



NWEH
NorthWest EHealth

Using Electronic Health Records for Real World Trials (Salford Lung Studies)

CDISC UK Network | 05th July 2018 | NorthWest EHealth



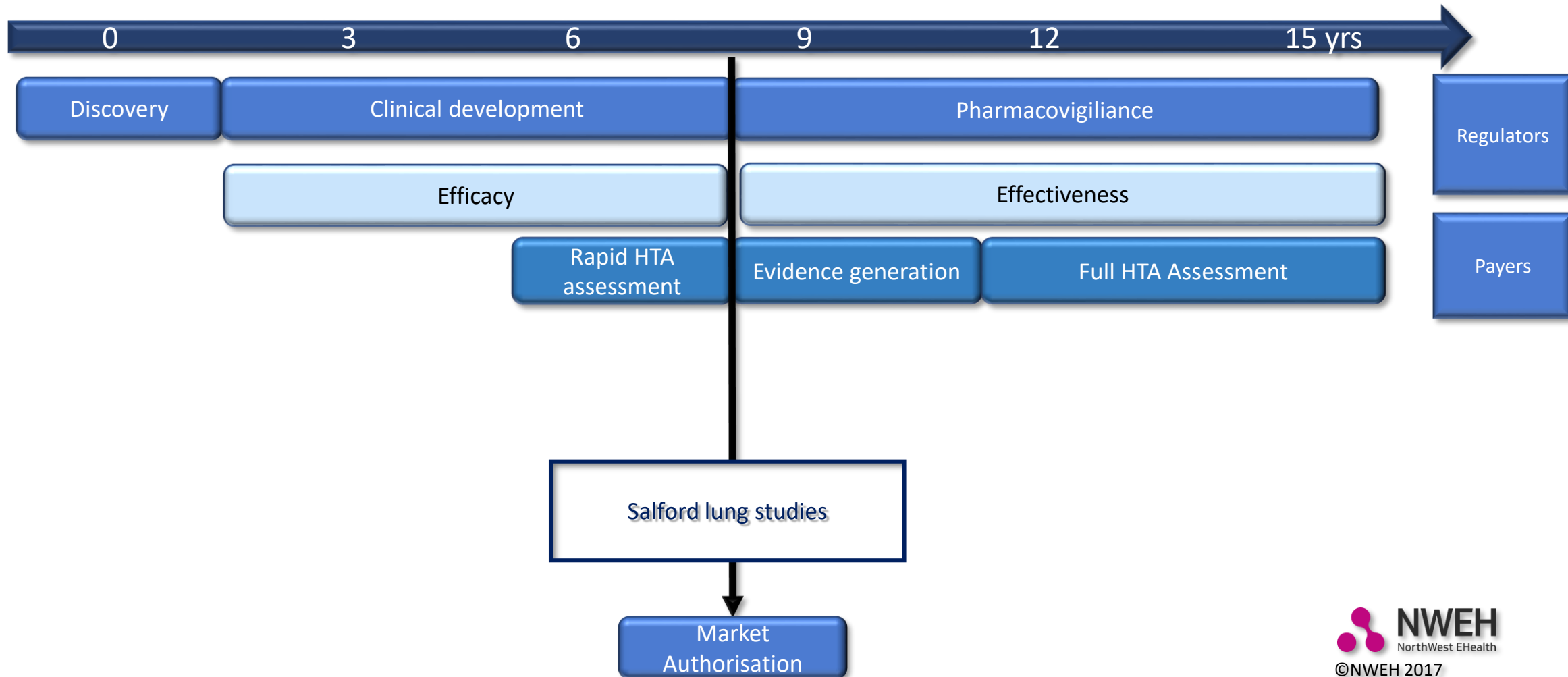
The Salford Lung Studies

Where is Salford?



- Two late phase pRCT in Salford UK and surrounding areas sponsored by GSK.
- Over 7200 patients were monitored in near real-time for safety and outcomes using city-wide linked electronic health records.
- First study in the world to have evaluated the effectiveness of a pre-licence medication in a real world setting.
- The study demonstrated the success of Relvar Ellipta (FF/VI) when used in everyday clinical practice for the treatment of COPD and Asthma.
- Results of both the Asthma and COPD studies were positive.
- COPD: N Engl J Med 2016; 375:1253-1260
- Asthma: Lancet 2017; 390:2247–2255

Clinical evaluation lifecycle





Why the UK and why Salford?

- The National Health Service (NHS)
- Single unique identifier (NHS number)
- Long-established use of electronic health records in primary care
- A national infrastructure to support research (NIHR)
- Stable Salford population (~240 000) serviced by a single large university hospital with an enterprise-wide EHR in place
- Salford integrated primary and secondary care electronic records from 2002
- A track record of close working between community and hospital care
- Manchester based NorthWest EHealth established 2008

- A 'Connected Community of Care'

Salford Lung Study design

Aim: To compare the effectiveness and safety of study Rx to usual care on meaningful patient-centred outcomes in COPD (rate of moderate/severe exacerbations)

 **2,802 patients**

- Patients in primary care
- Aged 40+ years
- GP diagnosis of COPD
- Taking ICS and/or LABA and/or LAMA
- Exacerbation in last 3 years
- Consented

Randomisation**

Constant real-time data collection of all interventions and safety monitoring

Study Treatment

Randomisation visit

- Routine respiratory review
- Device instruction
- CAT

12 months of usual care

3 phone calls
(if no regular visits)

