The main document that is returned to the physician is the “TreatmentDocument”, this document contains the suggested drug, that is connected to its toxicity information, as well as the cohort information on the studies that recommend the drug. The steps it follows to answer this question is as follows.

First, a patient’s profile is input into the system, we use the diagnosis guideline detailed in the second chapter of the ADA guideline to diagnose the patient (that is the Hemoglobin A1C level, Fasting Plasma Glucose levels), we also take into consideration the presence of comorbid conditions and drug contraindications while generating a recommendation, for example, metformin the first line of treatment for diabetic patients, but patients with renal disorder have to be placed on other drugs. All these details are encoded within the ontology, and for a given patient the recommended pharmaceutical intervention is obtained following the ADA guideline.

For each suggested drug, toxicity information is returned to the user. However, to have a more comprehensive understanding of the toxicity, the system returns the toxicity of not only the suggested drug, but also a drug similar to it by target and target mechanism. This is assuming that a drug with the same target and interaction to its target, also has similar toxicity. To do this, the system finds a similar drug by target and target mechanism to the suggested drug, and returns the toxicity information of it too. Thus, each instance of a Drug class hasSimilarDrug, hasTarget and hasTargetMechanism – to find the similar drug, as well as hasToxicity – to relay the toxicity of both the suggested drug and the similar drug. The toxicity information contains information on the study the toxicity was found in (isStudiedIn “Research Study”), the species the toxicity was found to effect (impacts “Species”), and the associated dosage level (associatedWithDosage: Low/Medium/High) of the toxicity found. In this manner, a comprehensive toxicity possibilities of a suggested drug and its similar drug is returned to the user.

Finally, the system also returns the cohort information, connected to the suggestions the system makes. Each suggested drug is found by connecting a patient’s characteristics to previously studied clinical trials and research studies. However, each study is conducted on a specific group of people – a cohort. Thus, the system compares this cohort to the patient in terms of demographics, to give an indication of how related the research study that suggests a drug really is to the patient.
Q. What is the recommended pharmaceutical intervention for patient Sam?
Q. What is the recommended pharmaceutical intervention for patient Sam?

The following are the steps to return the pharmaceutical intervention for any given patient?

In order to obtain the drug for a patient, the system first looks at the patient's hemoglobin A1C level and ensures it is greater than 6.5 according to the ADA guideline. This ensures that the given patient has diabetes mellitus. After the diagnosis has been confirmed, the system begins to reason about the pharmaceutical interventions for the patient firstly by categorizing the patient into his/her drug subplan, that is if the patient is in monotherapy, dual therapy or triple therapy. After the subplan is identified the comorbidities and/or contraindications are identified, as the presence of any of these will greatly affect the type of drug available to the patient. The ADA guidelines provides recommendations for several common comorbid conditions such as hypertension, neuropathy, nephropathy, stroke, obesity and so on. They also take into consideration the patient’s estimated glomerular filtration rate (eGFR) and the cardiovascular risk before the make recommendations. The contraindications for the drugs are outlined in table 8.1 of chapter 8 of ADA guidelines. Finally, the system obtains a recommended drug for the patient by following the recommendations described within chapter 8 of ADA standards of care guideline.
Q. What are the toxicities to Metformin and to drugs similar to Metformin?
Q. What are the toxicities to Metformin and to drugs similar to Metformin?

The following are the steps to return toxicities of a suggested drug and a drug similar to it by target and target mechanism.

