



ITHACA Board Meeting

2020 December 10 – 12

Satellite Meetings : Friday Dec. 11th

WG 10 Spina Bifida

From 11 to 12:50 AM

(WG10) Work Groups / Satellite Meetings : Friday December 11th



Time Slot (Virtual Zoom Rooms)	W10 : Spina Bifida Chair : Andrea Manunta /Giovanni Mosiello	SPEAKER PM contact : Anne Hugon
11h00	Welcome to new members, Structure of the group : An Inter - ERN WG Patient perspective on the assessment framework	Sylvia Roozen, Andrea Manunta, Giovanni Mosiello, Ammi Sundqvist-Andersson
11h15	Update on dysraphisms classification and Orphacodes revision	Ferdinand Dhombres
11h35	Guidelines redaction on urological management of SB, methodology	Andrea Manunta, Benoit Peyronnet
11h40	Transition Guidelines	Dan Wood
11h55	Pediatric Guidelines	Giovanni Mosiello, K. Abrahamsson
12h10	Adult Guidelines	Andrea Manunta, Benoit Peyronnet
12h20	Discussion on guidelines	All attendees
12h30	SBWG research workshop within the EJP RD call - ERN RD Training and Support Program	Giovanni Mosiello
12h35	Participation to Cross ERN surgical-based working group, contact with BOND ERN	Andrea Manunta
12h40	Agenda 2021	All attendees

European
Reference
Network
for rare or low prevalence
complex diseases

AMMI SUNDQVIST - ASSESSMENT FRAMEWORK MEASURES



	Num.	Measures
Goal 1: Improve quality of care, diagnosis and treatment	1	Listed as co-authors of consensus statements and Clinical Practice Guidelines
Goal 2: Ensure patient-centric ERNs that meet our community needs - Needs of patient community inform all ERN activities and their structure (for example, ERN covering in equal terms adult and paediatric care, MDT, etc)	2	Percentage of ERN WGs with ePAG advocates participating as members
	3	Patient representatives are members of the ERN Registry governance structure and/or ERN Registry Working Group (Yes/No)
	4.1	Number of patient journeys or surveys to capture patients' needs that have been discussed with ERN clinicians
	4.2	Percentage of sub-thematic areas where patient needs have been captured through a Patient Journey (or a survey on patients') and results have been discussed with ERN clinicians
	5	Perceptions or level of satisfaction on how ePAG advocates and clinicians are working together as a team to advance the ERN goals
	6	Percentage of outcome measures identified with the input of ePAG advocates
	7	Number of posters/presentations on ERNs delivered in national or international meetings (conferences and workshops)
Goal 3. Ensure a good level of awareness among the patient community about ERNs and their work (so that all can benefit)	8.1	Perception on how the ePAG has organised the outreach to its wider patient community (DISSEMINATION)
	8.2	Perception on how the ePAG has organised the outreach to its wider patient community (CAPTURING FEEDBACK AND PATIENTS NEEDS)

European



- 2016 « informal » Spina Bifida Working Group under the implusion from IF
- 01 April 2019 → cross ERN working group (WG) on Spina Bifida merging ITHACA and EUROGEN groups

August 2019 Web meeting → Objectives



1. Build the WG SB → identify experts in different fields
2. Draft EU recommendations on urological management of patients with Spinal Dysraphism
3. Orphacodes revision
4. Patient Registry

Orphanet Codes Revision

Ferdinand Dhombres, Hôp Trousseau Paris
Thimotey de Saint Denis, Hôp Necker Paris

Orphacodes Revision



- Orphanet asked for support with the revision of the Orphacodes for Spinal Dysraphism
-
- Currently → classification is mainly anatomical and incomplete
- More recent entities like LDM do not fit well in the present classification
- Need for a new classification not only anatomical but also clinical and prognostic and defining new entities
- → To be validated on a multicentric project analysing the next 100 cases of spinal dysraphism

