Transfer of expertise on rare metabolic disease in adults: the TEAM-study

Karolinska Hospital, Stockholm
May 11, 2001
EU-programmes

Community Action on Rare Diseases

1: Information databases
2: Training of professionals
3: Support of patient groups
4: Epidemiologic surveillance
TEAM-study

Transfer of Expertise on Rare Metabolic diseases in adults

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TEAM-study

Essential starting points
• Lack of knowledge on a new patient group
• Available information is scattered among experts and not easily found
• Available information is not easily conceptually accessible and quality or scientific foundation of information (very) uncertain
TEAM-study

Potential consequences

- Delay in diagnosis
- Delay in initiation treatment
- Erroneous choice of treatment
- Negative influence on prognosis and quality-of-life
The birth of the TEAM-study

- Choice of the item in the EU-programme (#2)
- Elements of a EU-grant proposal
  - background & aims and objectives
  - project mechanism & feasibility of the mechanism
  - deliverables
  - subsidiarity
  - community-wide application
  - after the project has come to an end….
TEAM-study

Essentials of the TEAM-study
Background & aims and objectives

“Mission statement”

“To provide quality assessment of current knowledge on aetiology, epidemiology, diagnosis, treatment, complications and prognosis in adult patients with rare metabolic diseases; design, creation and try-out of trainings for professionals based on an elementary consensus after conclusion of quality assessment”
Quality assessment

“Consensus"

Training sessions

Dissemination of quality-assessed expertise
What’s happening in a physician’s mind

Clinical process

Clinical problem
- medical history
- physical examination

Hypothesis
- Knowledge
- Experience
- Intuition
- Luck
- …………

Tests

Database

Diagnosis

Database

Database

Therapy & Prognosis
TEAM-study

Essentials of the TEAM-study
Mechanism of the project & feasibility of mechanism

- Formation of groups of diseases
- Choice of experts in the field (6)
- Recruiting them for the TEAM-approach
- Quality assessment mechanism (Cochrane)
- Consensus
- Design and creation of trainings
- Try-out of trainings
TEAM-study

The different expert groups

Group 1: Amino acids I

- Phenylketonuria
- Alkaptonuria
- Tyrosinaemia

Utrecht, The Netherlands
Example expert-group

Amino acid disorder I
  Head-coordinator

  Phenylketonuria
    Subgroup-coordinator
      Members

  Alkaptonuria
    Subgroup-coordinator
      Members

  Tyrosinaemia
    Subgroup-coordinator
      Members
TEAM-study

The different expert groups
Group 2: Amino acids II
- Homocystinuria
- Maple syrup disease
- Urea cycle defects
- Hyperornithinemia

Padova, Italy
TEAM-study

The different expert groups

Group 3: Carbohydrate disorders

- Galactosaemia
- Glycogen storage diseases
- Fructose disorders

London, UK
TEAM-study

The different expert groups

Group 4: Organic acidurias

- Propionic acidemia (PA)
- Methylmalonic aciduria (MMA)
- Isovaleric aciduria (IVA)

Madrid, Spain
TEAM-study

The different expert groups

Group 5: Fatty acid disorders

- LCHAD, MCAD, LCAD, SCAD
- CPT
- vLCAD
- TFP

Lisbon, Portugal
TEAM-study

The different expert groups
Group 6: Other disorders
- ALD
- Lysosomal disorders
- Peroxisomal disorders

Paris, France
Basic considerations of the **TEAM**-approach

- **Systematic** review of current expertise

  - systematic review of publications

- **Systematic** means:
  - adequate and comprehensive search strategy
  - accountability of inclusion or exclusion
  - reproducibility of inclusion or exclusion

- Applies to all types of studies
Systematic review (1)

Systematic reviews

- Unit of research: publication (abstracts included?)
- Definition of a research question
- Definition of the search strategy
- Accountability of inclusion non-inclusion: selection
- Judgment on the merits of publications: appraisal
- Transparent presentation of the results: review

Prevention of bias as much as possible
Systematic reviews (2)

The making of a systematic review
1: Definition of a research question
2: Writing of a specific protocol
3: Search strategy including various items
4: Selection and appraisal of publications
5: Pooling of data if possible and indicated
6: Presentation of the data
Systematic reviews (3)

Selection strategy

• Selection of publications: In/exclusion criteria
  - age
  - sex
  - intervention
  - follow-up duration

• Transparent selection on predesigned form

• Entry of all publications in Reference manager by coordinating center
Systematic reviews (4)

Selection of publications
• No restriction in language (Tower of Babel bias)
• Unpublished results or abstracts-only research
  -publication bias?
  -quality deficit of unpublished results?
  -presentation bias
• Blinded selection
Systematic reviews (5)

Appraisal of publications
• Internal validity
• External validity
• Quantitative aspects (data presentation)
• Other relevant items encountered
Systematic reviews (6)

Major items in appraisal of relevant publications
- Description of the studied population
- Diagnostic procedures
- Randomization
- Study intervention
- Assessment
- Follow-up
- Side-effects
Specific review question

- The specific review question determines search strategy
- The better specified the question, the more tailored the search strategy

EXAMPLE:
- frequency of congenital abnormalities in MPKU
- follow-up of adults with PKU
- is premature dementia a symptom of carriers of methylmammonic aciduria

- More than one question on a specific item is possible
Items to be considered

• Epidemiology of the disease (prevalence)
• Causes and genetics
• Clinical presentation
• Diagnostic procedures
• Therapeutic interventions and strategies
• Prognosis
Structure

Specific review question

Type of study → Search strategy

Selection of studies → Appraisal of studies

Results → Pooling/synthesis

Discussion & Conclusion
Collective (EU-programme)

Cochrane initiative

Expert group
Expert group
Expert group
Expert group
Expert group
Expert group

Cochrane analyses
Other products

Consensus

Trainings

Other initiatives
TEAM-study

Essentials of the TEAM-study

Deliverables

- Trainings on rare metabolic diseases in adults based on quality-assessed expertise and based on subsequent elementary consensus
- Trainings for professionals to provide dissemination of new and applicable knowledge
- Accessible knowledge in a database; electronic and non-electronic dissemination
- Trainings in different languages and for other professionals
TEAM-study

Essentials of the TEAM-study
Subsidiarity
• Participation of and input from different centers and countries of the EU
TEAM-study

Essentials of the TEAM-study
Community-wide application
• Accessible information database by Internet
• Accessible database by non-electronic means
• Trainings in different countries and different languages, accommodating differences in culture
TEAM-study

**Essentials of the TEAM-study**

After the project has come to an end

- Continuation of the trainings (fees for participation, other sources)
- Updating of the trainings
- TEAM-study as initiator of collaborative networks