

IST-2004-027749

HeC

Health-e-Child

Instrument: Integrated Project
Thematic Priority: IST

D9.2 Status report on database population and data collection status

Due date of delivery: 30 June 2009
Actual Submission date: 13 August 2009

Start date of project: 1 January 2006
Ending: 31 December 2009

Organisation name of lead contractor for this deliverable: P03IGG - I.R.C.C.S. Giannina Gaslini

Revision 4

Project co-funded by the European Commission within the FP6 (2002-2006)		
Dissemination level		
PU	Public	X
PP	Restricted to other programmes participants	
RE	Restricted to a group specified by the Consortium	
CO	Confidential	

Document Classification

Title	Status report on database population and data collection status
Deliverable	9.2
Reporting Period:	Month 30 - Month 42
Authors	Dr. Anwar Baban, Dr. Gianluca Trocchio, Prof. Giacomo Pongiglione
Work package	9
Version	1
Keywords	Data collection, Database population

Document History

Name	Remark	Version	Date
Anwar Baban		V 1	12.08.2009
Gianluca Trocchio		V 2	12.08.2009
Giacomo Pongiglione		V 3	12.08.2009

Health-e-Child Consortium

The partners in this project are:

- 01 Siemens AG (Siemens)
- 02 Lynkeus Srl (Lynkeus)
- 03 I.R.C.C.S. Giannina Gaslini (IGG)
- 04 University College London – Great Ormond Street Children’s Hospital (UCL)
- 05 Assistance Publique Hopitaux de Paris – Necker (APHP)
- 06 Ospedale Pediatrico Bambino Gesù (OPBG)
- 06 European Organisation for Nuclear Research (CERN)
- 09 University of the West of England (UWE)
- 10 University of Athens (UoA)
- 11 Università degli Studi di Genova (DISI)
- 12 The French National Institute for Research on Computer Science and Control (INRIA)
- 13 European Genetics Foundation (EGF)
- 14 Aktsiaselts ASPER BIOTECH (Asper)
- 15 Gerolamo Gaslini Foundation (FGG)
- 16 Maat G Knowledge (MAAT)
17. I.R.C.C.S. Ospedale Pediatrico Bambino Gesù (OPBG)



List of contributors

Name	Affiliation	Co-author of:
Giacomo Pongiglione	OPBG	
Maurizio Marasini	IGG	
Alberto Martini	IGG	
Anwar Baban	IGG	
Gianluca Trocchio	IGG	
Clara Malattia	IGG	
Maria Luisa Garrè	IGG	
Valeria Capra	IGG	
Andrew Taylor	UCL	
Patricia Woo	UCL	
Katherine Owens	UCL	
Younes Boudjemline	APHP	
Julie Blanc	APHP	
Ilona Alova	APHP	
Pierre Quartier	APHP	
Sonia Volpe	OPBG	
Ludmilla Mantione	OPBG	
Elisabetta Cortis	OPBG	
Claudia Bracaglia	OPBG	

List of reviewers

Name	Affiliation

Table of contents

1. Introduction	5
2. Data collection status	6
I.R.C.C.S. Giannina Gaslini (IGG).....	6
2.1.1. Paediatric Heart Diseases	6
2.1.2. Inflammatory Diseases	6
2.1.3. Brain Tumours.....	6
Assistance Publique Hopitaux de Paris – Necker (APHP).....	7
2.1.4. Paediatric Heart Diseases	7
2.1.5. Inflammatory Diseases	7
University College London – Great Ormond Street Children’s Hospital (UCL)	8
2.1.6. Paediatric Heart Diseases	8
2.1.7. Inflammatory Diseases	8
Ospedale Pediatrico Bambino Gesù (OPBG).....	9
2.1.8. Paediatric Heart Diseases	9
2.1.9. Inflammatory Diseases	9
3. Problems encountered during the reporting period	10
IGG.....	10
APHP.....	10
UCL	10
OPBG	10
4. Plan for the next period for each participating centre	11
IGG.....	11
APHP.....	11
UCL	11
OPBG	11
5. Status with regard to Self Assessment Plan	13
6. References.....	14