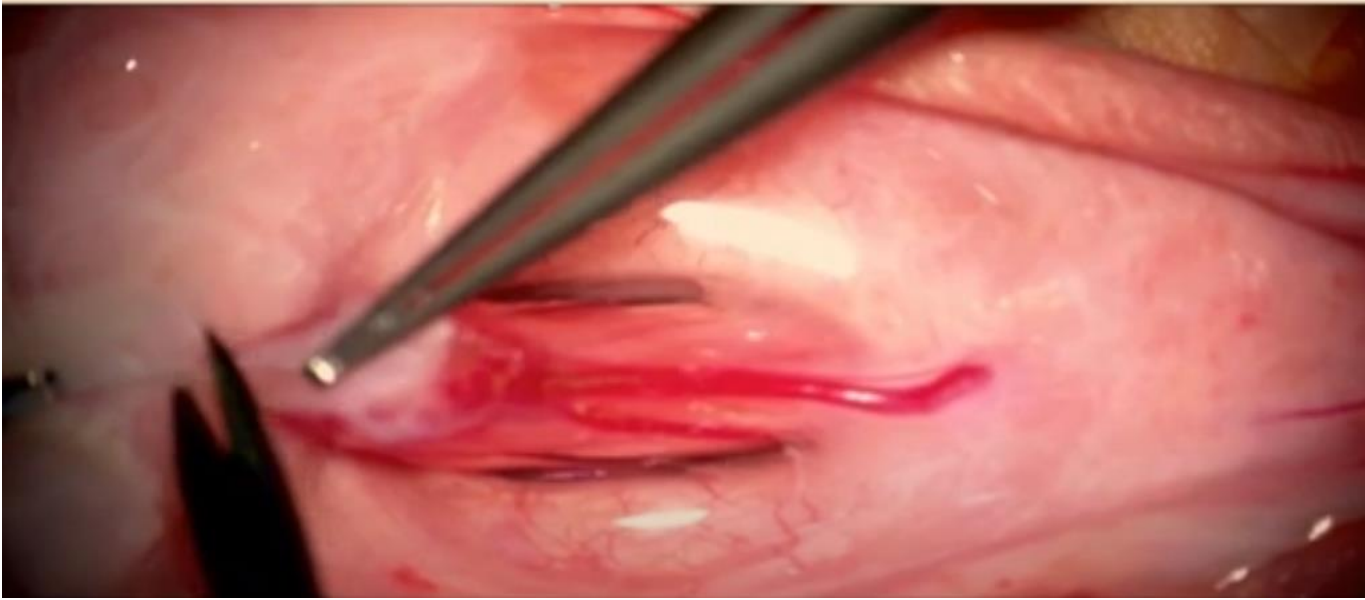


Birth of Y.
CS, 4180g



2:52

27



- **Limited Dorsal Myeloschisis not to be confused with MMC**
- **Excellent outlook**
- **No indication for fetal surgery**
- **No code orphanet for this entity**



Methodology proposal for the redaction of European Guidelines on spinal dysraphism

B Peyronnet – A Manunta

Centre de Référence Spina Bifida – Dysraphismes

Rennes

France

Guidelines on urological management of patients with Spina Bifida



Why ?

90% of children with SB are born with normal upper urinary tract → 50% upper urinary tract damage if untreated

2019 French national survey on causes of death in SB

Urologic Congenitalism

Urologic Disorders are Still the Leading Cause of In-hospital Death in Patients With Spina Bifida



Benoit Peyronnet, Fei Gao, Charlene Brochard, Emmanuel Oger, Lucie-Marie Scailteux, Frédéric Balusson, Juliette Hascoet, Quentin Alimi, Zine-eddine Khene, Sahar Bayat, Magali Jezequel, Camille Olivari, Caroline Voiry, Jacques Kerdraon, Guillaume Bouguen, Xavier Game, Laurent Siproudhis, and Andrea Manunta

UROLOGY 137: 200–204, 2020. © 2019 Elsevier Inc.



European
Reference
Network
for rare or low prevalence
complex diseases

Network
Intellectual Disability
and Congenital
Malformations (ERN ITHACA)

Guidelines already exist



American guidelines on SB, very comprehensive but...

“18+ years

Clinical Questions

- 1. What is optimal surveillance of the upper and lower urinary tract? What cancer screening is needed?

