SimulConsult®

A Simultaneous Consult On Your Patient's Diagnosis

Guide to Phenome Analyzer 2019

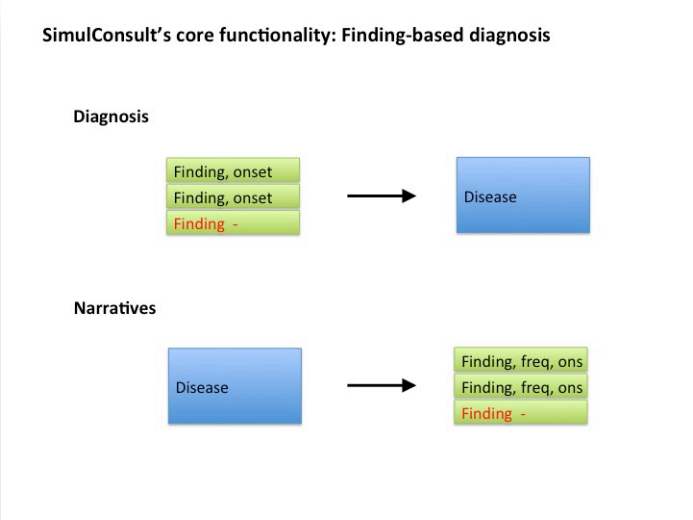
AI-based, human-curated Diagnostic Decision Support Software

Table of contents

WELCOME!

Narrative medical resources enable medical professionals to start with a disease and learn about its findings (symptoms, signs and tests). Patients, of course, appear the other way: with findings that medical professionals need to use to deduce the diagnosis from thousands of known disease phenotypes. The group of all such disease phenotypes is called the "Phenome". SimulConsult has been built to help solve this diagnostic problem, enabling clinicians to start with findings and get to the correct diagnosis. In doing so, it offers a "differential diagnosis" consisting of a list of likely diseases with some indication of their relative probability.

Figure 1: SimulConsult's core functionality: finding-based Diagnosis



SimulConsult 2.0 comprises a proprietary computational database of diseases and their characteristics, patented AI-based algorithms and intuitive, easy to use user interface.

- **Database.** Specialists curate and update the database continuously with information from the peer-reviewed literature and relevant unpublished disease characteristics. The company has a well-established, efficient approach to data-gathering. Each year, the database grows by 500-1,000 diseases.
- **Patented algorithms.** The company has received 4 issued U.S. patents (6,212,519; 6,754,655; 7,742,932 & 9,524,373)
- **User interface.** The user interface **simplifies input** of onset (or absence) of patient symptoms and physician-observed signs and test results ("findings"); **computes and displays** likelihood-weighted potential diagnoses ("differential diagnosis") that evolves as data is entered; **suggests** the most useful clinical findings and tests, which are most likely to shorten the list of diagnoses; and **connects** instantly to precise narrative resources about the disease or finding under consideration. The results improve accuracy, lower costs and increase physician productivity.

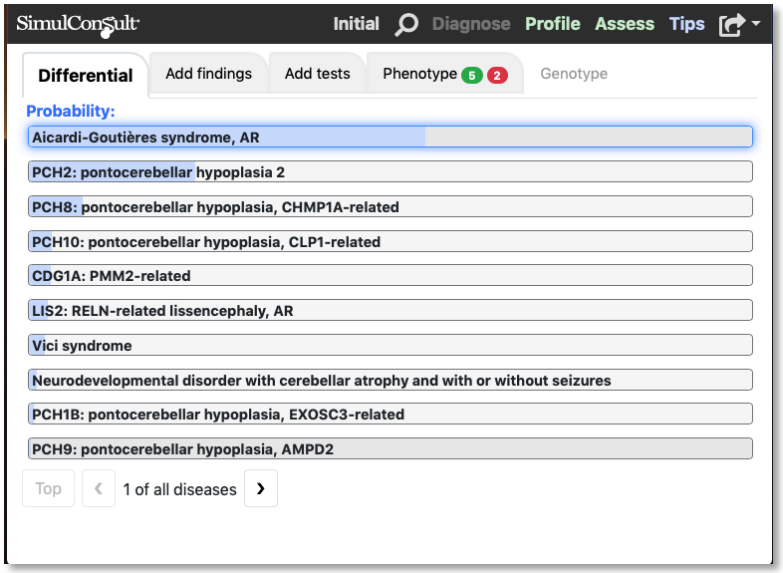
A Genome-Phenome Module that enables interpretation of genomic results in the clinical context is an optional upgrade.

INTRODUCTION TO A FEW SIMULCONSULT CONVENTIONS

Colors and their meaning

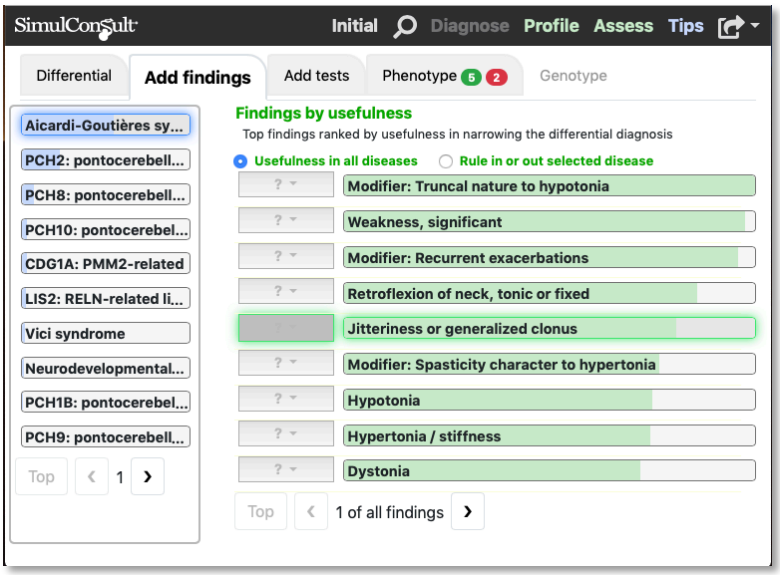
Diseases are **blue**. Findings are **green.**

Figure 2: The Differential Diagnosis with likelihood shown in blue



The main diagnostic screen shows a miniaturized differential diagnosis, together with other useful information. In this case, the software shows suggested useful clinical findings.

Figure 3: Suggested findings ranked in order of Usefulness in Narrowing the Differential Diagnosis



PATIENT CASE USED FOR ILLUSTRATIONS

This Very Low Density Lipoprotein Receptor (VLDLR) case was published by Dixon and Salazar in 2012 and will be used throughout for illustrating the points.

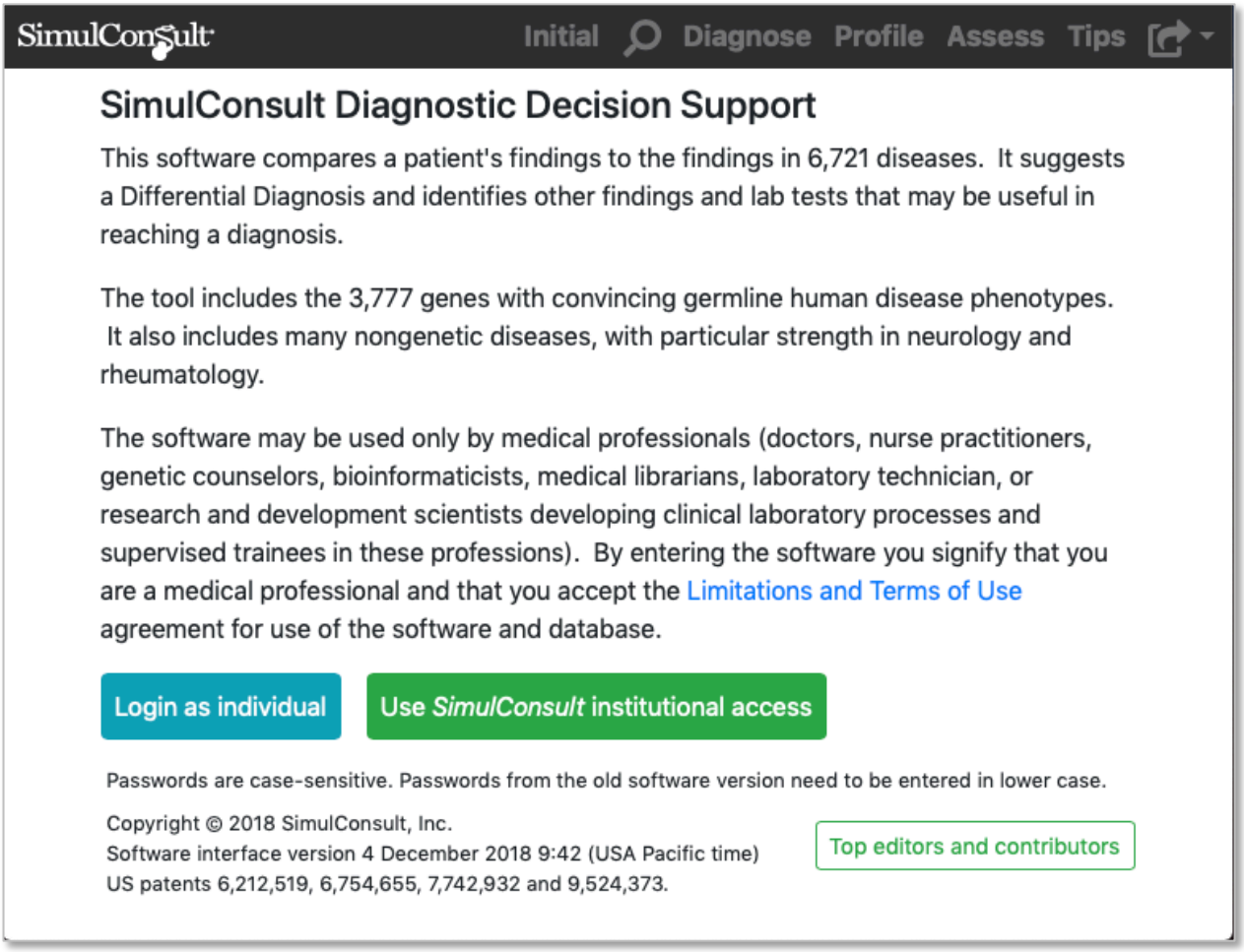
A 2-year old boy from the Middle East

- **Family history:**
  - Neither parent affected
  - 1 of 2 brothers affected
  - Parent consanguinity: first cousins
- **At 1 month:** microcephaly
- **By 1 month:** Nystagmus, non-rotary
- **By 6 months:** hyperreflexia
- **Absent:** regression
- **MRI:** pan cerebellar hypoplasia

GET STARTED

On the login page you can see the number of diseases and genes covered. The editors and contributors can also be seen using the link from this page.

Figure 4: Login



Note that on the above page we publish the number of genes and diseases currently in the database.

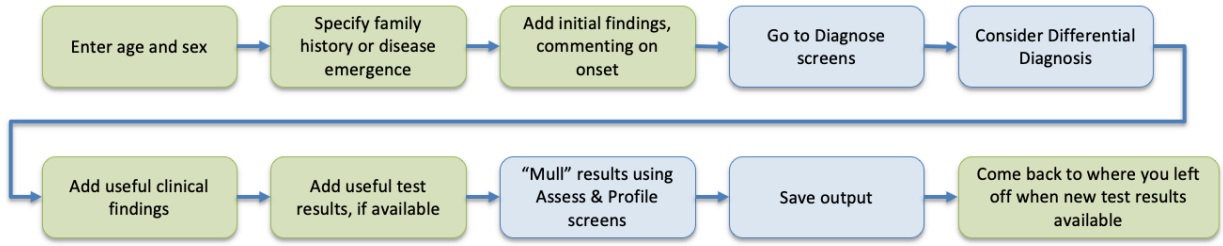
Enterprise version (Health system or Laboratory): Access from within EHR or LIM.

If you have the electronic health record or laboratory information system integrated version, please see the companion document for how to launch SimulConsult from within your system.

Basic process

Diagnosis is usually an iterative task. SimulConsult 2.0 emulates the doctor's iterative decision making process, especially for more complex cases.

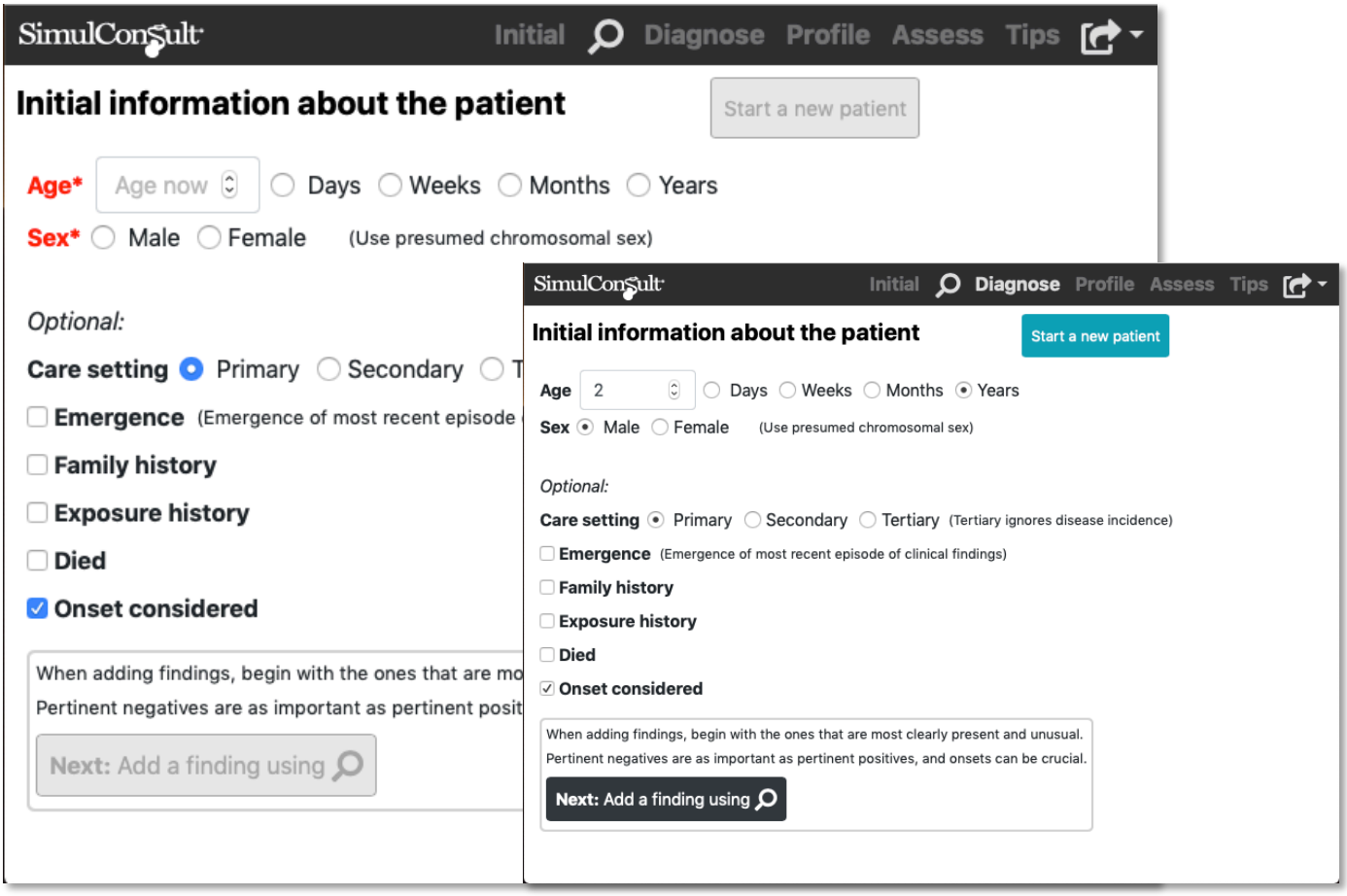
Figure 5: Process flow for diagnosis using SimulConsult



Start a new patient, by entering age and sex

Once the age and sex are entered, you have multiple options for entering findings. Note that in the Enterprise version integrated with the electronic health record (**EHR**), age and sex are automatically imported.

