



Use of FHIR in Clinical Research: From Electronic Medical Records to Analysis

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This Project Extends the Initial Research on FHIR (RoF) Project



PhUSE 2017

Paper RW04

Use of Fast Healthcare Interoperability Resources (FHIR) in the Generation of Real World Evidence (RWE)

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Consider reading the papers in order if you are new to eSource and HL7 FHIR

What We Did



- Test use of HL7 FHIR standard for data exchange
- Extracted data for diabetic type 2 patients from the MITRE SyntheticMass Synthea Health Information Exchange (HIE) in FHIR format
- Mapped certain data points from FHIR to CDASH & SDTM
- Generated CDASH-compliant CRFs
- Generated SDTM-compliant datasets
- Realized further exploration & more work is needed



This Project Extends the Initial Research on FHIR (RoF) Project



PhUSE EU Connect 2018

Paper RW02

**Use of HL7 FHIR as eSource to Pre-populate CDASH Case Report Forms
using a CDISC ODM API**

Sam Hume, CDISC, State College, PA, USA
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What We Did



- Automate populating EDC from eSource/EHR
- Adds FHIR API use to the initial Research on FHIR (RoF) paper
- Demonstrates how data standards, workflows, and APIs reduce eSource implementation barriers
- Develops and demonstrates the use of new extensions to the CDISC ODM and CDASH standards metadata
- Provides access to the E2C FHIR mapping for CDASH variables in ODM using the SHARE API
- Tests the new ResearchStudy and ResearchSubject FHIR resources



Clinical Resources

Summary

AllergyIntolerance 3
AdverseEvent 0
Condition (Problem) 3
Procedure 3
FamilyMemberHistory 2
ClinicalImpression 0
DetectedIssue 1

Medication

MedicationRequest 3
MedicationAdministration 2
MedicationDispense 2
MedicationStatement 3
Medication 3
MedicationKnowledge 0
Immunization 3
ImmunizationEvaluation 0
ImmunizationRecommendation 1

Public Health & Research

Research Study 0
ResearchSubject 0

Care Provision

CarePlan 2
CareTeam 2
Goal 2
ServiceRequest 2
NutritionalOrder 2
VisionPrescription 2
RiskAssessment 1
RequestGroup 2

Diagnostics

Observation 5
Media 1
DiagnosticRequest 3
Specimen 2
BodyStructure 1
ImagingStudy 3
QuestionnaireResponse 3
MolecularSequence 1

<https://www.hl7.org/fhir/resourcelist.html>

Project Purpose



- Build on previous two projects by RoF team
- Can FHIR provide near real time analytics from EHRs
- Can FHIR provide standardized data for input to ADaM
- Develop a model/automated process to
 - extract EHR data using FHIR resources and APIs
 - create ADaM datasets from FHIR formatted inputs
 - Generate safety related analytics

Business Case



- Importance of subject safety
- Ability of study teams to look at safety data ASAP
- Eliminate gap between initial data collection and entry into study EDC
- Monitor safety in long term follow-up/post-marketing studies

Methods (1)

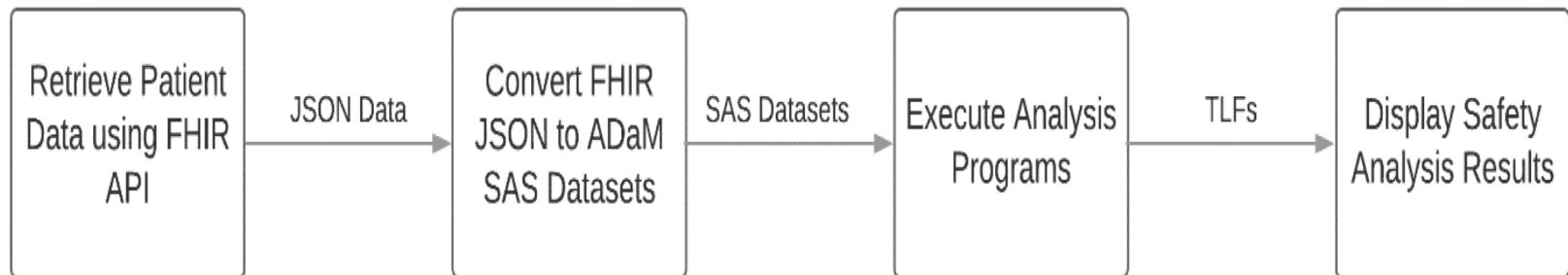


- Same database as in our two previous papers
- Adult subjects (greater than 18 years of age) with Diabetes Mellitus Type 2 with at least two encounters in the SyntheticMass Database
- Data domains
 - demographics
 - medications
 - medical history
 - adverse events
 - laboratory and vital signs
- Data manually mapped from FHIR to ADaM

