MINUTES

5TH MEETING OF THE EUPHORIC PROJECT

INNSBRUCK, *27 – 28 MARCH 2008*
(9:00-13:00 and 14:00-17:00) – (9:00-13:00)

UNIVERSITY OF INNSBRUCK,
INNSBRUCK UNIVERSITY HOSPITAL
SEMINAR ROOM NO. 3

Participants:

MB: Torre Marina and Manno Valerio – Istituto Superiore di Sanità (ISS), Rome (Italy)
AB: Weimin Ye – Karolinska Institutet (KAR), Stockholm (Sweden)
AB: Häkkinen Unto – Centre for Health Economics at Stakes (STAKES), Helsinki (Finland)
AB: Fusco Danilo and Carbone Anna Patrizia – Department of Epidemiology ASL RM E (DEASL), Rome (Italy)
AB: Labek Gerold and Fechter Renate – EFORT-EAR Innsbruck Medical University (EAR), Innsbruck (Austria)
AB: Marrugat Jaume and Ferrer Yolanda – Institut Municipal d'Investigació Mèdica (IMIM), Barcelona (Spain)
AB: Psaltopoulou Dora – National and Kapodistrian University of Athens (NKUA), Athens (Greece)
CP: Mathis Stefan – Ludwig Boltzmann Institute (LBI), Vienna (Austria)
CP: Behar Shlomo – Israel Society for the Prevention of Heart Attacks at NRCI (Israel)

Absentees:

CP: Allepuz Alejandro – Catalan Agency for Health Technology Assessment and Research (CAHTA), Barcelona (Spain)
CP: Lyubomirova Karolina – National Center of Public Health Protection (NHCPH), Sofia (Bulgaria)
CP: Oberaigner Willy – Department of Clinical Epidemiology of the Tyrolean State Hospitals Ltd, Innsbruck (Austria)
CP: Delaunay Christian – French Society of Orthopaedic and Trauma Surgery (SOFCOT), Paris (France)
CP: Nečas Libor – Slovak Arthroplasty Register, Slovak Republic

THURSDAY 27 MARCH

1. Welcome

Marina Torre welcomes all the participants, expresses gratitude to both pilot leaders and to all the participants for their help during 2007, having been a very intensive year of activity. She also thanks Gerold Labek for hosting the meeting. Since this meeting is the last general meeting before the end of the project (the project will end on 14 December 2008 and the next general meeting will coincide with the final workshop of the project) she underlines the importance of focussing attention on the analysis of the first results available from the project in order to finely tune and plan the final phase of activity.

She passes on the EUPHORIC EU Officer's, Artur Furtado, greetings to all the participants and his apologies for not being able to attend the meeting.

She announces that Prof. Shlomo Behar joined the project in December 2007 and since then has been cooperating with Jaume Marrugat on the development of the CV pilot.

2. Approval of the agenda

The agenda is approved.

3. Updating EUPHORIC's progress (Marina Torre)

- WP 1 Management of the project (Marina Torre)

  The Second Interim Report together with all
  the documents was submitted on 15 March in order to request an amendment.
  Marina Torre gives all the participants a CD which includes the Second Interim Report and all the deliverables prepared in 2007 and submitted to the Commission.
  Marina Torre announces that partner GRI withdrew from the project on February 6 2008 and that the relevant amendment was submitted to the Commission together with the Second Interim Report.

  The amendment referred to:
  1. The transfer of part of the ISS budget to both pilots
  2. The transfer of the residual GRI budget to both pilots. Additional WPs were submitted to the EU Commission and approved (attached to the Interim Report)
  3. The reorganization of the ISS budget
  4. The request sent by KAR to reorganize their human resources without any modification to their budget.

- WP 2 Dissemination strategy (Marina Torre)

  LEAFLETS
  The leaflets translated into the language of the participating countries were put on the website. All partners are requested to check them. Prof. Shlomo Behar is invited to translate the leaflet into Jewish.

  DISSEMINATION PLAN
  The dissemination plan has been submitted in its first revised form. Marina Torre invites all the partners to send ISS any new proposals for its update (new report, participation in conferences, etc).

  CASPUR and ZADIG
  The reorganization of the ISS budget included in the submitted amendment is aimed at improving the dissemination of the results. Additional contracts with CASPUR (to improve and update the website) and with an editorial and publishing company (ZADIG) have been considered. A list of activities that will be performed by both subcontractors was shown.

  i. Preparation of the final workshop
     The final EUPHORIC workshop will take place at the ISS on 11-12 December 2008. A draft preliminary programme was presented.

