

Synthesize Your SDTMs!

Realistic Simulated SDTMs When You Need Them

Matt Travell, 07-Nov-2023

Introduction

- (1) Scene Setting and Challenge**
- (2) Opportunity**
- (3) Approach**
- (4) Outcome**
- (5) Lessons Learned**
- (6) What's Next**





Scene Setting

- Rapidly expanding small Biopharma internalizing and modernizing its data analytics capabilities
- Moving into new molecule entities
- No first-in-human study internal processes in-place
- Newly formed Integrated Data Analytics and Statistical Programming Group (IDSAP)

Challenge

Deliver analysis to support dose-escalation decision making in-house

- Formal TLFs
- Exploratory interactive app
- With-in 2 months
- No study test data available
- 2-day window on analysis generation 5-days after dosing starts



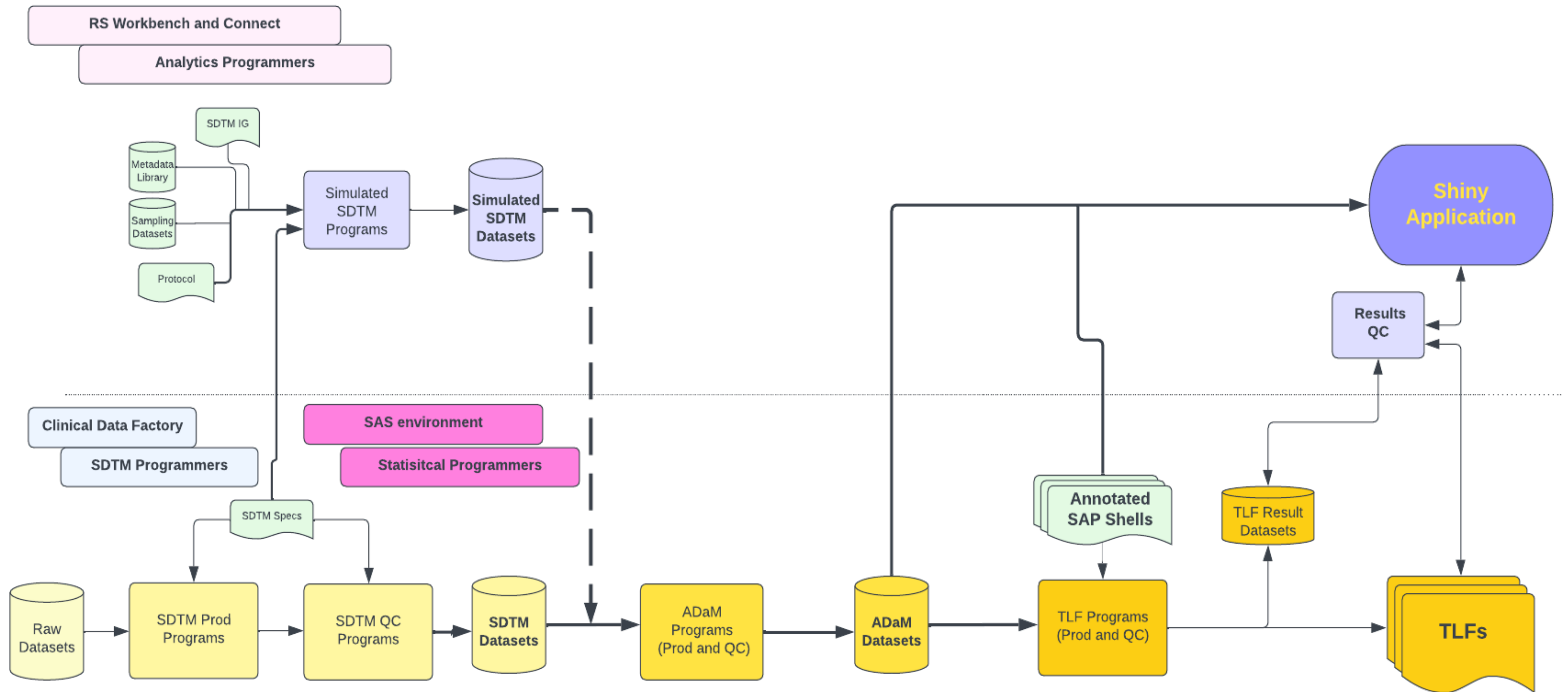
Opportunity

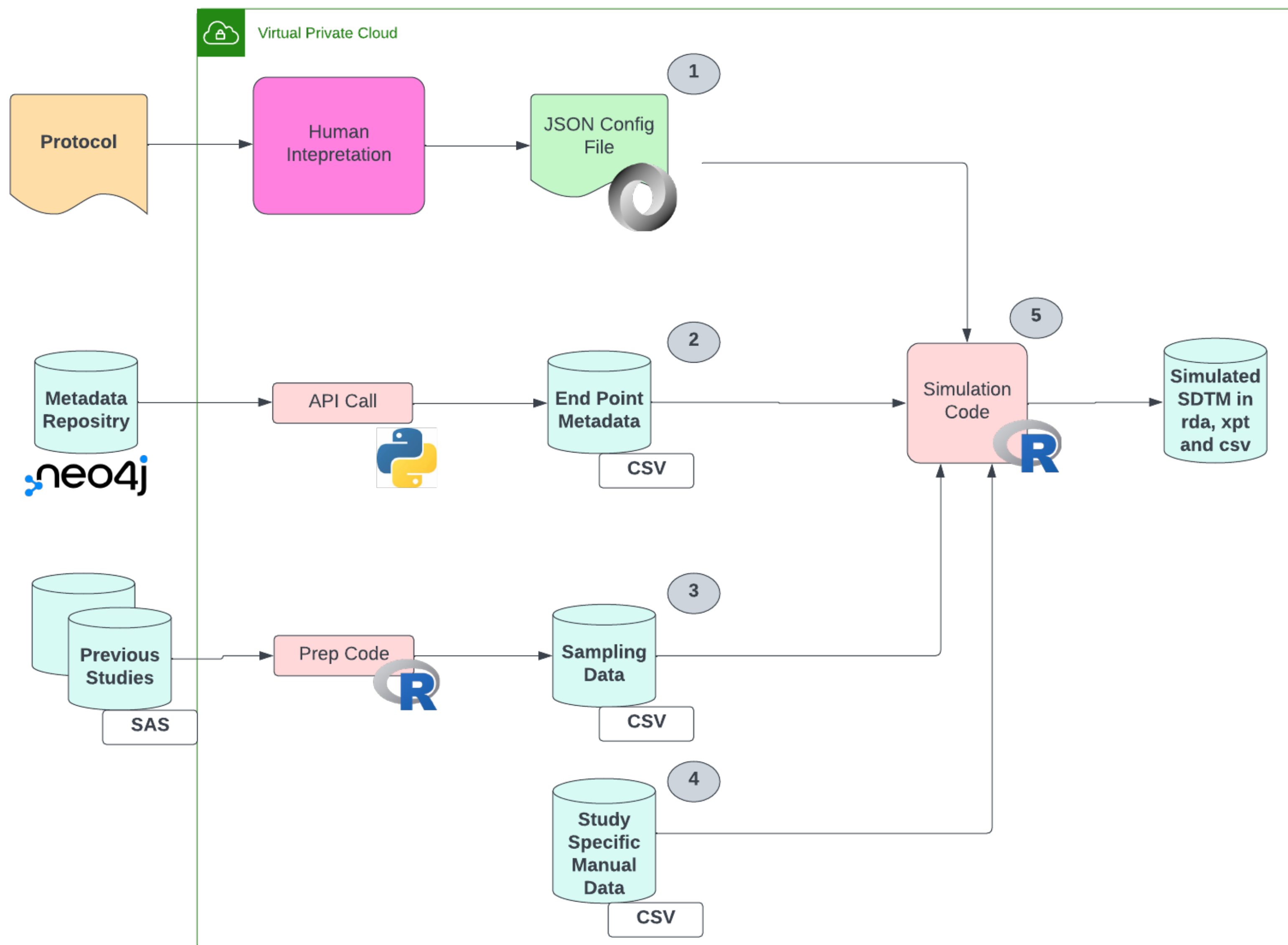
- Simulation of study data had previously been discussed as possible option to augment and improve the test data available at study set-up
- Provided a specific need where the potential value could be evaluated



