The Use of Big Medicare Data and LHC Data Capture Forms in FHIR

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Big Data from Medicare's VRDC

aka CMS Enclave

A brilliant approach to big data access with no privacy tears

The Core Honeypot

- Medicare Part A and Part B (includes coded in office medications) from 1991
  - Includes encounter events, Diagnoses, surgical procedures (lots of outcomes)
- Medicare Part D- all out patient prescription from Oct 2006
- Around 100 M enrollees all together
- If you focus only on PART A/B/D excluding capitated patients, its about 24 million
- Vital status (they link to SS death tapes)
- A per patient database of 50 algorithms defined nearly chronic disease per 50
- Lots of other info can also be obtained on smaller populations (e.g. Medicaid

Process For Getting Data

- Make application with study rational and what databases you want
- ResDac (U. of Minneapolis) will help you
  - https://www.resdac.org/cms-data/request/cms-virtual-research-data-center
- Pay fee around $25 K per year for one seat – cost depends on # of seats)
- Wait for approval or request for revisions (can take 2+ months)
- They set up your computer with special software help you figure out databases you really need

Tools Available for Analysis

- SAS with an SQL data base
- STATA
- Can upload and link (with consents for uploaded patients)
- Can download but only statistical summary
- Machine time is free
- More info:
  - http://resdac.umn.edu/sites/resdac.umn.edu/files/Introduction%20to%20the%20Virtual%20Research%20Data%20Center%20(VRDC)%20-

Cox Regression: A Most Powerful Tool for Temporal Data

- Typically predicts time to an outcome, e.g. death
- Can take binary, categorical, or continuous covariates
- Accommodates censuring, lost to follow up, etc.
- Can (Usually should) use time varying coefficients
  - Such variables reflect changes in test values or drug use over time
  - Just don't use variables that peak into the future (Like "any" occurrence)
- Lots of variants on the COX method exist

Cox is Ingenious

- It pivots on the outcome event (e.g. death) for each patient
- It develops a statistic for that patient, based on the state of all of the remaining study individuals. So when a patient dies, it looks at the value of all of the other remaining patients AT THAT POINT IN TIME. Generates a statistic for the index patient based on that data
- Then repeats the process for all other events
- Finally averages over all of those calculations to figure the hazard due to each covariate

What We Are Looking At NLM

- Unexpected harms (Non-harm) or benefits from treatments (especially drugs)
- Looked at the risk of Alzheimer's from androgen suppression therapy
  - Paper last year said it was 2-fold. We found almost zero risk[1].
- Looking at risk of PPIs for death (reported to increase death risk by 15-30%)
  - 15 to 20% of the adult population is taking PPIs –so that be huge bump in death rate.
- Did 12 different analyses using 38 chronic diseases, demographics, Medicare status, rural status, and use of PPIs and of H2 blockers as covariates. See only positive effects of PPIs. (Hope to results publish soon)
- Other studies of metformin (the so called fountain of youth drug), and of statins and BP meds on Alzheimer's and death and Opioid abuse
- Working with other big medical databases as well, e.g MIMIC II

1. Baik, S, PhD, Kury F, MD McDonald C, MD. DOI: 10.1200/JCO.2017.72.6109 *Journal of Clinical Oncology* 35, no. 30 (October 2017) 3401-3409.

LHC-Forms

LHC-Forms- how does it work and what can it do?

- A fast, web open source JavaScript widget program (300kB) generates live forms from JSON form descriptions on the fly
- Based on Meaningful Use standards
- Accommodates nested groups and repeating groups of questions
- Has all of the usual form functions: Skip logic, rich validation checks, auto complete menus, score calculation, etc.
- Many different layout styles and a responsive design that fits any screen size

LHC forms are standards based

- All 2000+ LOINC panels including hundreds of validated surveys. Are LHC forms
- UCUM for units of measure
- Tied to many external, MU standards, and genetic standard coding systems, including NPI (National Provider Identifier)

Background on Standards Medical forms

- FHIR forms
  - FHIR Questionnaire- defines a simple questionnaire without special features such as skip logic
  - FHIR SDC Questionnaire – an extension on Questionnaire, with lots of additional features like skip logic – more sophisticatederror checking, etc.
- IHE
  - Has an SDC form- but it is different from, https://ihe.net/uploadedFiles/Documents/QRPH/IHE_QRPH_Suppl_SDC.pdf
- LHC forms has a native form definition based on LOINC panels, which we can transform into either of the FHIR questionnaires and possibly into IHE questionnaire

Overall Technology

- Mixture of Web widgets and applications, namely : LHC-Forms Widget, Clinical Table Search Service, Form Builder, UCUM validator
- All software- applications and widgets are written in JavaScript
- Development uses Google AngularJS
- All data (including form definition and content of populated form) is represented as JSON
- Most content stored in ElasticSearch (with Lucene) https://www.elastic.co/
- Size of LHC forms renderer that loads into browser –about 240K to compress

LHC forms and FHIR

LHC-Forms and FHIR SDC Questionnaire

- Most common features are compatible.
  - Form structure, code, name, data types, etc.
  - Most FHIR Questionnaire resources could be loaded into LHC-Forms widget and displayed as actionable forms
  - LHC-Forms form definition data can be exported as FHIR Questionnaire
  - Form data can be exported as FHIR Questionnaire Response or Diagnostic Report
- LHC-Forms has additional features
  - Skip logic, Display control and etc. support more functions

LHC forms via SMART on FHIR

SMART® App Gallery

Add New Listing Your Listings Search Login

LHC-Forms on FHIR

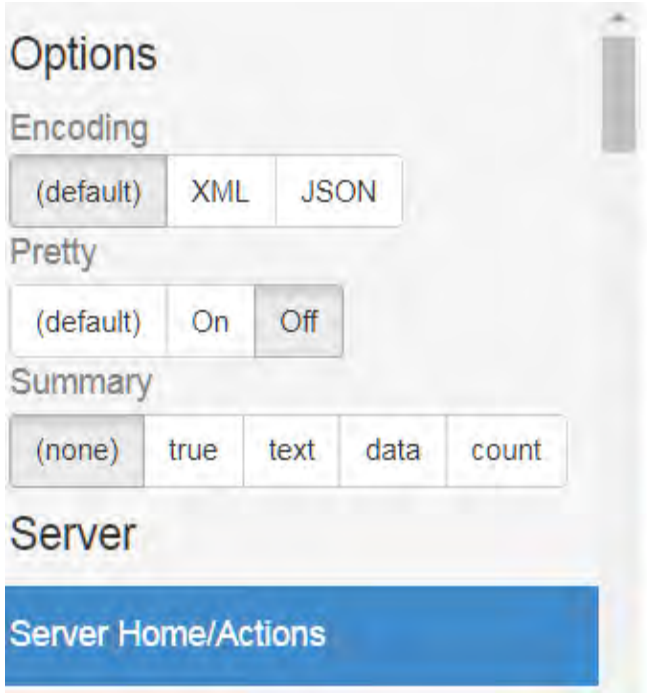
Lister Hill National Center for Biomedical Communications (LHNCBC)

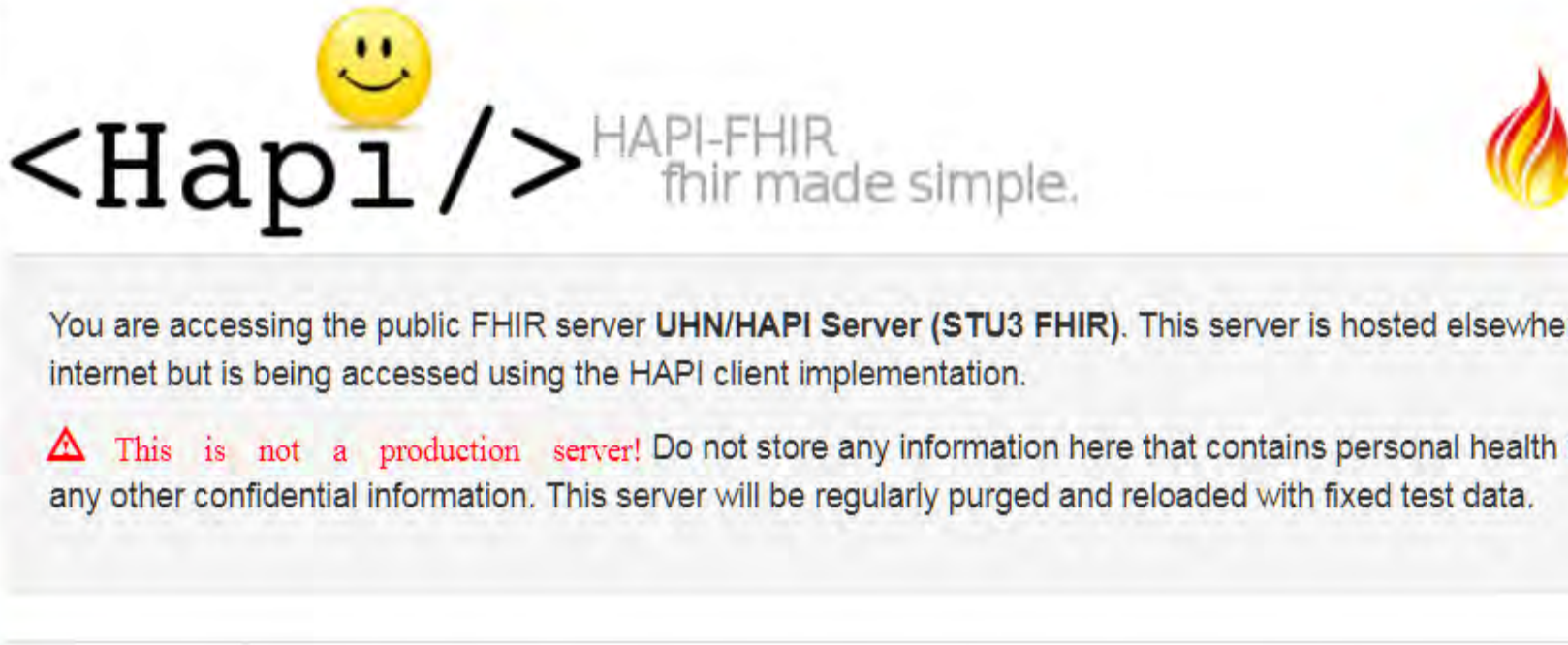
Website Try App Contact

LHC-Forms (a.k.a. "LForms") is a widget that generates input forms, based on definition files, for Web-based applications or to integrate into electronic health records (EHRs), personal health records (PHRs), and mobile health apps. The input forms support repeating sections and questions, hiding and showing questions via skip logic based on the user's answers to other questions, coded answer lists, scored answers, and more.

