

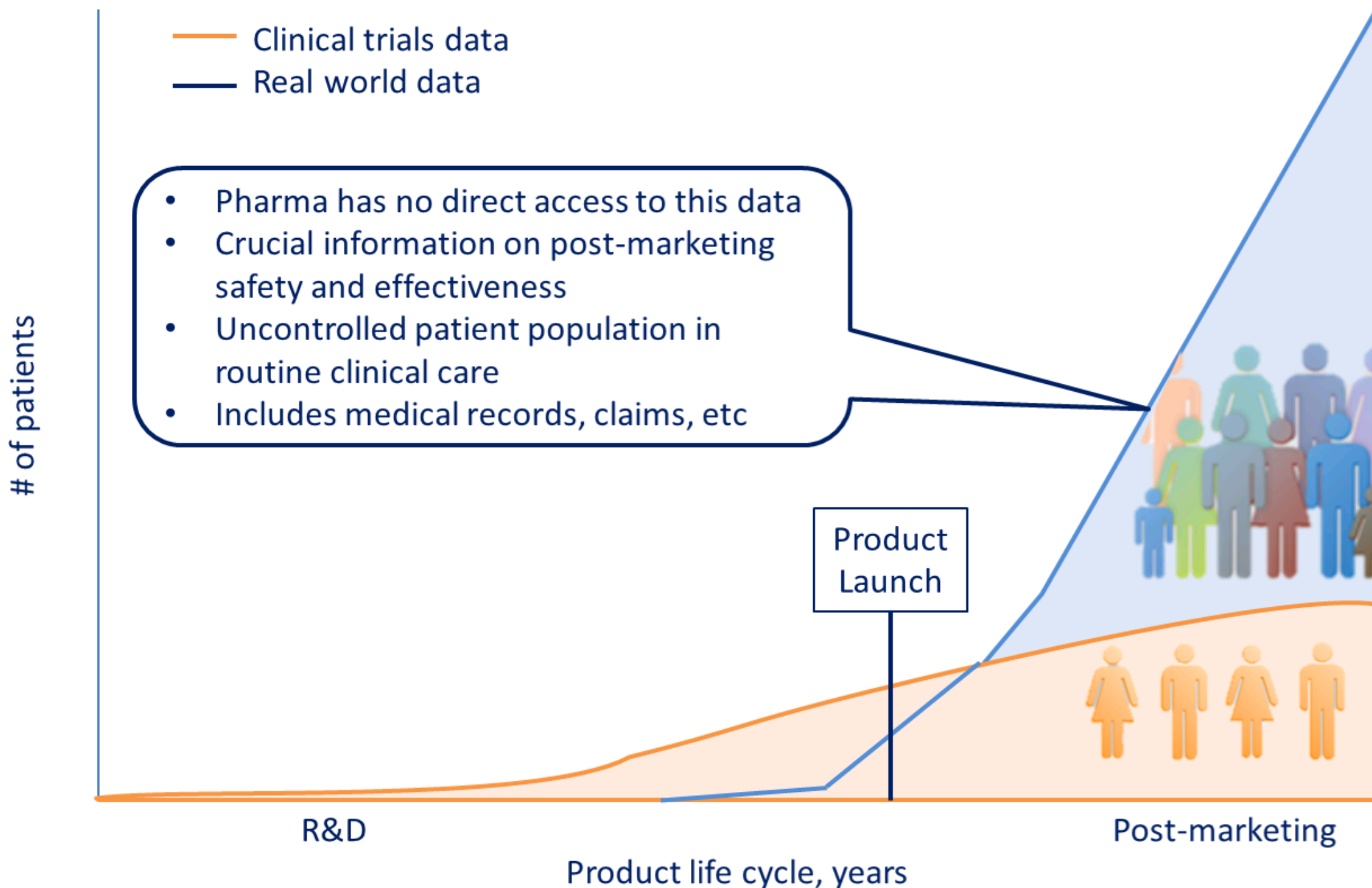
**A comparison between countries –
common data models and SAS macro catalogs**

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Introduction: the Real World Evidence challenge



Introduction: the multi-country challenge (1)

EMA: multi-country perspective required

- Rare products or outcomes
- Different populations, risk profiles
- Different markets, health care systems
- Different types of electronic medical records
- Different settings



Introduction: the multi-country challenge (2)

- Similar protocols – similar execution?