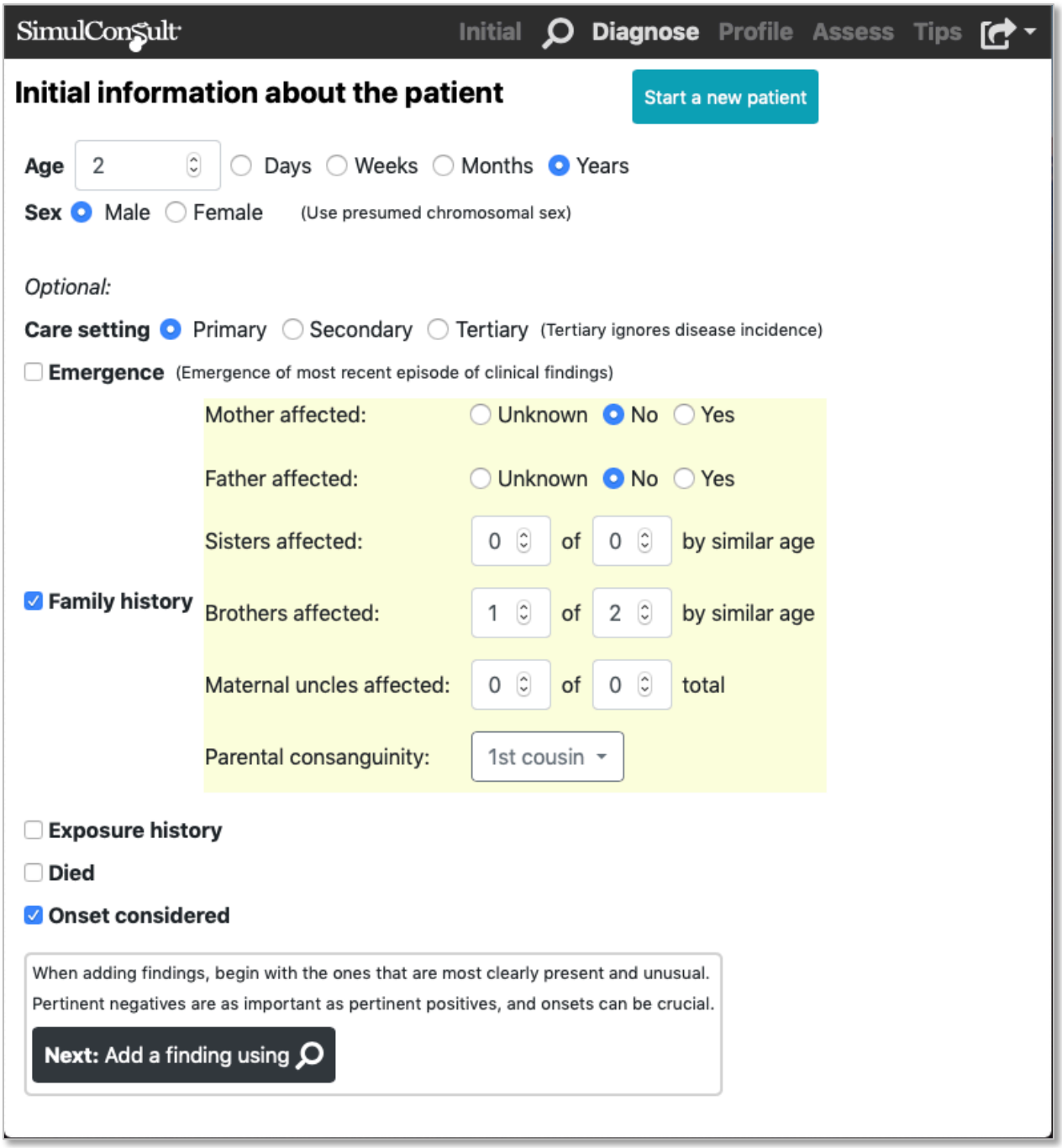
Figure 6: Initial screen, where you specify the age, units and sex



Enter Family history

You can enter family history if you know it by checking family history. While the family history shown here will obviously increase the probability of the diagnosis being a recessive disease, non-genetic diseases continue to be considered.

Figure 7: Entering family history



ENTER INITIAL KEY FINDINGS

The process of entering clinical findings (signs, symptoms) and test results has been optimized for speed, including prompting the clinician to comment on findings most helpful in narrowing the evolving differential diagnosis (the probability weighted list of potential diagnoses relevant for this patient based on findings entered).

Modes for entering findings

You have several search modes for locating **the initial** findings, each of which is illustrated below.

1. **Core finding lists** (common findings in genetics, neurology, rheumatology and ancestry, as well as an interface for family history)
2. **Search** for findings (one or more terms)
3. **Disease profile** is useful if you have a strong hypothesis. Once 3-5 findings are entered, move to the general diagnose screen to get the benefit of suggestions based on the evolving differential diagnosis.
4. **Useful findings** and **Useful tests** tabs will often be the most convenient way to add findings once the user has gotten an initial differential diagnosis.

Enter using “Core finding lists”

Using the “**Neurology Core finding lists**” you can add a set of pertinent positives and negatives.

Core finding lists are developed as a set of up to 46 findings most often used in the referrals to the specialty. Core finding lists allow the user to increase the speed with which the software focuses on the relevant subset of diseases. To ensure the Core Finding List is most useful, the curation process for new and updated disease reviews the findings in the Core Finding List to ensure complete coverage.

With the addition of new specialties, new Core Finding Lists are added

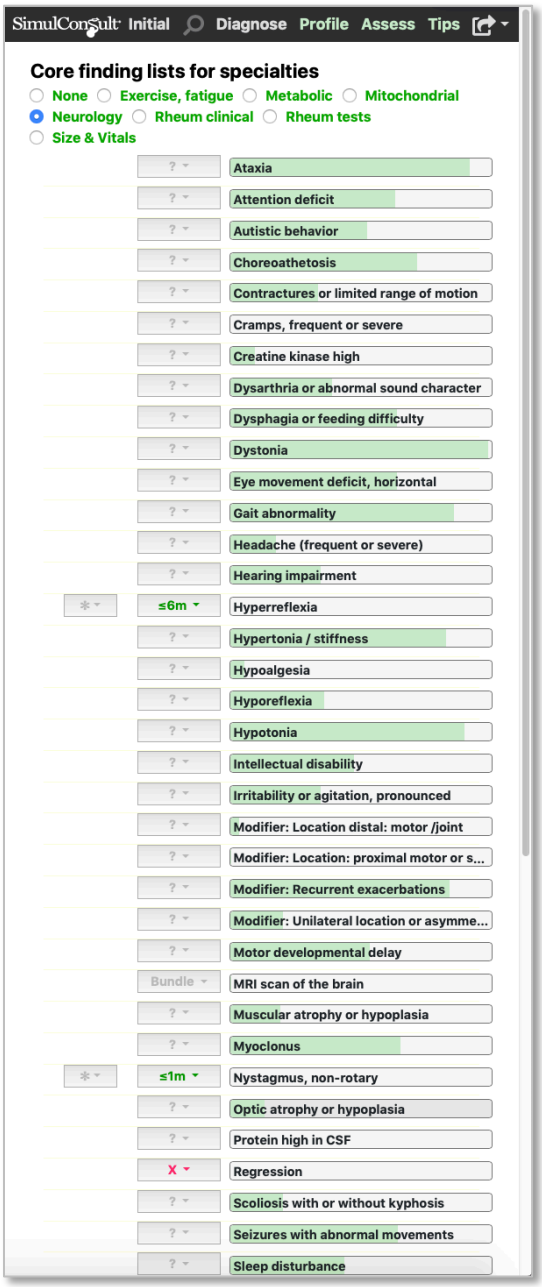
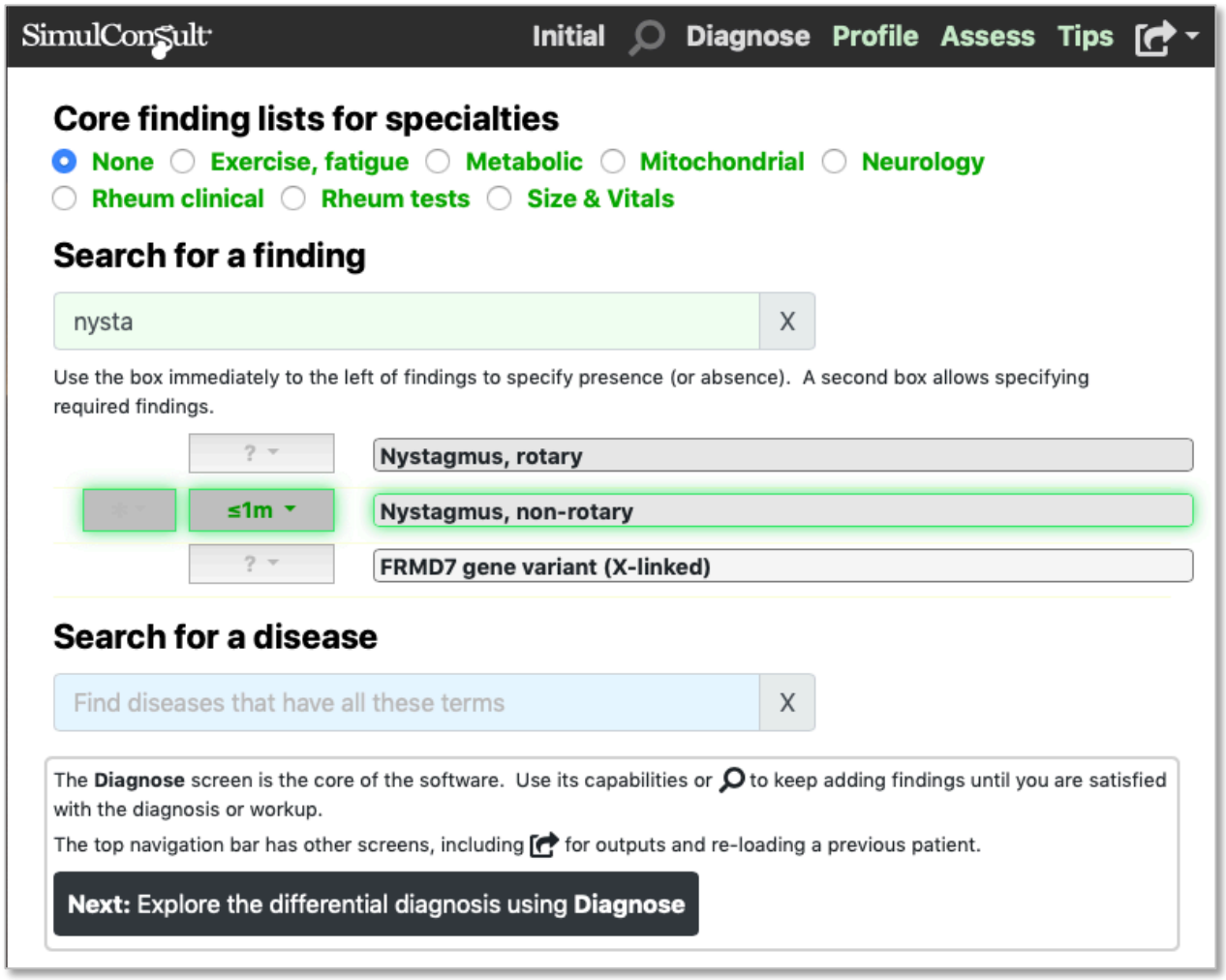


Figure 8: Entering findings using the Neurology Core finding lists

Enter findings using search

As the user types into the search box, all the findings appear as buttons below. The search considers both the finding name and the synonyms known for that finding. SimulConsult supports many synonyms. You can put more than one search term in the box at a time, separate them with a space. Often it is best to use a word fragment if different endings are used, such as “nyst” for nystagmus.