1. Introduction

This document reports the progress made in WP 9 Data Collection from month 30 to month 42. The goal of this work package is to collect the necessary clinical, imaging and genetic patient data. This activity supplies core data for the three applications of disease modelling, decision support, and knowledge discovery. Biomedical data are collected for three disease groups, namely Paediatric Heart Diseases, Inflammatory Diseases, Brain Tumours [1].

Collecting as comprehensive as possible biomedical data for each patient entering the Health-e-Child system is critical. This step not only serves the purpose of testing the data integration mechanism, but also provides training and testing data for the construction of integrated disease modelling, decision support, and knowledge discovery systems.

Our four hospitals (IGG, Genoa; APHP, Paris; UCL, London; and OPBG, Rome) are collecting patient data for Paediatric Heart Diseases and Inflammatory Diseases. Moreover, Brain Tumours study is ongoing only at IGG.

The following chapters deal with the three disease classes of Health-e-Child, they include: data collection status, problems encountered during the reporting period, plan for the next period for each participating centre and status with regard to the Self Assessment Plan.

2. Data collection status

I.R.C.C.S. Giannina Gaslini (IGG)

2.1.1. Paediatric Heart Diseases

The totally enrolled patients are 103. no further follow-up has been undertaken. Seventy three reports have been released with the cytogenetics results (Conventional Karyotyping and Array-CGH). Results of the molecular genetic screening will shortly be released and delivered.

Most of the data have been already inputted in the database and released to IT partners. Further data will be shortly inputted in the database and released.

Blood samples for genetic test have also been collected for 88 RVO patients. Seventy three reports have been released with the cytogenetics results (Conventional Karyotyping and Array-CGH). Results of the molecular genetic screening will shortly be released and delivered.

In conclusion regarding Pediatric heart disease recruitment at IGG: the global progress assessment rate was 103.

2.1.2. Inflammatory Diseases

156 MRI scans have been collected coupled with standard rheumatologic examination and biochemical analysis. In particular we are going on collecting follow up data. Up to date we have collected 31 wrist 1 year follow-up MRI scans and 11 wrist two-years MRI scans; as far as hip MRI is concerned, 16 patients performed hip MRI after 1 year from the enrollment into the study and 4 patients performed hip MRI after two years from the enrollment. Follow up data are essential in order to perform analysis aimed at find out predictors of outcome. As far as the final MRI scoring system for JIA is concerned, an international group of radiologists and rheumatologists is working in order to devise a paediatric targeted semiquantitative scoring system for the assessment of the disease activity and damage in JIA. This score is essential in order to proceed with the vertical integration of clinical, radiological, genetic and immunological data. A quantitative computer-assisted system for the measurements of the inflamed synovial membrane volume has been developed. The validation of the tool is ongoing on 66 patients with wrist involvement.

Furthermore we are analysing the follow up MRI scans of JIA patients in order to identify early imaging predictors of joint damage progression. We observed that carpal bones with bone marrow oedema at baseline MRI are at a significantly higher risk of developing MRI erosion at the same site at 1 year follow-up. Multivariate analysis is ongoing in order to confirm this preliminary results.

2.1.3. Brain Tumours

A total of 77 cases have been enrolled for the study. The clinical data of all 49 patients have been collected and the other 28 clinical information are currently added into the database. We finished to hybridize all the cases using the Affimetrix Gene-Chip U133 Arrays (IGG). The gene expression data (microarray) has been completed for the total 64 tumour samples and the expression data of 63 out cases is currently being analysed by Siemens, DISI and UoA and soon will be validated using quantitative PCR analysis. One sample was not adequate for the chip analysis. We have further amplified 13 samples with the Two-Cycle cDNA Synthesis Kit. The information that will come out of these 13 samples will be compared and validated with the other 64 cases.



