

APRICOT

APRICOT : **A**naesthesia **PR**actice **I**n Children **O**bservational **T**rial

European prospective multicentre observational study

Epidemiology of severe critical events

Sponsored by the European Society of Anaesthesiology

and endorsed by ESPA

The steering committee



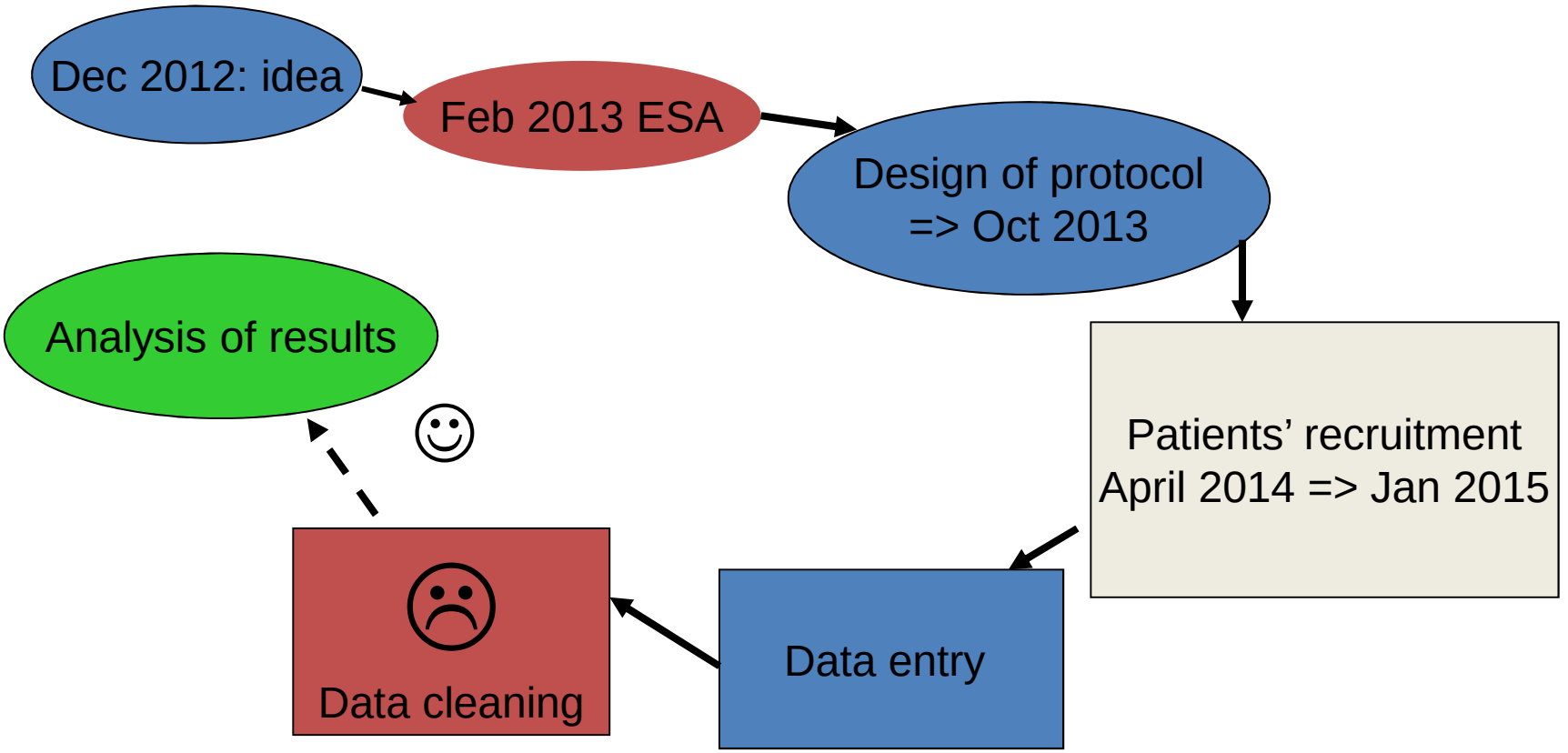
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Conflict of interest

