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PER LA RICERCA FARMACOLOGICA
GIANNI BENZI
ONLUS

THE EUROPEAN MEDICINES REGULATORY NETWORK:
PRESENT AND FUTURE
X Foresight Training Course

Pavia, 28th October 2017

Involve the younger in safe medicinal development plans

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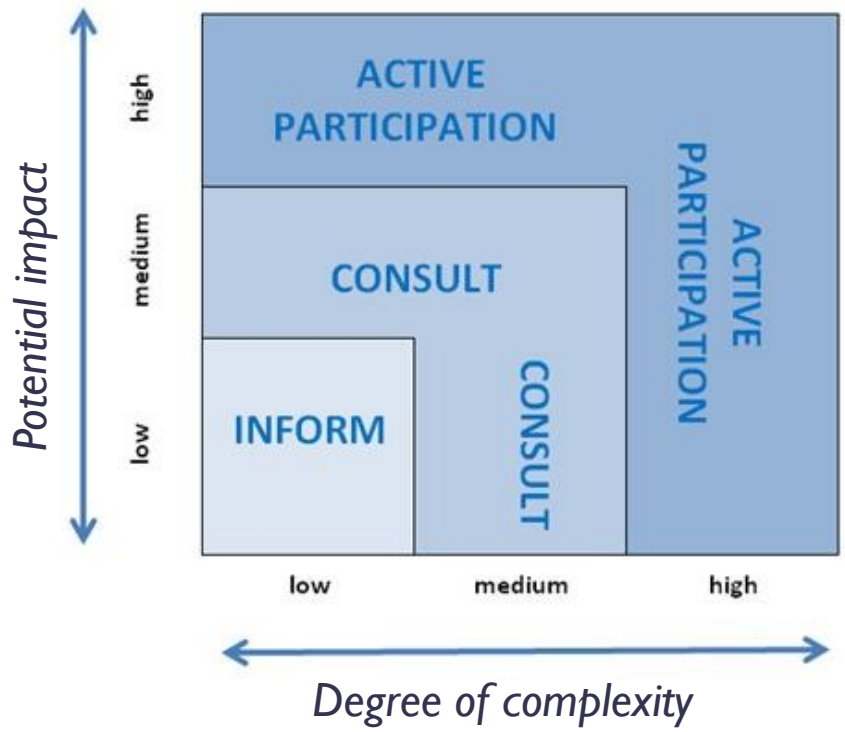
Patients' participation in medicines research and development



Empowered Patient model

Who?

The expert patient:

The expert patient is an educated patient, at Eu level, on the drug development process, that is experienced and able to work in synergy with other patients, focused on specific diseases. The common interest is that the patients' voice is recognised, respected and considered as reference point. In this perspective, training and knowledge are milestones for patients' active participation and for their collaboration.

Paola Kruger, EUPATI Expert Patient, Quotidiano Sanità, April 2017

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Patients' participation in medicines research and development: some examples

EXPERT PATIENT ADDED VALUE

How?

- Identification of research priorities
- Participation in Advisory and Steering Groups
- Co-management of research projects
- Documents review
- Participation in results draft and communication
- Training (specific workshops/initiatives)
- Evaluation surveys

What?

- Transparency and dissemination of information
- Information on the product, including 'EPARs' and PLs
- Pharmacovigilance (ENCePP)
- Interaction with the European Medicines Agency and its scientific committees

