deutsche gesellschaft für humangenetik e.v.

Indication Criteria for Genetic Testing
Evaluation of validity and clinical utility

Indication criteria for disease:
Prader-Willi syndrome [SNRPN]

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2. Disease characteristics

2.1 Name of the Disease (Synonyms): *Prader-Willi syndrome*

2.2 OMIM# of the Disease: *176270*

2.3 Name of the Analysed Genes or DNA/Chromosome Segments:
SNRPN / #15q11-q13

2.4 OMIM# of the Gene(s): *182279*

2.5 Mutational Spectrum:
70% paternal deletion 15q11-q13,
25-30% maternal uniparental disomy 15 [upd(15)mat],
1% imprinting defect,
rarely a balanced translocation with breakpoint in the SNRPN locus.

2.6 Analytical Methods:
Methylation test, FISH, microsatellite analysis, MLPA

2.7 Analytical Validation
Parallel analysis of negative and positive controls

2.8 Estimated Frequency of the Disease in Germany
(Incidence at birth ("birth prevalence") or population prevalence):
Prevalence at birth 1:10,000 to 1:25,000

2.9 If applicable, prevalence in the ethnic group of investigated person:
not applicable

2.10 Diagnostic Setting:

	Yes.	No.
A. (Differential)diagnostics	☒	☐
B. Predictive Testing	☐	☒
C. Risk assessment in Relatives	☒	☐
D. Prenatal	☒	☐

Comment:

3. Test characteristics

		genotype or disease	
		present	absent
test	pos.	A	B
	neg.	C	D

A: true positives C: false negatives
B: false positives D: true negatives

sensitivity:	A/(A+C)
specificity:	D/(D+B)
pos. predict. value:	A/(A+B)
neg. predict. value:	D/(C+D)

3.1 **Analytical Sensitivity**
(proportion of positive tests if the genotype is present)
nearly 100%

3.2 **Analytical Specificity**
(proportion of negative tests if the genotype is not present)
nearly 100%

3.3 **Clinical Sensitivity**
(proportion of positive tests if the disease is present)
The clinical sensitivity can be dependent on variable factors such as age or family history. In such cases a general statement should be given, even if a quantification can only be made case by case.
nearly 100%

3.4 **Clinical Specificity**
(proportion of negative tests if the disease is not present)
The clinical specificity can be dependent on variable factors such as age or family history. In such cases a general statement should be given, even if a quantification can only be made case by case.
nearly 100%

3.5 **Positive clinical predictive value**
(life time risk to develop the disease if the test is positive).
nearly 100%

3.6 **Negative clinical predictive value**
(Probability not to develop the disease if the test is negative).
Assume an increased risk based on family history for a non-affected person. Allelic and locus heterogeneity may need to be considered.

Index case in that family had been tested:
nearly 100%

Index case in that family had not been tested:
Can only be resolved by analysis of the not afflicted individual.

4. Clinical Utility

4.1 (Differential)diagnosis: The tested person ist clinically affected
(To be answered if in 2.10 "A" was marked)

4.1.1 Can a diagnosis be made other than through a genetic test?

No. ☒ (continue with 4.1.4)
Yes, ☐
- clinically. ☐
- imaging. ☐
- endoscopy. ☐
- biochemistry. ☐
- electrophysiology. ☐
- other (please describe)

4.1.2 Describe the burden of alternative diagnostic methods to the patient

4.1.3 How ist the cost effectiveness of alternative diagnostic methods to be judged?

4.1.4 Will disease management be influenced by the result of a genetic test?

No. ☐

Yes. ☒

Therapy (please describe)	*Growth hormone, diet, sports, psychological care*
Prognosis (please describe)	*Despite good care and acceptance of aids rather poor. Therapy with growth hormone improves the fat/lean body mass relation and final hight.*
Management (please describe)	*Difficult, because in most cases there is only slight understanding of necessary measures.*

4.2 Predictive Setting: The tested person is clinically unaffected but carries an increased risk based on family history
(To be answered if in 2.10 "B" was marked)

4.2.1 Will the result of a genetic test influence lifestyle and prevention?

If the test result is positive (please describe)

If the test result is negative (please describe)

4.2.2 Which options in view of lifestyle and prevention does a person at-risk have if no genetic test has been done (please describe)?

4.3 Genetic risk assessment in family members of a diseased person
(To be answered if in 2.10 "C" was marked)

4.3.1 Does the result of a genetic test resolve the genetic situation in that family?
No.

4.3.2 Can a genetic test in the index patient save genetic or other tests in family members?
No.

4.3.3 Does a positive genetic test result in the index patient enable a predictive test in a family member?
No.

4.4 Prenatal diagnosis
(To be answered if in 2.10 "D" was marked)

4.4.1 Does a positive genetic test result in the index patient enable a prenatal diagnostic?
Yes.

5. If applicable, further consequences of testing
Please assume that the result of a genetic test has no immediate medical consequences. Is there any evidence that a genetic test is nevertheless useful for the patient or his/her relatives? (Please describe)
For the parents the result conveys clarity about the eventual cause of the disease.
It may bring relief from own feelings of guilt.
A positive test is prerequisite for growth hormone therapy.