



Dysmorphology Diagnostic System (DDS)

Pilot Study

(19.12.08 – 30.04.09)

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DYSCERNE: A Network of Centres of Expertise for Dysmorphology

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DDS Pilot Study Report: Summary

Introduction

- The pilot of DYSCERNE's Dysmorphology Diagnostic System (DDS) started on Friday, 19th December 2008 and ran until 30th April 2009 (19 weeks). DYSCERNE Expert Case Reports (DECERs) produced after 30th April 2009, for cases submitted during the pilot are included in this report.

Methodology

- The pilot was split into 3 phases (table 1) to allow the Coordinating Centre to offer maximum support to the participants of each phase as they familiarised themselves with the DDS.

Table 1. Phases of DDS Pilot

Pilot Phase	Dates	No. of Submitting Nodes	No. of Expert Panel members
1	19.12.08 – 17.02.09	7	11
2	18.02 – 19.03.09	7	26
3	20.03 – 30.04.09	22	26

- **Phase 1** involved 7 Submitting Nodes (the DYSCERNE Partner Centres: Leuven, Manchester, Marseille, Nijmegen, San Giovanni Rotondo and Warsaw; plus an additional, non-partner, Istanbul) submitting 1-2 cases for review by the DYSCERNE Partner clinicians.
- **Phase 2** increased the number of Experts able to review cases to include all Expert Panel members.
- During **Phase 3** Case Submitter access was extended to all members of the DDS Expert Panel, giving an additional 15 Submitting Nodes (table 1).
- The duration of the pilot was extended from the originally planned 8 weeks to 19 weeks, partly to allow for what was expected to be a slow start to the pilot over the Christmas period, but also to give the participants of each phase time to fully familiarise themselves with the system before introducing new users who would require support from the Coordinating Centre.
- Throughout the pilot the DYSCERNE Coordinating Centre provided support for DDS users via email and telephone as required.

Overview of the DDS workflow

- **Case Submission**
 - Patient Information & Consent forms were distributed to all Submitting Nodes. Translations were available in Dutch, English, French, Italian and Polish. There are 3 different levels of patient consent:
 - DDS only: patient details submitted to DDS only
 - DDS Archive: the patient details submitted to the DDS may be stored in the DDS archive
 - Scientific meeting: the patient details submitted to the DDS & stored in the DDS archive, may also be presented at scientific meetings
 - Submitting Nodes completed the online case submission form with the patient's clinical details. Clinical images were uploaded and submitted to the DDS along with the case submission form.

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• Internal Review

- Submitted cases were reviewed by the DYSCERNE Clinical Fellow to make sure they were suitable for the DDS and that enough information had been provided.
- The outcome of the Internal Review for a case could be abandoned, returned to the case submitter or accepted onto the DDS.

• Expert Review

- Members of the Expert Panel reviewed the anonymised details of accepted cases and submitted their opinions on an Expert Case Review form or via the secure discussion forum available for each case.

• Production of the DYSCERNE Expert Case Report (DECR)

- The DECR was compiled by the DYSCERNE Clinical Fellow from the opinions received from Expert Panel members, and sent to the relevant Submitting Node.
- A provisional deadline for the production of the DECR was set at 4 weeks after case acceptance. However, because for some cases only a small number of Expert reviews had been received by this time, the deadline was extended so that the reports would be as comprehensive and clinically informative as possible.

Results

Case Submission

- A total of 23 cases were submitted to the DDS during the 19 weeks of the pilot (figure 1.), an average of 5 per month.