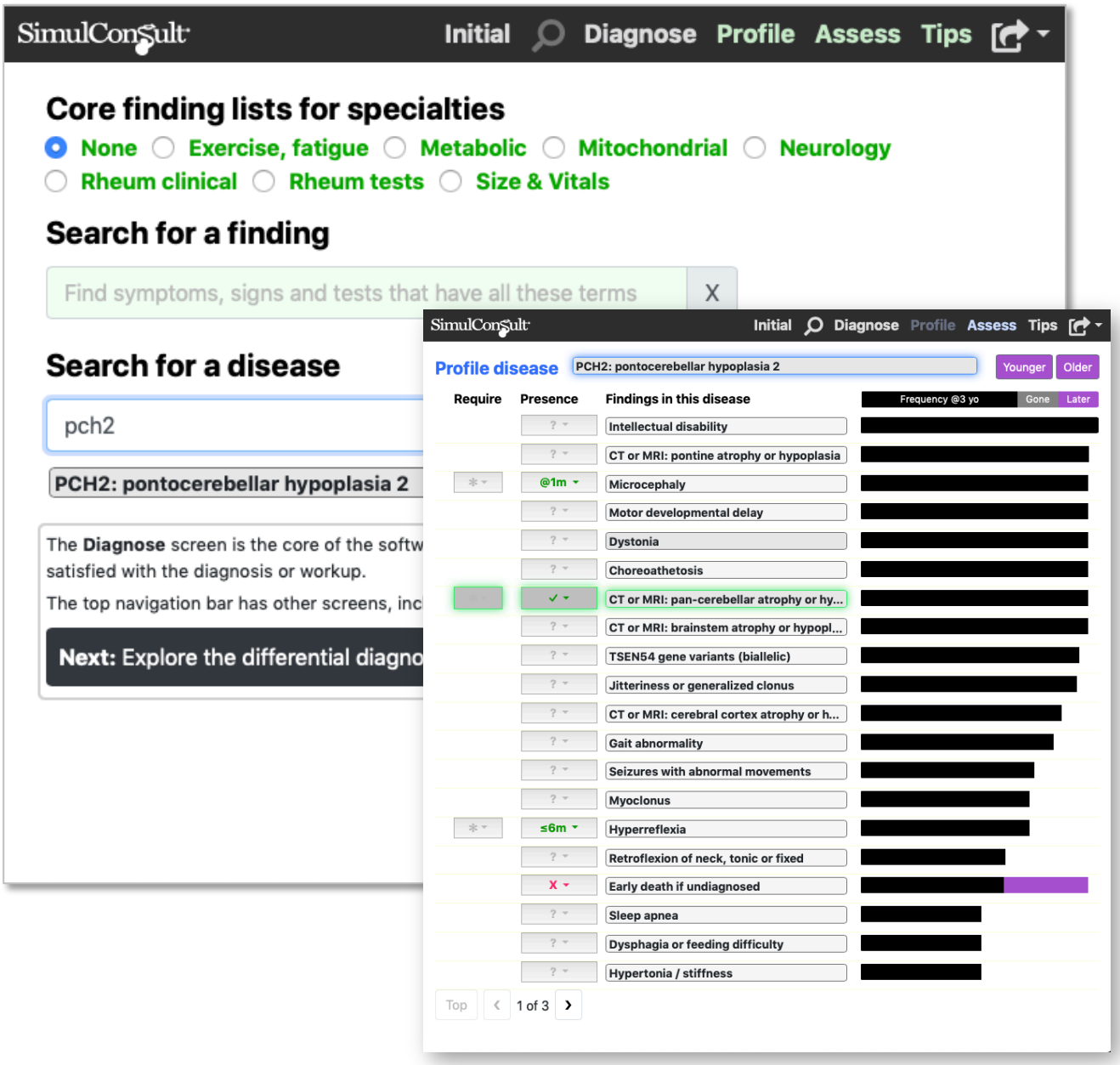
Figure 9: Entering findings via search



Enter findings using a disease where there is a strong hypothesis

If the user has a strong hypothesis of the diagnosis, they can begin by typing the disease name into the blue disease search box. Matching diseases appear as buttons below. Then by clicking on the disease button and the profile option, the user can begin by entering findings associated with that disease. It is best not to add more than 3-5 pertinent positives before going to the general diagnose screen, so as not to over specify the answer.

Figure 10: Entering findings via the disease profile

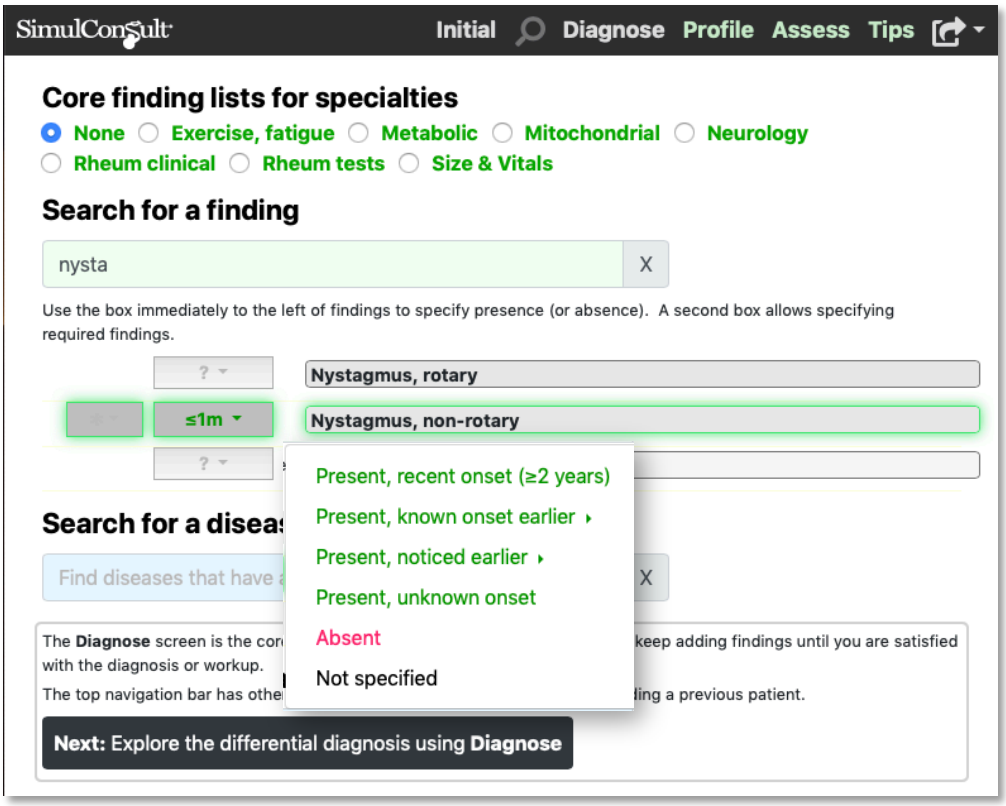


The importance of onset information

Most genetic diseases unfold over time, and as a result, using information available about the **onset of particular findings** is helpful in narrowing the differential diagnosis. Clicking on the box next to the finding brings up a dialog box of onset options. After you specify the onset the box automatically closes and a short-hand appears in the box next to finding. To enter a finding, click to the left of the finding where you see the "**? and the down arrow."** The menu will appear. Click on the selection you want.

1. **Pertinent positive options**
    a. Onset **at** a particular age
    b. Present **by** a particular age, onset unknown (not as informative as option "a" but sometimes all that is known)
    c. Present, onset unknown
2. **Pertinent negative option**
    a. Absent now

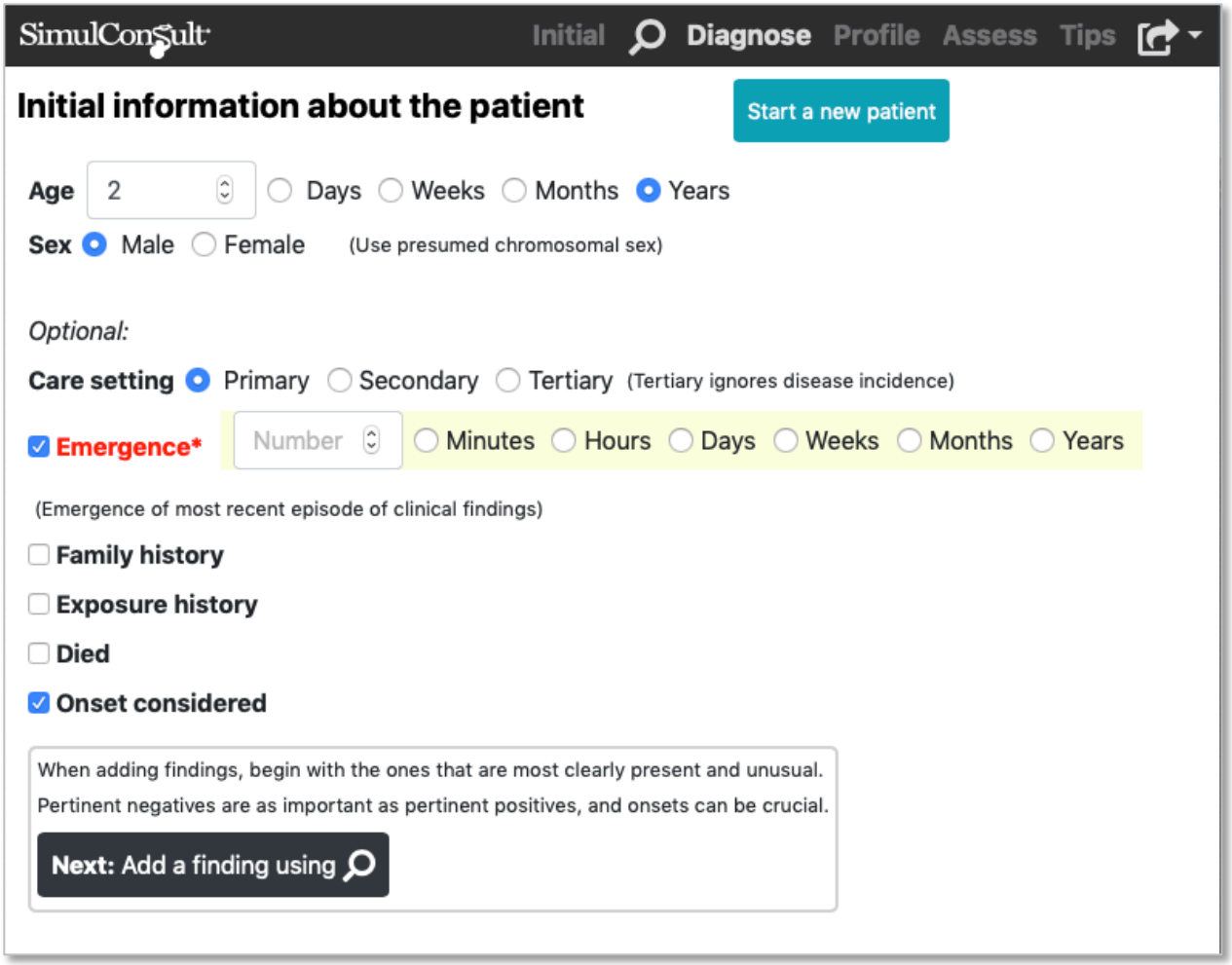
Figure 11: Specifying Onset



The importance of emergence

For other diseases, such as those in rheumatology, the **speed of emergence** is key. This is done at the macro level for all findings on the Initial screen.

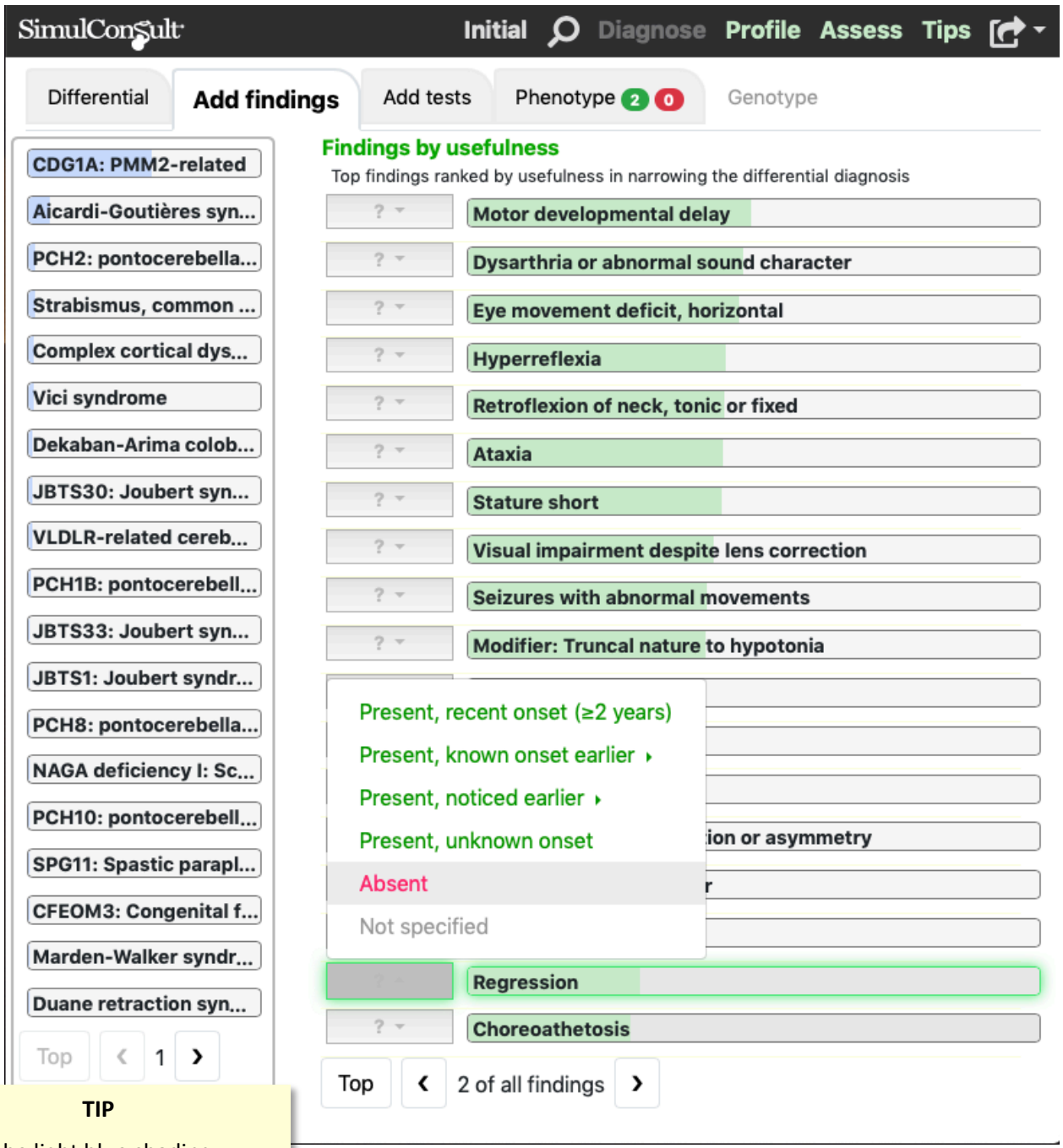
Figure 12: Commenting on the speed of Emergence



The importance of pertinent negatives

Because many genetic diseases share multiple findings, geneticists usually make heavy use of the absence of pertinent findings during the process of diagnosis. The software also supports this option.

