

Evaluation, Validation & Implementation  
of a  
Computerized Diagnostic Decision Support System in  
Primary Practice

By

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Evaluation, Validation, and Implementation  
of a  
Computerized Diagnostic Decision Support System in Primary Practice

A  
Translational Project Paper

Presented to the Faculty of  
The University of Texas  
Health Science Center at Houston  
School of Biomedical Informatics  
in Partial Fulfillment of the Requirements for the Degree of  
Doctorate in Health Informatics

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2022

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## Acknowledgments

- Doctorate in Health Informatics Committee
  - Robert E. Murphy, MD
  - Amy Franklin, Ph.D.
  - Hardeep Singh, MD, MPH
- Doctorate in Health Informatics Program
  - Susan Fenton, Ph.D.
  - Angela Ross, DNP, MPH, PMP, PHCNS-BC
  - Deborah Simmons, Ph.D., RN, CCNS, FAAN
- Baylor College of Medicine
  - Ashley N. D. Meyer, Ph.D.
- UTPhysicians
  - Martin J. Citardi, MD
  - Carmel B. Dyer, MD (Deceased)
  - Kevin O. Hwang, MD
  - Eric J. Thomas, MD
  - Thomas J. Murphy, MD
  - Holly Holmes, MD
  - Babatope O. Fatuyi, MD
  - Jeffrey W. Chen, MD
  - Rohit V. Goswamy, MD

- UTHHealth
  - Giuseppe Colasurdo, MD, President
  - Michael Blackburn, PhD, EVP
  - Jiajie Zhang, PhD, Dean, School of Biomedical Informatics
  - Kevin Dillon, MBA, CPA, Sr.EVP & COO
  - Amar Yousif, MBA, VP & CIO
  - Dr. James Griffiths, MD
- University of Michigan Medical School, Department of Learning Health Sciences
  - Dr. Charles P. Friedman

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## Abstract

### Evaluation, Validation, and Implementation of a Computerized Diagnostic Decision Support System in Primary Practice

**Background:** Medical diagnosis may be the most complex task attempted by humans. Studies estimate that 95% of diagnoses in outpatient care are accurate, implying that the annual rate of inaccurate diagnoses is 12 million in the US alone, with the potential for patient harm in about half. A well-researched differential might reduce inaccurate diagnoses by offering alternatives matching the patient's symptoms. This study searched the literature for articles evaluating the diagnostic performance of commercially available computerized diagnostic decision support systems. This search led to selecting Isabel Pro, developed by Isabel Healthcare, Ltd. of Haslemere, UK.

**Evaluation and Validation:** A computerized diagnostic decision support system should respond adequately to four questions: What is the "diagnostic retrieval accuracy"? Does it perform as well as clinicians? When provided with the differential, do clinicians improve diagnostic accuracy? Is it easily incorporated into routine practice?

The project validated the diagnostic retrieval accuracy of Isabel Pro using 46 cases with a previously confirmed diagnosis. The confirmed diagnosis appeared in Isabel Pro's differential in 24 cases (52.2%), outperforming even internal medicine faculty (47%).

Using those 24 cases and the differentials produced, the author conducted a diagnostic challenge that involved 120 McGovern Medical School residents. The residents produced 406 diagnoses, of which 105 (25.9%) were correct without the differentials, and 37 were correct post-consultation, a 9.1% absolute improvement. In responses, 75.1% of the participants agreed the

differentials would be helpful in routine practice, and 64.1% agreed they would consult the differentials if available.

**Implementation:** The project successfully proposed Isabel Pro as a solution to UT practice leadership on September 16, 2021, and incorporated the system into the Epic EHR as a menu line link on November 30, 2021. This system-wide integration also included a QR code for downloading Isabel Pro to a mobile device. Usage of Isabel Pro in the practices of UT Physicians began on December 8, 2021.

**Results:** The project concluded data collection after 86 days on March 4, 2022, with usage showing a steady increase in the final three weeks. The project produced 73 unique users (37 faculty and 36 residents). The user survey responses showed 83.3% agreeing they would consult the differential generated by Isabel Pro if available at every patient encounter (+19.2% compared to the challenge survey) and 77.8% agreeing that the suggestions would be helpful in routine practice (+2.7% compared to the challenge survey). More than one-third (36.8%) responded that they changed their diagnosis in response to the differential.

**Limitations:** Only usage statistics were analyzed; the system records no reason for the clinician discontinuing a diagnostic session. Only 20 participants responded out of 73 (27.4%), so even though the respondents represented a spread of experience levels, the results may not represent the total number of potential users. The project covered a limited period of 86 days.

**Conclusions:** Diagnostic inaccuracy is a significant patient safety concern. Studies show that computerized diagnostic decision support systems improve diagnostic accuracy, but they are not wide implementation lags despite these findings. This project demonstrated the feasibility of implementing such a well-known system in academic medical practice. The responses to the

surveys demonstrate favorable opinions about the system's perceived usefulness. Active communication and dissemination programs may be essential to improve and sustain use.

## Section 1: Introduction

According to the World Health Organization, the prevalence of inaccurate diagnoses in today's healthcare system is among the world's most critical patient safety issues (World Health Organization, 2021, p. 77). Estimates of diagnostic accuracy in primary or outpatient care in the United States and the United Kingdom vary. However, well-researched studies suggest a figure between 95% and 96% (Singh et al., 2014, p. 3; Cheraghi-Sohi et al., 2021, p. 5), leaving inaccurate diagnoses at roughly 12 million annually in the US and 15 million in the UK, half of which are estimated to result in patient harm, even death. This estimate implies that one of every twenty patients may be inaccurately diagnosed, with patient harm accruing to half of those inaccurately diagnosed patients.

An earlier study noted that in 74% of the cases of an inaccurate diagnosis, all the elements necessary to reach an accurate diagnosis were present at the initial encounter. Further, of those cases of an inaccurate diagnosis, only one out of five documented a differential diagnosis listing in the clinical record. (Singh et al., 2013, p. 3). A comprehensive differential diagnosis listing would likely improve the diagnostic accuracy of almost any diagnostician. However, as the study suggests, such a listing is infrequently prepared in today's busy primary care practices, and, even if prepared, the clinician has no place to record it in the electronic health record. (Berner & Graber, 2008, p. 11). This project aims to evaluate, validate, and select a commercially available diagnostic decision support system and then implement that system in the primary care and outpatient medical practices of UTPhysicians. The goal is that by using only the patient demographics, chief complaint, symptoms, signs, medications, and medical history available at the outset of the physician-patient encounter, the diagnostician might be

presented with a well-researched differential diagnosis listing allowing consideration of likely diagnoses that might be alternatives to an early, possibly premature, conclusion.

Diagnosis is one of the most, if not the most, complex tasks attempted by humans. (Newman-Toker & Makary, 2013, para. 4; Graber, 2021, p. 1). A relatively small set of signs and symptoms (roughly 200) appear in many diseases (more than 10,000). There are numerous definitions of an inaccurate diagnosis, but there is no single, generally accepted definition for an inaccurate diagnosis, and there exists much disagreement about what constitutes an inaccurate diagnosis (Olson et al., 2018). Further adding to the disagreement, the often-used term “diagnostic error” conveys a lack of competence or a sense of irresponsibility on the part of the diagnostician that is unhelpful to the detection, prevention, and learning feedback process necessary to deal with the matter effectively.

Inaccurate diagnoses or missed diagnostic opportunities are, as mentioned earlier, far more common in primary care medical practice than is generally acknowledged. However, unless the diagnostic error results in identifiable patient harm, the inaccurate diagnosis typically goes unnoticed, especially in delayed diagnosis of progressive conditions, such as colorectal cancer (Singh et al. 2014). Many malpractice claims, both those adjudicated and the out-of-court settlements, are judged attributable to inaccurate diagnoses, many of which were preventable, had the physicians not ignored the guidance of the diagnostic decision support systems already in place (Schiff et al., 2013). Despite this, in the literature research for this paper, the author has yet to find evidence of any institutional, well-researched, widely used program to detect, prevent, and give physicians feedback on instances of inaccurate diagnosis. In a 2018 article by Drs. Olson, Graber, and Singh, the authors observed:

“Multiple national health care and governmental organizations have recently identified the need to improve diagnostic safety as a high priority. A major barrier, however, is the lack of standardized, reliable methods for measuring diagnostic safety....Multiple approaches have been suggested but none widely adopted.” (Olson et al., 2018, p. 1)

The seminal study on inaccurate diagnosis was the treatise published in 2015 by the Institute of Medicine’s Committee on Diagnostic Error in Health Care, entitled *Improving Diagnosis in Health Care*. (Balogh et al., 2015). Inaccurate diagnosis was characterized as a decades-long blind spot in healthcare delivery, expressing the opinion that each of us would suffer an inaccurate diagnosis of meaningful consequence in our lifetimes. Considering the United States population of 320 million, averaging a lifespan of 80 years, the implication is 4 million meaningful inaccurate diagnoses annually, an estimate only slightly more conservative than the 2014 Singh et al. study.

Several thorough articles, discussed more fully in Section 2 of this report, support the potential for reducing inaccurate diagnoses using a diagnostic decision support system (Henderson & Rubin, 2013; Barbieri et al., 2015; Riches et al., 2016; Sibbald et al., 2021). Several other well-researched studies show a small but statistically significant improvement in physicians' diagnostic accuracy when using a diagnostic decision support system. (Friedman et al., 1999; Kostopoulou et al., 2015; Kostopoulou et al., 2017; Sibbald et al., 2021). Studies of malpractice claims suggest a demonstrable improvement in the physician's diagnostic accuracy when using clinical decision support. (Schiff et al., 2013; Zuccotti et al., 2014).

Another difficulty for any physician is staying current with the best in evidence-based scientific research, a challenging, if not virtually impossible, task given the rapid pace of new



research produced every year, much of which disagrees with or at least brings into question earlier recommendations. (Delaney & Kostopoulou, 2017). The need to remain abreast of current developments in evidence-based medicine is where diagnostic decision support systems offer a window of opportunity for accomplishing this vital task. Today's systems use the latest in search technology to interrogate peer-reviewed clinical literature sources that are routinely and frequently updated to produce diagnostic alternatives that are current and clinically relevant. Web-based diagnostic decision support systems provide accurate and relevant diagnostic alternatives (an electronically prepared differential diagnosis list), improve physicians' diagnostic accuracy, perform as well as clinicians, and are hampered mainly by the absence of smooth integration with the electronic health record (Riches et al., 2016; Graber et al., 2017; Segal et al., 2017; Cheraghi-Sohi et al., 2020).

Computerized diagnostic support systems are not universally used or even widely used in routine clinical practice. Dr. Mark Graber, in October 2021, devoted his entire editorial to the issue of the broader use of computerized diagnostic decision support systems and lamented the underutilization of them by clinicians in the real world of patient diagnosis in their practices. Dr. Graber noted:

“Especially in view of their potential to improve diagnosis, usage of CDS-Dx systems to date is underwhelming. Even when they are available, clinicians most often do not consult them.” (Graber, 2021, p. 2).

Until this project, the outpatient and primary care practices at the UTHealth academic medical practices, UTPhysicians, did not employ a computerized diagnostic decision support system of the type envisioned by Dr. Graber. The clinicians have had access to UpToDate as a digitized medical reference source for some time, and the clinicians access UpToDate in their

practices frequently. UpToDate, or any other medical reference source, is generally accessed to investigate a diagnosis already made. If the diagnosis is correct, UpToDate is an excellent diagnostic resource for the clinician. In the case of an inaccurate diagnosis, however, this method likely will not reveal alternatives that should be considered and may lead only to confirmation of what will prove to be an inaccurate diagnosis.

