



## Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

<b>Topic exploration report number:</b>	TER354
<b>Topic:</b>	Processed or cadaveric nerve allografts (PNA) to repair peripheral nerve discontinuities for people with peripheral nerve damage.
<b>Summary of findings:</b>	<p>Health Technology Wales identified one NICE interventional procedures guidance entitled 'Processed nerve allografts to repair peripheral nerve discontinuities' published in 2017. Their search covered the period from their start to January 2017 and we have therefore searched for any additional evidence since January 2017.</p> <p>The guidance recommends that the evidence on the safety and efficacy of PNA was adequate to support the procedure provided that standard arrangements are in place for clinical governance, consent, and audit. The guidance also stated that for indications other than digital nerve repair, the procedure should only be used with special arrangements for clinical governance, consent and audit or research. The guidance recommendations were based on one randomised controlled trial (RCT), one non-randomised controlled trial, and six observational studies, although findings were mixed.</p> <p>We were able to review the full text of one additional systematic review. This review suggests that PNA and autografts may have similar outcomes. Although, the review suggests PNA may have fewer poor outcomes and lower complication rates than other types of grafts. We also identified two more recent primary studies reporting on failure rates for PNA. These studies suggest that failures may be higher than reported in studies included in the review.</p> <p>There are several uncertainties that could not be addressed in this report, including what comparators represents standard care in Wales, what other factors would influence procedural success, such as experience of the surgeon, and whether the intervention is cost-effective.</p>

## Introduction and aims

Autologous nerve grafting or autograft (using another nerve from the same patient) is usually used for people with peripheral nerve damage. PNA are nerves from deceased human donors that have had their immunogenic components removed using tissue processing techniques. The aim of the procedure is to bridge the peripheral nerve discontinuity to allow axonal regeneration and growth through the allograft towards the distal nerve (restoring the function of the damaged nerve). The procedure is done under general anaesthesia.

Health Technology Wales researchers searched for evidence on the safety and clinical effectiveness of PNA when compared to other graft types, such as autografts, conduit, and primary repair.

## Evidence overview

### Guidance

NICE produced interventional procedures guidance in 2017 on PNA to repair peripheral nerve discontinuities (NICE 2017). The guidance recommended that evidence on the safety and efficacy of PNA was adequate to support the procedure for digital nerves provided that standard arrangements are in place for clinical governance, consent, and audit. The guidance also stated that for other nerve sites (e.g., ulnar, radial, median) evidence was less clear and the procedure should only be used with special arrangements for clinical governance, consent and audit or research.

The guidance recommendations were based on one randomised controlled trial (RCT), one non-randomised controlled trial, and six observational studies and findings across studies were mixed. Evidence from the randomised controlled trial focused on patients needing digital nerve repair and this study reported significant improvements in some pressure tests, thermal sensation but null findings on other outcomes relating to pressure sensing, disability, and pain. The evidence on the safety of PNA to repair peripheral nerve discontinuities in other sites raised no major safety concerns.

### Systematic reviews

HTW researchers identified three systematic reviews on PNA published since the NICE guidance (Le Donne et al. 2022, Mauch et al. 2019, Pedrini et al. 2019). However, only one full text could be accessed during this topic exploration report (Mauch et al. 2019).

Mauch et al. (2019) aimed to examine the effectiveness of digital nerve gap reconstruction with PNA, autograft, and conduits compared to primary repair on sensory outcomes for patients with digital nerve damage. The review included 18 studies with four studies evaluating PNA. Two of these studies were referenced in the NICE guidance. The review reports that autograft and PNA repairs are superior to other approaches and have comparable outcomes based on average response on sensory measures, but they suggest that rates of poor outcomes are lower for PNA repairs. The review also reports that complication rates differ across interventions. PNA had fewer complications (3.0%) than autograft (5.7%) and conduit (10.9%) but more than primary repair (0.4%). It is important to note that the review did not use statistical tests to compare outcomes across interventions and there appeared to be differences in patient populations across the included trials which may have influenced their findings.

### Primary studies

We identified two primary studies published since the publication of the systematic review above about procedural failures. One retrospective case series of peripheral mixed nerve reconstruction

failures using PNA found that no patients (n=14) at their 10-month postoperative visit, had any motor or sensory improvement. Four patients underwent or were planned for subsequent revision surgery (Huddleston et al. 2021). Another study examined the clinical and histological findings in failed cases of PNA procedures (Thomson et al. 2021). Eight failed procedures were identified from a database of 99 separate allograft records on 74 patients.

#### *Economic evaluations*

We did not identify any economic evaluations relating to PNA.

### **Areas of uncertainty**

The evidence included in this report was based on a series of small-scale studies and the available review. A range of comparators appears to be used in trials of PNA and it is unclear which would represent standard care in Wales. Consideration of this and confirmation of currently used approaches in Wales would be needed in a fuller review.

Due to the nature of PNA, it is possible that there is variability in how procedures are completed and there may be an impact of surgeon skill and experience. These issues were not possible to explore in this report and would need to be explored more in a fuller review.

Finally, we did not identify any economic evaluations on the use of PNA and it is uncertain whether any improvements in clinical outcomes would translate into cost-effectiveness.

## Literature search results

### Health technology assessments and guidance

NICE. (2017). Processed nerve allografts to repair peripheral nerve discontinuities. Interventional procedures guidance [IPG597]. National Institute for Health and Care Excellence. Available at: <https://www.nice.org.uk/guidance/ipg597/> [Accessed 7 April].

### Evidence reviews and economic evaluations

Mauch JT, Bae A, Shubinets V, et al. (2019). A Systematic Review of Sensory Outcomes of Digital Nerve Gap Reconstruction With Autograft, Allograft, and Conduit. *Ann Plast Surg.* 82(4S Suppl 3): S247-s55. doi: 10.1097/sap.0000000000001851 <https://pubmed.ncbi.nlm.nih.gov/30855395/>

### Individual studies

Huddleston HP, Kurtzman JS, Connors KM, et al. (2021). A Retrospective Case Series of Peripheral Mixed Nerve Reconstruction Failures Using Processed Nerve Allografts. *Plast Reconstr Surg Glob Open.* 9(12): e3983. doi: 10.1097/gox.0000000000003983

Thomson C, Schneider JM, Pohl U, et al. (2021). Failed Acellular Nerve Allografts: A Critical Review. *Ann Plast Surg.* doi: 10.1097/sap.0000000000003055 <https://pubmed.ncbi.nlm.nih.gov/34864747/>

### Ongoing research

We did not identify any on-going trials relating to PNA that are due to be completed within the next six to 12 months.

**Date of search:**

April 2022

**Concepts used:**

Cadaveric nerve allografts; processed nerve allografts; allografts; peripheral nerve discontinuities; peripheral nerve damage