Ripping up the protocol

Pairing USDM and ICH M11 to inform real-time study builds

Meet the Speaker

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A Software Engineer specialising in the development and enhancement of cutting-edge clinical trial software at Lindus Health. With a passion for leveraging technology to improve patient outcomes and streamline research processes, he has contributed to the creation of robust and secure software solutions tailored for the unique demands of clinical research.

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Agenda

1. A Brief History of Clinical Trial Protocols
2. Postmodernity
3. A New Paradigm

A Brief History of Clinical Trial Protocols

From word-of-mouth to digital documents

Classical Era

The Book of Daniel

Around 600 BC, the age-old question was trialled: does a diet of only meat and wine leave you more nourished than one of vegetables and water? Nebuchadnezzar II and Daniel sought to find the answer.

- n = 4
- Ten day intervention of some amount of vegetables and water
- The rest of the Babylonian army as a control?
- Primary endpoint was how good they looked
- Daniel and friends proved to be better nourished and were allowed to continue their diet

- Not uploaded to **clinicaltrials.gov**

Early Modern Era

James Lind

In 1747, the Scottish naval surgeon James Lind was at sea with an entourage of very sick sailors.

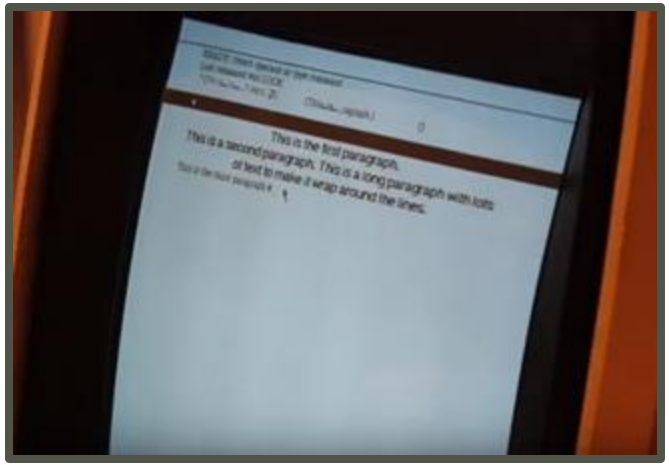
- n = 12
- Six interventions, controlling for other factors
  - Quart of cider
  - Elixir of vitriol
  - Two spoonfuls of vinegar
  - A pint of sea water
  - A spicy nutmeg paste and some barley water
  - Two oranges and a lemon
- The citrus fruits proved to be incredibly effective at treating the scurvy
- Methodology and results were detailed in his “Treatise of the Scurvy”

Modern Era

Paper to Digital

A move away from publishing trial design retrospectively with the results, to having a distinct, prospective protocol.

- **Foundation Course in Clinical Trials** by Cyril Maxwell, 1968
  - Likely first publication to have section devoted to clinical trial protocols
- **Declaration of Helsinki** revision by the 29th World Medical Assembly, 1975
  - First international guidance on necessitating a clinical trial protocol



- **Bravo, a WYSIWYG Editor** by Xerox Parc, 1972-1974
  - Harbinger of death for paper processes

Postmodernity

It’s not enough to be digital

The pains of paper protocols

- Cumbersome to manage and redistribute different versions, amendments
- No integration with clinical trial management solutions

The pains of PDF protocols

- Cumbersome to manage and redistribute different versions, amendments
- No integration with clinical trial management solutions

Solving for the user

What people like about protocol writing 🙂

- The ability to be creative in trial design
- Collaboration with multidisciplinary groups
- Discussing challenges and finding solutions

What people dislike about protocol writing 😤

- Writing a first draft, and aligning on a final draft
- Missing small details that eventually become evident and cause issues
- Hard to understand the impact of any changes
- Formatting

A truly digital protocol

- Protocols are almost entirely composed of unstructured text
- Could a protocol be considered as both **data** and **content** instead?

