

Esophageal atresia WG

Chair: F Gottrand

Co-Chair: L Dall'Oglio

Secretary: U Krishnan



Agenda

- **Introduction: what is going on in the EA planet (ERNICA, INoEA, Covid...) (Frederic Gottrand)**
- **Update on the EoE register in EA patients: current status of agreements and inclusion; preliminary results of the first 45 cases (Frederic Gottrand, Usha Krishnan, Katialine Groff)**
- **Progress of Transition consensus (Usha Krishnan)**
- **Comparison of Balloon and Savary dilalation study: current status (Renato Tambucci)**
- **First results of the mucosal bridge (Matthieu Antoine)**
- **Announcement of the next world congress on EA in Cincinnati Oct 10-14 2022 (Mike Rutter)**
- **Update of the STEPS-EA trial (Anne-Fleur van Hal)**
- **Other project/proposal (?)**

Summary of activities 2020

O'Donnell JEM, Purcell M, Mousa H, Dall'Oglio L, Rosen R, Faure C, Gottrand F, Krishnan U. Clinician Knowledge of Societal Guidelines on Management of Gastrointestinal Complications in Esophageal Atresia. J Pediatr Gastroenterol Nutr. 2021 Feb 1;72(2):232-238.

Ten Kate CA, Tambucci R, Vlot J, Spaander MCW, Gottrand F, Wijnen RMH, Dall'Oglio L. An international survey on anastomotic stricture management after esophageal atresia repair: considerations and advisory statements. Surg Endosc. 2020 Aug 3. doi: 10.1007/s00464-020-07844-6. Epub ahead of print.



Esophageal Atresia COVID19 International Network on Esophageal Atresia Registry INoEA.org March 22, 2021

	EA/TEF n=17
Gender	9M/8F
EA type C / A / other	11 / 3 / 2 (missing n=1)
Mean Age	6.8 years
Associated respiratory problems	Asthma n=3 Tracheomalacia n=7 Recurrent chest infections n=3
Associated malformation	Cardiac n=6
Associated digestive problems	Anastomotic strictures n=7
Medication prior to COVID19	PPI n=4 fluticasone n=3 bronchodilators n=2 furosemide, enalapril n=1
Number of days since onset of illness (days) to reach the peak of COVID-19	4.1 days Asymptomatic n=2 Pneumonia n=1
Outcome	No hospitalization n=14 Admitted on the ward and discharged n=3 Exudative retinopathy n=1
Respiratory support at peak of COVID-19	O2 n=1
Ped ICU admission	None



INoEA International Network of Esophageal Atresia

- In addition, 3 adults (2 males, 30 years) with EA/TEF (1 type A, 1 type B, 1 type C) have been reported to be infected by SARS-CoV-2, (1 from India, 1 from Italy, 1 from France). Two were admitted on the ward. All three had an uneventful outcome.

Anastassios C. Koumbourlis, Yvonne Belessis, Mary Cataletto, Renato Cutrera, Emily DeBoer, Mikhail Kazachkov, Sophie Leberge, Jonathan Popler, Federica Porcaro, Thomas Kovesi. Care Recommendations for the Respiratory Complications of Esophageal Atresia-Tracheoesophageal Fistula The International Network of Esophageal Atresia, Respiratory Complications Working Group. [Pediatr Pulmonol. 2020 Jul 27. doi: 10.1002/ppul.24982.](#)

ERNICA: European Reference Network for rare Inherited and Congenital (digestive and gastrointestinal) Anomalies

Dingemann C, Eaton S, Aksnes G, Bagolan P, Cross KM, De Coppi P, Fruithof J, Gamba P, Goldschmidt I, Gottrand F, Pirr S, Rasmussen L, Sfeir R, Slater G, Suominen J, Svensson JF, Thorup JM, Tytgat SHAJ, van der Zee DC, Wessel L, Widenmann-Grolig A, Wijnen R, Zetterquist W, Ure BM. ERNICA Consensus Conference on the Management of Patients with Long-Gap Esophageal Atresia: Perioperative, Surgical, and Long-Term Management. Eur J Pediatr Surg. 2021 Jun;31(3):214-225.



[CAN EAT - Care and Nutrition in Esophageal Atresia: An ERNICA animation for parents and families - YouTube](https://www.youtube.com/watch?v=6sdwKlbZZoc&list=PLdmabVdgL6xlijhHaXmWQp111W8vUOZNn)

<https://www.youtube.com/watch?v=6sdwKlbZZoc&list=PLdmabVdgL6xlijhHaXmWQp111W8vUOZNn>

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EOE EA network

- **Due to General Data Protection Regulation issues impossible to send data from European citizen to Australia (database finally moved to Lille): all Agreements (ethical, privacy...) obtained in France!**
- **E-CRF retrospective ready and functioning**
- **Agreements still in process with several participating centers!**



EOE_RETRO

Working Group Meetings – WCPGHAN

11/06/2021



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Agreement signed

Country	Site	PI
France	Hospital J de Flandre, Lille	Prof Frederic Gottrand
	Sydney Children's Hospital	Dr Usha Krishnan
Australia	Canberra Hospital	Pr David Croaker
	The Royal Children's Hospital, Melbourne	Dr Michael Nightingale
	Schneider Children's Medical Center of Israel	Professor Raanan Shamir
Israel		Dr Noam Zevit
	Soroka University Medical Center	Dr Ari Silbermintz
		Dr Baruch Yerushalmi
Netherlands	Emma Children's Hospital	Dr Michiel van Wjik
Finland	Children's Hospital, Helsinki	Antti Ilmari Koivusalo

Agreement in review

Country	Site	PI
Belgium	Universitair Kinderziekenhuis, Brussels	Prof Yvan Vandenplas Dr Gigi Veereman Dr Koen Huysentruyt
	CHC Clinique Saint-Joseph	Dr Olivia Bauraind
	Ghent University hospital	Dr Stephanie Van Biervliet
		Dr Saskia Vandevelde