LHC forms direct to FHIR

- Integrates with plain 'ole FHIR servers- HAPI works well for us
  - https://fhirtest.uhn.ca/

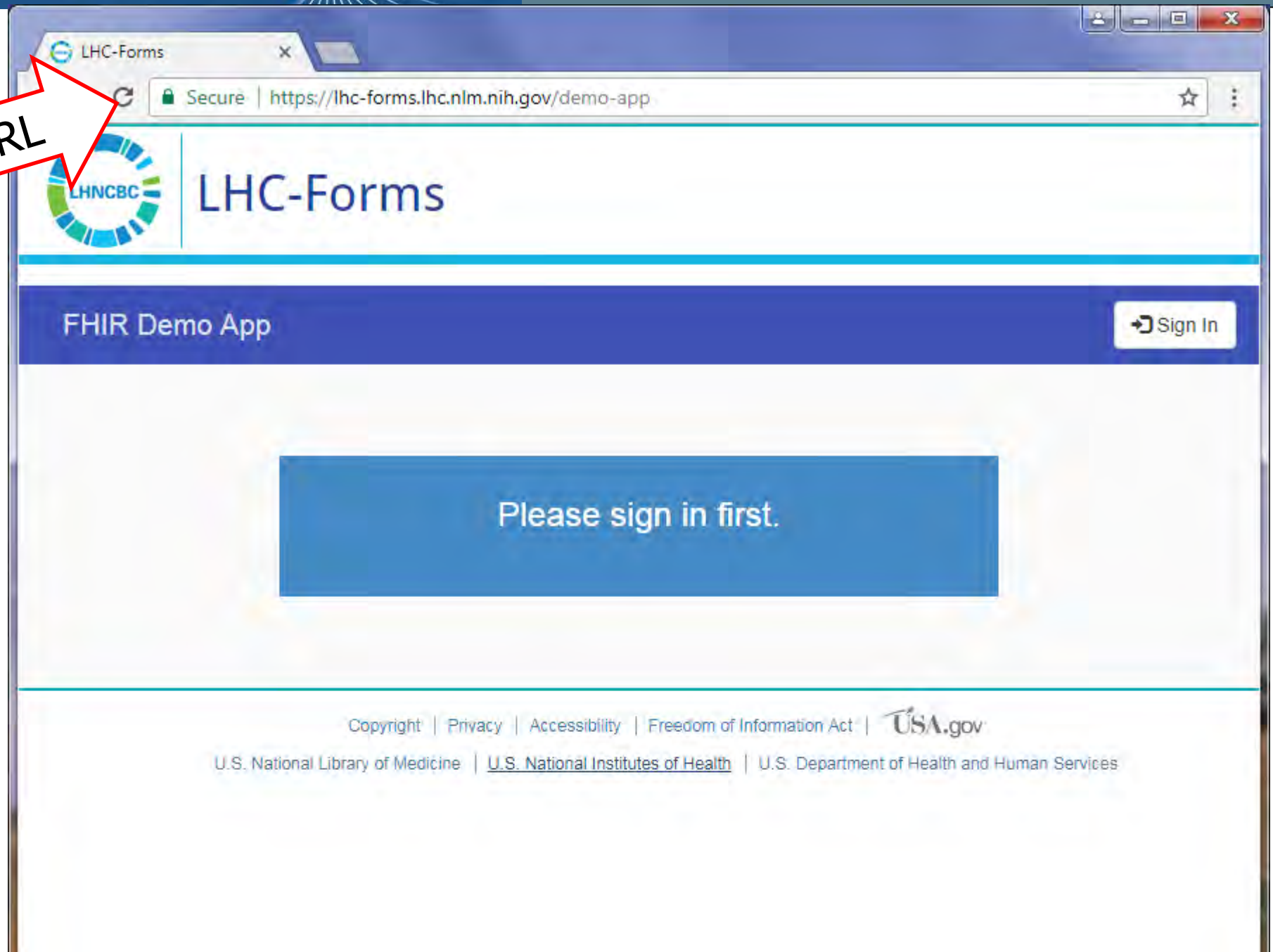




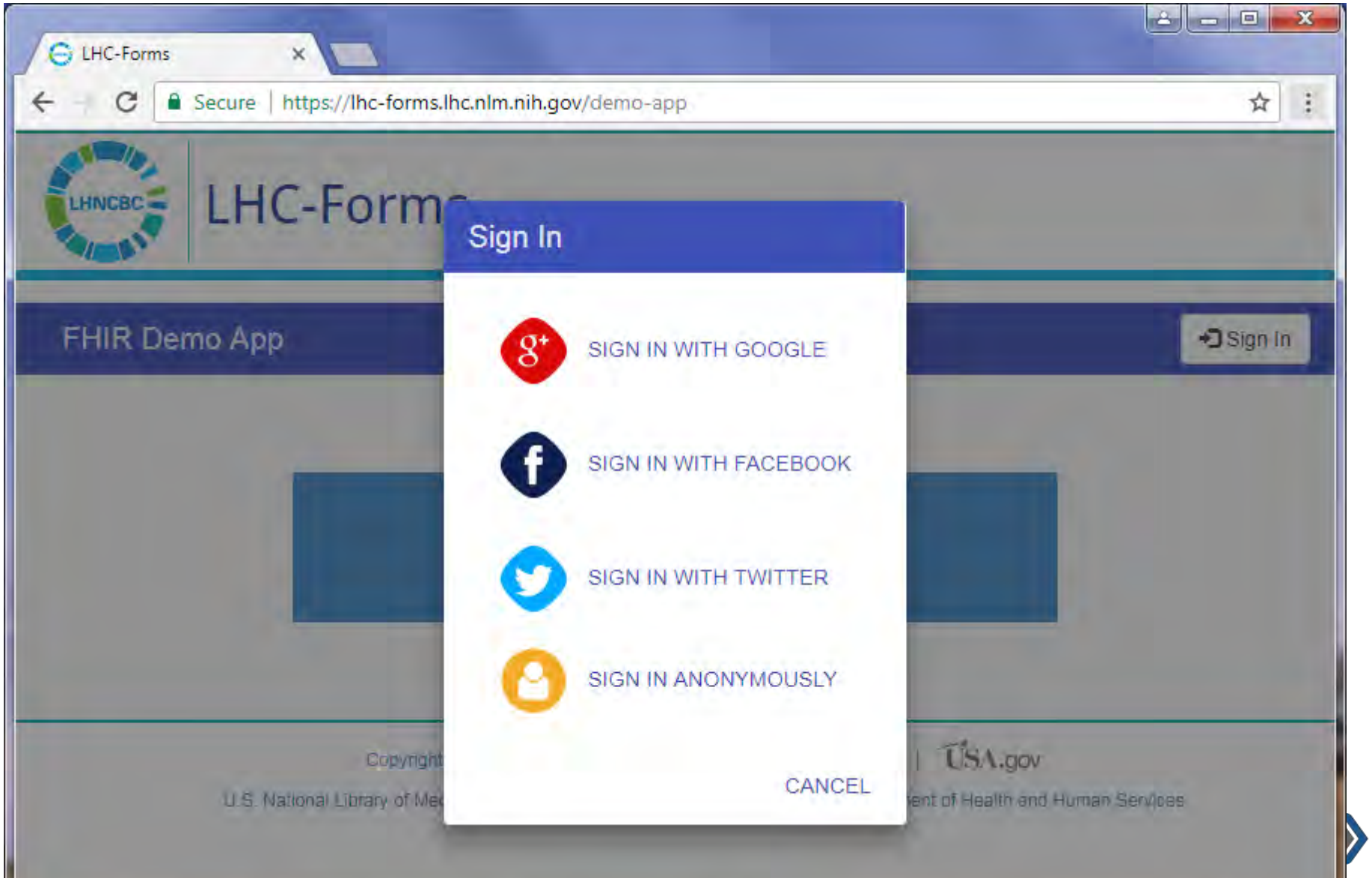
Walk through of direct to FHIR option

What we will show is an application that controls the use of different LHC Forms tied to an example FHIR server with most of the Tables/Objects (called resources in FHIR), such as patients, orders, etc. that you would find in an EMR. Gives us an Ecosystem in which to use FHIR. Can LHC forms equally well with SMART on FHIR

