



# **GRiP – Global Research in Paediatrics**

## **Pediatric Pharmacoepidemiology Platform**

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**On behalf of the GRiP Network of Excellence**



# Global Research in Paediatrics Network of Excellence

home Who we are Objectives and results

## OVERVIEW



What is GRiP?



GRiP Virtual Learning Environment  
Click to login and access GRiP educational resources on paediatric clinical pharmacology

## OUR WORK

Training and education

Epidemiological and post-marketing studies

Tools for interoperability

Paediatric clinical studies

Paediatric formulations

Drug development in neonates

ENCePP DB sites with pediatric data

Enpr-EMA

To improve the comprehensive infrastructure in paediatric pharmacology and will build use of research capacity.



# Objectives WP 2

- To **develop an integrated electronic infrastructure** for pediatric (pharmaco)epidemiological research
- This infrastructure will exploit and link existing healthcare databases around the world to assess the occurrence of diseases in children, plus the use and effects of drugs (including vaccines) on a large scale.
- Methodologies for harmonization, data exchange across national boundaries (including ethical and governance issues), data mining and comparative safety and effectiveness studies will be developed and tested

# What is the current status regarding evidence on effects of drugs in pediatrics?



- Many complaints about lack of data in pediatrics
- Many studies showing the off-label use of drugs in children
- Several pediatric regulations/initiatives to boost trials in children in the beginning of 2000 (FDA/EMA/WHO)
- Pediatric drug safety still often the cause for regulatory action (in 2001-2007 for 28 medicines or drug classes safety warnings (Clavenna A et al. Archives of disease in childhood. Sep 2009;94(9):724-728)
- Postmarketing data need to be utilized, as many children are exposed very day and this information should be utilized.
- No single database has enough power to study serious safety issues in children.  
E.g. EU-ADR:
  - 4.8 million children/adolescents across 7 databases in 4 countries, 25 Million PY
  - Total 2,170 drugs prescribed / dispensed
  - *Anaphylactic shock (3/100,000): only for 8 drugs power to demonstrate RR>4*
  - *UGIB (10/100,000) only for 39 drugs power to demonstrate RR> 4*

**TO BUILD a SUSTAINABLE & TESTED GLOBAL  
PLATFORM TO IMPROVE INFORMATION ON  
THE USE & EFFECTS OF DRUGS IN CHILDREN**

# Key Products WP 2



- 1) A technical operational research infrastructure for collaborative data sharing / analysis accessible around the world
- 2) A catalogue of databases with contact and meta-data on pediatric patients that can be approached for collaborative pharmacoepidemiological studies
- 3) Description of ethical and governance issues related to secondary use of health care data across the world
- 4) Description of paediatric spontaneous reports in WHO-VIGIBASE, EUDRAVIGILANCE, AERS and VAERS
- 5) Catalogue of disease codes for different pediatric events to be extracted in SRS and EHR databases

