Care and Trial Site Registry – CTSR
A Powerful Tool for Clinical Research in Rare Diseases

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TREAT-NMD TGDOC meeting
Washington, December 2015
CTSR

I. Global database for feasibility enquiries
II. Temporary and/or regional questionnaires
III. Combination of the CTSR and the patient registries
I. Feasibility Database

Data collected:

- Patient cohorts of 32 diseases sub-divided into age groups
- Diagnostic tools
- Personnel and experience in clinical trials
- Equipment
- Care settings
- Research and education
- Networking
• openly accessible
• hosted by the University Medical Center Freiburg (Germany)

https://ctsr.uniklinik-freiburg.de
Number of sites since 2008
Neurodegenerative diseases

• In 2013 the CTSR expanded to cover NDD specialist centres.
  • Ataxias
  • Huntington’s
  • Hereditary spastic paraplegia
  • Fronto-temporal lobe dementia

• Part of the Neuromics project (www.rd-neuromics.eu)

• 75 NDD centres have registered (11 NDD only)
330 registered sites worldwide
Patient numbers since 2008
64,000 patients in 48 countries
CTSR Usage

In 2015:

- Four feasibility reports for major pharmaceutical companies
- Two surveys for UK patient organizations
II. Temporary and/or regional questionnaires

Flexible

Visible only to certain countries/centers

Examples:

- Country specific monitoring of care sites
- Find partners for projects
Muscular Dystrophy UK audit on neuromuscular services

- Second audit using the CTSR to collect data
- The first audit in 2012 resulted in 7 centers being recognized as Centres of Neuromuscular Clinical Excellence or Centres of Neuromuscular Clinical and Research Excellence
- 27 centers gave quite detailed answers to 23 questions

Section 1: Overview of service

Note: If you filled out the previous questionnaire in 2012, the data is shown below. Please check, if it is still up-to-date.

1. Name the consultants and allied health professionals directly involved in your service, their specialist expertise and the approximate number of hours per week devoted to the service.

2. Explain how patients from within your hospital trust and your local and more distant community access your services. Give average waiting times for urgent new; routine new and urgent follow-up consultations.

3. Approximately how many new referrals for each neuromuscular disease do you receive per year?

4. List all your regular clinics for adults and children. Describe which clinics provide a national service.
Muscular Dystrophy UK Audit 2015 Questions

• Name of the consultants, their expertise and the number of hours per week devoted to the service

• Average waiting times for urgent and routine consultations

• How many new referrals for each neuromuscular disease received per year

• Literature or websites produced by the center to inform patients about neuromuscular disease, its management and your services

• List of the centers 10 most important publications in the last three years

• Care plans

• Time taken up by non-health related issues

• …
Reach out to sites

- Contact sites via mail
- Gather information for a specific project through temporary questionnaire with restricted visibility

Example MYO-SEQ:

Search for undiagnosed patients with unexplained limb-girdle weakness for WES project

Restricted to Europe
**Patient identification:**

The project aims at the identification of patients aged 10 years and above with the characteristics listed below.

<table>
<thead>
<tr>
<th>Number of undiagnosed patients already known at your centre</th>
<th>n≤10</th>
<th>n&gt;10</th>
<th>n&gt;30</th>
<th>n&gt;50</th>
<th>Exact number if known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with elevated serum CK activity only</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients with at least 2 of the following characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• elevated serum CK activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• unexplained limb girdle weakness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• unexplained respiratory weakness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>WES data already generated</th>
<th>n≤10</th>
<th>n&gt;10</th>
<th>n&gt;30</th>
<th>n&gt;50</th>
<th>Exact number if known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients belonging to the above groups with WES data already generated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reimbursement policy</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>
Exome sequencing in 1000 patients with limb girdle weakness of unknown origin
- Older than 10 years
- Elevated serum CK activity

PI: Volker Straub
IV. CTSR and patient registries

• Complementary information, industry often requests information from both databases

• Two distinct sources of information

Patient registries:
– each entry represents a single patient
– more exact information on individual patient
– allows direct contact with individual patients

Care and Trial Site Registry:
– database of neuromuscular centres
– contains only the number of patients in an age group
– patient numbers are often only estimates
### Patient numbers

#### Example Duchenne in Germany

<table>
<thead>
<tr>
<th>CTSR</th>
<th>Patient registry</th>
<th>Approx. Prevalence (Incidence 1:3500 boys)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1303</td>
<td>857</td>
<td>2100</td>
</tr>
</tbody>
</table>
## Example SMA in Germany

<table>
<thead>
<tr>
<th>CTSR</th>
<th>Patient registry</th>
<th>Approx. Prevalence (Incidence 1:10000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>698</td>
<td>580</td>
<td>3000-4000 ?</td>
</tr>
</tbody>
</table>
CTSR outlook I

• Improve *geographic coverage* of CTSR:
  – Most but not all important neuromuscular centers are registered
  – Some countries are underrepresented

• Suggestion: Collaborate with registry curators to motivate national centres to register
  – CTSR could provide a list to national curators with all registered centres in a specific country
  – Curator could review the list and suggest additional centres
CTSR outlook II

- Improve **linkage** between CTSR and patient registries:
  - Currently two separate datasets
  - It is not known at which center an individual patient is seen

- Suggestion: Integrate information about care centre in patient registries
  - CTSR could provide a data file that patient registries could integrate as a dropdown menu
CTSR conclusions

• The CTSR is complementary to TREAT-NMD patient registries and is increasingly used by industry and academia

• Flexible application, which can be used for country specific monitoring of care sites or finding project partners

• Improving geographical coverage and linkage between patient registries and CTSR would further improve the utility of the CTSR
Thank you

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Kirsten König

Contact us: ctsr@uniklinik-freiburg.de