Different results: real or artefact?

Modifiable?

- coding harmonization , health care system, population
- (unconscious) decisions during programming:
e.g.
 - < vs. ≤
 - included duration of history
 - methods for e.g. determining prescription durations
 - ...

no

yes

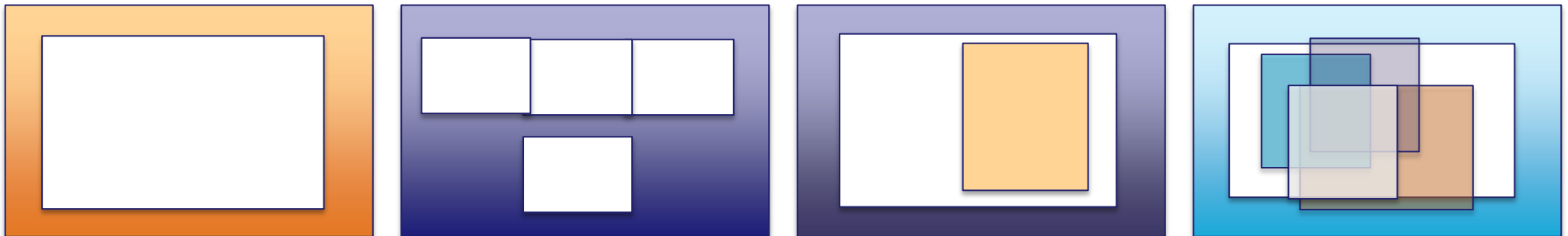
- Local governance / legislation restricts data access:
 - Only non-commercial parties
 - Only aggregated data exports

The PHARMO approach

- Study specific common data model
- Shared exportable SAS macro catalogs
- Making use of local expertise
 - Data Permissions
 - Health care system
 - Coding
 - Database structure

Common data model (CDM) - concept

- Stringent variable specifications for input datasets
 - Dictated by study protocol
 - Provided by study coordinator
 - Fits programming requirements
- Local expertise of database custodians
 - Governance
 - Health care system
 - Language
 - Coding system
 - Database structure



