Towards clinical trial readiness and reduction of burden for Duchenne and Becker patients in the Netherlands

Two intertwined, standardized data collection projects

Introduction

Trial readiness and reduction of patient burden is essential in view of the number of compounds currently in development for Duchenne and Becker (DBMD) patients. This can be facilitated by collecting natural history data from clinical care. In 2016, the Duchenne Centre Netherlands (DCN) was founded to facilitate and integrate clinical care and research in the Netherlands. In the DCN, 3 academic partners (LUMC, Radboudumc and Kempenhaeghe-MUMC+) and the two patient organizations Duchenne Parent Project and Spierziekten Nederland collaborate and have set up six research projects including two intertwined projects on natural history data collection described here.

Project 1: Dutch Dystrophinopathy Database (DDD): a registry for all DBMD patients

Background: originally founded in 2008 by the LUMC with the aim to include all DBMD patients in the Netherlands. In 2019, the structure was renewed due to the DCN collaboration and new privacy regulations.

Design: we built 4 registration options of which only the first one is essential. See table 1.

Data management system: Castor EDC (web-based).

Privacy regulations: access can be granted to (de)decoded data separately, is supervised by a database manager and is approved by the DCN scientific advisory board.

Project 2: the Dutch Parell initiative, a national biobank

Background: the National Biobank is founded to integrate clinical care and research. Figure 1 shows an overview.

Design: standardized collection of clinical care data, prospectively and anonymized (including blood and urine samples). The dataset is consensus derived (between all 7 UMCs involved in DBMD care) and based on international DMD care guidelines. All UMC pediatric physiotherapists were trained according to international standards for clinical trials. Centers for Home Ventilation (CHVs) include a specific data set.

Data management system: each center has its own Castor system. SNOMED and HPO will be implemented to enhance information exchange under FAIR principles.

Privacy regulations: Data are coded in each center. Aggregated and anonymized data can be extracted after approval.

Table 1. Registration options in the DDD

<table>
<thead>
<tr>
<th>Option</th>
<th>Content</th>
<th>Reasoning</th>
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<tbody>
<tr>
<td>1.</td>
<td>Registration of name, contact details and disease.</td>
<td>Enabling the approach of patients for clinical trials</td>
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<td>2.</td>
<td>Yearly questionnaire on disease milestones and use of medication</td>
<td>Comprehensive insight in natural history and epidemiology</td>
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<td>3.</td>
<td>Store clinical data acquired as part of regular care (only for patients visiting one of the DCN centers for care).</td>
<td>Re-use of data, a reduction for patients and caregivers in participation of investigator-initiated studies</td>
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<td>4.</td>
<td>Exchange coded and aggregated data with non commercial partners</td>
<td>Participation in collaborations with academical partners and requests from, for example, TREAT-NMD</td>
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<td>5.</td>
<td>Exchange coded and aggregated data with commercial partners</td>
<td>International collaboration with commercial research</td>
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Conclusions

The two presented projects complement each other:

- Project 1 is a low-threshold national registry collecting personal data from all Dutch patients who want to be approached for new (clinical) trials.
- Project 2 is embedded in clinical care and provides the opportunity to collect longitudinal clinical data and blood and urine samples for biomarkers from a large cohort of Dutch DBMD patients from all ages, without predefined study end-points. This allows for research questions to be defined afterwards and data to be used as natural history controls in future studies.

Both projects will facilitate a more detailed understanding of the natural history of DBMD and the development of new outcome measures in the future.

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