

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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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 accesible and quality or scientific foundation of information (very) uncertain

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Potential consequences

- Delay in diagnosis
- Delay in initiation treatment
- Erroneous choice of treatment
- Negative influence on prognosis and quality-of-life

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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....

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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

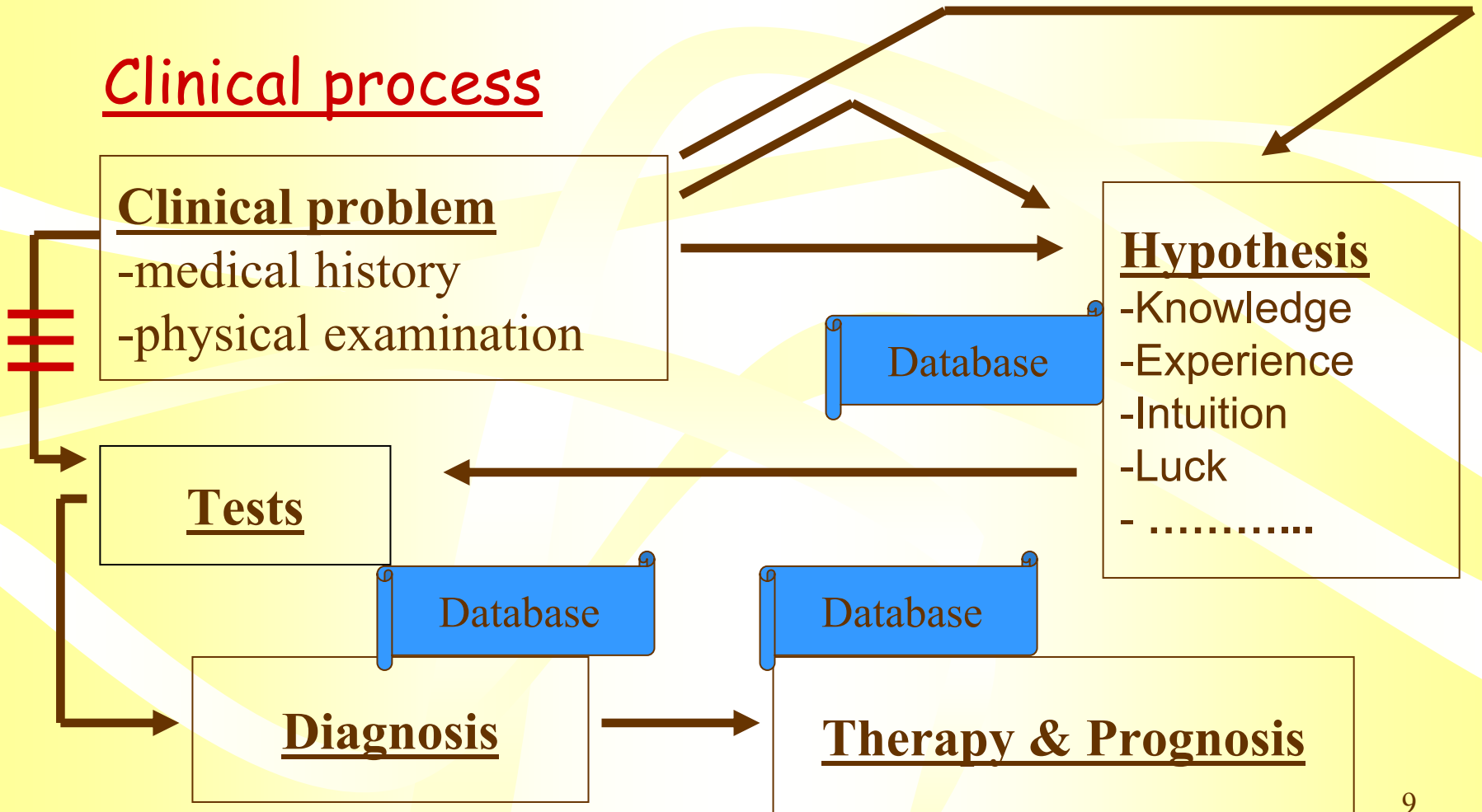
“Consensus”