End of study visit

- Routine respiratory review
- CAT

Usual care

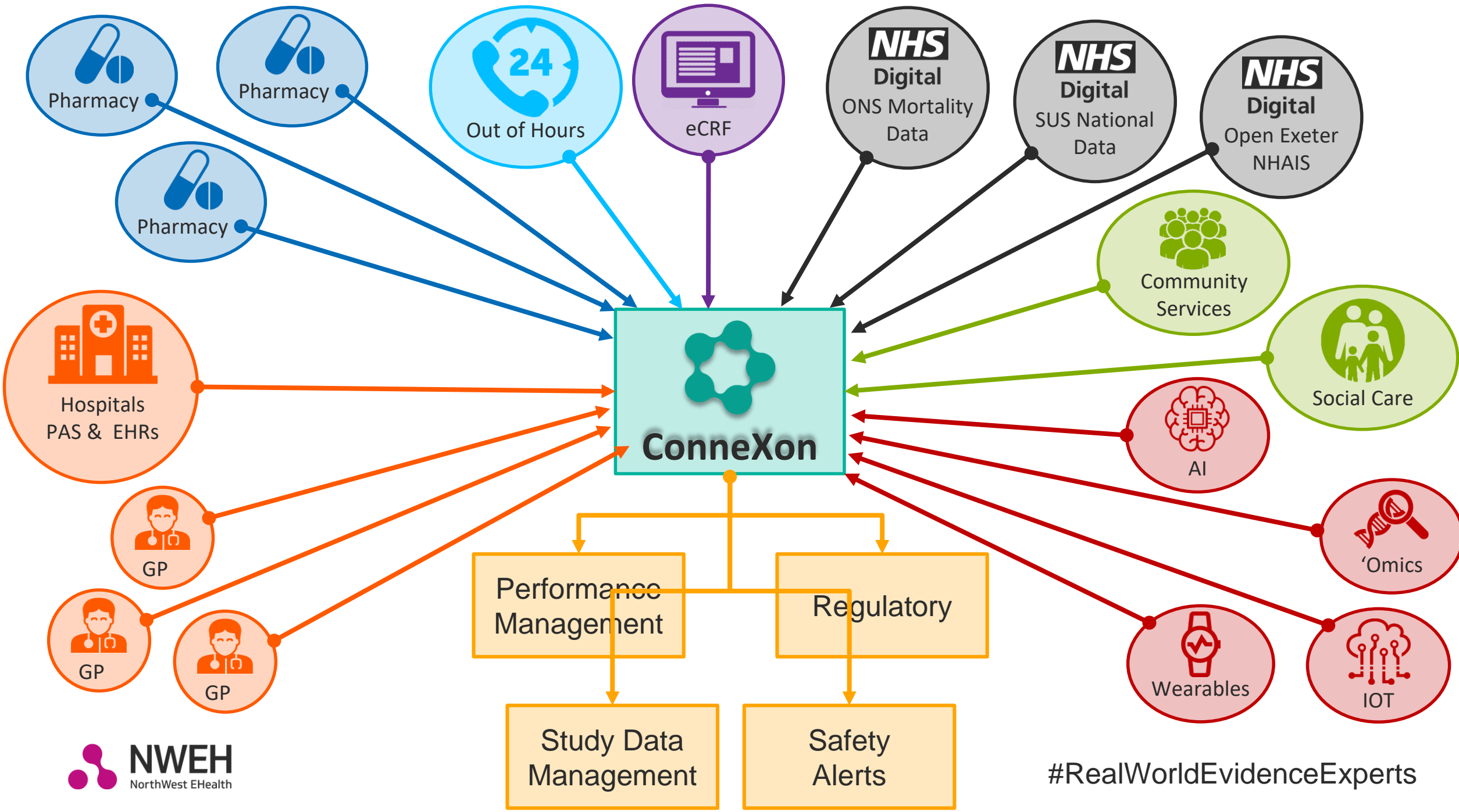
During the 12 month treatment period, patients can have their maintenance treatment adjusted (stepping-up, stepping-down or switch) in both arms, at the GP's/Investigator's discretion as would be normal clinical practice



1

Real World Data

Where does it come from? What does it look like?



Examples of hospital data

Category	Subcategory	Reason	Location	HRG	Tariff(£)
Admission	AE Visit	Hallucinations	Majors HD	VB07Z	£119.00
Admission	AE Visit	Diarrhoea and Vomiting	Majors HD	VB04Z	£139.00
Admission	Day Case	Contusion of lower leg Oesophageal obstruction (disorder)	Majors HD	FZ25/B08Z	£196.00
Admission	AE Visit	Unwell Adult	Majors	VB05Z	£130.00
Admission	AE Visit	Septicemia (disorder)	Majors	WA0307Z	£1,290.00

Example of Primary Care prescription data

readcode	rubric	entrydate	codevalue	codeunits
f41z.	METFORMIN tabs 850mg	20011113	90	ONE THREE TIMES A DAY

Example of data after NWEH transformation

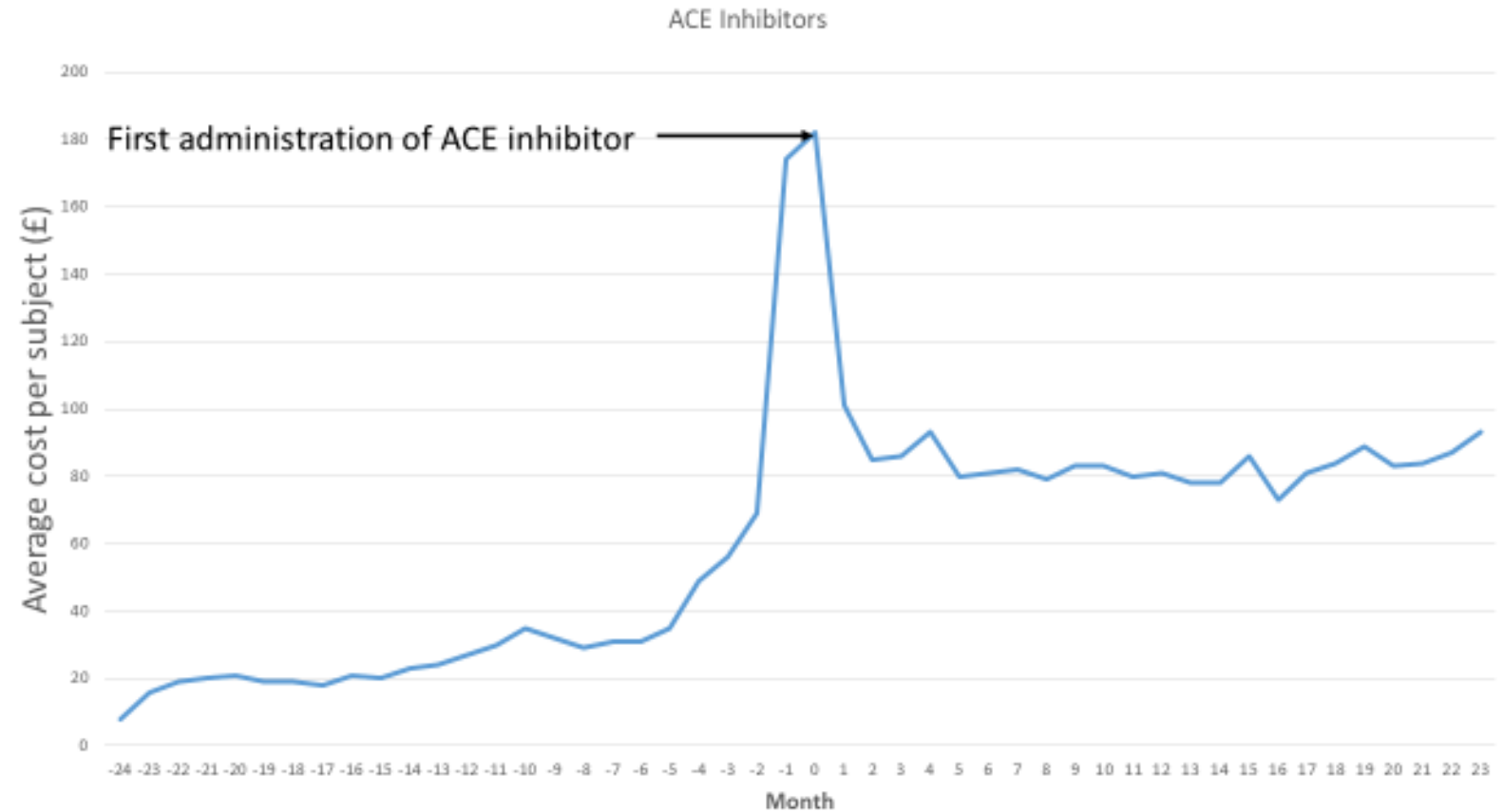
SDTMClass	SDTMDomain	readcode	drug	dose	form	bnf_version	amount
INTERVENTIONS	CM	f41z.	METFORMIN	850mg	tablets	06.01.02.02	90