This study searched the literature for commercially available computerized diagnostic decision support systems to find a system that best met all the requirements for diagnostic performance, settling on Isabel Pro. Isabel Pro is a web-based differential diagnosis tool designed by Isabel Healthcare, Ltd., a company with head offices in Haslemere, United Kingdom, and Ann Arbor, Michigan. This study then evaluated the diagnostic retrieval accuracy of Isabel Pro using only those signs, symptoms, and medical history elements known at the outset of the patient encounter. The system searches a well-maintained medical reference literature database and produces an evidence-based differential diagnosis list for the physician to review before reaching any diagnostic conclusion about the patient. The thought is that the best way to reduce inaccurate diagnosis is to prevent its occurrence in the first place, preventing premature closure on an inaccurate diagnosis. The project also aims to smoothly integrate the diagnostic decision support system into the routine outpatient and primary care clinical practices at UTPhysicians.

In the Doctorate of Health Informatics Program at the School of Biomedical Informatics at the University of Texas Health Science Center at Houston, a translational project always begins with a PICO statement: Problem, Intervention, Comparison, and Outcome. For the project, the PICO Statement is as follows:

- **Problem:**

- Inaccurate diagnosis in outpatient and primary care
- **Intervention:**
  - Introduce a validated computerized diagnostic decision support system at the outset of the physician-patient encounter
- **Comparison:**
  - The diagnostic alternatives presented by the system to the confirmed case diagnoses
  - The system's performance to that of clinicians
  - The improvement in the performance of clinicians using system suggestions
- **Outcome:**
  - The system returns valid, relevant diagnoses matching the patient demographics and clinical features
  - The diagnostic retrieval accuracy of the system exceeds that of the clinicians alone
  - The clinicians' performance improves with access to the system's diagnostic alternatives
  - Introduction of the system for use in routine clinical practice at UTPhysicians

In the Doctorate of Health Informatics Program, the project is then succinctly described in a SMART statement, a series of statements designed to meet the requirements of the acronym; Specific, Measurable, Achievable, Relevant, and Time-bound. For this project, the SMART statement is:

- **By May 1, 2022**

- Evaluate a commercially available computerized diagnostic decision support system
- Assess physician opinions on usefulness in practice
- Propose the system to UTPhysicians for routine clinical usage in primary care practices
- Develop a process to capture a patient's presentation inputs into the system
- Develop a process to monitor system usage and a survey sequence to assess clinician satisfaction with the system

The last item in a Doctorate of Health Informatics Program project is the choice of a framework or model to follow in conducting the project from visualization to initiation to implementation, and finally to completion. There are numerous frameworks or methodologies available depending to a great extent on the nature and extent of the project. For this project, a traditional project development model, the “Structured Analysis Methodology,” lends itself most appropriately to the process, proceeding in phases. (Tilley, 2020, pp. 17–20). In this project, the phases, in sequence, are

- **First:**
  - Literature Search to choose the diagnostic decision support system
- **Second:**
  - Validate the system with actual cases
- **Third:**
  - Obtain buy-in and approval of UTPhysicians
- **Fourth:**
  - Introduce the system into the primary care practice

- **Fifth:**
  - Develop the procedure for tracking usage and surveying users

This project aimed to determine the answers to four critical questions regarding the performance of Isabel Pro in primary care practice.

- First:
  - Did the system offer accurate and relevant diagnoses?
  - With what frequency did the correct diagnosis appear in the list of diagnostic alternatives?
  - What was the ranking of the correct diagnosis among the alternatives produced?
  - What was the match of the inputs to the scientific literature on each alternative?
- Second:
  - Did the system perform as well as clinicians?
- Third:
  - Did the system's suggestions improve the physicians' diagnostic accuracy using them?
- Fourth:
  - What are the barriers to using the system in routine clinical practice and integrating it with the electronic health record?
  - Do physicians report that the system was helpful in routine clinical practice and that they would use it if available?

In the sections that follow, the details of the project are covered, beginning with the Evidence-Based Practice Review, then Methodology, Results, Discussion, Study Limitations, and finally, Conclusions.

## Section 2: Evidence-Based Practice Review

In preparation for this report, the literature review resulted in a robust listing of scholarly articles on several topics essential to the author's translational project for the Doctorate of Health Informatics Program. The project aims to evaluate the validity and utility of a diagnostic decision support system in primary medical practice using only a patient's presenting chief complaint, signs, symptoms, medications, and medical history. The search interrogated the National Library of Medicine's National Center for Biotechnology Information database, PubMed.gov. A Research & Instruction Librarian and Liaison to UT Health Science Center Houston, located at the Texas Medical Center Library, acted as the research consultant in developing the search strategy. Developing the search strategy was a multi-step process beginning with submitting a series of keywords that might yield topics of interest such as diagnostic error, missed diagnosis, delayed diagnosis, Isabel, VisualDX, and others. The search strategy for article retrieval used the following search string:

```
(((diagnostic error* OR diagnostic differential* OR "diagnosis"[Subheading] OR "Diagnosis"[Mesh] OR "Diagnostic Errors"[Mesh] OR diagnostic accuracy*) AND ("Diagnostic Decision Support" OR "visualdx" OR "Ada dx" OR "isabel healthcare"))))
```

Using a combination of Medical Search Headings (MeSH) terms, title-only restrictions, and title-abstract restrictions, combined with the search's requirement to contain both the initial and secondary terms, the search returned 159 articles. The author also reviewed previous papers submitted in BMI6328 (Bridges, April 12, 2020), BMI6002 (Bridges, May 1, 2020), and BMI7350 (Bridges, August 10, 2020). Those papers yielded an additional 31 articles to review. The articles were then sequentially excluded using the technique identified as PRISMA -

Preferred Reporting Items for Systematic reviews and Meta-Analyses. The author conducted a manual review of the 190 articles in a three-step process, looking first for titles specific enough to exclude an article using the title information alone. This title review excluded a total of seventy-seven articles. Second, reading the abstracts of the remaining articles excluded fourteen articles. Finally, each remaining article's full reading excluded forty-three remaining articles, leaving fifty-six articles for the Translational Project Reference List. Three articles, published after completing the PRISMA reduction process, were subsequently included as part of the project. The resulting references establish the foundation for the validation study on a diagnostic decision support system. The evidence-based practice review for this translational project covered nine elements:

- Seminal studies in improving diagnosis (two studies, Table 1),
- The detection and frequency of inaccurate diagnoses in primary practice (two studies, Table 2),
- Procedural recommendations for diagnosis from recognized experts in the field (seven studies, Table 3),
- The history of diagnostic decision support systems (one study, Table 4),
- The various diagnostic decision support systems developed over the years (six studies, Table 5),
- Assessments of the diagnostic performance of various diagnostic decision support systems (fifteen studies, Table 6),
- Assessments of the improvement in physician diagnostic accuracy when using a diagnostic decision support system (seventeen studies, Table 7),
- Issues of physician acceptance of these systems (seven studies, Table 8), and

- Issues related to integrating a diagnostic decision support system within the electronic health record (one study. Table 9).

The seminal publication in medical diagnosis is *Improving Diagnosis in Healthcare* (Balogh et al., 2015). This publication is the culmination of investigations conducted by the Committee on Diagnostic Error in Healthcare, formed by the Institute of Medicine's Board on Healthcare Services at the request of the Society for the Improvement of Diagnosis in Medicine (SIDM) in 2013. The board charged the committee with presenting an additional publication to add to the *Crossing the Quality Chasm* series. The origin and types of inaccurate diagnoses in primary care are also well-documented in a publication by a research team led by Dr. Hardeep Singh (Singh et al., 2013). These two studies (see Table 1) conclude that inaccurate diagnoses occur with greater frequency than typically thought and are often of relatively common conditions rather than rare ones. The studies found that inaccurate diagnoses are frequently the result of inadequacies in the physician-patient exchange (including the absence of a differential diagnosis list that can be provided automatically by a diagnostic decision support system) and represent slightly over 5% of all primary care encounters. About half are judged likely to result in significant patient harm, including death. The studies suggest a potential for severe patient harm ranging from 4 million to six million inaccurate diagnoses annually.

The frequency and detection of inaccurate diagnoses in primary care are well-documented in two companion publications (Singh et al., 2012; Singh et al., 2014). The articles (see Table 2) report on aspects of a study conducted at two sizeable integrated medical facilities with robust electronic health record systems using a full year of data on encounters as the dataset. The studies are thorough, well-researched, and suggest an electronic error detection protocol. The first article reports on a program to detect inaccurate diagnoses using a trigger



algorithm to interrogate the electronic health record for cases showing a return visit within fourteen days of the index visit. A team of experienced review physicians focused on whether the presenting information was sufficient to have determined the final diagnosis at the index encounter. Of the 674 cases flagged by the trigger algorithm, 141 were determined to be a missed diagnostic opportunity. The second study took the frequency of occurrence from the earlier studies and two studies of chronic conditions to extrapolate an estimate of inaccurate diagnoses in the entire United States.

The review found seven publications on the topic of diagnosis recommendations, listed in Table 3, authored by various highly regarded experts opining on aspects of diagnosis in medicine, each with a series of recommendations to improve the procedures involved or an assessment of the impediments to improving the diagnostic process from roughly 2005 to date. In general, the publications examine the nature and cause of inaccurate diagnoses in search of common themes, causes or failures, and a common language for studying and discussing inaccurate diagnoses. The first of these articles addressed inaccurate diagnoses in internal medicine and examined 100 cases of known inaccurate diagnoses by internists to categorize the errors and produce a system for uniformly classifying the nature of the inaccuracies (Graber et al., 2005). The report found only seven no-fault missed diagnostic opportunities, with the remainder generally characterized by both system and cognitive elements. Of note for this project was the observation that 74% of the cases involved cognitive issues, with premature closure (the failure to consider diagnostic alternatives, a central element provided by diagnostic decision support) being the single most common cause. The third study (Schiff et al., 2013) analyzed Massachusetts' malpractice claims against primary care providers. The finding in this

study most pertinent to this project is that 72% of the claims were allegations related to a failure to diagnose.

The next segment, Diagnostic Decision Support Systems History, is a single article listed in Table 4. Dr. Arthur Elstein, a co-author of the book *Medical Problem Solving* published in 1981 and one of the landmark research sources on clinical judgment, reflects on his long career with observations about diagnostic reasoning. Especially relevant to this project are his observations on strategies to reduce the frequency of inaccurate diagnoses, particularly the promise of computerized diagnostic decision support systems and the advantages of including the consideration of diagnostic alternatives. Two quotations encapsulate the opinions expressed in this paper and their implications for this project (Elstein, 2009).

“Given that our intuition is not perfect, and that rational analytic thought is too time consuming, when should we trust our clinical intuition and when is a more systematic rational approach needed? How should we decide that question?”

“The method of hypothesis generation and testing is a form of reflection. It offers the opportunity for a physician to think about alternatives...Developers of systems for computer-assisted diagnosis hoped that they would provide convenient, inexpensive, and accurate second opinions... It is possible that the findings in the electronic medical record of a multi-problem patient could be automatically entered into a diagnostic decision support system that would be sufficiently intelligent to distinguish the unknown problem from the list of diagnoses already identified. To my knowledge, such a system is not yet available, but given the pace of development of computer applications, it would be foolhardy to forecast the future.”