- none
- Member of the Steering Committee

Where we are…


Dec 2012: idea
Feb 2013 ESA
Design of protocol
=> Oct 2013
Patients' recruitment
April 2014 => Jan 2015
Data entry
Data cleaning
Analysis of results

Enrollment criteria

- ALL consecutive patients from birth to 15 years old
- Inpatient or outpatient procedures
- Under sedation or general anaesthesia with or without regional analgesia or under regional anaesthesia alone.
- All diagnostic and surgical procedures
- In the OR or outside the OR
- Including an urgent or emergency procedure performed in- or out-of-hours.
- During a two weeks period

Exclusion criteria

- Children admitted intubated from the intensive care unit to the operating room

- Anaesthesia procedures performed in the intensive care unit

9 Critical events recordec

- Bronchospasm
- Laryngospasm
- Inhalation of gastric content
- Drug error
- Anaphylaxis
- Hemodynamic instability
- Neurologic complication
- Cardiac arrest
- Stridor post-anesthesia

Initial estimation

Sample size

- incidence of 0.1% of severe critical events
- sample size of 25,000 patients

  to allow detecting a 3 times difference in the probability of severe critical events due to difference in practice with a power of 0.9

  and an alpha error of 0.05
- expected inclusions per center: 20 to 200 patients
- at least 200 centers needed

Results … today

More than 300 Sites

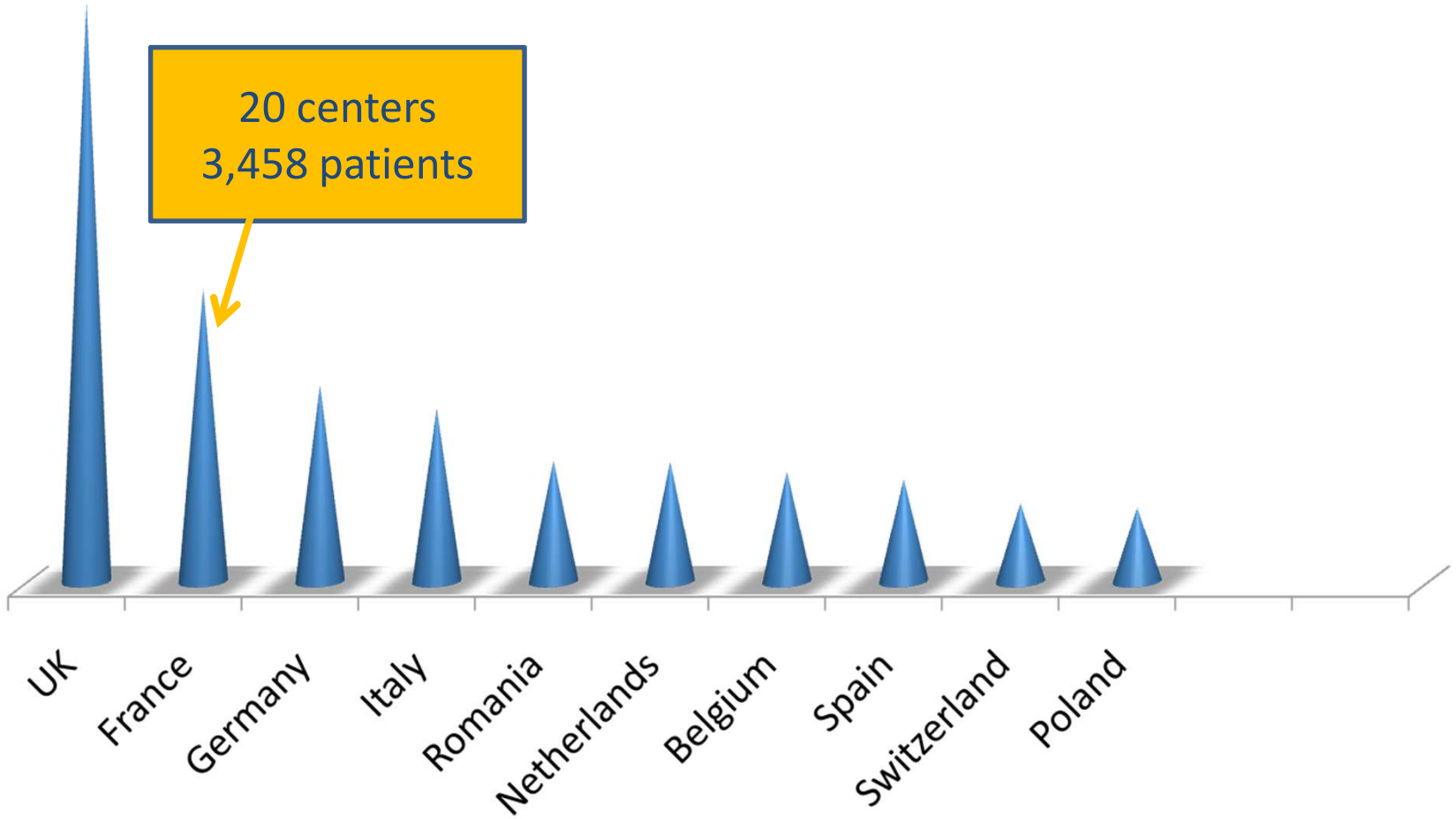
Austria
Belgium
Croatia
Czech Republic
Denmark
Estonia
Finland
France
Georgia
Germany
Gibraltar
Greece
Ireland
Israel