PrescriptionDate	DosageDirections
2001-11-13 00:00:00.000	ONE THREE TIMES A DAY

drugCategory	drugSubCategory	SnomedFullySpecifiedName
ENDOCRINE DRUGS	BIGUANIDES	Metformin hydrochloride 850mg tablet - product

Mapping costs of health resource utilisation

ACE Inhibitors – 5213 anonymised subjects



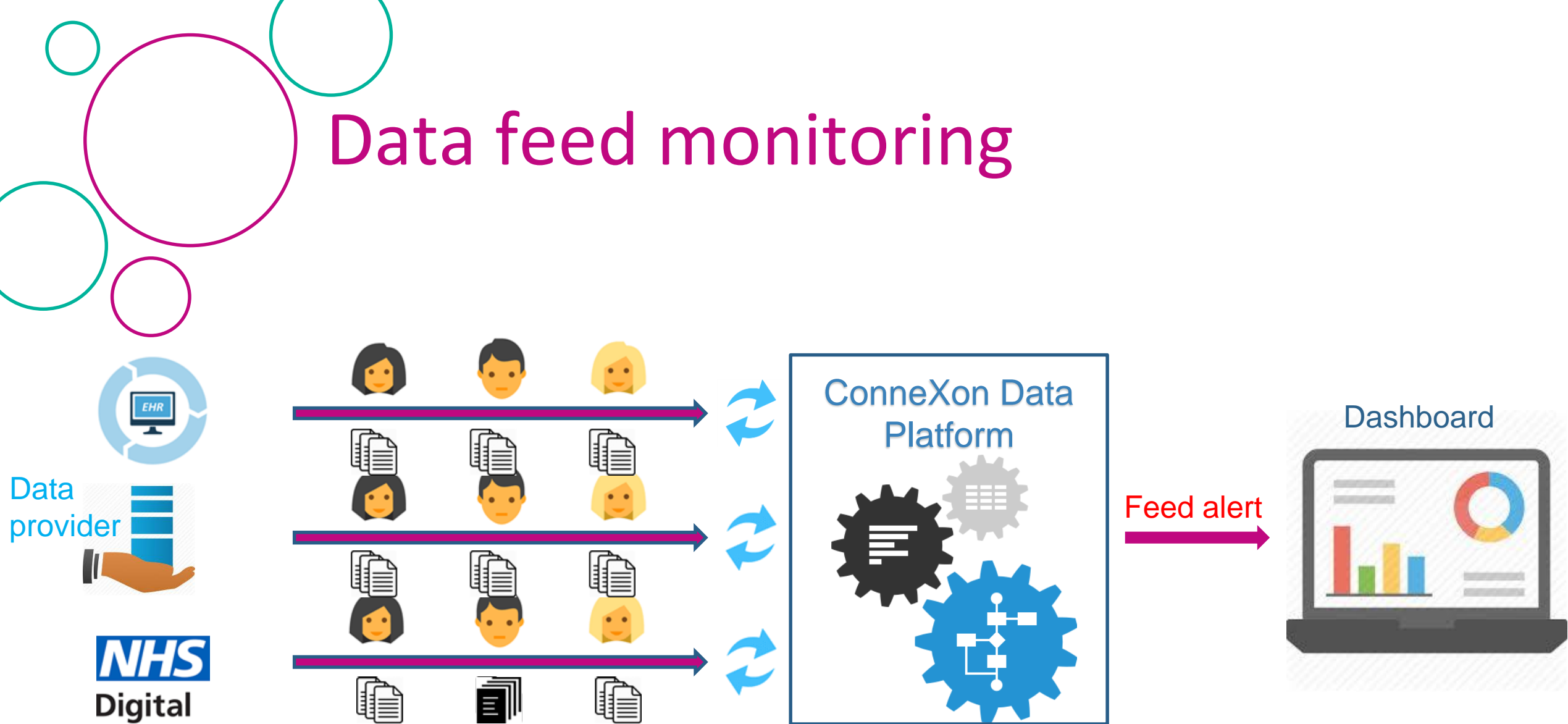


2

Data quality service

Can Real World Data *actually* be used for the statistical analysis of clinical trials. How do we prevent poor quality data

Data feed monitoring



Data provider



ConneXon Data Platform

Feed alert

Dashboard

Automated data quality checks

Source data	Check
A&E Inpatient spells	If an inpatient is admitted via A&E it should be possible to link the A&E visit to the inpatient spell
Outpatients	Follow up appointments should heavily outnumber new appointments
Inpatient episodes Prescriptions	Distribution number of episodes in a spell should be roughly an exponential decay Maximum number of prescriptions per patient per year should not exceed 1000
Dispensing	There should be no patients with substantial numbers of prescriptions but no dispenses
Laboratory tests Inpatient episodes	Instances of more than 1 admission per patient per day should be very low Histogram of values should be relatively smooth
ALL	Number of records as a function of time should generally reflect number of active patients



3

Data normalization

Real World Data comes from multiple sources with different structure and coding. How do we prevent duplication and improve data quality without changing the meaning of the original data



“The nice thing about standards is that you have so many to choose from.”

Andrew S. Tanenbaum – Computer Scientist

NWEH Integration Engine



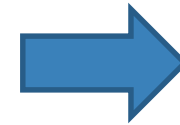
ORION
HEALTH



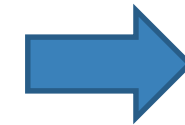
InterSystems
Health | Business | Government