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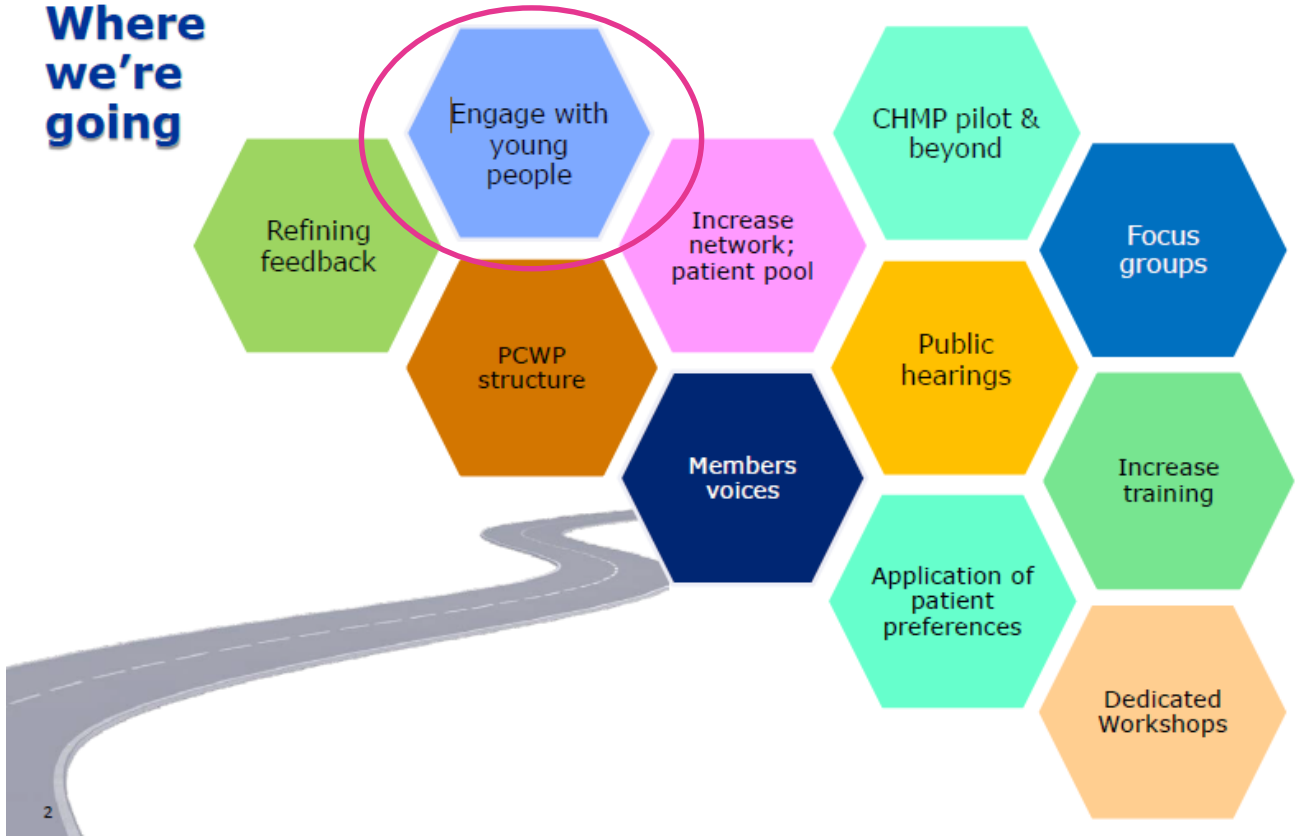
EMA Patients and Consumers working party



Source: Nathalie Bere Patients and Consumers: where are we going? European Medicines Agency, Patients and Consumers Working Party – 30th November 2016

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Are children entitled to enter this process?

International Convention of the Rights of the Child (UN)

Fundamental principles underpinning the rights of the child in Europe

principles of the
"Best interests"
"Evolving capacities"
of the child

"States Parties recognize the right of the child to the enjoyment of the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health. States Parties shall strive to ensure that no child is deprived of his or her right of access to such health care services." (Art. 24)

"The child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child, the views of the child being given due weight in accordance with the age and maturity of the child." (Art. 12)

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Paediatric patients' participation in medicines research and development

1. understanding by the patient of his/her role
2. acquisition by patients of sufficient knowledge to be able to engage with their healthcare provider
3. patient skills
4. presence of a facilitating environment

ASPECTS TO CONSIDER IN PAEDIATRICS:

- Children awareness about their status
- Information and knowledge on disease-related aspects
- Individual maturation level
- Adequate language and means of communication, dedicated initiatives
- Parents' wills