Approach

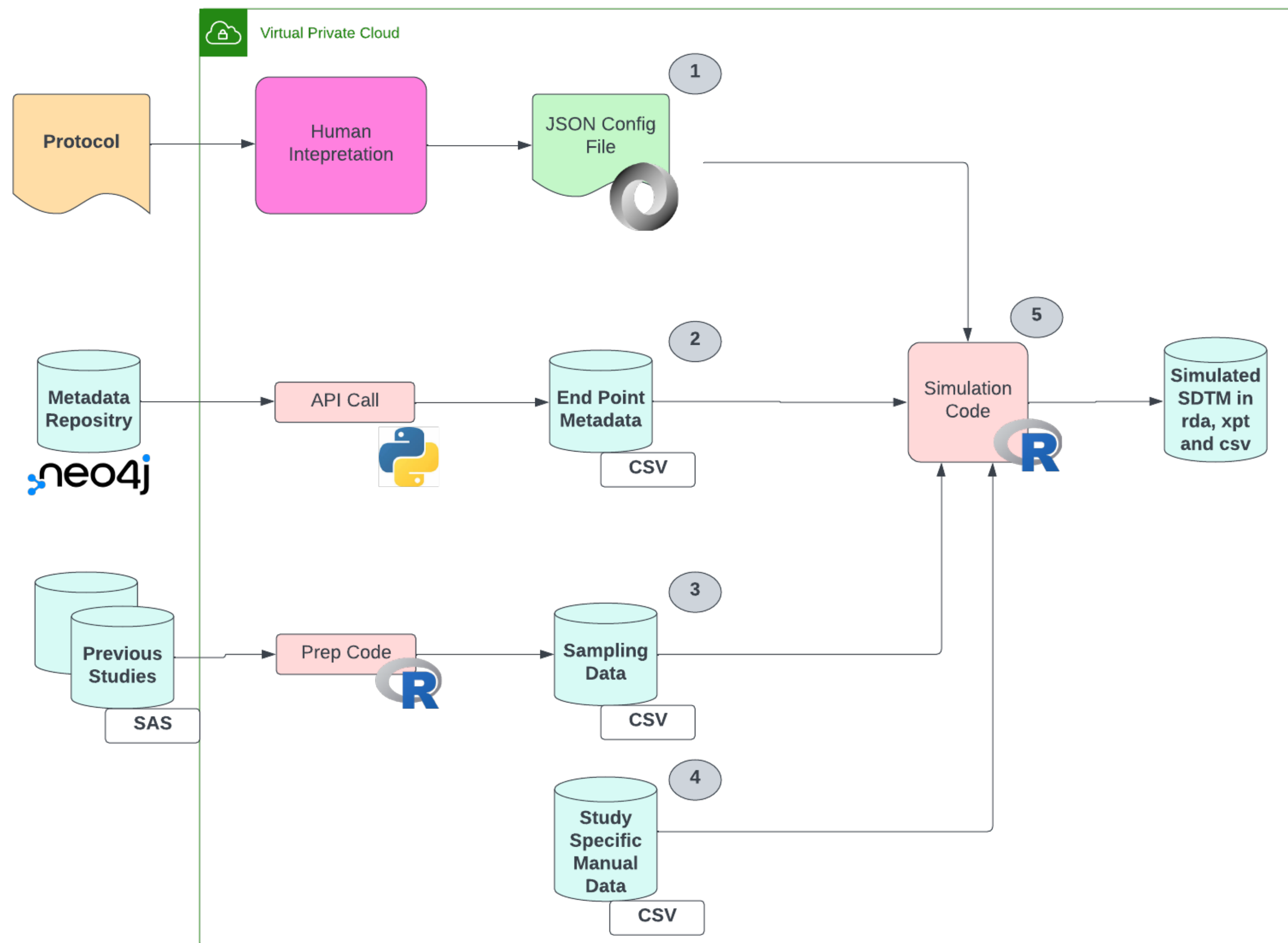
- Generate full set of SDTM datasets that are:
 - Fully structurally identical to the production datasets (easy bit)
 - More **critically**, closely mimic the expected different **subject data profiles** (hard bit)
- Enable all analysis activities to be completed prior to study start and support a frictionless transition of code to actual data once available
- Use modern tool set and readily available open-source packages
- Full agile scrum approach:
 - 2-week sprint cycles
 - Cross functional developers from SDTM, Statistical and Analytics programmers
 - Product Owner and Scrum Master roles