Training sessions

Dissemination of
quality-assessed expertise

What's happening in a physician's mind

Clinical process



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

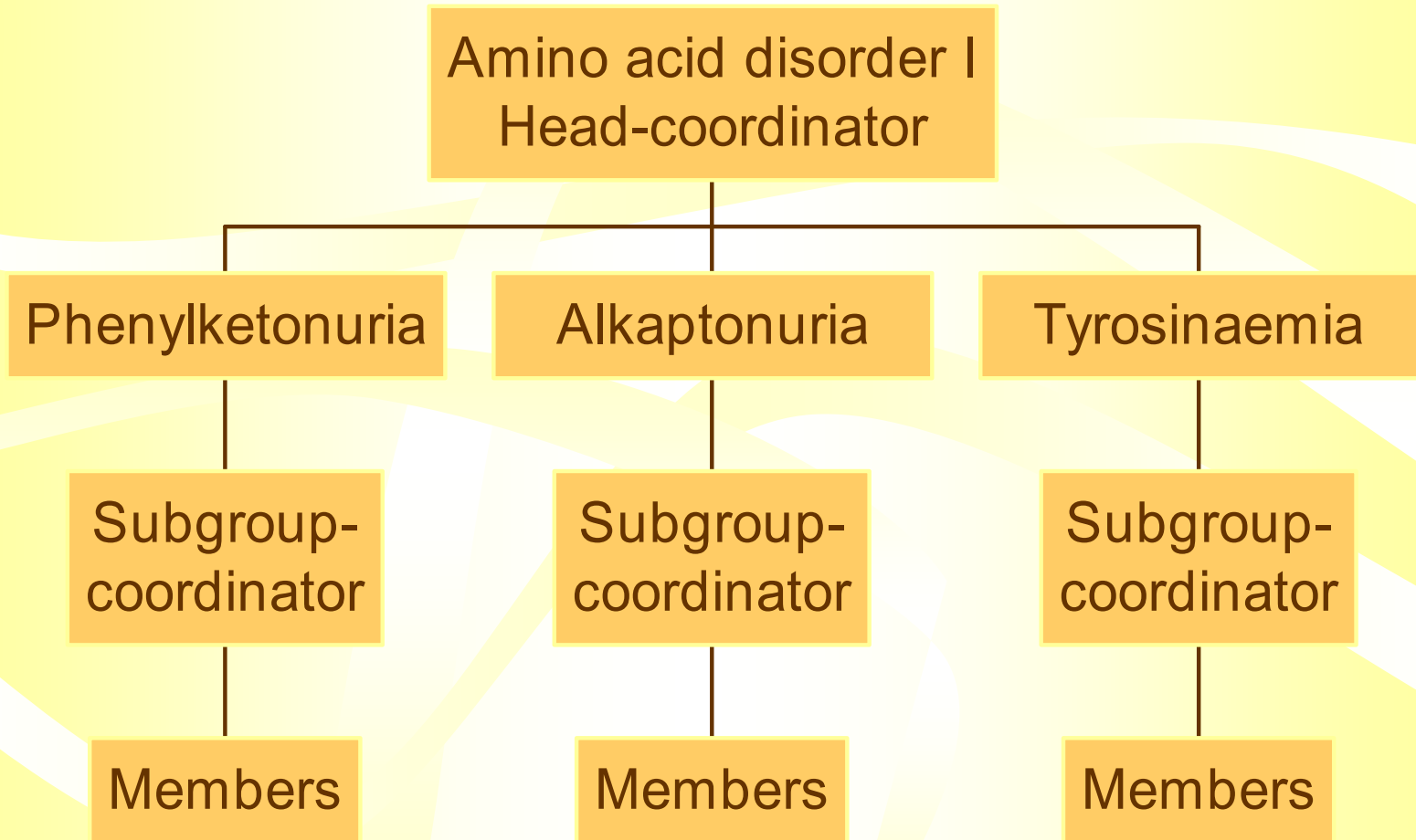
The different expert groups

Group 1: Amino acids I

- Phenylketonuria
- Alkaptonuria
- Tyrosinaemia

Utrecht, The Netherlands

Example expert-group



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

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The different expert groups

Group 4: Organic acidurias

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

Madrid, Spain

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The different expert groups

Group 5: Fatty acid disorders

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

Lisbon, Portugal

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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