No agreement

Country	Site	PI
UK	Great Ormond Street Hospital for Sick Children	Dr Osvaldo Borelli
	Epson and ST Helier University Hospitals	Dr Sonny Chong
	Bristol Royal Hospital for Children	Dr Christine Spray
Germany	University of Munich Medical Center	Dr Sibylle Koletzko
Greece	Iaso General Pediatric Hospital, Athens	Dr Ioanna Panayotou – Angelakopoulou
	Athens Children's Hospital	Prof Alexandra Papadopoulou Prof Luigi Dalloglio
Italy	Bambino Gesù Children's Hospital, IRCCS, Rome	Dr Francesca Rea Dr Renata Tambucci
	University of Messina Hospital	Dr Paola Deangelis
	Policlinico Hospital, Bari	Dr Claudio Romano
		Baldassarre
	Sapienza-University of Rome	Dr Salvatore Olivia

No agreement

Country	Site	PI
Sweden	Karolinska University Hospital	Dr Jan Svensson
Lebanon	Makassed University General Hospital, Lebanon	Dr Aziz Koleilat Dr Shrine Mneimneh
Slovenia	Children's Hospital, Ljubljana	Prof Rok Orel
Lithuania	Vilnius University Children's Hospital	Dr Vaidotas Urbonas
Switzerland	University Hospital Lausanne	Dr Andreas Nydegger Dr Sabine Vasseur
	Rady Children's Hospital-San Diego	Dr Hayat Mousa
	Cincinnati Children's Hospital Medical Center	Dr Von Allmen, Daniel
USA	Boston's children hospital	Dr Peter Ngo Dr Mike Manfredi
	NYU Langone Medical Center	Dr Russell W. Jennings Dr Mikhail Kazachkov
Canada	Hospital Pediatrics at Alberta Health Services - Calgary,	Michelle Bailey
Dubai	Al Jalila Children's Specialty Hospital, Dubai ,UAE	Dr Christos Tzivinikos

e-CRF ACCESS

CENTER	SITE_NAME	FIRST_NAME	LAST_NAME	N° patients included n = 49
01	Sydney Children's Hospital, AUSTRALIA	USHA	KRISHNAN	28
02	Hospital J de Flandre, FRANCE	FREDERIC	GOTTRAND	19
08	Israel	ARI	SILBERMINTZ	0
08	Israel	RAANAN	SHAMIR	0
08	Israel	NOAM	ZEVIT	0
12	Amsterdam	MICHIEL	VAN WJIK	0
21	Finland	ANTTI	KOIVUSALO	0
30	Al Jalila Children's Specialty Hospital, DUBAI	CHRISTOS	TZIVINIKOS	2

EOE EA network

- **How can we help you expediting Agreements signature in your centers? This is the only way to get access to the e-CRF**



EOE EA: Preliminary data

- 47 patients analysed

Type A	Type B	Type C	Type D	Type E
7	1	31	1	2
17%	2%	74%	2%	5%

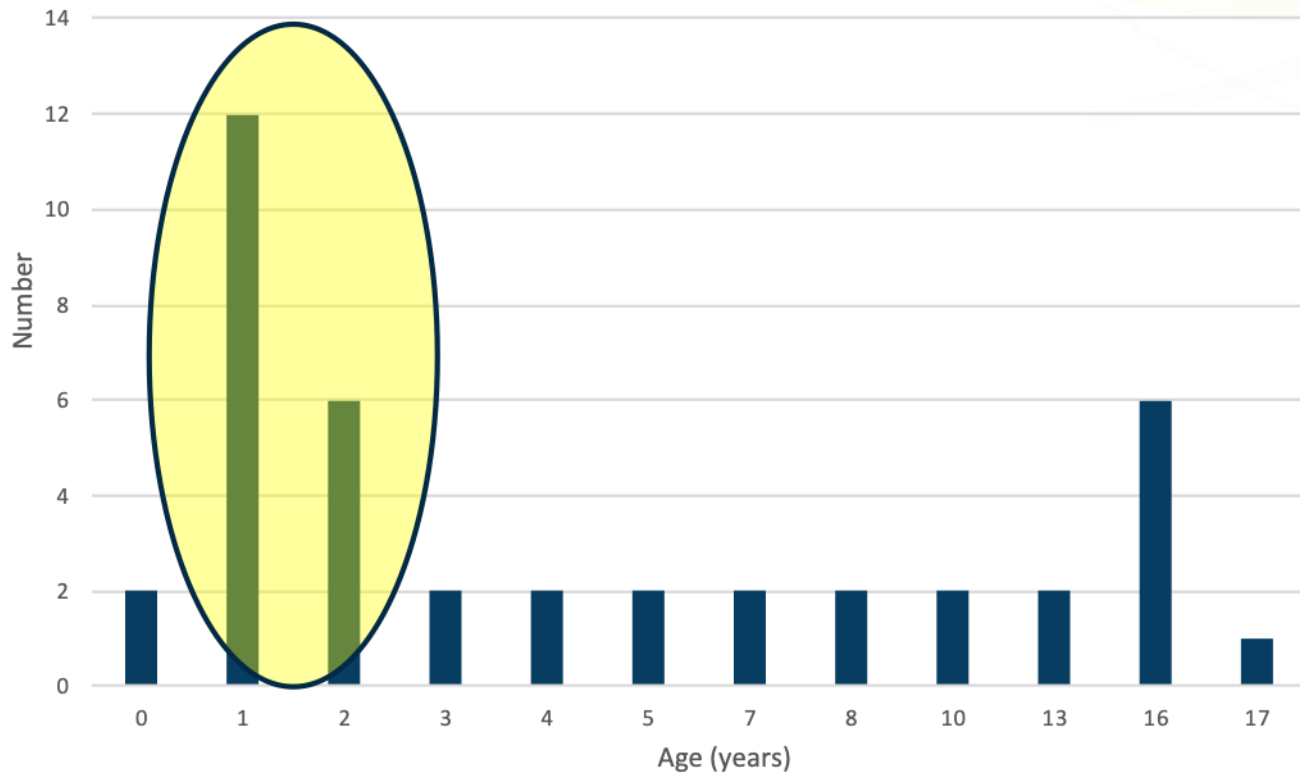
(n=42)