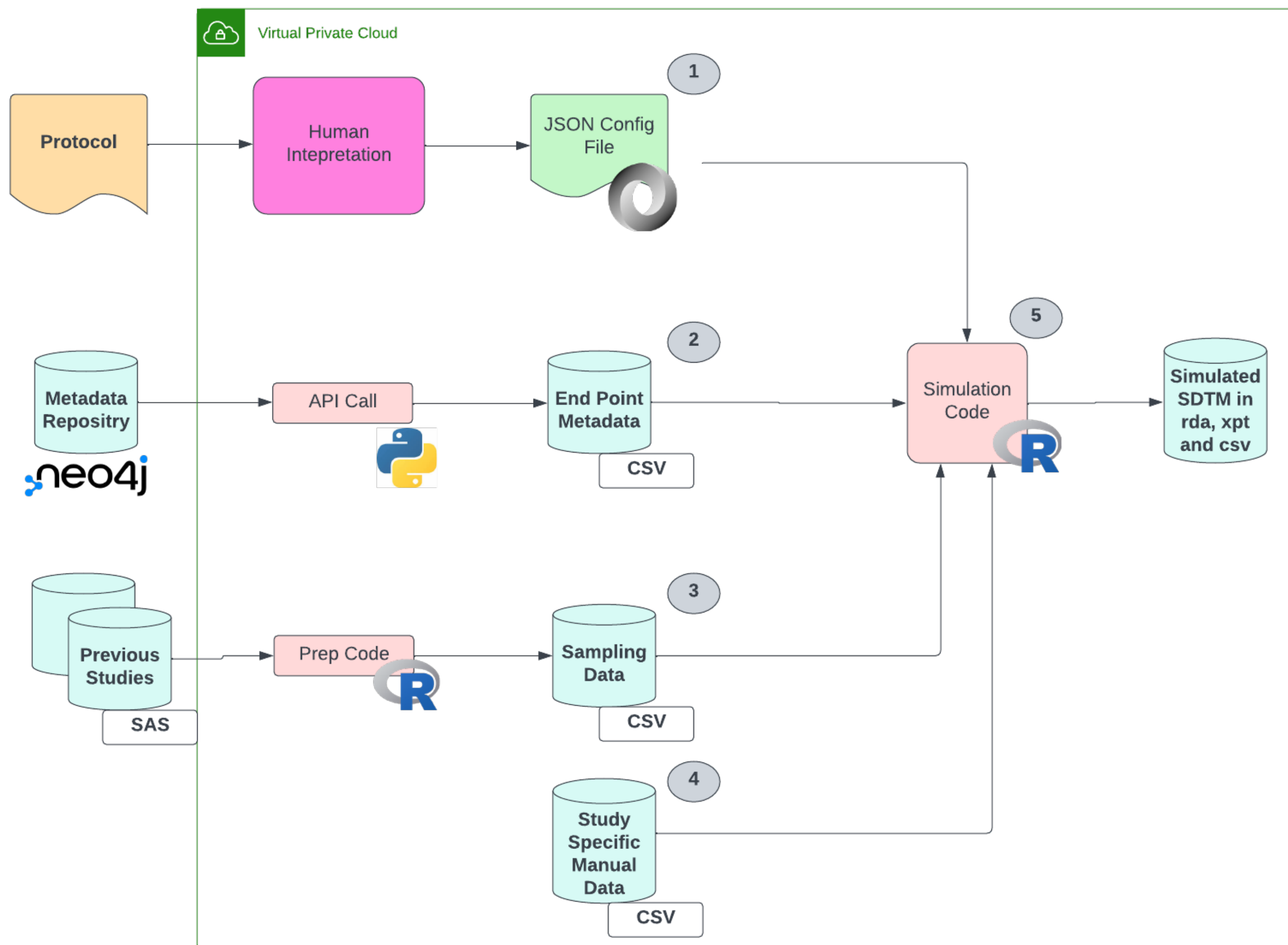
(1) JSON Configuration File

- Study design level information
- Population information
- End points in the study
- Time points per endpoint in the study
- Subject pathway information