- WP 3 Liaison with other EU projects, EU programmes and health stakeholders (Unto Häkkinen)

  Marina Torre conveys that very useful cooperation with ECHIM has been set up. A selected set of EUPHORIC indicators was submitted to be included as a potential entry in the short list.

- WP 4 Indicators development (Marina Torre)

  WP 4 can be considered concluded. The deliverable including all sheets describing in detail all 54 indicators selected was submitted to the Commission with the Second Interim Report.

- WP 6 Setting up and maintaining an indicators database (Marina Torre)

  Valerio Manno illustrates the web-based database. All partners are requested to check and update the information considered for each country. Jaume Marrugat suggested integrating two

additional fields: 1) availability (Yes/No) of the source of data; 2) contact (website, institution, etc) so as to have information about the data.

Information collected in the Deliverable "Indicators sheets" will be immediately uploaded on the website in the members' area.

4. WP 5 Development of an adverse-outcome risk indicator in real clinical and register databases, and its possible use in systematic administrative databases (Jaume Marrugat, Gerold Labek, Danilo Fusco)

- WP 5.2 Orthopaedic pilot (Gerold Labek)

i. Progress reporting (Development and implementation of the WP)

WP 5.2.1: Assessment and summary of the existing arthroplasty registers and related projects (Scotland, Austria, Tyrol, Hungary). Underway according to schedule.

WP 5.2.2: Comparison of clinical studies and register results based on example analyses. Continuing well ahead of schedule.

WP 5.2.3: Quality control mechanisms and quality control procedures by manufacturers: first documents have arrived. Work progress slightly behind schedule because confidential material has to be obtained.

WP 5.2.4: Significance of the indicators proposed from the medical expert's point of view. Making good progress – also ahead of schedule.

WP 5.2.5: Public health-related data sources and their linkage. As decided in Stockholm, the reports from KAR and STAKES are expected in May (Unto Häkkinen's part being ahead of schedule and Weimin Ye's part will also be finished in time for the meeting in June).

WP 5.2.6: Summary of basic data concerning the indicators from international databases. According to the schedule, work on this WP has not yet started.

ii. First results (Deliverable and outcomes achieved)

WP 5.2.2: The literature review revealed a significant bias in clinical studies. The comparison between metanalyses and register publications has shown that relatively few articles are published in peer-reviewed journals. Moreover, clinical studies tend to underestimate the actual failure rate, revision rates differing by a factor of two as compared to register-based data. A highly significant deviation was stated regarding the case numbers at observation. While clinical studies usually refer to numbers around 100 (300 cases are an exception), Swedish register studies, for instance, have treated an average of about 18,000 cases for the same issue.

Register data were also found to demonstrate an improvement in performance over the years, depending on training and other influence factors. All in all, our findings so far suggest that register results are a highly valuable data source. However, register data are not available on a European scale, and they are subject to country variability. For proper use they must therefore be adjusted to the individual country concerned.
Adjustments to general patient characteristics, such as sex or age are possible since these data are included in the data collection. For variables concerning the national health system, e.g. hospital specifications, the given data are inconsistent.
Other observations include that there are few publications on implants available on the market (even though patients are still at risk), that scientific peer- reviewed journals tend to focus on recent issues rather than following matters up, and that publications usually follow a particular mainstream focus.

The absence of authors' publications, repeated design revisions at about five years, as well as a low number of publications in peer-reviewed journals were identified as being indicators of inferior outcome.
In conclusion, due to the high variability in study design and inhomogeneous patient cohorts, as well as a high amount of uncontrolled bias, peer-reviewed journals do not seem to be an appropriate source for valid assessment. Discharge records are also biased (depending on the purpose they are produced for) and, for various reasons, cannot provide the broad range and quality of data needed. Compared to these two sources, register databases offer the best quality and are particularly valid for the area they cover. Standardizations and adaptations are suited to make them appropriate for large-scale use.
As a conclusion for the final statement, Gerold Labek suggests pointing out that

- Registers offer the best preconditions to serve as a monitoring and outcome measurement tool; and that
- Standardization in definitions, internal procedures, evaluation and reporting is required.

WP 5.2.3: SOPs have so far been provided by one manufacturer (Link, Hamburg). A particular incident at our clinic will be used as a complaint example. In addition, we are waiting for another set of SOPs to be able to analyze differences in approach between the companies.