- 62% male and 38 % female



➔ Male-female ratio: 1.61

Age at diagnosis:



Symptoms:

Asymptomatic	Regurgitation	Dysphagia	Vomiting	Feeding difficulties
4	9	21	18	21
9%	20%	47%	40%	47%

- 2 congenital stenosis → 4%
- PPI at the time of diagnosis: 25/27 → 93%



Endoscopy:

- (n=40)

Normal	Anastomotic Stricture	Rings	Exsudate	Edema	Furrow	Trachealisation
11	17	0	3	4	8	0
23%	36%	0%	6%	9%	40%	0%

Biopsies (n=47): N° EoE/Hpf

Esophagus	Proximal	Mid	Distal
mean	26	26	33
ranges	2-91	0-80	1-96

Treatment:

- ($n=30$)

Fluticasone	Budesonide	PPI increased
5	16	22
17%	53%	73%

- ($n=29$)

Targeted elimination diet	Elemental formula	No diet therapy
4	2	23
14%	7%	79%



Post treatment

- Remission ($n=37$):

YES	NO
29	8
78%	22%

- Relapse post treatment ($n=33$):



14 patients → 42%

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INoEA Transition Working Group Update




Members

- Sub-speciality groups
- **Pediatric and Adult Gastroenterology** : Prof Christophe Faure (Lead), Prof Frederic Gottrand,, Dr Benjamin Gold, Dr Usha Krishnan, Dr David Seguy, Dr Andrew Taylor
- **Surgery** : Prof Rene Wijnen (Lead), Prof Luigi Dall'oglio, **Dr Mario Constantini**
- **Pulmonology** : Prof Anastassios Koumbouralis and Prof Tom Kovesi (Joint Leads)
- **ENT** : Prof Mike Rutter (Lead)
- **Feeding and Nutrition** : Gastroenterologist: Dr Usha Krishnan (Lead), Dietician: Ms Jessica Menzies, Ms Audrey Vanmalleghem and Deglutologist: Dr Nathalie Rommel
- **Psychology and QOL** : Ms Michaela Dellenmark Blom (Lead), **Dr Vuokko Wallace, Ms Evelyn Culnane**
- **Parent/Patient support groups** : Mr Graham Slater (Lead, President of EAT)
- **Literature Review**: **Dr Michael Dumont and Dr Hayley Slater**

Steps Completed

- Literature Review
- Summary Tables based on Literature Review
- Draft questions from sub groups
- Drafting of sections, recommendations, referencing based on the questions and literature review by each sub group
 - Psychology and QOL
 - Respiratory
 - Feeding and Nutrition

Next Steps.....

- **Drafting of sections, recommendations, referencing based on the questions and literature review by each sub group**
 - **Gastroenterology** 
 - **Surgery** 
 - **ENT** 
- **Online/F2F/Hybrid Voting on recommendations methodology**

Next Steps.....

- Collating all sections and drafting whole paper and circulating amongst whole group
- Deciding which journal to submit to
 - Diseases of Esophagus (both adult and paed GI/Surgeons read it but not so much from other specialities)
 - Frontiers (Open Access, includes all disciplines)
- Presentation in INoEA Congress in 2022
- Creation of Transition App for EA patients with funding support from ERNICA





WORK FROM
HOMER

Stay Safe

Update on Old/New projects

- International survey on management of GERD in EA patients
- Survey Monkey link sent to ESPGHAN EA WG and INoEA members
- 40 respondents from 23 hospitals in 19 countries
- 87.5% aware of guidelines
- 35% prescribe PPI during first year
- 65% performed endoscopy/pH metry/Impedance testing for GERD screening
- 62.5% performed investigations as recommended by guidelines prior to fundoplication
- But only 22.5% performed fundoplication for refractory GERD as recommended in guidelines
- Paper currently being finalised for submission

New Project

- In the survey 25 centres had indicated that they were interested in taking part in a multicentre study evaluating “Fundoplication outcomes in children with Esophageal Atresia”, using Pressure Flow Analysis metrics (PFA) on Swallow Gateway Platform with High Resolution Impedance Manometry (HRIM) of the esophagus
- High-resolution manometry combined with impedance measurements, helps characterize the interplay between esophageal motor function and bolus clearance.
- PFA can offer new insights in this area and potentially help predict the likelihood of developing dysphagia post fundoplication and help with patient selection for anti reflux surgery

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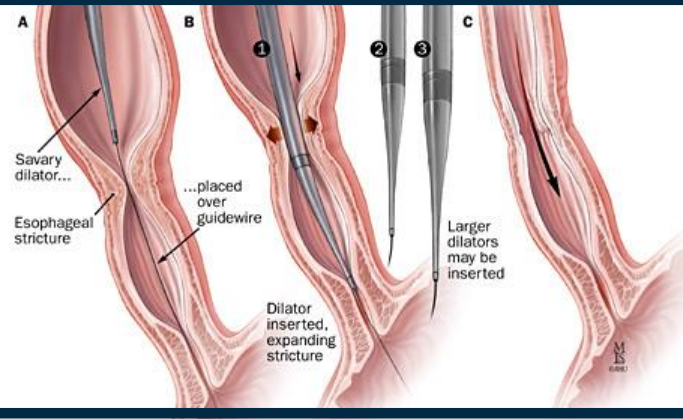
51st Annual Meeting of the ESPGHAN