# Key Products WP 2



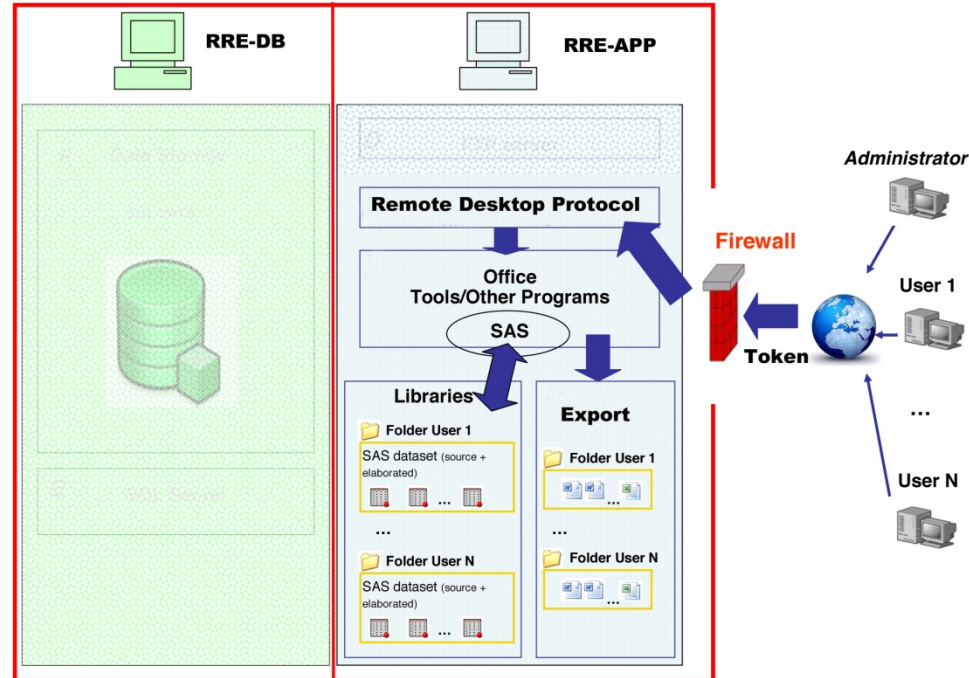
- 6) Reference set of positive and negative controls for signal detection to be used (vaccines/drugs)
- 7) Tested methods for Signal detection in pediatrics (SRS/EHR) and a comparison between databases and methods, together with EMA, PROTECT & OMOP
- 8) Templates and global proof of concept studies on drug/vaccine use, disease incidence, drug safety and effectiveness
- 9) Pediatric pharmacoepidemiology courses (e-learning)



Some outputs.. so far



# Platform for data-sharing (Octopus)



- Functional platform in ARITMO, SAFEGUARD, GRIP
- Shared aggregated data within firewalls
- Remote access to work together and analyse and rotate coordinator ship