Note the URL

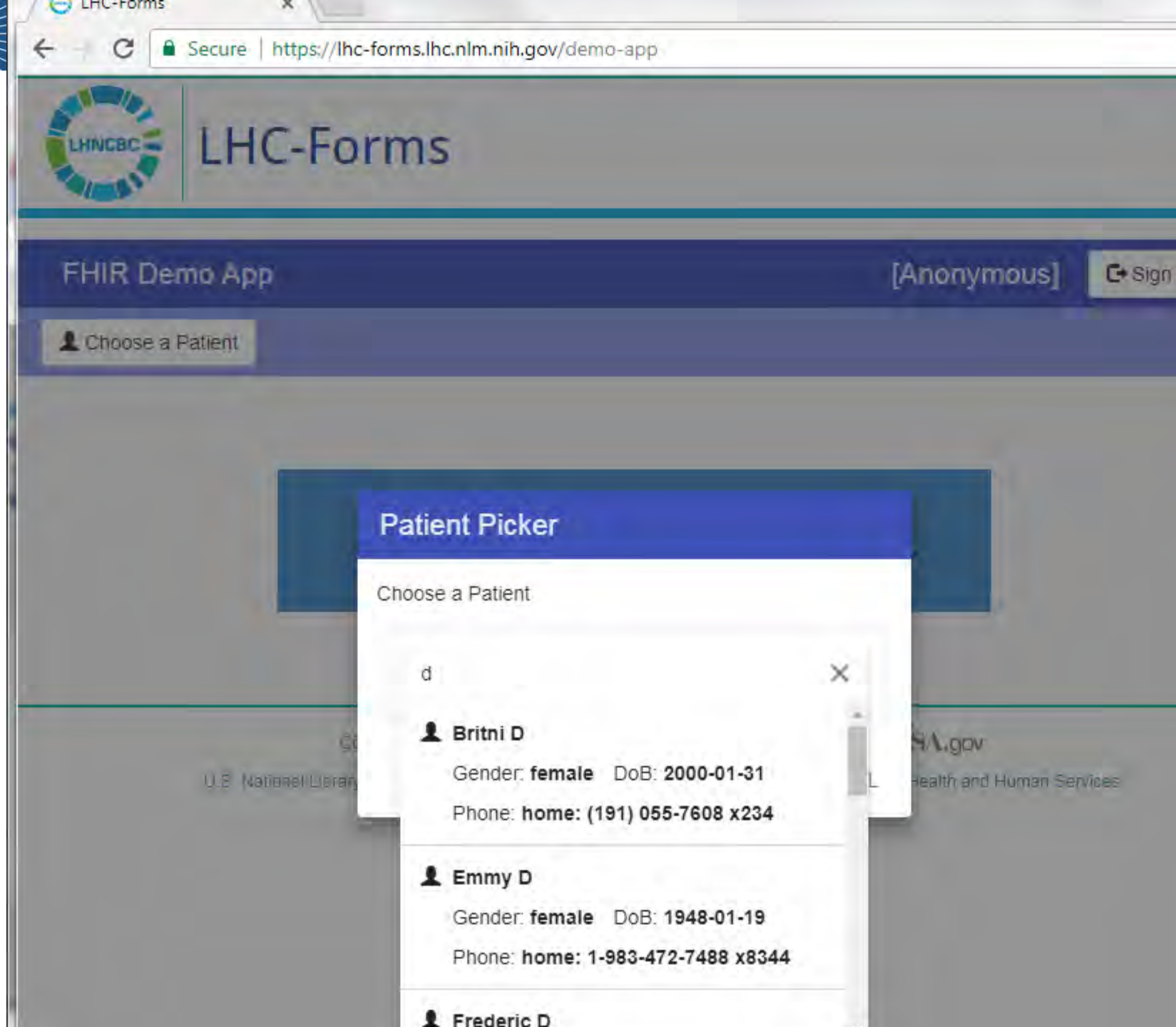

LHC-Forms
Secure | https://lhc-forms.lhc.nlm.nih.gov/demo-app
LHNCBC
LHC-Forms
FHIR Demo App
Sign In
Please sign in first.
Copyright | Privacy | Accessibility | Freedom of Information Act | USA.gov
U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health and Human Services

Sign in if you want to save what you do. All standards sign ins work



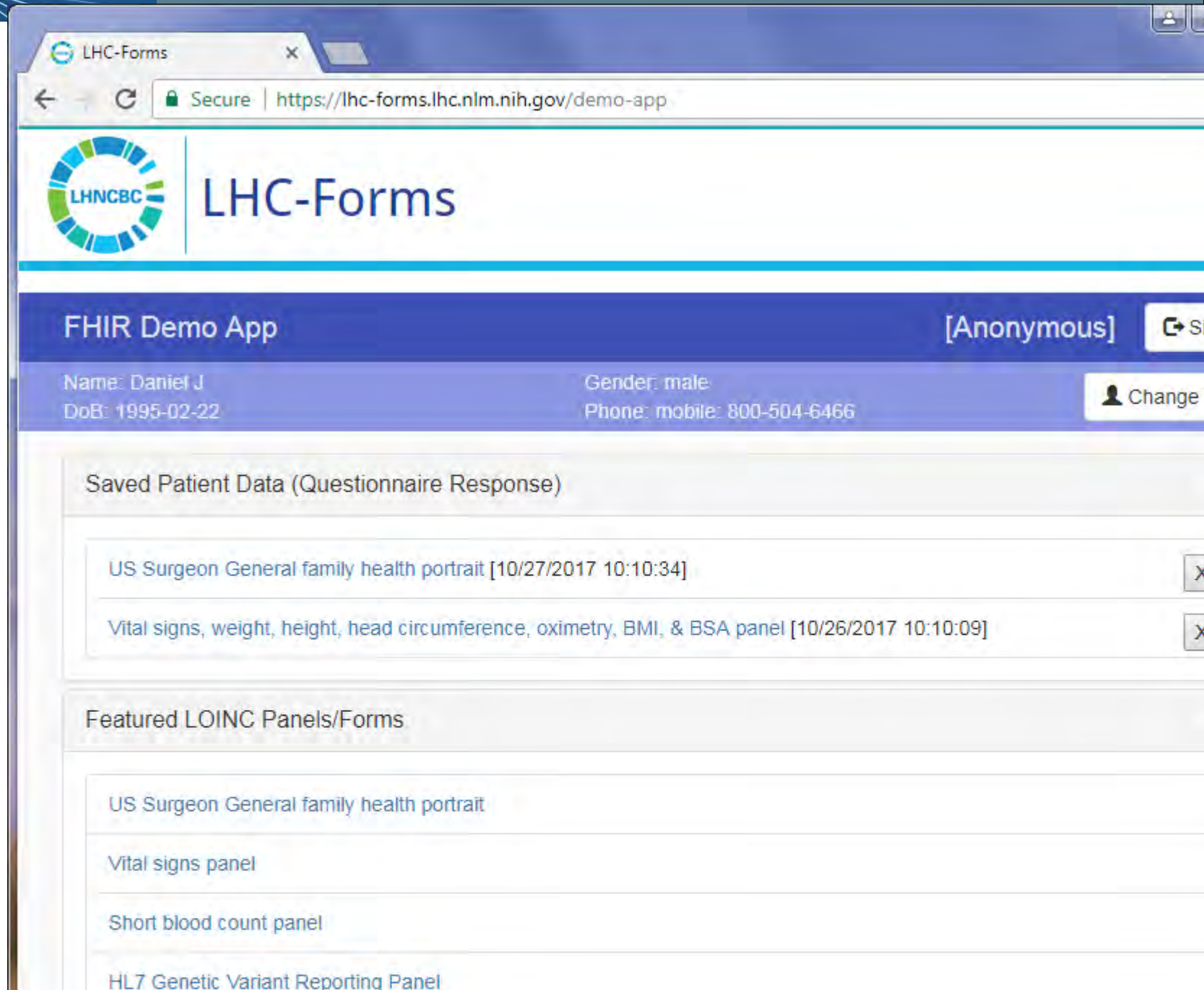
Pick a patient

- Autocomplete choice from the Hapi FHIR server

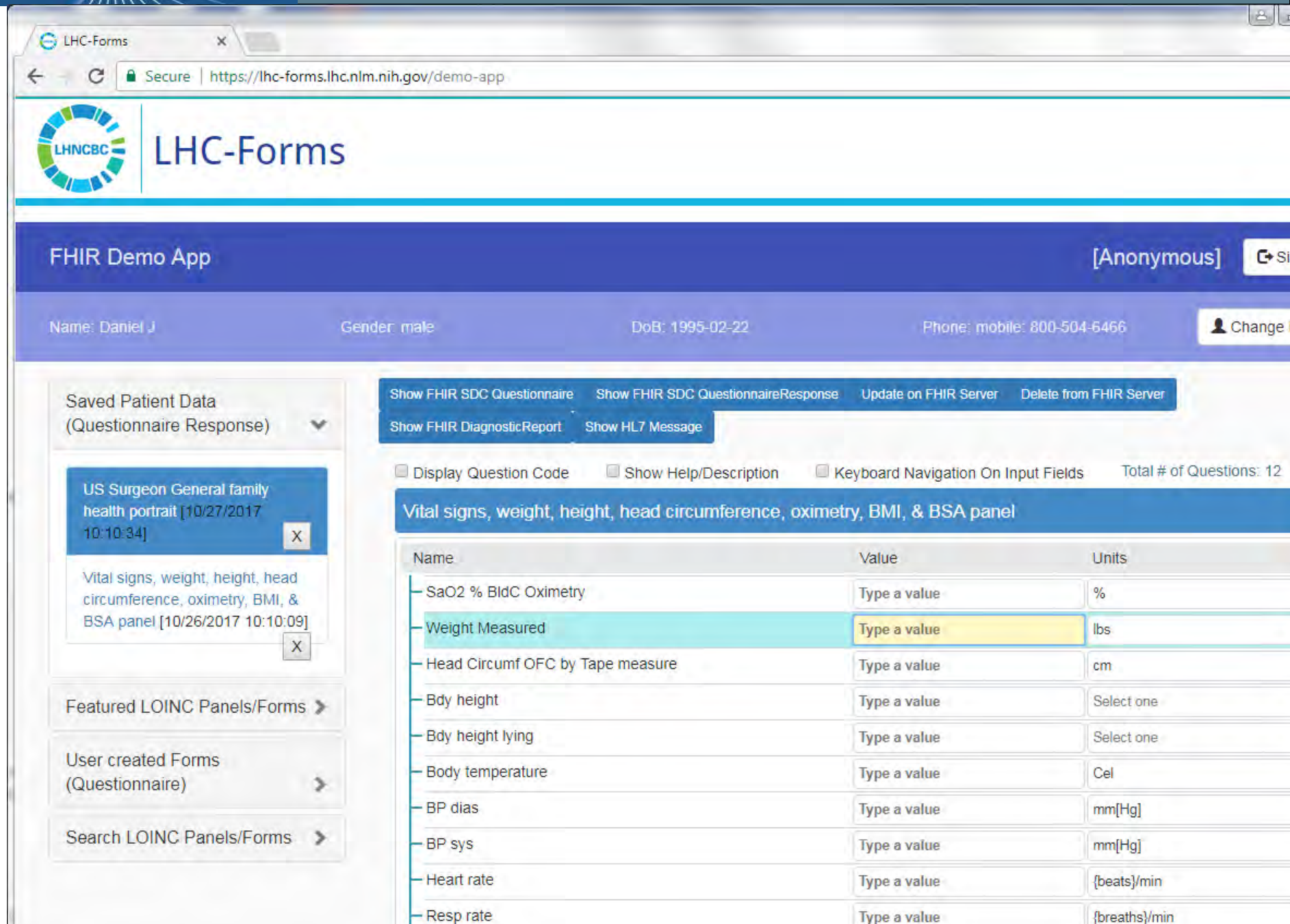


Pick A form

- Can pull a previously saved form for review and/or editing
- Can pull a new form