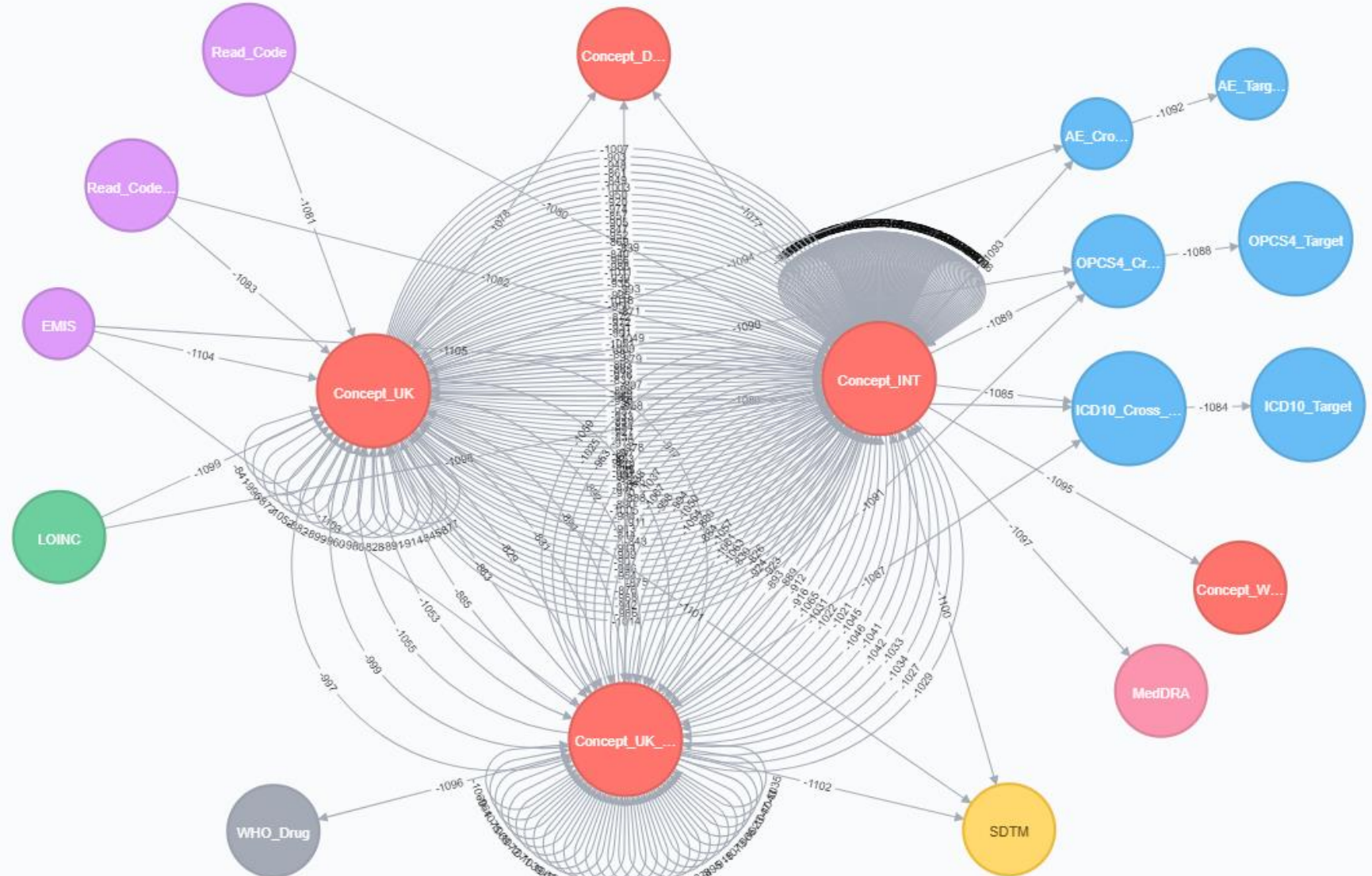
INTERFACEWARE



NWEH Data Extractor

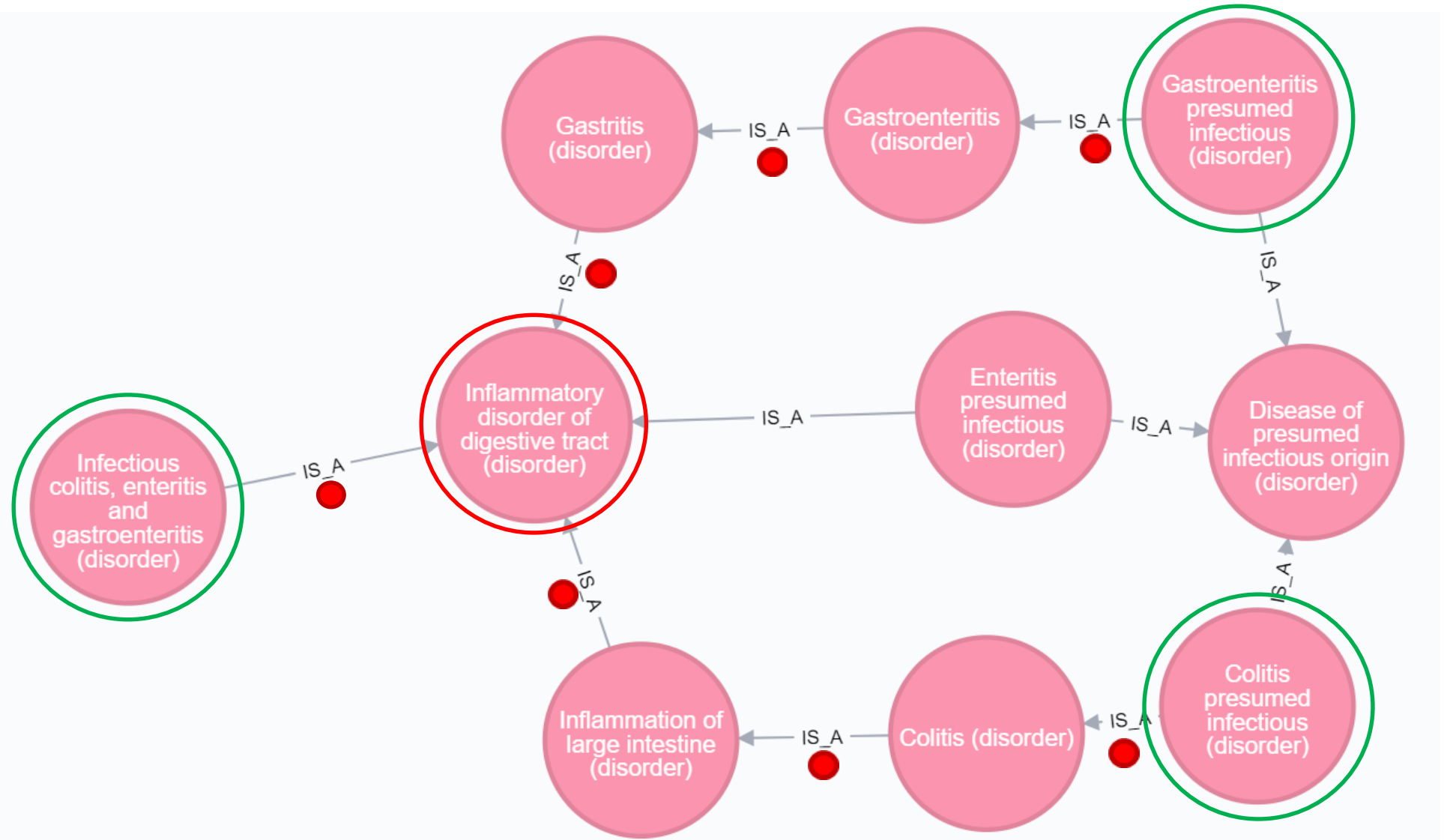


The ConneXon Data Platform transforms all coding to Snomed CT



LPG Mapping Example: Concept of common 'proximal supertypes'

ICD to code A09
'Other gastroenteritis
& supertypes' using
the Cypsa and
language 'infectious
origin'
maps to these 3
Snomed CT codes