Geneva, 09-12 May 2018

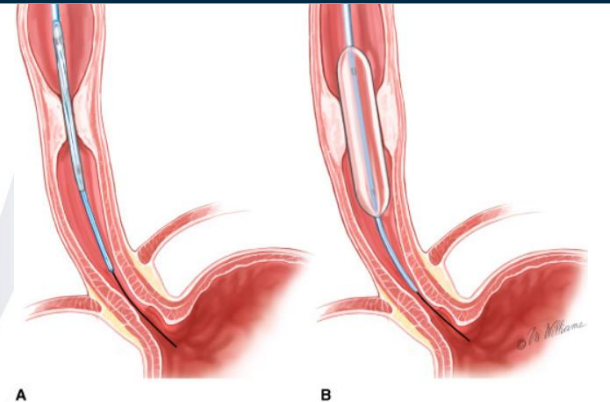
Anastomotic stricture in esophageal atresia: comparison of balloon vs bougie dilation

Two main categories of dilators exist:

fixed-diameter push-type dilators (bougie dilators)



radial expanding balloon dilators



No clear advantage of either balloon or bougie dilation has been demonstrated

Data coming from two randomized, controlled trials comparing bougie with balloons dilators for benign strictures in adults found no differences in terms of efficacy and safety at 1 year.



www.espghan.org

Saeed ZA. *Gastrointest Endosc*
1995;41:189-95.

Currently there are no controlled trials comparing efficacy and safety of hydrostatic balloon with bougie dilator for treatment of AS in EA patients

Therefore, due to the lack of strong evidences, the choice between balloon dilation and bougie is based only on operator experience and comfort with the equipment



www.espghan.org

Krishnan U. JPGN 2016;63:550-70.

Tambucci R. Front Pediatr 2017;

ESPGHAN multicenter collaborative study

Bougie vs Balloon dilators



www.espghan.org

All data being collected and patient interactions
are a part of routine patient care

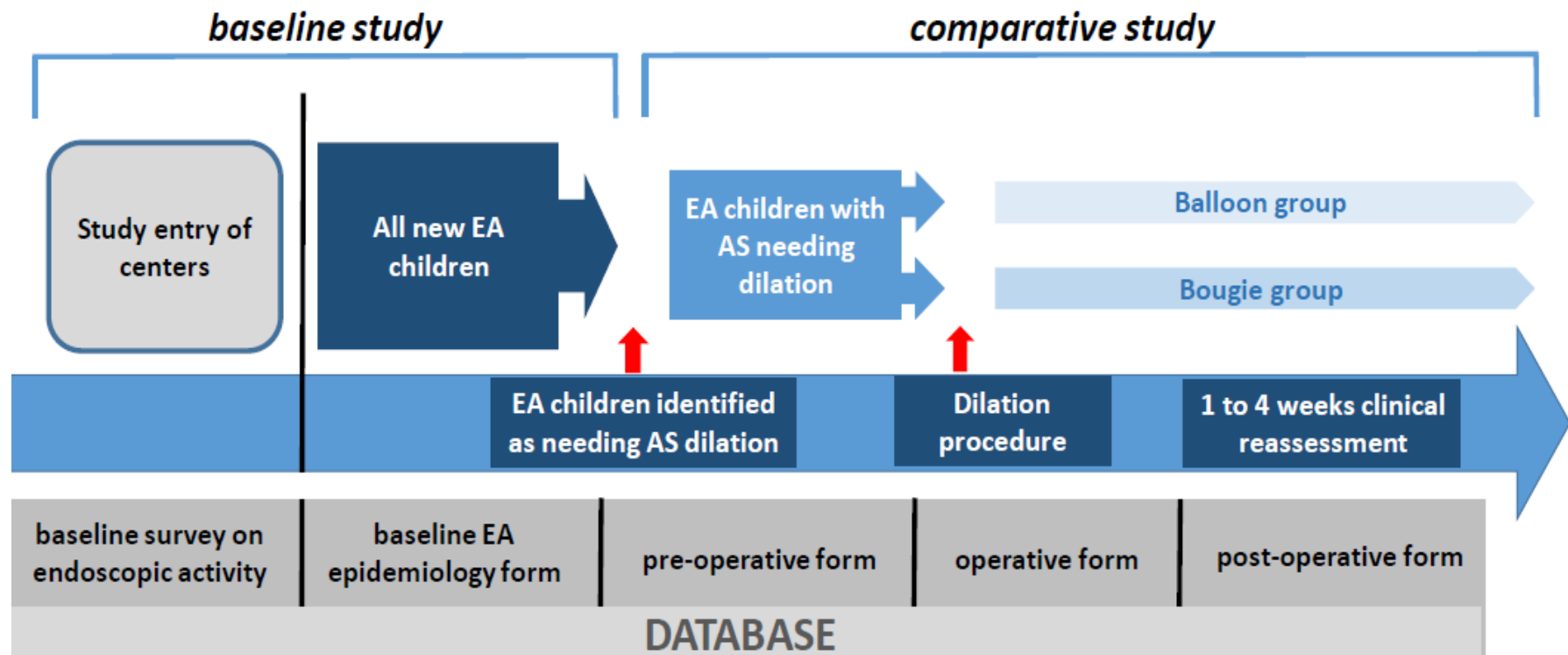
Primary endpoint

Compare the efficacy of the balloon vs bougie dilations in terms of number of dilatation sessions per patients needed to achieve stricture resolution