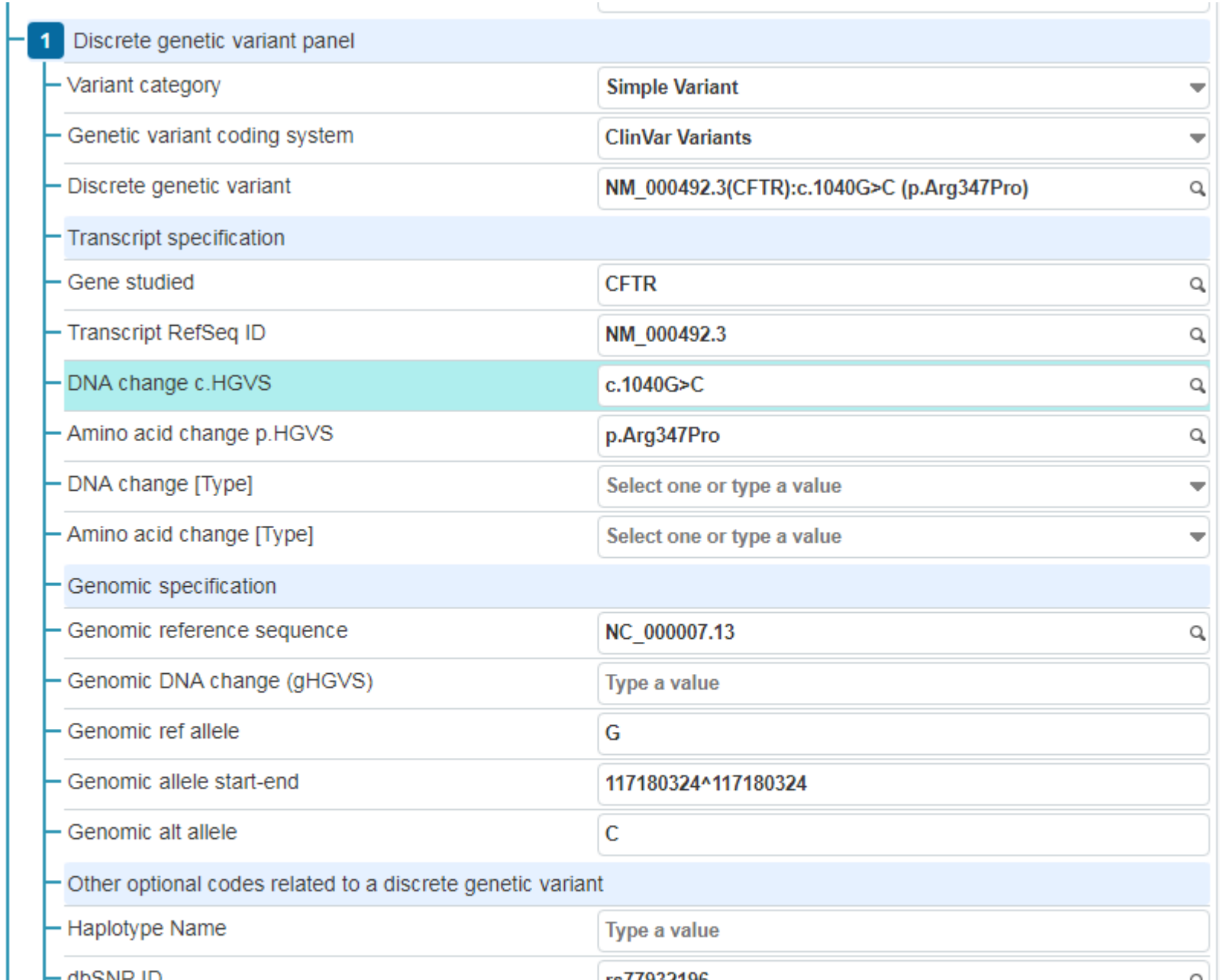


- Here we show a new form for vital signs with no data yet entered



One LOINC pane (v2 genetics)

- Here we show data entered into the genetics report form
- The output examples below based on this content



Load existing form from local file

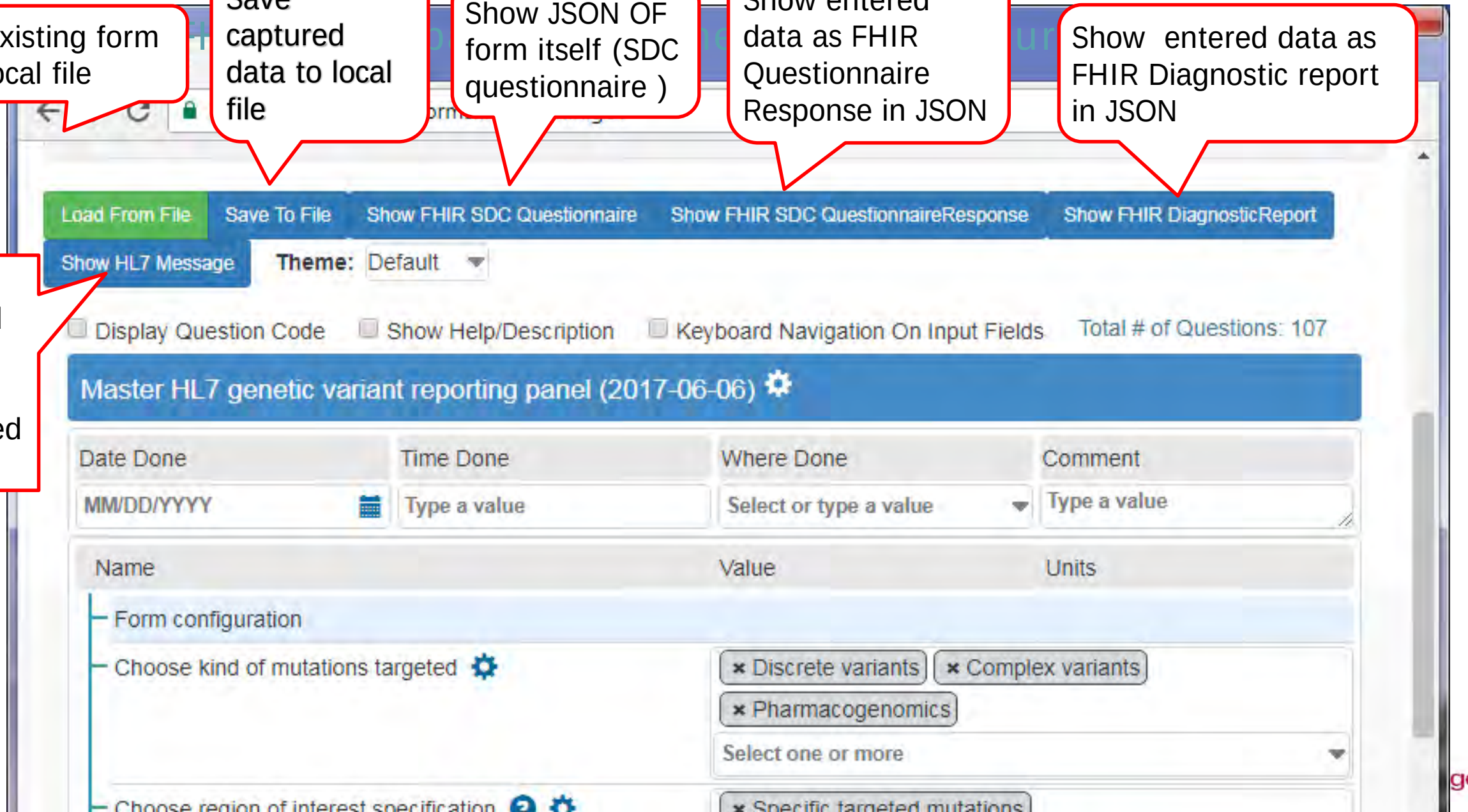
Save captured data to local file

Show JSON OF form itself (SDC questionnaire)

Show entered data as FHIR Questionnaire Response in JSON

Show entered data as FHIR Diagnostic report in JSON

Show entered data as HL7 V2 delimited file



gov

Click HL7 and you get this almost most of the message

Click Questionnaire response and get this-JSON- It extends for a long way below

HL7 OBR & OBX Segments

Please note that this is still a work in progress, and the code system values might be incorrect in some places.

```
OBR|1|81247-9^Master HL7 genetic variant reporting panel (2017-06-06)^LN|
OBX|1|CNE|XXXXX-12^Choose kind of mutations targeted^LN|a|C01^Discrete variants^LN|
OBX|1|CNE|XXXXX-12^Choose kind of mutations targeted^LN|b|C02^Complex variants^LN|
OBX|1|CNE|XXXXX-12^Choose kind of mutations targeted^LN|c|C04^Pharmacogenomics^LN|
OBX|2|CNE|XXXXX-10^Choose region of interest specification^LN|a|C01^Specific targeted mutat
OBX|2|CNE|XXXXX-10^Choose region of interest specification^LN|b|C02^Range targeted in the r
OBX|3|CNE|83005-9^Variant category^LN|2a|LA26801-3^Simple Variant^LN|
OBX|4|CWE|82122-3^Genetic variant coding system^LN|2a|CLINVAR-V^ClinVar Variants^LN|
OBX|5|CWE|81252-9^Discrete genetic variant^LN|2a|7110^NM_000492.3(CFTR):c.1040G>C (p.Arg347
OBX|6|CWE|48018-6^Gene studied^LN|2a|1884^CFTR^HGNC-Symb|
OBX|7|CWE|51958-7^Transcript RefSeq ID^LN|2a|NM_000492.3^NM_000492.3^RefSeq-T|
OBX|8|CWE|41103-3^DNA change c.HGVS^LN|2a|c.1040G>C^c.1040G>C^HGVS.c|
OBX|9|CWE|48005-3^Amino acid change p.HGVS^LN|2a|p.Arg347Pro^p.Arg347Pro^HGVS.p|
OBX|10|CWE|48013-7^Genomic reference sequence^LN|2a|NC_000007.13^NC_000007.13^RefSeq-G|
OBX|11|ST|69547-8^Genomic ref allele^LN|2a|G|
OBX|12|NR|81254-5^Genomic allele start-end^LN|2a|117180324^117180324|
OBX|13|ST|69551-0^Genomic alt allele^LN|2a|C|
OBX|14|CNE|81255-2^dbSNP ID^LN|2a|7110^rs77932196^dbSNP|
OBX|15|CWE|48001-2^Cytogenetic (chromosome) location^LN|2a|^^^^^^^^7q31.2|
OBX|16|CWE|81259-4^Probable associated phenotype^LN|2a|CN169374^not specified^Medgen-Dis|
OBX|17|CNE|83005-9^Variant category^LN|3a.1a|LA26801-3^Simple Variant^LN|
OBX|18|CWE|82122-3^Genetic variant coding system^LN|3a.1a|CLINVAR-V^ClinVar Variants^LN|
```