A protocol as data

- **USDM** allows a study to be modelled and read in a computer-friendly way
- The populated study model is the data that all artefacts are derived from downstream
- Define once, consume many
  - Generate a protocol with ICH M11
  - Statistical analysis plans
  - Informed consent forms
  - Configure your EDC, CTMS, etc.

A protocol as content

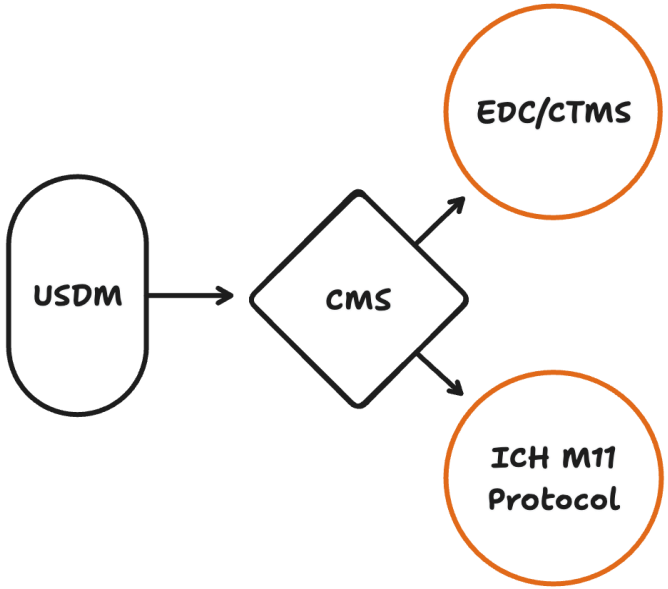
- **Content management systems** (CMS) are used to create, edit, and manage content for blogs, recipe sites, online stores, etc.
- Provides an interface to manage and represent the study model
- Users don't need to access code directly to make changes