WP 5.2.4: The indicators E1-E7 very rarely appear in scientific publications concerning arthroplasty and trauma. As well, they seem to be irrelevant for both scientific issues and physicians in their daily decisions related to outcome measurement and quality control. A statement from the medical expert's point of view is presently being prepared. This statement does not include a statement on the quality of the indicators collected in the 1st phase of EUPHORIC for the use for public health issues, where a focus on organisation and procedures has a higher priority than for physicians working in a given system.

iii. Planning of future actions

Our main emphasis will be placed on the following issues:

- Focus on WP 5.2.1 (register assessment)
- Statistical analysis of the results of WP 5.2.2 together with ISS
- Publication and dissemination activities (EFORT Congress in Nice in May; EHS Meeting in Madrid in June; EFORT Congress 2009 in Vienna; journal publications)
- Support of other partners (KAR and STAKES / WP 5.2.5; DEASL / WP 5.3)
- Grant amendment: subcontracts for new activities (Romanian register: collection of economic data and link to outcome data in one institution; comparison of discharge records and register data in Tyrol)
- Start activities regarding validation of clinical forms according to their validity and potential contribution to outcome measurement
- Limited assessment of surgical procedures (MIS) – in addition to the initial work plan (easily obtainable from WOMAC validation data).

iv. Partners involved

- KAR and STAKES (in compliance with decisions made at the Stockholm meeting)
- DEASL (support for WP 5.3 – to be defined in detail; questionnaires expected)
- Additional subcontracts with Romanian and Tyrolean registers
- In addition to the points of the agenda, Gerold Labek reported on the PHEA Info Day held in Luxembourg on 12 March, and pointed out the main issues presented and tips given for preparing a promising grant application.

– WP 5.3 Validation of the datasets: discharge records, registers, surveys and clinical studies available in participant countries (Danilo Fusco)

Danilo Fusco gives an overview of the decisions made during the extra meeting of the statistical working group of 26 March 2008 (see the relevant minutes) and presents the future planned actions:

a) Pilot target group:
   - Collecting information from registers (pilots); changing items on questionnaire;
   - List of computable indicators;
   - Possible linking with health care information datasets.

b) Health Care Information System target group:
   - Leadership: STAKES

   The question of whether it would be possible to get and use data from an existing Finnish EU project (website; OECD web page; etc.) will be clarified by e-mail with Unto Häkkinen.
   If required, Danilo Fusco will then forward a list of his additional needs to Marina Torre.

   Danilo Fusco raises the question whether predictive functions can be shared by different countries. Unto Häkkinen suggests e-mailing a statistical system to Danilo that may be appropriate for his purposes.

c) For each indicator proposed by the pilots, the following information will be needed:
   - definition of the extended protocol;
   - shared inclusion and exclusion criteria;
   - variables to be used for risk assessment and statistical methodology (use one country as a reference).

   At this point, Marina Torre suggests working on the information contained in the protocol first and then deciding what will be further needed.

   Discussion:
   It was stated that different approaches to the subject constitute another point of interest: while Finland, for instance, is primarily interested in describing and comparing the outcome per hospital, from an orthopaedic point of view the emphasis is placed on the causes of good or bad performance, such as implants, among others.
   This implies different levels of consideration: e.g. comparing costs, etc. from a public health point of view versus the patient's perspective ("Where to go to get the best implant?").

d) Planning of future actions
   Focus on deliverables and outcomes:
   - Deliverable No. 4 "Review on Risk Adjustment Methods";
   - Questionnaire on registers included in pilot studies;
   - Indicator protocols to be used in participating countries;
   - Deliverable on identification and definition of risk factors that could be used for comparative evaluation of the outcomes being studied in participating countries;
   - Deliverables on statistical procedures that will be applied for the comparative evaluation of outcomes;
   - Papers about WP 5.3 results.

   Work plan: Planned Coordinating Meeting in September; Finalization.

Additional arrangements:

- Protocol modifications will be sent to all participants of the meeting;
- Deadlines must be set in order to avoid running out of time. (e.g. protocols: "next week").

FRIDAY 28 MARCH

4. WP 5 Development of an adverse-outcome risk indicator in real clinical and register databases, and its possible use in systematic administrative databases (Jaume Marrugat, Gerold Labek, Danilo Fusco) (continued)

- WP 5.1 Cardiovascular pilot (Jaume Marrugat)

The following three register components of the joint EUPHORIC database containing 24,533 ACS patients were being used for model fitting: ACSIS 2004 and 2006, MASCARA 2005 and EHS-ACS 2000 and 2005 registers. The number of patients included was:

	Mascara	ESURVEY1	ESURVEY2	ACSIS 2004	ACSIS 2006
Non-ST Elevation ACS	2,142 (44.8%)	5,209 (54.8%)	2,444 (49.9%)	1,003 (49.5%)	1,074 (54.5%)
ST Elevation ACS	2,635 (55.2%)	4,305 (45.2%)	2,449 (50.1%)	1,025 (50.5%)	896 (45.5%)

Professor Shlomo Behar presents the ACSIS (Acute Coronary Syndrome in Israel) and EHS-ACS (Euro Heart Survey on Acute Coronary Syndrome), and Jaume Marrugat the MASCARA characteristics. It has become clear that ACSIS and MASCARA are representative of the populations of Israel and Spain, respectively, and guarantee consecutiveness of recruitment.