CDM– specifications example

- Patient ID key variable in all files

Patient file

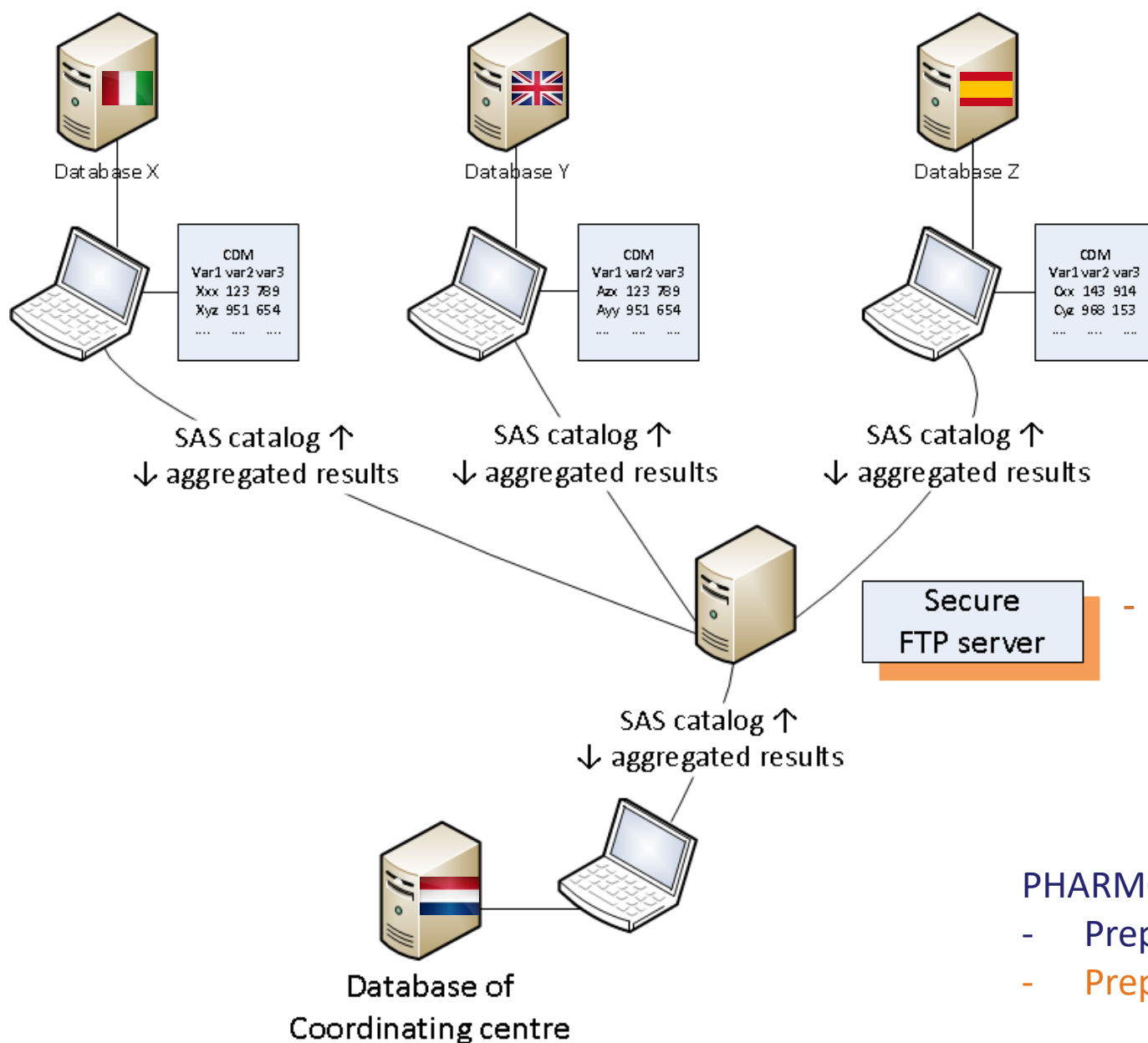
Variable	Description	Format	Requirements
PatID	Patient identifier	\$20.	Identical to PatID in drug and assessment input files
Byear	Birth year	Numeric	Valid year between 1900 and 2012
Gender	Gender	\$1.	F (=Female) or M (=Male)
...			

Prescription file

Variable	Description	Format	Requirements
PatID	Patient identifier	\$20.	Identical to PatID in patient and assessment input files
ATC	ATC code	\$7.	Any ATC code starting with A10, 7 characters, according to WHO table
RxDate	Date of prescription	date9.	Valid date between start and end of enrolment
...			

Variable	Description	Format	Requirements
PatID	Patient identifier	\$20.	Identical to PatID in patient and drug input files
Measure	Description of type of measurement	\$8.	One of the following categories: HBA1C BMI SBP DBP
Date	Date of measurement	date9.	Valid date between start and end of study period
Value	Value of measurement	5.1	HBA1C between 4 and 14 etc.

Multi-country RWE study execution concept



Partner databases:

- Get approval for data use
- Create CDM input datasets
- Run test/summary scripts
- Send summary results
- Run SAS catalog
- Send aggregated results

- File transfer through secure server

PHARMO study coordinator:

- Prepare instructions & SAS catalog
- Prepare study report

Data due diligence

- Summary tables prior to analyses: check
 - Units
 - pounds vs kilograms, HbA1c % vs mmol/l, etc.
 - Distributions
 - range numeric variables
 - predefined categories, explain missing categories
- Build checks into your catalog
 - Check logic of variables of input datasets
 - Relations between variables (e.g. start before end)
 - Dates within study period
 - Prompt error messages pointing out problem
 - Stop execution until problem is fixed

SAS compiled macro catalog - concept

- Storage of macros in SASMACR library
- Compilation decreases overhead processing time
- Version control:
 - Accessible by many
 - Modifiable by few

SAS macro catalog – sharing programs between organisations

- SASMACR library stored on SAS server as one file
- Different organisations use different servers
- Catalog file can be transferred
 - instructions where to save
 - and how to access

Compatibility requirements (1)

Using a SAS stored compiled macro catalog on a different operating system may result in the following error:

ERROR: File libref.SASMACR.CATALOG was created for a different operating system.