This project's premise is that early diagnostic suggestions may prevent missed diagnostic opportunities and that almost any physician's diagnostic accuracy improves with a differential diagnosis list. The initial presentation of a differential diagnosis list is the premise of this report, automatically prepared with the patient's presenting issues and available to the physician at the outset of the encounter.

The next segment of six articles all report on one or more diagnostic decision support systems, including DXplain, an early system still in use today at Massachusetts General Hospital and available by institutional subscription on a limited basis. The articles listed in Table 5 describe various systems, including Isabel Pro, the system chosen by the author of this report for the translational project. Excluded from the review were systems limited in application, systems dealing with a single condition only, or systems addressing only rare conditions. The relevance of the included articles to this project is an overview of the various attempts at developing a computerized diagnostic decision system, the problems encountered, and the systems' eventual evolution toward an assistive or augmentative relationship with the diagnostician. The United Kingdom, in the continuation of a project for a learning health system referred to as TRANSFoRm, has developed a prototype decision support system that integrates with an electronic health record commonly used in the UK and provides for knowledge base updating using interrogation of electronic health records for current patient information. Despite years of effort, the system remains a prototype limited to only three Reasons for Encounter (chief complaints) and still exhibits difficulty dealing with inconsistent coding in the EHR. These articles progressively lead to only two broadly applicable systems today: DXplain and Isabel Pro, with Isabel Pro being the most easily used and producing high diagnostic retrieval accuracy (Wood, 2014). These features are essential when the goal is to employ a system at the outset of

the encounter using only presenting symptoms. VisualDX, first developed for dermatology diagnosis, has expanded its diagnostic options to more general medical conditions, but the system is difficult to use and requires structured inputs that limit its usefulness in initial encounter situations.

The next set of articles, listed in Table 6, describes a series of performance evaluations or comparisons for computerized diagnostic decision support systems, some comparing several systems, one with another, and some being performance evaluations of a single system. Some articles report on the performance evaluation process elements, such as determining the “gold standard” final diagnosis. Several articles evaluate the systems’ performance in a particular aspect of medicine, such as emergency department, pediatrics, or primary care. The articles outline a variety of performance measures, but the most recent studies concentrate on the concept of diagnostic retrieval accuracy; that is, was the final, “gold standard” diagnosis among the diagnostic alternatives presented by the system, and where did that final diagnosis appear in the ranking of the list of the diagnostic presentations. These concepts are the essence of validation and this project's essence.

In tracing the history of diagnostic decision support systems, validation efforts were the topic of studies beginning as early as 1996, even earlier for some systems no longer maintained or available (such as Quick Medical Reference (QMR) or INTERNIST1). The earliest articles focused on assessing the capabilities of so-called "Oracle" systems, those systems expected to produce "the" diagnosis, essentially replacing the physician as a diagnostician. Later validation efforts focused on assessing the improvement in physician diagnostic accuracy before and after diagnostic decision support system consultation, generally by comparing the physician's

differential diagnosis list prepared before consultation with the one prepared afterward (Kostopoulou et al., 2015; Kostopoulou et al., 2017).

The most extensive validation study found in this literature search is an article published in 2016 by Riches et al., listed in Table 6 as item 13. The authors performed a systematic review and meta-analysis of thirty-six articles addressing differential diagnosis generators in this study. Their search included sixteen databases, included all the references in the articles retrieved, and addressed several specialist patient safety databases. The study assessed the clinical effectiveness of the systems by seeking answers to four critical research questions: did the system retrieve accurate diagnoses (as measured by the percentage of correct diagnoses returned and the average ranking of the final diagnoses); did the system perform as well as clinicians; did the system improve the diagnostic list of the physicians; and what enablers or barriers are likely to affect clinical practice?

The study reported several conclusions relevant to diagnostic decision support systems and their ultimate use in routine clinical practice. 'Diagnostic Accuracy' is typically cited as the primary goal and typically defined as the frequency with which the correct diagnosis appears in what can be a lengthy output list. The authors felt this term was too broad and proposed 'Accurate Diagnosis Retrieval' as a preferred term. The newest tools, including Isabel Pro, posted the highest accurate diagnosis retrieval rates, suggesting continued system accuracy improvement with further development. However, even when 'Accurate Diagnosis Retrieval' is high, the correct diagnosis is frequently well down on a lengthy list. This concept's clinical relevance is questionable since an accurate diagnosis that fails to show up in the top twenty, perhaps even the top ten, is quite likely to be ignored. In a small group of the studies reviewed, the systems matched clinicians in presenting the correct diagnosis, and preliminary evidence

indicates a modest but statistically significant improvement in the clinicians' assignment of an accurate diagnosis after consulting the system (Kostopoulou et al., 2015; Kostopoulou et al., 2017).

The authors presented several caveats for consideration in assessing these conclusions. The studies invariably assumed that the 'gold standard' clinicians' diagnoses are always correct. The authors noted that the underlying studies always used carefully prepared cases, but the conclusions drawn depend significantly on the validity of those studies. The authors also noted that accurate diagnosis retrieval alone does not predict the possible use and effectiveness of diagnostic decision support systems in clinical settings. Other essential factors were the specificity of the diagnostic list, the time required, the availability and access to the system, the cost-effectiveness, and the speed of use. Speed is no minor contributor to the usefulness of a system, and the authors noted that some of the newer tools are significantly faster to use, a critical implication for use in routine clinical practice.

The next to last article in Table 6 describes a study of the utility of such a system in routine clinical practice in the United Kingdom's general medical practice. In the absence of physicians' training in diagnostic decision support systems and smooth integration with the EHR with minimal re-entry of patient information, the article concludes that the outlook for routine clinical use is not promising (Cheraghi-Sohi et al., 2020). The study, however, has relatively limited generalizability since the hospital chosen for the study had limited IT capabilities and little computer support for physicians, either in training or equipment.

The next set of articles (see Table 7) report on the improvement (or lack of improvement) in a physician's diagnostic accuracy using diagnostic suggestions or prompts from a computerized diagnostic decision support system. One study in particular is relevant to this

project since this project includes the cases from that study (Friedman et al., 2005). This study examined the agreement between physicians' confidence in their diagnoses and accuracy. The study, conducted at three academic medical centers, involved 72 senior medical students, 72 senior medical residents, and 72 faculty internists. The participants studied synopses of 9 of 36 diagnostically challenging medical cases (each with a correct definitive diagnosis) and generated a differential diagnosis for each case. Participants indicated their level of confidence in each diagnosis. A differential was "correct" if the correct definitive diagnosis appeared in that subject's hypothesis list. The study assessed confidence by asking participants to rate the likelihood of seeking assistance in reaching a diagnosis when they generated the differential. This project conducted a "Diagnostic Challenge" during the Spring of 2021 using some of these same cases to evaluate the improvement in diagnostic retrieval accuracy using Isabel Pro's suggestions. Participants produced a differential diagnosis list after reviewing a case, then reviewed the case a second time with the diagnostic suggestions from Isabel Pro for reconsideration of their original differential. The challenge aimed to determine if Isabel Pro is as accurate as clinicians and whether clinicians' diagnostic accuracy improved with early diagnostic suggestions.

After completing the literature search described above, another article, published in September 2021 (Sibbald et al., 2021), reported on a study using Isabel Pro as a computerized diagnostic decision support system. Participants were in two groups, the first group using Isabel Pro early in the diagnostic process and the second group using Isabel Pro after performing additional tests and accumulating additional diagnostic information. The study reported a 7% improvement in diagnostic accuracy when using the system early and an 8% improvement when

using the system later. When using the system later in the diagnostic process, the improvement in diagnostic accuracy applied to all experience levels, from students to faculty.

The article reviewing malpractice claims (Zuccotti et al., 2014) demonstrates the benefits of clinical decision support in preventing inaccurate diagnoses that result in malpractice claims. This study reported the proportion of malpractice claims potentially preventable by clinical decision support (CDS). The study conducted a cross-sectional review of closed malpractice claims over seven years from one malpractice insurance company and seven hospitals in the Boston area. A panel of experts assessed the clinical opportunities to intervene to avert the malpractice event in each case. The expert panel also searched for the presence or absence of CDS that might have prevented the event. The study noted that CDS systems and other forms of health information technology (HIT) had not previously been evaluated for their potential to mitigate risk. This study suggests that CDS systems within HIT have a potential role in decreasing malpractice payments in addition to their known benefits for quality and safety. The study concluded that more than half of malpractice events and over \$40 million in indemnity payments were potentially preventable with CDS. The implication for this project is the possibility that this technique might lead to the financial justification for a diagnostic decision support system.

These studies generally show a small but statistically significant improvement in physician accuracy. Confirming this improvement will be essential for adopting such systems in routine clinical practice. Furthermore, the systems must demonstrate improvement in diagnostic accuracy for newly practicing physicians, medical students, and seasoned clinicians. This demonstration may not be all that is necessary for widespread usage, but its absence will prevent widespread acceptance.



The next segment of articles, listed in Table 8, covers the topic of physician acceptance of a diagnostic decision support system. One editorial, a commentary by Dr. Eta Berner (an icon in the study of diagnostic error and decision support), speaks to topics necessary to increase the use of diagnostic decision support systems. To quote her purposes: “This essay explores why diagnostic decision support systems are underutilized despite growing concern about diagnostic errors” (Berner, 2014). One issue stands out; routine clinical care fails to provide the feedback necessary for improvement. There can be no motivation to use diagnostic support if there is no awareness of the occurrence of inaccurate diagnosis.

Another publication of particular significance is the editorial by Dr. Brendan Delaney and Dr. Olga Kostopoulou, two of the most highly regarded and widely published researchers in the UK to improve diagnosis in healthcare (Delaney & Kostopoulou, 2017). Their essential comment is that computerized diagnostic decision support is essential in this era of time-constrained medical practice and the explosion of research in medicine. The article is a well-founded commentary on the need for diagnostic decision support in primary practice, the factors that have hindered adoption to date, and the encouraging technological developments that point to improvements in the diagnostic process.

While many of the issues revolve around time constraints, data entry requirements, integration with the electronic health record, and the smooth workflow of routine clinical practice, much of the reluctance is simply the physician seemingly unable to see the system's advantage. This inability (or unwillingness) to see an advantage, as reported in several of the earlier articles in this review, is frequently attributed to overconfidence in the physician's diagnosis. In other cases, the reluctance is merely unfamiliarity with the systems or the difficulty of using a system within the clinical workflow. Not least, the concern that a record of diagnoses

discarded may be discoverable and result in a claim of malpractice ranks high on the list of reasons for reluctance. The reports listed in Table 8 speak to these issues and provide chronological documentation of progress in this area.

The last segment of the evidence-based literature search found one article about integrating a diagnostic decision support system with the electronic health record. (Segal et al., 2017). This article underscores the difficulties of achieving this much sought-after integration. At the end of the effort described in this article, the study successfully integrated the diagnostic decision support system into the Epic EHR at Geisinger. However, tension arose between physicians holding opposing views of the wisdom of storing intermediate diagnostic steps in a discoverable format. The physicians responsible for direct treatment of the patients expressed concern about legal discoverability and the liability that might arise from the record of diagnoses considered and discarded. On the other hand, several specialists, such as imaging and pathology, were interested in a rich recording of diagnostic alternatives and diagnostic steps taken during the patient's overall encounter. The study achieved only incomplete reconciliation of these issues.