Guidelines

- 1. Obtain a renal/bladder ultrasound yearly. (clinical consensus)
- 2. Obtain a renal/bladder ultrasound, as needed if the adult has recurring symptomatic UTIs or if urodynamic testing identifies bladder hostility. (clinical consensus)
- 3. Obtain a serum creatinine test yearly. If the adult has low muscle mass, consider an alternative measure of renal function. (clinical consensus)”

ERN ITHACA - eUROGEN WG10 Spina Bifida



ITHACA Project Manager Contact anne.hugon@aphp.fr



Chair Andrea Manunta
Co Chair Giovanni Mosiello

International Federation for
Spina Bifida & Hydrocephalus (IF)
Sylvia Roozen – Secretary General
Ammi Sundqvist-Anderson

Task Force Teams

Pediatric Guidelines

Coordinated by Giovanni MOSIELLO
(Italy) and Kate ABRAHAMSSON
(Sweden)

Guidelines on Transition

Coordinated by Dan WOOD (UK)

Adult Guidelines

Coordinated by Andrea MANUNTA and
Benoit PEYRONNET (France)

Proposed roadmap



Jan 2021

- The coordinators of each section identify a panel of relevant experts within and/or outside the SBWG members
- Coordinators:
 - divide their sections of the guidelines in different chapters
 - identify an expert responsible for each chapter who will coordinate the literature search and chapter redaction

Feb 2021

- Systematic review of Medline and Embase databases + Cochrane library → all relevant articles in English language up to the 11th of december 2020
- Keywords adapted to the different chapters
- No search for unpublished literature
- Systematic reviews complying with the PRISMA statement included (if applicable)
- Search might be expanded to include articles on neurological bladder dysfunction related to traumatic lesions of the spinal cord

- Levels of evidence → Oxford Centre for Evidence-Based Medicine
- Strength of recommendations → « GRADE » system
- Max 5000 words for each section of the recommendations

April 2021

- the drafts of the different chapters are written and sent to the section coordinator and modified as required

Mai 2021

- Amended text → final review by a panel composed by all the authors of the three sections, i.e. authors of pediatric guidelines will read and comment transition and adult guidelines and vice-versa and all the members of the Spina Bifida Working Group
- The text is amended according to the modifications suggested by the review panel
- The Delphi method might be used if specific statements are controversial