A New Paradigm

Going with the flow

Digital Data Flow

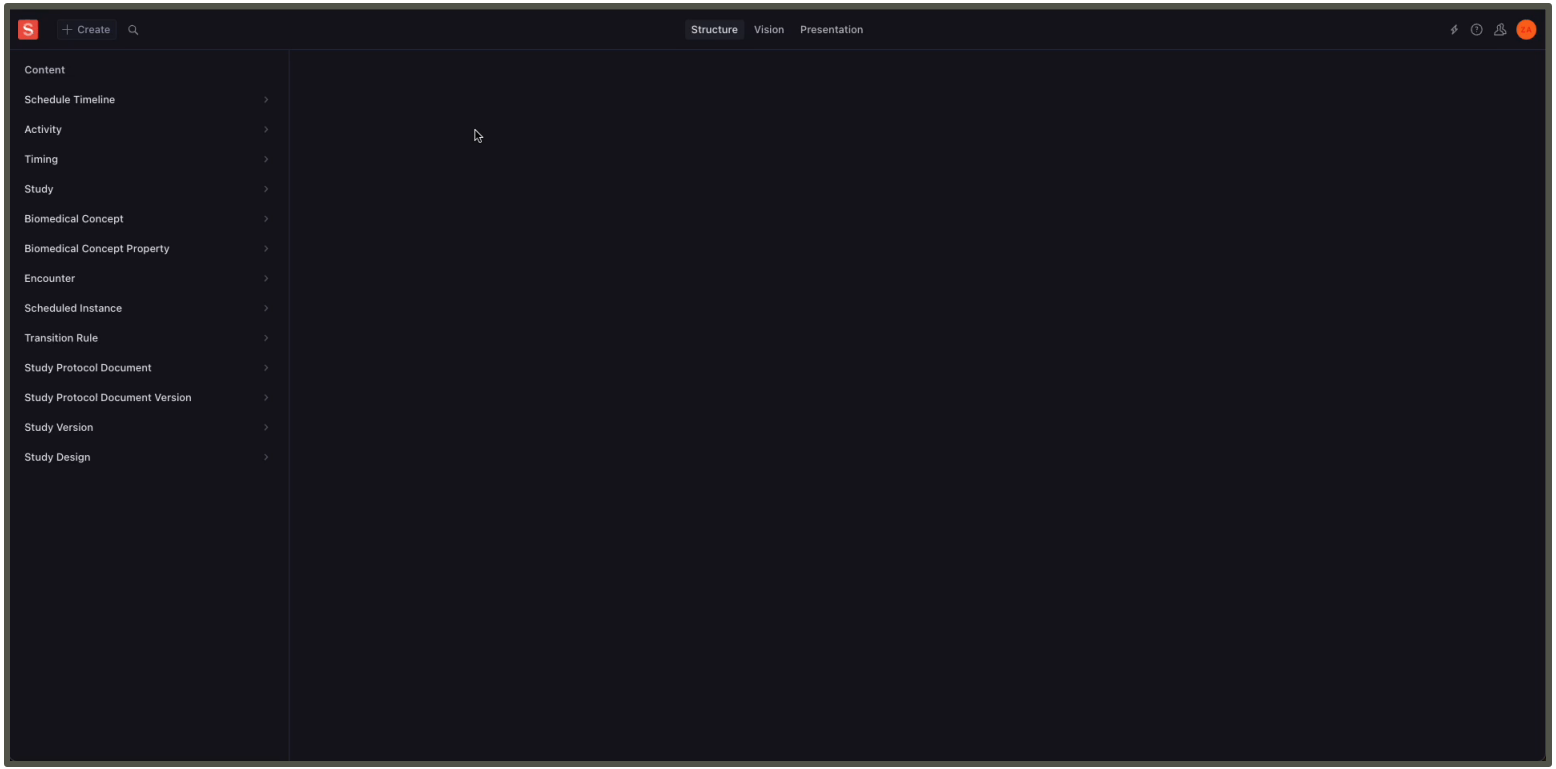
- Population of the study model using the CMS
- A representation of the protocol that updates in real-time helps visualise the study in a familiar format
- With a truly digital protocol, it can be integrated into EDCs and CTMSs to guarantee correct configuration and near-instant study launch



Modelling the Schedule of Activities

- **CMS** of choice is **Sanity.io**
- **USDM** defines multiple pieces related to an SoA
- **Encounters** and **Activities** represent what actions can be taken for a participant
  - Within **Activities**, **Procedures** and **Biomedical Concepts** detail these steps further
- **Timelines**, **Timings**, **Scheduled Instances** represent the journey of a participant