Methods (2): Process



RESEARCH ON FHIR: USING EHR DATA AND CDISC ADAM FOR SAFETY ANALYSIS



Methods (3): Convert FHIR JSON to CDISC ADaM

- Conversion of FHIR Data
 - Converted JSON formatted data to CSV
 - CSV converted to SAS datasets
- Safety ADaM datasets created for analysis
 - ADSL
 - ADAE
 - ADLB
 - ADVS

Methods (4): Execute Analysis Programs

- Safety summary tables and figures created for AEs and Lab
- FHIR data extraction and refreshing of safety summaries are done by APIs/batch files in near real time
- Displays posted to web browser

Results (1): Mapping FHIR to ADaM

All variables needed for analysis successfully mapped from FHIR -> ADaM

Dataset	ADaM Variable	FHIR Resource	FHIR Field	Notes
ADSL	USUBJID	Patient	<u>Identifier.Value</u>	de-identify
	STUDYID			Assign (= 'CDISC01')
	TRT01A	Medication	<u>coding.code/coding.display</u>	Actual treatment 'Metformin Hydrochloride' or 'Comparator'
	TRTSDT	Medication Statement	<u>effectivePeriod.start</u>	
	TRTEDT	Medication Statement	<u>effectivePeriod.end</u>	
ADLB/ ADVS	USUBJID	Patient		ADSL.USUBJID
	STUDYID			ADSL.STUDYID
	TRTA			ADSL.TRT01A
	ADT	Observation	<u>effectiveDateTime</u>	date measure taken
	AVISITN			patient encounter number for each subject
	PARAM	Observation	<u>coding.code</u>	extract from LOINC code
	AVAL	Observation	<u>valueQuantity.value</u>	
	BASE			value of PARAM from first subject visit
	ABLFN			set to 1 if first patient visit
	CHG			AVAL - BASE
	ANRLO			assign from published standards
	ANRHI			assign from published standards

Results (2): Mapping FHIR to ADaM

LOINC Code	LOINC Description	LOINC Short Description	LBTEST/VSTEST	LBTESTCD/VSTESTCD
2339-0	Glucose [Mass/volume] in Blood	Glucose Bld-mCnc	Glucose	GLUC
4548-4	Hemoglobin A1c/Hemoglobin.total in Blood	Hgb A1c MFr Bld	Hemoglobin A1C/Hemoglobin	HBA1CHGB
14959-1	Microalbumin/Creatinine [Mass Ratio] in Urine	Microalbumin/Creat Ur	Albumin/Creatinine	ALBCREAT

Results (3): Retrieve EHR Data



- HSPC sandbox used as EHR system
- Developed FHIR client software in Python to request specific patients/variables
- FHIR API returned “resources”
 - structured according to the FHIR resource specifications
 - Represented in JSON format