Figure 13: Noting a pertinent negative



TIP

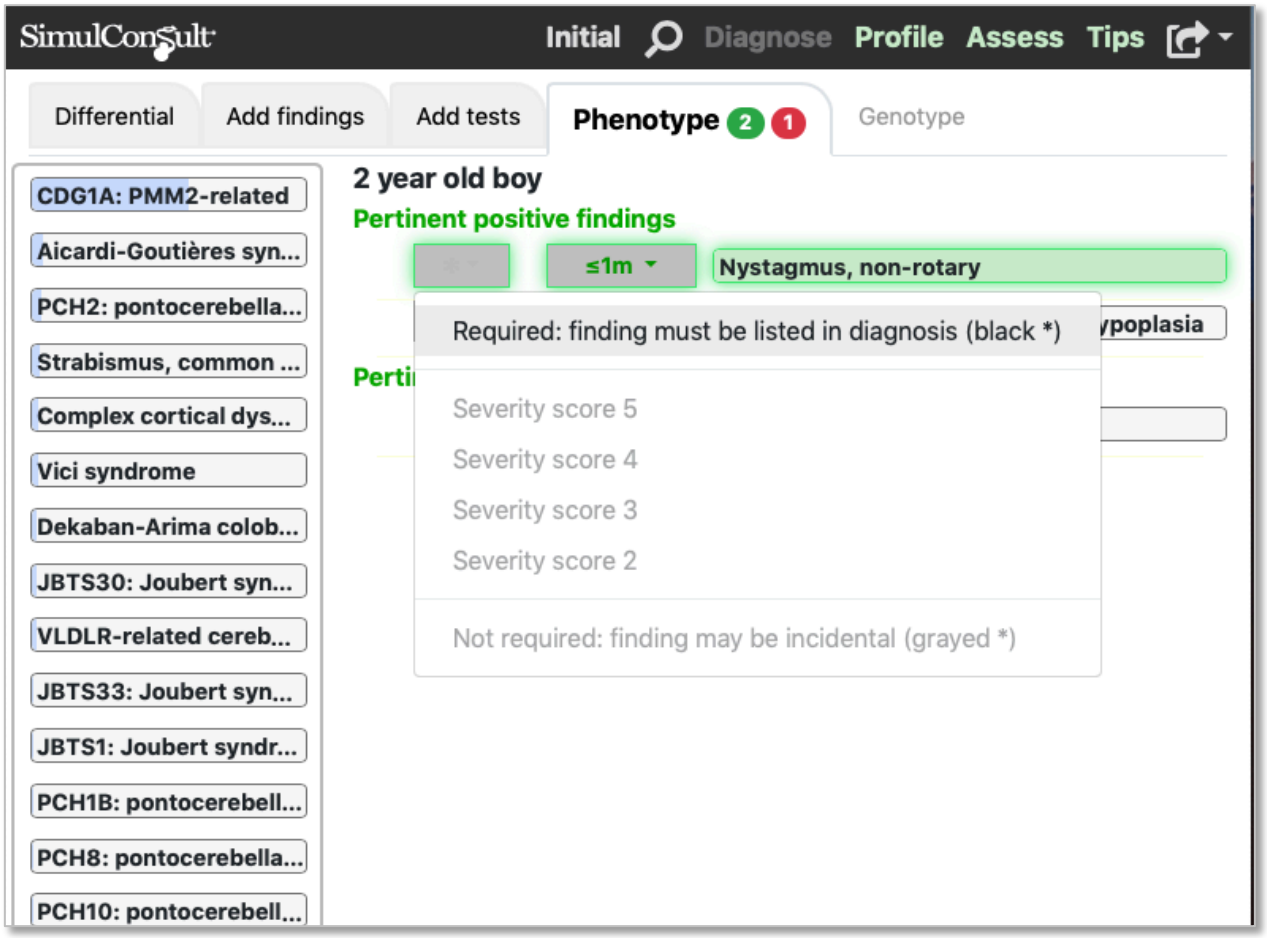
Notice the light blue shading representing the differential diagnosis overlay on the diseases.

The importance of requiring certain findings

The default in the software is to consider the possibility that a finding is not related to the primary diagnosis; the software has extensive probability information to make these assessments. However, when a common finding is particularly notable, such as a very high creatine kinase level, you have the ability to specify that you require it to be a finding in the diagnosis.

Similarly, one or more findings may be so striking or unusual that you only want to see diseases with that finding. You can require the finding, by selecting the box next to the onset box and selecting Required, which displays a "*" to the left of the onset, as is shown below for nystagmus.

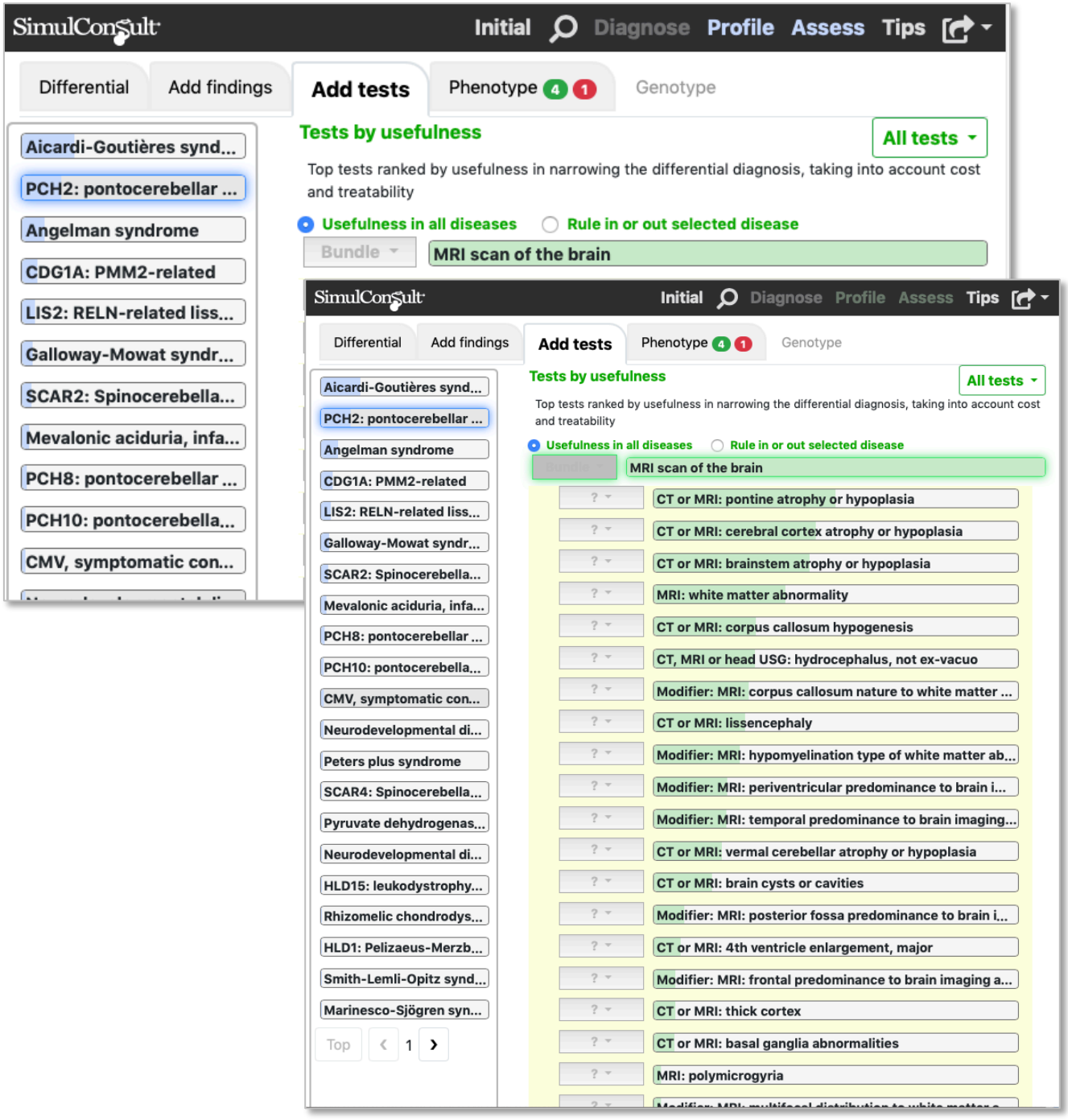
Figure 14: Requiring a finding



Entering tests results for tests that have multiple findings

In order to distinguish the test results from a particular laboratory or diagnostic testing panel from the general category of results, we call such collections "**Bundles**". Shown here is the bundle of test results that can come back from an MRI of the brain.

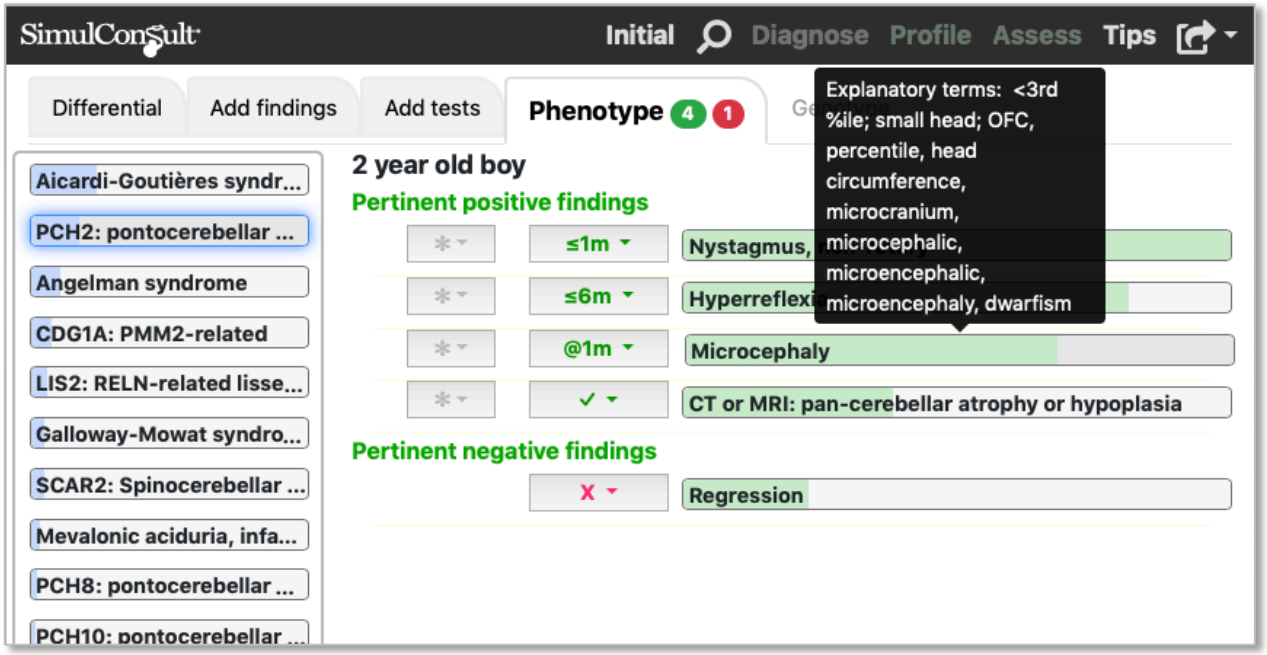
Figure 15: Entering test results for tests with multiple potential findings "Bundles"



View and use synonyms

Each disease and finding name may have synonyms, which the software also checks in search mode. To see the synonyms for a particular finding or disease hover your mouse over the button. The results display as shown here.

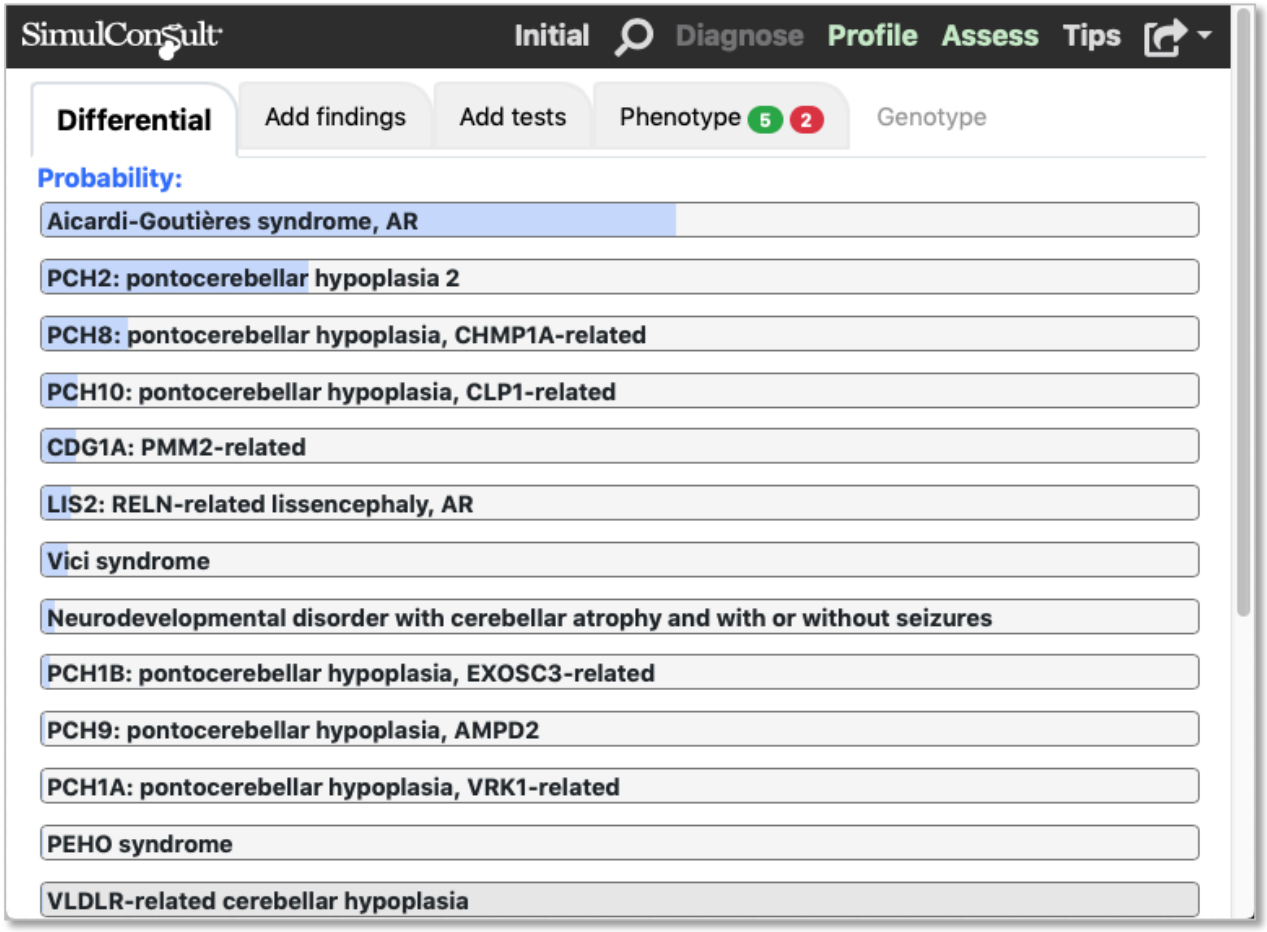
Figure 16: Viewing synonyms (basic mode)



VIEW THE DIFFERENTIAL DIAGNOSIS

After entering the initial findings, you can go to the differential diagnosis screen by pressing the "**Differential diagnosis**" button (see previous figure). From there you can add further findings to narrow the differential diagnosis.