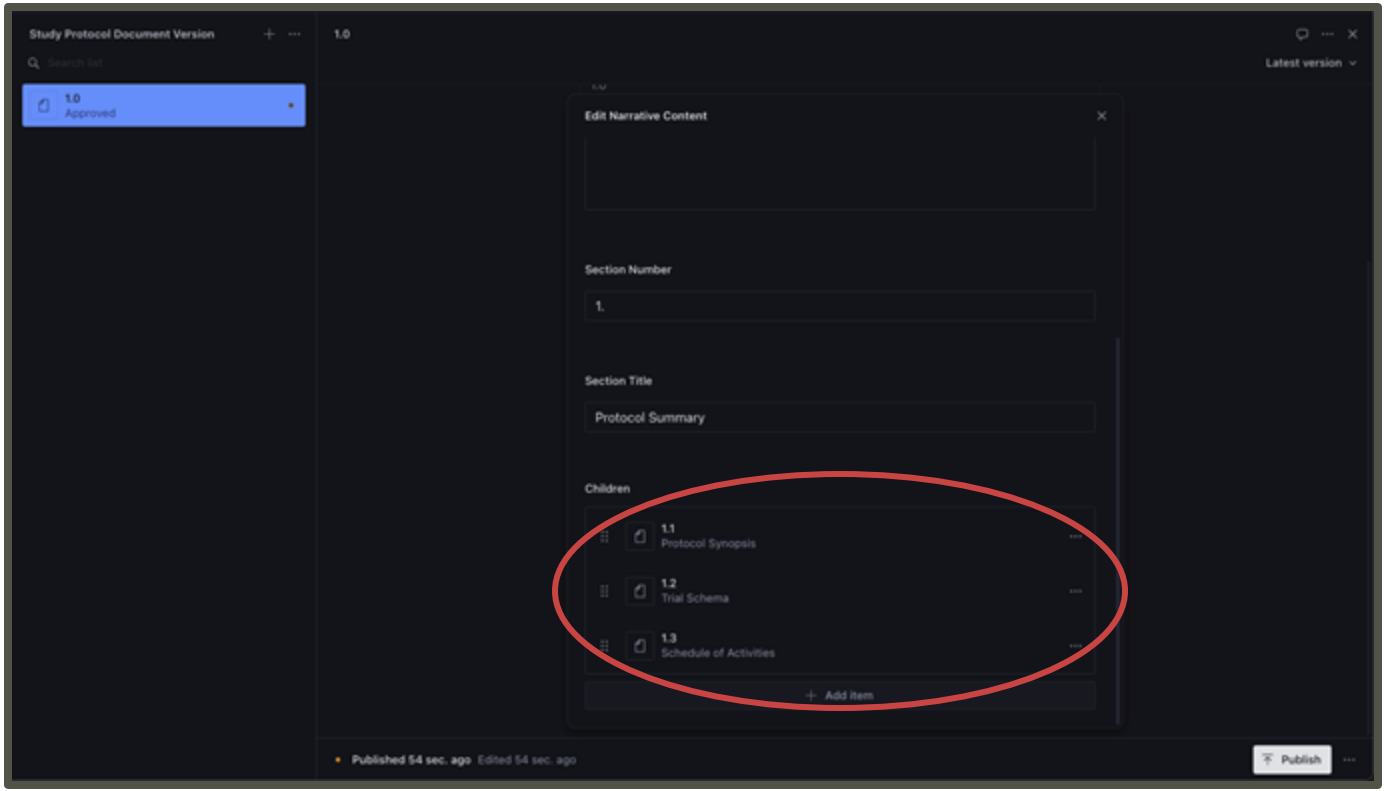
Modelling the Schedule of Activities



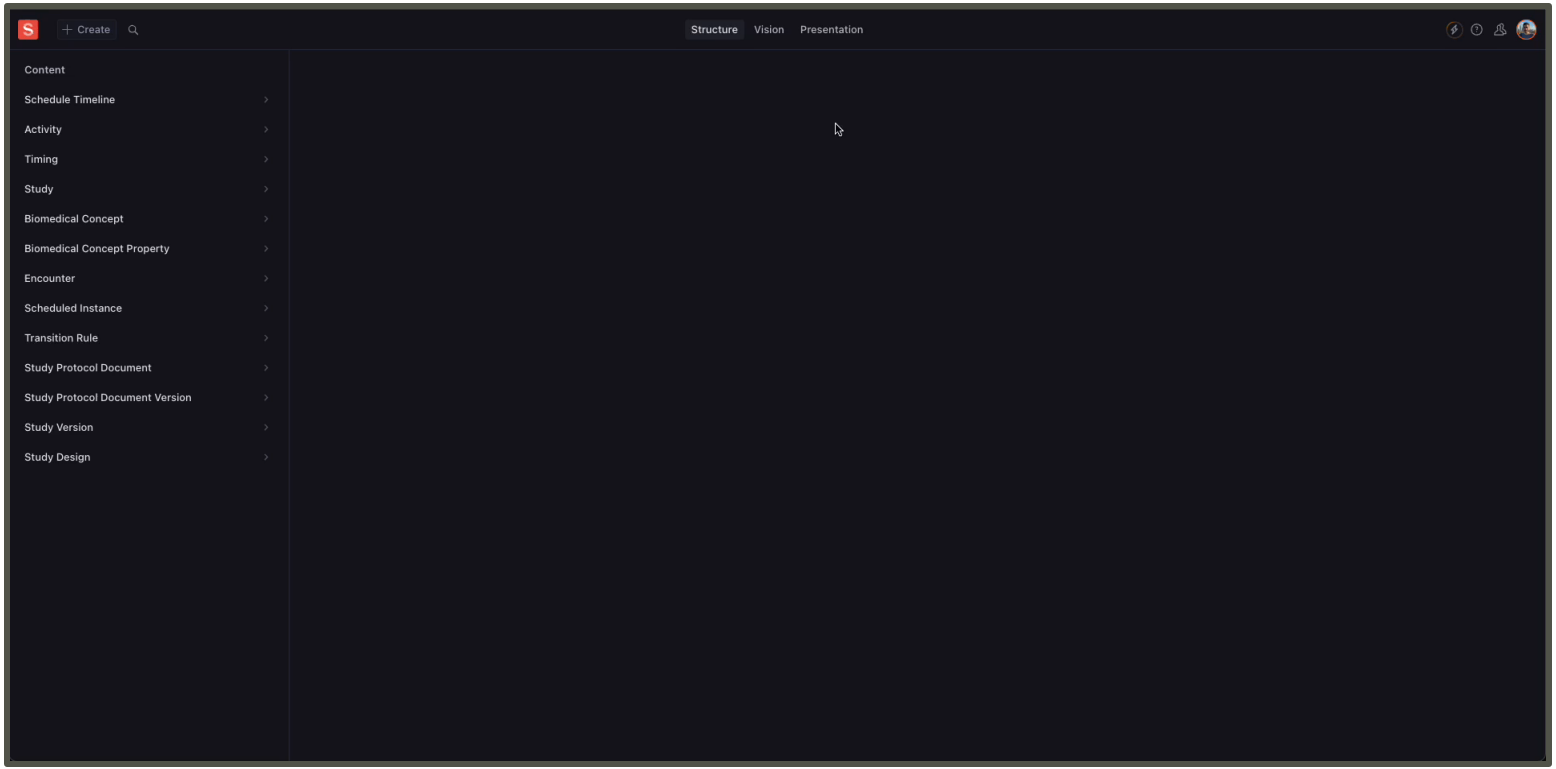
Pairing with ICH M11

- **ICH M11** specifies the headings and content of a protocol
- **1. Protocol Summary**
  - 1.1 Protocol Synopsis
  - 1.2 Trial Schema
  - 1.3 Schedule of Activities
- Some headings contain direct mappings to **USDM**
- **Narrative Content** class exists in cases where they don't