### Section 3: Methodology (Setting and Project Design)

This project lends itself to a series of sequential steps or phases – evaluation, validation, and implementation. Each of these phases may have two or more sub-phases, but the project methodology is a traditional project management process categorized in the literature as a “Structured Analysis Methodology.” (Tilley, 2020, pp. 17–20).

#### Evaluation

The purpose of a diagnostic decision support system has evolved, moving from a means of replacing the diagnostician (the “Oracle” idea) to the reasonably well-accepted notion today of augmenting the diagnostician, primarily assisting in staying abreast of advances in evidence-based clinical literature. The articles listed in Table 6 provide a chronology of performance evaluation methods for diagnostic decision support systems. The most extensive of these articles (Riches et al., 2016) was a systematic review of the literature on the subject (covering some thirty-six articles, all the references in those articles, and several patient safety databases) and concluded that a diagnostic decision support system should successfully answer four fundamental questions:

1. What is the system’s “diagnostic retrieval accuracy” (with what frequency is the correct diagnosis produced, and where did the correct diagnosis appear in the differential diagnoses' listing)?
2. Does the system perform as well as or better than clinicians based on these criteria?
3. Do clinicians improve their diagnostic accuracy when provided with the differential diagnosis suggestions produced by the system?
4. Is the system easily incorporated into routine clinical practice?

The literature search for a commercially available computerized diagnostic decision support system has been covered in detail in the preceding section, leading to the choice of Isabel Pro as the system meeting all the selection criteria. Isabel Healthcare, Ltd. of Hazelmere, UK, and Ann Arbor, Michigan, US produces Isabel Pro. In the 2016 systematic review and meta-analysis by Dr. Nicholas Riches and his co-authors (Riches et al., 2016, p. 11,17,18), Isabel Pro showed the highest accurate diagnosis retrieval rate with a pooled rate of 89% (the proportion of searches with the correct diagnosis). Isabel Pro was the fastest in the speed of retrieval, showing in three studies a retrieval rate of 60 seconds, 98 seconds, and six minutes, compared to 22 minutes for MEDITEL, 30 minutes for DxPLAIN, and up to 240 minutes for QMR. Isabel Pro also produced the most comprehensive differential diagnosis list, with the gold standard diagnosis appearing in the differential diagnosis listing 87% of the time. In one study, Isabel Pro reduced the number of incorrect diagnoses, and another study found Isabel Pro frequently used when available to clinicians.

### **Validation**

The validation methodology chosen for this project uses the process outlined in that 2016 study by Riches et al., following the conclusion in the author's final paper in BMI 6328 Healthcare Delivery in EHR Enabled Environment (Bridges, April 12, 2020). The validation process begins with searching for primary care cases where the presenting chief complaints, symptoms, signs, medications, and medical history can be input to the Isabel Pro Diagnostic Decision Support System (Isabel Pro). Cases suitable for this validation methodology have two essential components: an initial diagnosis different from the final diagnosis and a conclusive final diagnosis for comparison. The validation effort secured forty-six cases, two from

UTPhysicians, eight from McGovern Medical School, and thirty-six from the Learning Health Sciences Department at the University of Michigan Medical School

In preparation for this validation project, the author applied to the Committee for the Protection of Human Subjects at the University of Texas Health Science Center at Houston for approval to conduct a Quality Improvement Project. The application sought approval to evaluate the performance of the diagnostic decision support system, Isabel Pro, using cases from the primary care practice of UTPhysicians. The approval request is in Appendix D of this report. The project's approval notification occurred on November 12, 2019, and appears in this report as Appendix E. The application contemplated obtaining ten 'diagnostic dilemma' cases from each of three physicians at UTPhysicians, where the ultimate diagnosis was subsequently confirmed but was not among the diagnoses considered at the outset of the encounter. That process anticipated thirty cases for use in the validation process. Unfortunately, that case selection and the de-identification process proved unduly burdensome for the physicians and yielded only two cases. The author subsequently requested the Chief Resident at the McGovern Medical School for cases presented at the weekly resident conference as part of the medical school curriculum. That request yielded eight additional cases. This Quality Improvement Project concluded with a final report submitted to the Committee for the Protection of Human Subjects on September 24, 2020, attached to this report as Appendix F.

The author subsequently obtained thirty-six cases from the library of Dr. Charles P. Friedman, Professor, Head of the Learning Health Sciences Department at the University of Michigan Medical School. These cases offer the presenting chief complaint, symptoms, signs, medications, and medical history, together with a 'gold standard' diagnosis and an assessment of case difficulty, using a scale of one (least difficult) to seven (most difficult), provided by a team

of experienced physicians. These cases were considered imminently suitable for the validation process.

In applying the validation methodology to the cases available, the author entered the signs and symptoms from the cases into the Isabel Pro Differential Diagnosis System. The author entered the data from the case that would have been available at the outset of an encounter, including all chief complaints, symptoms, signs, medications, and medical history. The ultimate diagnosis of each case was unknown to the author until after producing the Isabel Pro diagnostic alternatives. The author cataloged the resulting presentation of diagnostic alternatives and matched the results to the actual diagnoses that accompanied the cases. The author further tabulated the correct diagnosis's ranking among the differential presentation and the percentage match of the inputs to the scientific literature for each condition. The author accumulated the individual case results in an aggregate presentation of outcomes included in Table 10, and the case information and the detailed diagnostic outputs are included as Exhibits 1 through 46. These case results represent the answers to the first question in the validation methodology process. For the forty-six cases, Isabel Pro returned the correct diagnosis twenty-four times (52.2%), with an average ranking of 10 and a range of 1 to 40.

In attempting to answer the second and third questions in the validation methodology process, the author sponsored the “JMB Diagnostic Challenge,” aggregating twenty-four cases from Dr. Friedman into four groups of six cases for which the correct diagnosis was in Isabel Pro differential. Dr. Jeffrey Chen, Chief Resident for Quality Improvement at McGovern Medical School, agreed that four of his Chief Resident’s conferences would be devoted to the “JMB Diagnostic Challenge.” Approximately 120 internal medicine residents in groups of 30 residents from the McGovern Medical School attended each of the weekly Chief Resident’s conferences.

The residents diagnosed a case, produced a differential diagnosis list, and then diagnosed the same case again but presented with the differential diagnosis list from Isabel Pro. The aim of the challenge was twofold. First, assess the performance of Isabel Pro compared to the residents' performance. Second, assess the improvement in the residents' diagnostic accuracy using diagnostic suggestions from the Isabel Pro differential diagnosis listing. A follow-up survey seeking responses on seven statements (strongly disagree, disagree, agree, or strongly agree) assessed the participant's opinions of the Isabel Pro differential and its effectiveness in augmenting their diagnostic process. The results of the "JMB Diagnostic Challenge" are covered in the Results section of this paper.

### **Implementation**

The author successfully defended the translational project in a presentation on Monday, September 13, 2021, allowing for the project's implementation phase commencement. In the world of organizational change management, an essential step is building a group of influential, highly respected opinion leaders whose guidance will steer the project through the intricacies of the organization. These individuals are those the organization values as opinion leaders and will follow their lead in introducing a project. Since physician acceptance is probably the most significant barrier to using the system in routine clinical practice, Outpatient and Primary Care Physician Leaders' support is essential to this project. For this segment of the project, the author has been fortunate to receive support from Dr. Eric Thomas, Professor and Associate Dean for Healthcare Quality, Dr. Thomas Murphy, Associate Dean for Community Affairs and Health Policy, Dr. Holly Holmes, Associate Professor, Internal Medicine, Geriatrics, and Dr. Rohit Goswamy, Chief Resident, Internal Medicine, McGovern Medical School.

Information Technology is another essential segment of this project, as the smooth incorporation of the system into routine clinical practice requires system implementation and presentation methodology. None of this would have been possible without specialized IT involvement. The author is fortunate to have received the support of Mr. Amar Yousef, Vice President and Chief Information Officer, in vendor contract negotiations and project funding, and Dr. James Griffiths, Associate Vice President of Healthcare IT, for the integration of a link to Isabel Pro into the menu bar of the Epic EHR immediately to the right of the link to UpToDate.

These individuals are the “Guiding Coalition” on whom the project has relied to accomplish a remarkable timetable from approval to introduce Isabel Pro by the UTPhysicians’ Outpatient Quality Council to the introduction of Isabel Pro into the practices in just under 12 weeks. The timeline is summarized below:

- September 13 – Advance to Candidacy Defense Presentation
- September 16 – Outpatient Quality Council Approval
- November 1 – Vendor Contract Executed, Funded for 1-year Pilot
- November 30 – Link to Isabel Pro incorporated into the Epic EHR
- December 8 – Introduced into Routine Clinical Practice

Isabel Pro usage statistics are captured automatically by the Isabel Pro system using a session identifier to track unique user usage from initiation of a session to its closing. The system captures all input and output details, from demographics to clinical features to the differentials produced and subsequent queries for research on specific diagnoses. The analysis format captured usage statistics weekly to show growth in usage, segregated by faculty or resident, segregated by access method, time of day, and day of the week. Using the same statements and



format as the JMB Diagnostic Challenge, the author sent a User Survey on February 21, 2022, with the responses collected and analyzed through March 4, 2022.

An article on Isabel Pro and the project, published on January 18, 2022, in the weekly newsletter “Inside UTHealth Houston,” announced Isabel Pro's availability and some of the system’s features. The author also made presentations to the residents attending the Chief Resident’s Conferences on February 2, 7, 21, and 28. Each presentation included a download of the Isabel Pro application to the residents’ mobile devices for their use in diagnosing a case sent by email to arrive during the presentation. The residents received the hands-on experience, and the download allowed them to retain access to Isabel Pro for future use.

Collection of both usage statistics and user responses for inclusion in this report ended as of March 4, 2022, allowing time to analyze the data in preparation for the Translational Project Defense Presentation on Friday, March 11, 2022. The defense presentation concluded that same day successfully.

UTPhysicians implemented the Epic electronic health record into the practices with a Go-Live date in May 2021. The implementation of the Epic EHR was a massive undertaking but, fortunately, was far enough along in November 2021 to allow a link to Isabel Pro to be added to the menu line on the Epic EHR immediately to the right of the UpToDate link. The clinical IT team at UTHealth collaborated with the Isabel Healthcare IT personnel to incorporate the link in just under one month. The link is very accessible and convenient but requires the clinician to manually enter the patient demographics and clinical features. Automatically capturing that information from the EHR would unquestionably be an advantage for increased program usage. Few physicians are interested in performing additional computer entries. An application's ability to read from and write to the Epic system is quite restrictive. The inclusion of Isabel Pro in the

Epic “App Orchard” would allow the automatic population of Isabel Pro, and while inclusion is under consideration at this time, the outcome of this effort is unclear.

## Section 4: Results

This study involved three specific endeavors – evaluation, validation, and implementation.

### **Evaluation**

As detailed in the literature search description earlier in this report, the first step evaluated commercially available computerized diagnostic decision support systems searching for the system producing the best diagnostic accuracy and showing the most efficient entry and retrieval features. Isabel Pro stood out among the systems available for use in practice. The most thorough analysis of differential diagnosis generators found in the literature search was the systematic review and meta-analysis performed by Dr. Nicholas Riches and his co-authors published in 2016. (Riches et al., 2016). That publication reviewed thirty-six articles covering eleven differential diagnosis generators and reported their performance in several diagnostic aspects. As noted earlier in this report, Isabel Pro showed the most accurate diagnostic retrieval rate (89%), was the fastest in retrieval, produced the most comprehensive differential diagnosis listing, reduced the number of incorrect diagnoses, and was frequently used by clinicians when available. That endeavor concluded with the selection of Isabel Pro based on superior diagnostic accuracy and speed of input and output of results.