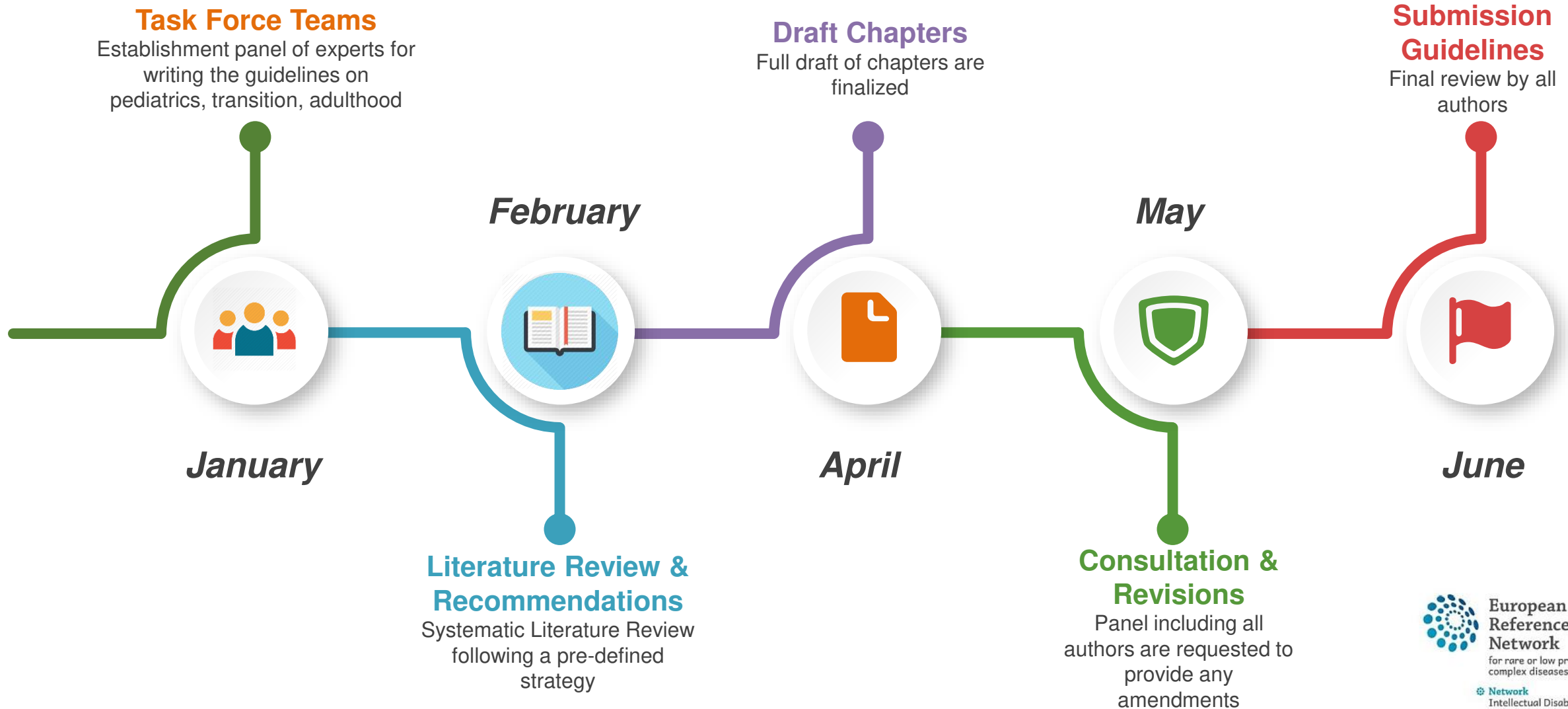
Juin 2021

- final text sent for a final reading to the panel of reviewers and in the absence of further comments is sent to a peer reviewed journal for publication
- The guidelines should be widely diffused on ITHACA and eUROGEN as well as on patients' associations internet sites
- We aim to publish each section of the guidelines as a separate article in a peer reviewed journal

- The acknowledgement section of the article should state that these guidelines were coordinated by the European Spina Bifida Working group within the ITHACA and eUROGEN European Reference Networks on rare diseases

Pediatric Guidelines

Timeline 2021



Pediatric Guidelines

G Mosiello – Rome – Italy

K Abrahamsson – Gotheborg - Sweden



Pediatric Urology

Early Start to Therapy Preserves Kidney Function in Spina Bifida Patients

Pieter Dik, Aart J. Klijn, Jan D. van Gool, Catherine C.E. de Jong-de Vos van Steenwijk,
Tom P.V.M. de Jong*

Results: Data of 144 children of 176 could be evaluated by the end of the study: 5 patients had pre-existing renal abnormalities, 69 had an overactive sphincter, 27 had reflux, and six had renal scarring. None are currently developing end-stage renal disease. All patients with spina bifida aperta started CIC and

Table 2 – Detrusor and sphincter behaviour in 144 patients with neurogenic bladder