Figure 17: Differential Diagnosis

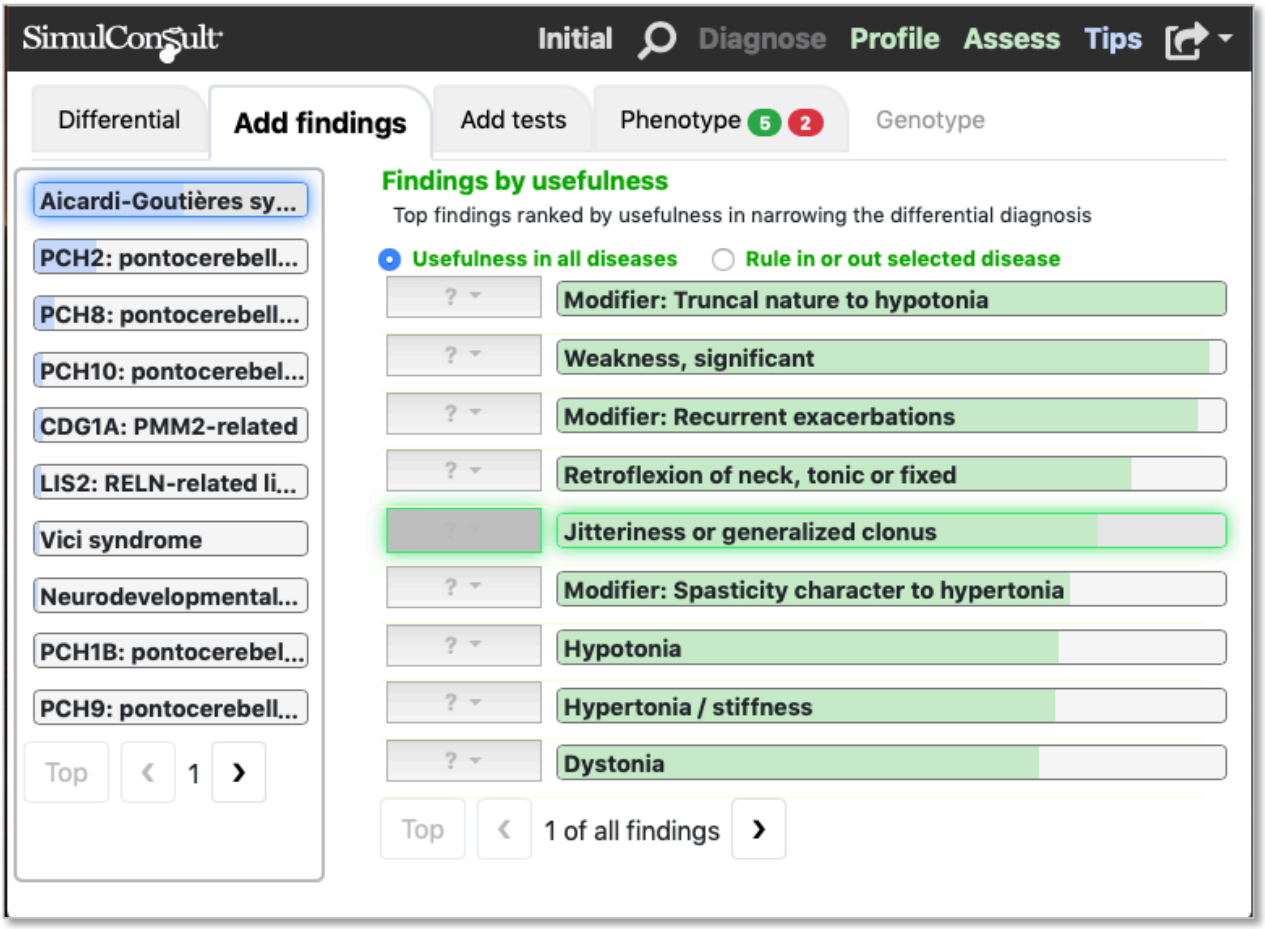


ADD FINDINGS BASED ON USEFULNESS

One of the key ways to use SimulConsult is on the diagnose screen with either the clinical finding or test results tabs. The software provides suggestions based on usefulness in narrowing the differential.

Add Useful Clinical Findings

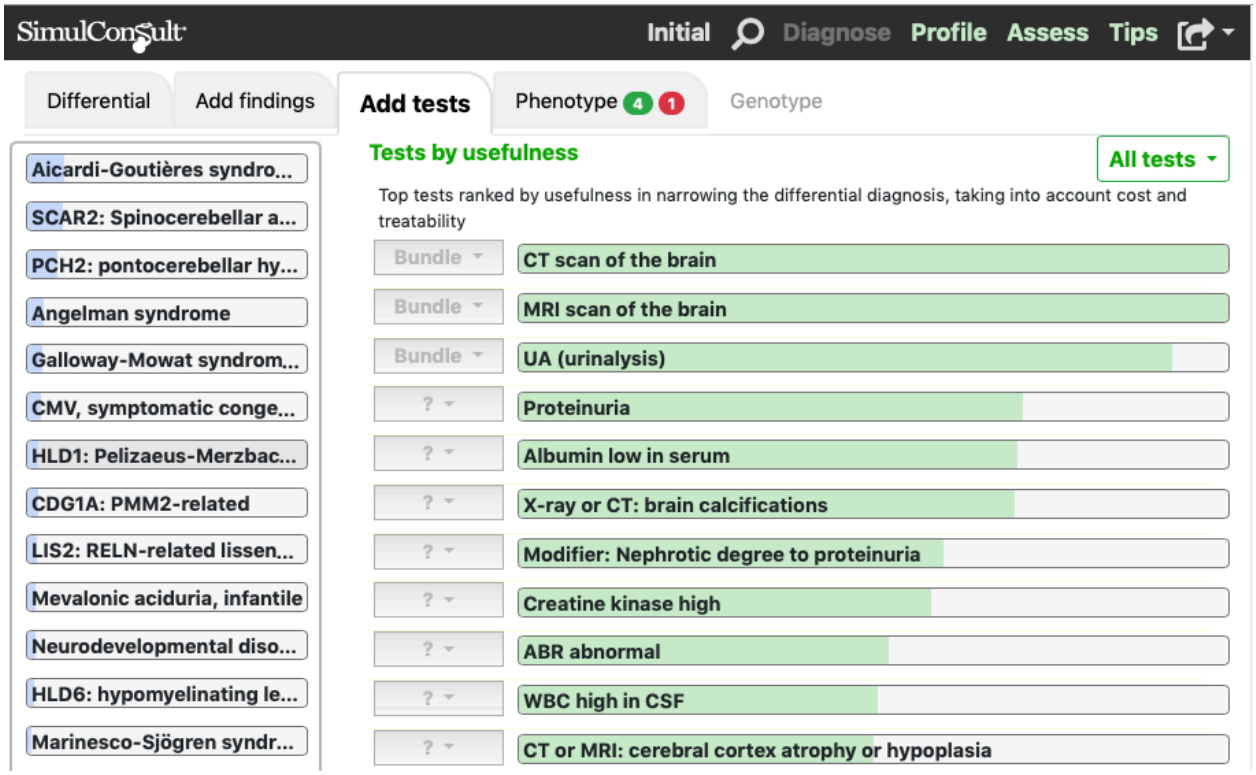
Figure 18: Add clinical findings based on usefulness



Add Useful Test Results

Here you can add test results you have, and you can learn which ones might be useful. The usefulness considers how much the result will narrow the differential diagnosis, and also, cost and any danger to the patient. It prioritizes low cost safe tests, where the results will make a difference.

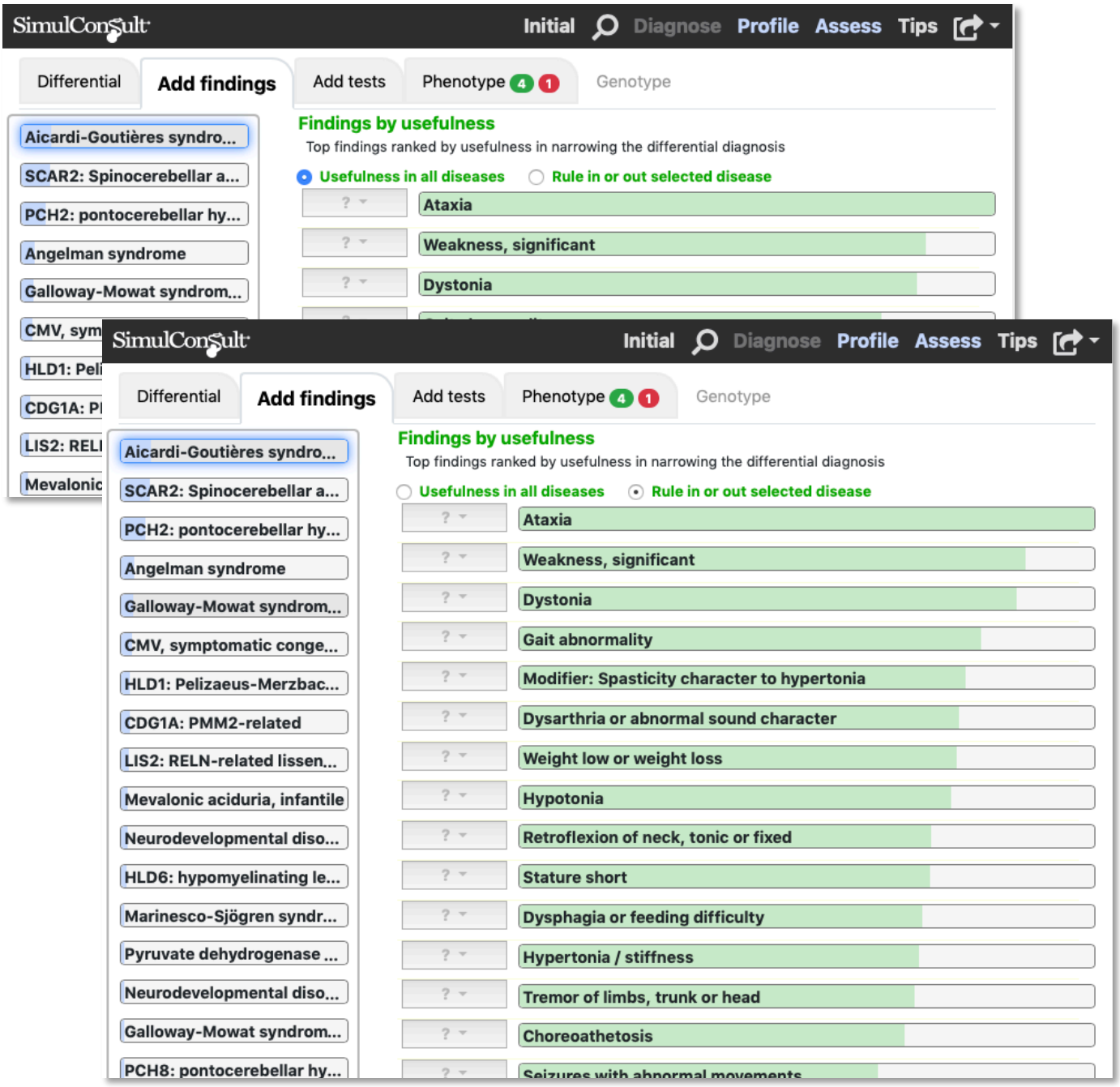
Figure 19: Add useful test results



Rule in or out a specific disease

Sometimes you want to rule in or out a disease high in the differential diagnosis. To do so, click to select the disease, and then you will be offered (on both Add findings and Add tests) the option to “Rule in or out selected disease” rather than the default of “Usefulness in all diseases”.

