Healthcare Improvement Scotland | SIGN Evidence-based clinical guidelines

SIGN 156

Children and young people exposed prenatally to alcohol

A national clinical guideline

January 2019

NHS SCOTLAND

Key to evidence statements and recommendations

Levels of evidence

1^{++}	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1^{+}	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2^{++}	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2^{+}	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2^{-}	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion

Recommendations

Some recommendations can be made with more certainty than others. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the 'strength' of the recommendation).

The 'strength' of a recommendation takes into account the quality (level) of the evidence. Although higher-quality evidence is more likely to be associated with strong recommendations than lower-quality evidence, a particular level of quality does not automatically lead to a particular strength of recommendation.

Other factors that are taken into account when forming recommendations include: relevance to the NHS in Scotland; applicability of published evidence to the target population; consistency of the body of evidence, and the balance of benefits and harms of the options.

R For **'strong'** recommendations on interventions that **'should'** be used, the guideline development group is confident that, for the vast majority of people, the intervention (or interventions) will do more good than harm. For **'strong'** recommendations on interventions that **'should not'** be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more harm than good.

R For **'conditional'** recommendations on interventions that should be **'considered'**, the guideline development group is confident that the intervention will do more good than harm for most patients. The choice of intervention is therefore more likely to vary depending on a person's values and preferences, and so the healthcare professional should spend more time discussing the options with the patient.

Good-practice points

✓ Recommended best practice based on the clinical experience of the guideline development group.

NICE accredited
www.nice.org.uk/accreditation

NICE has accredited the process used by Scottish Intercollegiate Guidelines Network to produce clinical guidelines. The accreditation term is valid until 31 March 2020 and is applicable to guidance produced using the processes described in SIGN 50: a guideline developer's handbook, 2015 edition (https://www.sign.ac.uk/assets/sign50_2015.pdf). More information on accreditation can be viewed at www.nice.org.uk/accreditation

Healthcare Improvement Scotland (HIS) is committed to equality and diversity and assesses all its publications for likely impact on the six equality groups defined by age, disability, gender, race, religion/belief and sexual orientation.

SIGN guidelines are produced using a standard methodology that has been **equality impact assessed** to ensure that these equality aims are addressed in every guideline. This methodology is set out in the current version of SIGN 50, our guideline manual, which can be found at www.sign.ac.uk/sign-50.html. The EQIA assessment of the manual can be seen at www.sign.ac.uk/assets/sign50eqia.pdf. The full report in paper form and/or alternative format is available on request from the Healthcare Improvement Scotland Equality and Diversity Officer.

Every care is taken to ensure that this publication is correct in every detail at the time of publication. However, in the event of errors or omissions corrections will be published in the web version of this document, which is the definitive version at all times. This version can be found on our web site www.sign.ac.uk

Scottish Intercollegiate Guidelines Network

Children and young people exposed prenatally to alcohol

A national clinical guideline

January 2019

Scottish Intercollegiate Guidelines Network
Gyle Square, 1 South Gyle Crescent
Edinburgh EH12 9EB

www.sign.ac.uk

First published January 2019

ISBN 978-1-909103-67-2

Citation text

Scottish Intercollegiate Guidelines Network (SIGN).
Children and young people exposed prenatally to alcohol. Edinburgh: SIGN; 2019.
(SIGN publication no. 156). [January 2019]. Available from URL: http://www.sign.ac.uk

Contents

1	**Introduction**	**1**
1.1	The need for guidance	1
1.2	Remit of the document	3
1.3	Definitions and terminology	3
1.4	Origin of this guidance	8
1.5	Statement of intent	9
2	**Identification of children at risk of FASD**	**10**
2.1	Maternal alcohol history	10
3	**Identification and assessment of children and young people affected by prenatal alcohol exposure**	**15**
3.1	Diagnostic criteria	15
3.2	Medical assessment	17
3.3	Sentinel facial features	18
3.4	Neurodevelopmental assessment	19
3.5	Special considerations in the assessment of infants, children and young people	23
3.6	Special considerations in the assessment of adolescents and adults	23
3.7	The assessment team	25
4	**Management and follow up**	**26**
4.1	Developing a management plan	26
5	**Implementing the recommendations**	**29**
5.1	Implementation strategy	29
5.2	Resource implications	30
5.3	Auditing current practice	31
5.4	Supporting materials	32
6	**Development of the guidance**	**33**
6.1	Introduction	33
6.2	Methods used to develop this guidance	33
6.3	The guidance development group	34
6.4	Acknowledgements	35
6.5	Editorial group	36
7	**The evidence base**	**37**
7.1	Systematic literature review	37
7.2	Recommendations for research	38
7.3	Review and updating	38
Abbreviations		**39**
Annexes		**40**
References		**49**

1 Introduction

1.1 The need for guidance

In Scotland, alcohol consumption in women of childbearing age is common and is recognised as a significant public health issue. While surveys show a pattern of decline in self-reported alcohol consumption in Scotland, the majority of women still drink some alcohol. This proportion has decreased from 87% in 2003 to 82% in 2017 with the abstinence rate among women aged 16–34 years being 18%, falling to 13% in 35–44 year olds. Women in the least deprived areas are most likely to drink and those in most deprived areas are least likely to drink at all, but those living in deprivation who do drink are more likely to drink heavily.[1] Alcohol consumption in women of childbearing age reflects the consumption across the population and the whole population approach adopted by the Scottish Government, informed by World Health Organization guidance, is designed to reduce general consumption.[2]

Alcohol consumption in pregnancy has the potential to cause significant fetal damage.[3-5] While no woman wishes to intentionally harm her unborn child, this preventable cause of damage to the fetus continues to occur for a variety of reasons. In 1973, a cluster of birth defects resulting from prenatal alcohol exposure was first described as a clinical entity called fetal alcohol syndrome (FAS).[6] The syndrome has been characterised with specific diagnostic criteria which include evidence of prenatal alcohol exposure, evidence of structural or functional central nervous system (CNS) abnormalities, a specific pattern of three facial abnormalities and growth impairment (either prenatally, after birth or both).

As experience with children prenatally exposed to alcohol grew, other definitions were introduced in an attempt to provide better descriptions of a range of clinically diverse presentations. Such terms have included 'fetal alcohol effects' (FAE) which was used to describe children whose behaviour and cognitive function were assumed to have been affected by prenatal alcohol exposure (PAE) but whose growth and facial features, as well as global cognitive function, were normal or did not meet specific deficits. Further terms used in this situation include 'alcohol-related birth defects (ARBD), alcohol-related neurodevelopment disorder (ARND), partial fetal alcohol syndrome (pFAS)' and 'neurodevelopmental disorder – prenatal alcohol exposure (ND-PAE)' *(see section 1.3)*.

These wider patterns of effects, along with FAS, constitute the continuum of structural anomalies and neurocognitive and behavioural disabilities associated with prenatal exposure to alcohol which has been labelled fetal alcohol spectrum disorder (FASD).

It is estimated that PAE detrimentally affects 7.7 per 1,000 population worldwide (95% confidence interval (CI) 4.9 to 11.7) with prevalence of FASD in the UK rising to 32.4 per 1,000 (95% CI 20.0 to 49.0) making neurodevelopmental disorder related to PAE one of the commonest preventable causes of impairment.[7-9] In Scotland, many fewer children than predicted by international studies in similar populations are identified as having been affected by PAE, suggesting that we are failing to identify, and therefore adequately support, these children. Between 2010 and 2015 a passive surveillance study funded by the Chief Scientist's Office and Child and Maternal Health Division of Scottish Government, identified only 41 reported cases of FAS.[10] The study recorded diagnoses in children below the age of six years.

Based on clinical experience and published evidence, the reasons for this low incidence reporting include:

- failure to consider PAE as a possible cause of neurodevelopmental delay and/or behavioural difficulties[11]
- a lack of standardised diagnostic approach and training in its use[12]

- a lack of expertise and/or confidence in making the diagnosis[13]
- non-referral for appropriate assessment of children suspected of having significant PAE[11]
- reluctance to make the diagnosis, as this is perceived as unhelpful or more damaging than not making the diagnosis[11,14]
- additional substance abuse in mothers which overshadows the features of FASD.[15]

Currently, for many children PAE is not considered and/or acknowledged as a possible cause of their neurodevelopmental disorder, particularly those children with attention deficit and hyperkinetic disorders (ADHD) and autism spectrum disorder (ASD). This may contribute to an adverse outcome for the child, and, just as importantly, misses the opportunity to protect subsequent pregnancies. Information from New Zealand and Canada suggests that identification of FASD can be a potent motivator for mothers to abstain from alcohol in subsequent pregnancies.[16]

Although birth mothers are generally reticent in identifying themselves because of the stigma attached to the diagnosis, those who present their views publicly confirm that they would have been better able to manage their child's difficulties if they had understood the underlying brain damage that the child had sustained. Staff in the education sector may also be more supportive if they are aware of alcohol-related prenatal brain damage in a child.

With the development of better, more targeted, educational and social support programmes for these children and their families there is an urgent need to make the appropriate diagnosis at the earliest opportunity. Early diagnosis and intervention from birth and in the first years of life can make significant differences to the developmental progress of the affected child, and better understanding of the condition can help parents and professionals cope more appropriately with the child's difficulties.[17]

Poor awareness and lack of training in available standardised diagnostic and screening tools for healthcare staff may result in the failure to recognise these children. Additionally, alcohol use may be overshadowed by other substance use in mothers,[15] which may result in poor recording of alcohol use in the context of illicit substance use.

FASD is a lifelong condition. If difficulties are not anticipated and understood, educational opportunities will not be optimised and some affected children and young people will have poor educational attainment, develop mental health problems, have a higher risk of becoming addicted to alcohol and other drugs thus continuing the cycle.[18] These children and young people are also more likely to become involved in criminal activity,[18,19] and die prematurely from violence, accident or suicide.[20] Evidence suggests that receiving an accurate and early diagnosis allows parents and carers to best accommodate the child's environment to meet their needs and allows access to early interventions that may help to prevent secondary disabilities.[21,22]

1.1.1 Patient perspective

Patients may have different perspectives on healthcare processes and outcomes from those of healthcare professionals. The involvement of patients in developing guidance is therefore important to ensure that guidance reflect their needs and concerns and address issues that matter to them.

Common concerns raised by patient and carer groups and through research include:

- late diagnosis and difficulties in accessing services
- poor communication between different agencies involved in assessment and management
- accuracy of diagnosis
- the perceived lack of confidence among healthcare professionals in making a diagnosis of FASD
- coping with challenging behaviour or symptoms before a diagnosis is made
- lack of follow up of 'at risk' individuals exposed prenatally to alcohol but who have not yet displayed signs or symptoms of FASD.

1.2 Remit of the document

1.2.1 Overall objectives

This document provides recommendations based on best available evidence and consensus for the assessment and diagnosis of children and young people affected by PAE. It includes evidence-based recommendations on measurement of alcohol consumption in pregnancy and consensus-based recommendations on:

- identification of children at risk of FASD
- criteria for diagnosis and use of FASD as a descriptor
- medical assessment
- physical examination
- sentinel features
- neurodevelopmental assessment
- the multidisciplinary assessment team
- special considerations in the neurodevelopmental assessment
- management and follow up of children and young people affected by PAE.

Detailed treatment options for individuals affected by PAE are not included.

1.2.2 Comorbidities to consider when managing patients at risk of FASD

Common comorbidities and coexisting health issues which have been considered when reviewing the evidence for this guidance are:

- ADHD
- ASD
- mood disorders.

1.2.3 Target users

These recommendations will be of interest to individuals involved in the assessment and diagnosis of people at risk of FASD, including child development specialists, clinical and educational psychologists, clinical geneticists, general practitioners (GPs) and members of the primary care team, health visitors, members of the judicial system, midwives, neonatologists, nurses (eg school, learning disability and others), obstetricians, occupational therapists, paediatricians, physicians, physiotherapists, psychiatrists, social workers and speech and language therapists. It will also be of interest to people at risk of FASD, their parents and carers, adoptive and fostering services, supportive organisations in the voluntary sector and policy makers.

1.2.4 Patient version

A patient version is available from the Scottish Intercollegiate Guidelines Network (SIGN) website, www.sign.ac.uk

1.3 Definitions and terminology

Diagnosis is based on a thorough history and examination, however, because alcohol has broad and varied effects on brain development, there is no unique clinical pattern of impairment that is sensitive or specific enough to confirm the diagnosis of FASD. A number of diagnostic criteria exist *(see Table 1)*. Although these criteria share some common features, differences exist in terminology which may be confusing and be associated with lower confidence in reaching a valid diagnosis.

1.3.1 Existing diagnostic criteria

The Institute of Medicine (IOM) criteria for fetal alcohol syndrome were published in 1996 and provided the first systematic approach to delineating diagnostic categories for children adversely affected by prenatal alcohol exposure.[23] They were developed by a panel of experts, based on review of a large number of children with clinical abnormalities who were born in the USA following confirmed prenatal alcohol exposure. An update was published in 2005 which revised the diagnostic criteria for FAS and pFAS and defined alcohol-related birth defects (ARBD) and alcohol-related neurodevelopmental disorder (ARND).[24] A second update was published in 2016 which included cut-off points for measurements of growth and palpebral fissure length and stricter criteria for ARBD.[25]

The IOM diagnostic categories are:

- FAS,
- partial FAS,
- ARND, and
- ARBD.

The Fetal Alcohol Spectrum Disorders 4-digit diagnostic code was developed in 2000 to ensure objectivity and reproducibility in the diagnosis of FAS through specifying cut-off points (for example, for growth parameters and palpebral fissure length).[26] The concept of the 4-digit diagnostic code was introduced to give greater diagnostic scope for describing children adversely affected by alcohol but who did not fulfil the diagnostic criteria for FAS. This system introduces the use of a number of other terms to describe clinical patterns, including the terms 'static encephalopathy – alcohol exposed', and 'neurobehavioural disorder - alcohol exposed'.

There are a total of 256 diagnostic codes arranged into 22 diagnostic categories in the 4-digit diagnostic code system:

- FAS (alcohol exposed)
- FAS (alcohol exposure unknown)
- partial FAS (alcohol exposed)
- FAS phenocopy (no alcohol exposure)
- sentinel physical finding(s) / static encephalopathy (alcohol exposed)
- static encephalopathy (alcohol exposed)
- sentinel physical finding(s) / neurobehavioural disorder (alcohol exposed)
- neurobehavioral disorder (alcohol exposed)
- sentinel physical finding(s) (alcohol exposed)
- no sentinel physical findings or CNS abnormalities detected (alcohol exposed)
- sentinel physical finding(s) / static encephalopathy (alcohol exposure unknown)
- static encephalopathy (alcohol exposure unknown)
- sentinel physical finding(s) / neurobehavioural disorder (alcohol exposure unknown)
- neurobehavioural disorder (alcohol exposure unknown)
- sentinel physical finding(s) (alcohol exposure unknown)
- no sentinel physical findings or CNS abnormalities detected (alcohol exposure unknown)
- sentinel physical finding(s) / static encephalopathy (no alcohol exposure)
- static encephalopathy (no alcohol exposure)
- sentinel physical finding(s) / neurobehavioural disorder (no alcohol exposure)
- neurobehavioural disorder (no alcohol exposure)
- sentinel physical finding(s) (no alcohol exposure)
- no sentinel physical findings or CNS abnormalities detected (no alcohol exposure).

A committee of experts, mandated by US federal law, was convened by the Centers for Disease Control and Prevention (CDC) to update and refine the diagnostic criteria for FAS in 2004.[27] Only criteria for FAS were developed because there was deemed to be lack of evidence to support the development of reliable diagnostic criteria for the rest of the spectrum. The committee then introduced the term FASD as an umbrella term to encompass the full range of individuals along a broad continuum of clinical deficits related to PAE.

The first Canadian guideline for diagnosis of FASD, published in 2005, included elements of both the IOM criteria and the 4-digit diagnostic code and provided specific cut-off values for growth parameters.[28] The criteria for CNS involvement were more stringent than other classifications, requiring evidence of deficits in three or more CNS domains. An updated version of the guideline, published in 2016, was the first system to recommend the use of the term FASD as a diagnostic classification rather than a collective category.[29] It removed growth impairment as a diagnostic criterion and modified the domains of neurodevelopmental deficit required for diagnosis.

The Canadian diagnostic categories are:

- FASD with sentinel facial features
- FASD without sentinel facial features.

A further designation of 'at risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure' was introduced to describe individuals with confirmed PAE and some indication of neurodevelopmental concerns, who do not meet the criteria for either of the FASD diagnostic categories.