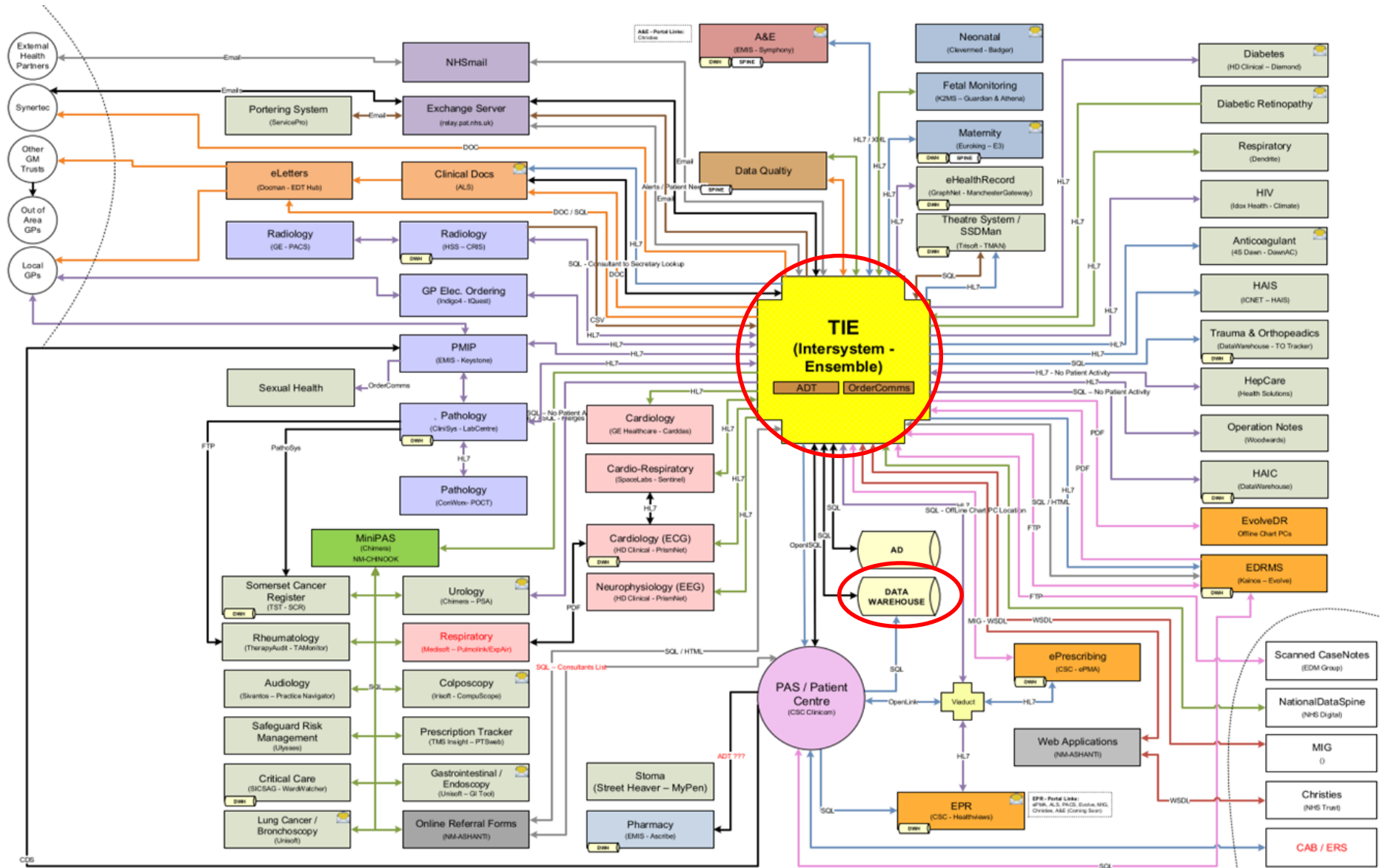




4

Data from complex and legacy systems

Example hospital system





5

Pharmacy data

Dispensing and collection

Cohens Chemist.





Variations of drug term in the electronic health record

Result:

CMTERM

DOSETX

DRUGFORM

Fluticasone furoate + Vilanterol

92micrograms / 22micrograms

inhaler

Fluticasone Furoate + Vilanterol 92/22microgram Inhaled 1 Puff/s Morning Flucicasone / Vilanterol Inhaled 1 Puff/s Morning

Flucitasone furoate + vilenterol inhaler (92 microgram + 22 microgram) Inhaled 1 Blister/s Morning