### **Validation**

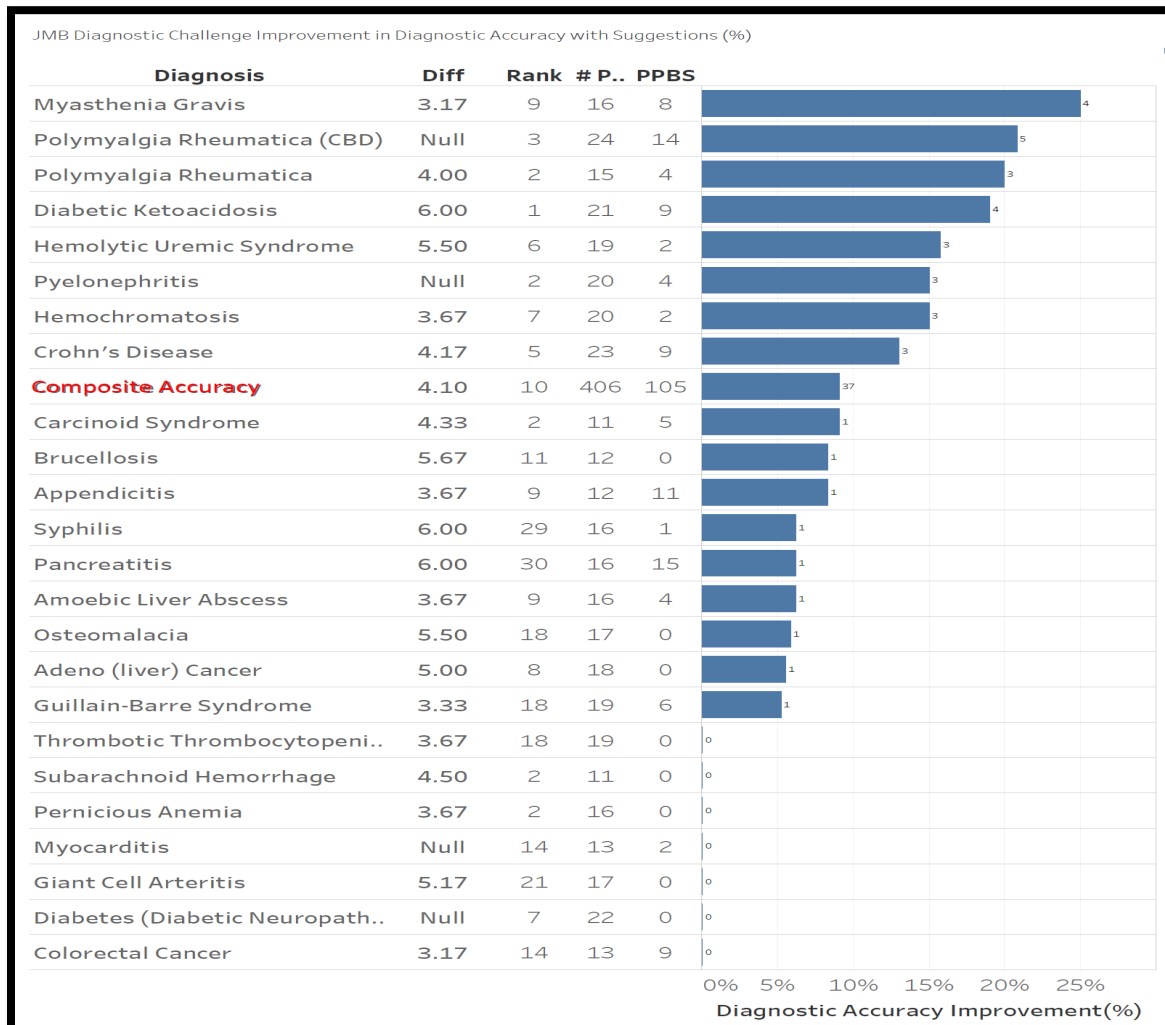
The next phase validated the system, first by determining the diagnostic accuracy using the 36 cases furnished by Dr. Charles Friedman, the two cases from the practices of UTPhysicians, and the eight cases from the McGovern Medical School Chief Resident's Conferences. This step establishes that Isabel Pro produces accurate and relevant diagnoses. Entering only the presenting patient demographics and clinical features, Isabel Pro returned the

correct diagnosis for 24 cases (52.5%), with the ranking of the diagnoses ranging from 1 to 40. Table 10 summarizes the results, while Exhibits 1 through 46 present the case details and the diagnostic outputs.

The second step in the validation phase tested Isabel Pro in action. The “JMB Diagnostic Challenge,” conducted during Spring 2021, presented 24 cases for which the diagnostic retrieval accuracy of Isabel Pro was 100%. For this phase of the project, the definition of Diagnostic retrieval accuracy is the correct diagnosis appearing anywhere in the participant’s differential. Approximately 120 Internal Medicine residents from McGovern Medical School, while attending a Chief Resident’s Conference (30 residents each in four conferences), diagnosed the cases in groups of 6, first without suggestions, then with Isabel Pro suggestions provided for the reconsideration of their earlier differential.

The residents produced 406 diagnoses, of which 105 (25.9%) were correct without suggestions; 37 (9.1%) additional correct diagnoses were produced after reviewing the Isabel Pro suggestions, for 142 (35.0%) total correct diagnoses. After reviewing the Isabel Pro suggestions, the participants showed an absolute improvement in diagnostic accuracy averaging 9.1%. The bar graph below shows the outcome of the challenge by case, from the case where the Isabel Pro suggestions produced the most improvement (25% for Myasthenia Gravis) to the seven cases showing no improvement.

Figure 1

*JMB Diagnostic Challenge – Bar Chart of Improvement in Diagnostic Accuracy*

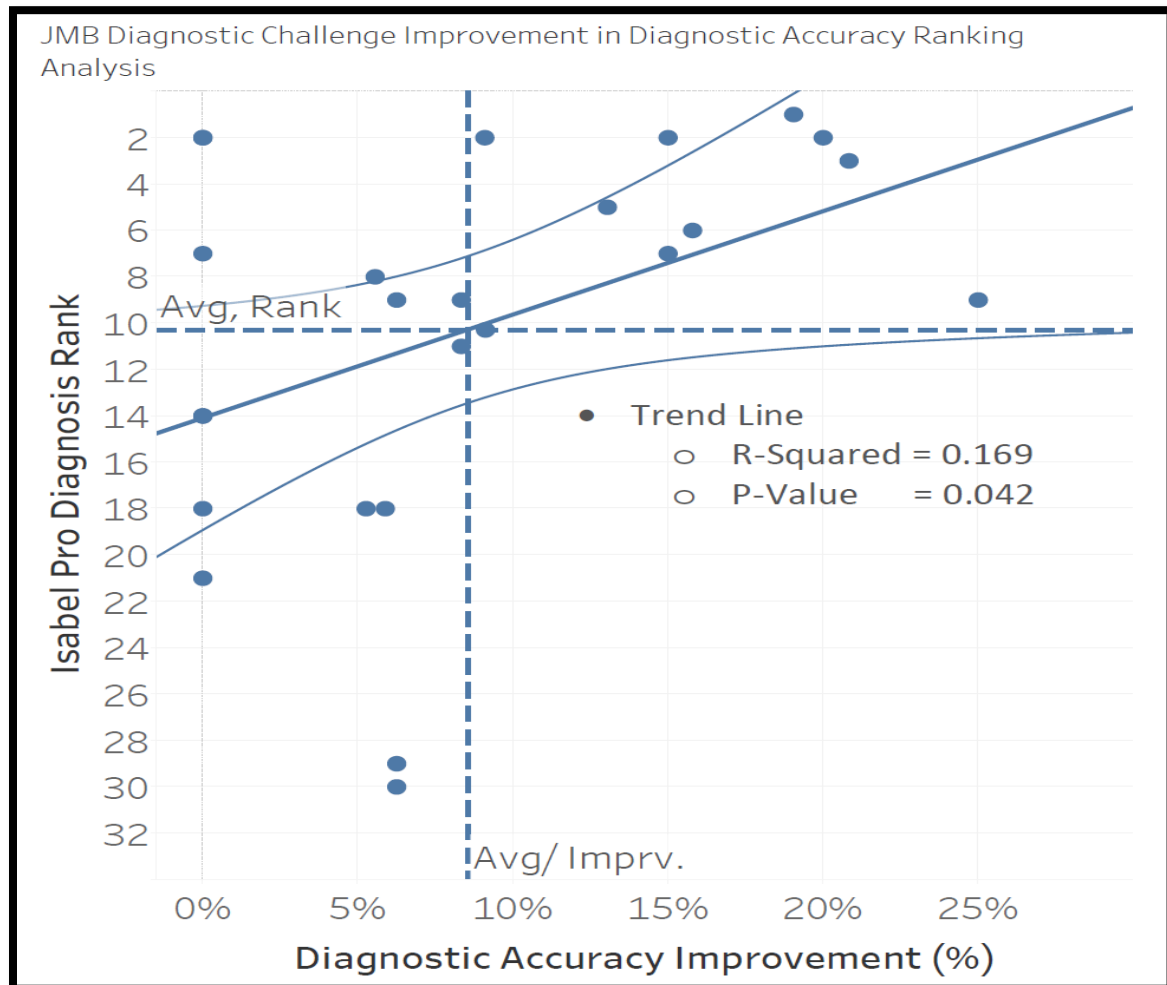
Two questions almost immediately arise from this bar chart. “Does the ranking of the diagnosis influence the improvement in diagnostic accuracy?” “Does case difficulty influence the improvement in diagnostic accuracy?”

In answer to the first of the two questions, the figure below is a scatter plot of diagnosis rank plotted against improvement in diagnostic accuracy. The Isabel Pro presentation rank of the correct diagnosis is on the vertical axis. The range is from 1, the highest, at the axis top to 35 at

the axis bottom. The Absolute Improvement in Diagnostic Accuracy for each case is on the horizontal axis, ranging from 0% to 25%. Each dot represents a case with the improvement in diagnostic accuracy for that case plotted against the diagnosis ranking for that case by Isabel Pro. The trend line shows an R-squared of 0.169 produced from data with much variance around the trend. Nevertheless, the trend line indicates that the higher the presentation rank, the greater the improvement in diagnostic accuracy. Even though the zero-percent improvement intercept is at a ranking of 14, merely observing the data suggests that achieving the most improvement in diagnostic accuracy likely occurs if the ranking is within the first ten presentations.