While FAS is a clinical diagnosis, reached through any of the systems noted above, ND-PAE is a new psychiatric diagnosis introduced in the Diagnostic and Statistical Manual of Mental Disorders fifth edition (DSM-5) classification in 2014.[30] It is included as an appendix representing a condition requiring further study, however, is also used as an example of 'other specified neurodevelopmental disorder', (code 315.8). The current International Classification of Diseases 10th revision (ICD-10) includes a diagnostic description for fetal alcohol syndrome. A further diagnosis of 'neurodevelopmental syndrome due to prenatal alcohol exposure', reserved for patients in whom no other neurodevelopmental disorder can be diagnosed, is anticipated with the implementation of the 11th revision in 2022.

A study assessed the consistency and differences between five diagnostic systems for FASD in 1,581 consecutively registered patients, ages 0 to 21, who applied for a multidisciplinary diagnostic evaluation at a university-based clinic specialising in the care of children with prenatal alcohol and drug exposure.[31] Despite overlapping diagnostic criteria, there was only fair to moderate agreement between diagnostic outcomes across the five systems, with different systems resulting in the proportion of participants who received any FASD-related diagnosis ranging from 4.74% to 59.58%. The authors noted that rather than representing a matter of degree, for example an individual receiving a diagnosis of pFAS in one system, and a diagnosis of FAS in another (based on the number of criteria required in each system) there were cases where an individual might be diagnosed with FAS in one system and receive no diagnosis in another. This lack of convergent validity was ascribed to a range of factors, including the fact that there is no gold standard for diagnosis against which to measure competing systems. In addition, there is a wide variety of measures and thresholds in meeting the neurodevelopmental diagnostic criteria and there is inconsistency among them. The choice of facial features across different diagnostic approaches have not, in general, been made using empirical evidence but rather rely on clinical judgement. The authors note that the concordance between systems is improved when diagnostic categories are collapsed into FASD versus no diagnosis. Such an approach is designed into the 2016 Canadian system.

A comparison of diagnostic criteria for FAS across different systems is contained in Table 1.

Table 1: Comparison of five international systems for diagnosis of FAS(D)

	IOM (1996)	Revised IOM (2005)	4-digit (2000)
Diagnostic term	FAS	FAS	22 terms
Prenatal alcohol exposure	Confirmed-excessive or unknown	Confirmed-excessive or unknown	Confirmed or unknown
Facial features	Characteristic pattern that includes features such as short PFL, flat upper lip, flattened philtrum, and flat midface.	2 or more of the following: • PFL <10th percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5	All 3 of the following at any age: • PFL < 3rd percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5
Neuro developmental impairment	At least 1 of the following: • Structural/ neurological: - Decreased cranial size at birth - Abnormal structure (eg microcephaly, partial/complete agenesis of the corpus callosum, cerebellar hypoplasia) - Neurological hard/ soft signs	At least 1 of the following: • Structural - OFC <10th percentile - Abnormal structure	At least 1 of the following: • Structural/ neurological: (eg OFC <3rd percentile, abnormal structure, seizure disorder, hard signs) • Severe dysfunction: (3 or more domains of function with impairment 2 or more SDs below the mean)
Growth impairment	At least 1 of the following: • Low birth weight • Low weight for height • Decelerating weight	Prenatal and/or postnatal height or weight • <10th percentile	Prenatal and/or postnatal height or weight • <10th percentile

CDC (2004)	Canadian (2005)	Canadian (2015)	
FAS	FAS	FASD with sentinel facial features	FASD without sentinel facial features
Confirmed or unknown	Confirmed or unknown	Confirmed or unknown	Confirmed
All 3 of the following at any age: • PFL <3rd percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5	All 3 of the following at any age: • PFL <3rd percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5	All 3 of the following at any age: • PFL <3rd percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5	<3 of the following: • PFL <3rd percentile • Smooth philtrum Rank 4 or 5 • Thin upper lip Rank 4 or 5
At least 1 of the following: • Structural/neurological: (eg OFC <10th percentile, abnormal structure, seizure disorder, hard/soft signs) • Dysfunction: - 3 or more domains of function with impairment 1 or more SDs below the mean - Global deficit (2 or more SDs below the mean)	At least 3 of the following domains with impairment: • Hard/soft signs, structure, cognition, communication academic achievement, memory, executive functioning, abstract reasoning, ADD, adaptive behaviour, social skills, or communication	At least 3 of the following domains with impairment: • motor skills • neuroanatomy/ neurophysiology • cognition • language • academic achievement • memory • attention • executive function, including impulse control and hyperactivity • affect regulation, and • adaptive behaviour, social skills or social communication	At least 3 of the following domains with impairment: • motor skills • neuroanatomy/ neurophysiology • cognition • language • academic achievement • memory • attention • executive function, including impulse control and hyperactivity • affect regulation, and • adaptive behaviour, social skills or social communication
Prenatal and/or postnatal height or weight • <10th percentile	At least 1 of the following: • Prenatal and/or postnatal height or weight <10th percentile • Weight-to-height ratio (<10th percentile)	N/A	N/A

1.3.2 Terminology

In addition to differences between the diagnostic criteria included in existing published systems *(see section 1.3.1)* there are also differences in terminology used to describe symptoms and impairments. In order to facilitate recognition of the adverse effects of PAE in Scotland and contribute to ongoing international research, the working group felt that using contemporary worldwide terminology would be beneficial. In adopting the most recent Canadian Guidelines, which recognise FASD with or without sentinel features as diagnostic categories, we believe that it is clinically and practically useful to define and identify these two groups of affected individuals.

We acknowledge that this terminology does not match the ICD-10 and DSM-5 classifications, in which only FAS (presence of sentinel facial features alongside developmental delay and typical behavioural characteristics – similar to the Canadian FASD with sentinel facial features diagnosis) and ND-PAE, respectively, are recognised as diagnostic categories. We intend to use the Canadian terminology 'FASD without sentinel features' (which describes cases with confirmed prenatal alcohol exposure and severe pervasive neurodevelopmental impairment in the context of fewer than three sentinel facial features) as a descriptor rather than a diagnostic term.

We also acknowledge that the way in which the Canadian guideline uses the term 'domain' to identify both anatomical structure, and individual areas of assessment of brain function is conceptually problematic. The term does, however, allow for easier identification of at least three differing areas of brain impairment; this is critical in attributing dysfunction to PAE, and is an internationally accepted term.

In this document we will denote 'domain' as an area of assessment.

1.4 Origin of this guidance

The topic of diagnosis of FAS and FASD was accepted by SIGN for development as an evidence-based clinical guideline. However, the systematic literature review conducted to inform this guideline identified insufficient relevant evidence of adequate quality to support the development of evidence-based recommendations (with the exception of the issue of screening for alcohol consumption during pregnancy). The literature review also identified the existence of a number of published consensus guidelines on the topic, and the guidance development group explored these in further detail to determine whether these could be used in Scotland. The group agreed that development of a new consensus guideline for Scotland without reference to existing guidance would not be practical or efficient and may increase the inconsistencies between different diagnostic systems used across the world *(see section 1.3.1)*. After assessment, the group concluded that adaptation of the revised Canadian guideline on diagnosis of FASD[29] offered the best balance of methodological quality and clinical topic coverage. Elements of the Australian guide to the diagnosis of FASD have also been incorporated.[32]

The multidisciplinary development group has derived this guidance, with permission, from the Canadian guideline developers by considering each recommendation from the source in detail and making minor revisions to align the guidance with practice in Scotland. This includes differences in the use of diagnostic criteria for behavioural conditions in the two countries. In Scotland, diagnoses are generally made on the basis of the classification developed by the World Health Organization (ICD-10), whereas DSM-5 is used in Canada. The rationale for these revisions is explained in the body of this guidance. Where the group felt specific advice was not required, recommendations have been excluded. The supporting text which underpins each recommendation is drawn mostly from the Canadian guideline with additional material and references added from the SIGN systematic review. The only new recommendations added are drawn from the evidence-based review of the literature on screening for alcohol use during pregnancy *(see section 2.1.3)*. Further details on the methods used to develop this guidance are contained in section 6.2.

1.4.1 Layout of the guidance

In order to maintain the integrity of the consensus process used by the Canadian guideline developers in the formulation of their recommendations, this guidance has preserved as much of the original recommendations as possible, and made only minor revisions to the wording to align these with the Scottish context. These revisions are fully described in the guidance and the original Canadian recommendations are listed in Annex 3. To allow the reader to understand the source of the information in this document, text which is taken from the Canadian guideline is reproduced within green boxes. Text generated by the Scottish development group does not appear in boxes (unless replacing or adding to Canadian text in which case it appears in a grey font). In section 2.1 a recommendation has been reproduced from the UK Chief Medical Officers' Low Risk Drinking Guidelines and is reproduced within a dark blue box for clarity.

1.5 Statement of intent

This guidance is based on the consensus developed by a clinical expert group and is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results.

The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at through a process of shared decision making with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guidance or any local guidelines derived from it should be documented in the patient's medical records at the time the relevant decision is taken.

1.5.1 Influence of financial and other interests

It has been recognised that financial interests in, or close working relationships with, pharmaceutical companies may have an influence on the interpretation of evidence from clinical studies.

It is not possible to completely eliminate any possible bias from this source, nor even to quantify the degree of bias with any certainty. SIGN requires that all those involved in the work of guideline development should declare all financial interests, whether direct or indirect, annually for as long as they are actively working with the organisation. By being explicit about the influences to which contributors are subjected, SIGN acknowledges the risk of bias and makes it possible for guideline users or reviewers to assess for themselves how likely it is that the conclusions and guideline recommendations are based on a biased interpretation of the evidence.

Signed copies of declaration of interests forms are retained by the SIGN Executive and a register of interests is available in the supporting material section for this guidance at www.sign.ac.uk

2 Identification of children at risk of FASD

The current consideration of FASD as a cause of neurodevelopmental dysfunction is very poor in Scotland. Identification of potentially-affected children depends on the clear recording of alcohol consumption in women of childbearing age, particularly those planning to become pregnant, or presenting in the antenatal period. Proactive routine recording of alcohol consumption during pregnancy and access to this information across key clinical and social stakeholders is important. This section looks at methods of recording alcohol intake and initiating referral for comprehensive assessment of effects caused by PAE.

2.1 Maternal alcohol history

A reliable and accurate maternal alcohol history is the best screening tool for identifying risk of FASD. It is therefore critical for service providers to effectively and appropriately determine alcohol use among all women of childbearing age. A variety of factors can impact a woman's consumption of alcohol during pregnancy,[33] including a prior history of alcohol consumption,[34,35] a family background of alcohol use,[23,36] a history of inpatient treatment for problematic alcohol and/or substance use and/or a history of mental health problems,[37,38] the previous birth of a child with FASD,[36,39] lack of contraception/unplanned pregnancy,[37] a history of physical/emotional/sexual abuse,[37] low income and/or limited access to health care.[34,37,38]

At the request of the UK Chief Medical Officers (CMOs), three groups of independent experts reviewed evidence from over 40 systematic reviews and meta-analyses; consulted with international experts and the Committee on Carcinogenicity on the effects of alcohol on a range of cancers and commissioned new modelling of the impact of alcohol consumption on morbidity and mortality, based on UK population data. In making their recommendations to the UK CMOs, the expert group took account of evidence of risks and benefits, but noted that studying the effects of low levels of alcohol on the fetus was difficult, not least because women will not know they are pregnant at the earliest stages. They noted that relevant good-quality studies were few, meaning that, despite little evidence of harm from low levels of drinking, it was not possible to say that such drinking carries no risks of harm to the fetus at all. It is plausible scientifically that alcohol, even at such low levels, could cause some harm. Based on evidence that risks of low birth weight, preterm birth, and being small for gestational age may all be increased in mothers drinking above 1–2 units/day during pregnancy and the need for clarity and simplicity in providing helpful advice for women and the uncertainties that exist about any completely safe level, the CMO guideline recommended a 'precautionary' approach that it is safest to avoid drinking any alcohol in pregnancy.[40]

CMO

The Chief Medical Officers' guideline is that:

- **if you are pregnant or think you could become pregnant, the safest approach is not to drink alcohol at all, to keep risks to your baby to a minimum**
- **drinking in pregnancy can lead to long-term harm to the baby, with the more you drink the greater the risk.**

The risk of harm to the baby is likely to be low if you have drunk only small amounts of alcohol before you knew you were pregnant or during pregnancy.

If you find out you are pregnant after you have drunk alcohol during early pregnancy, you should avoid further drinking. You should be aware that it is unlikely in most cases that your baby has been affected. If you are worried about alcohol use during pregnancy do talk to your doctor or midwife.

There is no known safe level of alcohol consumption during pregnancy. Even low to moderate levels of PAE can negatively impact a fetus and these adverse consequences can persist into adulthood.[41-44] A lack of access to accurate antenatal health records can be a significant barrier to diagnosis. It is critical for healthcare providers to discuss alcohol use during pregnancy, to document concerns and to ensure that appropriate supportive follow-up care is provided. Although information about quantity, frequency and pattern of alcohol consumption during pregnancy is important, it is difficult to determine for a number of reasons, including under-reporting.[45,46]

R **All pregnant and postpartum women should be screened for alcohol use with validated measurement tools by service providers who have received appropriate training in their use. All women should be advised not to consume alcohol in pregnancy; additionally those women drinking above the low-risk guideline for the general population should be offered early, brief interventions (ie counselling and/or other services).**

✓ Women identified as having a pattern of risky or harmful alcohol use should be offered an intervention appropriate to their needs. This could range from a single structured conversation about alcohol risk (a brief intervention) to intensive treatment including detoxification and relapse prevention work.

Rationale for revision

Canadian recommendations 1.1 and *1.3* have been amalgamated for impact and clarity. The revision brings the recommendation in line with Scottish Government drinking limits rather than the more vague "risk of heavy alcohol use".

2.1.1 Assessing likely prenatal alcohol exposure

As most of the published data relating to drinking alcohol during pregnancy are collected from mothers either prospectively or retrospectively, they may be inherently flawed. Studies have shown that women tend to under-report (or not report) their alcohol consumption during pregnancy.[47-49]

The presence of all three facial features has such high specificity to prenatal alcohol exposure and FASD that confirmation of alcohol exposure is not required when they are present. The presence of fewer than three facial features does not have the same degree of specificity and therefore requires other confirmation.

R **Confirmation of PAE requires documentation that the biological mother consumed alcohol during the index pregnancy based on:**

- **reliable clinical observation**
- **self report or reports by a reliable source**
- **medical records documenting positive blood alcohol concentrations, or**
- **alcohol treatment or other social, legal or medical problems related to drinking during the pregnancy.**

Rationale for revision

Canadian recommendation 2.2 noted that in the presence of all three facial sentinel features, confirmation of prenatal alcohol exposure was not required to make an FASD diagnosis. However, the development group felt that introduction of the sentinel facial features within the recommendation was not directly relevant to screening for alcohol use. Furthermore, in the absence of confirmed alcohol exposure, there are a number of possible genetic causes which may account for facial dysmorphology. We have therefore moved the reference to facial features to the supporting text and added a statement to the recommendation in section 3.1.1 that genetic causes should be considered (and excluded, where possible) before arriving at a diagnosis/descriptor of FASD.

2.1.2 Recording the pattern of alcohol consumption

Differences in gender, ethnicity, history and genetics[50-52] are some of the factors influencing or contributing to alcohol's effects, as is the timing, frequency and quantity of alcohol consumed. Although dose per occasion is likely more important than drinking frequency,[53] binge drinking does occur in all types of prenatal alcohol consuming women – low/light, moderate and heavy.

R **The number of type(s) of alcoholic beverages consumed (dose), the pattern of drinking and the frequency of drinking in pregnancy should all be documented.**

✓ This information should be routinely recorded by the midwife in antenatal notes and communicated to the GP and Health Visitor in Transfer of Care documentation. This will ensure that PAE information (confirmed/confirmed absent/unknown) will be more easily accessed and remain within the child's health records.

R **Sources for confirmed prenatal alcohol history must be reliable and devoid of any conflict of interest. Unsubstantiated information, lifestyle alone, other drug use or history of alcohol exposure in previous pregnancies cannot, in isolation, confirm alcohol consumption in the index pregnancy. However, co-occurring disorders, significant psychosocial stressors and prenatal exposure to other substances (eg smoking, licit or illicit drugs) in the index and previous pregnancies should still be recorded, based on the known interactions of these substances and their effects on pregnancy outcomes for both the mother and her offspring.**

Rationale for revision

Canadian recommendation 2.3 has been retained in full and clarified that the documentation should refer to alcohol consumption during pregnancy. *Canadian recommendation 2.4* has been retained in full.