= 30,874 patients !

Italy
Kosovo
Latvia
Malta
Lithuania
Netherlands
Norway
Poland
Portugal
Romania
Russia
Serbia
Slovakia
Slovenia
Spain
Sweden
Switzerland
Turkey
Ukraine
United Kingdom


Iceland
Finland
Sweden
Norway
Russia
Estonia
Latvia
Den-
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Lithuania
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Czech Republic
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Romania
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Croatia
Georgia
Bosnia and
Herzego-
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Serbia
Monaco
San
Marino
Monte-
negro
Bulgaria
Andorra
Portugal
Spain
Italy
Vatican City
Mace-
donia

The top 10 countries with the largest n of inclusions





APRICOT

France: 3,458

American Memorial Hospital CHU Reims	109
Centre Hospitalier de Tourcoing	28
Centre hospitalo-universitaire de Nantes	294
CHRU de Lille Hôpital Jeanne de Flandre	273
CHU Angers	127
CHU Bicêtre	75
CHU Bordeaux	186
CHU d'Amiens	106
CHU de Grenoble	163
CHU de Toulouse. Hôpital des enfants	218
CHU Nancy - Brabois	159
Clinique du Val d'Ouest Ecully	113
Hôpital Femme-Mère-Enfant - Bron (Lyon)	299
Hôpital Necker - Paris	300
Hôpital privé de Villeneuve d'Ascq	103
Hôpital Robert Debré.Université Paris Diderot, PRES Sorbonne Paris Cité.	316
Hopital Trousseau - Paris	149
Hopitaux Pédiatriques de Nice CHU Lenval	184
Hôpital Lapeyronie - Montpellier	146
Université Rennes	110
Grand Total	**3458**

Recruitment bias ?



Participating centers

Non-participating centers ?

Recruitment bias ?



Participating centers

Non-participating centers ?

- Academic-teaching Hosp
- Private practice
- procedures
- ages etc

Recruitment bias ?



