

Antenatal screening for syphilis is to identify women who have syphilis in early pregnancy and offer appropriate treatment to substantially reduce the risks of the fetus contracting congenital syphilis. The identification and treatment of this communicable disease also has potential health benefits for the mother.

Syphilis results from infection by the spirochete bacterium, treponema pallidum. Humans are the only host, and transmission can occur through sexual contact (adult syphilis) or following transmission across the placenta during pregnancy from an infected mother to her fetus (congenital syphilis).

Syphilis is passed from person to person through direct contact with a syphilis sore (chancre). Sores occur mainly on the external genitals, vagina, anus or in the rectum. They can also occur on the lips or in the mouth.

Stages and Symptoms of Maternal Infection and Chance of Transmission to Fetus

Stage of Infection	Maternal Symptoms	Risk of Vertical Transmission to Fetus in Untreated Mother
Primary syphilis	sore (chancre)	70% - 100%
Secondary syphilis	include disseminated disease including fever, malaise, maculopapular rash, hepatitis, meningitis, renal damage	Similar to primary syphilis
Latent syphilis	asymptomatic but moderately infectious	10% - 40%
Tertiary syphilis	2 to 40 years after infection many major symptoms including cardiovascular syphilis, neurosyphilis	Rare

Congenital Syphilis

Syphilis can be transmitted across the placenta at any stage of pregnancy and if untreated is associated with prematurity, low birth weight, non-immune hydrops and intrauterine death:

- Over 60% of fetus's with an infectious mother will be affected.