Results (4): EHR Data in JSON



```
{
  "resourceType": "Observation",
  "id": "f001",
  "text": {
    "status": "generated",
    "div": "<div xmlns='\"http://www.w3.org/1999/xhtml\"'><p><b>Generated Narrative with Details</b></p><p><b>id</b>: f001</p><p><b>identifier</b>: 6323 (OFFICIAL)</p><p><b>status</b>: final</p><p><b>code</b>: Glucose [Moles/volume] in Blood <span>(Details : {LOINC code '15074-8' = 'Glucose [Moles/volume] in Blood', given as 'Glucose [Moles/volume] in Blood'})</span></p><p><b>subject</b>: <a>P. van de Heuvel</a></p><p><b>effective</b>: Apr 2, 2013 9:30:10 AM --&gt; (ongoing)</p><p><b>issued</b>: Apr 3, 2013 3:30:10 PM</p><p><b>performer</b>: <a>A. Langeveld</a></p><p><b>value</b>: 6.3 mmol/l<span> (Details: UCUM code mmol/L = 'mmol/L')</span></p><p><b>interpretation</b>: High <span>(Details : {http://terminology.hl7.org/CodeSystem/v3-ObservationInterpretation code 'H' = 'High', given as 'High'})</span></p><h3>ReferenceRanges</h3><table><tr><td><b>Low</b></td><td><b>High</b></td></tr><tr><td>*</td><td>3.1 mmol/l<span> (Details: UCUM code mmol/L = 'mmol/L')</span></td><td>6.2 mmol/l<span> (Details: UCUM code mmol/L = 'mmol/L')</span></td></tr></table></div>"
  },
  "identifier": [
    {
      "use": "official",
      "system": "http://www.bmc.nl/zorgportal/identifiers/observations",
      "value": "6323"
    }
  ],
  "status": "final",
  "code": {
    "coding": [
      {
        "system": "http://loinc.org",
        "code": "15074-8",
        "display": "Glucose [Moles/volume] in Blood"
      }
    ]
  },
  "subject": {
    "reference": "Patient/f001",
    "display": "P. van de Heuvel"
  },
  "effectivePeriod": {
    "start": "2013-04-02T09:30:10+01:00"
  },
  "issued": "2013-04-03T15:30:10+01:00",
  "performer": [
    {
      "reference": "Practitioner/f005",
      "display": "A. Langeveld"
    }
  ],
  "valueQuantity": {
    "value": 6.3,
    "unit": "mmol/l",
    "system": "http://unitsofmeasure.org",
    "code": "mmol/L"
  },
  "interpretation": [
```

Results (5): Mapping Issues

- Treatment group / Arm
- Visit variables
- AEs
- Lack of harmonization between FHIR and CDISC
 - Coding system
 - Terminology

Results (6): ADaM Datasets



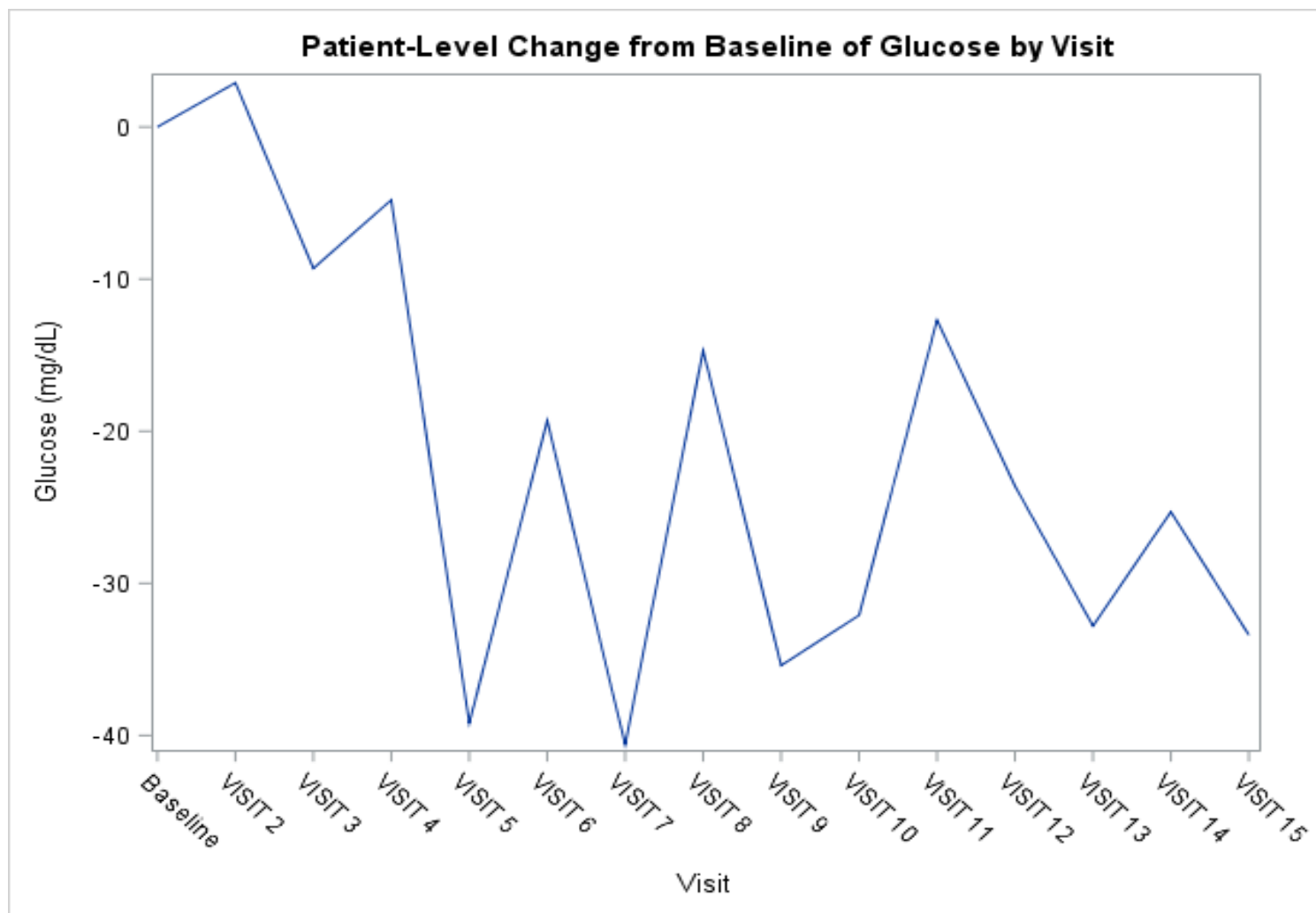
Script successfully retrieved EHR data and created ADaM datasets

