

Worcestershire Clinical Commissioning Policy Collaborative Brief Technology Assessment:

Sperm DNA Fragmentation Testing

<p>Background</p>	<p>Mammalian fertilisation and subsequent embryo development depend in part on the integrity of sperm DNA. Damage to sperm DNA may occur as a result of oxidative stress, protamine deficiency and other causes. The association between sperm DNA damage and diminished reproductive outcomes has led to the development and introduction of sperm DNA integrity testing. This is not assessed as part of the current semen analysis undertaken and a separate test is required for this purpose. There are a variety of DNA fragmentation tests available.</p> <p>Sperm DNA damage is reported to be associated with:</p> <ul style="list-style-type: none"> • Less fertilised eggs • Poor embryo development • Poor cleavage resulting in repeated early miscarriage • Failed fertilisation/implantation • Reduced pregnancy rate
<p>Evidence to support the Technology</p>	<p>There is no national policy or guidance and the topic was not considered within the NICE Clinical Guideline 156: Fertility assessment and treatment, which, therefore does not address this issue.</p> <p>The European Association of Urology published Guidelines on Male Infertility in 2015. This guideline briefly refers to “DNA fragmentation in spermatozoa”, citing “There is increased DNA damage in spermatozoa from men with oligozoospermia. This increase is associated with reduced chances of natural conception and an increased chance of early pregnancy loss.”</p> <p>The Practice Committee of the American Society for Reproductive Medicine published the following review in 2013: The Clinical Utility of Sperm DNA Integrity testing: a guideline. This review involved a systematic literature search and concluded: There is insufficient evidence to recommend the routine use of sperm DNA integrity tests in the evaluation and treatment of the infertile couple. This is on the basis of the following summary from the literature review:</p> <ul style="list-style-type: none"> • Existing data do not support a consistent relationship between abnormal DNA integrity and reproductive outcomes. • At present, the results of sperm DNA integrity testing alone do not predict pregnancy rates achieved though natural conception or with IUI, IVF, or ICSI. However further research may lead to validation of the clinical utility of these tests. <p>A full evidence review has not been undertaken. There are many aspects to consider including:</p> <ul style="list-style-type: none"> • The relative efficacy of different sperm DNA fragmentation tests • The efficacy of the tests in terms of what they demonstrate, how the results impact on patient management and ultimately outcomes in terms of live births. This would need to be considered for the different patient cohorts that the test is indicated for. <ul style="list-style-type: none"> ○ The safety of the test and its wider implications for the management pathway. ○ The evidence to support use of anti-oxidants
<p>Future Pathways of Care</p>	<p>There is currently no local NHS use of sperm DNA fragmentation testing. The number of Worcestershire patients presenting to secondary care with infertility is unknown. The annual incidence of infertility is estimated at 1.2 couples per 1,000 total general population equating to around 690 couples per annum across Worcestershire.</p> <p>The number of patients considered eligible for sperm DNA fragmentation</p>

	<p>testing is likely to be significantly greater because the test may be offered outside of the NHS in a primary care setting and also because it will be offered to couples who would not be managed via the NHS infertility pathway.</p>
<p>Financial implications arising from new pathway of care</p>	<p>SpermComet® (one of the available tests) costs around £400 per test (privately)</p> <p>Additional costs in relation to the impact of the test result on the management of patients may also be significant, for example:</p> <ul style="list-style-type: none"> • the additional cost of ICSI over IVF treatment (around £300 per cycle) • the potential cost of anti-oxidants • the cost of assisted conception treatment for patients who would not otherwise be eligible (around £3,000 per cycle).
<p>Implications</p>	<p>The issues of relevance include:</p> <ul style="list-style-type: none"> • Implications for the NHS assisted conception pathway in terms of how and when the test would best be undertaken (appropriateness of primary care and acceptance in tertiary care). • The impact of the test results on sperm selection techniques and recommended assisted conception treatment (note: the current assisted conception policy would not necessarily allow for the outcome of the test results to influence the treatment offered to eligible patients ie. IVF or ICSI) • Proposed management of patients including potential for use of antioxidants (and evidence to support that this is safe and makes a difference in terms of outcomes) • Private vs NHS patients and potential risk of co-funding • Defining patients/couples likely to benefit and the impact of this on current pathways (for example recurrent miscarriage would not ordinarily meet the eligibility requirements of the assisted conception policy) • Reliability of the evidence associated with the SpermComet® test in terms of what the results demonstrate, the impact on treatment and subsequent outcomes.
<p>CCPC Recommendations</p>	<ol style="list-style-type: none"> 1. A preliminary review of readily available systematic reviews and advice from authoritative bodies suggests that there is currently insufficient evidence to support this technology in Worcestershire. 2. The Clinical Commissioning Policy Collaborative will reconsider this position should new evidence or national advice become available. At this time, NHS Providers wishing to use this test, should complete and submit a new technology application form for consideration by CCPC. In view of the specialist nature of this intervention and the existing local commissioning arrangements for assisted conception services, it would be expected that such an application/request is received from a specialist provider. 3. Where the test is offered through a private provider, the outcome will not be considered or used as part of any subsequent NHS related service. It is incumbent on the service provider to ensure that patients are aware of this at the outset. 4. Anti-oxidants and other recommended supplements may not be prescribed at NHS expense though General Practitioners in Worcestershire.
<p>Approved by Worcestershire CETs:</p> <p>NHS Redditch & Bromsgrove CCG 07/10/2015 NHS South Worcestershire CCG 13/10/2015 NHS Wyre Forest CCG 27/10/2015</p>	<p>Date to Initiate Review: October 2018</p> <p>Documents will be reviewed as a minimum every 3 years. However, earlier revisions to the policy may be made in light of published updates to local and national evidence of effectiveness and cost effectiveness and/or recommendations and guidelines from local, national and international clinical professional bodies.</p>