# Improving recruitment to clinical trials through closer respiratory monitoring in ALS/MND


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# Background

- Good recruitment is critical to the success of clinical trials
- Limited disease modifying options for people with MND should mean easier recruitment
- Eligibility for MND trials has been highly dependent on respiratory measurement;
  - Patients often fail to meet eligibility criteria – SVC not met

# Problems with Recruitment

Eligibility criteria

Access to electronic health records

Clinicians & researchers based at different sites

Patients living in remote areas

# Clinical Management of MND in WA

- Approximately 180 people living with MND in WA (MNDAWA 2019)
- 3 MND multidisciplinary team clinics in WA
- The method and frequency of respiratory testing varies across the 3 MND sites

# Our Trial

- Phase 2 clinical drug trial - 450 MND patients required globally
- Our site agreed to enrol 8 patients
- 10 patients screened (Sept 2018- April 2019)
- 2 patients (20%) were eligible
- 8 patients failed to meet all eligibility criteria
  - 6/8 patients failed on Slow Vital Capacity (SVC) criteria of 65-90%

# Objective

To increase clinical trial recruitment through close monitoring of respiratory function

# Clinical Questions:

- Do we have a trajectory of respiratory deterioration in MND?
- What are the recommended procedures for monitoring respiratory function?
- How often is respiratory function measured in WA?

# Monitoring respiratory function – what is recommended?

- "Routinely perform respiratory function tests (Forced Vital Capacity and where possible Sniff Nasal Inspiratory Pressure) in all MND/ALS patients in outpatient clinics"
- Advised:
  - As soon as diagnosis is made
  - Ongoing – 'routinely check for symptoms and signs of respiratory insufficiency'.
  - No specific frequency determined
  - Propose measure every 3 months

**Any recommendations for monitoring frequency since then?**

- Ref: Heffernan et al (2006)

# Guidelines

BMJ Best practice

" Monitoring for respiratory decline (FVC) is recommended every 3 months"

NICE guideline

**Respiratory function tests:**

- As part of the initial assessment to diagnose MND
  - forced vital capacity (FVC) or vital capacity (VC)[5]

# Guidelines cont.

A healthcare professional with appropriate competencies should perform the respiratory function tests every 2–3 months, although tests may be performed more or less often depending on:

- whether there are any symptoms and signs of respiratory impairment
- the rate of progression of MND
- the person's preference and circumstances. **[2010, amended 2016]**

**How does our current practice of clinical respiratory measurement in WA compare to these standards ?**

# What is current practice in WA?

- Site 1
  - Physiotherapist has access to portable spirometry device to use when required -'as and when' basis
  - Otherwise, patients are reviewed approximately every 3-4 months at Respiratory Clinic
- Site 2
  - Patients reviewed approximately every 3-4 months at Respiratory Clinic
- Site 3
  - Patients reviewed approximately every 3-4 months at Respiratory Clinic

# How do respiratory measures correlate?

- FVC ( Forced vital capacity) and SVC ( Slow Vital Capacity)
- Study in 2017 of consecutive patients with ALS and PLS from 2000-2014. Tests at baseline and 4 months. ( Pinto and Carvalho, 2017)
- FVC and SVC in sitting position
- Both FVC and SVC were strongly correlated at baseline and 4 months $r^2=0.98$
- Mean decrease of FVC 2.15 % per month and SVC 2.08% per month

**Can we use this data to screen those borderline patients more regularly to improve their access to clinical trials?**

- Ref: Pinto S and De Carvalho M. (2017)

# Example based on evidence of respiratory decline

- Screening FVC 94% - ‘too good’ for inclusion

- If we apply mean decrease of 2.15% per month then they are then eligible at 2 months.

| 1 month | 2 months | 3 months |
|---|---|---|
| 91.85% | 89.7% | 87.55% |

- Ref: Pinto S and De Carvalho M. (2017)