To be evaluated in each country?
Total N anesthesia during recruitment period vs
vs N encoded in APRICOT:
e.g., network in Scotland

Problems encountered

Before starting

- Ethical Committee approval

Workload for local coordinator

After data collection ⇨ cleaning process

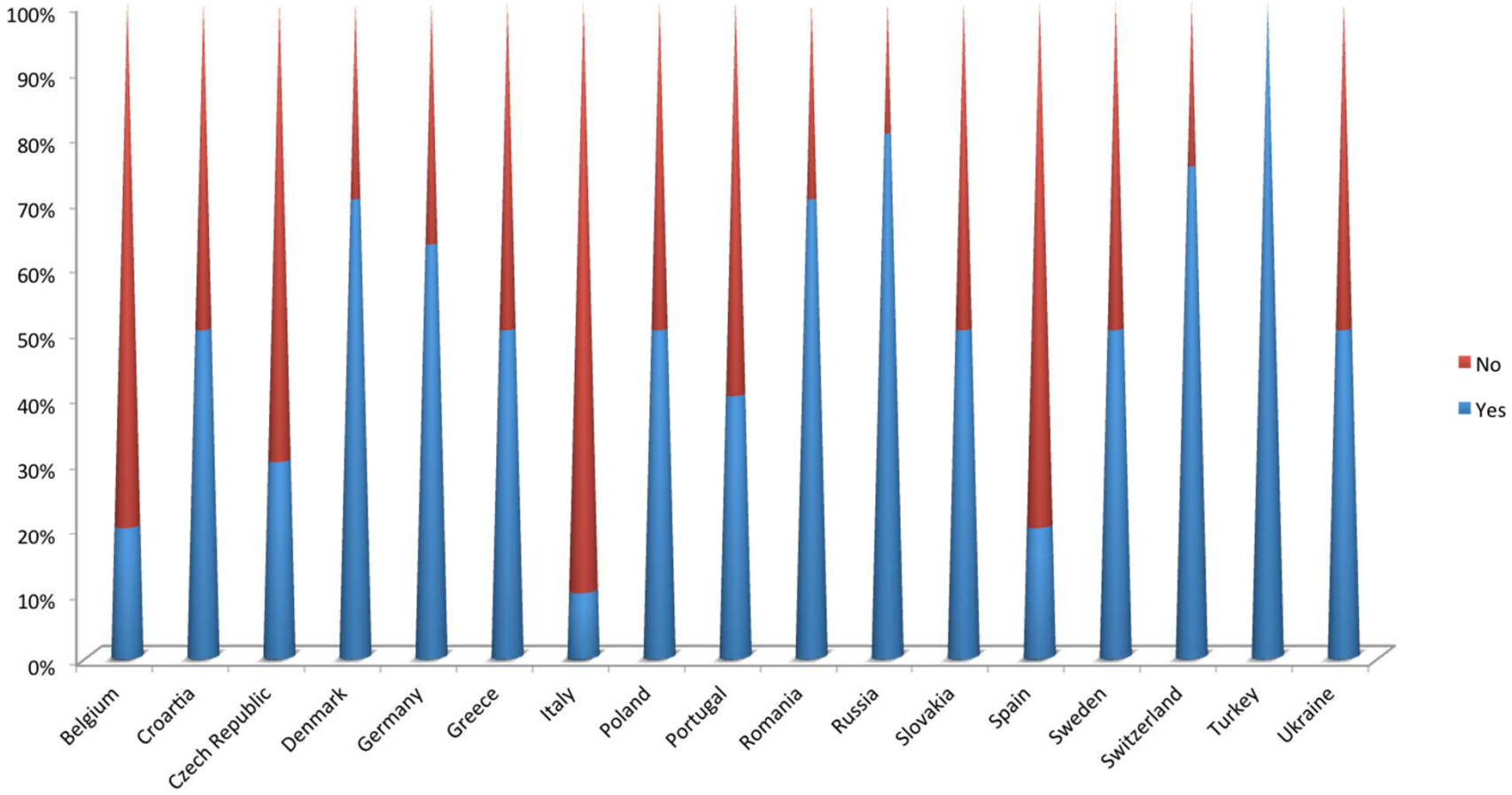
- More than 1 anesthesia in some patients
- Definition of complications
- Compliance with good clinical practice principles
- Unclear data reporting in CRF

EC/IRB Approval: a real challenge for observational studies

- National differences regarding ethical requirements and application details
- variable delay to obtain EC approval
- specific requirements for each EC/IRB
- only 10 countries agreed to waive the requirement to obtain a consent form:

(Estonia, France, Finland, Gibraltar, Ireland, UK, Kosovo, Latia, Lituania, Netherlands, Norway)

Need for parental consent: large variability within countries



Additional recruitment bias ?