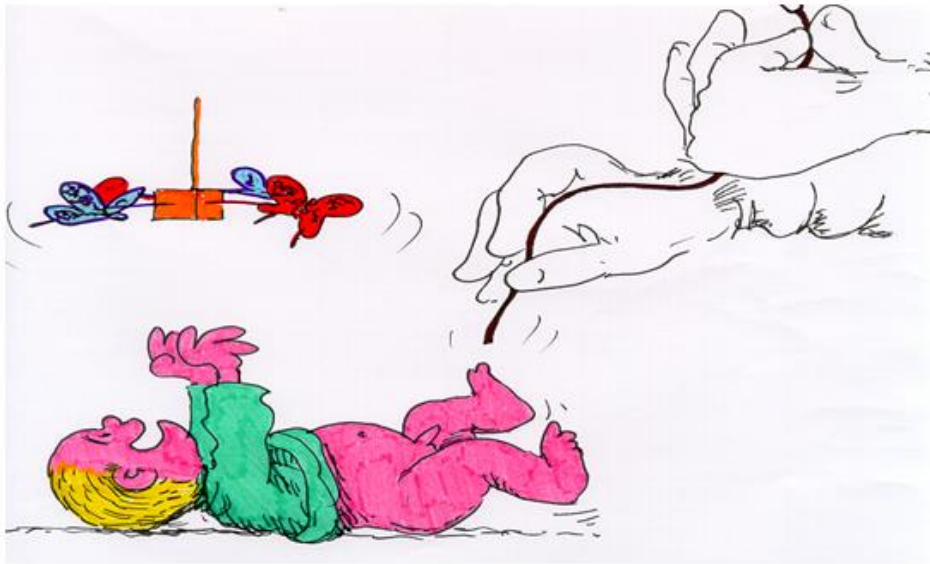
144 patients with spina bifida (70 boys, 74 girls)	Detrusor			
	Inactive		Active	
Sphincter				
Inactive	54	11 VUR 2 with renal scarring	21	4 VUR 1 with renal scarring
Active	29	4 VUR 1 with renal scarring	40	8 VUR 2 with renal scarring

3.7. Surgery

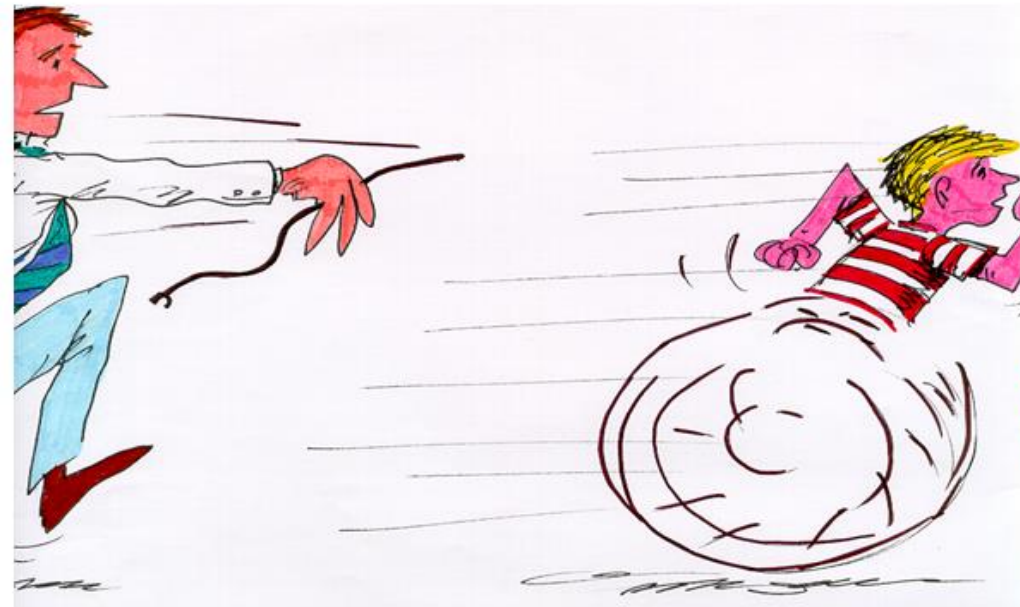
The ureter was reimplanted into the bladder (fiv bilaterally) in 14 girls and a left ureteral reimplan tation was done in one boy. To provide socia



CIC well accepted in infants



... not in ADOLESCENTS



Transition Guidelines

Dan Wood
University College Hospital
London

Why ?

90% of children with SB are born with normal upper urinary tract → 50% upper urinary tract damage if untreated

2019 French national survey
on causes of death in SB

Urologic Congenitalism

Urologic Disorders are Still the Leading Cause of In-hospital Death in Patients With Spina Bifida



Benoit Peyronnet, Fei Gao, Charlene Brochard, Emmanuel Oger, Lucie-Marie Scailteux, Frédéric Balusson, Juliette Hascoet, Quentin Alimi, Zine-eddine Khene, Sahar Bayat, Magali Jezequel, Camille Olivari, Caroline Voiry, Jacques Kerdraon, Guillaume Bouguen, Xavier Game, Laurent Siproudhis, and Andrea Manunta

UROLOGY 137: 200–204, 2020. © 2019 Elsevier Inc.