**NOTE: The SAS System was unable to open the macro library referenced by the
SASMSTORE = libref .**

WARNING: Apparent invocation of macro not resolved.

ERROR 180-322: Statement is not valid or it is used out of proper order.

Therefore check compatibility of operating systems up front

e.g. Windows 7 Ultimate x64

not compatible with

Windows 7 Ultimate 32 bit

Compatibility requirements (2)

Different SAS release versions may also cause errors

- Catalog created in 9.2 worked in 9.2 and higher (when using the same operating system)

Check:

- If catalog macros can be executed
- If resulting SAS datasets can be opened by coordinator

ERROR: File libref.member.DATA not compatible with this SAS version.

- New versions may contain new system options, default setting may cause problems, e.g.

Options EXTENDOBSCOUNTER = no;

Options can be incorporated in the execution macro in the catalog

SAS macro catalog – creation

- Location SAS macro catalog

```
options mstored sasmstore=TPcat;  
libname Tpcat  
    'Directory:\folder\Catalog_TP';
```

- Storing a macro in the catalog

- Without source code
allowing protection
of intellectual property

```
%macro macro_name (parameters) / store;  
    macro program code  
%mend macro_name;
```

- With source code

```
%macro macro_name (parameters)  
    / store source;  
    macro program code  
%mend macro_name;
```

SAS macro catalog – viewing source code

```
proc catalog catalog = tpcat.sasmacr;  
contents;  
quit;
```

creates list of all stored macros

```
%copy macro_name / source;
```

can be used to actually view the source code of a specific macro from the list

SAS macro catalog – useful options

options

Hides in the log file:

nonotes

- the notes associated with each data processing step, including the source code

nomprint

- display of the SAS statements that are generated by macro execution

nomlogic

- tracing of macro execution (the beginning and end of macro execution, values of macro parameters at invocation, execution of each macro program statement, whether each %IF condition is true or false)

nosymbolgen

- the results of resolving macro variable references

nosource

- source lines, except those that contain errors

nosource2;

- secondary source statements from files that are included with an %INCLUDE statement

SAS macro catalog – set up of study execution programs



```
/* start execution macro */  
%macro exec_tp(    RxDs = ,  
                  PtDs = ,  
                  endStudyPeriod = ,  
                  startStudyPeriod = ,  
                  inputdir = ,  
                  outputdir =  
                  accesskey = ) / store;
```

Macro variable definitions



```
/* check if the access key corresponds with the provided list */  
%access (key=&accesskey) ;
```

Invoke access key verification macro

```
/* make sure files can be read by lower SAS release versions */  
options EXTENDOBSCOUNTER = no;
```

System options compatibility

```
/* suppress log file notifications */  
options nonotes nomprint nomlogic nosymbolgen nosource nosource2;
```

Set log file suppression options



```
/* invoke processing and analyses macros in required order */  
%inputcheck (parameters);
```

Invoke macros to check input files






```
/* invoke processing and analyses macros in required order */  
%step1 (parameters);  
%step2 (parameters);  
%step3 (parameters);  
%step4 (parameters);
```

Invoke actual data processing
and analyses macros

```
/* reinstate log file notifications */  
options notes mprint mlogic symbolgen source source2;
```

Reset log file suppression options

```
%mend exec_tp;  
/* end execution macro */
```

Execution of the study catalog macros

➡ Execution macro and all macros invoked in it are compiled into one catalog
Only the execution macro needs to be invoked
after defining database specific macro variables and paths

```
%exec_TP  RxDs = rxfile
           /* Prescription dataset name */
, PtDs = patientfile
           /* Patient dataset name */
, endStudyPeriod = "31dec2011"d
           /* End study period */
, startStudyPeriod = "01jan2007"d
           /* Start study period */
, inputdir = Directory:\folder\input
           /* Directory of input data */
, outputdir = Directory:\folder\output
           /* Directory of output data */
, accesskey = qleBr8ew) ;
```

Conclusions

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- Common data models and SAS catalogs can be used to uniformly perform analyses across countries
- Knowledge of database custodians retained
- Ease of use: press-the-button
- Less resources needed per country
- Blinding of code is an option

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- System specifications need to match
- Expect some trouble shooting

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Questions



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