Figure 20: Use Rule in or out selected disease to narrow differential diagnosis



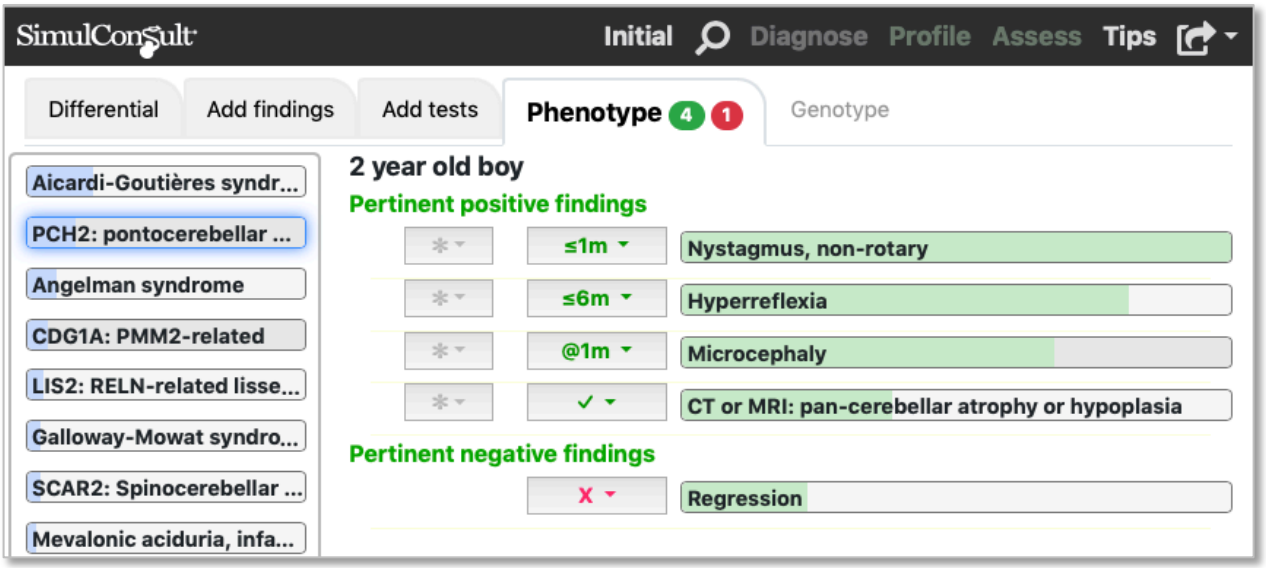
VIEW THE FINDINGS ALREADY ENTERED

To see the findings entered about this case, and their pertinence to the differential, click the "**Phenotype"** tab. The numbers on the tab indicate the pertinent positive and negative finding count already entered.

Note that by clicking the onset, one can always "un-specify" the finding to eliminate it from the patient findings by choosing "Not specified".

A mathematical representation of the common medical concept of "Pertinence" (as used in "pertinent positives and negatives") is represented by the green shading overlay on the patient's findings. Usefulness and pertinence are related concepts: pertinence is retrospective and usefulness prospective.

Figure 21: Phenotype of the patient



TIP
The higher the pertinence of the entered findings, the more important it is for you to be sure that the finding is reliably determined – since the high pertinence findings are (by definition) driving the diagnosis.

Get back to the "Core finding lists" and other search modes

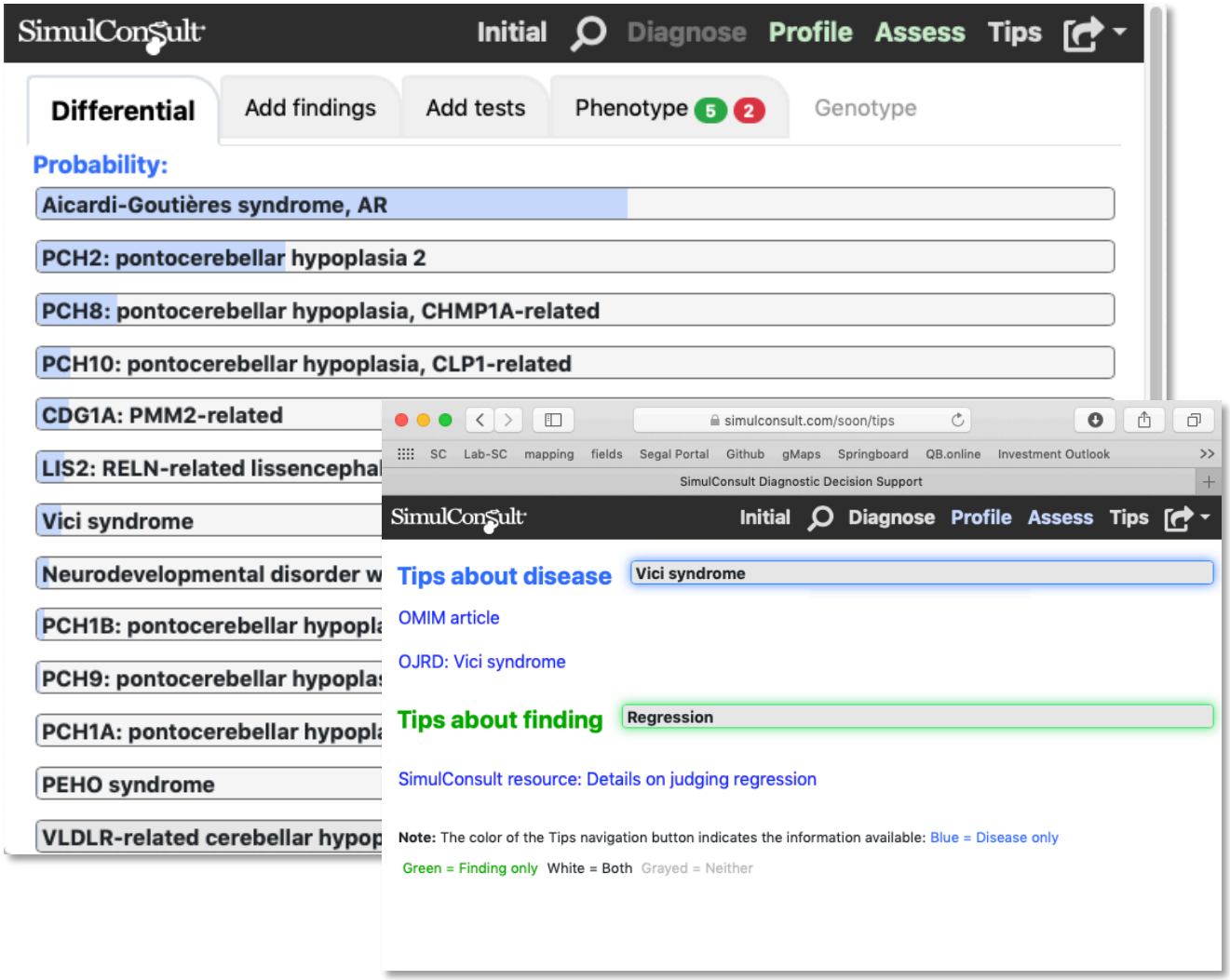
To return to Core finding lists or any of the other methods typically used for entering initial findings, click the search icon.

Contextual links

When you click on either the disease or finding, you can then access links to various resources with "Tips" at the top. Illustrated here is Vici Syndrome, and a link to a OJRD article and to OMIM. Since the last finding entered was Regression, one gets tips related to the finding. Clicking on a finding, and then Tips, gets Tips for the selected finding.

Regular sources include GeneReviews, OMIM (Online Mendelian Inheritance in Man), Orphanet, as well as many individual test books and articles. Links to disease associations, and various useful calculators are also included.

Figure 22: The user can click on a disease to show disease-related links

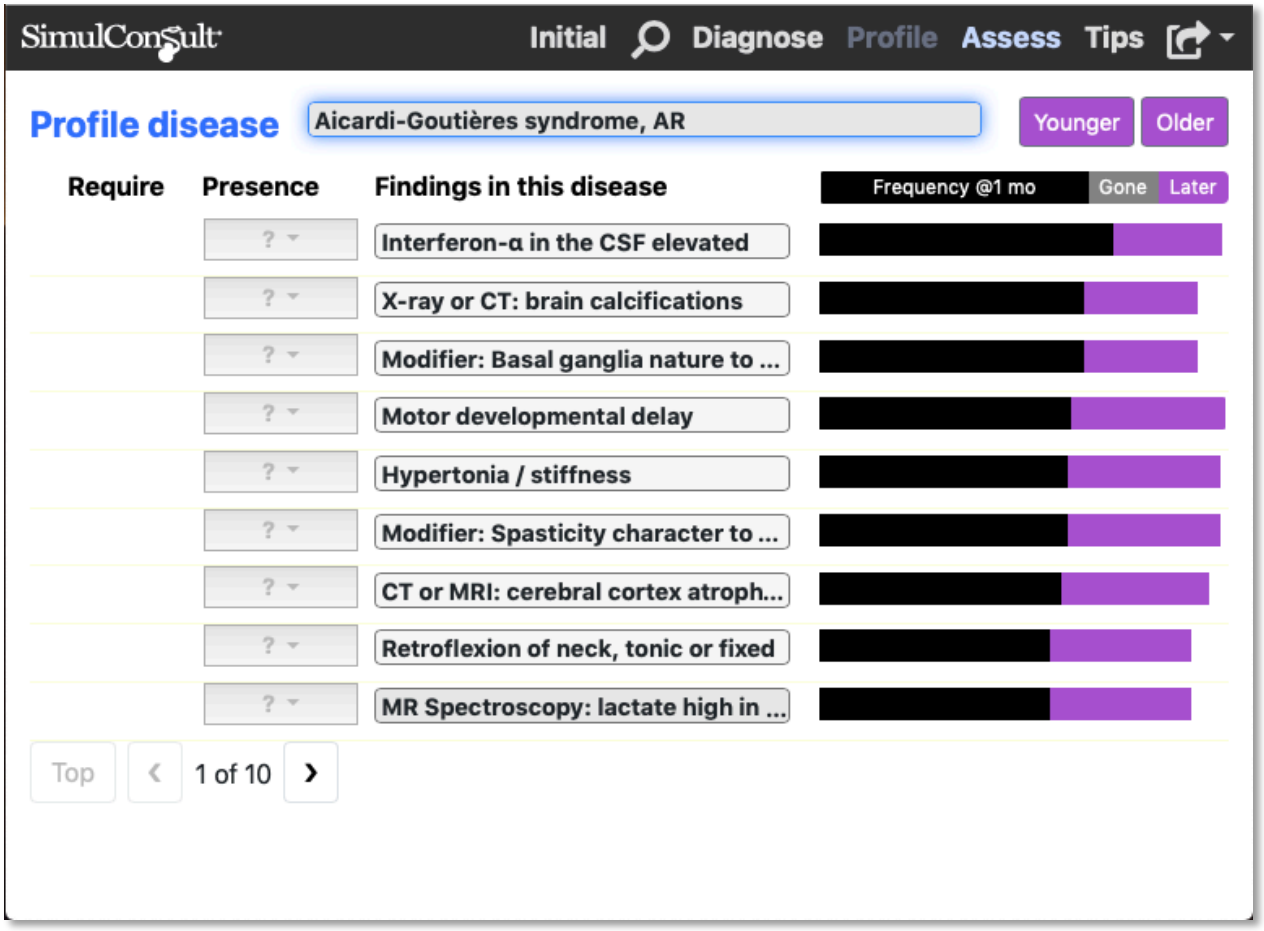


Profile Disease

If you click on a disease, you can get "**Assess"** and "**Profile"** screens.

Profile disease provides all the findings in a disease ranked by the frequency at the patient's age. Using the "younger" and "older" will allow rapid scrolling of those frequency at different ages.

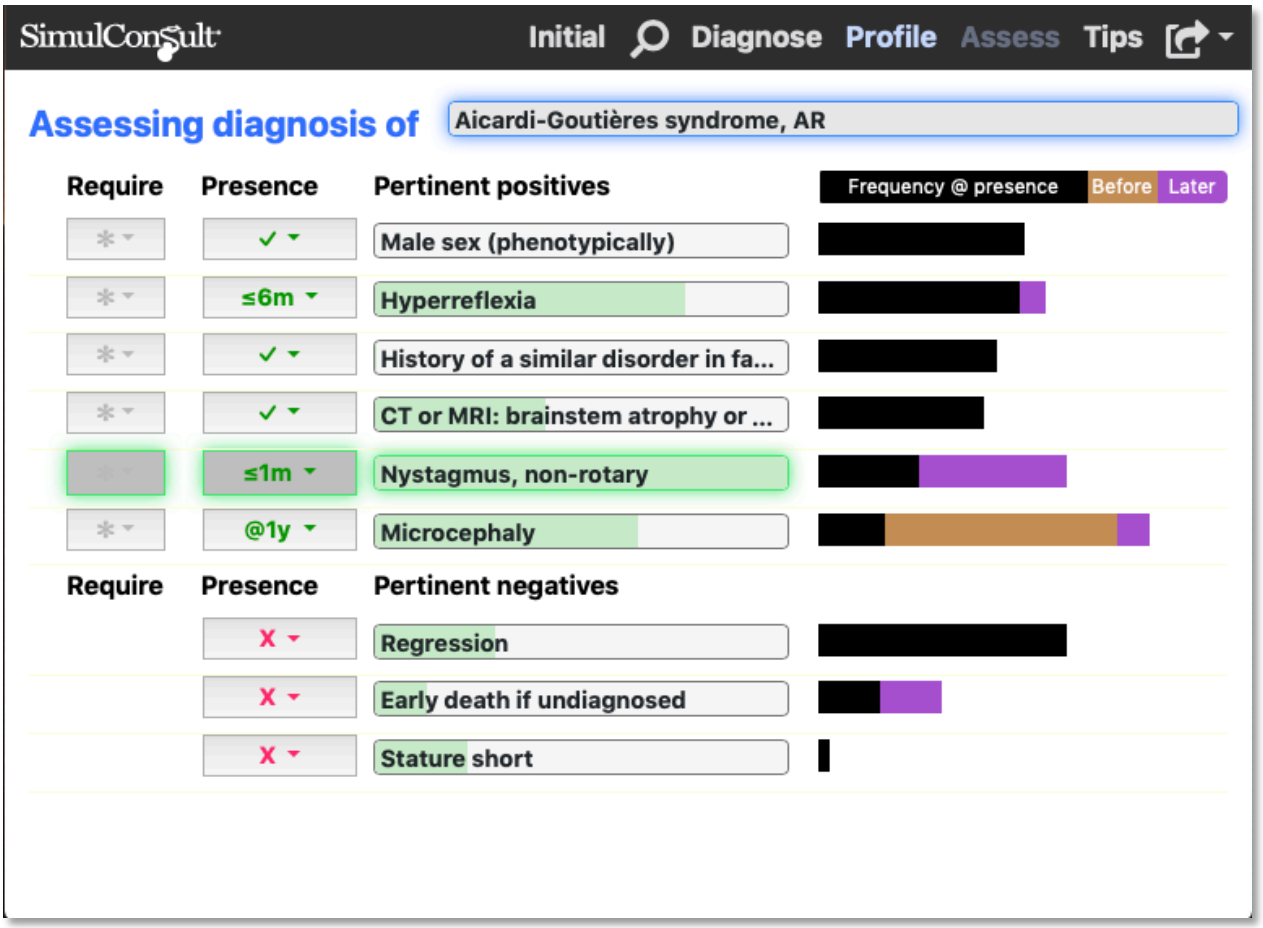
Figure 23: Profile Disease



Assess disease

Assess disease shows the fit of the patient's findings (positive and negative) with the disease. One can scroll down the differential to evaluate how good a case has been made for the diagnosis.

