

Implementation of a Clinical Trial Recruitment Support System Based on FHIR in a Cardiology Department

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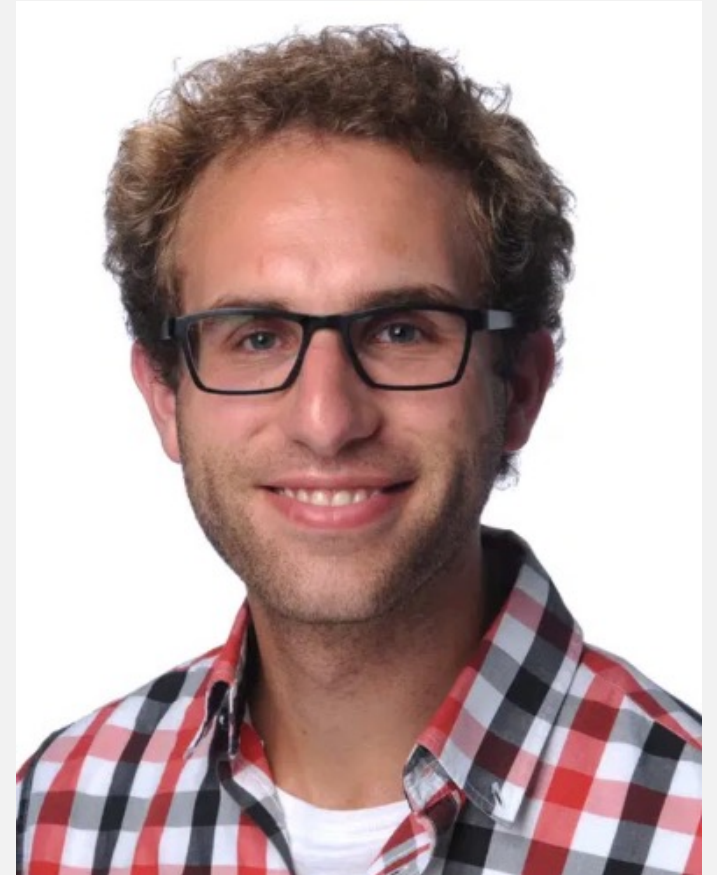
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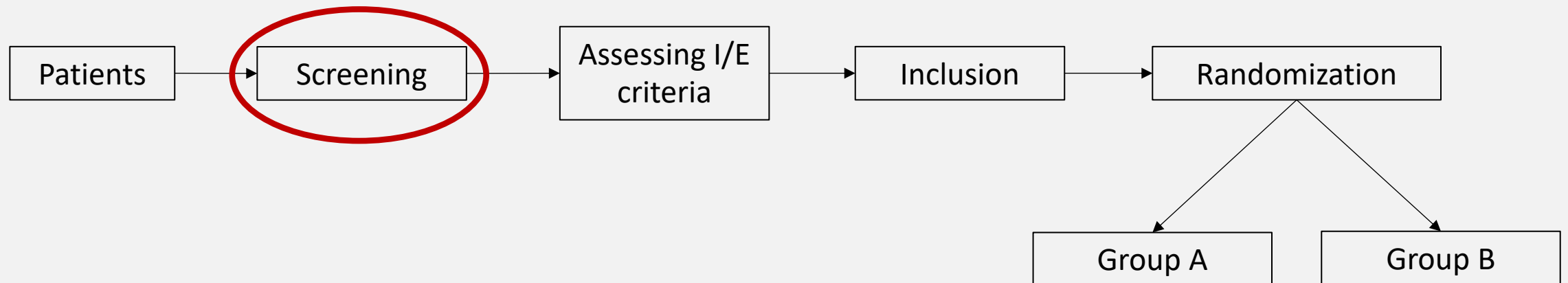
Who am I?