Pairing with ICH M11



Visualising the protocol



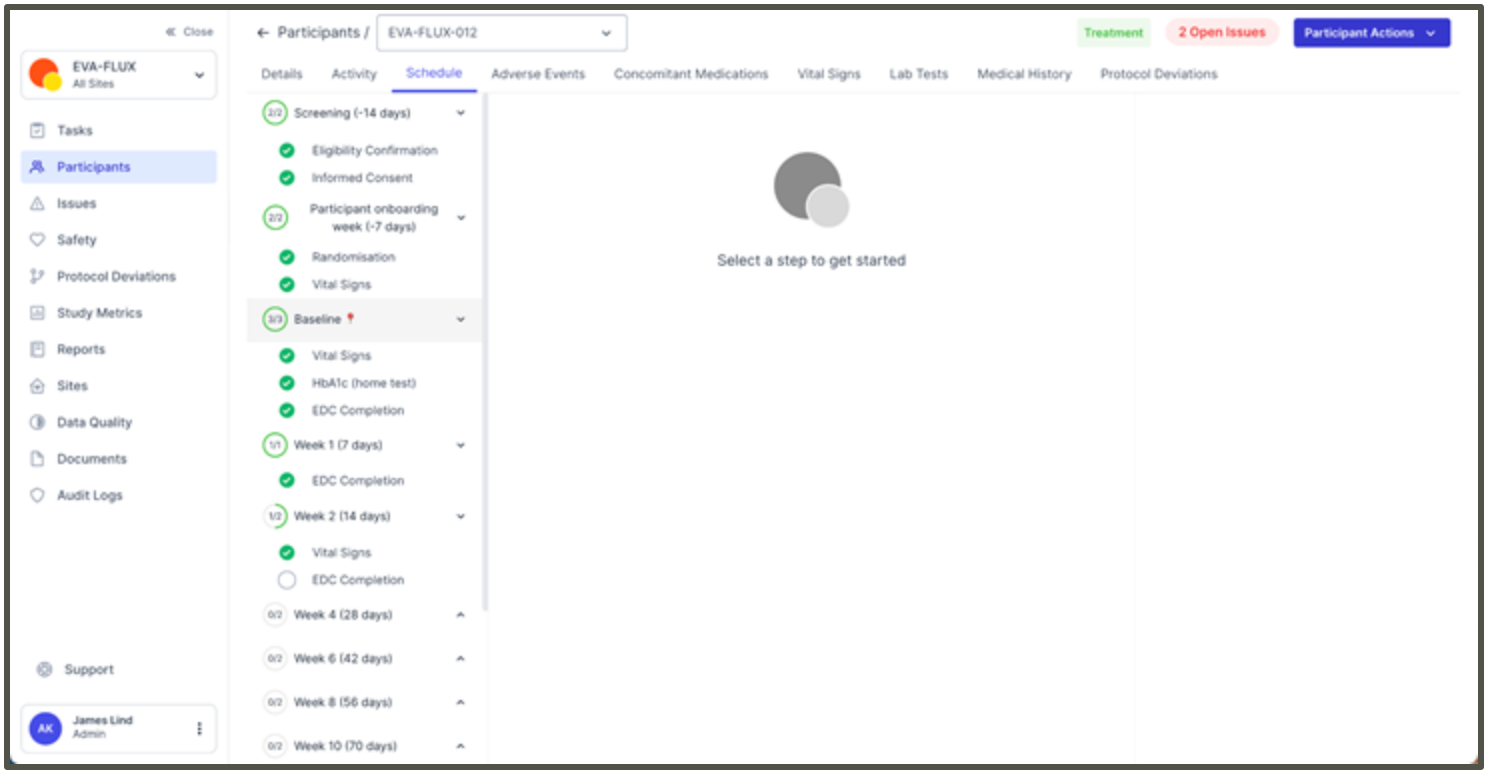
Visualising the protocol

Schedule of events	Screening	Participant onboarding week	Baseline	Week 1	Weeks 2, 4, 6, 8, 10	3 month	Weeks 14, 16, 18, 20, 22	6 month and End of RCT Study
		(Day -7 to 0)	(Week 0)			(Week 12)		(Week 24)
Control and Intervention Groups								
Informed e-consent and eligibility confirmation	X							
Randomisation		X						

1.3 Schedule of Activities

Activity	Screening -14 days	Participant onboarding week -7 days	Baseline	Week 1 7 days	Week 2 14 days	Week 4 28 days	Week 6 42 days	Week 8 56 days	Week 10 70 days	Week 12 (HbA1c) 84 days	Week 14 98 days
Eligibility Confirmation	✓										
Informed Consent	✓										

Define once, consume many



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- Formatting ✅

Turn of the tide

- A big shift in how trial design will work
- Make it easy to switch
- Eulogise the benefits
- Increase community development on USDM and ICH M11 related tools

Thank You!

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