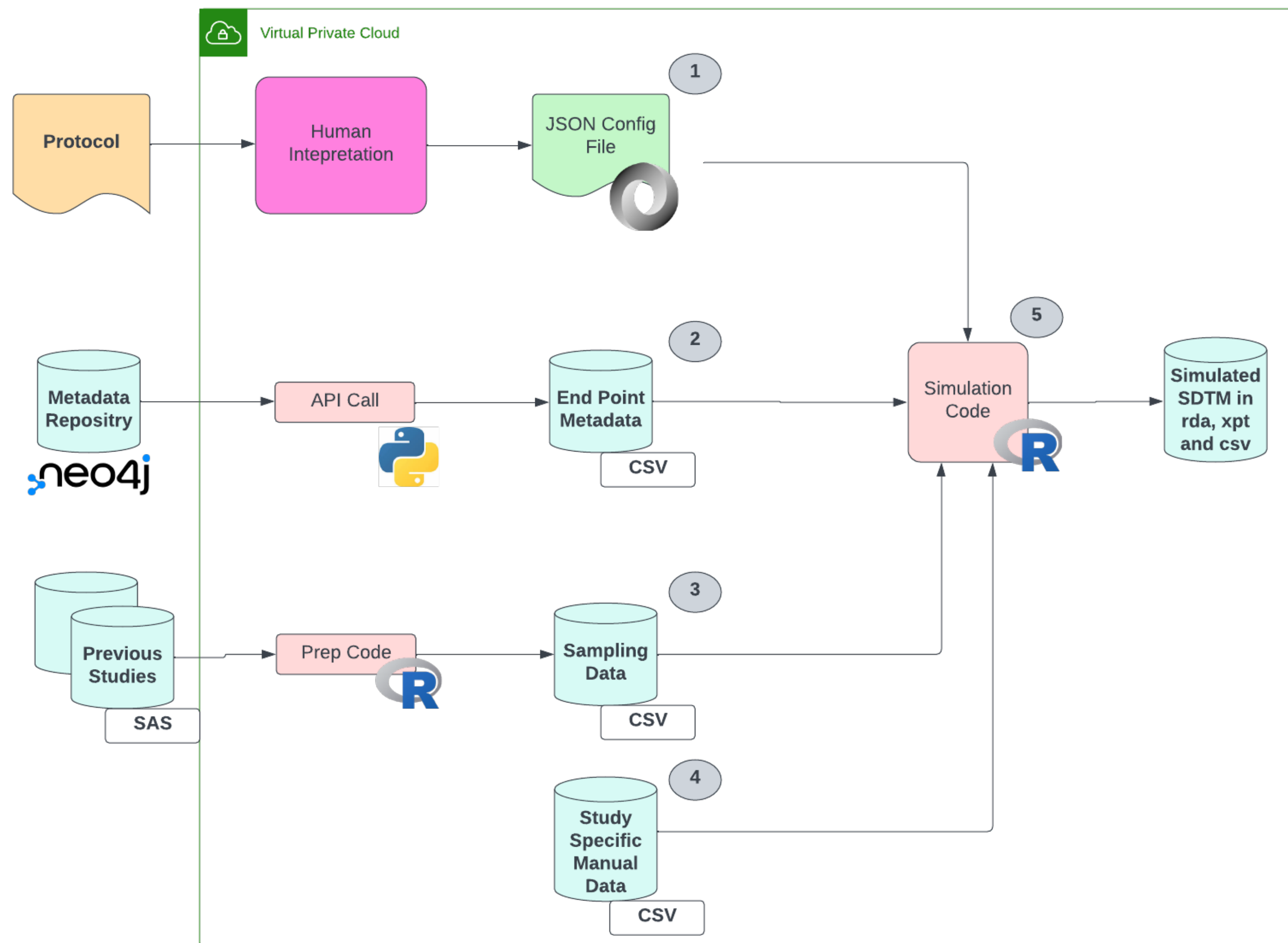
(2) End Point Metadata

- SDTM structural metadata
- Endpoint metadata taken from legacy studies
 - Distribution type
 - Estimate value
 - Variance
 - Minimum
 - Maximum
 - Categorical values and associated probability
 - Trend of end point over time