Figure 2

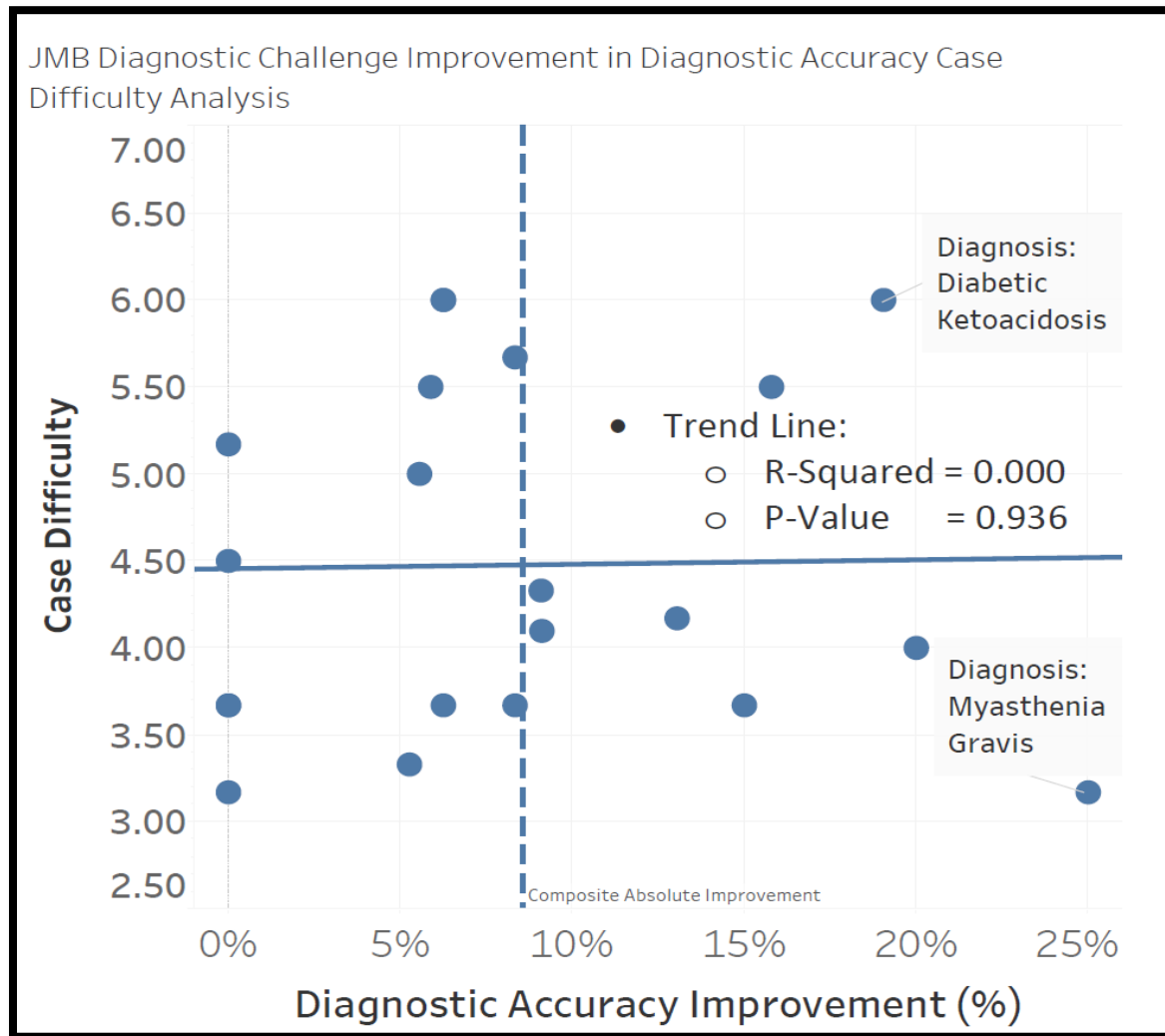
*Isabel Pro Diagnosis Rank versus Diagnostic Accuracy Improvement (%)*



The figure below addresses the second of the questions. In this scatter plot, the vertical axis plots case difficulty on a scale of maximum difficulty equal to 7.0. The horizontal axis, once again, is Absolute Improvement in Diagnostic Accuracy. Each dot represents a case with the improvement in diagnostic accuracy plotted against the case difficulty rating. Interestingly, this study's most significant improvement in diagnostic accuracy occurred in both the least difficult and the most difficult cases. The scatter plot shows little effect of case difficulty on improvement in diagnostic accuracy with an R-value of 0.000 and  $p = 0.916$ .

**Figure 3**

*Case Difficulty versus Improvement in Diagnostic Accuracy (%)*



The last item in the “JMB Diagnostic Challenge” was a survey requesting that residents respond to seven statements regarding their experience with the Isabel Pro suggestions. The responses were to “Strongly Disagree,” “Disagree,” “Agree,” or “Strongly Agree” with each statement on the perceived usefulness of the Isabel Pro suggestions. The figure below shows each statement and the percentage of respondents who chose “Agree” or “Strongly Agree.” The survey collected 197 responses out of a possible 240 responses.



**Figure 4**

*“JMB Diagnostic Challenge” Perceived Usefulness of Isabel Pro Diagnostic Suggestions*

RedCap Survey Questionnaire: “The Diagnostic Suggestions.....”	Agreed or Strongly Agreed (%) Non-Users (197 responses)
<b>Are reasonable and helpful</b>	<b>70.1%</b>
<b>Would consult if available at every patient encounter</b>	<b>64.1%</b>
<b>Would be helpful in routine clinical practice</b>	<b>75.1%</b>
<b>Early presentation improved diagnostic accuracy</b>	<b>55.8%</b>
<b>Prompted reconsideration of original diagnosis</b>	<b>57.4%</b>
<b>Ranking influenced diagnostic thinking process</b>	<b>43.9%</b>
<b>Prompted a change to original diagnosis</b>	<b>30.6%</b>

Underscoring the significance of these responses is that 75.1% of the respondents agreed that the suggestions would be helpful in routine clinical practice and 64.1% of the respondents agreed they would consult the differential if available at every patient encounter. These responses bode well for adoption and consistent usage of the system. Even the 30.6% of the respondents who changed their original diagnosis indicate the possibility of a significant improvement in diagnostic accuracy. A change in diagnosis does not necessarily mean the change will be to a correct diagnosis, but many will, and with 12 million inaccurate diagnoses annually, any improvement is welcome, however slight.

The “JMB Diagnostic Challenge” established that Isabel Pro performs well compared to clinicians alone, improves clinicians’ diagnostic accuracy when using the system, and, in the clinicians’ opinions, would be helpful in routine clinical practice. The “JMB Diagnostic Challenge” results compare favorably with the other similar studies reviewed in the literature search. (Friedman et al., 1999; Kostopoulou et al., 2015; Sibbald et al., 2021).

## Implementation

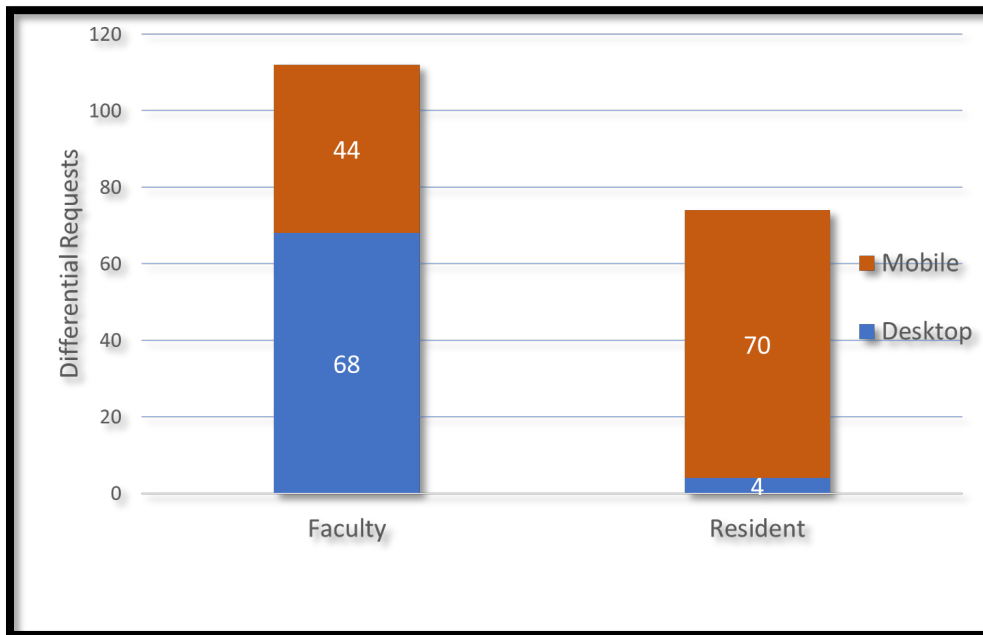
The third endeavor, implementation, began with a presentation to the Outpatient Quality Council of UTPhysicians on September 16, 2021, covering the evaluation and validation of Isabel Pro and proposing introducing the system into the outpatient practices UTPhysicians. The project was authorized for implementation to begin as soon as practicable. Negotiations for a one-year pilot project contract with the vendor Isabel Healthcare, Ltd. concluded with the execution of the contract on November 1, 2021. The UTHealth IT group began immediately to arrange access to Isabel Pro from the Epic EHR by way of a link on the EHR menu bar, situated just to the right of the existing link for UpToDate. When activated by an EHR user, the link brings up the Isabel Pro app for immediate use and displays a QR Code allowing a download of the Isabel Pro app to a mobile device if the user desires. The link became active on November 30.

On December 8, 2021, following activation of the Isabel Pro link in the Epic EHR, the UTPhysicians' practices received a notice of the availability of Isabel Pro, along with a QR Code, one for faculty and one for residents, for download of the app to a mobile device if desired. Usage of Isabel Pro began almost immediately. Anonymous usage statistics are collected automatically by Isabel Healthcare, Ltd., producing a rich dataset for analysis. The analysis combines usage statistics and responses from a survey of users in assessing the implementation project.

The first assessment question addresses the way the clinicians access the system – through the EHR by desktop or by their mobile devices. Figure 5 shows the faculty making most of their requests for differential through the EHR by desktop, a ratio of 1.5 to 1.0 over a mobile device. The residents, however, are primarily mobile users by a factor of nearly twenty to one.

**Figure 5**

*Users, Differential Requests by Access Method*



Usage statistics during the study period showed 73 unique users, 37 faculty, and 36 residents. Figure 6 shows users' breakdown by the number of differential requests made. Forty-two users (57.5%), evenly split between faculty and residents, used the system and requested a differential only a single time. Twenty-one users, again evenly split between faculty and residents, used the system and requested a differential between two and four times. Ten users, four faculty and six residents used the system and requested a differential five times or more. One faculty user made 37 requests for differential on several occasions over a roughly six-week period.