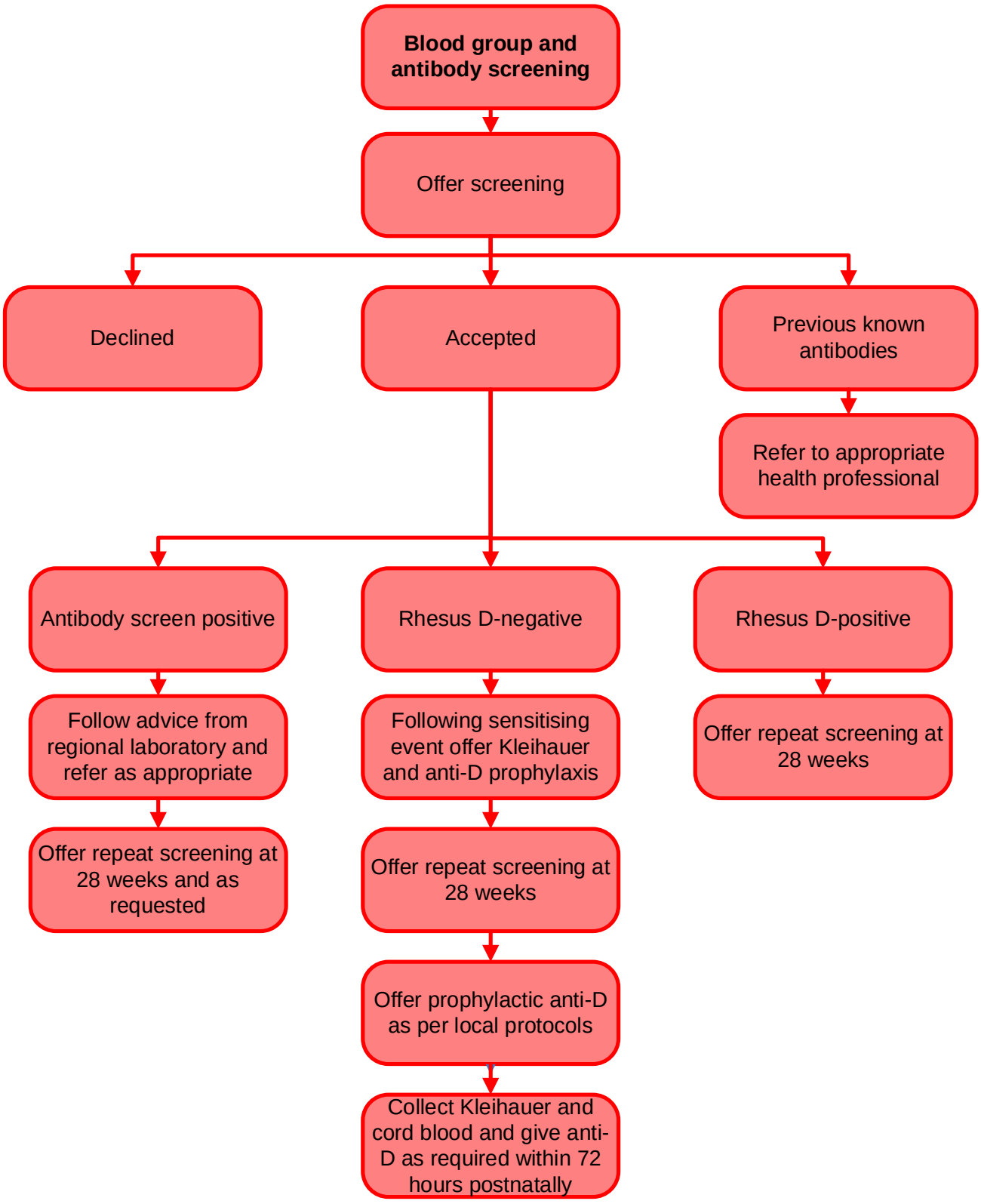
Incidence

- The total number of cases of infectious syphilis reported in Wales in recent years has been increasing. In 2016-2017 there were 98 reported cases, an 81% increase from the previous year. Most of this increase was with men-who-have-sex-with-men (MSM).
- There was also an increase noted in notifications of new antenatal diagnoses in Wales via the National Enhanced Surveillance of Infectious Syphilis Scheme (NESS) in 2017.

Screening Test Result

- A negative syphilis screening test result means the woman does not have syphilis infection at time of testing.
- Syphilis screening tests cannot always distinguish between syphilis and other non-communicable diseases, e.g. yaws, pinta, bejel or a previously treated syphilis infection. The laboratory result therefore needs expert interpretation by a consultant microbiologist/ virologist before the result is issued.

Blood Group and Antibody Screening Pathway



Blood Group and Antibodies Clinical Information

Aim

Antenatal screening for blood group and antibodies should be offered to all pregnant women in early pregnancy, irrespective of previous screening results as an integrated part of their antenatal care. If any antibodies are found, particularly anti D, anti Kell, or anti c, these may indicate a risk of haemolytic disease of the fetus and newborn (HDFN) and the antibodies can be monitored and appropriate obstetric management advised.

There are four main blood groups: group O, group A, group B and group AB. There is also another blood factor called the Rhesus (Rh) group and people have a blood group and Rh group, e.g. group O Rhesus D positive. RhD factor is the protein found in red cells in about 85% of people and its presence denotes a person is RhD positive and absence denotes the person is RhD negative.

Where the woman is RhD negative and the baby is RhD positive there is a possibility of maternal antibodies being produced (alloimmunisation) and passing from the maternal bloodstream into the fetus causing HDFN. Rhesus negative pregnant women should be offered prophylactic anti-D where there is a risk of alloimmunisation following a sensitising event and as part of normal antenatal care in the third trimester.

Inheritance Patterns

In genetic terms, the RhD positive allele is dominant (D) and the RhD negative allele (d) is recessive. Consequently, there are three possible genetic pairs for Rh alleles.

Genes	Blood Type
DD	RhD positive
Dd	RhD positive
dd	RhD negative

There are a number of possible combinations of RhD types in parents but the possibilities outlined here are only those that occur where the woman is RhD negative, because RhD positive women are not affected by this issue.

- If both of the parents are RhD negative, all babies will be RhD negative.
- If the woman is RhD negative and the biological father is RhD positive, the genetic (and potential clinical) outcomes are dependent upon whether the baby's biological father is homozygous RhD positive or heterozygous RhD positive.
- If the father is homozygous RhD positive (DD), all of his children will inherit one RhD positive allele from him (and one RhD negative allele from their mother) and all of the couple's babies will be heterozygous RhD positive.