Participating centers

Parental refusal

Non-participating centers ?



Risk for discouraging collaborative research in Europe

- « Strong dependency of the researcher on the local research Ethics Committee »
- « …., this dependency may appear rather arbitrary, because the procedures and requirements differ between European ECs »

Urgent need for a unique centralised European Research ethics approval process for multicentre studies

Stamer UM et al. *Eur J Anaesth* 2015; 32: 126-31

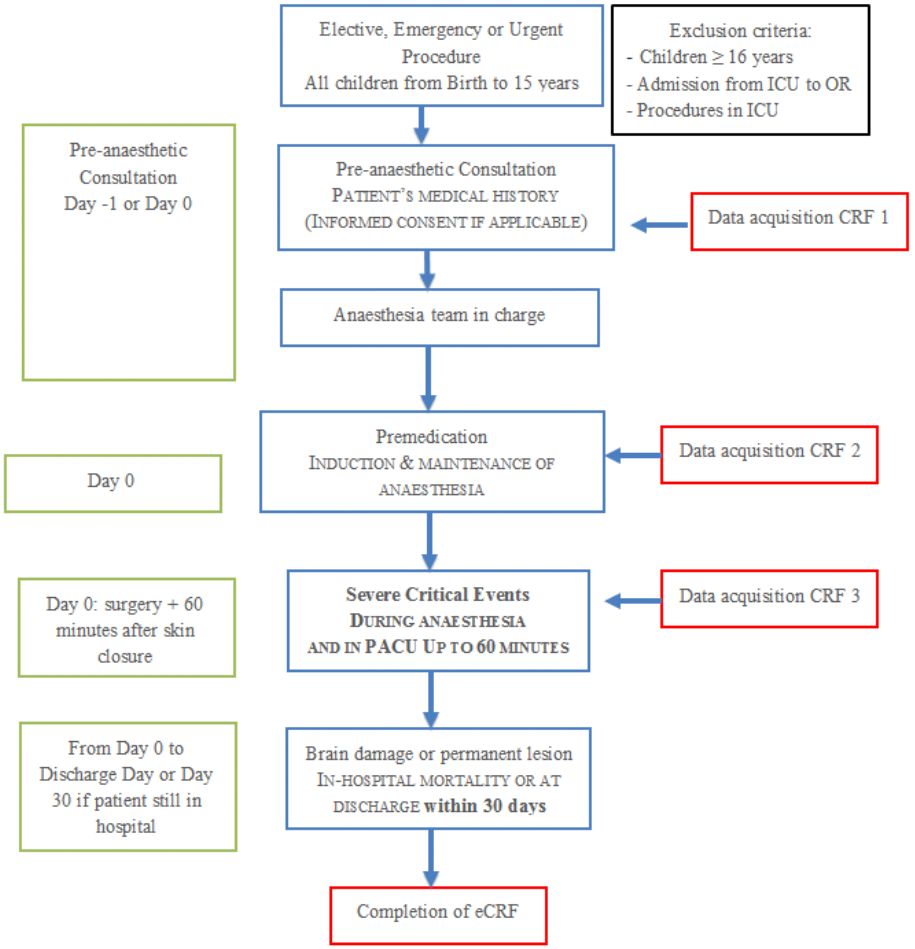
Legal definition of IC

Informed consent form : legal document used to inform a person about the hazards and potential dangers of a particuliar activity and obtain his/her permission to do it

Do prospective observational studies require informed consent ?
Should not we talk about **audit of routine clinical practice?**
quality improvement strategy?
and insist upon the fact the patient's data are anonymized !