2.1.3 Screening for prenatal alcohol exposure

While a number of systematic reviews and primary and pilot studies were identified by literature searching, following appraisal, only a few studies were considered by the group to answer this key question *(see Annex 1)* and be of adequate methodological quality. Three systematic reviews were identified that included evidence which addressed parts of the key question. The reviews were heterogeneous and addressed different research questions.

The first systematic review included studies involving brief screening questionnaires to identify drinking of alcohol in pregnancy.[54] All major screening tests were included. The findings showed that T-ACE, TWEAK and AUDIT-C could be helpful in screening for risky drinking, however, the authors recommended caution noting that further evaluations of questionnaires for prenatal alcohol consumption should be undertaken. (Evidence level 2++)

A further systematic review investigated the effectiveness of blood biomarkers.[55] Eight studies met the inclusion criteria and included a variety of blood biomarkers. Despite the included studies being rated as good methodological quality, none of the biomarkers had both high sensitivity and specificity compared with self report. There was some evidence that a combination of biomarkers, or combining biomarkers with self report, may increase accuracy. However, the blood biomarkers examined were of limited use in screening for low and moderate alcohol consumption in pregnancy compared with self report, although the authors stated that certain biomarkers such as carbohydrate deficient transferrin (CDT) and phosphatidylethanol (PEth) may complement self report and help improve the accuracy of diagnosis. (Evidence level 2++)

The third systematic review also explored the objective measures of biomarkers of prenatal alcohol exposure.[56] Eight biomarkers were assessed across 12 studies of heterogeneous populations, including women from particular high-risk groups. The authors concluded that the evidence reviewed was

insufficient to support the use of objective measures of prenatal alcohol exposure in practice. (Evidence level 2++)

There was some inconsistency between the two systematic reviews which assessed biomarkers in that one review cautiously suggested the use of certain measures such as CDT and PEth during pregnancy in complementary use, alongside women's self report,[55] while the other did not view biomarkers to have clear value in practice.[56] The latter review highlighted meconium and placental tissue as the objective measures with most promise, but this is only relevant to retrospective examination of levels of alcohol use once the pregnancy is over and therefore provides little opportunity to intervene when prevention of harm is still possible.

The development group also considered the relevance of this evidence to the Scottish population and the balance of benefits and harms of the proposed intervention. The group concluded that there are risks associated with not asking pregnant women about their alcohol use as there is then a missed opportunity to provide information about what is known about the risks of alcohol consumption in pregnancy and to support women with health behaviour change in this area. No evidence was identified to suggest that asking about alcohol history had a detrimental effect on attendance for care. There has been a national standard (formerly a Health Improvement, Efficiency, Access and Treatment (HEAT) target) on the delivery of alcohol brief interventions (ABIs) in antenatal settings since 2008[57] and therefore questions about alcohol have been routinely asked of pregnant women in Scotland by antenatal providers. Some group members did caution, however, that in their experience, adopting screening tools in isolation does not necessarily ensure that alcohol consumption in pregnancy is discussed effectively. The 'booking in' visit is one opportunity to ask questions sensitively about alcohol, as well as discussing other issues in the woman's life of relevance to her pregnancy,[58] such as paying due attention to potential risk factors such as high social class and experiences of violence and abuse. To enable health behaviour change, including reduction in alcohol consumption during pregnancy, supportive relationships between patients and caregivers are key.[59] (Evidence levels 2++, 2+ and 3)

The evidence highlights important additional issues for healthcare professionals and others concerned with the health and well-being of women of childbearing age and their children. For example, the likelihood that women drinking at higher and more problematic levels are least likely to accurately describe their alcohol use when asked has been reported.[60] Group members also expressed concern, based on their experience of implementing alcohol screening and ABIs in response to Scottish Government targets, that the validated screening tools did not contain language that was easily articulated in Scotland. At least one Scottish health board includes broad alcohol screening questions in the electronic maternity record rather than using a validated screening tool. Early identification and prompt intervention, based on the use of screening tools to support self-reported alcohol use during pregnancy, may benefit women and their families, including those affected by FASD. Recording an accurate alcohol history might, in turn, support a more thorough signposting process for additional support to obtain a diagnosis of FASD, which is a key issue for families. Nevertheless, group members were concerned that no evidence was identified which directly links a maternal history that has involved alcohol use to improved rates of diagnosis and better outcomes for a woman or her children. (Evidence level 2+)

R **Use of the T-ACE, TWEAK or AUDIT-C tools in screening women in the antenatal period for alcohol consumption should be considered.**

R **Associated use of particular biomarkers, such as CDT and Peth, alongside brief screening questionnaires, should be considered.**

A sample FASD assessment form, which includes sections for collection of maternal alcohol consumption in early pregnancy and standardised screening tools for alcohol exposure in pregnancy is available for download from the SIGN website.

2.1.4 Referral

A lack of knowledge and understanding of FASD among healthcare professionals means they often may not feel competent to carry out an assessment and make an appropriate diagnosis. Variation in knowledge and awareness poses a significant challenge to the implementation of a comprehensive and consistent approach to the management of FASD.[61]

Practitioners require to have a sound knowledge and understanding of the key principles of Scottish Government's practice models Getting It Right for Every Child (GIRFEC)[62] and Getting Our Priorities Right (GOPR)[63] when undertaking any assessment of need in relation to a child considered likely to be affected by maternal alcohol consumption.

R **Referral of individuals for consideration of PAE as a cause of possible neurodevelopmental disorder should be made sensitively and only when there is evidence of significant physical, developmental or behavioural concerns and probable PAE.**

Rationale for revision

In *Canadian recommendation 1.2*, referral was phrased to confirm a diagnosis of FASD only. In Scotland, the development group felt that referral should be for an assessment which may lead to a range of outcomes, which include the diagnosis of a neurodevelopmental disorder, diagnosis of FASD with sentinel facial features, descriptor of FASD without sentinel facial features or identification of other impairment not associated with any specific diagnosis. To avoid unmanageable increases in inappropriate referrals for any woman who has consumed significant amounts of alcohol during pregnancy, a referral should not be made in the absence of accompanying physical or developmental concerns in the child or young person. The development group also noted the potential for assessment or diagnosis to cause anxiety and stigma and emphasised that the process should be undertaken with sensitivity.

3 Identification and assessment of children and young people affected by prenatal alcohol exposure

Prenatal alcohol exposure should be actively considered as a possible underlying cause for neurodevelopmental delay, or an unexplained departure from a typical developmental profile. This section considers the process for assessment of those at risk of having been adversely affected by PAE and the criteria for application of the diagnosis/descriptor of FASD with or without sentinel features.

3.1 Diagnostic criteria

3.1.1 FASD

The term FASD was originally coined as an umbrella term to encompass a range of diagnoses (FAS, pFAS, FAE, ARND, ARBD) and the breadth of disabilities associated with PAE.[28] With the evolution of FASD-related language within different professions, it is critical to adopt standardised terminology wherever possible. Standard terminology and definitions are important for comparing data across different geographical settings.

R **A diagnosis of FASD with sentinel facial features* may be made if an individual meets the following criteria:**

- **simultaneous presentation of the three sentinel facial features (short palpebral fissures, smooth philtrum and thin upper lip); AND**
- **prenatal alcohol exposure confirmed or unknown; AND**
- **evidence of severe impairment in three or more of the identified neurodevelopmental areas of assessment or, in infants and young children, presence of microcephaly.**

R **A descriptor of FASD without sentinel facial features† may be used if an individual meets the following criteria:**

- **confirmation of prenatal alcohol exposure; AND**
- **evidence of severe impairment in three or more of the identified neurodevelopmental areas of assessment.**

For both diagnoses:

R

- **Contribution of genetic factors should be considered in all cases and referral may be indicated in atypical cases or where PAE is uncertain.**
- **Growth impairment and other birth defects and/or health issues should be documented if present.**
- **Hereditary, prenatal and postnatal factors that may influence developmental outcome should be recorded.**

* This has similarities to the diagnostic category FAS in ICD-10 and the diagnostic category ND-PAE in DSM-5

† There is no equivalent diagnostic category in ICD-10 or DSM-5

Rationale for revision

This recommendation is consistent with *Canadian recommendation 5.1*. "Severe" impairment has been added into this recommendation to make consistent with *Canadian recommendations 4.1* and *4.2*. Microcephaly (head circumference <2nd percentile for age) is either present or absent, so this is a simple

language clarification. Alcohol exposure is made consistent with Scottish Government recommendations on limits. Given the possible aetiological link between certain physical and neurodevelopmental impairments and genetic causes, the group felt it important that these are excluded before a diagnosis or descriptor of FASD is reached and have added a bullet point for consideration. The definition and use of the term 'neurodevelopmental domain' is now referred to as an area of assessment *(see section 1.3.2)*.

Standardised growth charts for UK boys and girls aged 0–4 years (©Department of Health 2009), and UK boys and girls aged 2–18 years (© Royal College of Paediatrics and Child Health 2012/13) which include WHO standards and UK birth and preterm data are available for download from the SIGN website.

R **The diagnostic/descriptive criteria for FASD are the same for adults as for younger individuals.**

Rationale for revision

Canadian recommendation 8.1 has been retained in full.

3.1.2 At risk for neurodevelopmental disorder and FASD

The designation 'at risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure' was created to describe individuals who have confirmed prenatal alcohol exposure and some indication of neurodevelopmental concerns, but who do not meet the criteria for either of the FASD categories. It is especially germane for young children. Research[64] and clinical observation suggest that some individuals who have been prenatally exposed to alcohol may develop normally at younger ages or show only mild deficits. Later, when reassessed, significant impairments become evident as they fail to develop the higher-level thinking skills that are the norm for their age. At the older ages a more comprehensive assessment can be conducted. The designation of 'at risk' when they are younger is important and may enable them to access services and supports, with the recommendation that a follow-up assessment in the future be done to confirm FASD or not. Postnatal factors that may influence developmental outcome (for example nutrition, stress or trauma) must always be considered and recorded.

R **The designation 'at risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure' should be given to individuals when:**

- **there is confirmation of prenatal alcohol exposure**
- **the CNS diagnostic/descriptive criteria for FASD are not met (see above)**
- **there is some indication of neurodevelopmental disorder in combination with a plausible explanation as to why the neurodevelopmental assessment results failed to meet the criteria for significant impairment (for example patient was too young; assessment was incomplete etc).**

In addition:

- **Growth impairment and other congenital anomalies should be documented if present.**
- **Hereditary, prenatal and postnatal factors that may influence developmental outcome should be recorded.**

Rationale for revision

The phrase from *Canadian recommendation 5.2.1* "the estimated dose at a level known to be associated with neurodevelopmental effects" which was used to describe a threshold for PAE has been removed to make consistent with the UK CMO advice for no safe level of alcohol consumption during pregnancy. A note has been added to reflect the possible outcome of assessment being a *descriptor* of FASD without sentinel facial features. The term 'birth defects' has been replaced with congenital anomalies.

R **The designation 'at risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure' may also be considered for individuals with all three sentinel facial features as described above who do not yet have documentation or evidence of abnormality in the requisite three or more neurodevelopmental area of assessment criteria or microcephaly. This designation should never be considered when prenatal alcohol exposure is confirmed absent.**

Rationale for revision

This recommendation is consistent with *Canadian recommendation 5.2.2*. The term 'domain' has been replaced with area of assessment *(see section 1.3.2)*.

3.1.3 The use of FASD as a diagnostic term

In some other diagnostic systems, the term FASD is not used as a diagnostic category *(see Table 1)*.[23,25-28] Based on recommendations in the Canadian guideline, we are recommending the adoption of FASD with sentinel facial features as a diagnostic term.[29] While the features associated with FASD represent a spectrum of effects, the severity of neurodevelopmental effects in all areas of assessment is not dependent upon whether facial features are present or absent.

R **FASD should now be used as a diagnostic/descriptor term when prenatal alcohol exposure is considered to be a significant contributor to observed deficits that cannot be fully explained by other aetiologies. Because the observed deficits are recognised as being multifactorial in origin, all other known relevant contributors (for example trauma or known genetic anomalies) should be documented with the FASD diagnosis/descriptor as they have significant impact on the functional and neurological challenges of the affected individuals.**

See Annex 2 for a diagnostic algorithm for FASD.

Rationale for revision

This recommendation is consistent with *Canadian recommendation 5.3*. In the Scottish context, we intend to use the Canadian terminology FASD without sentinel features as a descriptor rather than a diagnostic term *(see section 1.3.2)*.

A sample FASD assessment summary, which includes sections for recording alcohol exposure in pregnancy, sentinel facial features and neurodevelopmental areas of assessment is available for download from the SIGN website.

3.2 Medical assessment

It is critical that FASD is recognised as a physical, behavioural and neurodevelopmental health condition. Family history must be reviewed and, if possible, a three-generation family tree obtained. This allows the team to identify existing developmental disorders in the family and identify the potential for inheritable disorders, based on an occurrence in the parents, siblings or second- or third-generation relatives. Consanguinity in the parents may indicate a risk of certain inherited disorders. The presence of FASD in other siblings is a risk factor for having another affected child.[39,65-68]

Several structural deficits and/or birth defects involving the ears, eyes, palmar creases, digits, elbow, joints and heart have been associated with FASD. Children with FASD are also at increased risk of additional structural defects including congenital heart defects and orofacial clefts.[69-71]

R **The diagnostic process should include a family, social and medical history as well as complete physical examination.**

Rationale for revision

A minor revision from *Canadian recommendation 2.1* ensures that family history is gathered.

A sample FASD assessment form, which includes sections for collection of obstetric, developmental, medical and social history; other medical conditions and genetic and other investigations is available for download from the SIGN website.

3.3 Sentinel facial features

3.3.1 Overview

There is evidence to support the recommendation that the simultaneous presentation of the three characteristic facial features that discriminate individuals with PAE include:

- short palpebral fissures,
- indistinct philtrum and
- thin upper lip.[64,72]

In a longitudinal analysis that explored which facial measures were most predictive of prenatal alcohol exposure and whether the measurements changed with age, a set of 16 facial measurements were selected. The data revealed that measures of craniofacial width (minimal frontal), orbital width (palpebral fissure width) and ear and mandibular measures (ear length and lower facial depth) were consistently predictive of group membership across age groups (5 and 9 years old).[73] After evaluating a computational model that could be used to accurately identify children with FAS automatically using facial features from 3D scans, researchers found that prenatal alcohol exposure not only produced the specific dysmorphic features – short palpebral fissures, thin upper lip and flat philtrum – but also other more subtle features that made the overall gestalt of an FASD face.[74] Although variations in the facial features associated with prenatal alcohol exposure were found across different sample populations using computerised anthropometry, at least one measure involving the eye (for example shortened palpebral fissures, reduced outer canthal width, or reduced inner canthal width) was apparent in all of them,[75] suggesting that the palpebral fissure length measurement is particularly sensitive to PAE. Overall, the findings were consistent with the clinical description of facial features involving the orbital region (palpebral fissure size) and mid face (mid-facial hypoplasia and thin upper lip with flat philtrum) as discriminating features of PAE. Using data from active case ascertainment studies of three distinct populations of children with PAE, similarities and differences in dysmorphology, growth, and unique physical features were explored.[76] After combining the populations, their model revealed that the following variables predict dysmorphology unambiguously: small palpebral fissures, narrow vermillion, smooth philtrum, flat nasal bridge, and fifth finger clinodactyly.

FASD diagnostic data[64] revealed that the presence of all three sentinel facial features and microcephaly (head circumference ≥2 standard deviations (SD) below the mean) in children, who were old enough to undergo a complete neurodevelopmental assessment (>8 years), was always associated with significant neurodevelopmental impairment. Therefore, infants and young children presenting with all three sentinel facial features and microcephaly may receive a formal diagnosis of FASD with sentinel facial features, even if they have yet to meet the criteria for significant neurodevelopmental impairment.

3.3.2 Assessing the face

The University of Washington Lip-Philtrum Guides continue to be the standard for an objective evaluation of lip and philtrum development. As described by the FAS Diagnostic and Prevention Network (depts.washington.edu/fasdpn/htmls/lipphiltrum-guides.htm), the Lip-Philtrum Guides reflect the full range (or normal distribution) of lip thickness and philtrum depth one would see in a general population. The Rank 3 picture reflects the population mean (or 50th percentile). Ranks 1 and 5 reflect the extreme ends of the normal curve (<2.5th percentile and >97.5th percentile). In practice, the Lip-Philtrum Guides have been described as a Likert scale (which has often been

misunderstood as an equal interval scale). When understood as a quasinormal curve, the lip and philtrum rankings of '4' and '5' are understood as the extremes of development, with '3' as the average range. For the purposes of an FASD evaluation, rankings of '4' and '5' are the critical values. Standard deviation values can be conveniently computed using University of Washington software (depts.washington.edu/fasdpn/htmls/diagnostictools.htm#pfl).