FHIR SDC QuestionnaireResponse Content


```
    },
    {
      "linkId": "/81250-3/48018-6/1/1",
      "text": "Gene studied",
      "answer": [
        {
          "valueCoding": {
            "system": "http://loinc.org",
            "code": "1884",
            "display": "CFTR"
          }
        }
      ]
    },
    {
      "linkId": "/81250-3/51958-7/1/1",
      "text": "Transcript RefSeq ID",
      "answer": [
        {
          "valueCoding": {
            "system": "http://loinc.org",
            "code": "NM_000492.3",
            "display": "NM_000492.3"
          }
        }
      ]
    },
    {
      "linkId": "/81250-3/41103-3/1/1",
      "text": "DNA change c.HGVS",
      "answer": [
        {
          "valueCoding": {
            "system": "http://loinc.org",
            "code": "c.1040G>C",
```

Click FHIR Diagnostic Report and get this (only shows partial message)


```
{
 "resourceType": "DiagnosticReport",
 "id": "81247-9-juyptuxgwf",
 "status": "final",
 "code": {
  "coding": [
...
    "id": "XXXXX-10-ld6fmc8hwy9",
    "status": "final",
    "code": {
     "coding": [
      {
       "system": "http://loinc.org",
       "code": "XXXXX-10"
      }
     ],
     "text": "Choose region of interest
specification"
    },
    "valueCodeableConcept": {
     "coding": [
      {
       "system": "http://loinc.org",
       "code": "C01",
       "display": "Specific targeted
mutations"
      },
      {
       "system": "http://loinc.org",
       "code": "C02",
       "display": "Range targeted in the
reference sequence"
      }
     ]
    }
  },
  {
   "resourceType": "Observation",
   "id": "83005-9-yled6ihq58",
   "status": "final",
   "code": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "83005-9"
     }
    ],
    "text": "Variant category"
   },
   "valueCodeableConcept": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "LA26801-3",
      "display": "Simple Variant"
     }
    ],
    "text": "Simple Variant"
   }
  },
  {
   "resourceType": "Observation",
   "id": "82122-3-gp14b9abh7n",
   "status": "final",
   "code": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "82122-3"
     }
    ],
    "text": "Genetic variant coding
system"
   },
   "valueCodeableConcept": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "CLINVAR-V",
      "display": "ClinVar Variants"
     }
    ],
    "text": "ClinVar Variants"
   }
  },
  {
   "resourceType": "Observation",
   "id": "81252-9-4evwjg9v3d",
   "status": "final",
   "code": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "81252-9"
     }
    ],
    "text": "Discrete genetic variant"
   },
   "valueCodeableConcept": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "7110",
      "display":
"NM_000492.3(CFTR):c.1040G>C
(p.Arg347Pro)"
     }
    ],
    "text":
"NM_000492.3(CFTR):c.1040G>C
(p.Arg347Pro)"
   }
  },
  {
   "resourceType": "Observation",
   "id": "48018-6-pjkdllkrn4",
   "status": "final",
   "code": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "48018-6"
     }
    ],
    "text": "Gene studied"
   },
   "valueCodeableConcept": {
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      "code": "1884",
      "display": "CFTR"
     }
    ],
    "text": "CFTR"
   }
  },
  {
   "resourceType": "Observation",
   "id": "51958-7-i32tjamztpk",
   "status": "final",
   "code": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "51958-7"
     }
    ],
    "text": "Transcript RefSeq ID"
   },
   "valueCodeableConcept": {
    "coding": [
     {
      "system": "http://loinc.org",
      "code": "NM_000492.3",
      "display": "NM_000492.3"
     }
    ],
    "text": "NM_000492.3"
   }
  },
  {
   "resourceType": "Observation",
```

Examples from among the 2000+ forms

Associated Tools

** Clinical table linker for auto complete look-up when values come from big external tables
** Units validator and converter
** Form builder for creating new or editing existing forms

Secret Sauce in Clinical Table linker

- Via the URL, users can specify what fields in the external table are searched, and which answers are returned as part of selection grid, and which are stored in the index value field as hidden variables
- Other fields in the form can use these hidden variables as answer lists, default values, or help messages.
- Explore the tables we have created so far at:

  https://clin-table-search.lhc.nlm.nih.gov/
- Tables include IDC9, ICD10, genetic tables (ClinVar, dbSNP, etc.), RxTerms, NPI , etc.

Clinical Table Search Service: Demo page

Autocompletion Demo for the Alleles API

This page allows you to try the Alleles API and see the effects of different choices for search and display fields (specified with the "sf" and "df" query string parameters, as described on the API documentation page) on returned data, which is shown in the autocompletion list below.

Example autocompleter

The following autocompleter was constructed using the fields specified below.

Search for value

Show developer info

Database: alleles

The "Search" checkboxes control which data fields the autocompleter searches, and the "Display" checkboxes control which data fields show up in the autocompletion list. If none are checked, a default selection will be used.

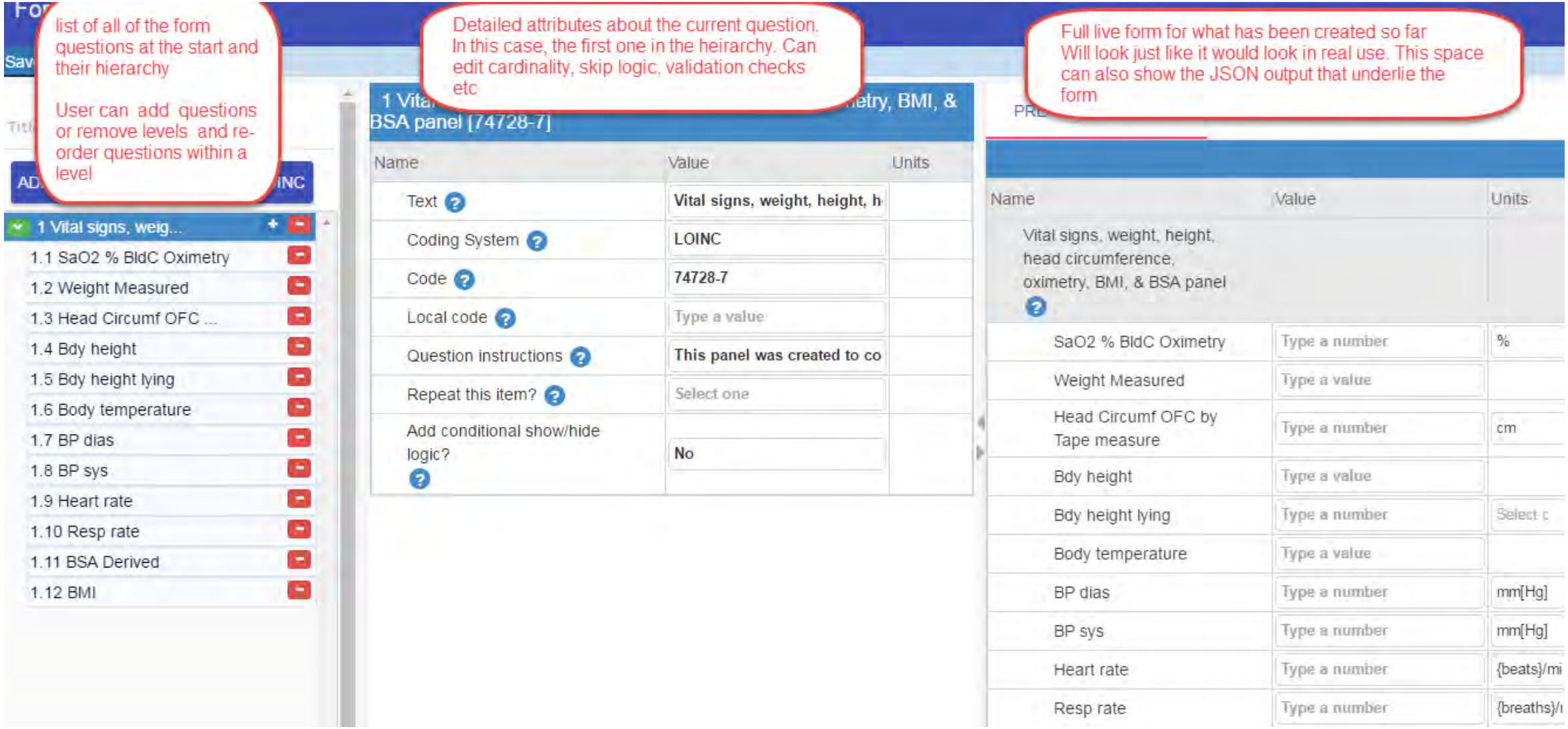
Field	Search All Default	Display All Default	Description
AlternateAllele	☐	☐	The value of the AlternateAllele field in the source file.
AlternateAllele_lbl	☐	☐	The value of the AlternateAllele field in the source file, but prefixed with "Alt=".
AlleleID	☐	☐	The ID of the allele as taken from the AlleleID column of the source file.
AminoAcidChange	☐	☐	This is the amino acid change (starting with "p.") parsed from the Name field.
Chromosome	☐	☐	The chromosome number, taken from the Chromosome field in the source file, but prefixed with "chr".
ChromosomeAccession	☐	☐	The chromosome accession number, taken from the ChromosomeAccession field in the source file.
Cytogenetic	☐	☐	The cytogenetic location of the allele, taken from the "Cytogenetic" field in the source file.
dbSNP	☐	☐	The "rs" ID number from dbSNP, taken from the "RS# (dbSNP)" field in the source file.
GeneID	☐	☐	The gene ID from NCBI's gene database.
GeneSymbol	☐	☐	This is the GeneSymbol field listed in the source file. It is the symbol for the gene that overlaps the variant.
GenomicLocation	☐	☐	This is an HL7-style concatenation of the Start and Stop fields, i.e., Start^Stop.
hgnc_id	☐	☐	A unique ID provided by the HGNC for each gene with an approved symbol. Although standard HGNC IDs are of the format HGNC:n, where n is a number, we have removed the "HGNC:" prefix, so that these values are just numbers.
HGVS_c	☐	☐	The "HGVS (c.)" field from the source file. (The "RefSeq cDNA-based HGVS expression".)
HGVS_p	☐	☐	The "HGVS (p.)" field from the source file. (The "RefSeq protein-based HGVS expression".)