The crucial point discussed regarded how representative the data used in a predictive model is. All participants agree that the representativeness of the data is a major difficulty because of the problematic nature of hospital data and discharge records, as well as the difficulties being further multiplied at country level.

Several suggestions are made to solve the problem:

- e.g. adjust four high-volume centres per country (as it is impossible to include all variables);
- perform a cross-over analysis (estimates based on various samples and trying to get a conclusion. Problem: exposure is needed to develop a function; and allows the comparison of hospitals, but is not representative);
- use a "EUROSCORE" subset (problem: not available for list of variables);
- use TIMISCORE (should be included to characterize the patient; only about six to ten variables; may prove useful);
- take a certain number of countries (representing about 75 % of the population) and use these data.

The discussion on the consequence of EHS-ACS's lack of country representation and little guarantee in consecutive recruitment leads to the question as to whether it is necessary to have these unbiased samples as an objective of the CV pilot. Arguments for: we are analysing the outcomes after some procedures or disease management. We need to ascertain that there are no severity biases with some subgroup analyses (sensitivity analyses) and with the

representative and consecutive patient registers (ACSIS and MASCARA and Finland). We will use a model that fits all the countries and check whether there are significant changes in the coefficient estimates when the model is adjusted to the representative registers. It is also important to check whether subanalyses in hospitals with >50 patients, or countries with >100 patients yield similar results.

Technical agreements:

1) Type of disease: Among ACS patients, we agreed to include not only AMI but also unstable angina patients.

2) Type of outcome: In-hospital mortality, in-hospital mortality angina or infarction extension

   We will make analyses of missing data for:
   a. 30-day mortality
   b. 30-day mortality angina or infarction extension

   and send them to the partners to decide which of the two periods (in-hospital or 30-day) to keep. In principle, we feel more inclined to keep the in-hospital period because there is a lower number of missing values.

3) Type of procedure: It was agreed to drop the analyses on CABG since there are only 1,000 patients and 37 deaths!

   We will keep:
   a. AMI+UA management
   b. Coronary angiography
   c. Thrombolysis
   d. PCI.

4) Questions:

   a. How do we solve the problem of selecting individual-level variables that may not be collected in administrative discharge data?

      Unto Häkkinen (STAKES) and Danilo Fusco (DEASL) will send the variables used in their registers for inspiration. In relation to this point, it was also agreed to take into account the clinical significance and not only the statistical significance, and to pay attention to the autocorrelation among variables during the variable selection. Severity measurements are to be found since they are of crucial importance to determine outcome. Killip class is not measured and perhaps TIMI score could be calculated: an attempt will be made by the CV coordinator (partner IMAS-IMIM).

   b. How many variables at individual-level do we consider?

      No more than six.

   c. Which hospital characteristics should we include in the models?

      Eliminate # hospital beds and keep the rest.

   d. Which country characteristics should we include in the models?

      Agreed to disregard total population.

5) Modelling with country characteristics: for countries in the database we use the country dummy variable and for others the average of all countries.

The CV pilot coordinator (partner IMAS-IMIM) will develop two sets of models: one to be used with data sets of individual information, and another with variables that synthesize patient characteristics in a hospital (e.g., proportion of diabetes, hypertensive, smoker, etc., and patients undergoing a particular procedure). The objective of this double approach is to provide hospitals with a method of benchmarking that does not need individual data. The abovementioned proportions can be obtained in a random sample of 100 patients, for example.

The resulting system will be posted on the intranet of the EUPHORIC website in July (Marina Torre and Jaume Marrugat being responsible).

5. Other business

Marina Torre proposes to send abstracts to the next EUPHA Congress (Lisbon, Portugal 6-7 November 2008; deadline for submission 1 May 2008). The abstract deals with a general description of the progress of the project and/or specific description of the results of the pilots. Partners are requested to send their proposal by 15 April 2008.

6. Closing of the meeting

The meeting closed at 13:00.