R **The following three sentinel facial features should be assessed:**

- **palpebral fissure length ≥2 SD below the mean**
- **philtrum rated 4 or 5 on 5-point scale of the University of Washington Lip-Philtrum Guide**
- **upper lip rated 4 or 5 on 5-point scale of the University of Washington Lip-Philtrum Guide.**

Rationale for revision

A minor rewording of *Canadian recommendation 3.1* has removed "must be present due to their specificity to prenatal alcohol exposure". The percentile threshold has been removed from the PFL criterion due the lack of standardised norms for this measure in the UK.

A sample FASD assessment form, which includes a section for recording of sentinel facial features is available for download from the SIGN website.

3.4 Neurodevelopmental assessment

3.4.1 Areas of assessment

The neurodevelopmental deficits associated with FASD are complex and multifaceted. It is well established that learning disabilities,[77] inattention,[78] social[79] and executive function deficits[80] can occur regardless of facial dysmorphology. There is no single neuropsychological measure, nor pattern of neuropsychological profiles that is specific to all individuals with FASD.[28,81-85] It is presumed that differences in the dose and timing of exposure,[86] as well as interacting genetic[87,88] and environmental influences[89-91] on brain development account for the variability in presentations. However, the most common neurodevelopmental disabilities include attention, executive function, spatial working memory, mathematics, communication, and adaptive behaviour.[81,92,93]

Canadian guidelines from 2005 and 2016 consistently recommend that significant deficits in at least three CNS areas of assessment are required for a diagnosis or descriptor of FASD.[28,29]

High levels of variance between index scores can emerge when assessing neurobehavioural function. If this discrepancy is found to be uncommon (ie a discrepancy analysis indicates this to occur in ≤3% of the population) and the lower of the two discrepant scores is at least one standard deviation below the mean, then this may be regarded as indicative of atypical development within that particular area of assessment.

Motor skills

Impairment is present when a composite score below the clinical cut-off or on multiple subtest scores is obtained on assessment of fine motor skills, gross motor skills, graphomotor skills, or visual-motor integration. Tone, reflexes, balance, co-ordination, strength and other abnormal findings on the neurological examination may be considered in combination with formal assessment of motor skills.

Neuroanatomy/neurophysiology

Impairment is present when occipitofrontal head circumference is <3rd percentile; a seizure disorder has been diagnosed not due to known postnatal influences; or when brain imaging shows convincing evidence of structural brain abnormalities known to be associated with PAE and other aetiologies have been excluded.[94,95] Although, a magnetic resonance imaging (MRI) scan is not required or necessary as a standard approach to assessing an individual suspected to have FASD, it may be an adjunct in determining the extent of effects on the brain or to rule out other disorders.

Cognition

Impairment is present when standardised tests of cognition or intelligence show a composite score below the clinical cut-off, a major subdomain score (such as verbal, nonverbal, or fluid reasoning) below the clinical cut off, or a large discrepancy among major subdomain scores, with a base rate below 3% and the lower of the two discrepant scores is at least one standard deviation below the mean.

Language

Impairment is present when a score below the clinical cut-off is obtained on a composite score assessing core language, receptive language, expressive language, or when multiple scores below the clinical cut off are seen on subtests assessing higher-level language skills (for example the integrative aspects of language such as narrative and complex comprehension abilities). Impairment is also present when there is a large discrepancy between receptive composite score and expressive composite score (as there are four index scores in language assessments), with a base rate of less than 3% and the lower of the two discrepant scores is at least one standard deviation below the mean.

Academic achievement

Impairment is present when a score below the clinical cut-off is obtained on standardised measures of reading, mathematics, and/or written expression, or when there is a large discrepancy between cognition and one of the above, with a base rate of less than 3% and an achievement score at least one standard deviation below the mean. The clinical team must determine that the individual has had consistent exposure to academic instruction before a deficit can be recorded.

Memory

Impairment is present when a score below the clinical cut-off is obtained on a composite measure of overall memory, verbal memory, or visual memory, or when there is a large discrepancy between verbal and non-verbal memory, with a base rate of less than 3% and the lower of the two discrepant scores is at least one standard deviation below the mean. A deficit in working memory should be considered under executive function rather than memory.

Attention

In many definitions and theories of brain function, attention overlaps with some of the executive functions. In order to distinguish these areas of assessment for diagnostic purposes, attention is here defined as sustained or selective attention and resistance to distractions. Deficits in inhibition, impulse control or hyperactivity should be considered under executive function rather than attention.

Impairment in attention by direct assessment is present when multiple subtest scores below the clinical cut-off are obtained on continuous processing tests or other neuropsychological measures of attention.

Impairment in attention by indirect assessment is present when a clinical assessment provides converging evidence of impairment from multiple sources, including clinical interview, questionnaire, file review and direct clinical observation during neurodevelopmental testing.

Executive function, including impulse control and hyperactivity

Executive function refers to a set of higher-level skills involved in organising and controlling one's own thoughts and behaviours in order to meet long-term goals. Although there is some overlap between attention and executive function in many conceptualisations, it is here defined as impairments in working memory, inhibition/impulse control, hyperactivity, planning and problem solving, or shifting and cognitive flexibility.

Impairment in executive function by direct assessment is present when multiple subtest scores below the clinical cut-off are obtained on neuropsychological measures of executive function.

Impairment in executive function by indirect assessment is present when a clinical assessment provides converging evidence of impairment from multiple sources, including scores at or below the clinical cut-off on standardised rating scales and supporting evidence from clinical interview, file review and direct clinical observation during neurodevelopmental testing.

Affect regulation

Impairment of affect regulation is manifested by high levels of emotional expression resulting in significant clinical impairment that may take the form of anxiety or depressive disorders, or as oppositional-defiant or conduct disorders. Possible types of anxiety disorder are panic disorder, phobic disorders, separation anxiety disorder or generalised anxiety disorder. A diagnosis of oppositional defiant disorder or conduct disorder is manifested (in part) by a frequent loss of temper, arguing, becoming easily angered or annoyed, showing vindictive or other negativistic behaviours. Disturbances of affect regulation should only be attributed to PAE if they longstanding, and should not be attributed to PAE if they are formulated to be in response to unfavourable life events or environmental conditions (for example, multiple foster placements) or are situationally specific (for example, specific phobias).

Adaptive behaviour, social skills or social communication

Impairment in social communication by direct assessment is present when a score below the clinical cut-off is obtained on the composite score from a measure of social language, social communication skills or pragmatic language skills. Impairment in adaptive behaviour or social skills by indirect assessment is present when according to a standardised interview or rating scale completed by a key informant, a score below the clinical cut-off is obtained on the global composite score or a major subdomain score. For children and most adolescents standardised indirect measures (ie by caregiver ratings) should be used. For adults and some adolescents who have not had a consistent caregiver within the last two years, clinicians may need to consider other methods of interview and use of historical records to rate adaptive function. For social language development a direct measure with the client should be used, if age-appropriate, in combination with reports and historical information. Observations and ratings should be across environments where appropriate (ie parents report on experiences at home and teachers can report on behaviour at school). Scores are considered significant when they are below the clinical cut-off.

R **A diagnosis/descriptor of FASD is made only when there is evidence of pervasive and long-standing brain dysfunction, which is defined by severe impairment (a global score or a major subdomain score on a standardised neurodevelopmental measure that is ≥2 SDs below the mean, with appropriate allowance for test error) in three of more of the following neurodevelopmental areas of assessment:**

- **motor skills**
- **neuroanatomy/neurophysiology**
- **cognition**
- **language**
- **academic achievement**
- **memory**
- **attention**
- **executive function, including impulse control and hyperactivity**
- **affect regulation, and**
- **adaptive behaviour, social skills or social communication.**

Rationale for revision

This recommendation is consistent with *Canadian recommendation 4.1*. The term 'domain' has been replaced with area of assessment *(see section 1.3.2)*. Adding 'long-standing' emphasises the existing

pervasive description and reinforces the concept that the impairment must be across different functional areas and not transient.

The definition of severe impairment has been added into this recommendation from original *Canadian recommendation 4.2* which is now not separately listed.

A sample FASD assessment form, which includes a section for recording of neurodevelopmental areas of assessment is available for download from the SIGN website.

3.4.2 Direct and indirect assessment methods

Clinical training and judgment are required to interpret test results and experienced clinicians will evaluate scores within the context of a complete assessment picture. *Canadian recommendations 4.3, 4.4* and *4.5* regarding the use of indirect assessments were developed as a result of extensive discussions regarding the strengths and weaknesses of different sources of information. Direct testing refers to standardised testing or physical measurements. The advantages of direct testing include the relative objectivity and lack of observer biases. The disadvantage of direct testing may be the absence of ecological validity; the relative calm, structure, and lack of ambiguity in the testing situation may not translate to real world situations. Indirect assessment, in contrast, may offer more ecological validity, but also carries risk of subjective bias. There is precedent for such a joint approach in the routine assessment of other common neurodevelopmental disorders, such as intellectual disabilities, which combine direct assessment of cognition with indirect assessment of adaptive function.

R **Direct standardised measures should be used whenever possible. We recognise, however, that in some cases, indirect assessment methods such as informant ratings, clinical interview, or historical assessment through file review may be more appropriate.**

Further details on the criteria for severe impairment in all areas of assessment and appropriate direct and indirect assessment methods for each is available for download from the SIGN website.

Rationale for revision

A minor revision of *Canadian recommendation 4.3* has been made to simplify language and remove reference to 'brain domains'.

R **If historical assessment, clinical interview, or file reviews are used for indirect assessment (for example assessing adaptive behaviour) deficits should be considered by the team to be at a severity level equal to or below the clinical cut-off, which is defined as ≥2 SD below the mean.**

Rationale for revision

A minor revision of *Canadian recommendation 4.4* has been made to clarify reference to the clinical cut-off.

It is incumbent that the clinician conducting the neuropsychological assessment considers the contribution from both the clinical interview and their clinical judgement as supporting evidence to confirm the significant brain impairment finding for areas of assessment that have fewer direct measurements.

R **When using indirect methods of assessment, clinicians should ensure that information comes from multiple sources rather than a single informant.**

Rationale for revision

Minor revision of *Canadian recommendation 4.5* has been made to remove reference to 'domains of function'.

3.5 Special considerations in the assessment of infants, children and young people

Research has suggested that measures of infant state regulation[96] and negative temperament[97] are important indicators of FASD. Other symptoms and signs include poor eating, poor sleeping, poor alertness and irritability.

Traditional tests of development in various areas of assessment are also available. The reliability of these tests tends to increase gradually with age, to a point where they become sufficiently reliable for decision-making purposes. Unfortunately, these 'thresholds of confidence' occur at different ages for different tests, and often exist as unwritten rules rather than published practice guidelines.

The development group has provided suggestions for example neurodevelopmental tests across the lifespan.

R **Infants and young children with confirmed prenatal alcohol exposure, but who do not meet the criteria for FASD should be designated as 'at risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure'. Those with all three facial features, but no microcephaly, should be referred to a clinical geneticist.**

✓ The record of a designation of 'at risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure' should be available to professionals undertaking childhood developmental surveillance.

Rationale for revision

Canadian recommendation 7.3 has been retained in full.

R **A neurodevelopmental assessment is recommended for all children with confirmed prenatal alcohol exposure and/or all three facial features in whom there are clinical concerns.**

Rationale for revision

Canadian recommendation 7.4 has been amended for clarity. Assessment of all children with a history of PAE was not thought to be practical. With the current universal developmental surveillance checks in place, health visitors should be aware of the potential increased risk and be proactive with early referral of children where there is cause for concern.

3.6 Special considerations in the assessment of adolescents and adults

Due to the current under-recognition of FASD in Scotland, presentation may occur at a later stage. Some young people and adults present with neurodevelopmental dysfunction where prenatal alcohol has not been considered as the underlying cause. Some may have already developed secondary mental health problems, or may have become involved in the judicial system. An awareness of the increased prevalence of people affected by prenatal alcohol in the mental health and judicial systems, and the need to review and reassess patients in these groups is required. The same guidance for assessment is relevant.

✓ Those working in organisations related to the care of 'looked after' and accommodated children and young people, individuals being seen by mental health services, or within the judicial system should be aware of the increased prevalence of prenatal alcohol exposure in these groups, and the need for referral for assessment of impairment.

R **When it is not possible to obtain a formal adaptive behaviour measure or when there is no suitable informant, historical or current information, derived from a file review, may be used as a proxy.**

Rationale for revision

Canadian recommendation 8.2 has been retained in full.

3.6.1 Individualising the assessment

An individual's social circumstances, such as homelessness, can present a significant challenge to the assessment process, especially their ability to attend appointments. They may also experience limited sleep and alcohol and substance abuse, which may affect the test results. A client-centred approach is needed such that the length of the assessment is tailored to the individual's needs and capacity. They may have low frustration tolerance and become tired easily, and may not attend all the assessment sessions needed. It is especially important to access any recent assessments so that the usual test battery can be modified. When asking about previous testing, individuals and their caregivers often do not realise that some of the same tests are used in a school assessment or a forensic assessment as in the FASD assessment. Pregnancy, breastfeeding, and childcare responsibilities are stressors that can impact test results and attendance. A chronic state of crisis or mental health involvement may mean that there is never an ideal time to be assessed but the clinical team must be confident that a reliable assessment can be obtained. An FASD diagnosis/descriptor based on unreliable data is not valid.

R **The length and structure of the assessment must accommodate the needs and capacity of the individual being assessed. It is important to recognise, for example, if the individual gets frustrated or tires easily; situational factors could invalidate the assessment.**

Rationale for revision

A minor revision has been made to *Canadian recommendation 8.3* in order to clarify the term "individual".

3.6.2 Making the assessment meaningful

The assessment and diagnosis/descriptor of FASD can help the individual, their family, and service providers to understand the challenges associated with a lifelong disability that requires accommodations and supports to maximise success.[98] It may help them access interventions and supports that address their biopsychosocial needs with recommendations for basic supports, general, physical and mental health.

R **Recommendations following the assessment must address basic and immediate needs of the individual being assessed, and assist them in accessing required resources.**

Rationale for revision

A minor revision has been made to *Canadian recommendation 8.4* in order to clarify the term "individual".

R **The core principles of bioethics, including autonomy and consent, confidentiality, beneficence, and non-maleficence must be carefully applied.**

Rationale for revision

A minor revision has been made to *Canadian recommendation 8.5* to cover people of all ages.

3.7 The assessment team

Because of the complexity of the outcomes related to PAE, a multidisciplinary team is essential for an accurate and comprehensive assessment and subsequent management recommendations. The multidisciplinary assessment team can be local, central or virtual; satellite clinics and telemedicine may be used to meet the needs of referrals from remote and rural locations. The team will vary according to the specific context and the age of the individuals being assessed. The team members should possess the necessary expertise to conduct all aspects of the assessment and have updated knowledge about FASD. New members of the team must receive appropriate training. Team members are outlined below and should always consist of professionals with appropriate qualifications, who have received appropriate training around obtaining sensitive information from birth families, especially when acquiring the prenatal alcohol exposure history.

R **Team members across the lifespan are:**

- **neonatologist/paediatrician/physician with competency in assessment of FASD**
- **child development specialists with the skillset to conduct physical and functional assessments (eg speech and language therapist, occupational therapist, clinical psychologist, educational psychologist).**

Further individuals who can provide valuable input into the diagnostic process may include parents and carers, advocates, childcare workers, clinical geneticists, cultural interpreters, family therapists, general practitioners, learning support, mental health professionals, mentors, nurses (eg school, learning disability, etc), neuropsychologists, probation officers, psychiatrists, social workers, substance misuse service staff, teachers and vocational counsellors.

Rationale for revision

Canadian recommendation 6.1 has been amended to remove the term 'core team', and to ensure terminology is appropriate to NHSScotland. It has been further amended to remove the stratification of team members by age of individual receiving assessment.

4 Management and follow up

4.1 Developing a management plan

Fetal alcohol spectrum disorder is a lifelong condition and individuals with FASD have varying needs across their lifespan. Each child is unique in their presentation, and so, no single approach is optimal for all cases. To allow people to live as independently as possible, services need to take a wide, varied and adaptable approach.

Following assessment, which should build a picture of the pattern of strengths and difficulties unique to the individual, management and follow up are critical to ensure that this specific profile of vulnerabilities is targeted for intervention. The assessment needs to be shared with the parents, carers and child or young person in an appropriate way, and the implications for the child's educational needs and how they can function within the living environment need to be documented in a practical way for those working closely with the child and their family. The lifelong and changing nature of the disorder needs to be understood, as does the need for reassessment at stages of transition to new situations.