- Clemens Scherer, MD
- Cardiologist at University Hospital, LMU Munich, Germany
- Fellow in intensive care medicine
- Research interest: cardiogenic shock
- Spare-time software developer and FHIR enthusiast → FHIR transformation
- Study doctor in 2017



Clinical trials

- Clinical trials → mainstay of medical advancement in modern times
- Compare effects of different drugs, techniques, medical devices, ...
- “Gold standard”: randomized, controlled, double-blind trials
- Enable evidenced-based medicine



Screening for clinical trials

- Tenacious recruiting due to
 - overestimation of eligible patients
 - insufficient identification by a healthcare providers
- Clinical trial recruitment support systems (CTRSS)
 - complete and accurate mapping of the inclusion and exclusion criteria is complex
 - missing interoperability
- Possible solution: Fast Healthcare Interoperability Resources (FHIR) + terminology systems (SNOMED-CT, LOINC)
 - R4: FHIR resources for CTRSS → low maturity level

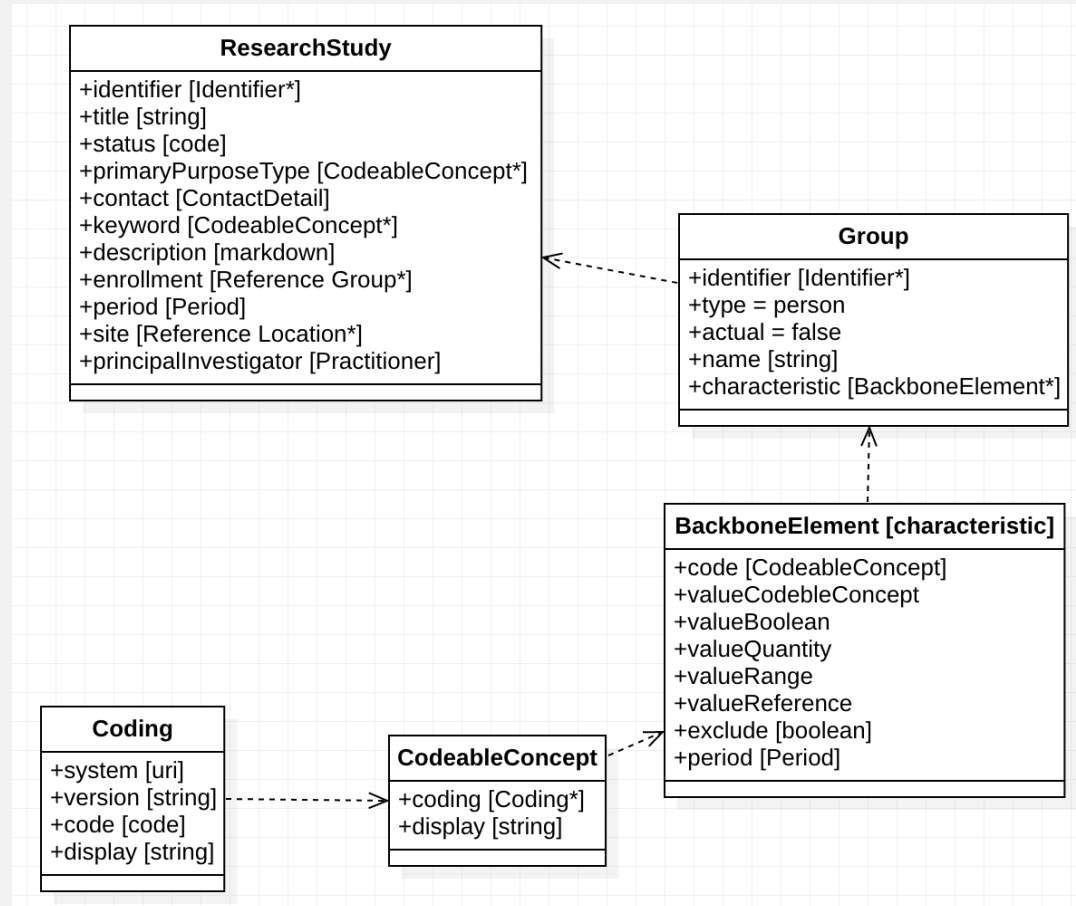
Motivation

- **Problem:** Insufficient recruitment, time-consuming screening
- Development of a clinical trial recruitment support system (CTRSS) based on FHIR R4 + SNOMED-CT, LOINC, ATC
- Evaluate its usage and features in cardiology department based on clinical trials