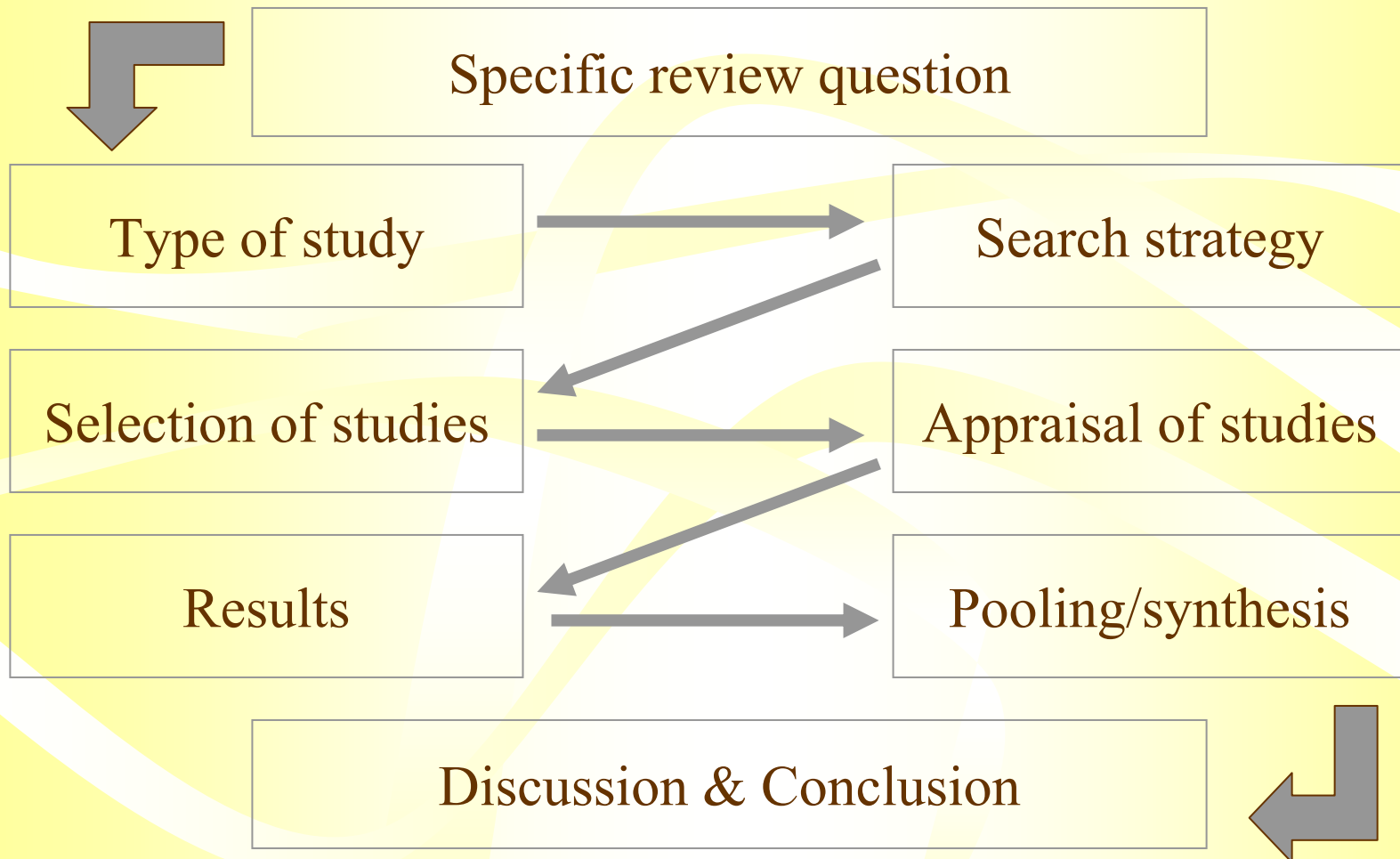
EXAMPLE:

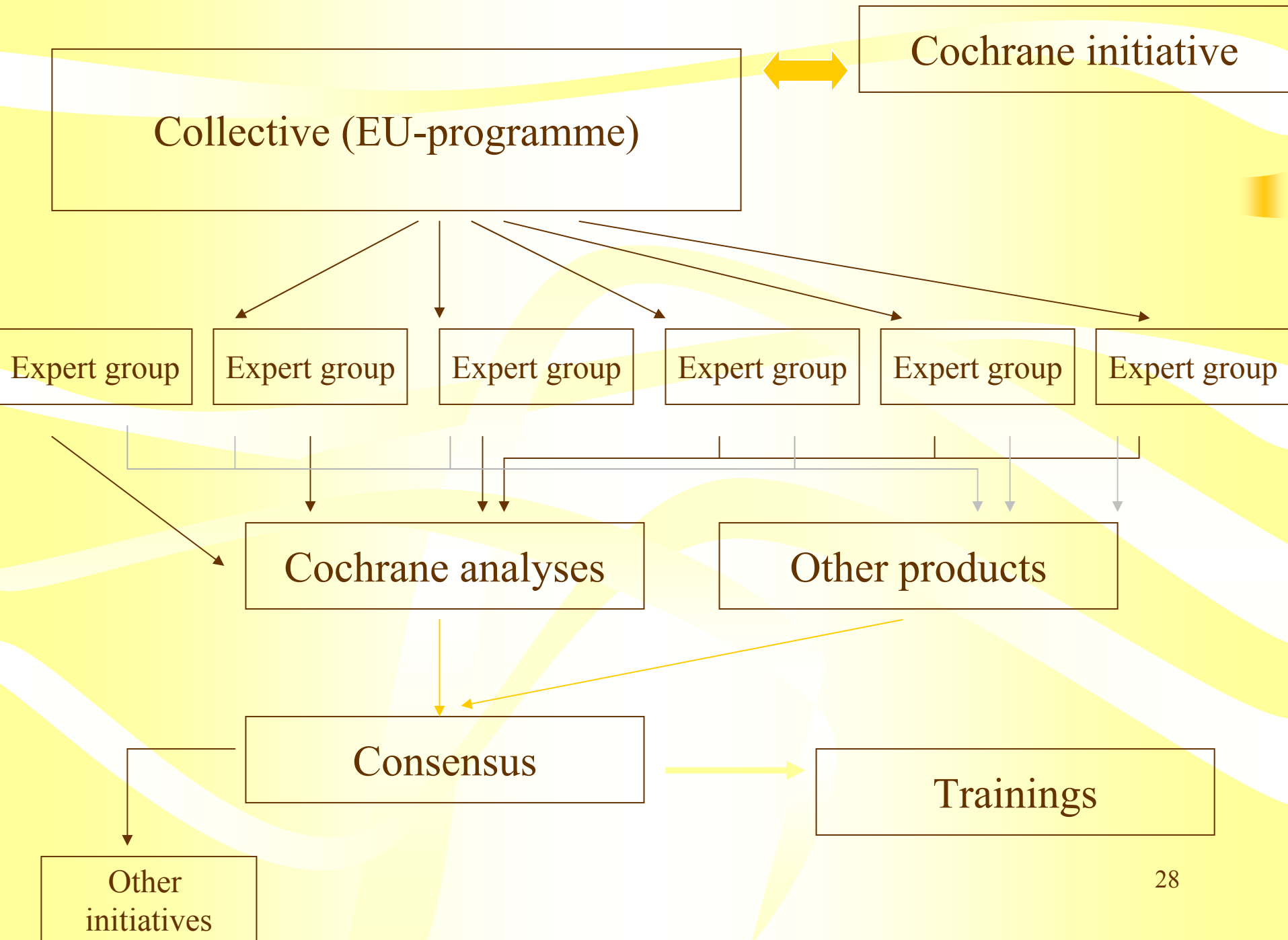
- frequency of congenital abnormalities in MPKU
- follow-up of adults with PKU
- is premature dementia a symptom of carriers of methylmalonic aciduria
- More than one question on a specific item is possible

Items to be considered

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

Structure





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, accomodating 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

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