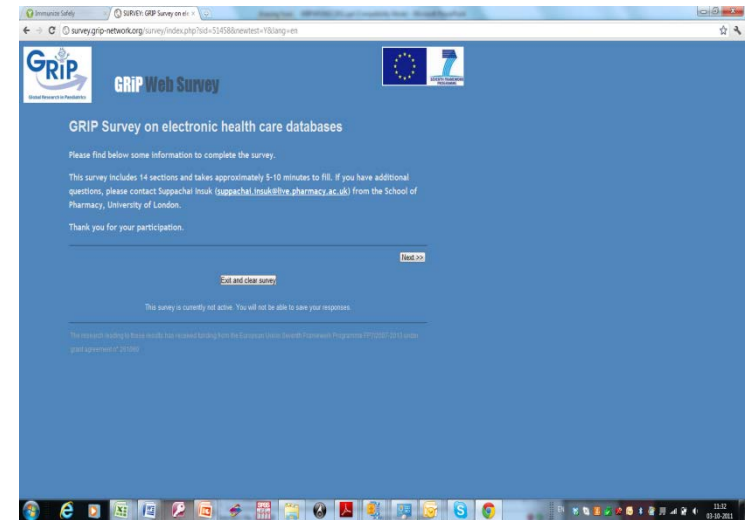
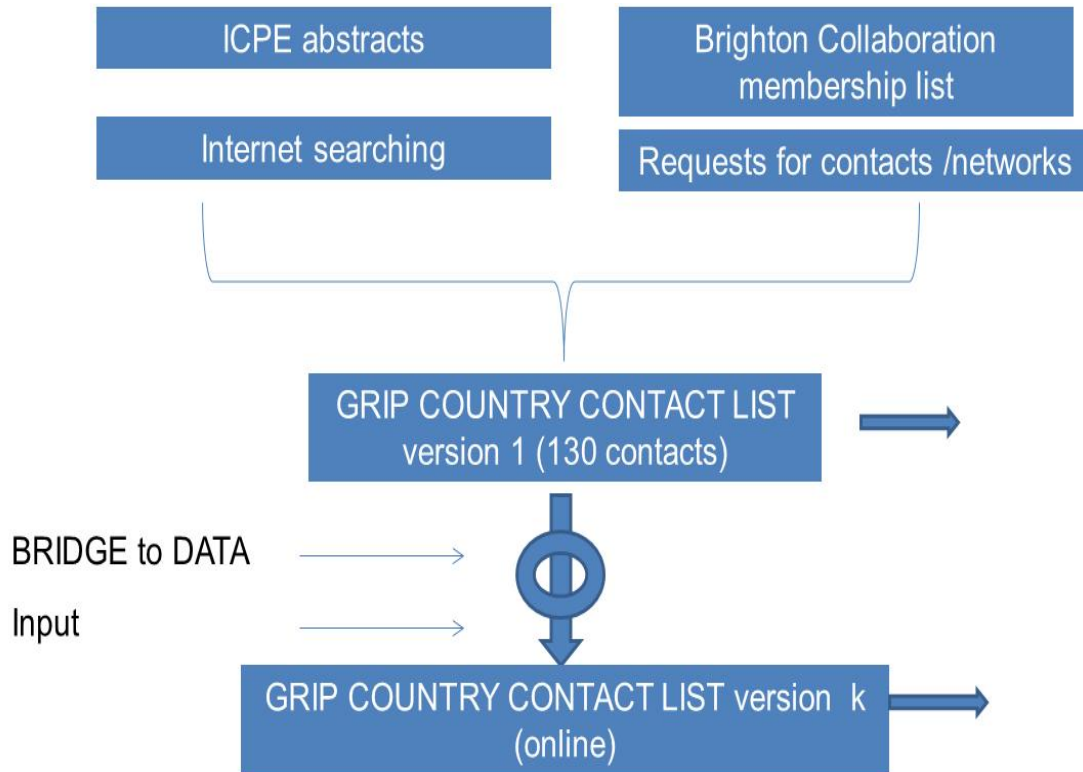
# Description of available spontaneous reports

(EUDRAVIGILANCE being analysed)

	Vigibase [1968-Feb2010]	AERS [2004-2011]	VAERS [1990-2011]	Overall
Age group	N [%]	N [%]	N [%]	N [%]
0-27 days	6,142 [2.3]	4,717 [4.4]	-	10,859 [2.0]
28 days - 23 months	38,205 [14.2]	16,096 [15.2]	80,760 [46.2]	135,061 [24.6]
2-11 years	124,321 [46.4]	47,248 [44.5]	68,726 [39.3]	240,295 [43.8]
12-17 years	99,477 [37.1]	38,061 [35.9]	25,463 [14.6]	163,001 [29.7]
Total	268,145 [100.0]	106,122 [100.0]	174,949 [100.0]	549,216 [100.0]