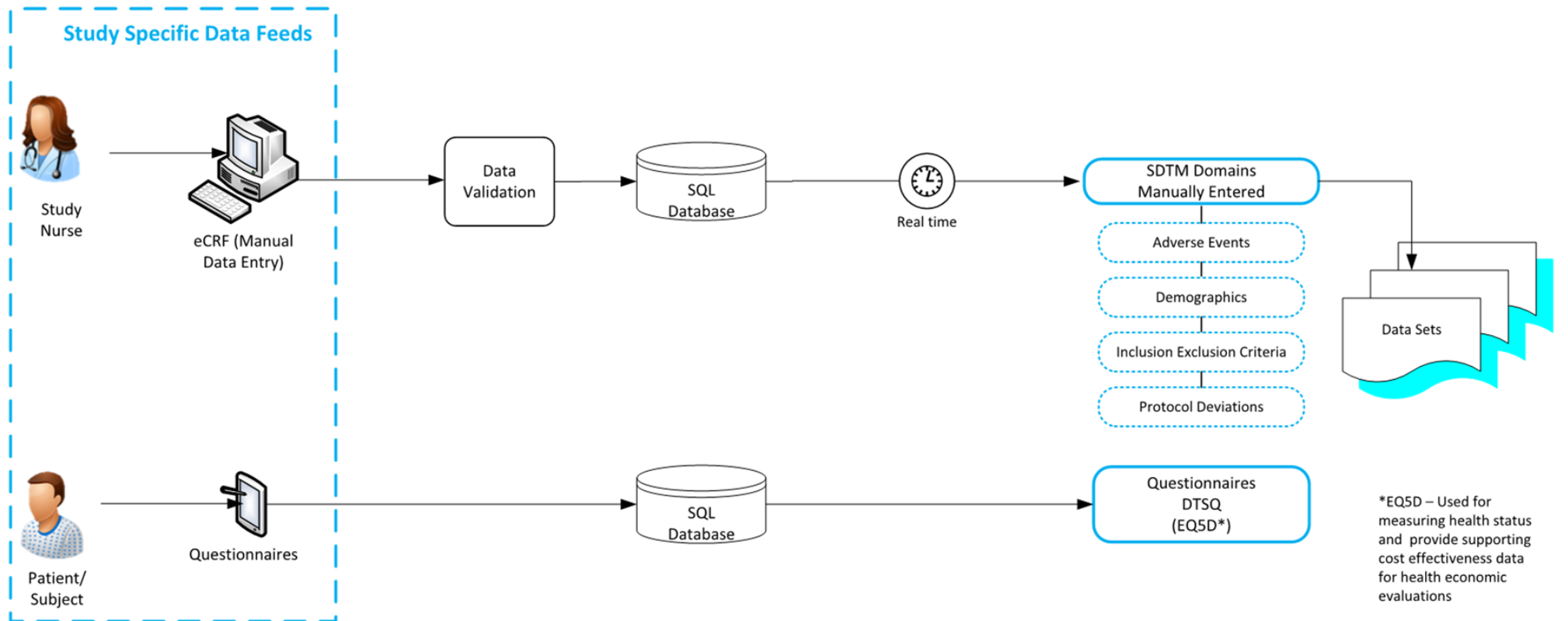


6

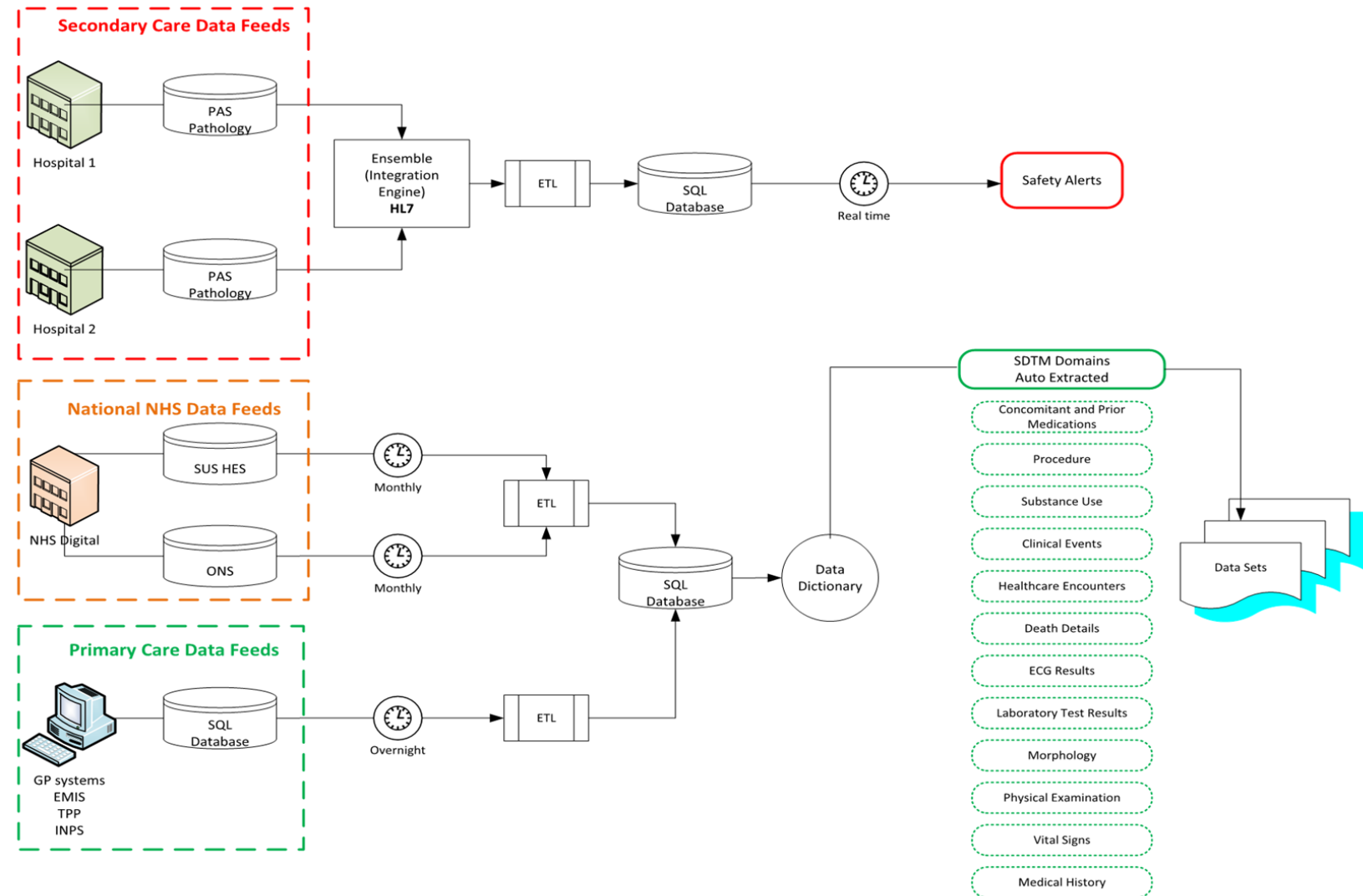
Creating datasets

Transforming Real World Data into CDISC Study Data Tabulation Model

Data collected through an eCRF



Electronic Medical Records automatically transformed into SDTM



How eCRF and EMR data populate datasets before, during and post study:

SDTM Domain	PRIOR	SCREEN	TREATMENT	FOLLOW-UP
CM	eDT	eDT	eDT	eDT
CM (e.g. study specific endpoint)	eDT	CRF	CRF	eDT
MH	eDT	eDT		eDT
AE			CRF	
CE	eDT	eDT	CRF	eDT

CM – Prior and Concomitant Medications

MH – Medical Histories

AE – Adverse Events

CE – Clinical Events

CDISC Clinical Terminology – coverage using ‘creatinine’ as an example

Readcode	ReadTerm	SDTM_Variable_Name	CDISC Submission Value	CDISC Synonym(s)
44lf.	Mercury/creatinine ratio	LBTESTCD	HGCREAT	
44lg.	Citrate/creatinine ratio	LBTESTCD	CITCREAT	Citrate/Creatinine; Citric Acid/Creatinine
44lh.	Cobalt/creatinine ratio	LBTESTCD	COCREAT	
44li.	Chromium/creatinine ratio	LBTESTCD	CRCREAT	
44ll.	Urine copper/creatinine ratio	LBTESTCD	UCUCREAT	
44lm.	Glycolate/creatinine ratio	LBTESTCD	GLYCOCRT	
44ln.	Phosphate/creatinine ratio	LBTESTCD	PHOSCRT	Phosphate/Creatinine
44lo.	Alanine/creatinine ratio	LBTESTCD	ALACREAT	
44lp.	Amylase/creatinine ratio	LBTESTCD	AMYCREAT	
44lq.	Aspartate/creatinine ratio	LBTESTCD	ASTCREAT	Aspartate/Creatinine
44lr.	Manganese/creatinine ratio	LBTESTCD	MNCREAT	
44ls.	Lead/creatinine ratio	LBTESTCD	PBCREAT	
44lt.	Urea/creatinine ratio	LBTESTCD	UREACRT	Urea/Creatinine
44lu.	Zinc/creatinine ratio	LBTESTCD	ZNCREAT	
44lv.	Cadmium/creatinine ratio	LBTESTCD	CDCREAT	
44lw.	Chloride/creatinine ratio	LBTESTCD	CLCREAT	Chloride/Creatinine
44lx.	Glutamate/creatinine ratio	LBTESTCD	GLUCREAT	
44ly.	Glycine/creatinine ratio	LBTESTCD	GLYCICRT	