Flow Chart

4.4 Protocol Flowchart: schematic diagram of trial design, procedures and stages:



☹ Heavy administrative workload for LC

Definitions: same language ?

- Precise definition of complications is crucial for outcomes statistics

- While the definitions were clearly stated on each CRF, we still had to send queries to confirm the occurrence of severe AE

Laryngospasm

" complete airway obstruction associated

- with rigidity of the abdominal and chest walls and leading to unsuccessful child's ventilation,
- or glottic closure associated with chest movement but silent unsuccessful child's respiratory efforts and assisted ventilation,
- unrelieved in both situations with simple jaw thrust and CPAP maneuvers and requiring the administration of medication (propofol, succinylcholine etc.) and/or tracheal intubation"

Agreement betwen eCRF and definition ?

2.2	Laryngospasm, specify Treatment: *(tick all that apply)* ☐ **Propofol** ☐ **Succinycholine** ☐ **Intubation** ☐ **Other**	*2.2.1 If other, specify*

Important number of corrections for laryngospasm

CPAP
Oxygen
Jaw thrust
Manual ventilation

Forgotten items ?

- bradycardia in hemodynamic instability
- hypoxia as a cause of cardiac arrest
- situation: Cannot Intubate Cannot Oxygenate

Compliance with GCP

Problems of compliance observed with:

- lost or not completed consent forms
- lost CRF/ patient records and impossibility to retrieve some information

Protocol compliance monitoring: a real challenge !

- Role of the National Coordinator

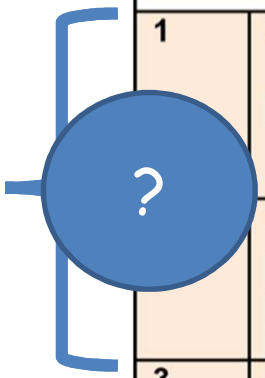
- Beneficial effect of the data cleaning process

Same for oncologists …

Responsible participants	Deficiencies	*n* (%)
Institution	Qualification requirements of hospitals were not met	6 (14.3)
	Lack of appropriate SOP	0 (0.0)
	All investigators were not identified in the contract	0 (0.0)
	Inappropriate contract	6 (14.3)
	Inappropriate informed consent	11 (26.2)
	CRFs filled incorrectly/and or insufficiently	8 (19.1)
	Problems related to archives	19 (45.2)
	Delay in communication of safety information	3 (7.1)
	Others	6 (14.3)

Yonemori K. et al. *Ann Oncol.* 2011; 22:1451-6.

Unclear data reporting on CRF



VI. FLUIDS

1	**Glucose-containing fluid?** ☐ Yes ☐ No	*1.1 If yes, provide concentration* ☐ 1% ☐ 2% ☐ 2.5% ☐ 5% ☐ 10% ☐ other %	
	Crystalloids administered: *(tick all that apply)* ☐ No ☐ Normal Saline ☐ Ringer Lactate ☐ Ringer acetate ☐ Hartmann solution ☐ Other		*2.1 If other, specify:*
3	**Colloids administered:** *(choose single most appropriate)* ☐ No ☐ Synthetic colloids ☐ Albumin ☐ Other		*3.1 If other, specify:*
4	**Blood products?** ☐ Yes ☐ No	*4.1 Packed RBCs:* ☐ Yes ☐ No	*4.1.1 # of packs RBC* |__|__| packs [1-99]
		4.2 FFP: ☐ Yes ☐ No	*4.2.1 # of packs FFP* |__|__| packs [1-99]
		4.3 Platelets: ☐ Yes ☐ No	
		4.4 Fibrinogen: ☐ Yes ☐ No	