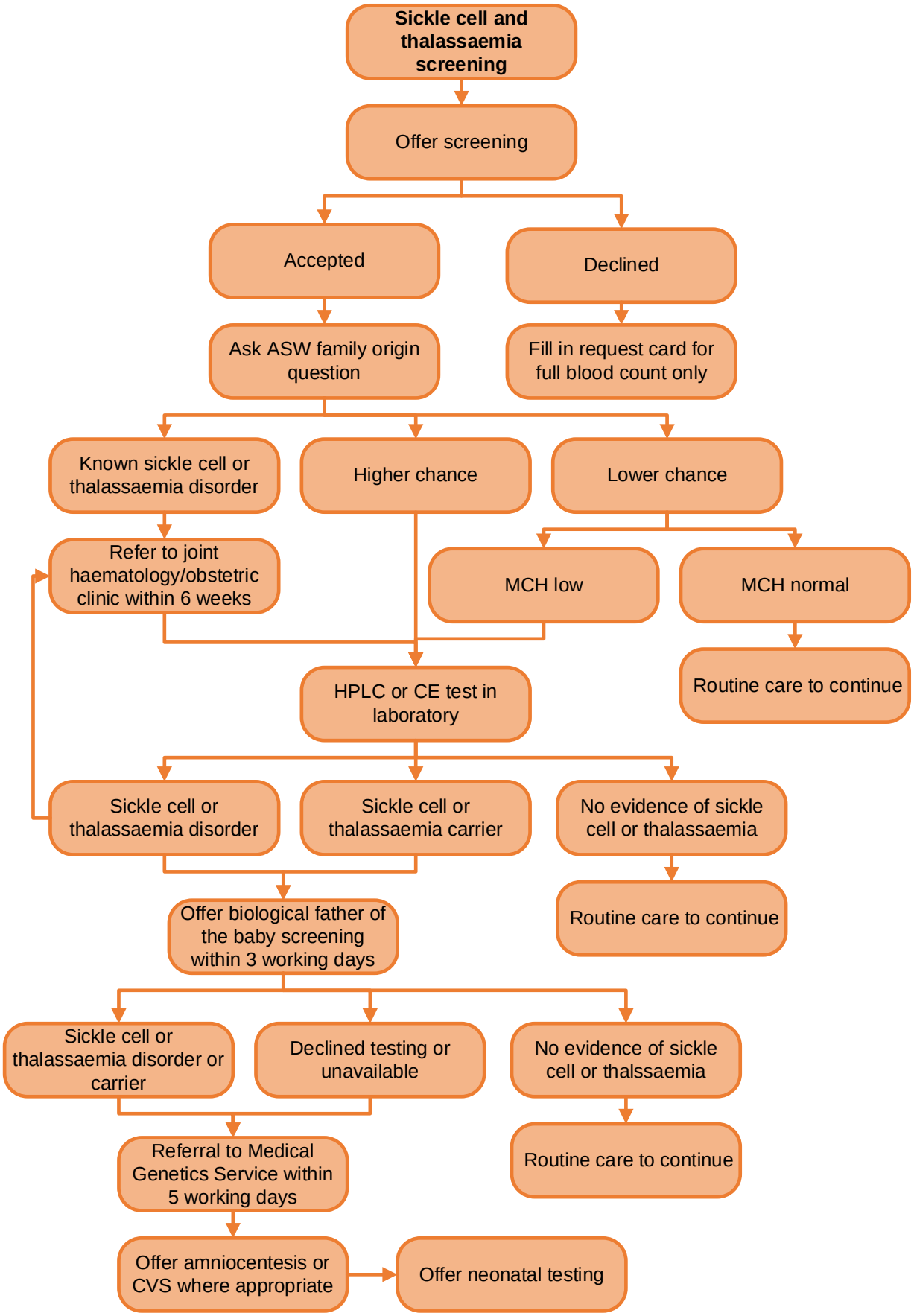
		Paternal	
		D	D
Maternal	d	Dd	Dd
	d	Dd	Dd

- If the father is heterozygous RhD positive (Dd), his children will have a 50% chance of inheriting an RhD positive allele from him and a 50% chance of inheriting an RhD negative allele from him. (Around 55% of RhD positive men are thought to be heterozygous).
- If the baby inherits the RhD positive allele from their father, they will be heterozygous RhD positive.
- If the baby inherits the RhD negative allele from their father and mother they will be RhD negative.

Incidence

The rate of alloimmunisation in the UK ranges between 0.17% and 0.28% and mortality caused by HDFN is 1.6/ 100 000 births.

Sickle Cell and Thalassaemia Screening Pathway



Sickle cell and Thalassaemia Clinical Information

Aim

Antenatal screening for sickle cell and thalassaemia is to identify women who have a high chance of having a fetus affected by a sickle cell disorder or thalassaemia major to enable decisions about whether to have invasive testing and continuing the pregnancy.

Sickle cell disorders

These are genetic conditions where an individual inherits sickle haemoglobin which affects the ability of the haemoglobin to function normally and results in chronic multi-system organ disease. The characteristics of sickle cell disease are:

- chronic haemolytic anaemia
- jaundice
- painful crisis
- organ damage where ‘sickling’ occurs
- susceptibility to infections
- strokes in childhood.

Thalassaemia

These are haemoglobin gene variants which affect the production of globin chains. They are classified according to the chain which is inefficiently produced, i.e. alpha or beta thalassaemia.