Angelmar R, Bermann BP. Patient empowerment and efficient health outcomes. Financing sustainable healthcare in Europe. 2007 :139–162.; http://www.sustainhealthcare.org/The_Cox_Report.pdf

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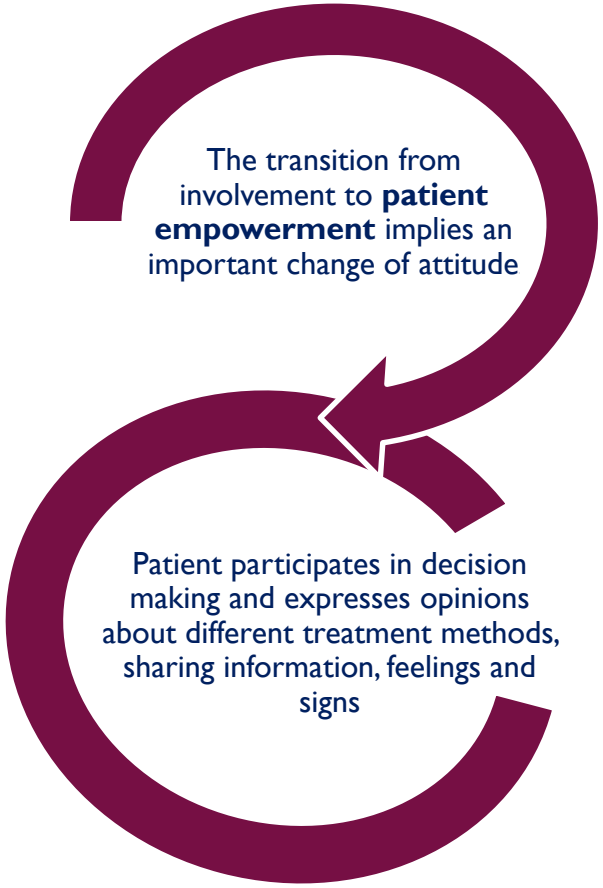