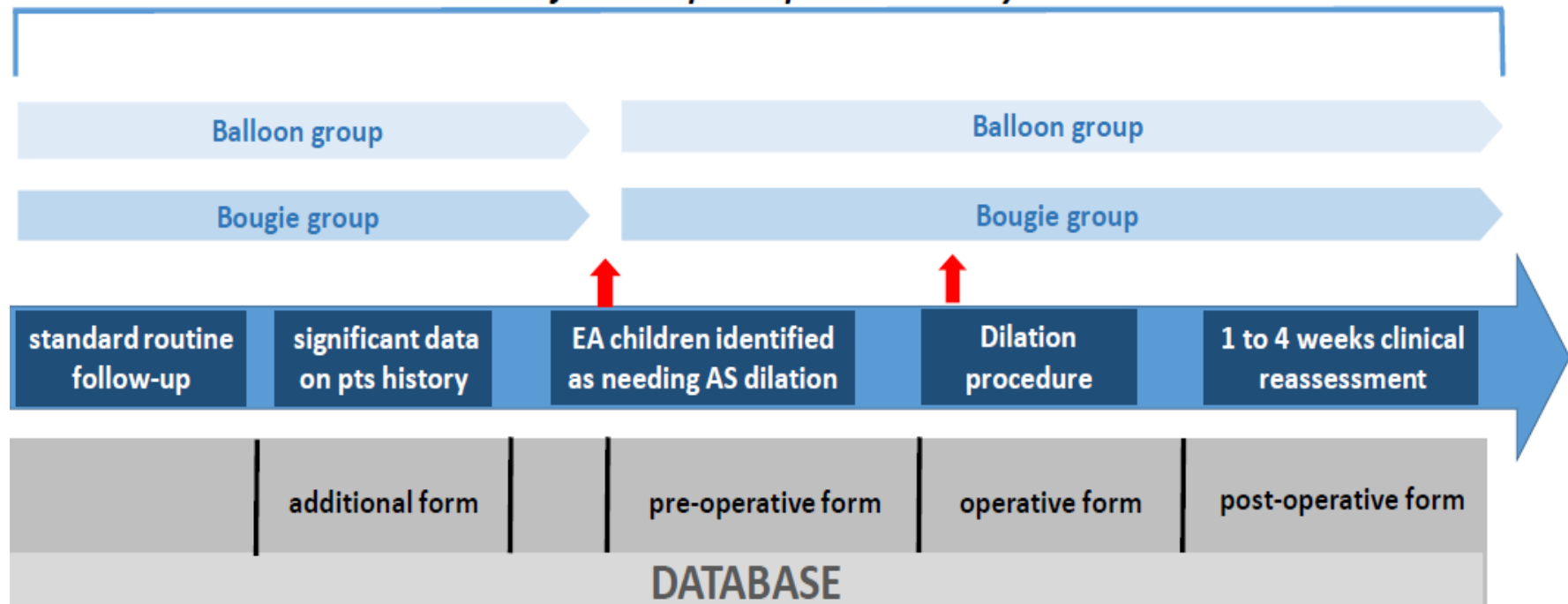


Secondary endpoints

- Develop a multi-center database to organize an international survey about the endoscopy activity on EA patients
- Compare the **safety profile** of bougie vs balloon dilations in terms of early and late complications occurrence
- Analyze **epidemiological data to describe the EA population** and evaluate AS incidence and identify risk factors for developing AS



follow-up comparative study



Inclusion criteria

- Infants undergoing surgical repair of congenital EA
- EA patients referred for endoscopic assessment

Exclusion criteria

- Patients with refractory/recurrent AS previously managed elsewhere
- Patients with insufficient medical history information



Anastomotic stricture after surgical repair of esophageal atresia: frequency, risk factors, and efficacy of esophageal bougie dilatations

Lydia Serhal, Frédéric Gottrand, Rony Sfeir, Dominique Guimber, Patrick Devos, Michel Bonnevalle, Laurent Storme, Dominique Turck, Laurent Michaud*

Stricture resolution occurred after a mean of 3.2 ± 1.74 dilatations per patient

Sample size of 150 patients (75 for each treatment group) could provide 80% power to detect a difference of 25% in number of dilations per patient with a CI 95% and

assuming the same SD

Management of anastomotic strictures after esophageal atresia repair: results of a global survey

Chantal ten Kate (c.tenkate@erasmusmc.nl)

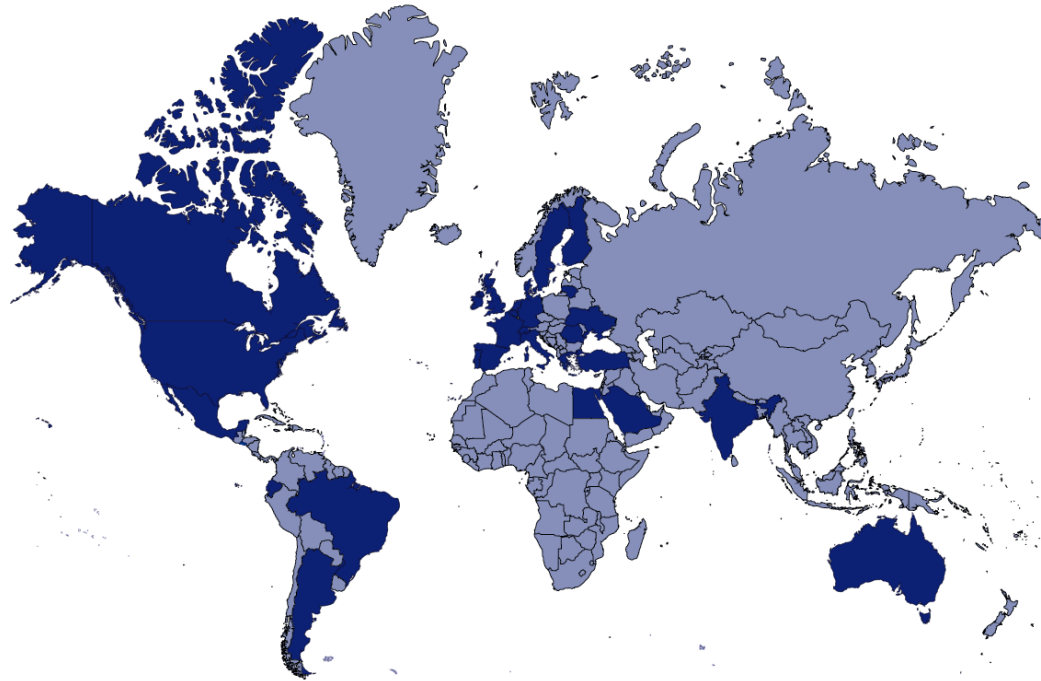
Renato Tambucci, [Frédéric Gottrand](#), Rene Wijnen, Luigi [Dall'Oglio](#)