The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 261060

# Catalogue of databases to identify pediatric data globally



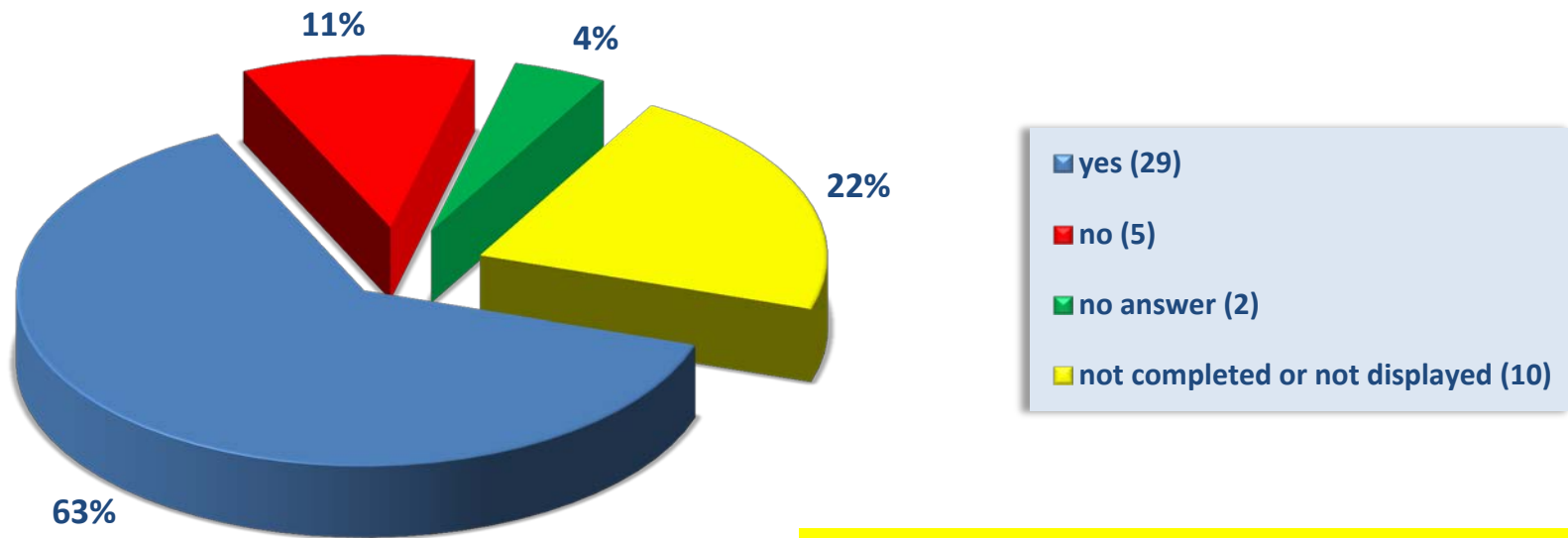
Databases are contacted and requested to fill out an online survey