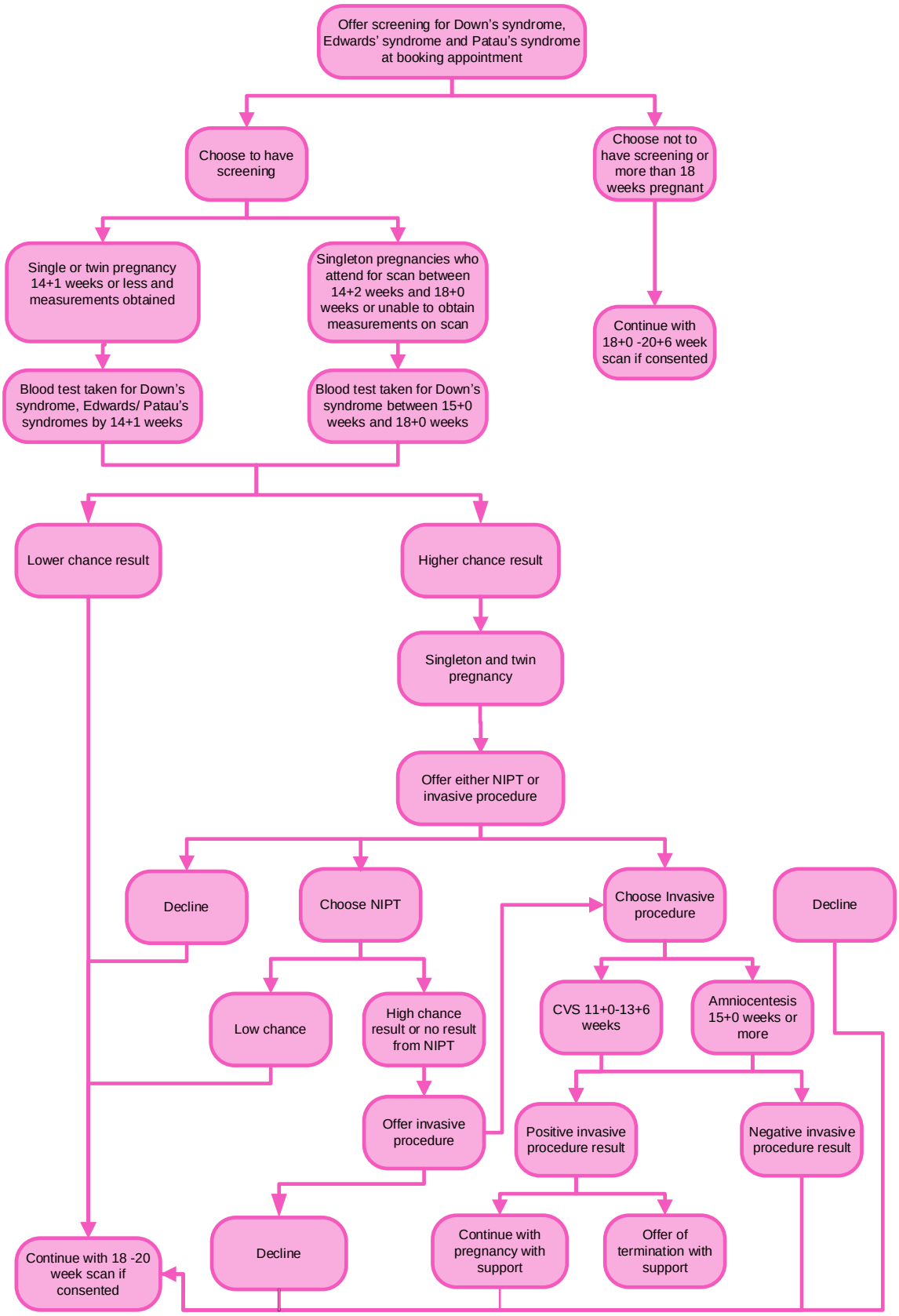
- Alpha thalassaemia is an inability to produce alpha globin chains. The fewer alpha globin genes the more serious the condition. Alpha thalassaemia major is incompatible with extra uterine life.
- Beta thalassaemia is an absence or reduced output of the beta globin chain synthesis and result in a reduced production of haemoglobin causing varying degrees of anaemia. Beta thalassaemia major can be life threatening requiring regular blood transfusion and iron chelation for survival. Beta thalassaemia major without treatment usually causes severe anaemia between the age of three and eighteen months and typically children do not live beyond early childhood.

Prevalence

Wales has a low prevalence of sickle cell disorders and thalassaemia major with approximately 20 pregnancies a year where, due to the mother and father’s result, the baby was predicted to be 'at risk' of having either sickle cell disorder or thalassaemia major.

Down's Syndrome, Edwards' Syndrome and Patau's Syndrome Screening Pathway

Note: At all stages in the pathway women should be offered appropriate counselling and support



Down's Syndrome, Edwards' Syndrome and Patau's Syndrome Clinical Information

Aim

Antenatal screening for Down's syndrome, Edwards' syndrome and Patau's syndrome offers women the choice to identify whether they have an increased chance of having a baby with one of these conditions to enable them to decide whether to have further testing and, if necessary, make choices about continuing the pregnancy.