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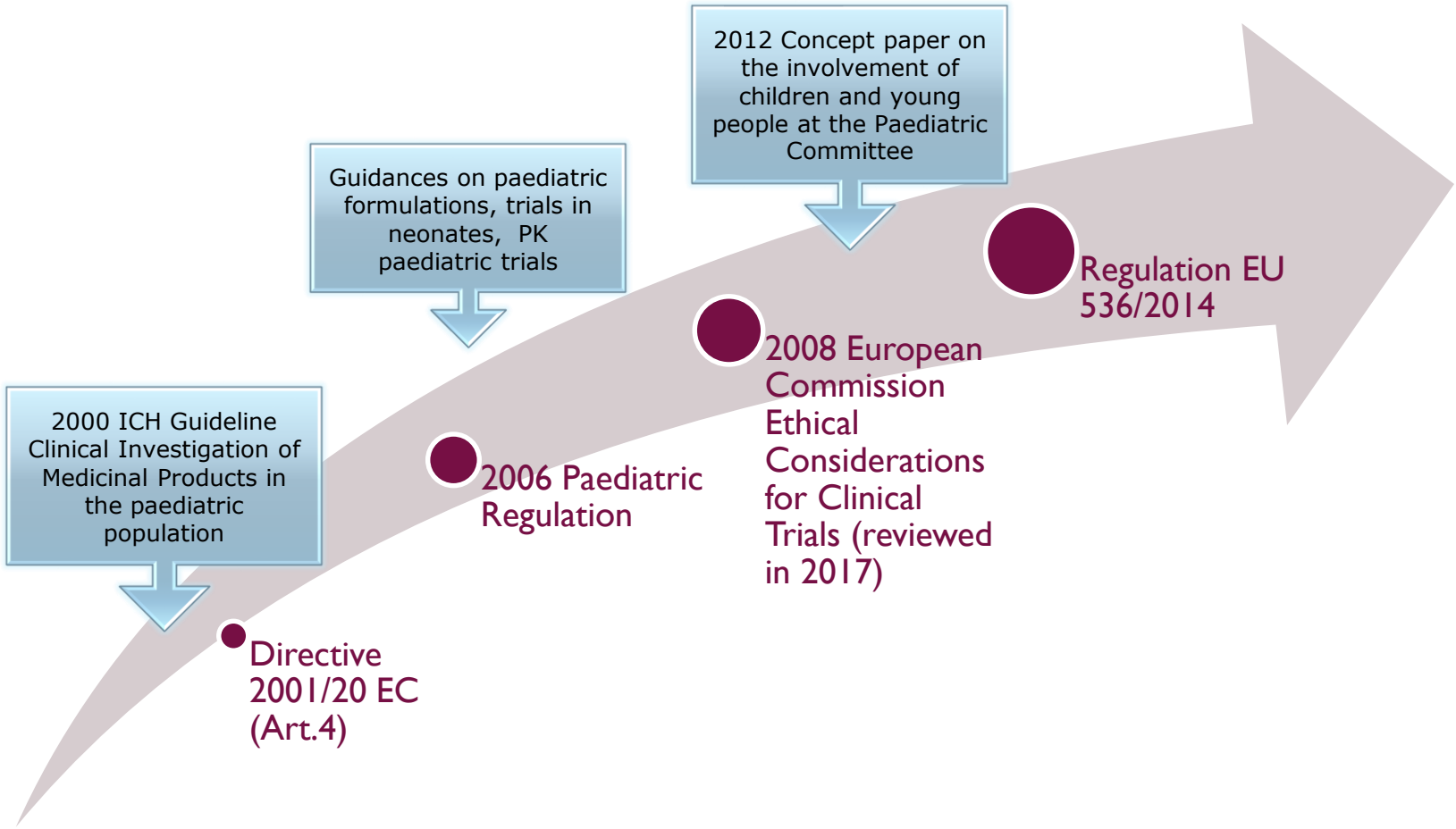
Children in medicines research and development - subjects or actors?



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Children in medicines research and development – the Eu Regulation on Clinical Trials

- Involvement of minors in the informed consent procedure according their age and mental maturity
- Respect of the explicit wish/refuse of a minor capable of forming an opinion
- If during a clinical trial the minor reaches the age of legal competence to give informed consent as defined in the law of the concerned MS, his or her express informed consent shall be obtained before that subject can continue to participate in the CT
- Need for paediatric expertise or advice in Ethics Committees

GRIP Global Research in Paediatrics

TEDDY NETWORK European Network of Excellence for Paediatric Clinical Research

But…

- What information should the children receive
- Which type of assent/agreement should be obtained (written? from what age?)
- How many parents or how many legal representatives should sign the consent

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Children in medicines research and development – the European Ethical Recommendations

2017 review: what is new?


Ethical considerations for clinical trials on medicinal products conducted with minors

Recommendations of the expert group on clinical trials for the implementation of Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use

Revision 1

18 September 2017

- More emphasis on the **evolving maturity of children,** underlying the requirement of the Regulation to respect the **explicit wish of a minor to refuse participation** in, or to withdraw from, a clinical trial at any time
- Requirement of **participation of the minor in the informed consent process** as a continual process (documented discussion) **and in the protocol design**
- Introduction of the term '**agreement**' = 'assent' in medical literature (the new CT Regulation reserves the term 'assent' to have legal value in some MSs)
- Updates on data protection on future (unknown) uses of data

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Children in medicines research and development – what to focus on?

- Support for initiatives requiring children active participation
- Define a methodology for the involvement of the paediatric population
- Identify fields of activity for which it is most relevant to have children's active participation: how to manage with the most difficult topics?
- Propose collaborative model children – families – healthcare professionals

Children in medicines research and development - the TEDDY network experience

TEDDY was born in the context of the FP6 (start date: 1st June **2005**, duration: 60 months)

Since **2010** TEDDY has revised its organisation and gathered new research centres and groups willing to be engaged in developing paediatric clinical research

TEDDY today is a category 1 Network Member of Enpr-EMA … is continuing working at facilitating the performance of good quality paediatric studies and research thanks to the voluntary efforts of its members.