# Results of the survey



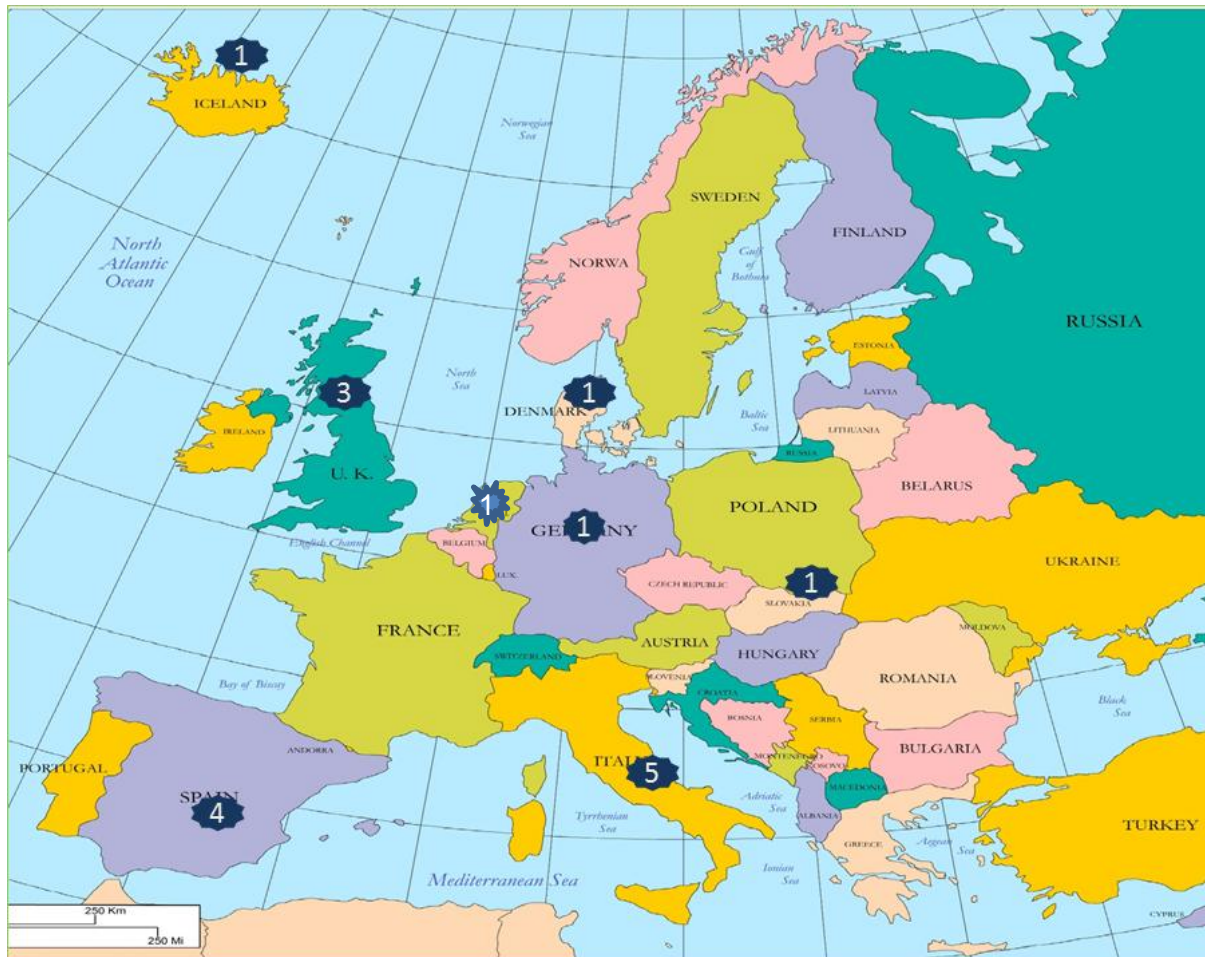
**N. of responders= 46 (35% of 130 DB contacted)  
only 20 from EU**

**Do you agree to be involved in the GRiP project?**



**FDA will make SENTINEL available  
as well for studies**

# DBs in EU participating



## ENCEPP sites

GB	21
ES	17
IT	16
FR	15
DE	12
NL	9
PT	7
DK	6
CH	5
FI	4
BE	3
SE	3
GR	2
IE	2
AT	1
NO	1
RO	1
SK	1

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# Invitation to ENCePP sites



- **Participate in GRiP**

- **What to do?**

- 1) Complete the survey if you have access to population-based data on drug/vaccine use / outcomes comprising children
- 2) Participate in proof of concept studies