Cause of death Malakounides et al 2013



Cause of death	Age
Sepsis (hindquarter amputation)	14
Sepis (post ileal conduit)	17
Sepsis (pressure sores)	??
Sepsis (pressure sores)	??
Blocked shunt	11
Not given	
Not given	

Mean age of death 14 (0-25 years) 4.4 % NONE FROM RENAL FAILURE

Previous series upto 1/3 death from renal failure (Singhal et al 1999)

Room for different models



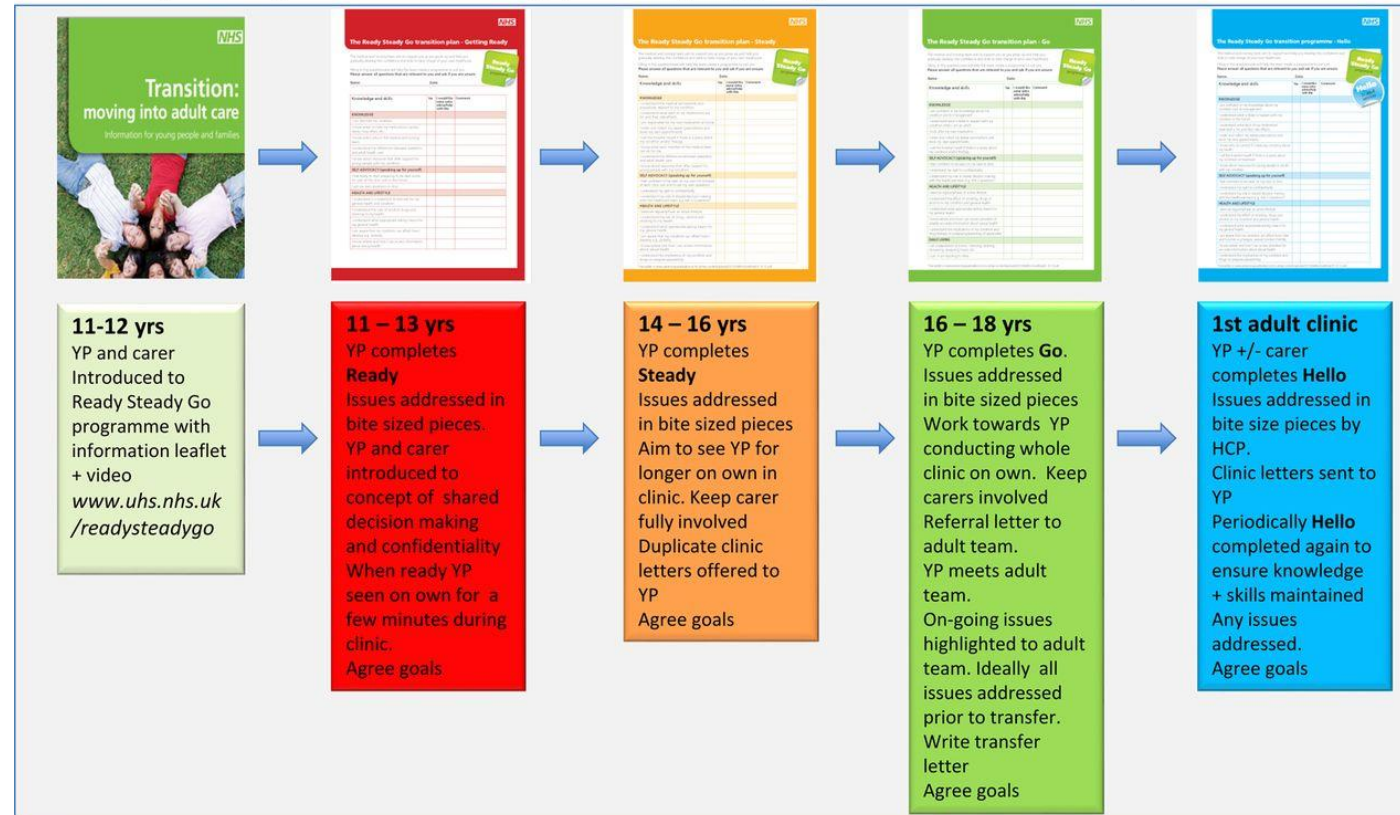
1. Paeds urologist follows the patient through in an integrated department
2. Paeds urologist continues to follow their patient into a separate adult department
3. The patient moves in adolescence to see an adult specialist in congenital urological disorders
4. The patient sees adult practitioners when needed