The assessment and diagnosis of FASD can help the individual, their family, and service providers to understand the challenges associated with a lifelong disability that requires accommodations and supports to maximise success.

Getting It Right For Every Child (GIRFEC)[62] aims to promote and support children and young people's well-being by making sure they have access to the right support when they need it. The co-ordination of services and collaboration between services as outlined in GIRFEC and related legislation is important for the provision of effective interventions and support *(see section 2.1.4)*.

Client- and family-centred approaches that are based on strengths, and sufficiently flexible to account for individual barriers, should be best practices for supporting adults with FASD. Recognising common risks for affected individuals and acting preventively can be beneficial. Prevention education must be incorporated into the assessment process when working with adolescents and adults to address issues of sexual health, birth control, and pregnancy. Modifications to the service delivery model, including team composition and ways of working may be needed to support individuals throughout the assessment process and implementation of their management plan. The multidisciplinary team provides recommendations to address the basic and immediate needs of the client, and aims to assist the individual and their family in accessing the needed supports and services.

4.1.1 Communicating the results of assessment

The results of the assessment should be presented to the family of the person being assessed (if a minor) and to the individual. A decision by the clinical team should be made regarding how to best present the findings to an adolescent or older child. The results should be presented in a written or graphical report that documents the social history, medical findings, results of the neurodevelopmental assessment, and diagnoses. FASD is a medical diagnosis or descriptor, and as such, there is unavoidable terminology that may not easily be understood by the individual and/or their family. The clinical team should do its best to simplify the findings when presented to the family and be available later to answer questions that may arise from the written report. The recommendations in the report should include services that might be available.

A sample diagnostic assessment summary form is available for download from the SIGN website.

R **Education about the impact of FASD and appropriate support for the individual and those involved with their care is recommended. The range of potential issues that might be expected to arise as a result of receiving the FASD diagnosis/descriptor should also be discussed. It is important that this information is communicated in a culturally sensitive manner using appropriate language.**

A range of information for individuals and caregivers, and for clinicians is available for download from the SIGN website. This includes information and resources about issues that individuals and their caregivers may experience during the FASD assessment process and after a diagnostic assessment.

Rationale for revision

Canadian recommendation 9.1 has been amended for terminology appropriate to NHSScotland. 'Appropriate' has been added as children who are affected and their families may not always require comprehensive support. 'Develop' has been changed to 'arise' to resolve unintended ambiguity that consequences of receiving a diagnosis or descriptor might represent a maturational change.

4.1.2 Follow up

Care plans[99] for affected individuals and those that support them are important to improve outcomes. Individuals with FASD experience a wide variety of complex physical, mental and behavioural health-related challenges that require a multifaceted approach to diagnosis and management. The complexity and persistence of FASD symptoms across the lifespan necessitates a long-term plan for management. The types of recommended services and supports will differ based on individual needs, and will often depend on where patients are assessed. Clinics may consider implementing staged care plans across the lifespan, with the opportunity to review a patient's current situation and anticipate upcoming problems at predetermined time intervals.

R **A member of the team around the child should follow up within a specified length of time to ensure that the recommendations have been addressed and to provide further support as needed.**

Rationale for revision

Canadian recommendation 9.2 has been amended to align with current GIRFEC scheme and language appropriate to NHSScotland. The addition of 'specified' ensures that follow up is predetermined, rather than arbitrary.

R **Individuals with FASD and their caregivers should be linked to resources that can improve outcomes. However, just because availability of services is limited, an individual should not be denied an assessment and management plan. Often the identification of need is the impetus that leads to the developmental of resources.**

Rationale for revision

In *Canadian recommendation 9.3* the term 'diagnosis' is used. Rather than change this to 'diagnosis/descriptor' the term 'identification of need' has been added to highlight the importance of the assessment process which may or may not result in a diagnosis, but will usually identify areas of need, prompting an individualised management plan.

R **When young adults are transitioning to independent or interdependent living situations, they may need to undergo a reassessment to identify any changes in their adaptive function scores and to make any subsequent adjustments to their management plan.**

Rationale for revision

A minor amendment has been made to *Canadian recommendation 9.4* for clarity only.

✓ It is particularly important given the changing and lifelong nature of FASD that reassessment and revision of care plans are considered at all transition stages in the child and young person's life. This should be linked to the GIRFEC process in Scotland and to the review of Individual Education Plans and transition to adulthood planning.

5 Implementing the recommendations

This section provides advice on the resource implications associated with implementing this guidance, and advice on audit as a tool to aid implementation.

5.1 Implementation strategy

Implementation of national clinical guidance is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guidance in individual hospitals, units and practices.

It will be important in assessing improvement in identification of children and young people who fit the diagnosis of FASD with sentinel features or the descriptor of FASD without sentinel features to have systems in place that will enable regular monitoring of diagnosis rates and epidemiology. For those health boards using the national Support Needs System (SNS) database two codes have been agreed to distinguish each of the conditions:

- FASD with sentinel features (PK80)
- FASD without sentinel features (L254).

Recording may be challenging for child and adolescent mental health services (CAMHS) colleagues as FASD with sentinel features almost maps to FAS in the ICD-10 coding system, but FASD without sentinel features is not recognised as a diagnosis or descriptor which can be coded using ICD-10 or DSM-5.

As the assessment is likely to be multidisciplinary, and CAMHS colleagues will be involved with others including paediatricians in the assessment process, it may be helpful to agree within health boards how best to record the identified children and young people in each category. For some this may involve the SNS system but where that is not in use a separate recording method may need to be established with the aim of facilitating monitoring the numbers of cases identified in each category year on year on a national basis.

NHS Education for Scotland has published an FASD diagnostic pathway which provides a framework for all statutory and voluntary agencies who are involved in supporting children or young adults affected by or thought to be affected by FASD. Compliance with the pathway, which offers a broad range of guidance for the identification and diagnosis of children and young people at risk of FASD, represents an implementation tool for many of the recommendations contained in this guidance.

www.knowledge.scot.nhs.uk/ecomscormplayer/fasdpathway/j459160/fasd-01.html

Following a commission from Scottish Government in 2016, the Mental Health Access Improvement Support Team (MHAIST) was established within Healthcare Improvement Scotland to improve access to Child and Adolescent Mental Health Services and Psychological Therapy services. The MHAIST is facilitating a neurodevelopmental collaborative working with teams across Scotland to improve the efficiency and effectiveness of their assessment and diagnostic pathways. This collaborative will run until the end of 2019 and is underpinned by quality improvement methodology (https://ihub.scot/improvement-programmes/mental-health-portfolio/mhaist/).

This guideline will assist those teams already involved in improving assessment and identification of FASD as well as supporting and monitoring of diagnostic rates. The collaborative will be a vehicle for implementation and future spread of best practice.

5.2 Resource implications

Additional resources are expected to be required as a result of these recommendations, but these will depend on several factors, including:

- the extent to which clinicians' current practices for identifying patients with, or at risk of, FASD may be underdiagnosing the true extent of FASD in the Scottish population, and if FASD is currently underdiagnosed, whether it is disproportionately patients who are less severely affected by FASD who are less likely to be diagnosed in practice.
- the extent to which implementation of these recommendations is able to rectify any underdiagnosis of FASD.
- whether any additional costs associated with implementing the recommendations may be offset by a reduction in costs that currently occur in clinical practice in the longer term, in that, by enabling earlier diagnosis of FASD and thereby enabling earlier treatment strategies to be put in place to help individuals with FASD and their families and/or carers, the level of unmet need that has longer-term implications for affected individuals is reduced.
- the extent to which expected additional pressures on services for FASD and individuals at risk of FASD will be borne predominantly by NHS providers, and/or social care partners and/or third sector organisations dedicated to working with people who have or are at risk of FASD.
- current and future trends in alcohol consumption during pregnancy.

In considering these issues, it is estimated that any resource impact is most likely to be felt in terms of staff costs, given the additional requirements associated with assessment and follow up of individuals who have (or are at risk of) an FASD diagnosis. There may also be additional costs to be borne by local authority social care partners and third sector organisations, which will depend on the identified social care needs of each individual with, or at risk of, FASD and the relevant staff members required to meet their needs.

Within Scotland, a recent evaluation funded by Scottish Government compared a pilot evaluation by NHS Ayrshire and Arran for the assessment and diagnosis of those with FASD using a Fetal Alcohol Assessment and Support Team, with treatment as usual using CAMHS and Community Paediatrics services. The pilot team was found to be less likely to struggle to provide access to multidisciplinary staff required for FASD assessment, and more confident in making a formal diagnosis related to prenatal alcohol exposure.

Whilst clinically successful, from a resource-use perspective it was noted that in the longer-term it would not be sustainable to provide FASD services in this way. It was therefore proposed FASD be managed within the context of wider neurodevelopmental services and mental health teams (and the service has since been integrated into existing CAMHS and Community Paediatrics services within NHS Ayrshire and Arran). This suggests it is possible to provide FASD services using existing resources, but the wider context in terms of the impact of altering existing service configurations needs to be considered.

A Children and Young People's Mental Health Task Force (https://www.gov.scot/publications/children-young-peoples-mental-health-task-force-preliminary-view-recommendations/) has been established by Scottish Government in collaboration with the Convention of Scottish Local Authorities to support and build on the actions in Scotland's ten-year Mental Health Strategy (https://www.gov.scot/publications/mental-health-strategy-2017-2027/) by setting out a whole systems approach to mental health services. The task force is investigating how services and community support can better meet the rapidly changing need seen across Scotland. It will look, in particular, at new provision for direct access to less intensive, education and community-based sources of help for young people, and will also develop a neurodevelopmental Service Framework and Specification that will improve support and care for children, young people and their families with neurodevelopmental concerns.

Preliminary findings of the task force have identified workforce shortages and waiting time pressures on CAMHS services and recognised that in addition to building capacity and capability across services there needs to be more innovation and flexibility in CAMHS team structures.

In order for change to be sustainable, the task force will tackle the current issues with waiting times for mental health services in young people, combined with more services for those who need support but who don't require a specialist service. It aims to improve coherence within the system, bringing in all of those who provide services to children and young people, including health boards, schools, social services, youth justice and the third sector.

The exact specifications of future workforce planning must be appropriate to local needs, and so any actual additional resource requirement cannot be quantified nationally at this stage.

Regardless of service reconfiguration, the implementation and staffing of sustainable FASD services in the long term is expected to require training by professionals to their NHS and social care colleagues. The NHS Ayrshire and Arran pilot delivered training, on average, to 137 health, education and social care professionals every month. While it is not clear how many still require initial training and what the requirements for refresh training will be, staff training should be an anticipated ongoing resource.

5.3 Auditing current practice

A first step in implementing a clinical practice guidance is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of recommendations requires good communication between staff and multidisciplinary team working.

The guidance development group has identified the following as key points to audit to assist with the implementation of this guidance:

- the proportion of pregnant women with complete alcohol histories recorded in antenatal records
- the proportion of pregnant women and mothers who hold a personal child health record that contains a complete prenatal alcohol history
- incidence and prevalence of diagnosis of FASD with sentinel facial features
- incidence and prevalence of descriptor of FASD without sentinel facial features
- the proportion of individuals with a diagnosis/descriptor of FASD who are linked to resources to improve outcomes or who receive an individualised management plan
- the proportion of young adults with a diagnosis/descriptor of FASD and who are transitioning to independent or interdependent living situations who undergo reassessment to identify changes in adaptive function scores or make adjustments to their management plan
- the proportion of individuals with a diagnosis/descriptor of FASD who are offered written information at the time of diagnosis.

5.4 Supporting materials

The following supporting materials are available for download from the SIGN website:

- qualitative synthesis on the experiences of caregivers looking after individuals with FASD
- sample FASD assessment form
- sample FASD assessment summary
- neurodevelopmental areas of assessment: criteria for severe impairment (includes examples of standardised tests)
- Department of Health and Royal College of Paediatrics and Child Health growth charts for boys and girls aged 0–4 years and 2–18 years (including weight, length/height and head circumference)
- information on FASD assessment for individuals and caregivers
- information for clinicians: issues that individuals and their caregivers may experience during the FASD assessment process
- information on FASD and support for individuals and caregivers after diagnosis
- information and resources for clinicians after diagnosis
- sample FASD management planning form.

6 Development of the guidance

6.1 Introduction

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of Healthcare Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising healthcare professionals using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in 'SIGN 50: A Guideline Developer's Handbook', available at www.sign.ac.uk

6.2 Methods used to develop this guidance

This guidance was initially developed using standard SIGN methodology. The multidisciplinary development group was recruited *(see section 6.3)*, key questions established *(see Annex 1)* and systematic review of the evidence carried out *(see section 7.1)* according to the methods published in SIGN 50. When it became clear that there was insufficient evidence available to answer key questions 2(a–e), 3 and 4, a systematic search for guidelines on diagnosis of FAS or FASD was completed. The identified documents were sifted based on relevance, scope, comprehensiveness and alignment with the original key questions.

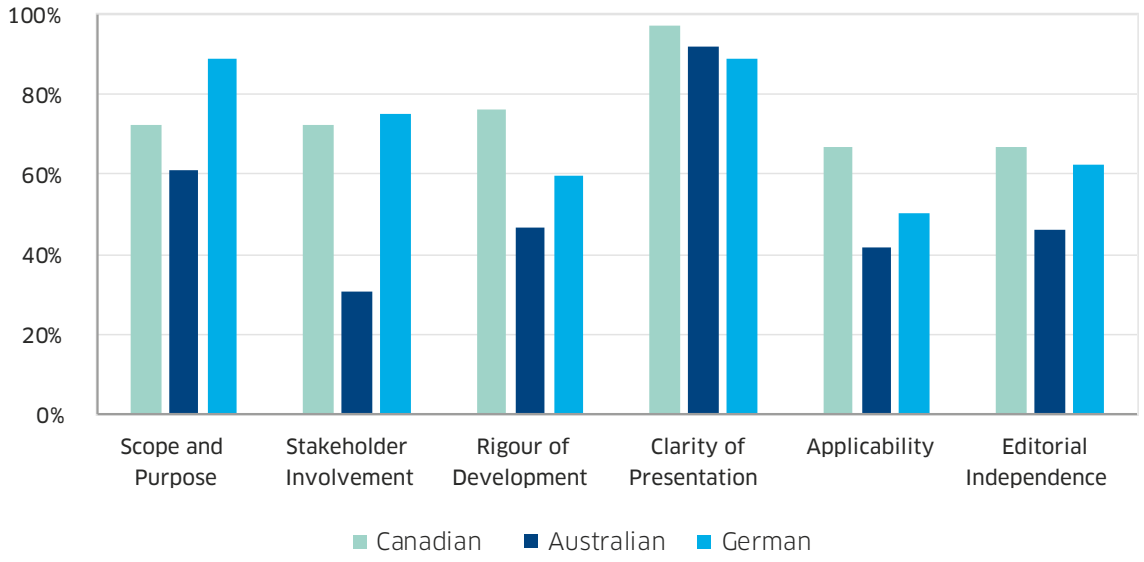
The guidelines selected were:

- the Canadian guideline for diagnosis of FASD[29]
- the Australian guide for the diagnosis of FASD[32]
- the German guideline for the diagnosis of FAS.[100]

The development group were invited to independently comment on each diagnostic system and provide feedback on their appropriateness, amenability to Scottish population and feasibility. The development group noted that the German guideline only included criteria for diagnosis of FAS and was less comprehensive than other systems and was not prioritised for adaptation. When considering the other candidates, the development group noted that the Australian guideline had been adapted from the Canadian guideline, though it was felt that the former had a more attractive interface and layout, including a comprehensive range of forms and appendices for recording of diagnostic outcomes and communicating these to parents and children. Evidence and Information Scientists also carried out an appraisal of guideline quality using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.[101] The Canadian guideline scored highest on four of the six subdomains of the AGREE instrument *(see Figure 1)* and was chosen by the development group as the preferred source for adaptation.

As key question 5 focuses on the experiences and views of parents and carers of individuals with FASD, the systematic review of quantitative studies used for other questions would not be an appropriate approach. Instead, a rapid synthesis of qualitative studies was completed to identify, appraise and summarise the evidence on the impact of providing care for people with FASD. This is available to download from the SIGN website.