UCUM-LHC: Unit Validation and Conversion

- For “Unified Code for Units of Measure” (UCUM)
- Website: https://lhncbc.github.io/ucum-lhc/
- Library can be downloaded from GitHub or installed with “bower”
- Library supports:
  - Validation of unit expressions
  - Conversion of values between different unit expressions
- Unit codes in UCUM are not always what one would expect, but there are synonyms
  - Some UCUM syntax is not in common vernacular, e.g. [lb_av], but synonyms ([lb_av] = pounds) will guide the users
- Some special syntax: “.” = multiplication, * = exponentiation

Presenter: Clem

Form Builder -After selecting a seed form



Example forms that illustrate the capabilities

"Matrix" style with Radio buttons-PROMIS Social isolation form

PROMIS item bank - social isolation - version 2.0 ©

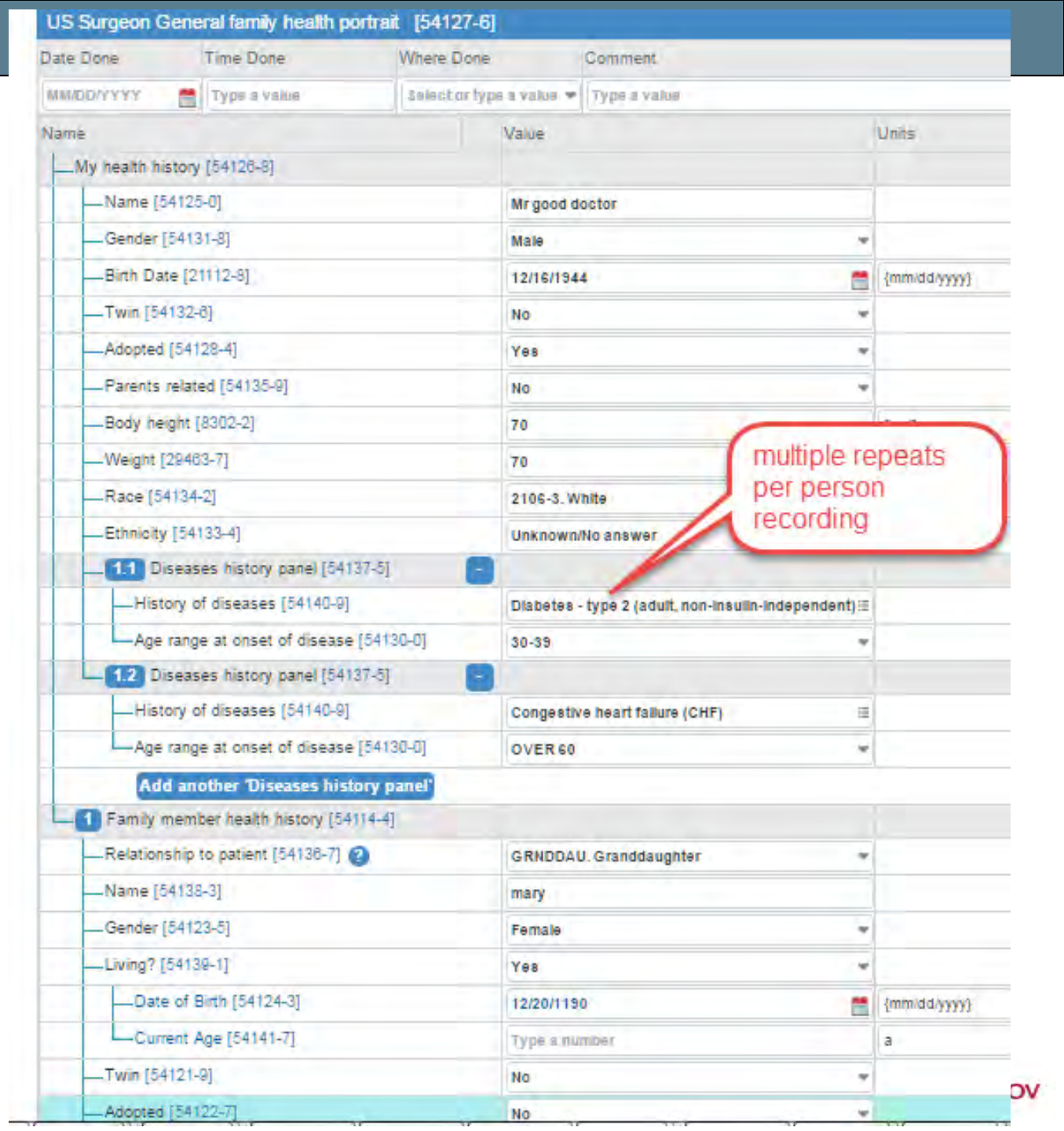
Date Done	Time Done	Where Done	Comment
MM/DD/YYYY	Type a value	Select or type a value	Type a value

	Never	Rarely	Sometimes	Usually	Always
People get the wrong idea about my situation ©	○	○	○	○	○
I feel isolated even when I am not alone ©	○	○	○	○	○
I feel that people avoid talking to me ©	○	○	○	○	○
I feel detached from other people ©	○	○	○	○	○
I feel that some of my friends avoid me ©	○	○	○	○	○
I feel that some of my family members avoid me ©	○	○	○	○	○
I feel that I am alone in my interests and ideas ©	○	○	○	○	○
I feel that people barely know me ©	○	○	○	○	○
I feel like a stranger to those around me ©	○	○	○	○	○
I find that friends or relatives have difficulty talking with me about my health ©	○	○	○	○	○
I feel that people are around me but not with me ©	○	○	○	○	○
I feel isolated from others ©	○	○	○	○	○
I feel left out ©	○	○	○	○	○
I feel that I am no longer close to anyone ©	○	○	○	○	○

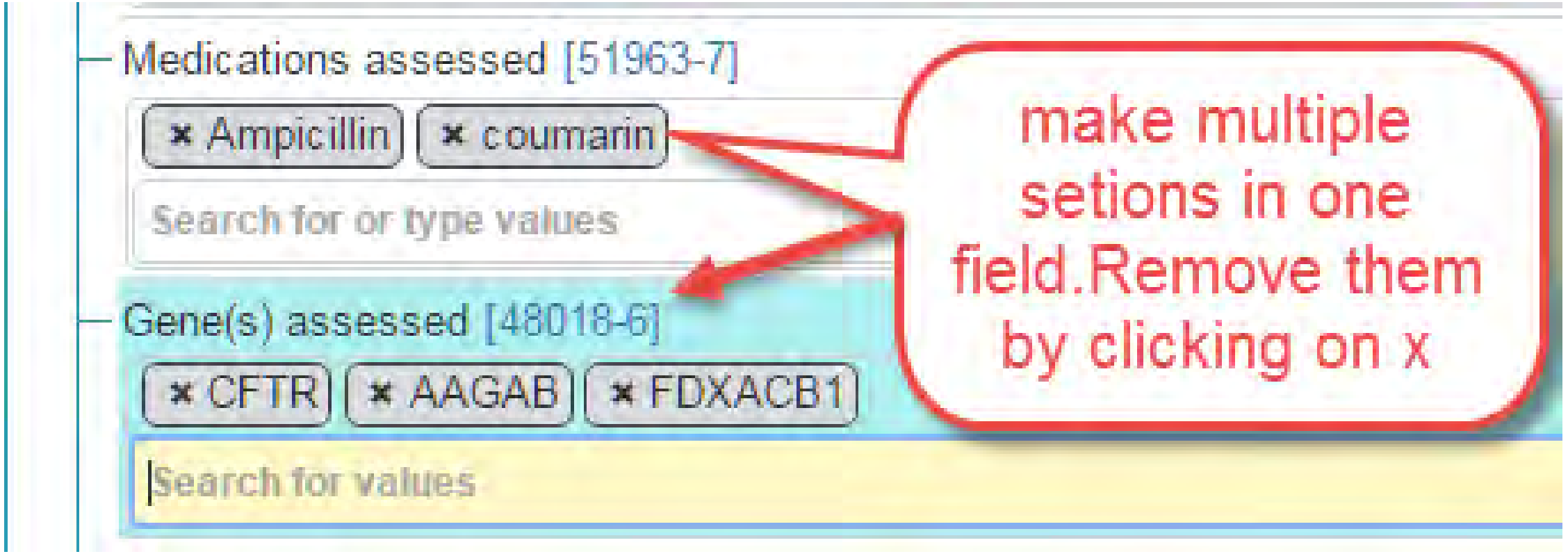
Surgeon Generals family health history as an LHC-Form

Illustrates repeating groups of nested questions.