Data sources

Type	Source	Mapping	FHIR resource / terminology system
Anamnesis, examination	Department FHIR server	-	Observation / SNOMED-CT
Allergies	Department FHIR server	-	AllergyIntolerance / ATC
Medication on admission	Department FHIR server	-	MedicationStatement / ATC
Diagnosis / Conditions	Department FHIR server	-/+	Condition / SNOMED-CT or text
Laboratory data	Hospital LIS	+	Observation / LOINC
Echocardiography	Microsoft SQL database	+	Observation / SNOMED-CT

Eligible criteria in FHIR R4



Example for inclusion / exclusion criteria

- Age (SNOMED-CT Code: 397669002) 18-80 years
- No HIV (SNOMED-CT Code: 86406008)
- No ischemic cardiomyopathy (SNOMED-CT Code: 426856002)
- OR statement:
 - Dilated cardiomyopathy (SNOMED-CT Code: 399020009) with LVEF (LOINC Code: 18043-0) \leq 45% **OR**
 - Hypertrophic cardiomyopathy (SNOMED-CT Code: 233873004) **OR**
 - Amyloidosis (SNOMED-CT Code: 17602002)

Example for inclusion / exclusion criteria

Group 1:

```
{
  "active": "true",
  "type": "person",
  "actual": "false",
  "name": "trialEnrollmentScreening",
  "characteristic":
  [
    {
      "code": {"text": "397669002"},
      "valueRange": {
        "low": {"value": 18},
        "high": {"value": 80}
      },
      "exclude": false
    },
    {
      "code": {"text": "86406008"},
      "valueBoolean": true,
      "exclude": true
    },
    {
      "code": {"text": "426856002"},
      "valueBoolean": true,
      "exclude": true
    },
    {
      "code": {"text": "399020009"},
      "valueBoolean": true,
      "exclude": false
    },
    {
      "code": {"text": "18043-0"},
      "valueQuantity": {
        "comparator": "<=",
        "value": 45
      },
      "exclude": false
    }
  ],
}
```

Group 2:

```
{
  "active": "true",
  "type": "person",
  "actual": "false",
  "name": "trialEnrollmentScreening",
  "characteristic":
  [
    {
      "code": {"text": "397669002"},
      "valueRange": {
        "low": {"value": 18},
        "high": {"value": 80}
      },
      "exclude": false
    },
    {
      "code": {"text": "86406008"},
      "valueBoolean": true,
      "exclude": true
    },
    {
      "code": {"text": "426856002"},
      "valueBoolean": true,
      "exclude": true
    },
    {
      "code": {"text": "233873004"},
      "valueBoolean": true,
      "exclude": false
    }
  ]
}
```

Group 3:

```
{
  "active": "true",
  "type": "person",
  "actual": "false",
  "name": "trialEnrollmentScreening",
  "characteristic":
  [
    {
      "code": {"text": "397669002"},
      "valueRange": {
        "low": {"value": 18},
        "high": {"value": 80}
      },
      "exclude": false
    },
    {
      "code": {"text": "86406008"},
      "valueBoolean": true,
      "exclude": true
    },
    {
      "code": {"text": "426856002"},
      "valueBoolean": true,
      "exclude": true
    },
    {
      "code": {"text": "17602002"},
      "valueBoolean": true,
      "exclude": false
    }
  ]
}
```

User interface

Include	▼	PatientAge	▼	:	Quantity	▼	>=	▼	18	▼	▼	🗑️	
Include	▼	Hemoglobin [Mass/volu...	▼	:	Range	▼	9	▼	-	14	▼	▼	🗑️
Include	▼	Left ventricular Ejection ...	▼	:	Quantity	▼	<=	▼	45	▼	▼	🗑️	