Figure 1: AGREE II instrument subdomain ratings of shortlisted FASD guidelines



6.3 The guidance development group

Dr Patricia Jackson OBE *(Co-Chair)*	*Senior Fellow, Royal College of Paediatrics and Child Health and Honorary Fellow, University of Edinburgh*
Dr Helen Mactier *(Co-Chair)*	*Consultant Neonatologist, Princess Royal Maternity, Glasgow and Honorary Clinical Associate Professor, University of Glasgow*
Ms Val Arbuckle	*Additional Support Midwifery Sister, Forth Valley Royal Hospital, Larbert*
Dr Jenny Bennison	*General practitioner, Niddrie Medical Practice, Edinburgh and Royal College of General Practitioners Scotland Executive Officer (Quality)*
Ms Juliet Brown	*Evidence and Information Scientist, Healthcare Improvement Scotland*
Dr Sarah Brown	*Consultant Paediatrician, Ayrshire Central Hospital, Irvine*
Ms Morag Burns	*Speech and Language Therapist, Newbattle Medical Practice, Mayfield*
Ms Eileen Calder	*Lay representative and Director, FASD Scotland, Hamilton*
Dr Elizabeth Ellis	*Associate Specialist Obstetrician, Princess Royal Maternity, Glasgow*
Ms Lorna Fulton	*Community Midwife, Ayrshire Maternity Unit*
Dr Shelagh Joss	*Consultant Clinical Geneticist, Royal Hospital for Children, Glasgow*
Dr Lindsay Logie	*Consultant Paediatrician, NHS Lothian*
Ms Angela McLeman	*Specialist Occupational Therapist, Musselburgh Primary Care Centre*
Ms Morag Murray	*Educational Psychologist, The City of Edinburgh Council*
Dr Moray Nairn	*Programme Manager, SIGN*

Dr Tessa Parkes	*Director, Salvation Army Centre for Addiction Services and Research, Faculty of Social Sciences, University of Stirling*
Dr Peter Rice	*Chair, Scottish Health Action on Alcohol Problems, Edinburgh*
Dr Jennifer Shields	*Principal Clinical Psychologist, Ayrshire Central Hospital*
Dr Justin Williams	*Senior Clinical Lecturer and Honorary Consultant in Child and Adolescent Psychiatry, Royal Cornhill Hospital, Aberdeen*

The membership of the guidance development group was confirmed following consultation with the member organisations of SIGN. All members of the guidance development group made declarations of interest. A register of interests is available in the supporting material section for this guidance at www.sign.ac.uk

Guidance development and literature review expertise, support and facilitation were provided by SIGN Executive and Healthcare Improvement Scotland staff. All members of the SIGN Executive make yearly declarations of interest. A register of interests is available on the contacts page of the SIGN website www.sign.ac.uk

Euan Bremner	*Project Officer*
Karen Graham	*Patient Involvement Officer*
Jenni Hislop	*Senior Health Economist, Healthcare Improvement Scotland*
Aimie Little	*Administration Officer*
Gaynor Rattray	*Guideline Co-ordinator*
Domenico Romano	*Publications Designer*
Dr Carolyn Sleith	*Evidence and Information Scientist, Healthcare Improvement Scotland*

6.4 Acknowledgements

SIGN is grateful to the following former members of the guidance development group and others who have contributed to the development of the guidance.

Mr Stephen Heller-Murphy	*Programme Manager, SIGN (former)*
Ms Anne Wilson	*Children's Health Scotland*

In addition, SIGN would like extend particular gratitude to members of Grandparents Parenting Again and Kinship Carers, Midlothian who participated in a focus group discussion to express views on the needs of carers of people at risk of FASD.

6.5 Editorial group

As a final quality control check, the guidance was reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council and senior management in Healthcare Improvement Scotland to ensure that risk of bias in the development process has been minimised. The editorial group for this guidance was as follows. All members of SIGN Council make yearly declarations of interest. A register of interests is available on the SIGN Council Membership page of the SIGN website www.sign.ac.uk

Professor John Kinsella	*Chair of SIGN; Co-Editor*
Dr Roberta James	*SIGN Programme Lead; Co-Editor*
Dr Sara Twaddle	*Director of Evidence, Healthcare Improvement Scotland*
Dr Karen Ritchie	*Head of Knowledge and Evidence, Healthcare Improvement Scotland*
Ms Alison Gray	*Allied Health Professional representative*
Mr David Hewitson	*Scottish Association of Social Workers*
Dr Jane Morris	*Royal College of Psychiatrists*
Professor Ronan O'Carroll	*British Psychological Society*
Dr Lydia Simpson	*Trainee representative*
Professor David Wilson	*Royal College of Paediatrics and Child Health*

7 The evidence base

7.1 Systematic literature review

The evidence base for section 2.1.3 of this guidance was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Evidence and Information Scientist. Databases searched include Medline, Embase, Cinahl, PsycINFO, EBSCO Psychology and Behavioural Sciences Collection, Midwives Information and Resource Service (MIDIRS) and the Cochrane Library. The year range covered was 2007–2017. Internet searches were carried out on various websites including the US National Guidelines Clearinghouse. The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by two Evidence and Information Scientists using standard SIGN methodological checklists before conclusions were considered as evidence by the development group.

The search strategies are available on the SIGN website, www.sign.ac.uk

7.1.1 Literature search for patient issues

At the start of the guideline development process, a SIGN Evidence and Information Scientist conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to diagnosis of FASD. Databases searched include Medline, Embase, Cinahl and PsycINFO, and the results were summarised by the SIGN Public Involvement Officer and presented to the development group.

7.1.2 Literature search for cost-effectiveness evidence

The development group identified key questions with potential cost-effectiveness implications, based on the following criteria, where it was judged particularly important to gain an understanding of the additional costs and benefits of different treatment strategies:

- treatments or assessments which may have a significant resource impact
- opportunities for significant disinvestment or resource release
- the potential need for significant service redesign
- cost-effectiveness evidence could aid implementation of a recommendation.

A systematic literature search for economic evidence for these questions was carried out by a SIGN Evidence and Information Scientist covering the years 2007–2017. Databases searched include Medline, Embase and NHS Economic Evaluation Database (NHS EED). No relevant economic evidence was identified.

7.2 Recommendations for research

The development group was not able to identify sufficient evidence to answer all of the key questions asked in this guidance *(see Annex 1)*. The following areas for further research have been identified:

- what is the epidemiology of FASD in Scotland?

Research should be supported by the implementation of diagnostic criteria recommended in this guidance and should include co-ordinated large-scale population-specific prevalence studies. As passive surveillance studies may underestimate the prevalence of FASD, future research should include active case ascertainment studies in a variety of settings including standard populations (nursery, primary schools, secondary school) and likely high-risk groups (ADHD clinics, looked-after and accommodated children, adopted children, individuals affected by homelessness or addictions and those involved with criminal justice).

- what are the optimal methods for discussing alcohol use before, during and after pregnancies?
- which methods of screening for alcohol use during pregnancy are most reliable in eliciting honest responses from those consuming alcohol?
- further feasibility studies on the use of meconium and placental biomarkers using large-scale population-based methods.
- charts for assessing palpebral fissure length standardised to the UK population.
- research into the relationship between membership of the assessment team and speed, quality and consistency of diagnostic outcomes.
- economic studies on the cost effectiveness of identification and screening for children and young people exposed prenatally to alcohol, and diagnostic strategies for FASD, respectively.

7.3 Review and updating

This guideline was issued in 2019 and will be considered for review in three years. The review history, and any updates to the guideline in the interim period, will be noted in the review report, which is available in the supporting material section for this guideline on the SIGN website: www.sign.ac.uk

Comments on new evidence that would update this guideline are welcome and should be sent to the SIGN Executive, Gyle Square, 1 South Gyle Crescent, Edinburgh, EH12 9EB (email: sign@sign.ac.uk).

Abbreviations

ABI	alcohol brief intervention
ADHD	attention deficit and hyperkinetic disorders
AGREE	Appraisal of Guidelines for Research and Evaluation
ARBD	alcohol-related birth defects
ARND	alcohol-related neurodevelopmental disorder
ASD	autism spectrum disorder
CAMHS	child and adolescent mental health services
CDC	Centers for Disease Control
CI	confidence interval
CMO	Chief Medical Officers
CDT	carbohydrate deficient transferrin
CNS	central nervous system
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, fifth edition
FAE	fetal alcohol effects
FAS	fetal alcohol syndrome
FASD	fetal alcohol spectrum disorder
GIRFEC	Getting It Right for Every Child
GOPR	Getting Our Priorities Right
GP	general practitioner
HEAT	Health Improvement, Efficiency, Access and Treatment
ICD-10	The International Classification of Diseases, 10th revision
IOM	Institute of Medicine
MHAIST	Mental Health Access Improvement Support Team
MIDIRS	Midwives Information and Resource Service
MRI	magnetic resonance imaging
ND-PAE	neurodevelopmental disorder – prenatal alcohol exposure
NHS EED	NHS Economic Evaluation Database
PAE	prenatal alcohol exposure
PEth	phosphatidylethanol
pFAS	partial fetal alcohol syndrome
PFL	palpebral fissure length
SD	standard deviation
SIGN	Scottish Intercollegiate Guidelines Network
SNS	Support Needs System

Annex 1

Key questions used to develop the guidance

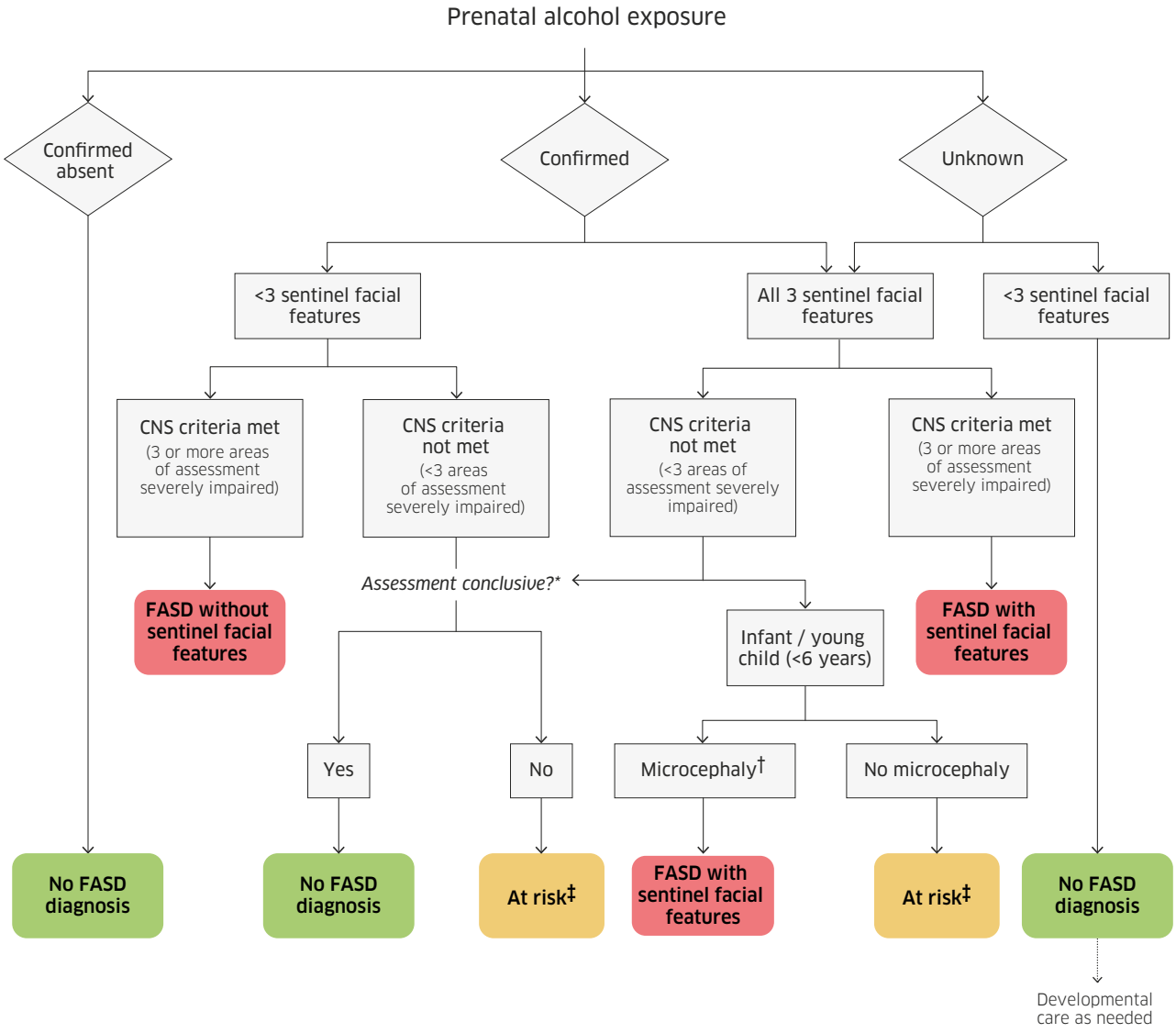
This guidance is based on a series of structured key questions that define the target population, the intervention, diagnostic test, or exposure under investigation, the comparison(s) used and the outcomes used to measure efficacy, effectiveness, or risk. These questions form the basis of the systematic literature search. With the exception of key question 1, insufficient evidence was identified to answer these questions and the majority of the recommendations in this guidance are adapted from the Canadian guideline for diagnosis of FASD which did not include recommendations on targeted screening or timing of diagnosis.[29]

Healthcare Improvement Scotland has published a synthesis of qualitative evidence on the experiences of caregivers looking after individuals with FASD to accompany this guidance which addresses key question 5.

1. How is alcohol consumption best measured and recorded (including methods of measurement, timing of measurement and information sharing between stakeholders)?
2. What social, medical and developmental factors in children are associated with a diagnosis of FASD?
    a) social history (eg foster care, maternal socioeconomic status, substance abuse among family members, parental history of criminal activity or domestic violence, maternal gravidity and parity, maternal age)
    b) medical and genetic history (eg hearing/visual impairment, cardiac effects, fragile X)
    c) physical examination (eg sentinel facial features, weight, height, microcephaly, skeletal effects)
    d) neurodevelopmental assessment (eg neuroanatomy, cognition, language, motor skills, memory, attention, executive function, affect)
    e) prenatal alcohol exposure
3. Should targeted screening or surveillance for FASD be carried out, and if so, how?
4. Does early diagnosis improve:
    a) any outcome for the child?
    b) odds of future normal pregnancy?
5. What is the impact on parents or carers of supporting individuals with FASD?

Annex 2

Diagnostic algorithm for FASD



* Assessment conclusive = clinician conducting the neurodevelopmental assessment is satisfied that the session was a true representation of the person's ability and that any deficits reported were not due to extenuating circumstances. Assessments may be inconclusive for children under six years of age, because some areas of assessment cannot be investigated with confidence until the person is older or because of other confounding factors, such as temporary life stress or illness.

† Microcephaly is not the only pathway to diagnosis for infants and young children; these individuals may also receive other FASD diagnoses, as specified elsewhere in the algorithm, if they show three areas of substantial impairment on neurodevelopmental tests.

‡ At risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure. An at-risk designation includes situations where a full neurodevelopmental assessment is not conclusive because of age or situational factors; therefore, FASD may not be the diagnoses. Clinical judgement is recommended.

Contribution of genetic factors should be considered in all cases and referral may be indicated in a typical cases or where PAE is uncertain.

Annex 3

Recommendations from the Canadian guideline

This guidance is adapted from the Canadian guideline for diagnosis of FASD.[29] While the guidance provides a rationale for revision to explain any changes which were made to each Canadian recommendation by the Scottish development group, the original unedited recommendations from the Canadian guideline are provided below for reference.

* **Strength of recommendation** The strength of a recommendation reflects the extent to which we can be confident that desirable effects of an intervention outweigh undesirable effects.

† **Quality of evidence** The quality of evidence reflects the extent to which confidence in an estimate of the effect is adequate to support a particular recommendation.