All LB Test codes must be unique



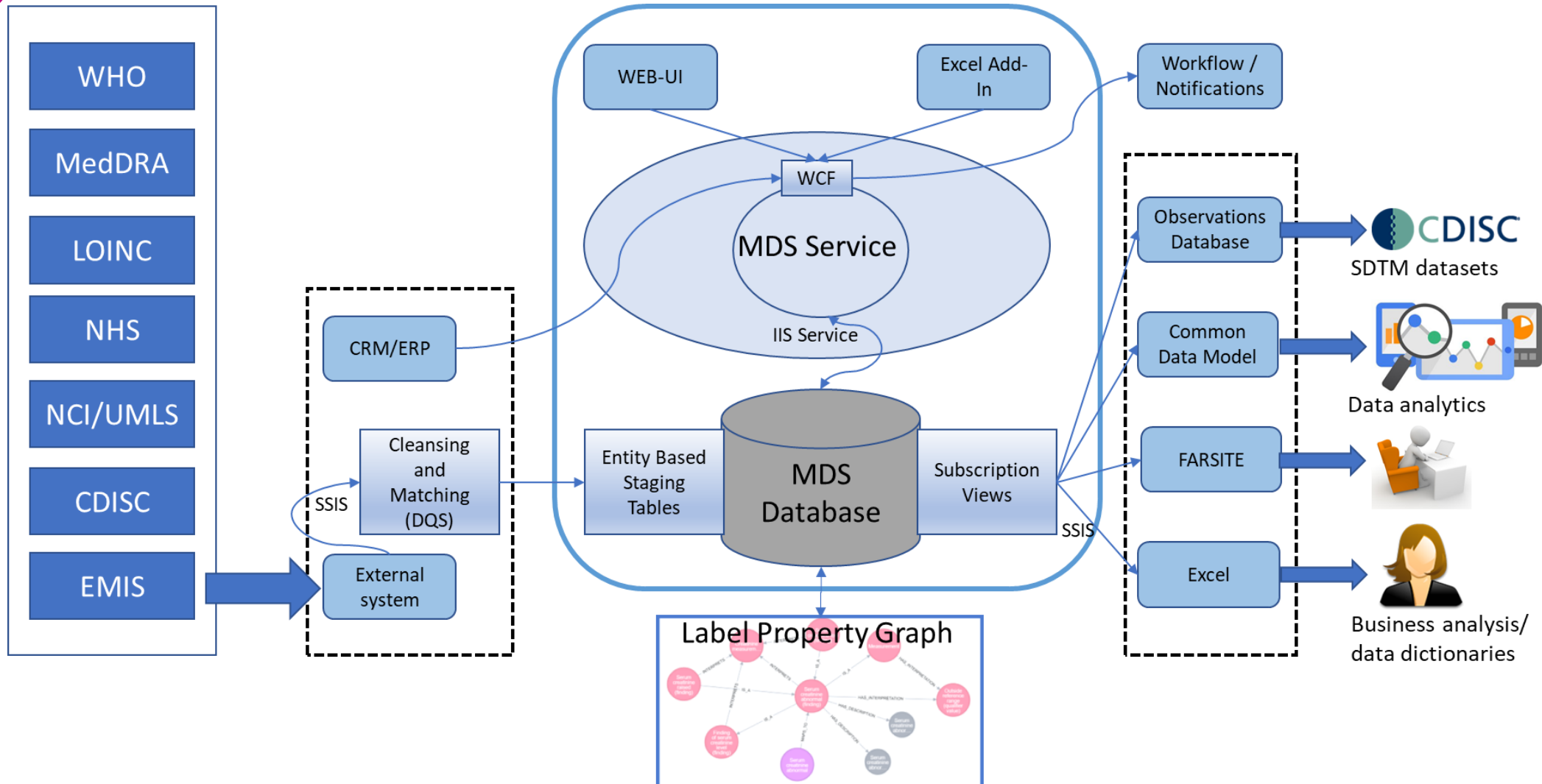
SDTM mapping example: MH

ICD10 CODE	ICD10 TERM
Q13	Congenital malformations of anterior segment of eye

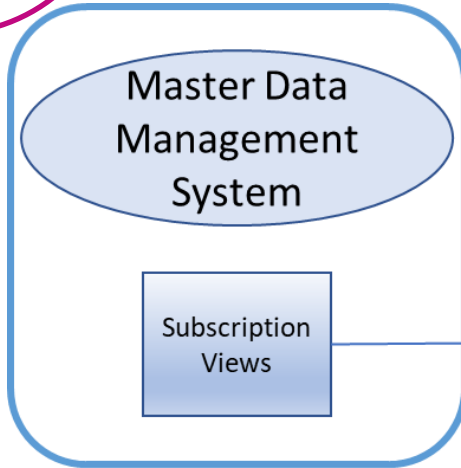
Concept ID	Snomed Term
429448005	Congenital anomaly of anterior segment of eye (disorder)

Concept ID	Snomed Term	SDTM Variable	CDISC Submission Value
276654001	Congenital malformation (disorder)	MHTERM	CONGENITAL MALFORMATION
255549009	Anterior (qualifier value)	MHDIR	ANTERIOR
264193995	Segment (qualifier value)	MHPORTOT	SEGMENT
244486005	Entire eye (body structure)	MHLOC	EYE

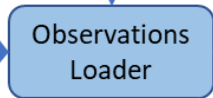
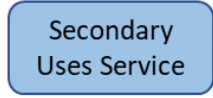
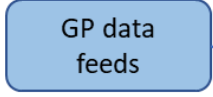
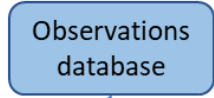
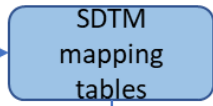
MDM System overview



SDTM Builder



VZ_CONCEPTID	FullySpecifiedName	SCT_CONCEPTID	SDTM_NCICode	DOMAIN	LBTESTCD	LBTEST
4414	Serum potassium (& level) (procedure)	166687002	C64853	LB	K	Potassium
44140	Normal serum potassium level (finding)	166688007	C64853	LB	K	Potassium
44141	Raised serum potassium level (finding)	166689004	C64853	LB	K	Potassium
44142	Low serum potassium level (finding)	166690008	C64853	LB	K	Potassium
4415	Serum sodium (& level) (procedure)	166691007	C64809	LB	SODIUM	Sodium
44150	Serum sodium level normal (finding)	166692000	C64809	LB	SODIUM	Sodium
44151	Serum sodium level abnormal (finding)	166693005	C64809	LB	SODIUM	Sodium