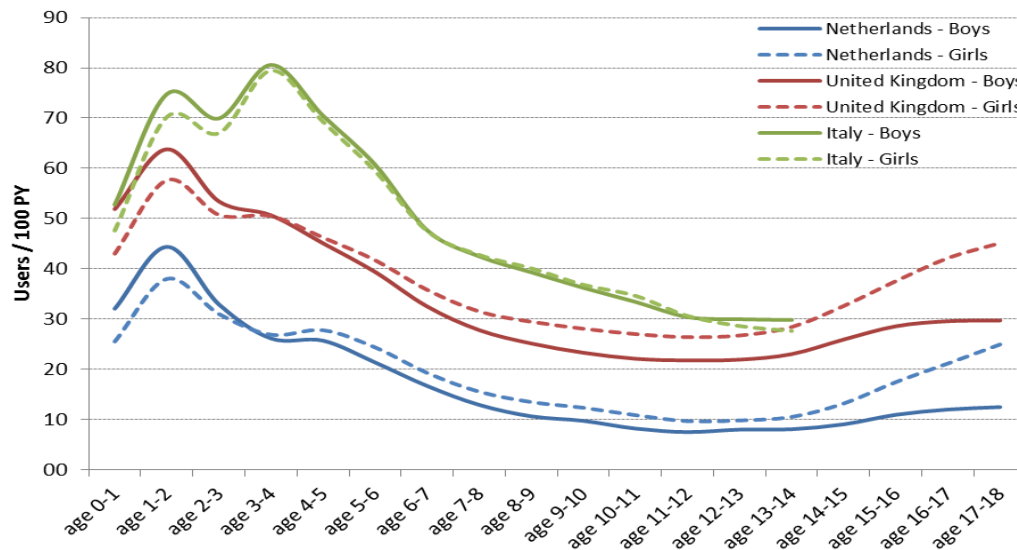
- **What do you get?**

- 1) Get access to the OCTOPUS platform to initiate & perform studies
- 2) Publish together & boost the field of pediatrics
- 3) Find your partners for collaborative studies in pediatrics around the world

# First proof of concept study proposal for collaboration



- Use & quality of prescribing of antibiotics in children globally
- ARPEC project (Mike Sharland): large differences in annual prevalence of use



# How to participate?



- **Indicate your interest**
- **Requirements:**
  - Access to prescription database & population database
  - Creation of two standardized input files locally
    - population: identifier, start follow-up, end follow-up, date of birth, sex
    - Prescriptions: identifier, date, ATC code, duration
  - Run JAVA or SAS script locally and share output table on RRE (in excel)
  - Get token for RRE access
  - Analyse/discuss /publish together with your colleagues



# What is being shared on RRE?



ATC7	AgeRange	Year	Month	PersonDays	PersonDays_	PersonDays_E	ExposedI	ExposedIn	NewUs	Prescript	Prevalence (p	Incidence (pe	Mean duration
J01CR02	age 15-19	1996	8	2	79365	79334	1	2565	1	1	4.602154602	4.603952908	30.94152047
J01CR02	age 15-19	1996	9	0	76506	76476	0	2556	0	0	0	0	29.93192488
J01CR02	age 15-19	1996	10	0	79612	79581	0	2572	0	0	0	0	30.9533437
J01CR02	age 15-19	1996	11	0	76839	76809	0	2570	0	0	0	0	29.89844358
J01CR02	age 15-19	1996	12	0	91177	91146	0	2947	0	0	0	0	30.93892094
J01CR02	age 15-19	1997	1	0	90559	90528	0	2929	0	0	0	0	30.91806077
J01CR02	age 15-19	1997	2	0	82134	82106	0	2943	0	0	0	0	27.90825688
J01CR02	age 15-19	1997	3	0	91171	91140	0	2941	0	0	0	0	31
J01CR02	age 15-19	1997	4	0	88383	88353	0	2949	0	0	0	0	29.97049847
J01CR02	age 15-19	1997	5	0	91490	91459	0	2960	0	0	0	0	30.90878378
G02CB03	age 15-19	1997	6	0	88323	88293	0	2947	0	0	0	0	29.97047845

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# Summary

- GRiP will provide a platform to work together
- ENCePP sites not yet well represented, whereas large USA sites will participate
- Opportunity to start working together (proof of concept) on a very relevant topic

# Participants– WP 2



## Major contributors

- **EMC** (Miriam Sturkenboom)
- **BF** (Jan Bonhoeffer)
- **AOPD** (Carlo Giaquinto)
- **CVBFTEDDY** (A. Ceci)
- **BIOEF** (Adolf Valls-i-Soler)
- **WHO** (Krisanta Weereasuriya)
- **FDA**
- **P-95**

## Minor contributors

- **NICHD-NIH** (S Hirschfeld)
- **EMA** (Agnes Saint Raymond)
- **ULIV-MCRN** (M. Turner)
- **INSERM** (E. Jacqz-Aigrain)
- **NCCHD** (Hidefumi Nakamura)
- **SGUL** (M. Sharland)
- **AMC** (M. Offringa)
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