

ECFS Neonatal Screening Working Group (NSWG)

Report for the Board, May 2014

It has been a busy year for the NSWG. The working group is going from strength to strength. With ongoing administrative support, there now is the resource to network and publicise the WG on a large scale. Attendance for the NSWG Annual Meeting is expected to rise from 70 in 2013 to 110 for 2014. We look forward to a productive meeting on the 11th June in Gothenburg and thank the ECFS for its continued support in the running of the WG meetings.

The most significant development for the WG has been the preparation of a bid (€3million) to the PTC6 funding stream of Horizon 2020. That bid (the CF EVE project) has been reviewed and we have been invited to submit a full application (deadline 19th August 2014).

Group members

We are now approaching 500 members on the NSWG database. Members come from a number of backgrounds, including physicians and scientists from across the globe.

Core Committee

The WG is co-ordinated by a Core Committee of volunteers,

- Kevin Southern (UK) (Co-ordinator)
- Jürg Barben (Switzerland)
- Carlo Castellani (Italy)
- Jeannette Dankert-Roelse (Netherlands)
- Silvia Gartner (Spain)
- Nataliya Kashirskaya (Russia) (New)
- Barry Linnane (Eire)
- Sarah Mayell (UK)
- Anne Munck (France)
- Dorota Sands (Poland)
- Olaf Sommerburg (Germany)

- Supported by Victoria Winters (UK)

Specific Aims of Working Group:

1. To support the implementation of newborn screening (NBS) for CF
2. To monitor performance and compare protocols to optimise effectiveness, whilst reducing negative impact
3. To encourage enrolment of all infants identified through NBS in clinical trials
4. To determine the optimal management of infants with an equivocal diagnosis following newborn screening

Broader objectives

1. To work in an open and inclusive manner
2. To encourage membership of the ECFS
3. To encourage participation from countries outside the EU

Progress report for each specific aim:

1. *To support the implementation of NBS for CF.*

This is the primary aim of the WG and is being addressed by the following:

- A. We are continuing to improve on our information network through the database. We now have 47 key country contacts in 36 countries.
- B. We have assisted in publishing the following – the Clinical Laboratory Standards Institute “Newborn Screening for Cystic Fibrosis; Approved Guidelines” (see attached document) (Carlo Castellani, Olaf Sommerburg, Kevin Southern).
- C. The Core group has produced the Standards of Care for Newborn Screening for CF
- D. Data from the Survey 2013 has now been analysed and will be presented at the poster session at the ECFC 2014. We aim to publish the results by the end of the year
- E. This year’s newsletters have included reports from Russia, Poland and on the New Standards for Early Life Care for infants screened for Cystic Fibrosis
- F. Support at international and national meetings. Meetings within the past year have included;
 - i. ECFS NSWG Annual Meeting, Lisbon, Portugal June 2013
 - ii. Diagnostic Network Working Group Annual Meeting Berlin February 2014
 - iii. The Latin America Meetings Lisbon 2013 and Gothenburg 2014
 - iv. Horizon 2020 CF-Eve Project Meeting Liverpool June 2014

2. *To monitor performance and compare protocols*

We will address this specific aim through the following strategies

- A. The database is in constant use as a functional tool to interact with WG members
- B. The Standards of Care for NBS have been developed. These were produced by a Delphi consensus methodology and reflect the comments of all members of the Core Committee.
- C. The Working Group has been involved in the application of Horizon 2020 bid. See appendices.
- D. NSWG Survey 2013 – results to be publish by year end
- E. Provided support to Jürg Barben (Switzerland) on a short questionnaire "Structures NBS for CF in Europe" – the findings were presented at the Diagnostic Network Working Group Meeting in Berlin (February 2014)

3. *To encourage enrolment of all infants identified in clinical trials*

This aim is being addressed by the following

- A. Establish close links with emerging registries. Provide database information for the purpose of encouraging recruitment to clinical trials, working closely with the ECFS Clinical Trials Network.
- B. CF START – A UK trial to examine routine use of anti-staphylococcal antibiotic prophylaxis. A £1.4 million application has been submitted to the UK HTA.