TEDDY activities up today

Participate in or promoting new EU **initiatives** in the paediatric fields (Enpr-EMA, FP7 and H2020 projects, EPCTRI, PedCRIN, EPTRI, c4c)

Develop educational, informative and empowerment **tools** for children and families (Education videos, age-appropriate leaflets and brochures, surveys for the evaluation of informative materia, focus groups).

Manage and mantain useful **databases** on paediatric medicinal products and related trials, studies, PIP, PUMA or paediatric variations

Inform the Network participants about new initiatives and circulate regulatory documents and scientific publicationsC

Contribute to the scientific and regulatory **debates** promoted by EU Institutions by stimulating participation and by submitting written contributions (public consultation)

Organisation of collaborative groups on the most relevant scientific novelties and out-standing issues in the paediatric medicines research scenario

Plan and execute **surveys** on specific themes and provide publications on the results

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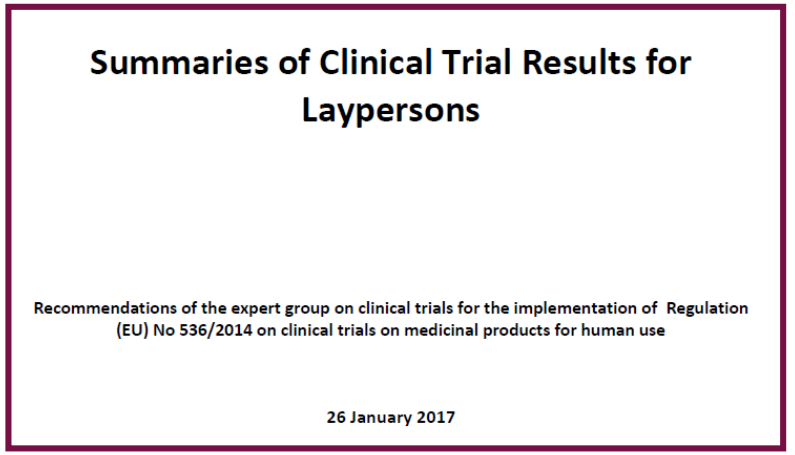
What TEDDY has achieved so far: : specific attention to paediatric population in communication of trial results

EU Clinical Trials Regulation 536/2014 foresees a dedicated section to communication of results to patients.

Article 37 requires sponsors to provide summary results of clinical trials in a format understandable to laypersons.
These lay person summaries will be made available in the EU Portal and Database. Annex V of the Regulation sets out the ten elements that must be addressed in the lay summaries.



This document includes **recommendations and templates to help authors when writing the lay summary**. Consistency in the way that trial results are presented will help to improve familiarity and comprehension for participants, patients and others.

What is missing: specific attention to paediatric population

The TEDDY Network participated in the public EU consultation, proposing to include the paediatric aspects in the consultation document.

A whole paragraph dedicated to paediatrics, including the TEDDY proposal, has been added into the final version of the document to develop **laypersons summary in age appropriate, simple and understandable language** to ensure easy reading by parents and by children.

More info at:
www.teddynetwork.net

Summaries of Clinical Trial Results for Laypersons

GENERAL PRINCIPLES

- Develop the summary for a general public audience and do not assume any prior knowledge of the trial
- Develop the layout and content for each section in terms of style, language and literacy level to meet the needs of the general public
- Keep the document as short as possible
- Focus on unambiguous, factual information
- Ensure that no promotional content is included
- Follow health literacy and numeracy principles
- Consider involving patients, patient representatives or advocates in the development and review of the summary information to ensure that it truly meets their needs.