Study Identifier	Unique Subject Identifier	Date of First Exposure to Treatment	Date of Last Exposure to Treatment	Actual Treatment	Analysis Date
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	1997-06-04
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	1998-06-10
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	1998-11-25
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	1999-03-24
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	1999-05-26
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	2000-01-19
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	2000-12-13
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	2001-08-08
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	2001-11-07
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	2002-04-17
CDISC01	054cfd5b-ccb0-4cb0-baf2-eacea220545f	1992-08-19		Metformin Hydrochloride	2002-07-10

ADLB continued:

Parameter	Analysis Value	Baseline Record Flag	Baseline Value	Analysis Visit	Analysis Visit (N)	Change from Baseline	Analysis Normal Range Lower Limit	Analysis Normal Range Lower Limit
Glucose (mg/dL)	141.8	Y	141.8	Baseline	1	0	65	110
Glucose (mg/dL)	159.5		141.8	VISIT 2	2	17.7	65	110
Glucose (mg/dL)	192.7		141.8	VISIT 3	3	50.9	65	110
Glucose (mg/dL)	137.6		141.8	VISIT 4	4	-4.2	65	110
Glucose (mg/dL)	160.5		141.8	VISIT 5	5	18.7	65	110
Glucose (mg/dL)	180.7		141.8	VISIT 6	6	38.9	65	110
Glucose (mg/dL)	141.8		141.8	VISIT 7	7	0	65	110
Glucose (mg/dL)	135.8		141.8	VISIT 8	8	-6	65	110
Glucose (mg/dL)	156.6		141.8	VISIT 9	9	14.8	65	110
Glucose (mg/dL)	199		141.8	VISIT 10	10	57.2	65	110
Glucose (mg/dL)	149.3		141.8	VISIT 11	11	7.5	65	110
Glucose (mg/dL)	186.7		141.8	VISIT 12	12	44.9	65	110