large number of different fluids

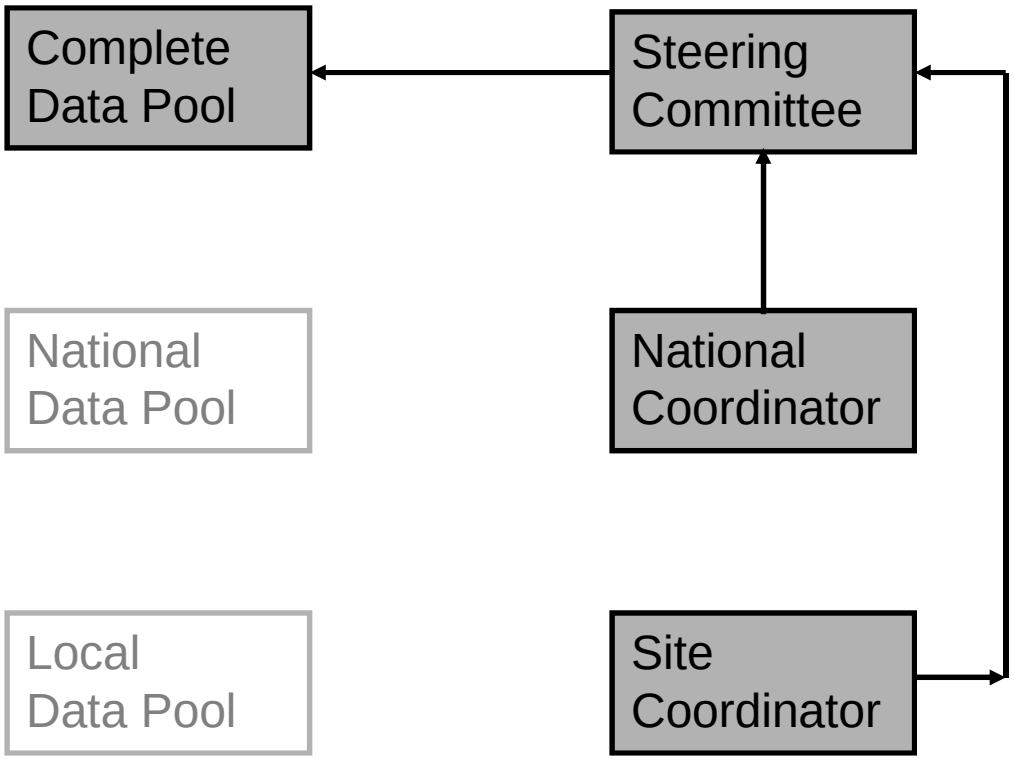
European Society of Anaesthesiology ESA



www.esahq.org

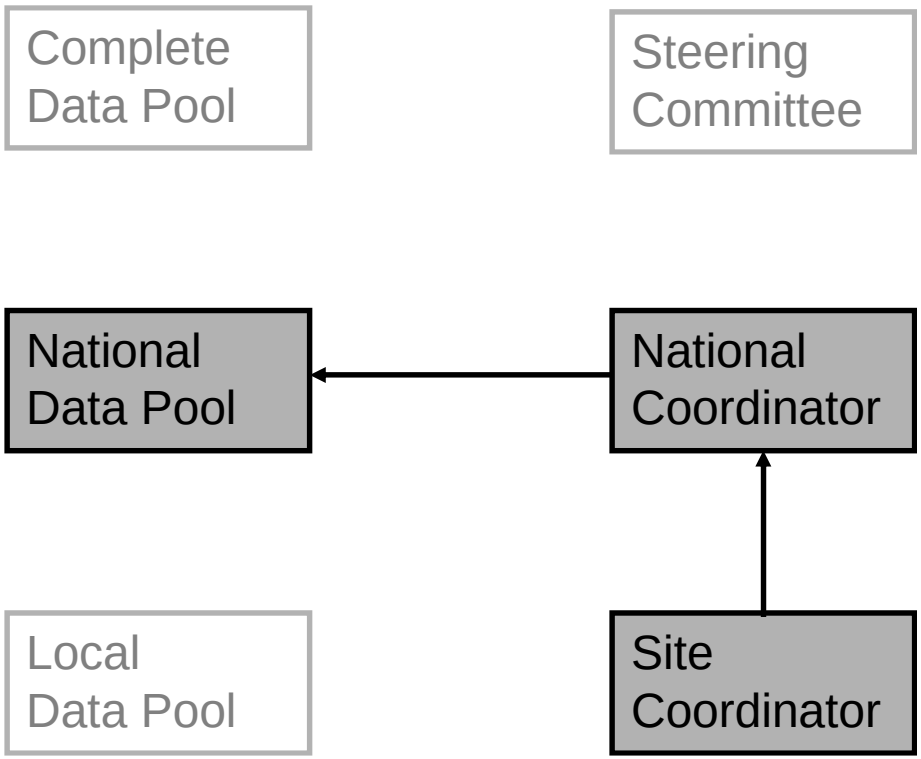
registration@esahq.org

Data Pool - Complete



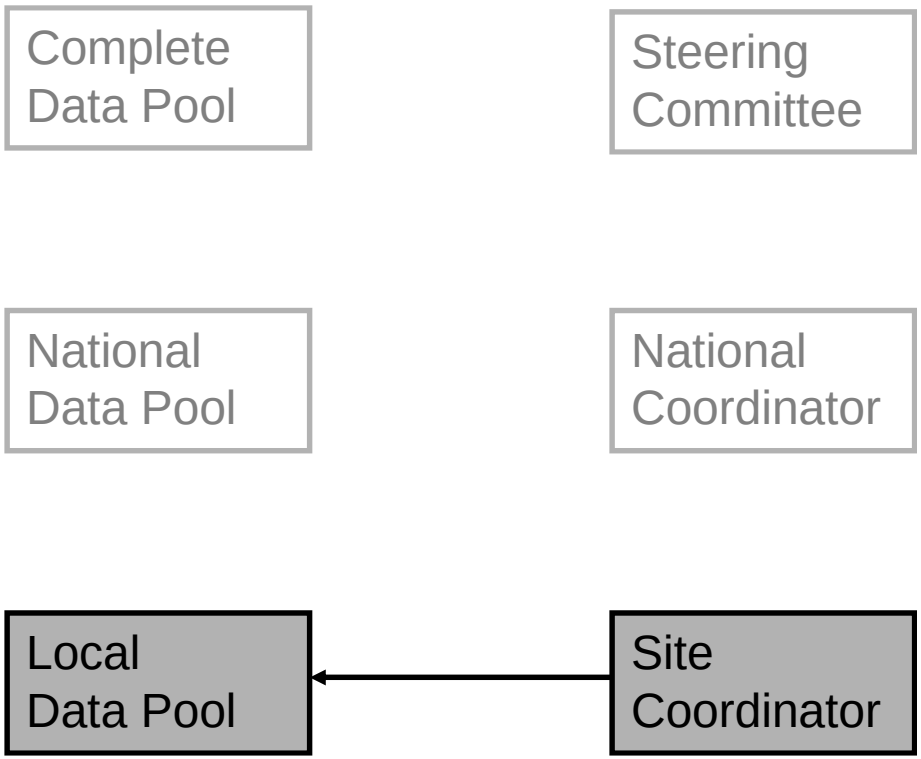
Complete Data Pool : Access to complete data-pool is provided after primary publication. After judgment by Steering of planned secondary analysis and approval by Steering of final manuscript

Data Pool - National



National Data Pool: Access to national data pool is available in consultation with National Coordinator

Data Pool - Local



Local Data Pool: Access to local data pool is available directly via data management team. For example for internal evaluation of practice

Many thanks to the ESA Clinical Trial Network & Research Dept



Brigitte Leva, Sandrine Damster, Julia Dowell
Benoit Plichon, Pierre Harlet,

Visit www.esahq.org/APRICOT

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Prospective, observational, multi-centre audit of clinical practice.

NECTARINE