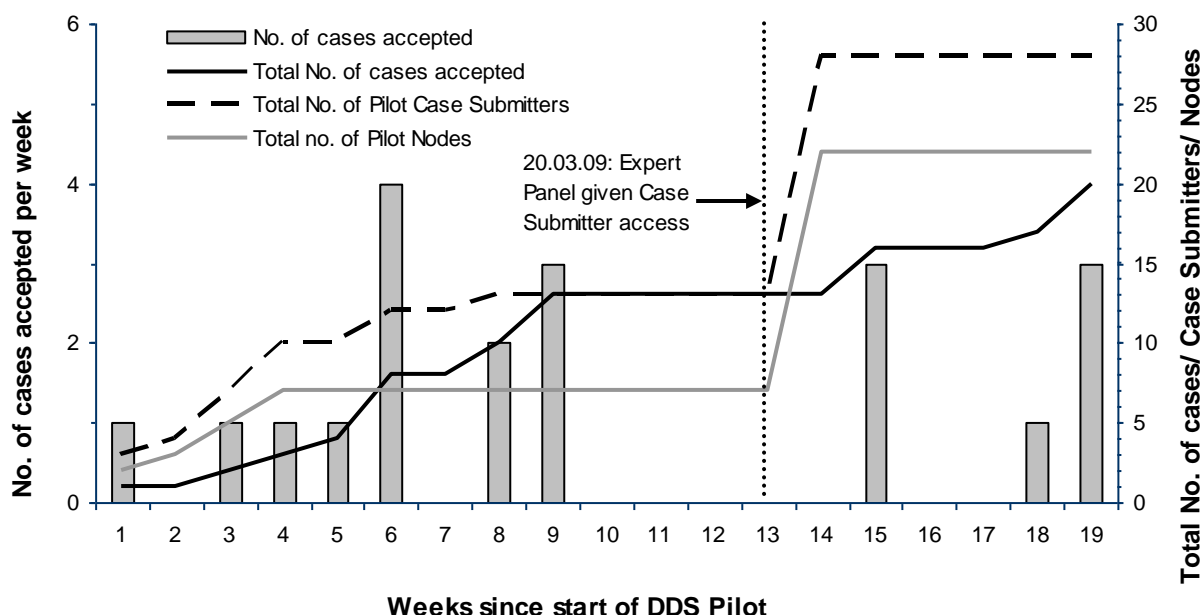


Figure 1. Number of case submitters and cases submitted per week

- Of the 20 patients whose cases were accepted during the pilot, a total of 10 (50%) consented to the storage of their medical details in the DDS archive.

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Internal Review

- Of the 23 submitted cases a total of 20 cases (87.0%) were accepted onto the DDS (7 at the 1st internal review and 13 after receipt of additional information). Three cases were abandoned due to duplicate or incomplete cases submissions.
- All cases received a final internal review decision within 8 working days (= 0.6 x full time) with over 82% being within 3 working days.

Expert Review

- The number of cases reviewed by Expert Panel members that took part in the pilot study ranged from 1 to 11, with 9 Experts reviewing 5 or more cases, and the average being 4.8.
- During the pilot the number of Expert reviews per case ranged from 2 to 10, with over half the cases receiving 5 or more reviews (figure 2), and the average being 5.1 reviews per case.

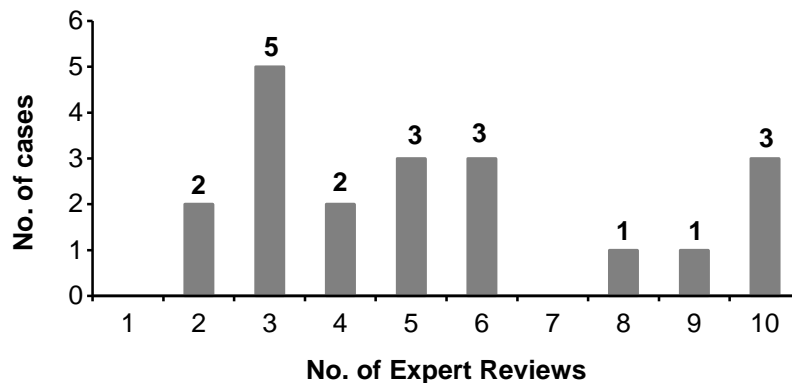


Figure 2. Number of Expert Reviews (ECR & DF)

Production of the DYSCERNE Expert Case Report (DECR)

- The original 4 week (28 days) deadline for production of DECRs was met for 8 out of the 20 (40%) submitted cases. On average DECRs were prepared 6 weeks (40 days) after case acceptance, depending on the timing & number of reviews received, with 80% completed within 8 weeks (56 days).
- All DECRs produced during the pilot were updated at the end of the pilot with any additional Expert reviews that had been received; the updated DECR was sent to the case submitters.
- **Clinical analysis:**
 - All the cases (100%) had further tests or investigations recommended, with 19 (95%) cases having a gene test suggested. The number of tests/ investigations suggested per case ranged from 1 to 5 per case (figure 3), with the average being 3.1.
 - All the cases (100%) had diagnoses suggested. The number suggested per case ranged from 1 to 7 (figure 4) with the average being 2.5 diagnoses per case.
 - All the cases (100%) could be described as complex phenotypes with combinations of dysmorphic features, varying congenital abnormalities affecting different body systems and a range of neurocognitive disabilities.
 - One case had confirmation of the suggested DDS clinical diagnosis of Coffin Lowry syndrome at a molecular level by the identification of a RSK2 mutation.

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- Two cases (a sibling pair) represent a possible new recessive condition which was recommended by the expert panel for publication as a case report.