Assistance Publique Hopitaux de Paris – Necker (APHP)

2.1.4. Paediatric Heart Diseases

Clinical data is integrated in the HEC database for 102 patients (68 RVO and 33 CMP). All 68 RVO (TOF) patients have had their first visit, 40 have had their second visit, 27 more follow-up visits are scheduled to go on until December 2008. Close to all RVO patients have undergone, exercise testing, ECG monitoring, and MRI. MRI data and exercise testing is currently being integrated in the database. 29 of the 33 cardiomyopathy patients have had their follow up visit, the other follow-up visits are scheduled to go on until October 2008.

2.1.5. Inflammatory Diseases

95 patients have been included at the end of June 2009: 56 of them have had a two-years control and 19 of them 3 year control. 1 of our patients have been lost to follow up and 3 did not like to continue the study.



University College London – Great Ormond Street Children’s Hospital (UCL)

2.1.6. Paediatric Heart Diseases

Recruitment for ToF has ceased as the total recruitment figures was achieved. Recruitment has begun and remains ongoing for Pre and Post op. patients to have MR scans to be submitted to HeC. 8/15 patients have been recruited thus far and will continue through the next phase.

2.1.7. Inflammatory Diseases

89 patients recruited and data collected in total. 62 6month follow-ups & 30 12month follow-ups completed in total by end of June 2009 (totals: 32 6month follow-ups and 17 12month follow-ups since January 2009).

Ospedale Pediatrico Bambino Gesù (OPBG)

2.1.8. Paediatric Heart Diseases

By the end of June, 96 patients have been enrolled. The aim of the study is to enroll patients with corrected Tetralogy of Fallot (TOF) only. For all enrolled patients clinical data, including patient's history, medications and physical examination, were entered. Imaging data have been gathered including: ECG, Holter 24h, exercise testings, spirometry and color-Doppler echocardiography.

Blood samples have been collected from 81 patients and stored in a biobank to perform genetic studies including the three candidate genes (*TXB5*, *GATA4*, *NKX 2.5*) We have the results of 45 patients. No disease-related mutations of pathogenic significance were detected in any of the three genes analyzed. A single nucleotide polymorphism (SNP) (namely, *rs2277923*) was found in *NKX 2.5* in 14 children (11% of alleles) whereas SNPs *rs3729856* in the 5'-UTR region of *GATA4* and SNP *rs12372585* in *TBX5* were detected in 4 (2% of alleles) and 5 cases (4% of alleles), respectively. One patient also carried the homozygous c.677C>T variant in the *MTHFR* gene.

2.1.9. Inflammatory Diseases

By the end of June 2009, 42 JIA patients aged from 5 to 18 years have been enrolled. The wrist was studied in 30 patients and the hip in 23 patients. Clinical and laboratory data were collected from all patients and X-Rays, US and MRI were performed for every patient. Clinical and ultrasound evaluation was performed in 20 patients after 6 months of follow-up. Four patients received also the 12 months of follow-up visit with clinical, laboratory and imaging evaluation. In those 4 patients a second MRI was performed.

Wrist X-Rays were scored according to the modified version of the Sharp/van der Heijde score and the radiographic damage was evaluated using the Poznanski score. US scoring system used was obtained according to the other involved Centers. As far as the final MRI scoring system for JIA is concerned, an international radiologists and rheumatologists group is working in order to develop and validate a semiquantitative MRI score for the assessment of disease activity and damage in JIA. As established during the last HeC meeting held in London in March 2009, this new score evaluates the presence/absence of bone edema, erosions, synovial thickening and enhancement, tenosynovitis of extensor and flexor tendons. In cooperation with the other centres involved in the study we are working to improve and to validate this score in order to use it for all HeC JIA patients.

Data entry on database is ongoing. We are proceeding on patient enrollment and follow-up.