Screening, referral and support

Number	Recommendation	Strength*	Quality†
1.1	All pregnant and post-partum women should be screened for alcohol use with validated measurement tools by service providers who have received appropriate training in their use. Women at risk for heavy alcohol use should receive early brief interventions (ie counselling and/or other services).	Strong	High
1.2	Referral of individuals for a possible FASD diagnosis should be made whenever there is evidence of or suspected prenatal alcohol exposure at levels associated with physical or developmental effects.	Strong	Moderate

The medical assessment: family history, maternal alcohol history, physical examination, and differential diagnosis,

Number	Recommendation	Strength	Quality
2.1	The diagnostic process should include compiling a social and medical history and complete physical examination.	Strong	High
2.2	Confirmation of prenatal alcohol exposure requires documentation that the biological mother consumed alcohol during the index pregnancy based on: reliable clinical observation; self-report; reports by a reliable source; medical records documenting positive blood alcohol concentrations; alcohol treatment or other social, legal or medical problems related to drinking during the pregnancy. The presence of all 3 facial features has such high specificity to alcohol exposure and FASD that confirmation of alcohol exposure is not required when they are present. The presence of fewer than 3 facial features does not have the same degree of specificity and therefore requires other confirmation.	Strong	Moderate

2.3	The number of type(s) of alcoholic beverages consumed (dose), the pattern of drinking and the frequency of drinking should all be documented, if possible.	Strong	High
2.4	Sources for confirmed prenatal alcohol history must be reliable and devoid of any conflict of interest. Unsubstantiated information, lifestyle alone, other drug use or history of alcohol exposure in previous pregnancies cannot, in isolation, confirm alcohol consumption in the index pregnancy. However, co-occurring disorders, significant psychosocial stressors and prenatal exposure to other substances (eg smoking, licit or illicit drugs) in the index and previous pregnancies should still be recorded, based on the known interactions of these substances and their effects on pregnancy outcomes for both the mother and her offspring.	Strong	Moderate

Sentinel facial features

Number	Recommendation	Strength	Quality
3.1	The following three sentinel facial features must be present due to their specificity to prenatal alcohol exposure: • palpebral fissure length below the 3rd percentile or 2 standard deviations below the mean • philtrum rated 4 or 5 on the 5-point scale of the University of Washington Lip-Philtrum Guides • upper lip rated 4 or 5 on the 5-point scale of the University of Washington Lip-Philtrum Guides.	Strong	High
3.2	Associated features (abnormalities such as mid-face hypoplasia, micrognathia, abnormal position or formation of the ears, high arched palate, epicanthic folds, limb abnormalities, palmar crease abnormalities, short-upturned nose, etc.) should be recorded, but do not contribute to confirming or refuting an FASD diagnosis.	Weak	Moderate
3.3	Clinicians should refer to the following references, which can be used for real time measurement as well as photographic analysis, to measure palpebral fissure length: • 29–32 weeks[102] • 32–40 weeks[102,103] • 0–6 years[102] • 6–16+ years.[102,104,105]	Strong	High

The neurodevelopmental assessment

Number	Recommendation	Strength	Quality
4.1	A diagnosis of FASD is only made when there is evidence of pervasive brain dysfunction, which is defined by severe impairment in three or more of the following neurodevelopmental domains: • motor skills • neuroanatomy/neurophysiology • cognition • language • academic achievement • memory • attention • executive function, including impulse control and hyperactivity • affect regulation • adaptive behaviour, social skills, or social communication.	Strong	High
4.2	Severe impairment is defined as a global score or a major subdomain score on a standardized neurodevelopmental measure that is 2 or more standard deviations (SD) below the mean with appropriate allowance for test error. In some domains, large discrepancies among subdomain scores may be considered when a difference of this size occurs with a very low base rate in the population (≤3% of the population). Clinical assessment with converging evidence from multiple sources and DSM-5 diagnostic criteria for certain disorders may also be considered in specific domains which are not easily assessed by standardized tests. For example, in the affect regulation domain the following diagnoses may be taken as an indication of severe impairment: major depressive disorder (with recurrent episodes), persistent depressive disorder, disruptive mood dysregulation disorder (DMDD), separation anxiety disorder, selective mutism, social anxiety disorder, panic disorder, agoraphobia, or generalized anxiety disorder.	Strong	Moderate
4.3	Direct standardized measures should be used to assess brain domains whenever possible and this is recommended for the majority of evidence for brain dysfunction. We recognize, however, that in some cases it is not possible to use direct measures. In these situations, indirect assessment methods such as informant ratings, clinical interview, or historical assessment through file review may be used.	Strong	High
4.4	If historical assessment, clinical interview, or file reviews are used for indirect assessment (eg assessing adaptive behaviour) deficits should be considered by the team to be at a severity level equal to the clinical cut-off, which is defined as 2 standard deviations below the mean.	Strong	Moderate
4.5	When using indirect methods of assessment, clinicians should ensure that information comes from multiple sources rather than a single informant rating multiple domains of function.	Strong	High

Nomenclature and terminology

Number	Recommendation	Strength	Quality
5.1	A diagnosis of FASD may be made if an individual meets either of the two sets of criteria outlined below:	Strong	High
5.1.1	FASD with sentinel facial features • simultaneous presentation of the 3 sentinel facial features (short palpebral fissures, smooth philtrum and thin upper lip), **AND** • prenatal alcohol exposure (PAE) confirmed or unknown. This diagnosis should not be made when PAE is confirmed absent or at a level definitely below that known to be associated with physical and/or developmental effects, **AND** • evidence of impairment in 3 or more of the identified neurodevelopmental domains, or, in infants and young children, evidence of microcephaly. • Growth impairment and other alcohol-related birth defects should be documented if present. • Hereditary, prenatal and postnatal factors that may influence developmental outcome should be recorded.		
	OR		
5.1.2	FASD without sentinel facial features • evidence of impairment in 3 or more of the identified neurodevelopmental domains, **AND** • confirmation of prenatal alcohol exposure, with the estimated dose at a level known to be associated with neurodevelopmental effects. • Growth impairment and other alcohol-related birth defects should be documented if present. • Hereditary, prenatal and postnatal factors that may influence developmental outcome should be recorded.		
5.2	At risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure		
5.2.1	This is not a diagnosis; this is a designation that should be given to individuals when: • there is confirmation of prenatal alcohol exposure, with the estimated dose at a level known to be associated with neurodevelopmental effects, **AND** • CNS criteria 5.1.1 and 5.1.2 are not met • there is some indication of neurodevelopmental disorder in combination with a plausible explanation as to why the neurodevelopmental assessment results failed to meet the criteria for significant impairment (eg patient was too young; assessment was incomplete, etc).		

	• Growth impairment and other alcohol-related birth defects should be documented if present. • Hereditary, prenatal and postnatal factors that may influence developmental outcome should be recorded.		
5.2.2	This designation may also be considered for individuals with all 3 sentinel facial features of FASD as described in 5.1.1, who do not yet have documentation or evidence for the requisite 3 or more neurodevelopmental domain criteria or true microcephaly. *(See recommendation 4.2)*. This designation should never be considered when PAE is confirmed absent.		
5.3	FASD should now be used as a diagnostic term when prenatal alcohol exposure is considered to be a significant contributor to observed deficits that cannot be fully explained by other etiologies. Because the observed deficits are recognized as being multifactorial in origin, all other known relevant contributors (eg trauma, known genetic anomalies) should be documented with the FASD diagnosis as they have significant impact on the functional and neurological challenges of the affected individuals.	Weak	Low

The diagnostic team

Number	Recommendation	Strength	Quality
6.1	Core team members across the lifespan are: Infants (<18 months): • Paediatrician/Physician • Child development specialist who has the skill set to conduct physical and functional assessments (ie Speech-language pathologist, Physiotherapist, Occupational therapist, Clinical psychologist). Preschoolers (18 months–5 years) • Paediatrician/Physician • Occupational therapist • Speech-language pathologist • Psychologist School-aged children (6 years–age of majority) • Paediatrician/Physician with expertise in FASD and differential diagnosis • Occupational therapist • Speech-language pathologist • Psychologist Adults • Physician • Psychologist • Speech-language pathologist or Psychologist with expertise in language assessment.	Strong	High

6.2	Additional individuals who can provide valuable input into the diagnostic process may include addiction counsellors, childcare workers, cultural interpreters, mental health professionals, parents or caregivers, advocates, mentors, probation officers, psychiatrists, teachers, vocational counsellors, nurses, clinical geneticists or dysmorphologists, neuropsychologists, social workers, nurse practitioners and family therapists.	Strong	High

Special considerations in the neurodevelopmental assessment of infants and young children

Number	Recommendation	Strength	Quality
7.1	Infants and young children with all 3 sentinel facial features and microcephaly should be diagnosed with FASD with sentinel facial features; these children have a high risk of neurodevelopmental disorder. They should also be referred to a clinical geneticist.	Strong	High
7.2	Infants and young children with all 3 facial features may be diagnosed with FASD with sentinel facial features, if they undergo a comprehensive neurodevelopmental assessment and demonstrate deficits in 3 or more brain domains. Infants and young children with confirmed prenatal alcohol exposure may be diagnosed with FASD without sentinel facial features if they undergo a comprehensive neurodevelopmental assessment and demonstrate deficits in 3 or more brain domains.	Strong	Moderate
7.3	Infants and young children with confirmed prenatal alcohol exposure, but who do not meet the criteria for FASD should be designated as at risk for neurodevelopmental disorder and FASD, associated with prenatal alcohol exposure. Those with all 3 facial features, but no microcephaly, should be referred to a clinical geneticist.	Strong	High
7.4	A complete neurodevelopmental assessment should be recommended at an age-appropriate time for all infants and young children with confirmed prenatal alcohol exposure and/or all 3 facial features.	Strong	High

Special considerations in the neurodevelopmental assessment of adolescents and adults

Number	Recommendation	Strength	Quality
8.1	The diagnostic criteria for FASD are the same for adults as for younger individuals.	Strong	Moderate
8.2	When it is not possible to obtain a formal adaptive behaviour measure or when there is no suitable informant, historical or current information, derived from a file review may be used as a proxy.	Weak	Low
8.3	The length and structure of the assessment must accommodate the individual's needs and capacity. It is important to recognize, for example, if the client gets frustrated or tires easily; situational factors could invalidate the assessment.	Strong	Low

8.4	Recommendations following the assessment must address basic and immediate needs of the client, and assist them in accessing required resources.	Strong	Moderate
8.5	The core principles of bioethics, including autonomy and consent, confidentiality, beneficence, and non-maleficence must be carefully considered, especially when dealing with adults.	Strong	Moderate

Management and follow up

Number	Recommendation	Strength	Quality
9.1	Education about the impact of FASD and support for the patient and those involved with their care is recommended. The potential psychosocial issues that might be expected to develop as a result of receiving the FASD diagnosis should also be discussed. It is important that this information is communicated in a culturally sensitive manner using appropriate language.	Strong	High
9.2	A member of the diagnostic team should follow up within a reasonable length of time to ensure that the recommendations have been addressed and to provide further support, if needed.	Strong	Low
9.3	Individuals with FASD and their caregivers should be linked to resources that can improve outcomes. However, just because availability of services is limited, an individual should not be denied an assessment and management plan. Often the diagnosis is the impetus that leads to the developmental of resources.	Strong	Low
9.4	When young adults are transitioning to independent living situations, it may require that they undergo a reassessment to identify any changes in their adaptive function scores and to make any subsequent adjustments to their management plan.	Strong	Low

References

1 Bardsley D, Dean L, Dougall I, Feng, Qingyang, Gray L, Karikoski M, et al. The Scottish Health Survey. Edinburgh: National Statistics. The Scottish Government; 2017. (Volume 1). [cited 11 Oct 2018]. Available from url: https://www.gov.scot/publications/scottish-health-survey-2017-volume-1-main-report/

2 Changing Scotland's Relationship with Alcohol: A Framework for Action. Edinburgh: The Scottish Government; 2009. [cited 11 Oct 2018]. Available from url: https://www2.gov.scot/Publications/2009/03/04144703/0

3 Beattie JO, Day RE, Cockburn F, Garg RA. Alcohol and the fetus in the west of Scotland. Br Med J (Clin Res Ed) 1983;287(6384):17-20.

4 Plant ML. Drinking in pregnancy and fetal harm: results from a Scottish prospective study. Midwifery 1986;2(2):81-5.

5 Sulaiman ND, Florey CD, Taylor DJ, Ogston SA. Alcohol consumption in Dundee primigravidas and its effects on outcome of pregnancy. Br Med J (Clin Res Ed) 1988;296(6635):1500-3.

6 Jones KL, Smith DW, Ulleland CN, Streissguth P. Pattern of malformation in offspring of chronic alcoholic mothers. Lancet 1973;1(7815):1267-71.

7 May PA, Gossage JP, Kalberg WO, Robinson LK, Buckley D, Manning M, et al. Prevalence and epidemiologic characteristics of FASD from various research methods with an emphasis on recent in-school studies. Dev Disabil Res Rev 2009;15(3):176-92.

8 Lange S, Probst C, Gmel G, Rehm J, Burd L, Popova S. Global Prevalence of Fetal Alcohol Spectrum Disorder Among Children and Youth: A Systematic Review and Meta-analysis. JAMA Pediatr 2017;171(10):948-56.

9 Roozen S, Peters GJ, Kok G, Townend D, Nijhuis J, Curfs L. Worldwide Prevalence of Fetal Alcohol Spectrum Disorders: A Systematic Literature Review Including Meta-Analysis. Alcohol Clin Exp Res 2016;40(1):18-32.

10 Steer C. Fetal alcohol spectrum disorder – what are the social care needs? The picture of FAS in Scotland – surveillance and vignettes. Edinburgh: Proceedings of The Scottish Government; 2013.

11 Elliott EJ, Payne J, Haan E, Bower C. Diagnosis of foetal alcohol syndrome and alcohol use in pregnancy: a survey of paediatricians' knowledge, attitudes and practice. J Paediatr Child Health 2006;42(11):698-703.

12 Gahagan S, Sharpe TT, Brimacombe M, Fry-Johnson Y, Levine R, Mengel M, et al. Pediatricians' knowledge, training, and experience in the care of children with fetal alcohol syndrome. Pediatrics 2006;118(3):e657-68.

13 Nevin AC, Parshuram C, Nulman I, Koren G, Einarson A. A survey of physicians knowledge regarding awareness of maternal alcohol use and the diagnosis of FAS. BMC Fam Pract 2002;3:2.

14 Payne J, Elliott E, D'Antoine H, O'Leary C, Mahony A, Haan E, et al. Health professionals' knowledge, practice and opinions about fetal alcohol syndrome and alcohol consumption in pregnancy. Aust N Z J Public Health 2005;29(6):558-64.

15 McGlone L, Mactier H, Hassan H, Cooper G. In utero drug and alcohol exposure in infants born to mothers prescribed maintenance methadone. Archives of Disease in Childhood - Fetal and Neonatal Edition 2013;98(6):F542.

16 May PA, Marais AS, Gossage JP, Barnard R, Joubert B, Cloete M, et al. Case Management Reduces Drinking During Pregnancy among High Risk Women. Int J Alcohol Drug Res 2013;2(3):61-70.

17 Paley B, O'Connor MJ. Intervention for individuals with fetal alcohol spectrum disorders: treatment approaches and case management. Dev Disabil Res Rev 2009;15(3):258-67.

18 Rasmussen C, Andrew G, Zwaigenbaum L, Tough S. Neurobehavioural outcomes of children with fetal alcohol spectrum disorders: A Canadian perspective. Paediatr Child Health 2008;13(3):185-91.

19 Popova S, Lange S, Bekmuradov D, Mihic A, Rehm J. Fetal alcohol spectrum disorder prevalence estimates in correctional systems: a systematic literature review. Can J Public Health 2011;102(5):336-40.

20 Easton B, Burd L, Sarnocinska-Hart A, Rehm J, Popova S. The cost of lost productivity due to fetal alcohol spectrum disorder-related premature mortality. J Popul Ther Clin Pharmacol 2015;22(1):e3-8.

21 Streissguth A, Kanter J. The challenge of fetal alcohol syndrome: Overcoming secondary disabilities. Seattle and London: University of Washington Press; 1997.

22 Coons KD, Watson SL, Schinke RJ, Yantzi NM. Adaptation in families raising children with fetal alcohol spectrum disorder. Part I: What has helped. J Intellect Dev Disabil 2016;41(2):150-65.

23 Stratton K, Howe C, Battaglia FC. Fetal alcohol syndrome: Diagnosis, epidemiology, prevention, and treatment. National Academies Press; 1996.

24 Hoyme HE, May PA, Kalberg WO, Kodituwakku P, Gossage JP, Trujillo PM, et al. A practical clinical approach to diagnosis of fetal alcohol spectrum disorders: clarification of the 1996 Institute of Medicine criteria. Pediatrics 2005;115(1):39-47.

25 Hoyme HE, Kalberg WO, Elliott AJ, Blankenship J, Buckley D, Marais A-S, et al. Updated clinical guidelines for diagnosing fetal alcohol spectrum disorders. Pediatrics 2016;138(2):e20154256.

26 Astley SJ. Diagnostic guide for fetal alcohol spectrum disorders: the 4-digit diagnostic code. [cited 02/11/2018]. Available from url: https://depts.washington.edu/fasdpn/htmls/4-digit-code.htm

27 Bertrand J, Floyd RL, Weber MK, O'Connor M, Riley EP, Johnson KA, et al. Fetal Alcohol Syndrome: Guidelines for Referral and Diagnosis. Atlanta, GA: Centers for Disease Control and Prevention; 2004. [cited 05 Sep 2018]. Available from url: https://www.cdc.gov/ncbddd/fasd/documents/FAS_guidelines_accessible.pdf

28 Chudley AE, Conry J, Cook JL, Loock C, Rosales T, LeBlanc N. Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. CMAJ 2005;172(5 suppl):S1-S21.