ESPGHAN Annual Meeting, Glasgow

EA working group 05-06-2019



Management of anastomotic strictures after esophageal atresia repair: results of a global survey



110 centers
worldwide interested in
partecipating



1. Universitair Ziekenhuis Gent (Gent, Belgio)
2. CHU Lille Pediatric Gastroenterology (Lille, France)
3. Hospital Italiano de Buenos Aires (Buenos Aires, Argentina)
4. Columbia University College (New York, USA)
5. Victor Babes University of Medicine and Pharmacy (Timisoara, Romania)
6. Hacettepe University Faculty of Medicine (Ankara, Turkey)
7. Istanbul Medeniyet University (Istanbul, Turkey)
8. Medical University of Warsaw (Warsaw, Poland)
9. Hospital de Emergencias Pediátricas (Lima, Perú)
10. Hospital General de Niños (Buenos Aires, Argentina)
11. Erasmus University of Rotterdam (Rotterdam, Paesi Bassi)
12. King Chulalongkorn Memorial Hospital (Bangkok, Thailand)
13. Ca' Granda Ospedale Maggiore Policlinico (Milano, Italy)
14. Universidad Central de Venezuela (Caracas, Venezuela)
15. A.O.R.N. Santobuono-Pausilipon (Napoli, Italia)
16. CHU Saint Etienne Neonatology Unit (Saint Etienne, Francia)
17. CHU – Toulouse – Hôpital des enfants (Toulouse, France)
18. CHU de Rennes Endoscopy (Rennes, France)
19. CHU de Reims Pediatric Surgery (Reims, France)
20. Trousseau University Hospital Pediatric Surgery (Paris, France)
21. Robert-Debré Hospital Pediatric Gastroenterology (Paris, France)
22. CHU Angers Pediatric unit (Angers, France)
23. CHU Bordeaux Pediatric Gastroenterology (Bordeaux, France)
24. CHU Grenoble Pediatric Department (Grenoble, France)
25. CHU Besançon Pediatric Gastroenterology (Besançon, France)
26. CHU Brest Pediatric Surgery (Brest, France)
27. CHU Strasbourg Pediatric Gastroenterology (Strasbourg, France)
28. CHR Orléans Pediatric Surgery (Orléans, France)

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7. Istanbul Medeniyet University (Istanbul, Turkey)
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Data of **11 patients**
are have been inserted into the
database!!



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Endoscopic management of esophageal mucosal bridges in children followed for esophageal atresia

M. Antoine, F. Gottrand

Hôpital Jeanne de Flandre, CHU Lille, France



www.espghan.org

Esophageal mucosal bridges (double-barrel esophagus)

Rare entity, cause of dysphagia, food blockage

Different etiologies: infections, inflammatory diseases, post-traumatic

Esophageal atresia: post-surgical, GERD, iatrogenic (nasogastric tube placement)

Endoscopic management:

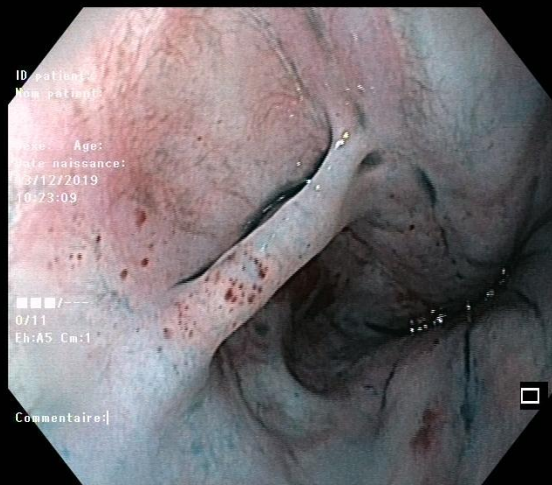
Argon plasma coagulation

Endoscopic knives/scissors

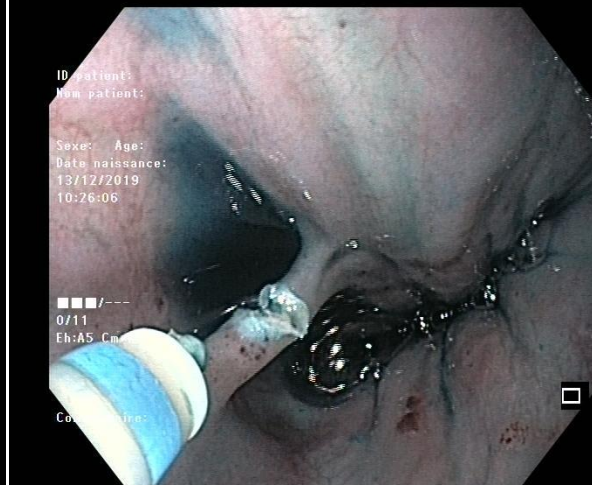
Electrocautery

Miniature staplers

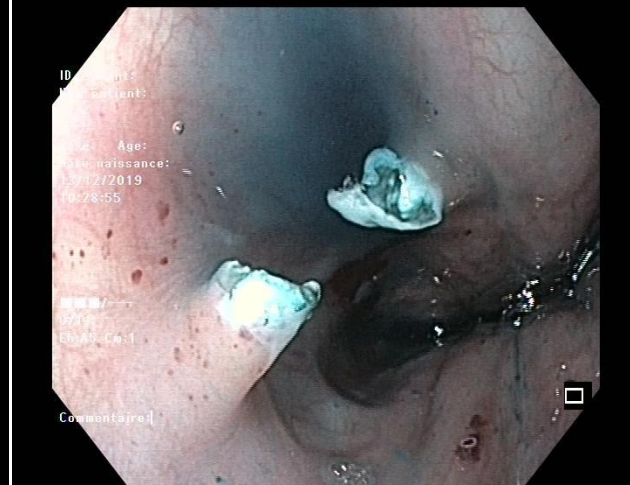




Mucosal bridge



Endoknife
(Dualknife 2mm)



Post section



Literature review

Only a few Case reported

N=4 children (with mucosal bridges at the site of esophaegal anastomosis followed for esophageal atresia) reported in **2 publications** :

- 3 treated with argon plasma coagulation (Chapuy and al., 2014)
- 1 treated with endoscopic miniature stapler (Kawano and Muensterer, 2019)

Objectives of the project:

- Collect a large number of cases at an international level
- Describe patients characteristics, mucosal bridges treatment, techniques, safety, efficacy and outcome



Preliminary results....