ODER-Kriterien: 🗑️

{

Include	▼	Ferritin [Mass/volume] i...	▼	:	Quantity	▼	<	▼	100	▼	▼	🗑️
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+ füge Kriterium hinzu + füge ODER-Kriterium hinzu














Include	▼	Ferritin [Mass/volume] i...	▼	:	Range	▼	100	▼	-	299	▼	▼	🗑️
Include	▼	Iron saturation [Mass Fr...	▼	:	Quantity	▼	<	▼	20	▼	▼	🗑️	

+ füge Kriterium hinzu + füge ODER-Kriterium hinzu

} + füge ODER-Kriterium hinzu

+ füge Kriterium hinzu + füge ODER-Kriterium hinzu

User interface

<u>Vorname</u> <u>Nachname</u>	XX.XX.XXXX	19.11.2021	MIGPM1hf	19.11.2021		Kandidat für Screening 
Name 2			MIGF4	19.11.2021		Kandidat für Screening 
Name 3			MIGF4	17.11.2021		Kandidat für Screening 
<u>Vorname</u> <u>Nachname</u>						
Name 2	<div style="background-color: #e0e0e0; padding: 5px;"> PatientAge: 46 HIV: No (19.11.2021) Ischämische Kardiomyopathie: No (19.11.2021) Dilatative Kardiomyopathie: Dilatative Kardiomyopathie ED 2013, 1 Bruder bereits verstorben, progredient im Verlauf, bei hochgradig dilatiertem LV mit hochgradig reduzierter LV-Pumpfunktion (19.11.2021) Left ventricular Ejection fraction by US: 26.2 (19.11.2021) 21.154 (19.11.2021) 28.763 (19.11.2021) 29 (19.11.2021) </div>					
Name 3						
<u>Vorname</u> <u>Nachname</u>	XX.XX.XXXX	19.11.2021	MIGPM1hf	19.11.2021		Kandidat für Screening  Kandidat für Screening Screening läuft E/A-Kriterien passend E/A-Kriterien nicht passend in Studie lehnt Studie ab
Name 2			MIGF4	19.11.2021		
Name 3			MIGF4	17.11.2021		

Evaluation

- CTRSS was used as an additional screening tool beginning from April 1st 2021 for four clinical trials (end of analysis: 23rd November 2021)
 - Problem: COVID19 pandemic

Trial name	Inclusion criteria	Exclusion criteria	Identified correctly
CLOSURE-AF	Age ≥18 years Atrial fibrillation	GFR < 15 mL/min Heart transplantation	4 / 5
FAIR-HF2	Age ≥18 years Hemoglobin 9-14 g/dL LVEF ≤ 45%		4 / 4
SPIRIT-HF	Age > 50 years LVEF ≥ 40% proBNP ≥ 200 pg/mL (E/E' medial ≥13 or E/E' lateral ≥13)	Aldosterone receptor antagonist GFR < 30 mL/min Hemoglobin < 10 g/dL No HCM, no Amyloidosis No aortic stenosis	2 / 2
TORCH-PLUS	Age 18-80 years (DCM with LVEF ≤ 45% OR HCM OR Amyloidosis OR LVNC OR ARVC OR Sarkoidosis OR Myocarditis)	HIV Ischemic cardiomyopathy	42 / 44
			52 / 55

Conclusion

- Interoperability regarding trial eligibility criteria can be achieved by using FHIR R4 resources, even for complex criteria
- Implementation was able to detect suitable patients based on eligibility criteria in an efficient way
- Experiences from the project were incorporated in the working group “Clinical research projects” of German Medical Informatics Initiative
- Eligibility criteria were altered for improved screening performance
- Handling „possible candidates“ with missing values?
- Newest FHIR snapshot: Tree-like structure of inclusion and exclusion criteria possible via *EvidenceVariable*

Contact

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