Results (7): Patient Level Displays



Results (8): Patient Level Displays

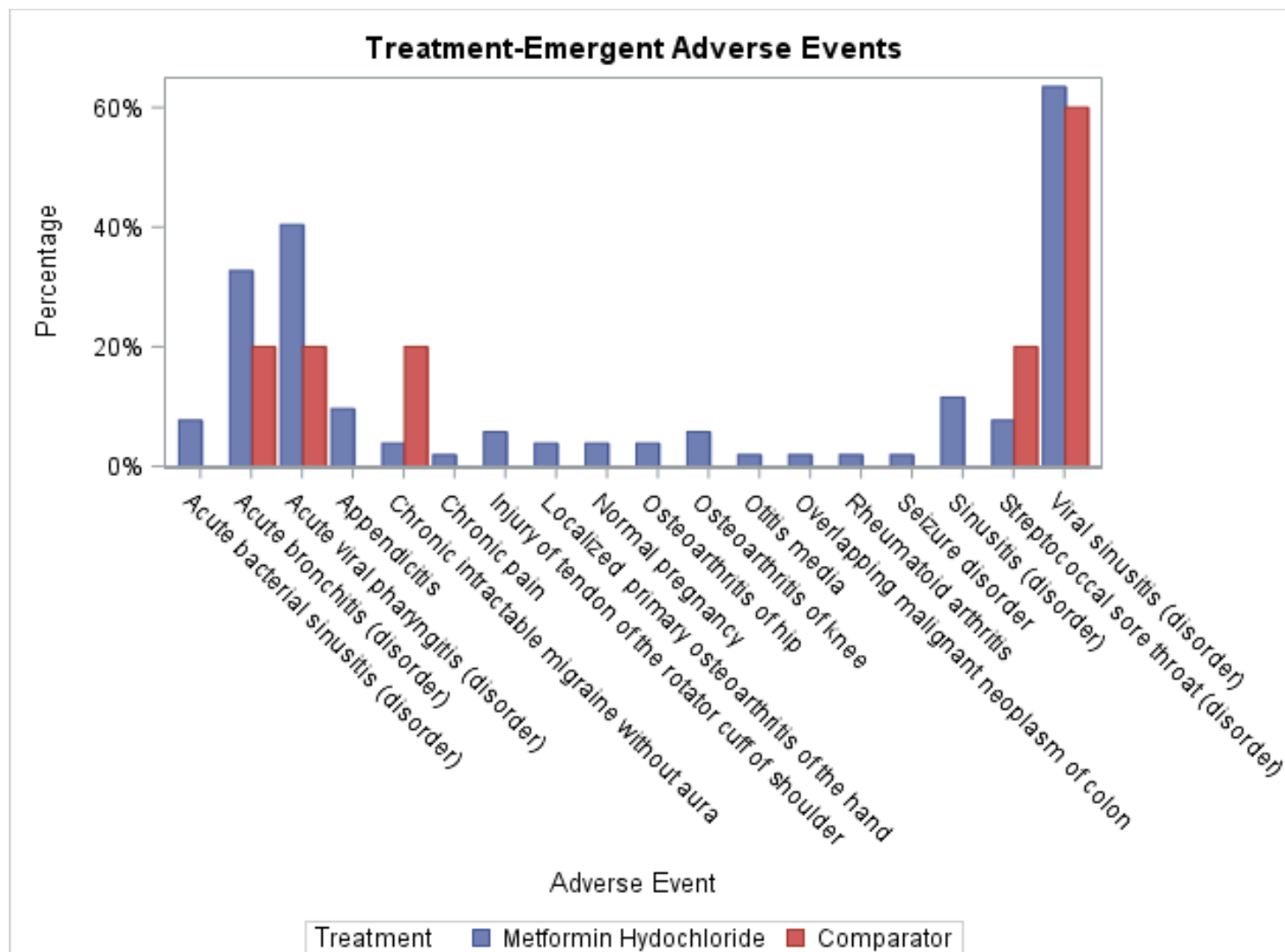


Treatment Emergent Adverse Event

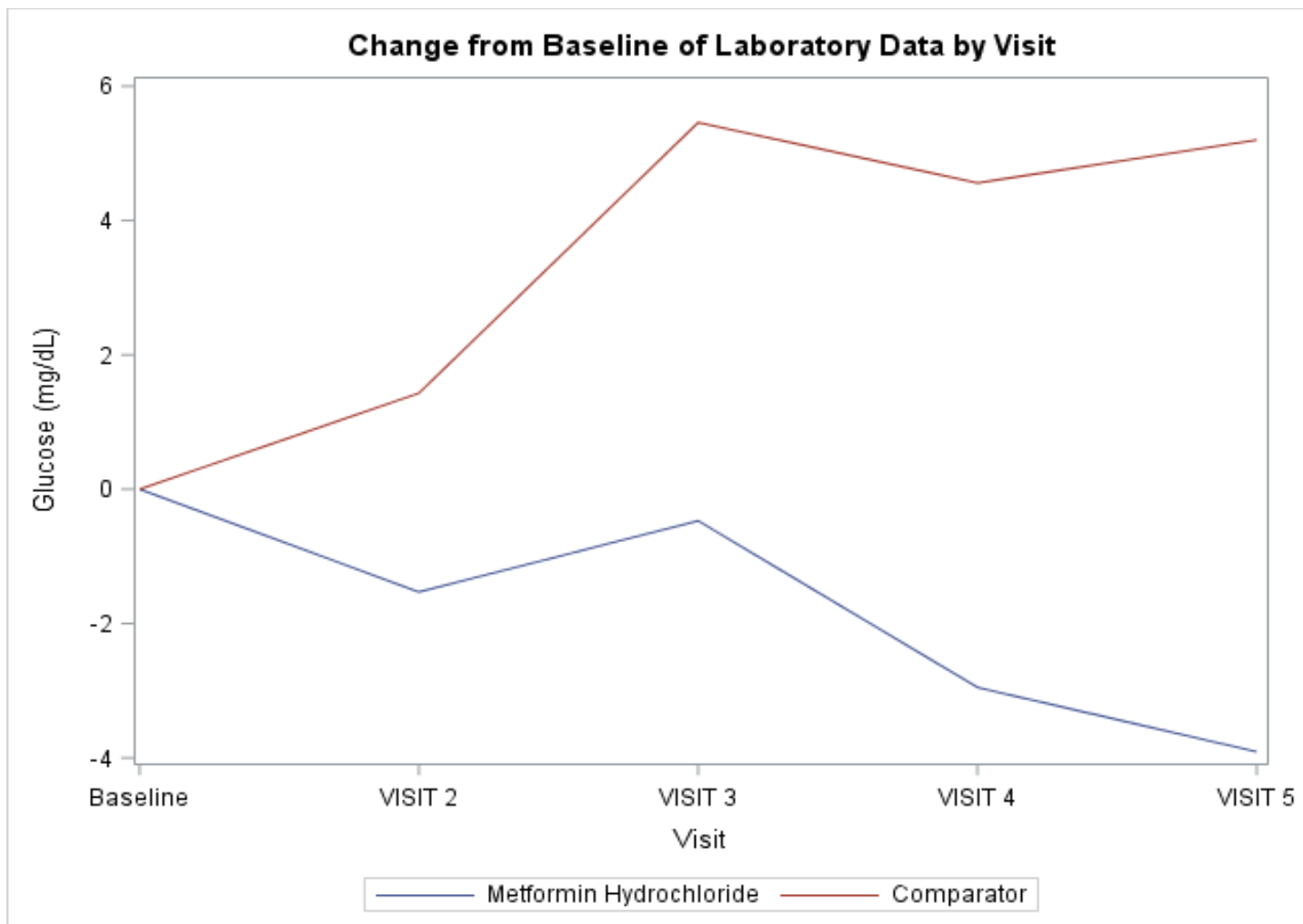
Treatment: Metformin Hydrochloride

Patient Number	Adverse Event	Start Date	End Date	Serious AE	Severity
1469e004-4c03-4244-b350-dbfd2 270ed48	Acute viral pharyngitis (disorder)	13-APR-1986	24-APR-1986	N	Mild
	Injury of tendon of the rotator cuff of shoulder	09-MAY-1989	15-JUL-1989	N	Mild
	Normal pregnancy	30-NOV-1981	07-DEC-1981	N	Mild
	Viral sinusitis (disorder)	02-FEB-1981	09-FEB-1981	N	Mild

Results (9): By Treatment Displays



Results (10): By Treatment Displays



Discussion (1): Retrieving EHR Patient Data using HL7 FHIR



- Why JSON
- SAS vs R/Python
- Python client software

```
from fhirclient import client
import fhirclient.models.patient as p
smart = client.FHIRClient(settings=settings)
patient = p.Patient.read('SMART-1288992', smart.server)
print(patient.name[0].given[0], patient.name[0].family)
print(patient.birthDate.isostring)
print(patient.gender)
```