18 patients in 9 centers (France: Lille, Paris Robert-Debré, Lyon, Amiens, Orléans; Hannover; Vilnius; Sydney; Dubai)

Mean age at diagnosis of mucosal bridge (MB): 5.8 ± 4.4 yo (7 months – 13.8 years)

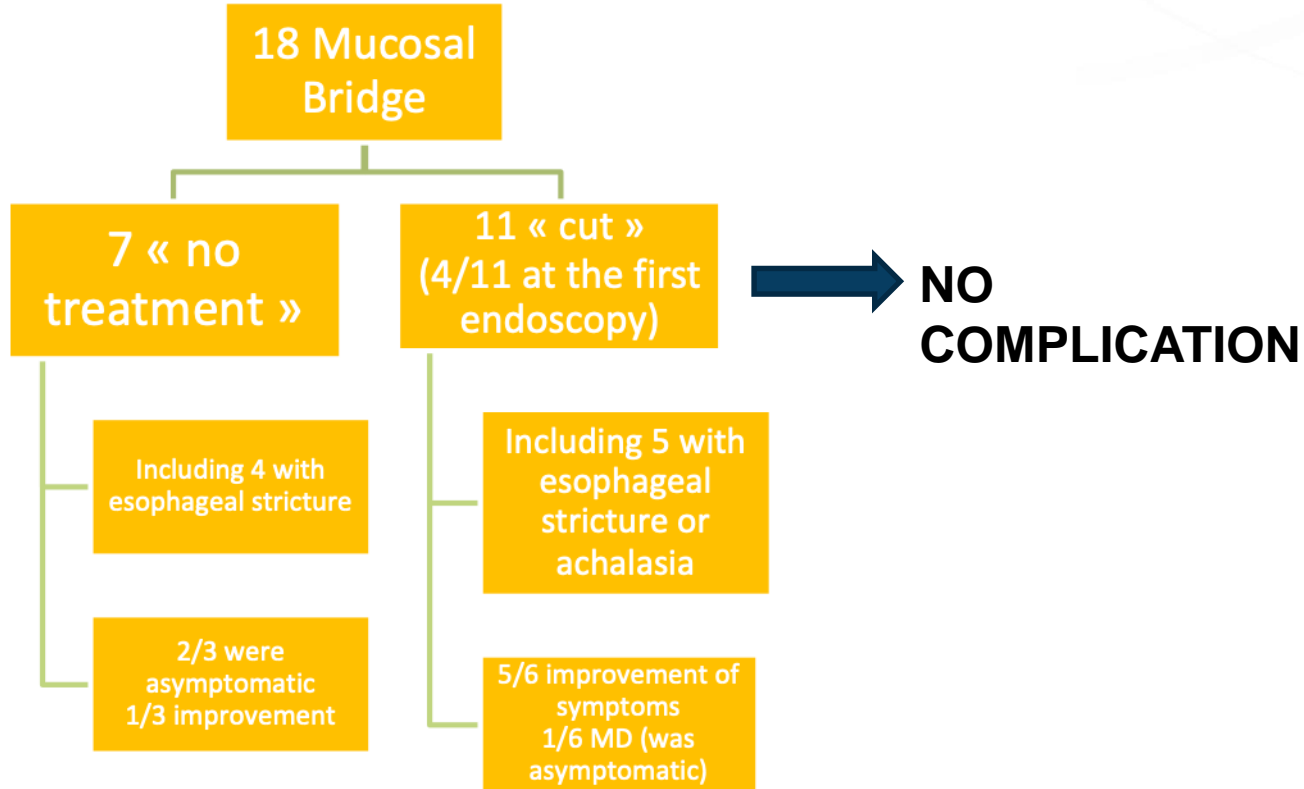
GERD (PPI 13/18, antireflux procedure 10/18)

Esophageal dilatations (13/18, >2 for 10/18)

No symptoms: 5/18



Preliminary results: treatment and outcome....



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Cincinnati, Ohio, October 10-14, 2022

The “QUAD” conference

- Including an INPAT session
- The Cincinnati Airway Course
- The Dysphagia Conference
- The Annual Aerodigestive Conference

INoEA 2022



October 2022	Saturday 8	Sunday 9	Monday 10	Tuesday 11	Wednesday 12	Thursday 13	Friday 14	Saturday 15	Sunday 16
Morning	1 Dysphagia Course FEES	3 Dysphagia Course FEES EAT Family Day INoEA / Ped Surg esophageal dissection	5 INoEA Dysphagia	7 INoEA Dysphagia	9 INoEA Airway	11 Airway Aero	13 Airway Aero	15 Airway Course Dissection A Flex bronch Sim A	17 Airway Course Dissection A Flex Bronch Sim A
Afternoon	2	4 Dysphagia Course Pharyngeal manometry EAT Family Day INoEA / Ped Surg esophageal dissection	6 INoEA Dysphagia	8 INoEA Dysphagia	10 INoEA Airway	12 Airway Aero	14 Airway Aero	16 Airway Course Dissection B	18
Evening		Welcome Cocktails	Faculty Dinner A Or evening at the Zoo		Joint Conference Banquet - Union Terminal / Museum Center		Faculty Dinner B		

Information Highlights



- Sessions will focus on interdisciplinary care
 - Pediatric to adult transitioning is an additional focus
- There will be breakout rooms for submitted papers
- We plan video poster boards
- The weekends either side of the conference will be for workshops and dissection courses
- There will be a competition for trainees
 - The prize will be 10 free registrations
- We can only accommodate 500 delegates
 - We will also be offering a virtual attendance option

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- Update on the EoE register in EA patients: current status of agreements and inclusion; preliminary results of the first 45 cases (Frederic Gottrand, Usha Krishnan, Katialine Groff)
- Progress of Transition consensus (Usha Krishnan)
- Comparison of Balloon and Savary dilalation study: current status (Renato Tambucci)
- First results of the mucosal bridge (Matthieu Antoine)
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- **Update of the STEPS-EA trial (Anne-Fleur van Hal)**
- Other project/proposal (?)