Preparation



Ready Steady Go: Moving through the programme

Ready Steady Go: Each Young person (YP) progresses at their own pace

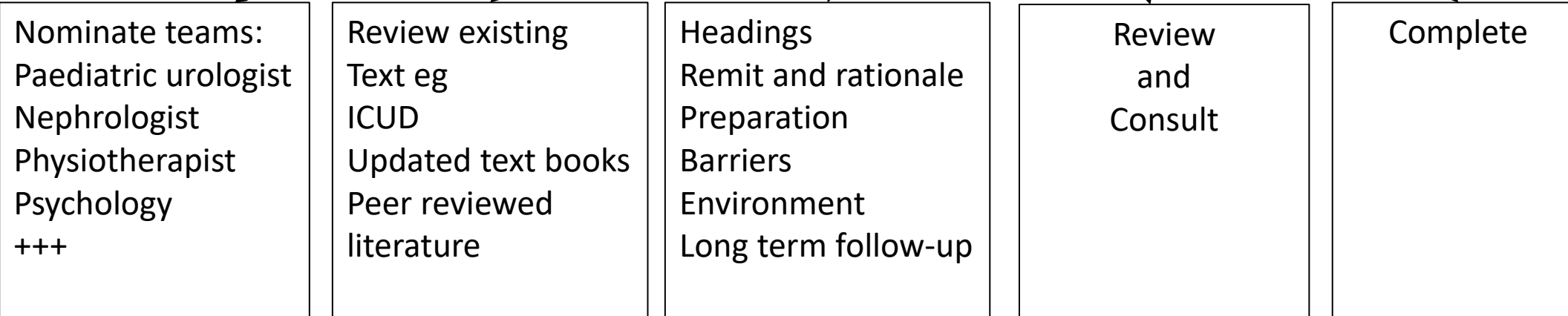


Carer completes parent/carers questionnaire alongside YP questionnaires. Any issues discussed. Goals agreed.

YP with learning difficulties completes as much as possible alongside carer who is YP advocate.

Arvind Nagra et al. Arch Dis Child Educ Pract Ed
2015;100:313-320

Transition guidelines plan



- Geography
- Resource
- Metrics
- Expertise
- Training
- MDT

Adult Guidelines

A Manunta – B Peyronnet, Rennes (France)

European Experts who have agreed to participate:

- David Castro Diaz (Sp) General Secretary of the International Continence Society
- Bertil F.M. Blok (NI) → endorsement by the neuro-urology EAU guidelines panel?
- Salvador Arlandis (Sp)
- Giulio Del Popolo (It)
- Gerard Amarenco (Fr)
- Xavier Gamé (Fr)
- Tufan Tarcan (Tur)
- Frank Van der Aa (Be)
- Rizwan Hamid (UK)
- Jan Krhut (Cz)
- Thomas Kessler (Ch)

- Introduction (Definition and classification, Prevalence, etiology and risk factors)
- Material and methods (in appendix in certain journals), database searched, keywords
- Diagnosis, long term follow up and outlook, risk of bladder cancer and of renal failure
- Conservative treatment of bladder dysfunction
 - self catheterisation
 - pharmacological treatment of NDO
 - low bladder compliance
 - treatment of recurrent UTIs
- Surgical treatment
 - Bladder augmentation
 - continent urinary diversion
 - ileal conduit
 - Surgical treatment of sphincteric deficiency

Trans-ERN Working Group for Spina Bifida Training: Workshop for future research on innovative diagnostic and interdisciplinary treatment

Giovanni Mosiello , MD, FEAPU, FEBPS,
Department of Urology and Neuro-Urology
Bambino Gesù Pediatric and Research Hospital, Rome , Italy
and

Andrea Manunta, MD, FRCS, FEBU ,
Department of Urology and Neuro-Urology.
Centre Hospitalier Universitaire de Rennes, France

EUROGEN (Wout Feitz) and ITHACA (Alain Verloes) EJP RD beneficiary.