Proband can have many diagnoses with dates AND many relatives who also have many diagnoses and dates

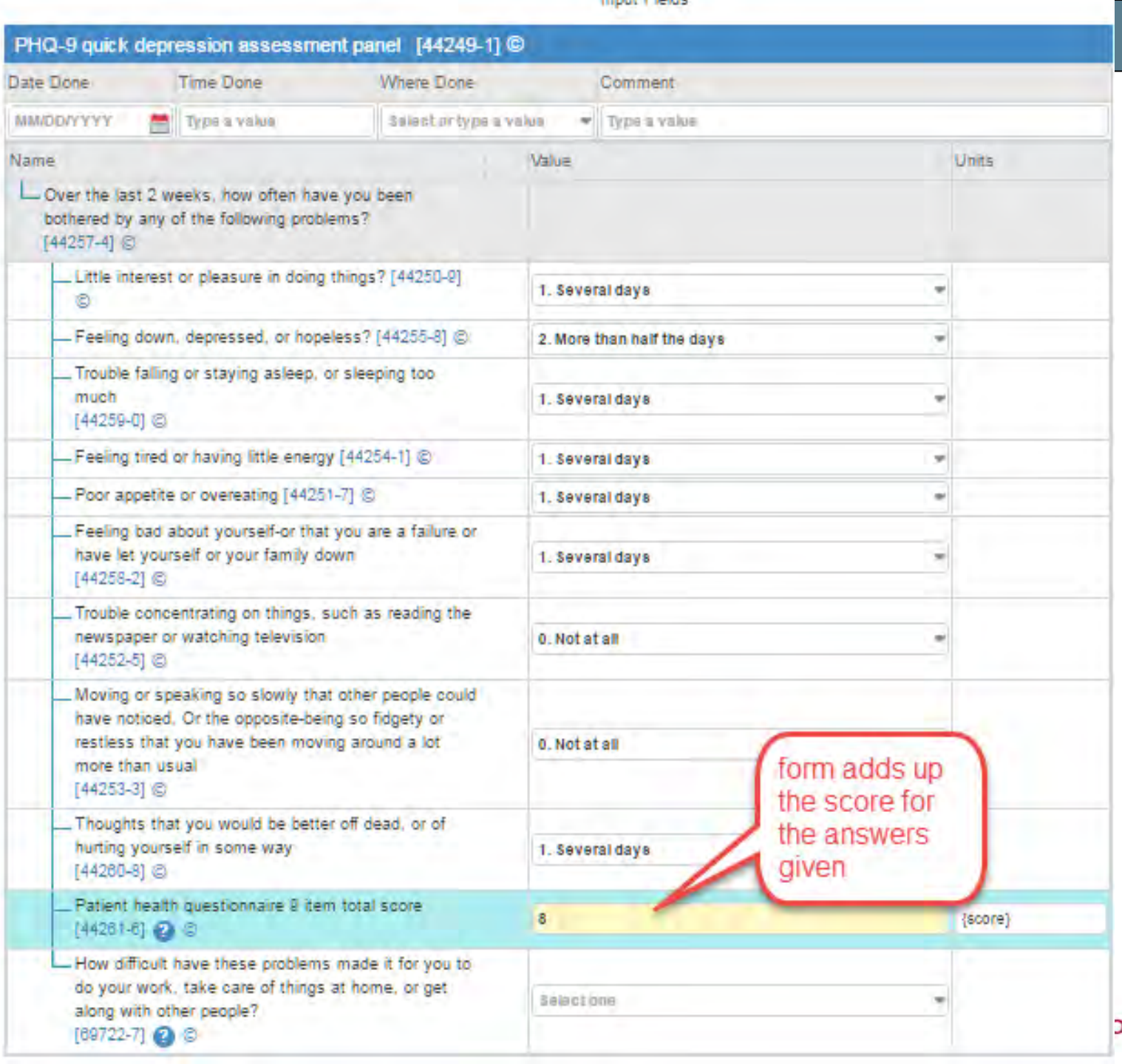


Can multiple values per field



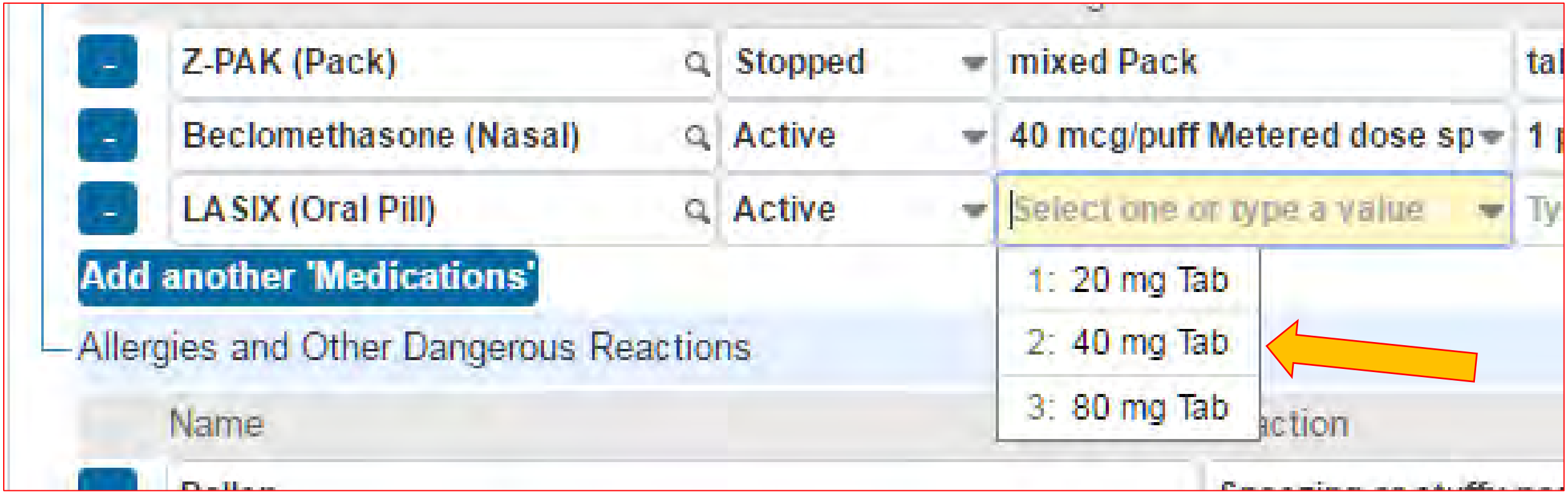
PHQ-9 Depression survey with score computed on the fly

As an LHC-Form



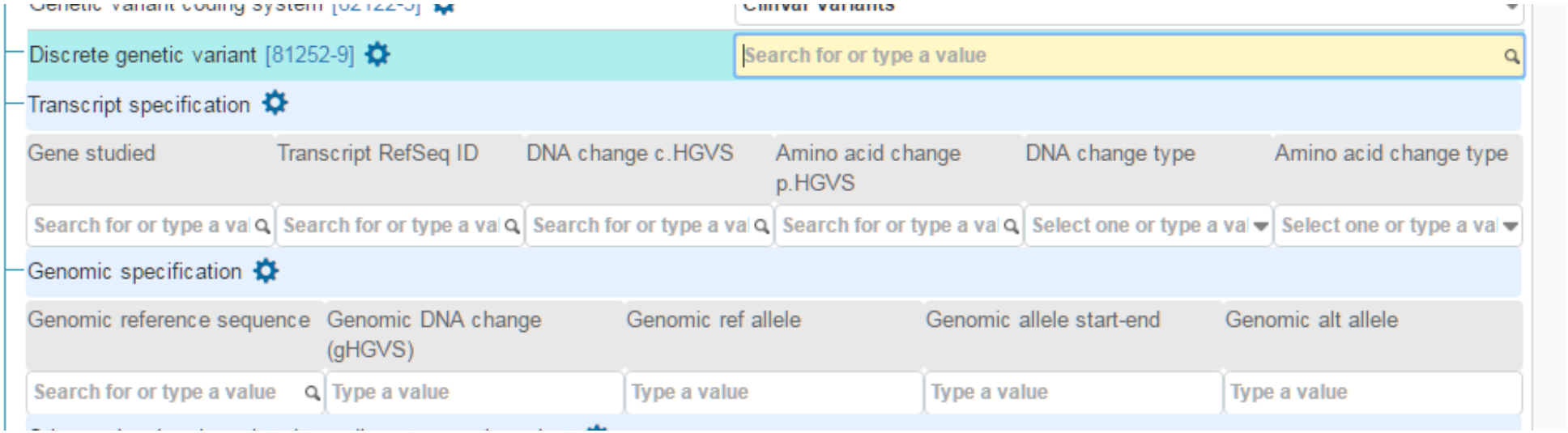
https://lhc-forms.lhc.nlm.nih.gov/

Secret sauce : Code stored in one field can generate code answer lists for succeeding fields- to be illustrated on the PHR form
Enter Lasix oral and get selection menu of available pill sizes

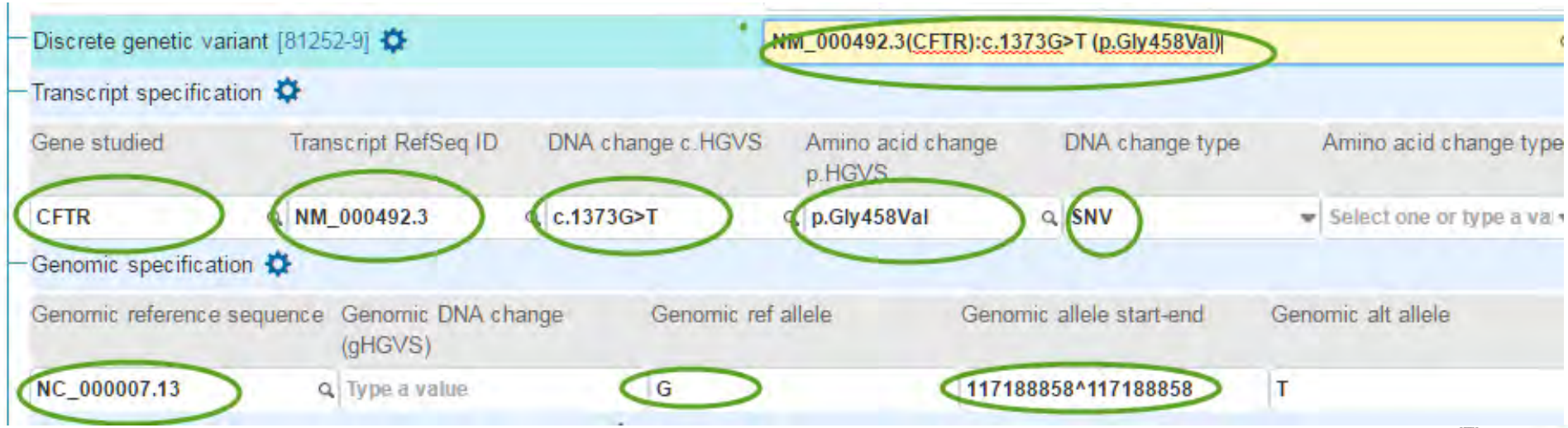


Secret sauce: Genetics form. Load variant ID and it fills in values for many other fields