STEPS-EA trial

Intralesional STeroid Injections to Prevent Refractory Strictures in Patients with Esophageal Atresia

Rene Wijnen, project leader

John Vlot, principal investigator

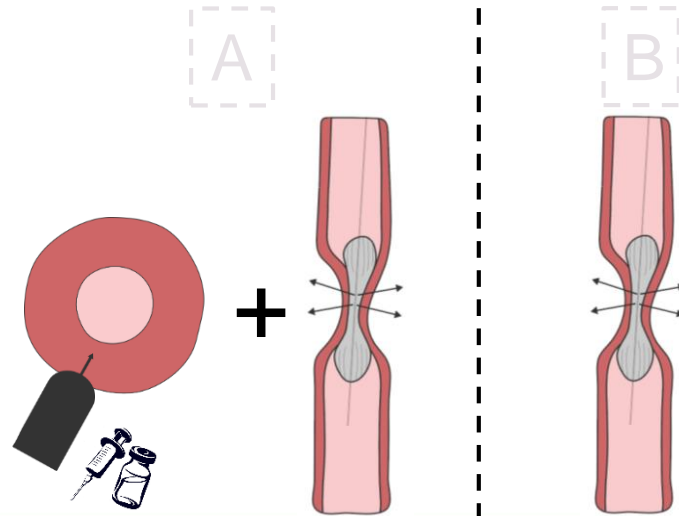
Anne-Fleur van Hal, coordinating investigator (steps.ea@erasmusmc.nl)



www.espghan.org

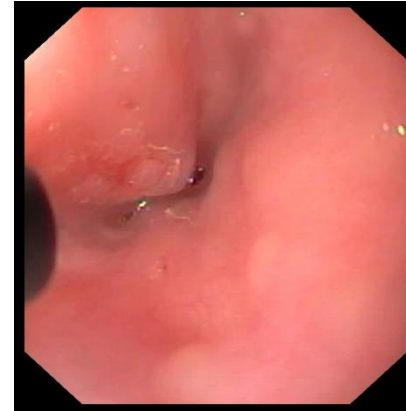
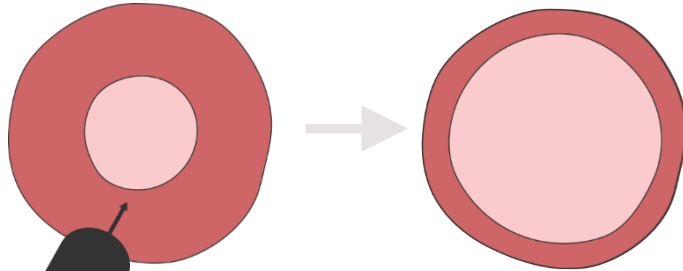
Quick recall

- Multicenter, single-blind randomized controlled trial.
 - → 1:1 randomization to injection with 10 mg/ml TAC (Kenacort-A 10) prior to balloon dilatation and balloon dilatation without any injection



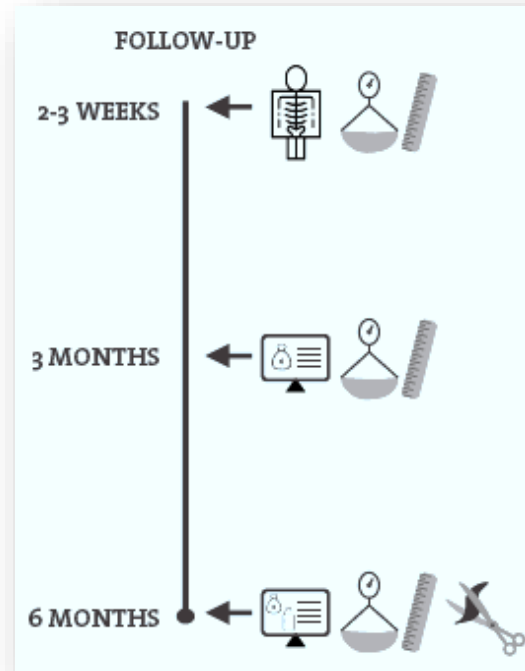
Quick recall

- Hypothesis: ↓ formation of collagen, ↑ breakdown of collagen, ↓ fibrotic healing
 - inhibition of scar formation
 - stenosis will not recur



Quick recall

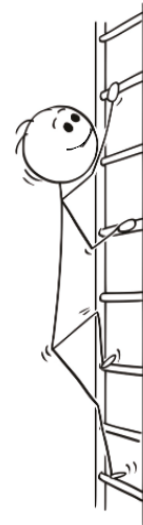
- Three main objectives:
 - Effectiveness
 - Safety
 - Cost-effectiveness



Where do we stand now?

- Grant from Sophia Foundation
 - Each center will receive €750,- per inclusion
- Inclusions N=4 Goal: N=110
- Three centers up and running, waiting for inclusions
 - Norway and France received ethical approval, starting in summer
- Still open for new participating centers if interested!
 - Contact: steps.ea@erasmusmc.nl

Road to success





steps.ea@erasmusmc.nl

STEPS-EA trial

 Network

Inherited and Congenital
Anomalies (ERNICA)



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