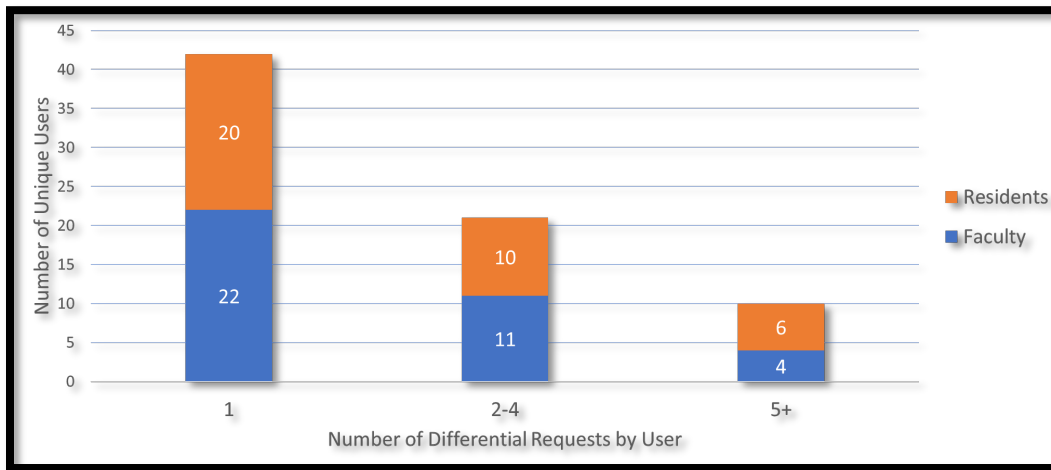
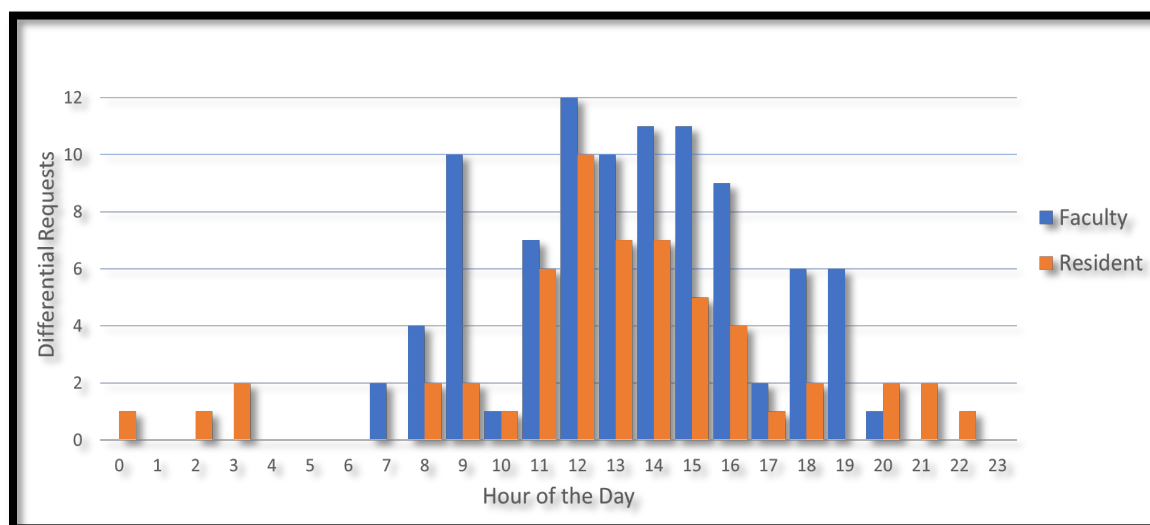
**Figure 6***Unique Users, Number of Requests for Differential*

Figure 7 below depicts the usage statistics by the time of day, showing the bulk of the usage between the hours of 7:00 a.m. and 7:00 p.m. Usage peaks for both faculty and residents from Noon to 4:00 p.m. The usage profile shows little difference between faculty and residents other than the residents being the only users late at night or in the very early morning hours.

**Figure 7***Users, Requests for Differential by Time of Day*

As shown in Figure 8 below, usage is relatively uniform throughout the week, with a peak for faculty on Friday as the week concludes and on Sunday in preparation for the upcoming week. Residents show a peak on Monday that corresponds to the faculty and are virtually the only users on Saturday.

**Figure 8**

*Users, Requests for Differential by Day of Week*

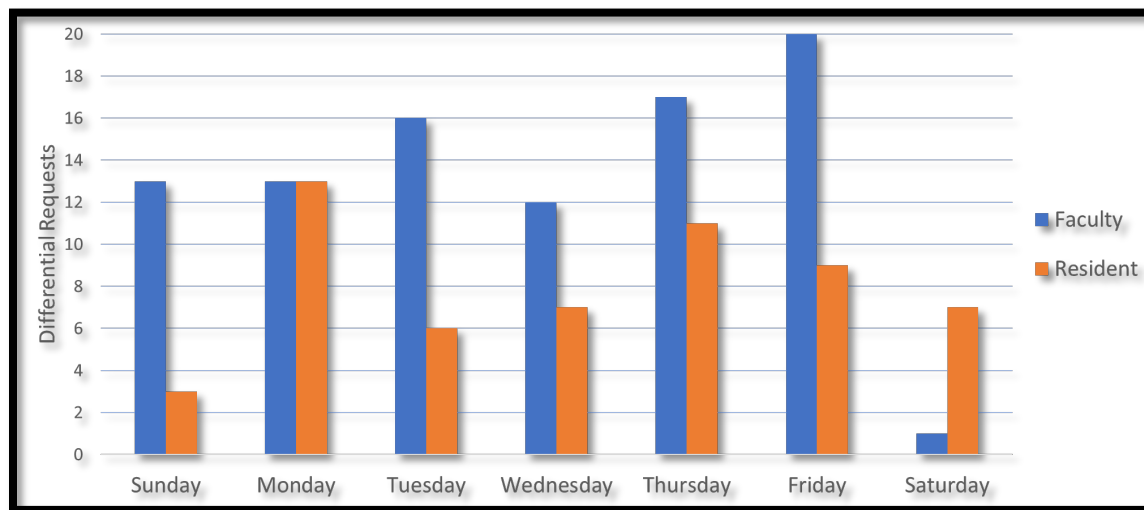


Figure 9 below shows the frequency of diagnosis requests by week since the introduction of the system into clinical practice on December 8, 2021. A rapid increase in usage followed as users tried the novel application in actual practice. A lull followed with the approach of Christmas and New Year, then resumed modestly with usage at roughly two times daily. An article on Isabel Pro appeared on January 18, 2022, in that week's edition of Inside UTHHealth. Usage increased sharply the following week, returning to the roughly twice daily rate. Presentations at the Chief Resident's conferences on February 2, 7, 21, and 28 produced a sharp increase in usage by residents following each presentation. The User Survey request was initiated on February 21 and may explain the growth in usage by the faculty during the following two

weeks. As the data collection period concluded on March 4, 2022, the usage by both faculty and residents was about twice daily for each.

**Figure 9**

*Users, Requests for Differential by Week*

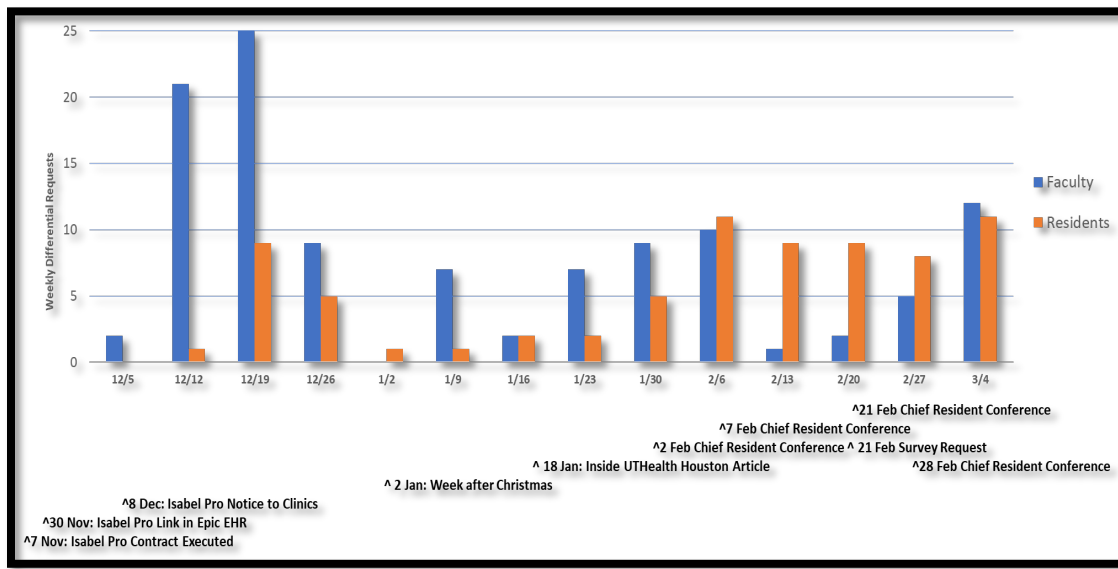
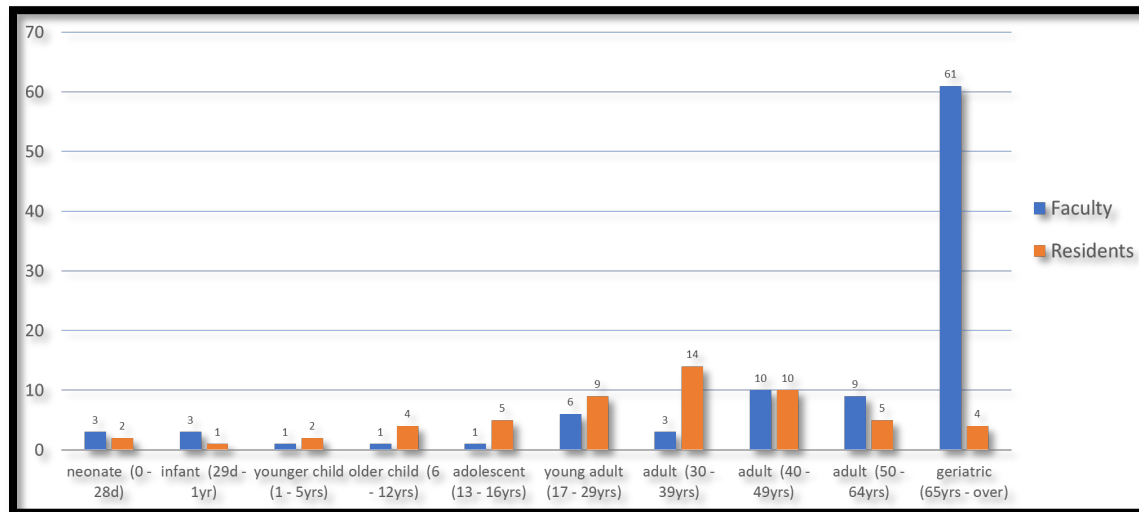


Figure 10 illustrates the system usage by patient age group. The bulk of the usage addresses geriatric patients, suggesting that usage is most frequent for patients presenting with multiple comorbidities. The faculty user making 37 differential requests distorts the geriatric usage somewhat but still leaves 24 requests from other geriatric clinicians, the bulk of the usage. Residents' conferences have increased usage, with most of the residents' requests for differential dealing with adults 17 to 49.

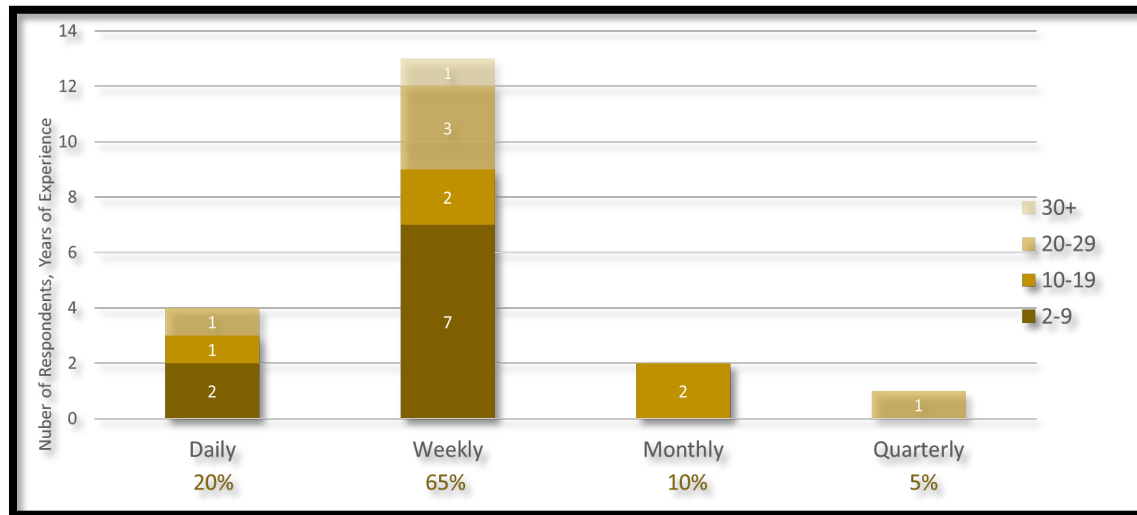
**Figure 10***Users, Requests for Differential by Patient Age Group*

The following figures display the responses to the clinician users' survey. Out of 73 unique users who might have responded, the survey request produced only 20 responses. While admittedly a small sample, the experience levels of the respondents nevertheless suggest that their responses may well be indicative of the user group as a whole.