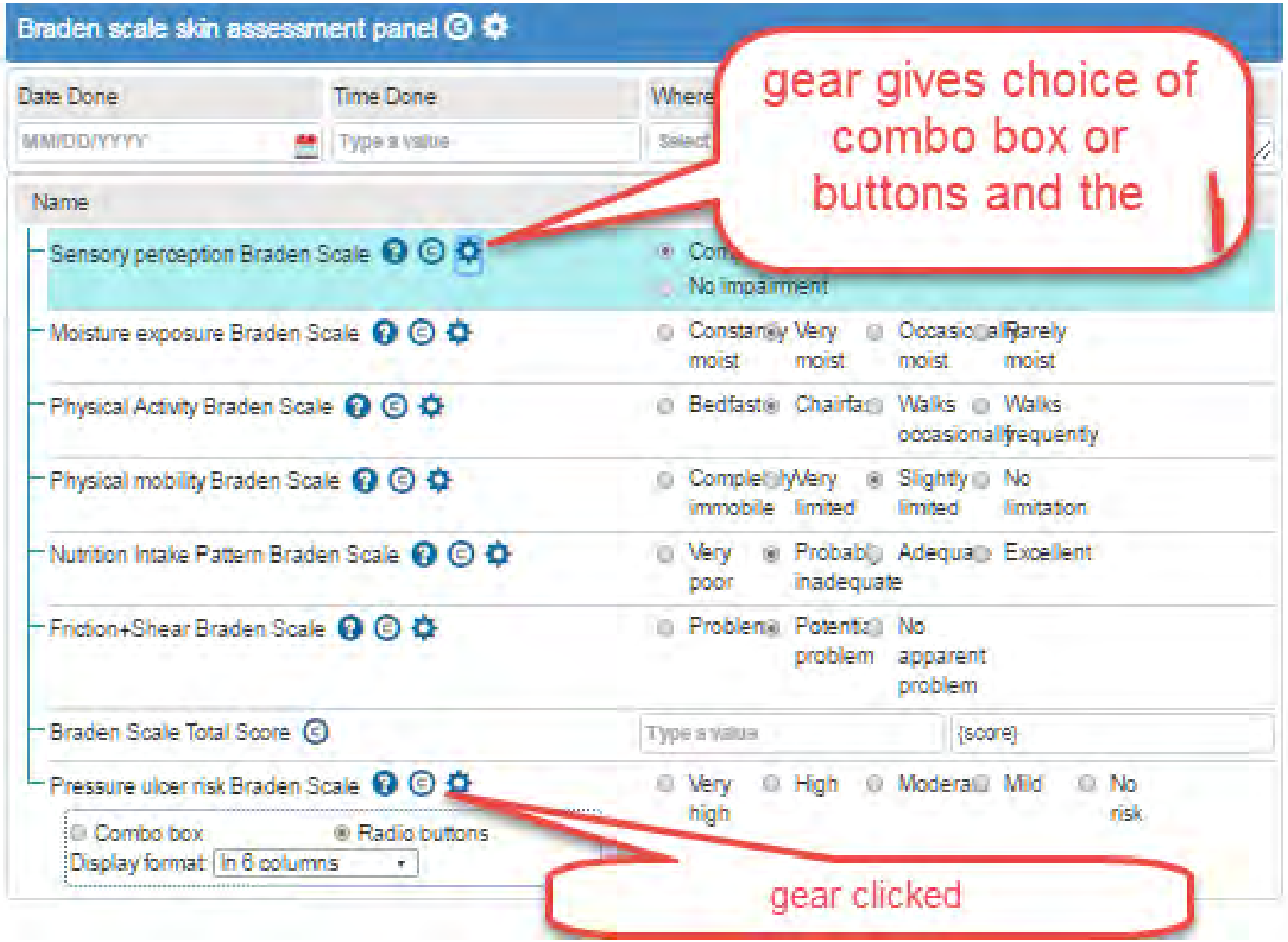
Before



After



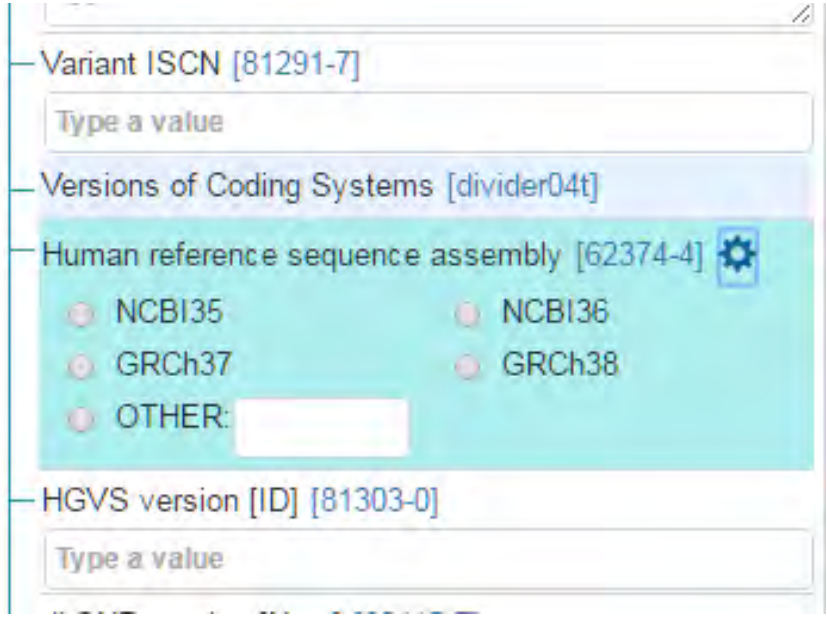
Choices of combo boxes, radio buttons, check boxes and grids when appropriate



Responsive design-example from HL7 V2 genetics reporting form

Wide screen

Skinny screen



A personal health record in one form

Save To File | Use "Label Above" Style | Use "Label on Left" Style | Show HL7 Message

☐ Display Question Code ☑ Show Help/Description ☐ Keyboard Navigation On Input Fields Total # of Questions: 44

Personal Health Record

Medical Conditions

Medical condition	Status	Started	Stopped	Description/Comment
Chest pain	Active	04/20/2016	MM/DD/YYYY	Sounds anginal. Worrse with exertion, but young and no family history
Pneumonia - bronchial	Inactive	03/17/2017	04/22/2016	Treated wish Zpack on ambulatorybais
Hay fever (allergic rhinitis)	Active	03/20/2012	MM/DD/YYYY	Every spring
bac	Select one or t	MM/DD/YYYY	MM/DD/YYYY	Type a value

Add another 'Medical Conditions'

Medications

Medication name	Status	Strength	Instructions	Started	Stopped	Why stopped	Resupply
Z-PAK (Pack)	Stopped	mixed Pack	take until gone	03/17/2016	04/22/2016	Finished the prescription	MM/DD/YYYY
Beclomethasone (Nasal)	Active	40 mcg/puff Metered dose sp	1 puff twice day in season	03/20/2012	MM/DD/YYYY	Select one or type a value	MM/DD/YYYY

Add another 'Medications'

Allergies and Other Dangerous Reactions

Name	Reaction	Started	Comment
Pollen	Sneezing or stuffy nose	03/15/2017	Worse when maple trees bloom
Select one or type a value	Select one or type a value	MM/DD/YYYY	Type a value

Add another 'Allergies and Other Dangerous Reactions'

Form Builder

URLS for exploring

(Ye Wang, Paul Lynch, Ajay Kanduru, Lee Mericle, Xiaocheng Luan, Clem McDonald)

- LHC-Forms
  - Project page: https://lhncbc.nlm.nih.gov/project/lforms
  - Software download and documentation: https://lhncbc.github.io/lforms
  - Demo site: https://lhc-forms.lhc.nlm.nih.gov/
- Lister Hill Table Connector (for autocompletion)
  - https://clin-table-search.lhc.nlm.nih.gov/
  - http://lhncbc.github.io/autocomplete-lhc
  - https://github.com/lhncbc/autocomplete-lhc
- Form Builder
  - https://lhc-formbuilder.lhc.nlm.nih.gov
- Units of measure (UCUM) validator and converter
  - http://lhncbc.github.io/ucum-lhc/

URLS for exploring - cont.

(Ye Wang, Paul Lynch, Ajay Kanduru, Lee Mericle, Clem McDonald)

- JSON & Screenshot of genetic form (use Chrome)
  - Screenshot: http://lhncbc.github.io/lforms/samples/genetic-panel/screenshot.png
  - - Form as FHIR Questionnaire: http://lhncbc.github.io/lforms/samples/genetic-panel/fhir-questionnaire.json
  - - Form response as FHIR Questionnaire Response: http://lhncbc.github.io/lforms/samples/genetic-panel/fhir-questionnaire-response.json
  - - Form response as FHIR Diagnostic Report: http://lhncbc.github.io/lforms/samples/genetic-panel/fhir-diagnostic-report.json
  - - LHC-Forms format (with user data): http://lhncbc.github.io/lforms/samples/genetic-panel/lforms-data.json

We would be interested in collaborators!