This involves:

- The offer of screening in the first trimester for Down's syndrome, Edwards' syndrome and Patau's syndrome using the combined test in singleton or twin pregnancies.
- The offer of a quadruple test for Down's syndrome for singleton pregnancies only, if too late for the combined test, or unable to get the required ultrasound measurements.

If the woman has a family member with Down's syndrome, Edwards' syndrome or Patau's syndrome, enquiries should be made into whether the type is known, as a familial translocation will increase the chance of inheriting Down's syndrome, Edwards' syndrome and Patau's syndrome. Referral to the All Wales Medical Genomics Service may be advised. Parental karyotyping or NIPT may be offered through the All Wales Medical Genomics Service

For women with a higher chance result from the combined or quadruple test, the choices are:

- No further testing
- Non-invasive prenatal testing (NIPT), or

Invasive testing- chorionic villus sampling (CVS) or amniocentesis

Down's syndrome

All people with Down's syndrome will have a learning disability. This means they may be delayed in their development and take longer to learn new things. There is a greater understanding these days of how children with Down's syndrome learn, and help is provided in education settings. Around 8 out of 10 (80%) of children with Down`s syndrome will go to mainstream primary schools, although individuals vary greatly in how they develop and will have different health and social needs. The antenatal tests cannot tell what the health and support needs of the baby may be.

Some family stories on living with Down's syndrome can be viewed here

There are support organisations available for pregnant women and for families who have a child with Down's syndrome. These include the Down's Syndrome Association (DSA). Helpline 0333 12 12 300.

Website: www.downs-syndrome.org.uk

Children and adults with Down's syndrome

In Wales 9 out of 10 (90%) children with Down's syndrome live past their 5th birthday. For babies without serious health challenges survival is similar to that of other children, and most people with Down's syndrome will live into their 60s. Most children and adults who have Down's syndrome lead healthy and fulfilled lives and are included in their community. Most say they enjoy their lives and relationships. Many adults are capable of work and live in their own accommodation, with support.

Health Conditions Associated with Down's syndrome

- In Wales about 6 out of 10 (60%) children with Down's syndrome will have a heart condition, and around 1 out of 3 (30%) will need an operation.
- Most children with Down's syndrome will have some vision impairment that will need monitoring or treatment. More serious sight impairment is less common, for example, 1 out of 250 (0.4%) children with Down's syndrome are born with cataracts.
- Around 6 out of 10 (60%) children with Down's syndrome will have some hearing loss which may cause challenges with speech and language.
- Infections of the ears, nose and throat are more likely.
- Leukaemia is more common in children with Down's syndrome and for most this will not cause any health conditions. 1 out of 200 (0.5%) children with Down's syndrome will need treatment for leukaemia. Following treatment, most children with leukaemia will recover with no related health issues.

Babies and children with Down's syndrome will be under the care of a specialist medical team who will be aware of the increased chances of these medical conditions and will do tests to look for them. Many of these conditions can be treated.

Incidence of Down's syndrome

In Wales, Down's syndrome occurs once in every 415 pregnancies with the incidence increasing with increasing maternal age.

Edwards' syndrome and Patau's syndrome

Most babies with Edwards' syndrome or Patau's syndrome will die before they are born or shortly after birth. Of the babies who survive, around 13% will live for more than a year. Some babies may survive to adulthood but this is rare.

Babies with Edwards' syndrome and Patau's syndrome have a range of specific challenges. All babies will have developmental delay and lifelong learning disability. Children with these conditions will take longer than usual to develop or learn. They will need to attend special school.

You can get more information about Edwards' syndrome, Patau's syndrome and living with people with these conditions from SOFT UK at www.soft.org.uk

Some family stories on living with Edwards' syndrome can be viewed here

Health Conditions Associated with Edwards' syndrome and Patau's syndrome

Babies with Edwards' syndrome and Patau's syndrome will have a narrow but often serious range of conditions.

- Significant developmental delay (all babies).
- Heart conditions (many babies).
- Feeding difficulties (many babies).

- Medically fragile, especially with respiratory conditions (most babies, especially when small).
- Cleft lip and palate (some babies).
- Babies with Edwards' syndrome and Patau's syndrome are more prone to conditions such as urinary tract infections (UTIs).

At the other end of the scale, research shows, for example, that:

- babies and children make progress, however slowly
- older babies and children show some level of communication
- some will stand and walk with help, and
- parents consistently report a high quality of life for their babies and children, because they are involved in family activities.
- Babies and children with Edwards' syndrome and Patau's syndrome will be under the care of a specialist medical team who will be aware of the increased chances of the medical conditions and will do tests to look for them. Some of these conditions can be treated.