In order to answer this question, first a similar drug to a suggested drug needs to be found. To help with this, the drugs are classified by two methods, one by FunctionBasedDrug – the classification by function of the drugs based on the ADA guidelines, and by TargetBasedDrug – classification by primary target of the drug, by the gene that encodes the protein it target based on the Kyoto Encyclopedia of Genes and Genomes (KEGG). Then each drug in the drug class is connected to a primary target (from KEGG) and a target mechanism (from DrugBank) in relation to this target. For instance, for the drug Metformin (instance of class Biguanide and AMPKDrug), it has a primary target of AMPK (instance of class CAMKLFamily), and a target mechanism of activate – in other words the drug Metformin activates its primary target AMPK, a protein kinase. For our purposes of augmenting to the toxicity information, we thus define a similar drug in terms of toxicity as one that has the same target and connected target mechanism, thus by a SPARQL query we are able to find that Phenformin (an instance of AMPKDrug) has both the same target (AMPK) and target mechanism (activate) as Metformin, and thus by a SPARQL query a triple is constructed :Metformin :hasSimilarDrug :Phenformin.

Now that we have the suggested drug and its similar drug, all of their toxicity information is stored in the Toxicity class. This contains cardiotoxicity, renal toxicity, and any Physical Adverse Events found for humans administered with this drug (ADA – for suggested drugs, PubChem – for similar drugs). Furthermore we can find out what dosage level (low, medium, high) a certain toxicity is associated with, from the data property of this class: associatedWithDosage, as well as the Research Study this toxicity was found in, and the Species this toxicity impacted. Thus, when a physician queries for a suggested drug from the treatment document, and are case, Metformin, connected to it is its similar drug (Phenformin), and all the toxicities of both it and its similar drug, to give the physician a more comprehensive understanding of the possible toxicities of Metformin.
Q. Do the ADA guidelines cover a diverse population, such that an African American diabetic patient on Metformin, can receive a recommendation?

The following are the steps to return descriptive statistics of the racial spread of patients utilized as study populations within research studies cited in the Chapter 8 of the ADA Standards of Care Guidelines. The above competency question and our focus for this project is on research studies, which administer Metformin as a form of medical intervention to treat diabetic patients.

In order to answer this question, first we identify the race of the patient whom the physician wants to ascertain a fit for amongst study populations. The patient is identified as an African American, and a query is framed which looks for African American population representations within study groups (PatientGroup). A ResearchStudy can contain multiple PatientGroup’s distinguished by study interventions and these are all collectively grouped within a Cohort. Patients within a study group (PatientGroup) share a set of characteristics which are broadly {AnthropometricProperty, Demographic, OrderedLaboratoryTestResult}, some Disease (sometimes Comorbid conditions) in addition to Diabetes Mellitus, and are administered MedicalIntervention in the form of Medication and Therapy. Since our recommendation system suggested Metformin as a form of medication for Sam, a physician who is also made aware of the Toxicity in terms of PhysicalAdverseEvent of Metformin, would want to delve deeper into the patient population utilized in the ClinicalTrial detailing the Long-term effects of Metformin. A query chain in this case is triggered on the path of ClinicalTrial – Cohort – PatientGroup – Medication – Race – AfricanAmerican, to retrieve percentage of AfricanAmerican patients administered Metformin as medication, and who are studied in the Long-term VitaminB12 effects of Metformin ClinicalTrial. Sometimes the characteristics of the population being queried for are not represented within the study, and in this case the system provides alternative ResearchStudy to the physician.

So under the closed-world assumption, a physician is shown that the percentage of AfricanAmerican patients in the Long-term effects study is 0. Another query is triggered to find the overall racial spread, in the only other ResearchStudy instantiated and which also administers Metformin as medication with Conventional Therapy to patients. A physician is shown percentage descriptions against each racial group employed as a part of the larger study group. During our modeling and deep dive into population descriptions of research studies cited in the ADA guidelines, we have seen that fractional measures and values like percentages tend to subset patient groups. For instance a subset of patients studied used for the 10 Year Follow Up Study were of African American descent, 7.4% to be precise. We have another alternative approach of instantiation on the same cohort portion of the concept map which leverages the natural notion of owl:Class as sets, and hence makes it easier to define study groups as XStudyPatient a owl:Class, rdfs:subClassOf dbt:Patient.

The cohort similarity to a patient can help the physician determine the applicability of evidence to his/her patient, and if not help identify a gap that the patient falls through within the guideline.