Discussion (2): Prototype Limitations



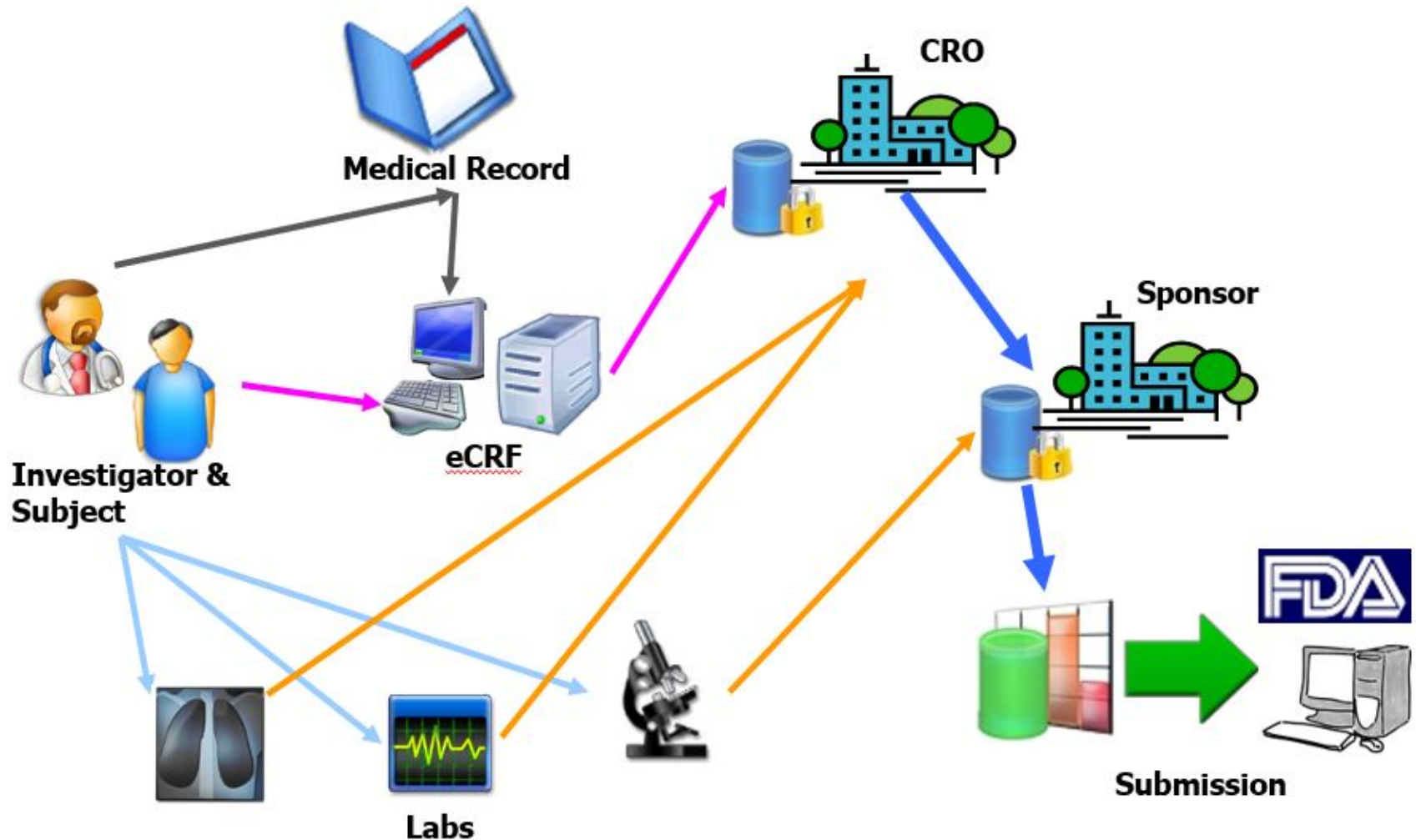
- Access/security
- Only 1 site
- Used basic mechanisms for slotting EHR data into the EDC visit structure
 - Visits
 - Treatment arms
- Limited scope of data: can other data be modelled in FHIR
- AEs
- FHIR/CDISC not harmonized

RoF Discussion Topics Warranting Additional Attention in Future Projects



- Test environment to limit mapping / data issues
- Consent and privacy rules
- Site-driven approach tradeoffs
- Data cleaning later in the lifecycle

Open, Standard APIs Improve Scalability of Data Exchange Solutions



Want to get involved?

Contact

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Thank You!