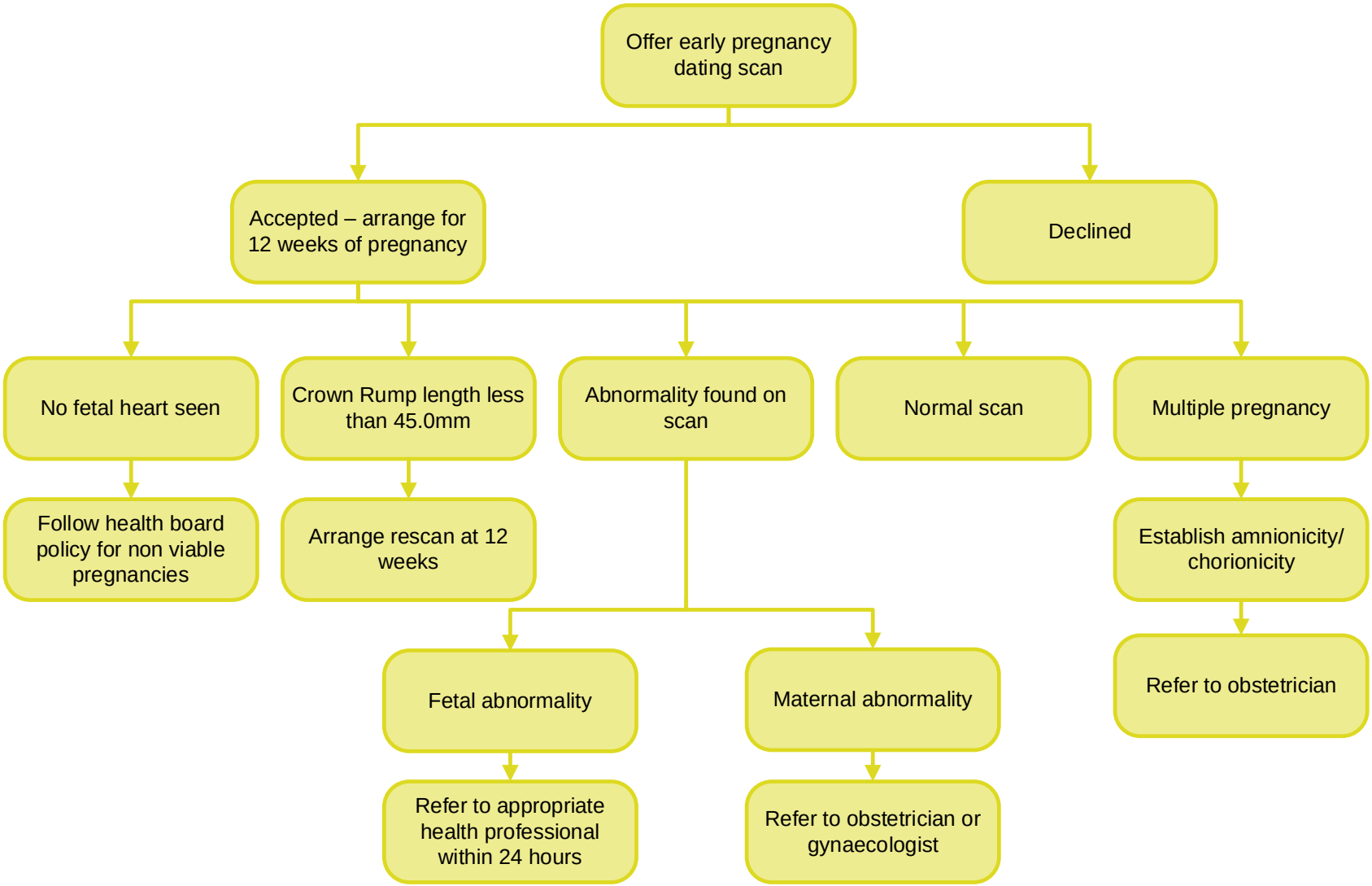
Incidence of Edwards' syndrome and Patau's syndrome

In Wales, Edwards' syndrome occurs once in every 1656 pregnancies and Patau's syndrome occurs once in every 4201 pregnancies with the incidence of both syndrome increasing with increasing maternal age.

Results

Between 97% and 98% of women who choose to have screening will receive a lower chance Down's syndrome, Edwards' syndrome and Patau's syndrome screening result. Around 2% to 3% of women will receive a higher chance result (result between 1 in 2 and 1 in 150) and will be offered either non-invasive prenatal testing (NIPT) or an invasive test.