Furthermore, this document provides recommendations about:

- Health Literacy →text should be suitable for people with a low/medium average level of literacy (level 2 or 3)
- Readability
- Use of plain language, numeracy and visuals

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Informed consent: Lack of harmonisation

Even if the requirements for the Informed Consent Form and Assent Form in paediatric clinical trials within European countries are similar and in accordance with the ICH GCP, there is a difference within individual countries, which are not harmonised in Europe. These discrepancies can present challenges for paediatric clinical trials.

CHALLENGE: there is a wide variation in age groups by national laws

Enpr-EMA (the European Network of Paediatric Research at the European Medicines Agency) Ethics WG suggested a "general template", that could be adopted and addressed to a wider population

What is missing: specific attention to paediatric population

- Rarely all the attempts for the patient involvement pay specific attention to the paediatric population needs.
- Available data and publications show that ad hoc strategies to inform minors to be enrolled in clinical trials are seldom produced.
- It is necessary to recognize that a standard model of information is not valid for all age groups above all for extreme groups.

An example of patients tailored approach: GAPP

The GAPP (GAbapentin in Paediatric Pain) project intends to improve the therapeutic perspectives of children who suffer from chronic pain, providing them with the drug " Gabapentin"

- **3 different BOOKLETS for each study** (GABA-1 e GABA-2) for different age groups
- **2 different ASSENT FORMS** for patients from 7 to 11 and from 12 to 17 years of age

Available in the 7 languages of the project (Albanian, French, Greek, English, Italian, Dutch and German)

More info at: http://pediatricpain.eu/

An example of patients age-tailored approach: DEEP

The objective of the DEEP project is the marketing of a new formulation of deferiprone for the treatment of iron overload in paediatric patients affected by congenital anaemias

- 3 different BOOKLETS explaining CTs aims and procedures and what they are going to experience
- 2 different ASSENT FORMS

Available in the 6 project languages (Albanian, Arabic, English, French, Greek, Italian)

More info at:
http://deepproject.eu/

Patient diary and booklets

Patient diary for each study (GABA-1 and GABA-2)

More info at: https://www.pediatricpain.eu/patients-and-families/

Informative videos

Two animated videos have been developed:

- presenting general information on clinical trials for young children
- presenting general information on clinical trials for teenagers

Videos are available at this link: https://www.pediatricpain.eu/patients-and-families/

An innovative approach for the patient involvement in the paediatric clinical research

YPAG (Young Persons Advisory Group)

A Young Persons Advisory Group, or YPAG, is an organization composed of youths, patients, carers and people interested in a health condition or in research, actively participating as partners, advising researchers and their teams in a full range of activities in various research projects and initiatives.

An innovative approach for the patient involvement in the paediatric clinical research: YPAGs

There are 21 different YPAGs across the world, included in the international iCAN Network. They collaborate all together to give voice to the children and their families about health, medicine, research and innovation issues.

At EU level **eYPAGnet** (member of Enpr-EMA) has been established with the mission to improve the capacity of collaboration with the different agents who participate in the research and development process of innovative drugs.

eYPAGnet
European Young Persons' Advisory Group Network

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CVBF in collaboration with the TEDDY Network and the paediatric University Hospital Azienda Ospedaliero-Universitaria Consorziale Policlinico di Bari – Ospedale Pediatrico "Giovanni XXIII" promotes the first italian YPAG in Bari corresponding to a new chapter of iCAN, named "KIDS Bari".

Launch event on 7th June 2017 in Bari

KIDS Objectives:
Peer support for young patients;
advocacy for children, patients and participants in clinical trials;
advise young people on research;
raising public awareness;
fundraising.

Consorzio per Valutazioni Biologiche e Farmacologiche – Dege e shoqerise se huaj, Albanian Branch Office in collaboration with the TEDDY Network and University Hospital Center Tirana "Mother Teresa", Service of Paediatrics), promoted the first YPAGin Albania, named KIDS Albania.

Launch event on 15th September 2017 in Tirana

Children's involvement and paediatric clinical research: what can be improved?

- Trials opened and completed on time
- Recruitment of patients to agreed target
- Retention of patient to completion
- Trials meet the needs of patients

The TEDDY Network could take care of these aspects

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