- 2 days workshop objective : to train researchers and clinicians on :
TBC
- Genetic neural tube defects , correlation with Orphacode and post natal outcome, -
- TRASCET :transamniotic stem cell therapy,
- Prenatal diagnosis correlating fetal MRI and Ultrasound, with post natal outcome, -
- Urinary marker on renal and bladder function,
- Fetal Surgery (different approaches), results on bladder function, etc
- Innovative urodynamic investigation on neurogenic bladder related to spina bifida (Radiomics),
- Long-term sequelae of continence treatment considering the specific spina bifida patient.

NB Patient's representatives will be present with Young and Senior Researcher.

- ITHACA, EUROGEN, ERKnet are the main beneficiary.
- The workshop is addressed to researcher and clinician involved in spina bifida management : neurologist, neurosurgeon, obstetrician, neonatologist, urologist, pediatric urologist, fetal and pediatric surgeon, nephrologist, genetician, epidemiologist, immunologist, etc. etc
- The workshop will consist : presentation by experts + hands-on session on to train participants, discussing clinical case or theoretical cross-ERN scientific studies project , in order to train participants and to gain practical insights.
- At the end of the workshop all participants will have gained more knowledge on new promising diagnostic procedures, new treatments defining their feasibility, safety efficacy for spina bifida patients.
- Defining trans-ERN multicentric clinical trial , based in Europe, according to EU rules , respecting ethical and legal requirements, in order to make research findable , accessible, interoperable and reusable for all.

EJP RD ERN Workshop Call 2020 (Q2)

Evaluation summary report

Application No. 4
EXCELLENCE
Highly transversal topic, high capacity of fostering ERN collaboration, covering 3 ERNs. Excellent list of multidimensional, innovative research topics to be covered. Clear objectives.
IMPACT
The topic induces and enhances collaboration within and between ERNs, which are significant benefits to the RD community. High potential translational value of research topics, which would benefit patients, researchers and clinicians, at different levels. Strong patient representation.
IMPLEMENTATION
Training methodology clearly presented. Realistic implementation. Detailed scientific program, realistic and clearly defined cost calculation.
FINAL ASSESSMENT
Recommended for funding

Logistic details



- Venue: Rome? Rennes ? Other?
- Speaker : 15
- Participants: 20
- All expenses supported by grant 24.030 Euro
- When?

Proposal of a cross ERN surgical-based working group



Irene Mathijssen coordinator of ERN CRANIO

Objectives:

- Promote surgical research in the field of rare diseases.
- Advance surgical-based research in the field.
- Standardise data collection for surgical-based ERN registries and inform the development of clinical guidelines

3 Priorities

1. Organisation of support for the development of ERN research studies in the field of surgery and rare diseases. Support includes: Study design, methodology, data cleaning, management of data sets, interpretation of data bases, statistics support.
2. Focus: on (long-term) outcomes, effectiveness of treatment (incl. implants/techniques/consequences of prophylactic surgery), cause of death and quality of life, standardising approaches across ERNs for the purpose of comparative research and joint studies across borders
3. Reaching out: Patient representatives/groups for discussions on surgical communication and expectation management (including aspects related to shared decision making); To industry for support in e.g. design of surgical tools, financial support

WP10	D10.1	Issue an expert consensus statement for SB after reviewing existing national care structures and recommendations	Provide expert consensus statement on SB elaborated by cross-ERN WG to stakeholders through ITHACA website	Report	Public	28 Feb 2022	Pending
------	-------	--	--	--------	--------	-------------	---------

- SB trans-ERN workgroup is working
 - Global recos vs system-specific recos
 - Extension to BOND (orthopedics)

That's all Folks!



European
Reference
Network

for rare or low prevalence
complex diseases

 **Network**
Intellectual Disability
and Congenital
Malformations (ERN ITHACA)