Early Pregnancy Dating Scan Pathway



Early Pregnancy Dating Scan Clinical Information

Aim

The early pregnancy dating scan is offered to determine viability, the gestational age and to detect multiple pregnancies (fetal number and chorionicity/ amnionicity). Some serious conditions may be detected, but this is not the primary purpose of this scan. Measurements to determine the gestational age are required for the Down's syndrome, Edwards' syndrome and Patau's syndrome screening programme and also an additional measurement if the scan is before 14 weeks and 1 day of pregnancy (maximum CRL 84.0mm). Using ultrasound derived gestation reduces the need for post term induction of labour.

Information Obtained from the Early Pregnancy Dating Scan

- Can identify a non viable pregnancy, a fetal demise or an empty sac.
- Will confirm if the pregnancy is intra-uterine.
- May identify multiple pregnancies.
- Measurements obtained are used to calculate the correct gestation and provide an accurate estimated date of delivery (EDD).
- Provides the measurements for Down's syndrome, Edwards' syndrome and Patau's syndrome screening:

  Combined test

  - Crown Rump Length (CRL) 45.0mm to 84.0mm and
  - Nuchal Translucency (NT)

  Quadruple test

  - Head Circumference (HC) 88.0mm to 147.0mm.

Possible Conditions Detected

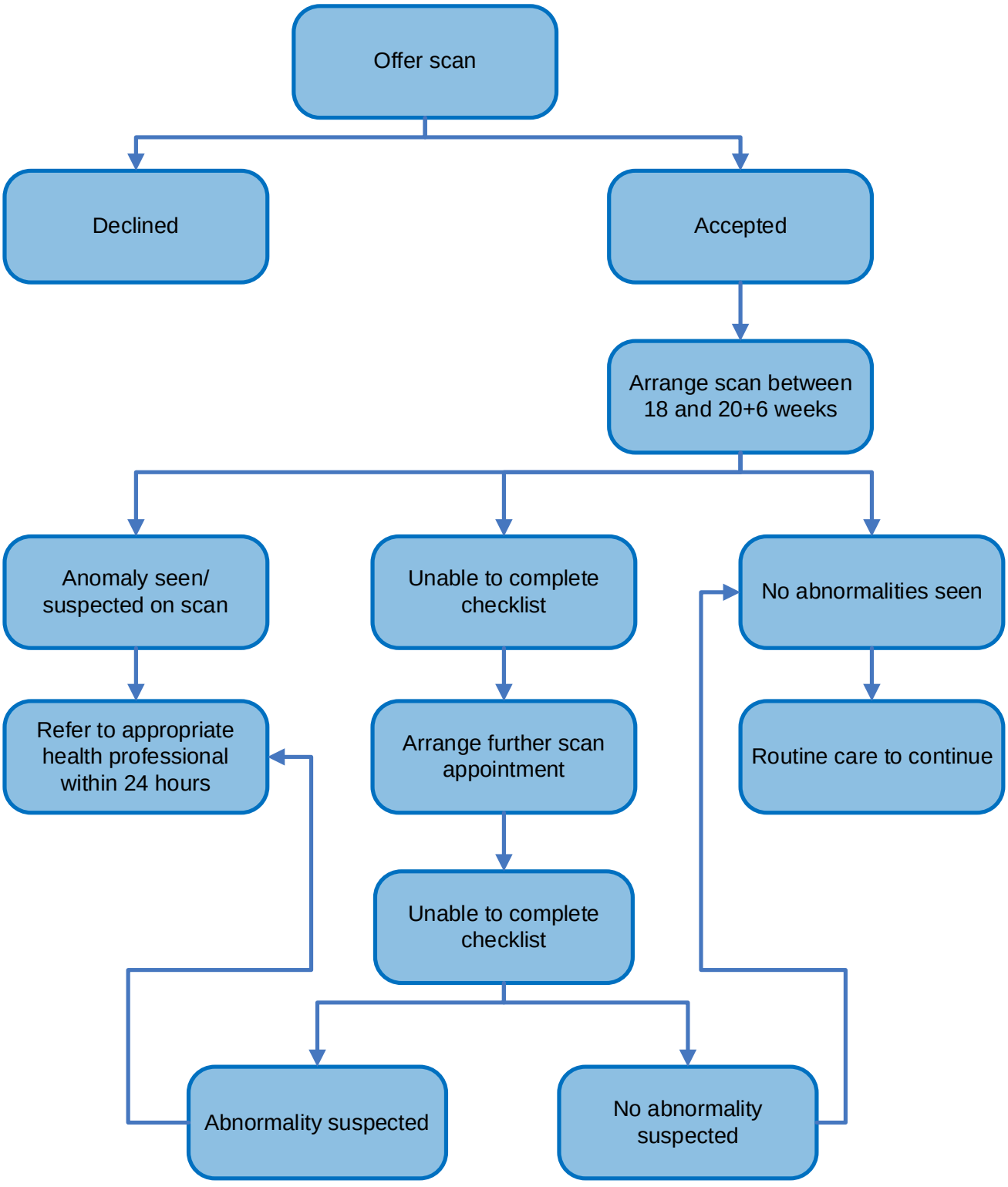
Some serious conditions may be detected:

- Anencephaly
- Enlarged Nuchal Translucency (3.5mm and above)
- Omphalocele
- Renal agenesis

Limitations of the Early Pregnancy Dating Scan

- Visualisation of the fetus will affect what can be seen on the scan. Some things that affect visualisation are:
  - Woman's body mass index
  - Position the fetus is lying
  - Uterine fibroids
  - Abdominal scarring
- Scans may give false reassurance as:
  - Some conditions may not become detectable until later in the pregnancy
  - Many conditions cannot be diagnosed by ultrasound scans
  - Fetuses with chromosomal changes cannot always be diagnosed by ultrasound.

Fetal Anomaly Ultrasound Scan Pathway



Fetal Anomaly Ultrasound Scan Clinical Information

Aim

The purpose of the fetal anomaly ultrasound scan is to detect significant structural fetal anomalies that are likely to have an adverse effect on the health of the mother and/ or baby and for which an effective intervention is available and warranted at 18 weeks and 0 days to 20 weeks and 6 days of pregnancy.

Information Obtained from the Fetal Anomaly Ultrasound Scan

At the fetal anomaly ultrasound scan the structures that are identified on the All Wales Fetal Anomaly Screening Scan Standard Checklist must all be visualised for the scan to be completed. The woman will be offered one further scan if not all structures are identified. If the check list **is not completed at the second visit** the woman **will not be rescanned** and this will need to be documented in the woman's All Wales Maternity Records.

Limitations of the Fetal Anomaly Ultrasound Scan

- Visualisation of the fetus will affect what can be seen on the scan. Some things that affect visualisation are:
    - Woman's body mass index
    - Position the fetus is lying
    - Uterine fibroids
    - Abdominal scarring
- Scans may give false reassurance as:
    - Some conditions may not become detectable until the third trimester
    - Fetuses with chromosomal changes cannot always be diagnosed by ultrasound.
    - Detection rates will be dependent on the conditions see chart below:

The condition	The chance of the condition being seen on an ultrasound anomaly scan at 18 to 20 weeks
Spina bifida (skin or bone not covering the spinal cord) Spina bifida is a fault in the development of the spine and spinal cord which leaves a gap in the spine. The spinal cord connects all parts of the body to the brain.	**90%**
Major heart condition, for example: **tetralogy of fallot** Tetralogy of fallot is a serious heart condition where the heart has not developed in the same way as a normal heart in the womb. This condition will need surgery usually in the first year of birth.	**73%**
Autism Autism cannot be picked up on scan as there is no structural abnormality. Autism is a lifelong developmental condition that affects how a person communicates with, and relates to, other people. It also affects how they make sense of the world around them.	**0%**

Appendix 1

Summary of Changes			
Date	Change	Page	Comments
Aug 2019	Front cover	1	Year/edition changed
Aug 2019	Contents page	3	Section titles changed
Aug 2019	HIV-Aim	5	Mother to child transmission changed to vertical transmission
Aug 2019	Global Incidence & Prevalence of HIV	5	Statistics updated
Aug 2019	HIV UK/Wales statistics	5	Statistics updated. As per National study of HIV in pregnancy and childhood
Aug 2019	Possible Outcome from a Hepatitis B infection	7	Percentages updated
Aug 2019	Prevalence of Hepatitis B	7	Figures updated
Aug 2019	UK/Wales Incidence of Hepatitis B in Pregnant Women	8	Figures updated
Aug 2019	Incidence of Syphilis	9	Figures updated
Aug 2019	Prevalence of Sickle cell and thalassaemia	13	Figures updated
Aug 2019	Down's syndrome, Edwards' syndrome, Patau's syndrome	15, 19	Terminology changed
Aug 2019	Characteristics of Down's syndrome	14 (5^{th} Edition 2018)	Section removed
Aug 2019	Associated health problems of Down's syndrome	15-16	Section amended
Jan 2021	Down's Syndrome, Edwards' Syndrome and Patau's Syndrome Clinical Information	15	Added Referral to All Wales Medical Genomics Service
Jan 2021	Associated health conditions of Down's syndrome	15-16	Section amended. Highest chance results amended from 1 in 5 to 1 in 2
Jan 2021	Edwards' syndrome and Patau's syndrome	17-18	Section amended
Jan 2021	Early Pregnancy Dating Scan Clinical Information	20	Section amended
Jan 2021	Fetal Anomaly Ultrasound Scan Clinical Information	21	Section amended