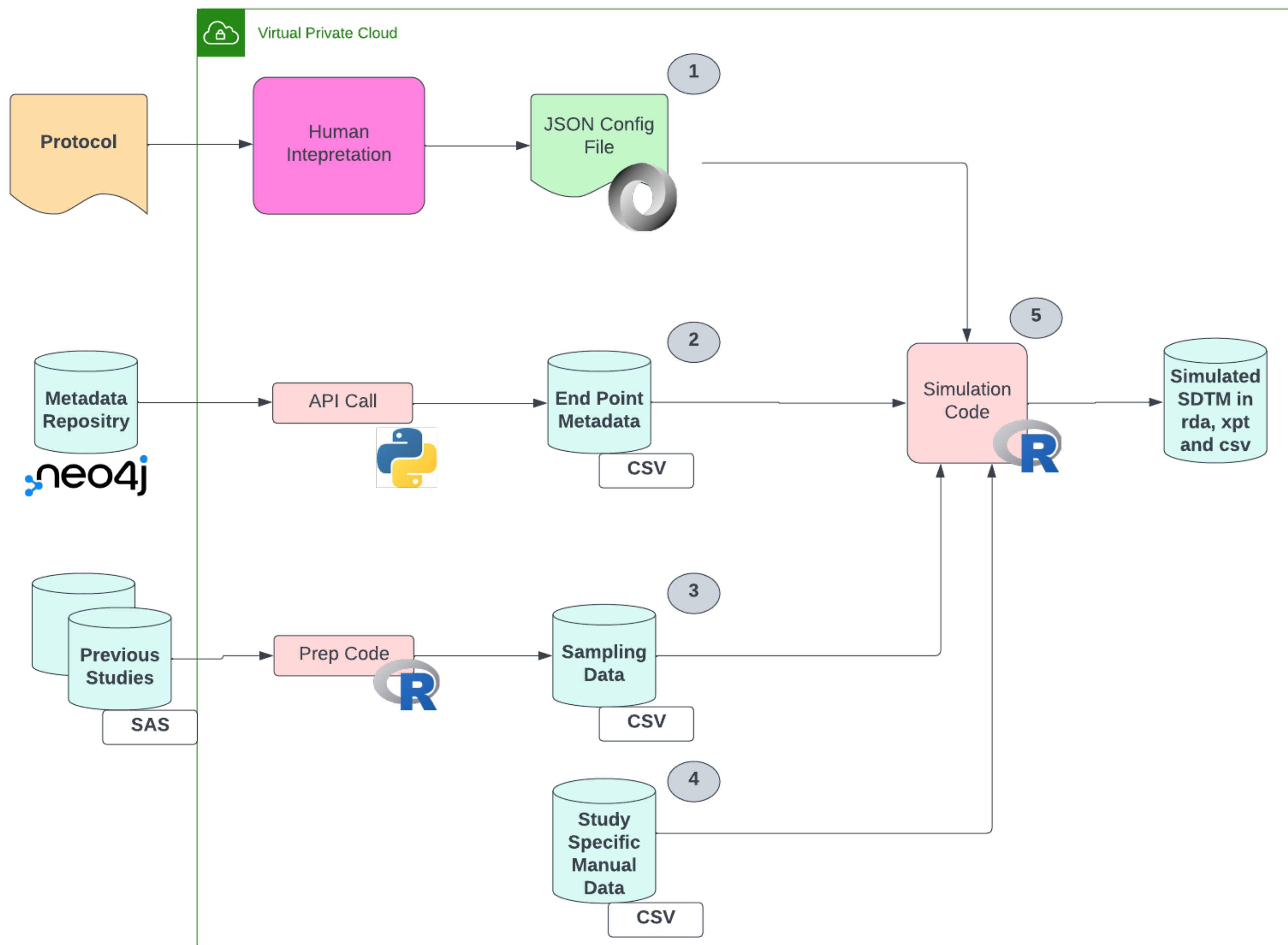
(3) Sampling Data

- Adverse Events, Medical History and Concomitant Medications from legacy studies



(4) Study Specific Manual Data

- Inject adverse event reaction profiles into subject data
- Adverse Event records
- Parameters records
- Event records
- Disposition records



(5) Simulation Code in R

- Metadata set-up
 - Usual packages
- Simulation result
 - “simstudy” package
- Processing into SDTM structure



Outcome

- Simulated SDTMs created in time enabling all analysis programming and stakeholder discussion to occur prior to study start

Jazz Pharmaceuticals
Protocol JZP

Table 9.1.1.1
Study Disposition
Randomized Analysis Set

Total Number, n (%)	Placebo (N=22)	JZP mg (N=20)	JZP mg (N=20)	JZP mg (N=10)
Participant Treatment Status				
Completed	22 (100)	18 (90.0)	19 (95.0)	10 (100)
Discontinued	0	2 (10.0)	1 (5.0)	0
Adverse Event	0	0	1 (5.0)	0
MET QTC STOPPING CRITERIA	0	2 (10.0)	0	0
MET VITAL SIGN STOPPING CRITERIA	0	0	0	0
Participant Study Status				
Completed	21 (95.5)	17 (85.0)	18 (90.0)	10 (100)
Ongoing	0	0	0	0
Discontinued	1 (4.5)	3 (15.0)	2 (10.0)	0
Adverse Event	0	2 (10.0)	1 (5.0)	0
Lost to Follow-up	1 (4.5)	1 (5.0)	1 (5.0)	0