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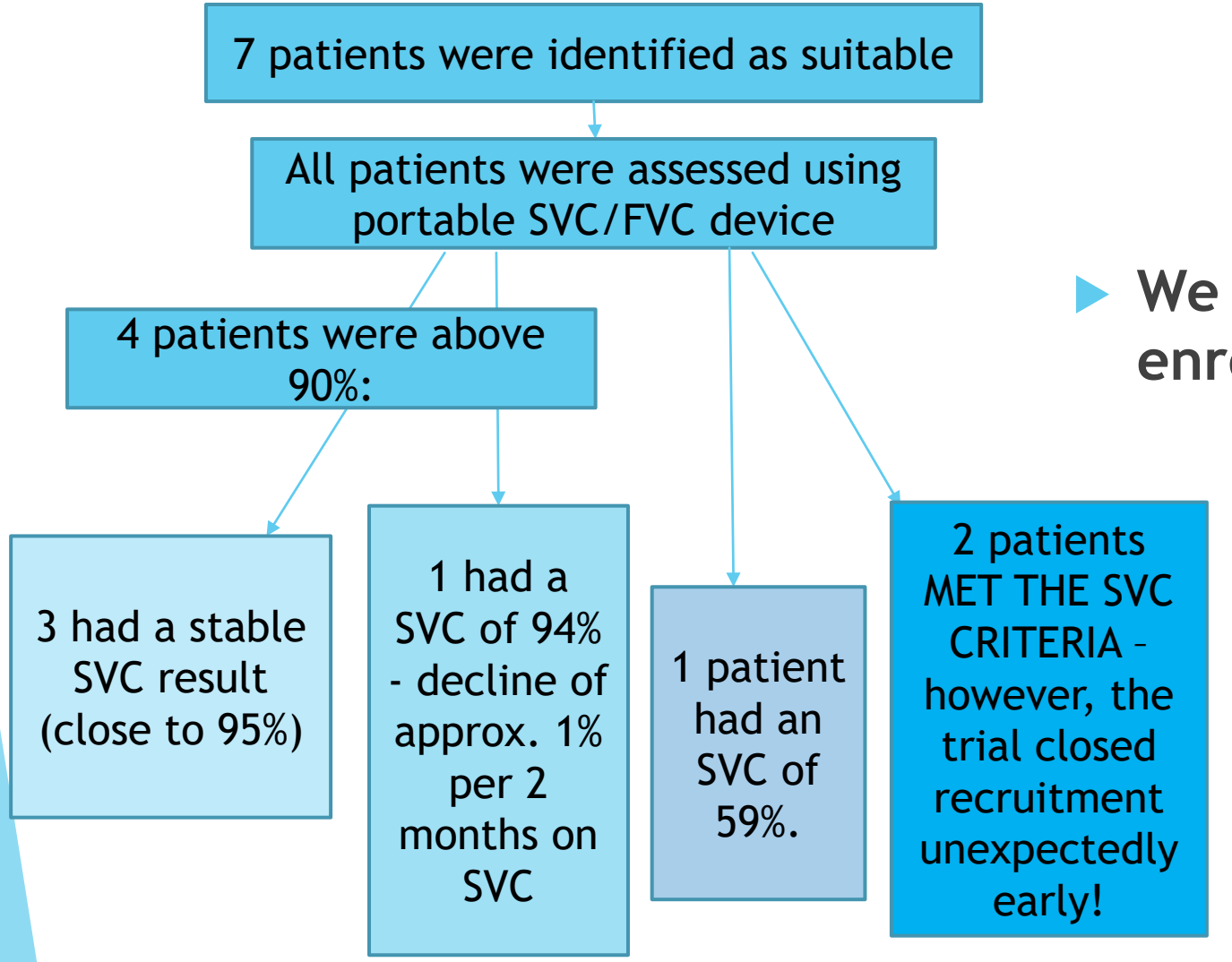
# Method

- Physiotherapist (PT) and & Speech Pathologist (SP) reviewed medical notes across 3 clinics between April & June 2019 to pre-screen potential patients

- PT/SP attended clinics to assess those patients identified as being close to but above  90% on recent respiratory measures- using portable spirometry device

# Results




- **We were unable to fulfil our enrolment goal.**

# So where to now?

We can’t change eligibility criteria for clinical trials BUT we can change our approach

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# Recommendations

SVC as ‘standard’ at MND clinic appointments

Clinical trials patient database

Earlier review of trial criteria

Education for AHPs

# Application of Recommendations

- Early tracking of SVC/FVC
- MND Database development
- Portable SVC assessment in clinics
  - Earlier detection of respiratory compromise
- Education for MDT AHPs

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# Thank you for listening!


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# Barriers to recommendations

- SVC **is not** routinely measured at MND Clinics
- Access to electronic medical records is a problem – consent issues as working across different health departments
- Patients who don't attend regular clinics may miss out on regular 'testing' and the opportunity to participate in trials
- There can often be a delay in receiving the eligibility criteria, which hinders our early planning
- Recruiting to clinical trials is not the main focus of MDT clinic