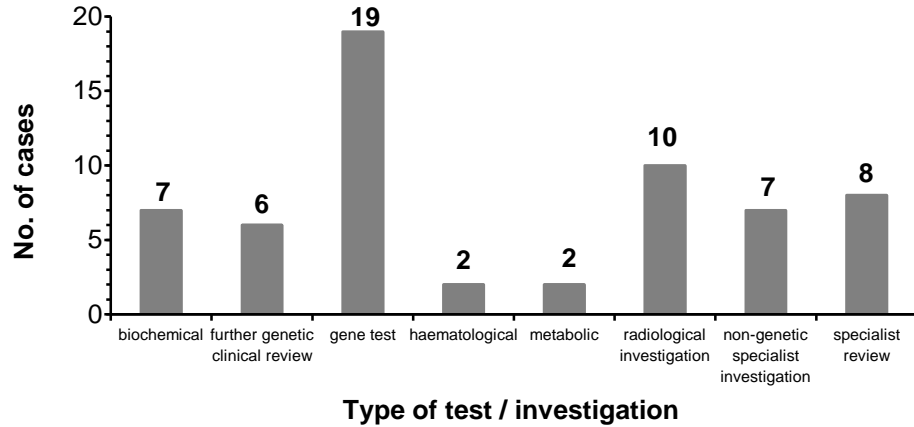


Figure 3: Types of test / investigation suggested by Expert Panel members

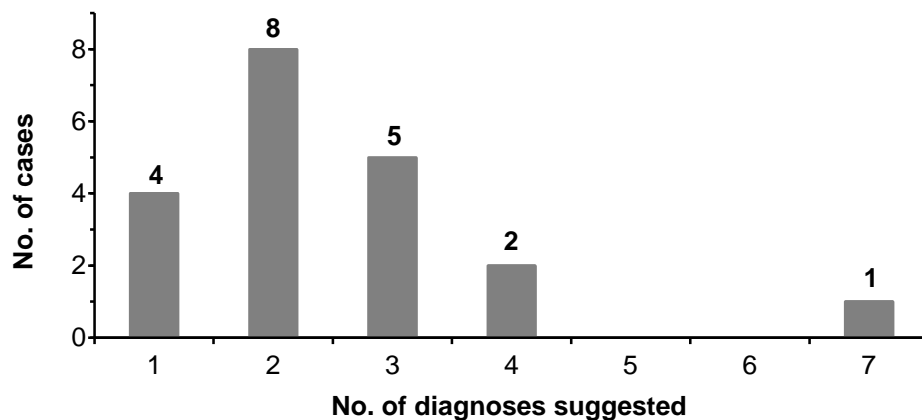


Figure 4: Number of diagnoses suggested by Expert Panel members

Discussion

Case submission

- Despite some issues noted by users overall case submission was less problematic than anticipated with a number of case submitters commenting that it was easier than they had expected.

Internal Review

- It is expected that as individual case submitters gain access to the DDS and become familiar with the case submission form and case submission requirements, the need to abandon or return cases at internal review while still occasionally arising, will occur less often.
- A more detailed section on how to complete a case submission form was written, which highlighted the most common reasons for returning cases, and is included in the 'Guides to the DDS' for Case Submitters and Expert Panel members.

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Expert Review

- A number of issues were noted by individual members of the Expert panel and also by the DYSCERNE Clinical Fellow and DDS Administrator. Discussions with the software company regarding these have been ongoing and a number of improvements are planned to the DDS software.

Production of the DYSCERNE Expert Case Report (DECR)

- A provisional 4 week deadline was set for the Expert Review of DDS cases. The number of Expert Reviews for each case was reviewed periodically by the DYSCERNE Clinical Fellow who, together with the DDS Administrator, took a decision on whether to extend the deadline for Expert Reviews if only a small number of Experts had reviewed a case. As it took longer than expected for the majority of the Expert Panel members to begin actively reviewing cases, the 4 week deadline was not met for over half of the cases (12 out of 20, 60%) submitted during the pilot. This should however be considered in the context of the more traditional route for such cases which would be presentation at national and international dysmorphology meetings, a process which can take many months.
- **Clinical Analysis.** Correct diagnosis and identification of a possible new recessive condition in a total of 3 out of 20 (15%) cases provides evidence that the system is viable and effective. These successes were fed back to the Expert Panel via email. Future feedback on clinical outcomes following DDS recommendations will partly be dependant on clinician input. It is also planned to periodically review cases and send relevant updates to the Expert Panel members.

Conclusions

- Improvements to the DDS software are underway and a new release is currently planned for late summer 2009, which will address a number of the problems highlighted by the pilot study. Further releases are planned for later in the year which will allow any additional issues to be addressed.
- Moving towards the full launch of the DDS, the remaining 54 proposed Submitting Nodes were invited to apply for DDS accounts from the beginning of April 2009 and by the end of May 2009, 34 of these centres had done so, giving a current total of 56 centres that are able to submit cases to the DDS.
- **Despite the full DDS workflow not being supported by the software during the pilot, this study has shown that the DDS is a viable and effective diagnostic system which will facilitate timely and equitable access for clinicians from across Europe to expert opinions, increasing capacity and accuracy of diagnoses and decreasing time from presentation to diagnosis.**