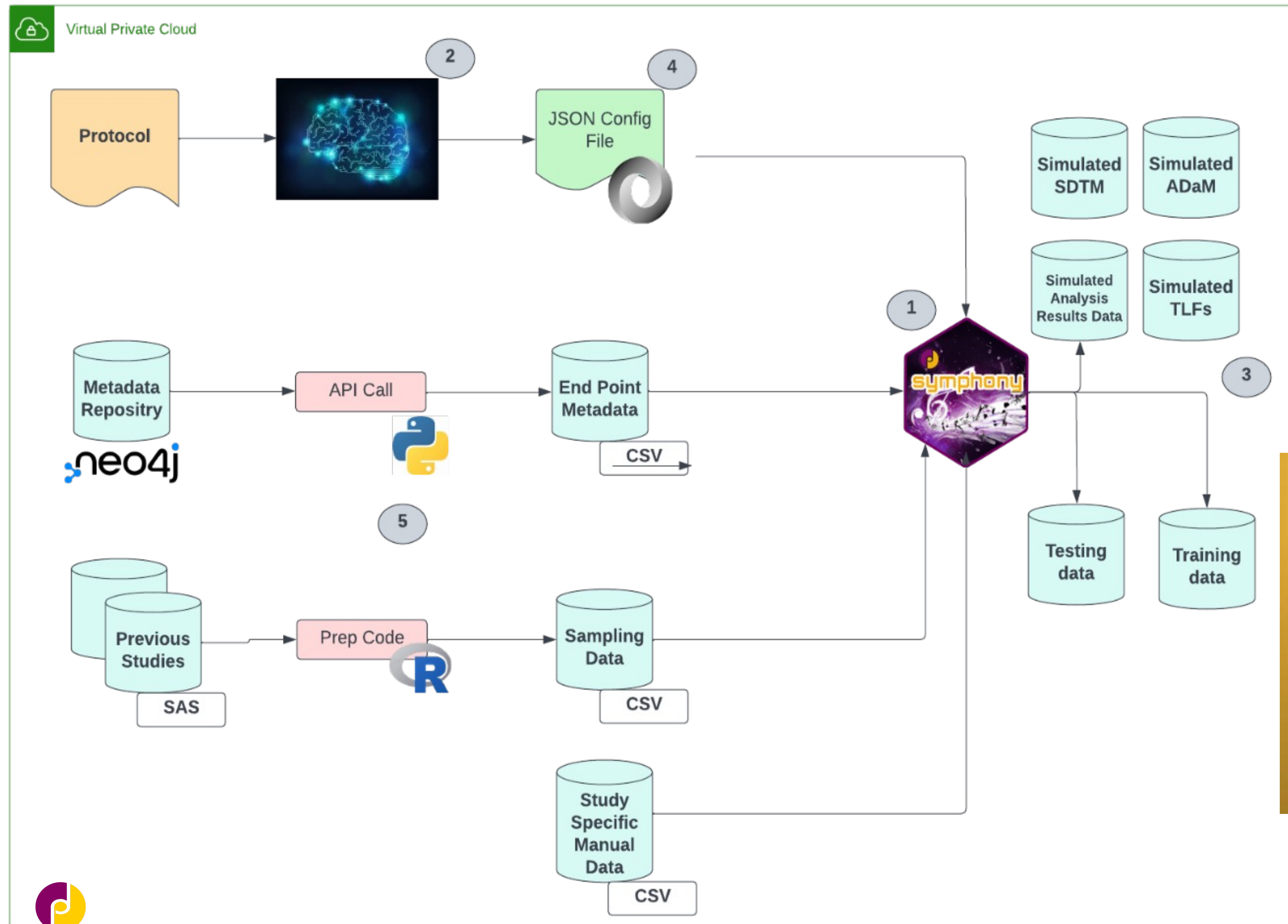
- Then seamless switch to production data





Lessons Learned

- Perceived benefits realised and opportunity to further develop the concept across other analysis component of ADaMs, Analysis Results Data, Mock TLFs and Code
- Need non-technical ability to digest a protocol to understand subject profiles
- Technical challenge was more in the multi-tool AWS environment than the simulation code itself
- End point distribution and trend information is not readily available
- Manual steps
- Still need to perform the raw to SDTM programming



Next Steps

- (1) Create an R package
- (2) Replace the human with ML
- (3) More use cases
- (4) Align with industry work (CDISC USDM)
- (5) Invest in “Knowledge Management”

WHAT'S NEXT?

Thank You – Questions?