3. Problems encountered during the reporting period

IGG

No significant problem was encountered for all three participating branches.

APHP

For **Paediatric Heart Diseases**, no major problems presented

Regarding the **Inflammatory Diseases** study, no major problems presented

UCL

No major problems were encountered.

OPBG

No major problems were encountered.

4. Plan for the next period for each participating centre

IGG

Paediatric Heart Diseases: the target number of enrolled patients has been achieved. Clinical, imaging and genetic data collection will continue in the next months for those with missing and / or follow-up data. Simultaneously, the data collected will be progressively inserted in the database and delivered to IT partners.

Inflammatory Diseases: to date it is not possible to share imaging data among the Centres. This issue is crucial in order to allow IT partner to proceed with the quantitative analysis of JIA pathological findings and in order to go on with the scoring system validation process. (i.e. to assess the multicentre reliability of the MRI scoring system etc). A preliminary version of the paediatric targeted MRI scoring system for the assessment of the disease activity and damage in JIA has been devised by all the radiologists and rheumatologists involved in the HeC study. The results of the radiological investigations will be integrated with the results of the clinical and laboratory assessments.

Brain Tumours, in the coming months the aim will be to complete the statistical and biological analysis of the expression data for the enrolled patients.

APHP

Paediatric Heart Diseases: data collection for follow up visits will continue in the coming months according to the protocol, and will be progressively inserted in the database and delivered to IT partners for analysis. No particular problem is anticipated.

Inflammatory Diseases: clinical, imaging and genetic data collection will continue in the next months; contemporary, the data collected will be progressively inserted in the database

UCL

Paediatric Heart Diseases: no major problems anticipated for next period. Minor setbacks may occur with getting data on to the database as some medical records required are prioritised for clinical use (as opposed to research) so can not always retrieve the records on demand but this should not have a significant impact on getting the data on the database in a timely manner.

Inflammatory Diseases: given that the procedures carried out for HeC at UCL there are not standard NHS procedures, parents can be less keen to go out of there way in order to participate. In order to accommodate the patient's wishes, we coordinate participation with patients' clinical visits as much as possible. However this is not always feasible due to patients' clinical time. Recruitment in the first month of the next phase may be more challenging due to the impending school holidays in the UK, where families traditionally go away on vacation. Nevertheless, we have been able to recruit some for July already and will continue to make this a priority, working with the patients in order to recruit as many as possible in the next phase.

OPBG



Inflammatory Diseases: patients enrolment is in progress. Clinical, laboratory and imaging data collection will continue in the next months. For each patient, we prepared a written document with radiographic, US and MRI findings. Moreover, at the moment we filled a form only for US. We are going to insert data collected also in the HeC database. We also think that, particularly for MRI, it's is crucial to validate a quantitative analysis of JIA pathological findings and to use scoring systems shared by all the Centers involved in the Project.

5. Status with regard to Self Assessment Plan

According to the self assessment plan, data collection at the four hospitals at month 42 (4a data collection at the four hospitals at month 42 in Paediatric Heart Diseases; 4b data collection at the three hospitals at month 42 in Inflammatory Diseases; 4c data collection at IGG at month 42 in Brain Tumours) is to be evaluated [2].

Data collection for Inflammatory Diseases started on month 6 at IGG, on month 10 at APHP, on month 19 at UCL and on month 28 at OPBG. Data collection for Paediatric Heart Diseases started on month 10 both at IGG and APHP, on month 17 at UCL and on month 30 at OPBG. Data collection for Brain Tumours started on month 11 at IGG.

The number of cases expected to be enrolled by the first three hospitals by month 30 was supposed to be completed in each subgroup while the deadline for terminating patient's enrolment at OPBG is month 42. This was respected in all participating groups.



6. References

- [1] Health-e-Child "Project Proposal, Annex I: Description of Work, Project Phase II"
- [2] Health-e-Child D.1.5.a Self Assessment Plan