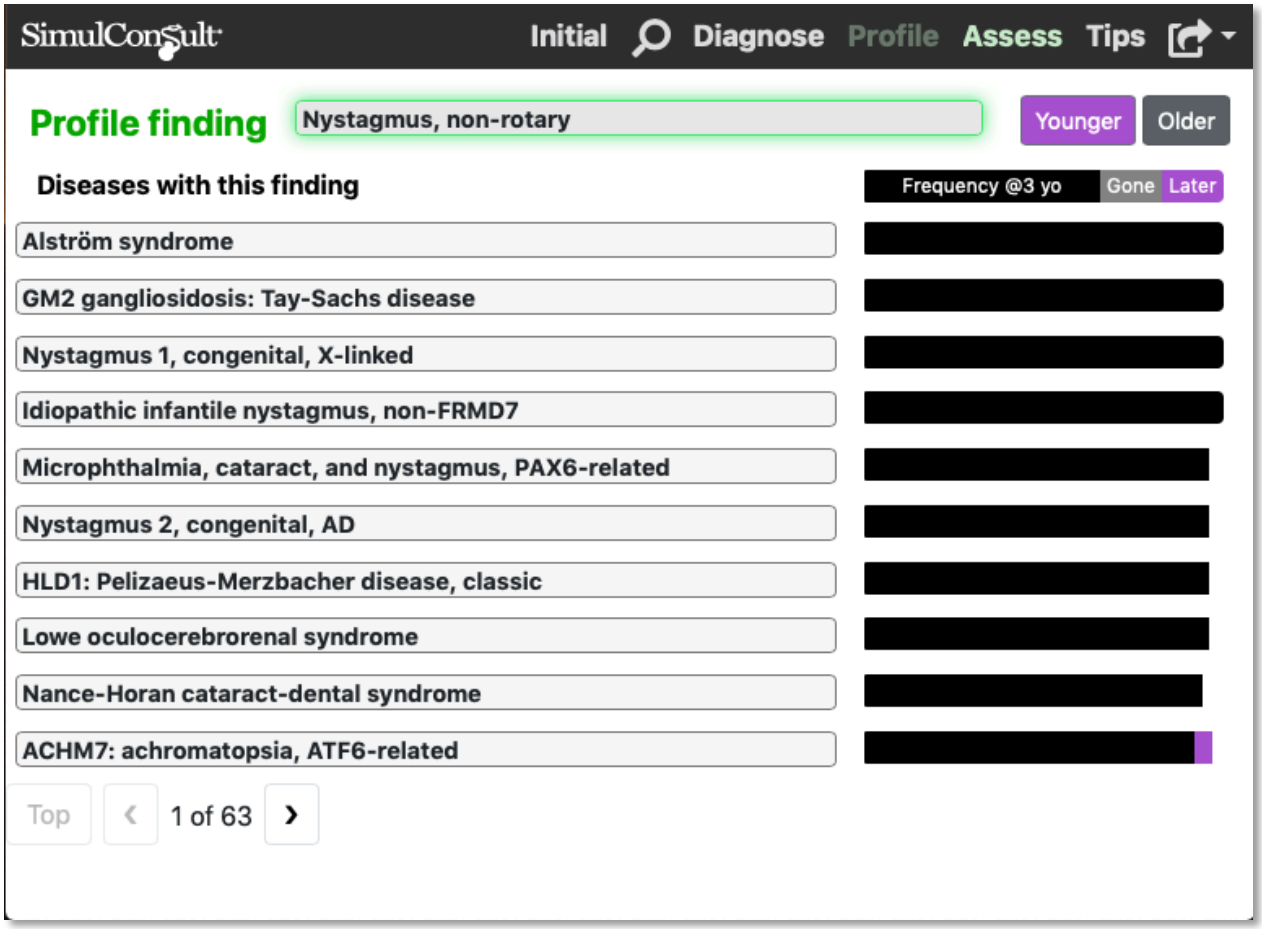
Figure 24: Assess Disease



Profile finding

Similarly, if you click on a finding, you will be offered choices related to the finding selected. By clicking on Nystagmus the "**Assess**" and "**Profile**" options appear. The Profile is in all diseases and the Assess is in the differential.

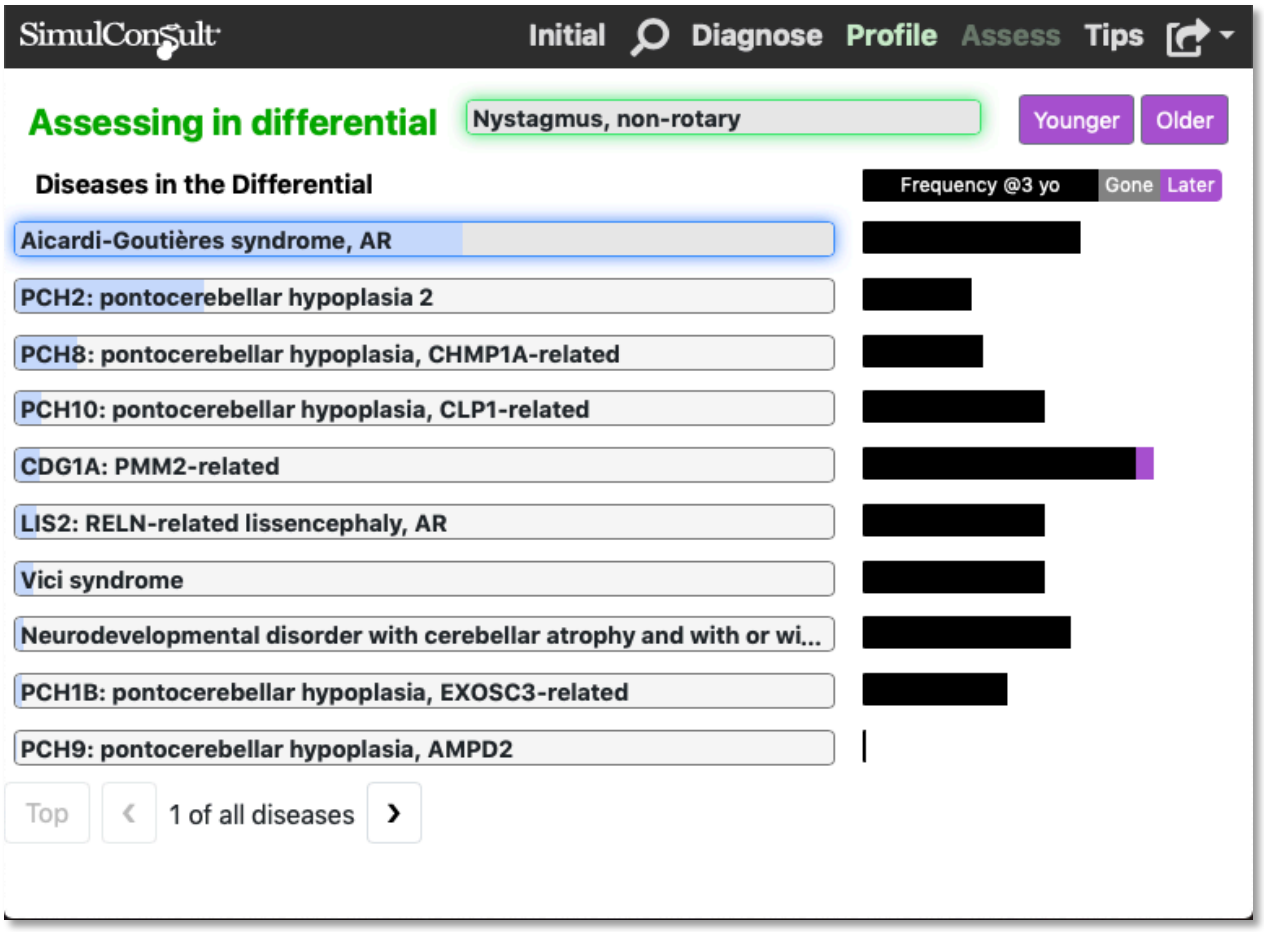
Figure 25: Profile Finding



Assess finding

Assess finding looks at the frequency of the selected finding in the diseases in the differential diagnosis.

Figure 26: Assess finding



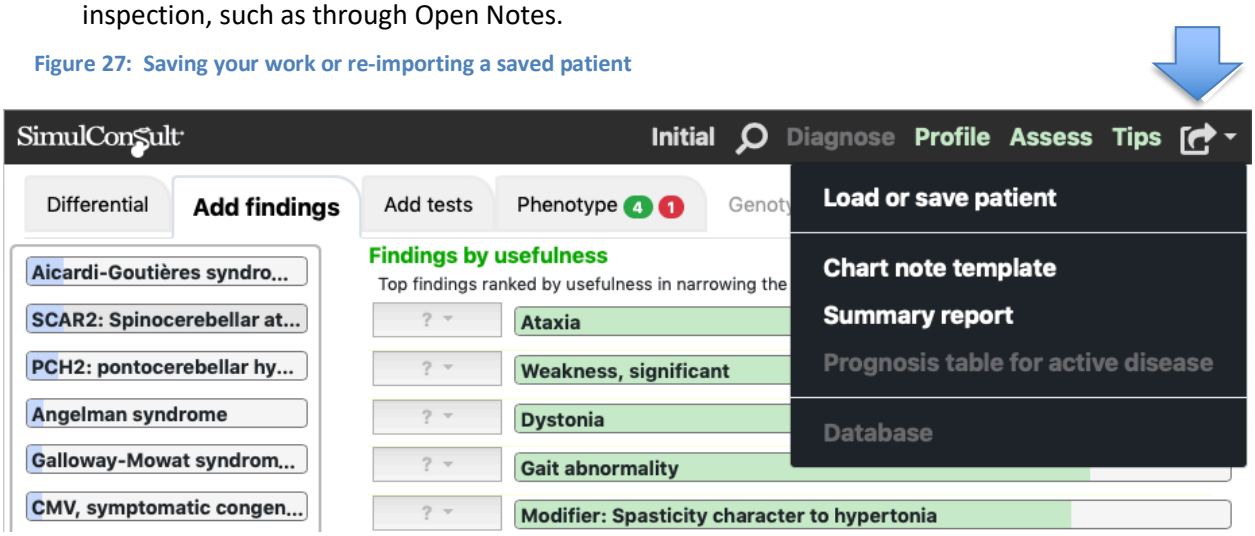
SAVE AND REOPEN PATIENT HISTORY

Output options

The software has three key outputs:

1. **Summary:** The Summary, a human readable "Informatics Lab Report" that provides a snapshot of the patient's findings as they were entered and run against the database with a particular date stamp. The display includes the pertinence of each finding and the likelihood of each disease in the Differential Diagnosis, as well as recommended tests.
2. **Text string:** SimulConsult has created special codes (in the form of a text string) that allow you to reopen SimulConsult with the previously entered findings already present. (Note: In the version of SimulConsult accessed from the cloud, the Summary is machine-readable because it has the text string embedded in it).
3. **Note:** The Note is in the classic "subjective, objective, assessment, and plan" (SOAP) note format used in clinical medicine. In the version of SimulConsult accessed from the cloud, it outputs a file that can be copied and pasted into a medical record as plain text and then edited. It also contains the text string that can be saved. Note: since only medical professionals may have direct access to SimulConsult it is not advised to put the text string in the note, if notes are open to patient inspection, such as through Open Notes.

Figure 27: Saving your work or re-importing a saved patient

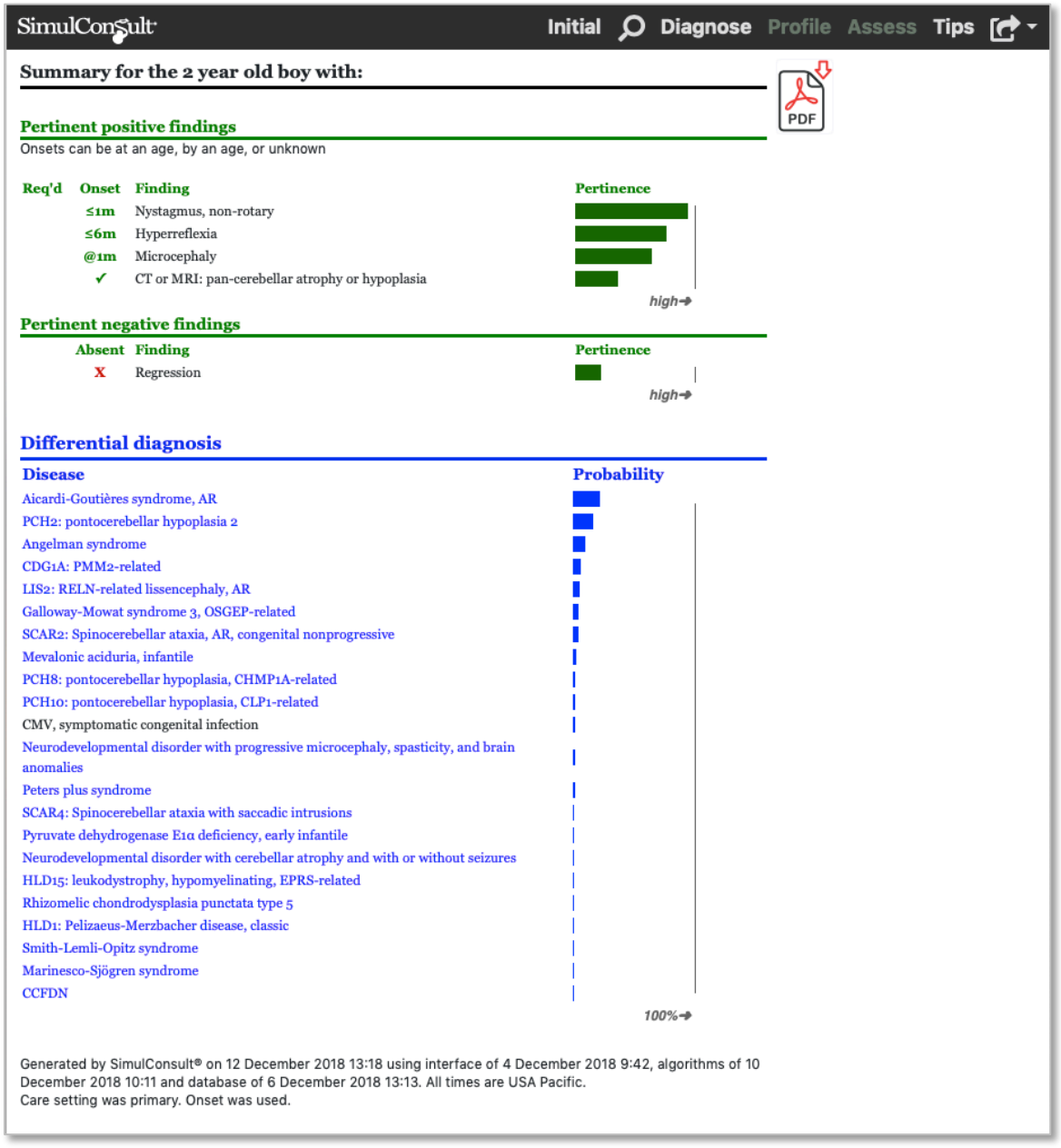


In addition, some coded outputs are possible within the Enterprise offerings.