Study Data Tabular Model

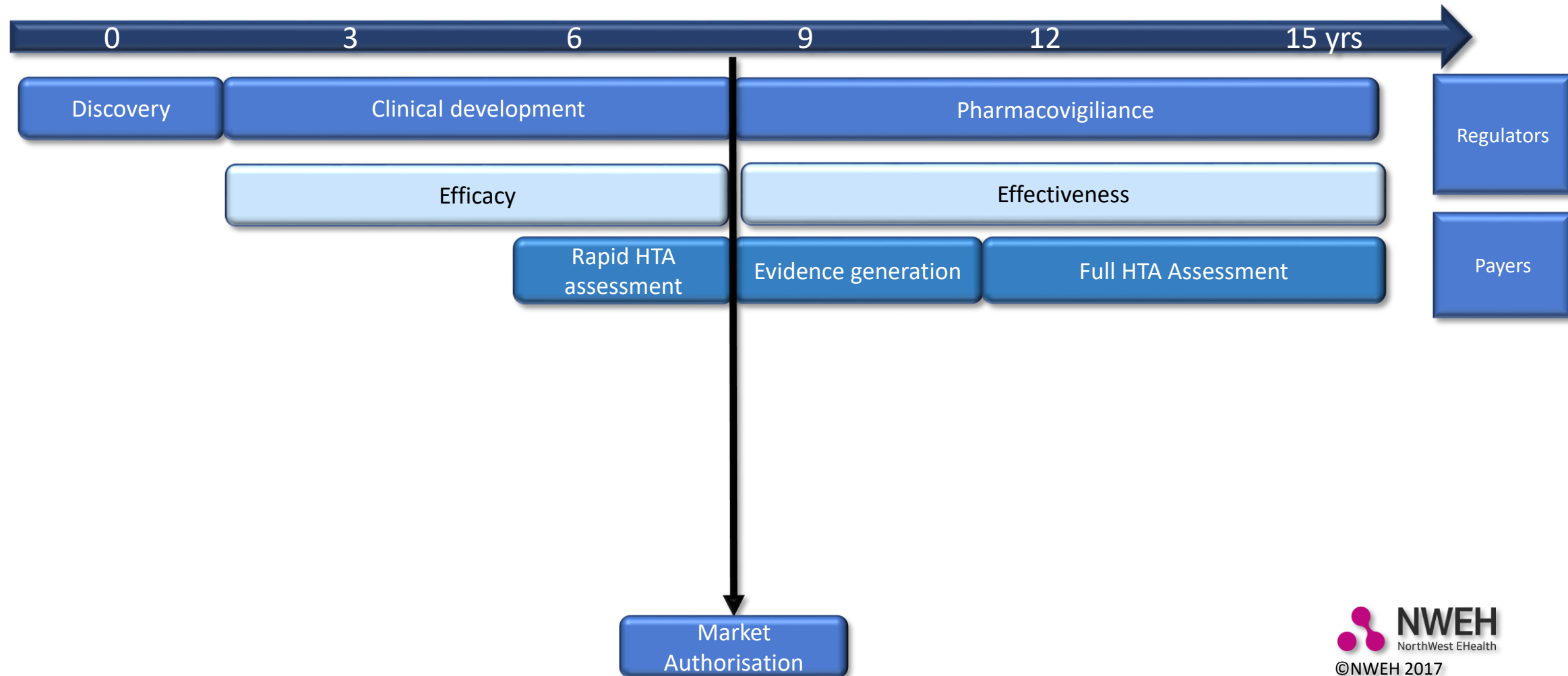
lb.xpt

Row	STUDYID	DOMAIN	USUBJID	LBSEQ	LBTESTCD	LBTEST	LBCAT
1	ABC	LB	ABC-001-001	1	ALB	Albumin	CHEMISTRY
2	ABC	LB	ABC-001-001	2	ALP	Alkaline Phosphatase	CHEMISTRY
3	ABC	LB	ABC-001-001	3	ALP	Alkaline Phosphatase	CHEMISTRY
4	ABC	LB	ABC-001-001	4	ALP	Alkaline Phosphatase	CHEMISTRY
5	ABC	LB	ABC-001-001	5	WBC	Leukocytes	HEMATOLOGY
6	ABC	LB	ABC-001-001	6	LYMLE	Lymphocytes	HEMATOLOGY
7	ABC	LB	ABC-001-001	7	NEUT	Neutrophils	HEMATOLOGY
8	ABC	LB	ABC-001-001	8	PH	pH	URINALYSIS

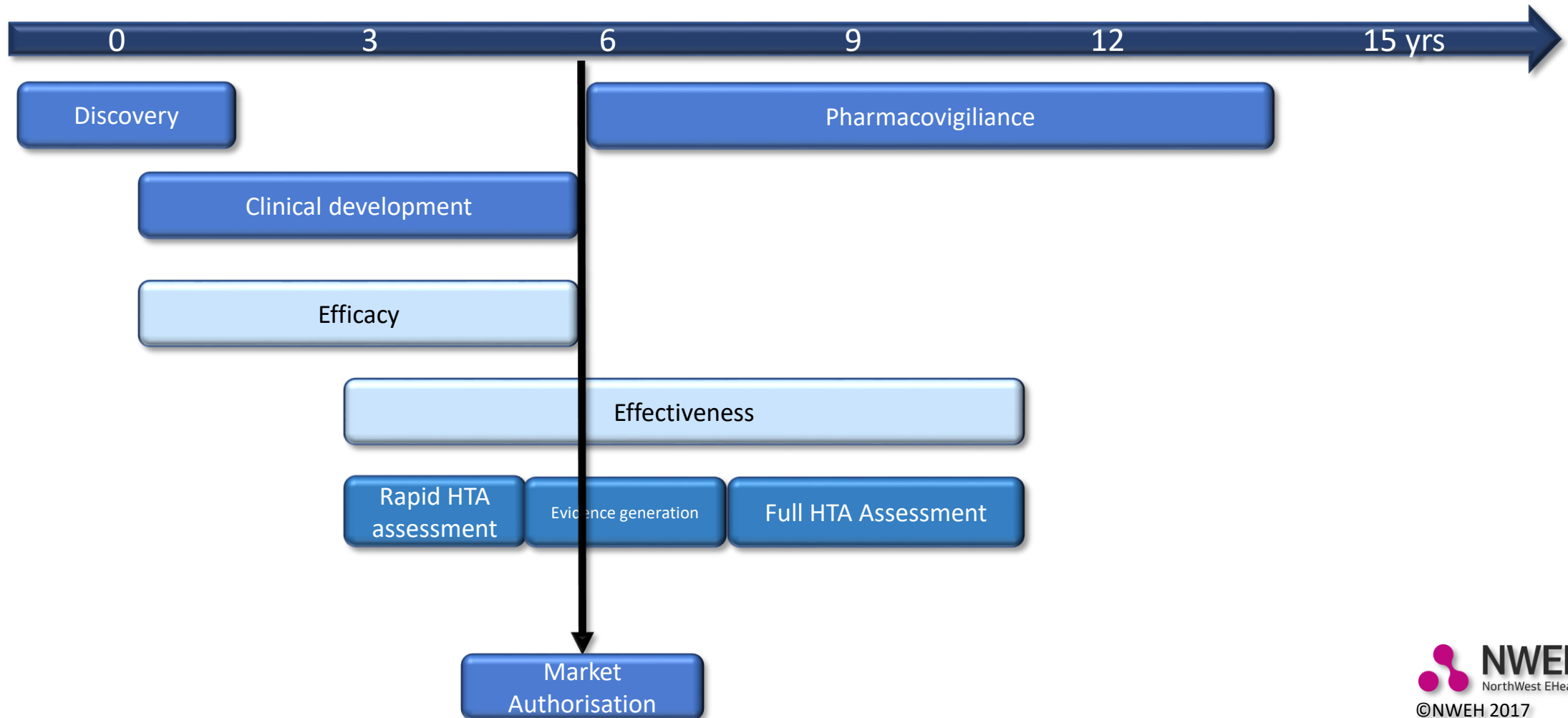
Operational Data Model

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        </ItemGroupData>
      </FormData>
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          <ItemDataString ItemOID="LBTESTCD">ALT</ItemDataString>
          <ItemDataString ItemOID="LBORRES">245</ItemDataString>
        </ItemGroupData>
      </FormData>
    </StudyEventData>
  </SubjectData>
</ClinicalData>
```


Future clinical evaluation lifecycle



Future clinical evaluation lifecycle



The background features a dark, textured surface with a network of thin, light-colored lines radiating from a central point. In the upper left corner, there are several circles of varying sizes, some outlined in cyan and others in magenta. The text 'NWEH ConneXon' is centered in a white, sans-serif font.

NWEH ConneXon