29 Cook JL, Green CR, Lilley CM, Anderson SM, Baldwin ME, Chudley AE, et al. Fetal alcohol spectrum disorder: a guideline for diagnosis across the lifespan. CMAJ 2016;188(3):191-7.

30 American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Association Publishing; 2013.

31 Coles CD, Gailey AR, Mulle JG, Kable JA, Lynch ME, Jones KL. A Comparison Among 5 Methods for the Clinical Diagnosis of Fetal Alcohol Spectrum Disorders. Alcohol Clin Exp Res 2016;40(5):1000-9.

32 Bower C, Elliott E, on behalf of the Steering Group. Report to the Australian Government Department of Health: "Australian Guide to the diagnosis of Fetal Alcohol Spectrum Disorder (FASD)". 2016. [cited 21 Sep 2018]. Available from url: https://www.fasdhub.org.au/siteassets/pdfs/australian-guide-to-diagnosis-of-fasd_all-appendices.pdf

33 Abel EL, Hannigan JH. Maternal risk factors in fetal alcohol syndrome: provocative and permissive influences. Neurotoxicol Teratol 1995;17(4):445-62.

34 Anderson A, Hure A, Forder P, Powers J, Kay-Lambkin F, Loxton D. Predictors of antenatal alcohol use among Australian women: a prospective cohort study. BJOG 2013;120(11):1366-74.

35 Bobo JK, Klepinger DH, Dong FB. Identifying social drinkers likely to consume alcohol during pregnancy: Findings from a prospective cohort study. Psychol Rep 2007;101(3):857-70.

36 Leonardson GR, Loudenburg R, Struck J. Factors predictive of alcohol use during pregnancy in three rural states. Behav Brain Funct 2007;3(1):8.

37 Astley SJ, Bailey D, Talbot C, Clarren SK. Fetal alcohol syndrome (FAS) primary prevention through FAS diagnosis: II. A comprehensive profile of 80 birth mothers of children with FAS. Alcohol Alcohol 2000;35(5):509-19.

38 Astley SJ, Bailey D, Talbot C, Clarren SK. Fetal alcohol syndrome (FAS) primary prevention through FAS diagnosis: I. Identification of high-risk birth mothers through the diagnosis of their children. Alcohol Alcohol 2000;35(5):499-508.

39 Kvigne VL, Leonardson GR, Borzelleca J, Brock E, Neff-Smith M, Welty TK. Characteristics of mothers who have children with fetal alcohol syndrome or some characteristics of fetal alcohol syndrome. J Am Board Fam Pract 2003;16(4):296-303.

40 UK Department of Health, The Scottish Government, The Welsh Government, Northern Ireland Department of Health. UK Chief Medical Officers' Low Risk Drinking Guidelines. 2016. [cited 11 Oct 2018]. Available from url: https://www.gov.scot/Resource/0050/00504757.pdf

41 Day NL, Helsel A, Sonon K, Goldschmidt L. The association between prenatal alcohol exposure and behavior at 22 years of age. Alcohol Clin Exp Res 2013;37(7):1171-8.

42 Eckstrand K, Ding Z, Dodge N, Cowan R, Jacobson J, Avison M, et al. Persistent Dose-dependent Changes In Brain Structure In Young Adults With Low-to-moderate Prenatal Alcohol Exposure. Alcohol Clin Exp Res 2012;36(11):1892-902.

43 Jacobson S, Jacobson J. Light and moderate drinking during pregnancy are not good for your child. BJOG 2010;117:1151.

44 Olson HC, Streissguth AP, Sampson PD, Barr HM, Bookstein FL, Thiede K. Association of prenatal alcohol exposure with behavioral and learning problems in early adolescence. J Am Acad Child Adolesc Psychiatry 1997;36(9):1187-94.

45 Hannigan JH, Chiodo LM, Sokol RJ, Janisse J, Ager JW, Greenwald MK, et al. A 14-year retrospective maternal report of alcohol consumption in pregnancy predicts pregnancy and teen outcomes. Alcohol 2010;44(7-8):583-94.

46 Merlob P, Sharan H, Weiss S. Maternal Report of Prenatal Alcohol Use. Pediatrics 2003;111(2):443-4.

47 Ernhart CB, Morrow-Tlucak M, Sokol RJ, Martier S. Underreporting of alcohol use in pregnancy. Alcohol Clin Exp Res 1988;12(4):506-11.

48 Jacobson SW, Jacobson JL, Sokol RJ, Martier SS, Ager JW, Kaplan MG. Maternal recall of alcohol, cocaine, and marijuana use during pregnancy. Neurotoxicol Teratol 1991;13(5):535-40.

49 Morrow-Tlucak M, Emhart CB, Sokol RJ, Martier S, Ager J. Underreporting of alcohol use in pregnancy: relationship to alcohol problem history. Alcohol Clin Exp Res 1989;13(3):399-401.

50 Chartier KG, Vaeth PA, Caetano R. Focus on: ethnicity and the social and health harms from drinking. Alcohol Res 2013;35(2):229-37.

51 Dick DM, Bierut LJ. The genetics of alcohol dependence. Curr Psychiatry Rep 2006;8(2):151-7.

52 Mumenthaler MS, Taylor JL, O'Hara R, Yesavage JA. Gender differences in moderate drinking effects. Alcohol Res Health 1999;23(1):55-64.

53 Streissguth AP, Barr HM, Olson HC, Sampson PD, Bookstein FL, Burgess DM. Drinking during pregnancy decreases word attack and arithmetic scores on standardized tests: Adolescent data from a population-based prospective study. Alcohol Clin Exp Res 1994;18(2):248-54.

54 Burns E, Gray R, Smith LA. Brief screening questionnaires to identify problem drinking during pregnancy: a systematic review. Addiction 2010;105(4):601-14.

55 Howlett H, Abernethy S, Brown NW, Rankin J, Gray WK. How strong is the evidence for using blood biomarkers alone to screen for alcohol consumption during pregnancy? A systematic review. Eur J Obstet Gynecol Reprod Biol 2017;213:45-52.

56 McQuire C, Paranjothy S, Hurt L, Mann M, Farewell D, Kemp A. Objective measures of prenatal alcohol exposure: A systematic review. Pediatrics 2016;138 (3) (no pagination)(e20160517).

57 Parkes T, Atherton I, Evans J, Gloyn S, McGhee S, Stoddart B, et al. An evaluation to assess the implementation of NHS delivered Alcohol Brief Interventions: Final Report. 2011. [cited 11 Oct 2018]. Available from url: http://www.healthscotland.com/documents/5438.aspx

58 Skagerstrom J, Chang G, Nilsen P. Predictors of drinking during pregnancy: A systematic review. J Womens Health 2011;20(6):901-13.

59 Parkes T, Poole N, Salmon A, Greaves L, Urquhart C. Double exposure: a better practices review on alcohol interventions during pregnancy. [cited Available from url: http://bccewh.bc.ca/wp-content/uploads/2014/08/Double-Exposure.pdf

60 Goecke TW, Burger P, Fasching PA, Bakdash A, Engel A, Häberle L, et al. Meconium Indicators of Maternal Alcohol Abuse during Pregnancy and Association with Patient Characteristics. Biomed Res Int 2014;2014(11):702848.

61 British Medical Association. Alcohol and pregnancy preventing and managing fetal alcohol spectrum disorders. London: British Medical Association; 2007 updated 2016.

62 The Scottish Government. A guide to getting it right for every child [cited 18 July 2018]. Available from url: https://www2.gov.scot/Topics/People/Young-People/gettingitright/publications/practice-guide

63 The Scottish Government. Getting our priorities right: good practice guidance. [cited 18 July 2018]. Available from url: https://beta.gov.scot/publications/getting-priorities-right/

64 Astley SJ. Validation of the fetal alcohol spectrum disorder (FASD) 4-Digit Diagnostic Code. J Popul Ther Clin Pharmacol 2013;20(3):e416-e67.

65 Astley SJ, Clarren SK. Diagnosing the full spectrum of fetal alcohol-exposed individuals: introducing the 4-digit diagnostic code. Alcohol Alcohol 2000;35(4):400-10.

66 Cannon MJ, Dominique Y, O'Leary LA, Sniezek JE, Floyd RL. Characteristics and behaviors of mothers who have a child with fetal alcohol syndrome. Neurotoxicol Teratol 2012;34(1):90-5.

67 May PA, Gossage JP, Brooke LE, Snell CL, Marais A-S, Hendricks LS, et al. Maternal risk factors for fetal alcohol syndrome in the Western cape province of South Africa: a population-based study. Am J Public Health 2005;95(7):1190-9.

68 May PA, Gossage JP, Marais AS, Hendricks LS, Snell CL, Tabachnick BG, et al. Maternal risk factors for fetal alcohol syndrome and partial fetal alcohol syndrome in South Africa: a third study. Alcohol Clin Exp Res 2008;32(5):738-53.

69 DeRoo LA, Wilcox AJ, Drevon CA, Lie RT. First-trimester maternal alcohol consumption and the risk of infant oral clefts in Norway: a population-based case-control study. Am J Epidemiol 2008;168(6):638-46.

70 Jones KL, Hoyme HE, Robinson LK, Del Campo M, Manning MA, Prewitt LM, et al. Fetal alcohol spectrum disorders: extending the range of structural defects. Am J Med Genet A 2010;152(11):2731-5.

71 O'Leary CM, Elliott EJ, Nassar N, Bower C. Exploring the potential to use data linkage for investigating the relationship between birth defects and prenatal alcohol exposure. Birth Defects Res A Clin Mol Teratol 2013;97(7):497-504.

72 Astley SJ. Comparison of the 4-digit diagnostic code and the Hoyme diagnostic guidelines for fetal alcohol spectrum disorders. Pediatrics 2006;118(4):1532-45.

73 Foroud T, Wetherill L, Vinci- Booher S, Moore ES, Ward RE, Hoyme HE, et al. Relation over time between facial measurements and cognitive outcomes in fetal alcohol- exposed children. Alcohol Clin Exp Res 2012;36(9):1634-46.

74 Fang S, McLaughlin J, Fang J, Huang J, Autti- Rämö I, Fagerlund Å, et al. Automated diagnosis of fetal alcohol syndrome using 3D facial image analysis. Orthod Craniofac Res 2008;11(3):162-71.

75 Moore ES, Ward RE, Wetherill LF, Rogers JL, Autti- Rämö I, Fagerlund Å, et al. Unique facial features distinguish fetal alcohol syndrome patients and controls in diverse ethnic populations. Alcohol Clin Exp Res 2007;31(10):1707-13.

76 May PA, Gossage JP, Smith M, Tabachnick BG, Robinson LK, Manning M, et al. Population differences in dysmorphic features among children with fetal alcohol spectrum disorders. J Dev Behav Pediatr 2010;31(4):304-16.

77 Greenbaum R, Nulman I, Rovet J, Koren G. The Toronto experience in diagnosing alcohol-related neurodevelopmental disorder: a unique profile of deficits and assets. Can J Clin Pharmacol 2002;9(4):215-25.

78 Malisza KL, Buss JL, Bolster RB, de Gervai PD, Woods-Frohlich L, Summers R, et al. Comparison of spatial working memory in children with prenatal alcohol exposure and those diagnosed with ADHD; A functional magnetic resonance imaging study. J Neurodev Disord 2012;4(1):12.

79 Kully-Martens K, Denys K, Treit S, Tamana S, Rasmussen C. A review of social skills deficits in individuals with fetal alcohol spectrum disorders and prenatal alcohol exposure: profiles, mechanisms, and interventions. Alcohol Clin Exp Res 2012;36(4):568-76.

80 Rasmussen C. Executive functioning and working memory in fetal alcohol spectrum disorder. Alcohol Clin Exp Res 2005;29(8):1359-67.

81 Kodituwakku P. Defining the behavioral phenotype in children with fetal alcohol spectrum disorders: a review. Neurosci Biobehav Rev 2007;31(2):192-201.

82 Nash K, Sheard E, Rovet J, Koren G. Understanding fetal alcohol spectrum disorders (FASDs): toward identification of a behavioral phenotype. ScientificWorldJournal 2008;8:873-82.

83 Paintner A, Williams AD, Burd L. Fetal alcohol spectrum disorders—implications for child neurology, part 2: diagnosis and management. J Child Neurol 2012;27(3):355-62.

84 Manning MA, Hoyme HE. Fetal alcohol spectrum disorders: a practical clinical approach to diagnosis. Neurosci Biobehav Rev 2007;31(2):230-8.

85 Riley EP, Infante MA, Warren KR. Fetal alcohol spectrum disorders: an overview. Neuropsychol Rev 2011;21(2):73-80.

86 Paintner A, Williams AD, Burd L. Fetal alcohol spectrum disorders—implications for child neurology, part 1: prenatal exposure and dosimetry. J Child Neurol 2012;27(2):258-63.

87 McCarthy N, Eberhart JK. Gene–ethanol interactions underlying fetal alcohol spectrum disorders. Cell Mol Life Sci 2014;71(14):2699-706.

88 Ungerer M, Knezovich J, Ramsay M. In utero alcohol exposure, epigenetic changes, and their consequences. Alcohol Res 2013;35(1):37-46.

89 Archer T. Effects of exogenous agents on brain development: stress, abuse and therapeutic compounds. CNS Neurosci Ther 2011;17(5):470-89.

90 Grossman AW, Churchill JD, McKinney BC, Kodish IM, Otte SL, Greenough WT. Experience effects on brain development: possible contributions to psychopathology. J Child Psychol Psychiatry 2003;44(1):33-63.

91 Zhang X, Sliwowska JH, Weinberg J. Prenatal alcohol exposure and fetal programming: effects on neuroendocrine and immune function. Exp Biol Med (Maywood) 2005;230(6):376-88.

92 Davis KM, Gagnier KR, Moore TE, Todorow M. Cognitive aspects of fetal alcohol spectrum disorder. Wiley Interdiscip Rev Cogn Sci 2013;4(1):81-92.

93 Mattson SN, Crocker N, Nguyen TT. Fetal alcohol spectrum disorders: neuropsychological and behavioral features. Neuropsychol Rev 2011;21(2):81-101.

94 Glass L, Ware AL, Mattson SN. Neurobehavioral, neurologic, and neuroimaging characteristics of fetal alcohol spectrum disorders. Handb Clin Neurol 2014;125:435-62.

95 Mattson SN, Schoenfeld AM, Riley EP. Teratogenic effects of alcohol on brain and behavior. Alcohol Res Health 2001;25(3):185-91.

96 Kelly SJ, Day N, Streissguth AP. Effects of prenatal alcohol exposure on social behavior in humans and other species. Neurotoxicol Teratol 2000;22(2):143-9.

97 Bayley N. Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III). [cited 21 Sep 2018]. Available from url: http://www.pearsonclinical.com/education/products/100000123/bayley-scales-of-infant-andtoddler-development-third-edition-bayley-iii.html.

98 Chudley AE, Kilgour AR, Cranston M, Edwards M. Challenges of diagnosis in fetal alcohol syndrome and fetal alcohol spectrum disorder in the adult. Am J Med Genet C Semin Med Genet 2007;145C(3):261-72.

99 Chudley AE, Longstaffe SE. Fetal alcohol syndrome and fetal alcohol spectrum disorder. In: Cassidy S, Allanson J, editors. Management of genetic syndromes. 3rd ed. New York, NY: John Wiley and Sons, Inc; 2010. p.363-80.

100 Landgraf MN, Nothacker M, Heinen F. Diagnosis of fetal alcohol syndrome (FAS): German guideline version 2013. Eur J Paediatr Neurol 2013;17(5):437-46.

101 Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. Canadian Medical Association Journal 2010;182(18):E839-E42.

102 Thomas I, Gaitantzis Y, Frias J. Palpebral fissure length from 29 weeks gestation to 14 years. The Journal of pediatrics 1987;111(2):267-8.

103 Jones KL, Hanson JW, Smith DW. Palpebral fissure size in newborn infants. The Journal of pediatrics 1978;92(5):787.

104 Clarren SK, Chudley AE, Wong L, Friesen J, Brant R. Normal distribution of palpebral fissure lengths in Canadian school age children. Can J Clin Pharmacol 2010;17(1):e67-e78.

105 Strömland K, Chen Y, Norberg T, Wennerström K, Michael G. Reference values of facial features in Scandinavian children measured with a range-camera technique. Scandinavian journal of plastic and reconstructive surgery and hand surgery 1999;33(1):59-65.

ISBN 978-1-909103-67-2

SIGN 156

Healthcare Improvement Scotland

Edinburgh Office
Gyle Square
1 South Gyle Crescent
Edinburgh
EH12 9EB

0131 623 4300

Glasgow Office
Delta House
50 West Nile Street
Glasgow
G1 2NP

0141 225 6999