Save the "Summary"

Select "**Summary report**" and then download the PDF to save to your desktop or the EHR. Note: this produces a version that is both human readable and also can be reopened and read by the software.

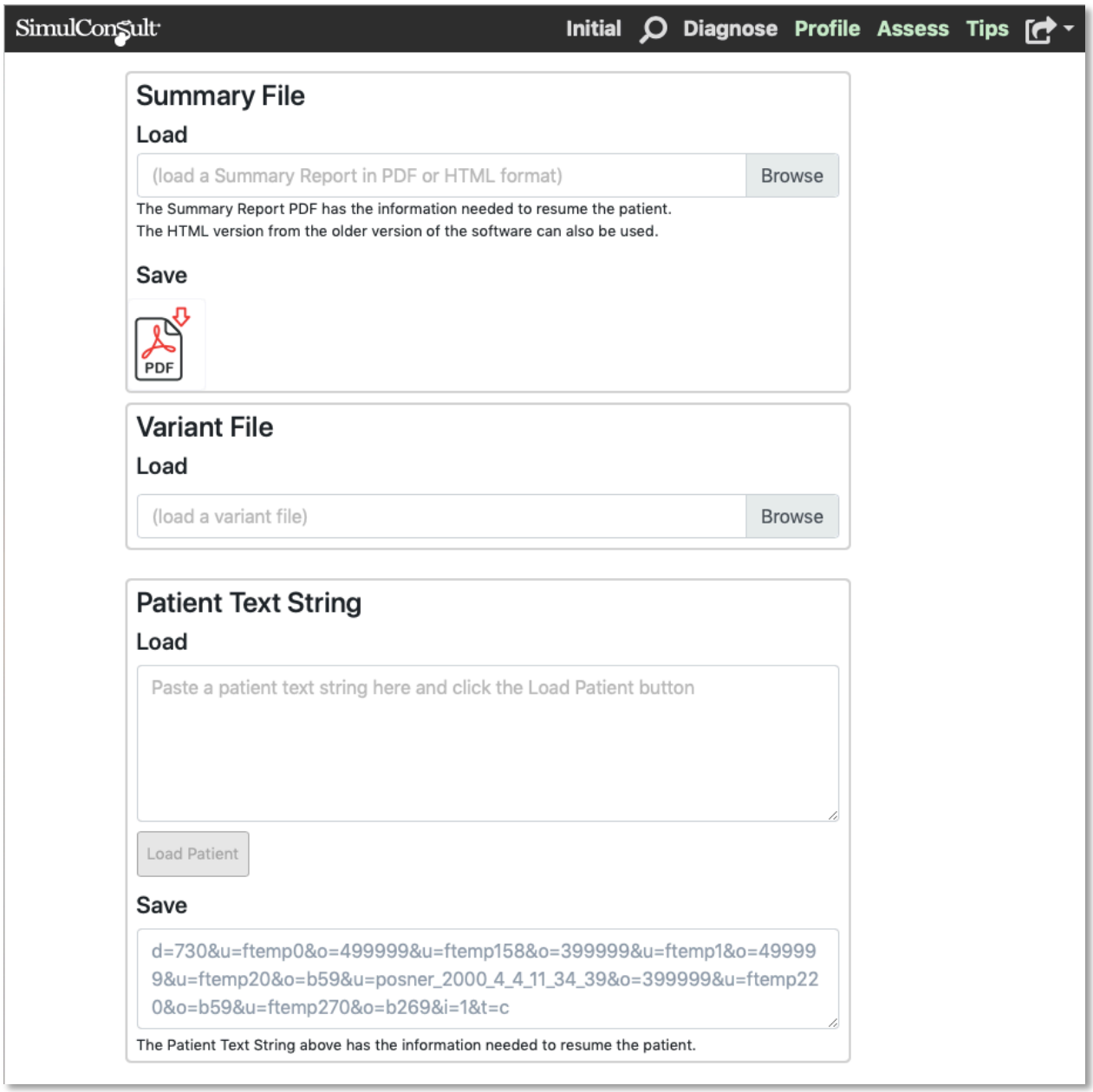
Figure 28: Generating the Patient Summary



Save the “text string”

Click **Load or save patient** and highlight the text in the bottom box to save it. Various APIs allow this information to be passed to other applications.

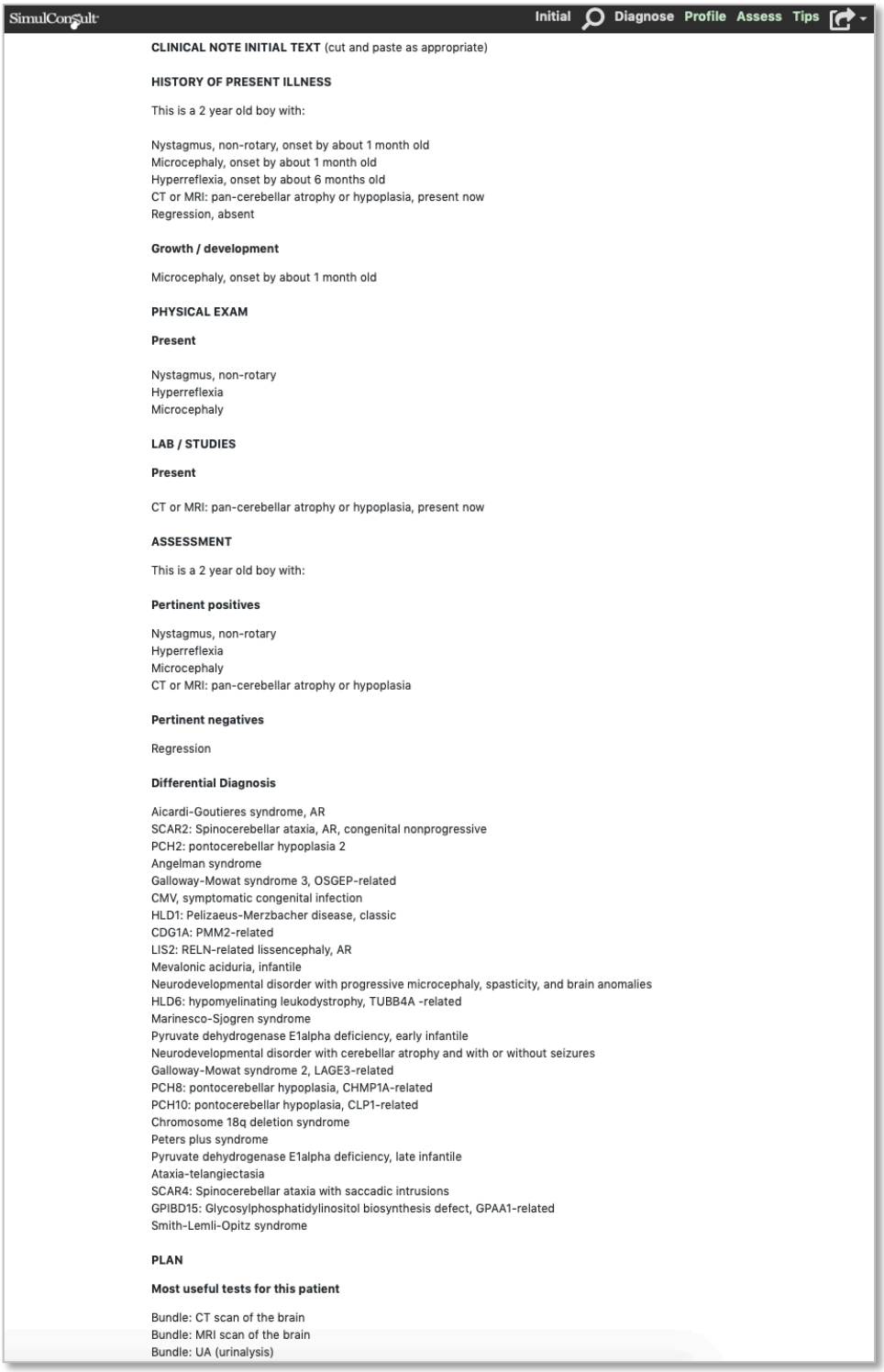
Figure 29: Load or save patient via a text string



Save the “Note”

This generates the raw text for a classic note, although in list form rather than prose.

Figure 30: Saving the Note, with sections for History, Assessment and Plan

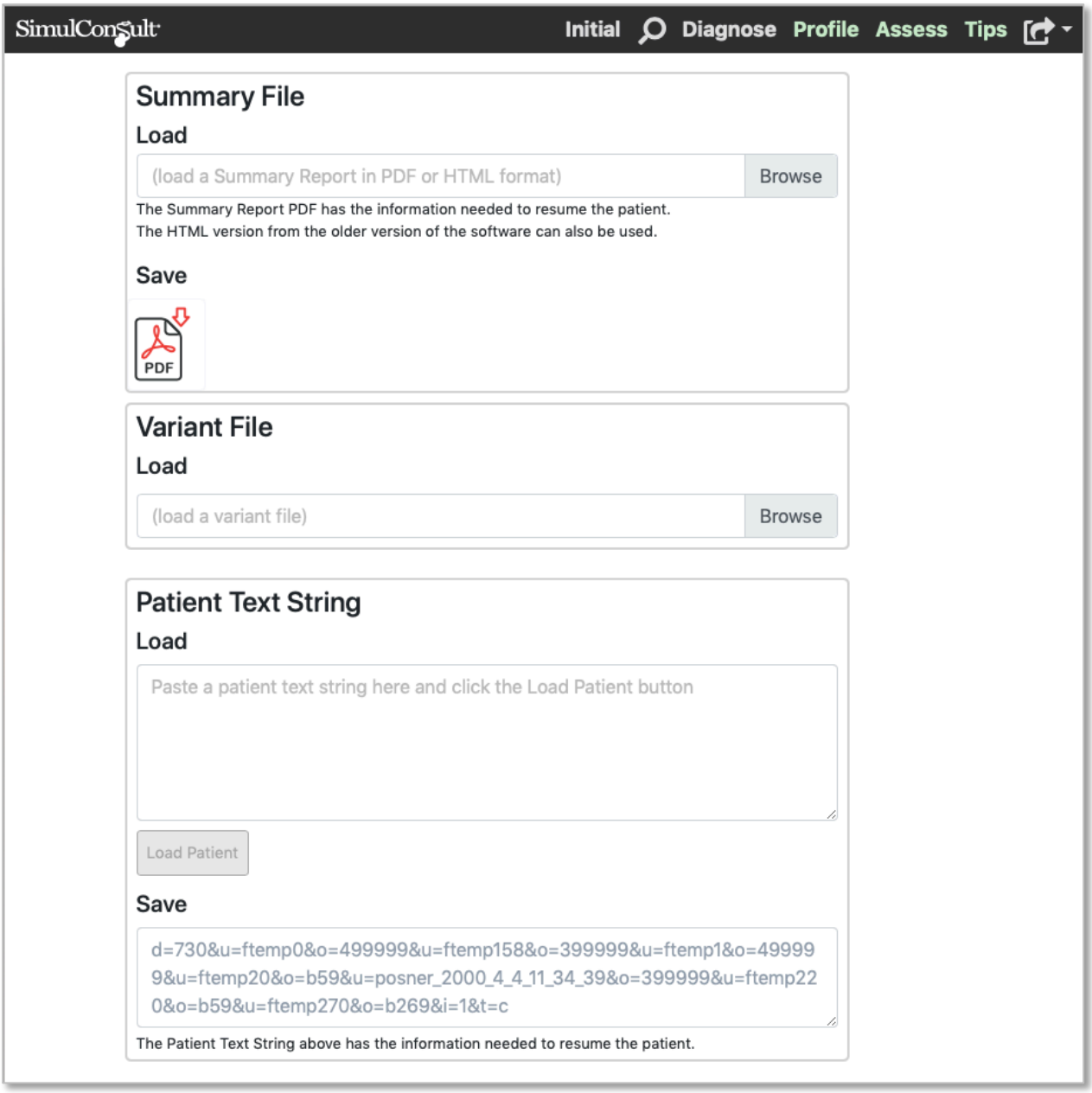


Open previously saved findings

Some users separate the task of collecting and entering clinical findings from subsequent interpretation or sharing with the lab. The tasks may be divided among people or by time.

In some radiology and genomics labs, some users are exploring ways to get the referring clinician to submit the Patient Summary as part of the referral, so that the clinical picture can include the most robust information about findings. In any of these scenarios, as well as one where you just need to save your work and come back later, you can reopen a patient summary easily.

Figure 31: Load patient data



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