4. *To determine the optimal management of infants with an equivocal diagnosis following newborn screening*

This aim is being addressed by the following:

The consensus process for Equivocal Diagnosis is now complete (appendices attached).

- A. Core statements were produced to establish clear guidance on the managements of these infant. (Shawcross, Southern and Mayell). We emailed the working group with 32 statements split between two groups:
 - i. Group A (Infants with 2 CFTR gene mutations, one of which has unclear clinical significance, and a normal sweat test $\leq 29\text{mmol/L}$)²
 - ii. Group B (Infants with an intermediate sweat test result (sweat chloride 30-59mmol/L) and 0 or 1 CFTR mutations).
- B. We worked with the CFF Special Interest Group (NBS) to form a global consensus on terminology and management of these infants. Richard Parad (Boston) contributed to the Delphi methodology.
- C. Overall there were 85 contributors to the Delphi Process with a core group of 7 (Kevin Southern, Jürg Barben, Nico Derichs, Sarah Mayell, Anne Munck, Richard Parad, Anna Shawcross)

- D. Out of thirty-two statements, at the end of the Delphi Consensus process 31 reached consensus with some modified.
- E. As part of the process the group took part in a designation exercise on how to “label” these infants. The group came to the conclusion that Cystic Fibrosis Screen Positive, Inconclusive Diagnosis (CFSPID) should be used (the term “equivocal” did not translate well into other languages)
- F. Results of the Equivocal Diagnosis Process to be presented at the NSWG Annual meeting by Anne Munck and at the ECFC by Sarah Mayell.

The term CF-SPID, to describe infants in this situation, is an important output from the WG.

Challenges achieved

1. An information network for members of the NSWG is now established
2. The Delphi process for “the Guidelines on the Management of Infants with an Equivocal Diagnosis following Newborn Screening for Cystic Fibrosis” - completed
3. Newborn Screening for Cystic Fibrosis - Standards of Care - completed
4. Data for the ECFS NSWG Survey 2013 collected – to be presented at the poster session at the ECFC
5. Ongoing regular WG newsletters
6. Through to the second stage for the Horizon 2020 Bid - Antenatal and newborn screening for cystic fibrosis (CF); Evaluating Validity and Effectiveness (CF-EVE)
7. A short survey on the “Structures of Newborn Screening for CF in European Countries with a National programme” – completed and presented at the DNWG Annual Meeting

Challenges on-going

1. In countries with NBS, supply annual progress reports for a database
2. To record the protocol undertaken in each country that has a regional programme (2013 Survey)
3. To record performance as determined by population screened and results (information being gathered by the 2013 Survey), including
 - a. Number of infants diagnosed with CF through NBS
 - b. Number of infants with an equivocal diagnosis following NBS
 - c. Number of assessments/sweat tests (and results when available)
 - d. Number of false negative NBS tests (true, meconium ileus or equivocal)
 - e. Incidence of CF
4. Key workers will be encouraged to join the ECFS and become members of the Core Group
5. To liaise with national and European Registry Groups to collect longer term outcome data (some crossover with the Diagnostic Network on this project)
6. To develop and maintain resources to support implementation
7. Paper to be completed by year end for the 2013 Survey

The success of CF EVE will provide an invaluable resource to determine the most effective and cost effective method to screen newborns for CF (see attached preliminary application).

Appendix

1. Application for Horizon 2020 Bid – CF-EVE.
2. The Clinical Laboratory Standards Institute “Newborn Screening for Cystic Fibrosis; Approved Guidelines”
3. The Delphi process for “the Guidelines on the Management of Infants with an Equivocal Diagnosis following Newborn Screening for Cystic Fibrosis”
4. The Standards of Care Document, which will be published with the Standards for other CF related topics.