Figure 11 depicts the responses to the question, "How often do you encounter a challenging diagnosis in your routine clinical practice?" The respondents report that challenging diagnoses are encountered as often as daily but most often weekly, with 85% of the challenging diagnoses encountered at least weekly. A range of experience levels sees the challenging diagnoses; about half of the respondents report fewer than ten years of experience and half ten or more. Although a small sample, the survey results suggest a weekly opportunity to employ diagnostic decision support.

**Figure 11**

*The Opportunity for Diagnostic Decision Support; Frequency of a Challenging Diagnosis, Experience Level (20 respondents out of 73 unique users)*

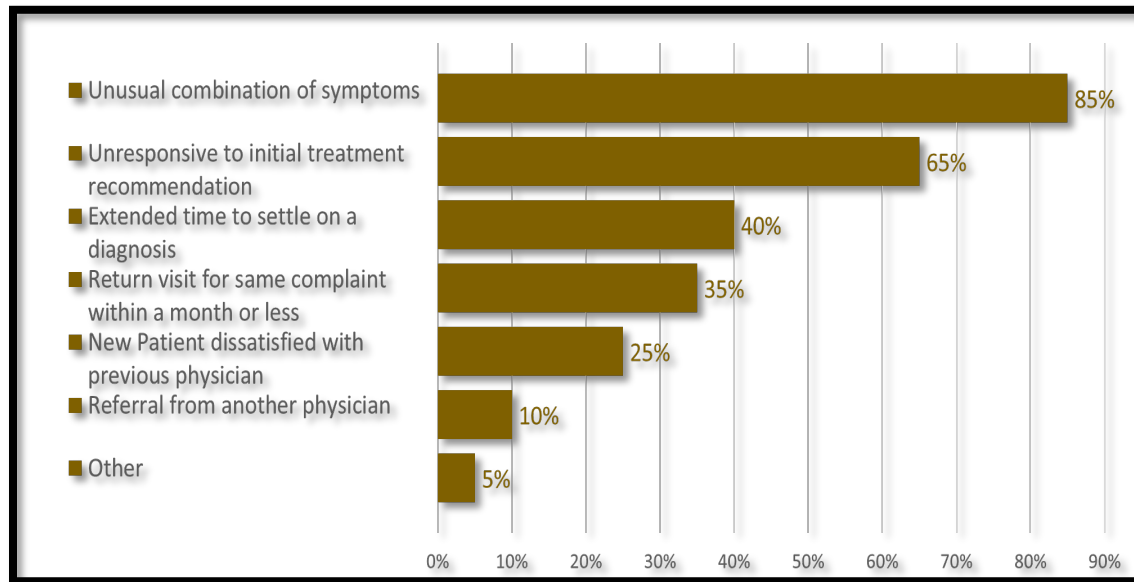


The survey then asked, “What are the typical indications of a challenging diagnosis?” The survey offered six preset alternatives for the respondents to select as many as appropriate to their experience. A seventh alternative allowed the respondents to enter any challenging diagnosis not among the first six alternatives offered if they wished. As shown in Figure 12, the respondents report that a challenging diagnosis is most often an unusual combination of symptoms; 85% of the respondents made this selection. A patient returning unresponsive to the initial diagnosis and treatment is the next most common source of a challenging diagnosis, with 65% of the respondents making this selection. More than one-third of the respondents reported a patient returning within a month unresponsive to the treatment prescribed as the challenging diagnosis. Each of these situations represents a prime opportunity for the use of diagnostic decision support.



**Figure 12**

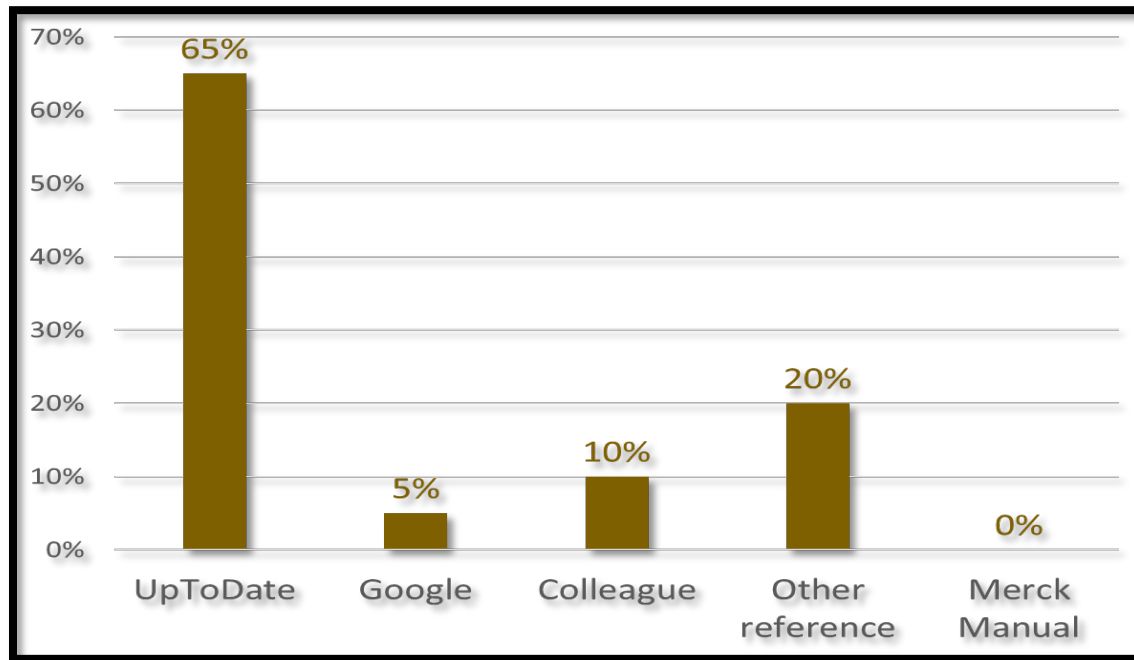
*Typical Indications of a Challenging Diagnosis, Respondent's Choice of Any or All (20 respondents out of 73 unique users)*



The survey asked, “What is your preferred medical reference source other than Isabel Pro?” The question offered four choices – UpToDate, Google, Merck Manual, or a colleague. The respondents could make another choice if preferred. Unsurprisingly, the most preferred reference source was UpToDate; almost two-thirds of respondents listed UpToDate as their preferred reference. UpToDate is now the default reference source in UTHHealth’s version of Isabel Pro, with the Merck Manual Professional, Google, and other reference sources available at the click of a mouse.

**Figure 13**

*Preferred Diagnostic Reference Source (20 respondents out of 73 unique users)*



At this point, the survey posed the same seven statements used in the survey accompanying the JMB Diagnostic Challenge conducted in the Spring of 2021. Figure 14 tabulates the responses from the survey distributed on February 21, 2022, to actual users of Isabel Pro in routine clinical practice, compared to the responses from the Spring 2021 survey when respondents viewed only the differentials produced by Isabel Pro. For each statement posed, the respondents chose to “Strongly Agree,” “Agree,” “Disagree,” or “Strongly Disagree” with the statement. The “Strongly Agree” and “Agree” responses improved for every statement, ranging from 0.5% to 19.2%. The Agree and Strongly Agree responses were very encouraging for the prospect of securing the use of Isabel Pro in routine clinical practice. For example, 83.3% of the users agreed they would consult the differential if available at every patient encounter, an improvement of 19.2% compared to the earlier study.

Furthermore, 77.8% of the respondents agreed that the suggestions would be helpful in routine clinical practice, an improvement of 2.7% over the earlier study. Of course, this is a small sample out of the 37 faculty and 36 resident users, but the favorable responses and the improvement from last spring's challenge bode well for a future increase in usage of the system at UTHealth. Of particular note is the response to whether the differential diagnosis listing led to a change in the respondent's earlier diagnosis – 36.8% reported a change in their earlier diagnosis. Consider the implication that of the twelve million inaccurate diagnoses annually in the US, the use of Isabel Pro might change more than four million of them. There is no evidence that the change from an inaccurate diagnosis would necessarily be to an accurate diagnosis, but the improvements in diagnostic accuracy of 7% to 8% from some studies suggest that nearly a million inaccurate diagnoses might be corrected annually.

**Figure 14***Perceived Usefulness of Isabel Pro Diagnostic Suggestions*

*JMB Challenge Responses (197 responses) versus Actual Users (20 respondents out of 73 unique users)*

RedCap Survey Questionnaire: "The Diagnostic Suggestions....." Agree or Strongly Agree Responses, (% of Total Responses)	JMB Challenge (Suggestions Only) Responses (197)	Actual Users (20 Respondents Out of 73 Users)	Positive Improvement from Users
Are reasonable and helpful	70.1%	84.2%	14.1%
Would consult if available at every patient encounter	64.1%	83.3%	19.2%
Would be helpful in routine clinical practice	75.1%	77.8%	2.7%
Early presentation improved diagnostic accuracy	55.8%	63.2%	7.4%
Prompted reconsideration of original diagnosis	57.4%	57.9%	0.5%
Ranking influenced diagnostic thinking process	43.9%	53.6%	9.7%
Prompted a change to original diagnosis	30.6%	36.8%	6.2%

## Section 5: Discussion

This project has presented a classic Organizational Change Management sequence – early usage when curiosity is highest, and the “New Toy” is available for exploration, followed by a drop-off in use after the newness wears off. Communication improves usage, as shown in the last three weeks of this project. The project requires a more continuous and focused communication plan as a near-term goal.

Physician acceptance of the need for computerized diagnostic decision support has shown to be a curious mix – few physicians say it is unnecessary, but frontline usage is lagging. As this project demonstrates, the relative advantage of a computerized diagnostic decision support system is unlikely to be realized with merely a single use out of curiosity. The system offers no relative advantage until a clinician encounters a patient presenting a particularly challenging diagnostic situation. The clinician then needs to seek assistance for diagnosis. Moreover, even at that point, the clinician must have a heightened appreciation of the system's assistance before using it.

Consulting with a colleague is a typical response when questioning clinicians on what steps they take when facing a challenging diagnosis. Having a “Clinical Champion,” a user respected among colleagues who successfully used the system to diagnose a challenging patient, may thus help. This project has yet to identify a “Clinical Champion” who can testify to the assistance provided by Isabel Pro and become that influential colleague that others turn to for assistance. One faculty user with 37 differential requests over six weeks may well be that “Clinical Champion.” Identifying that faculty member is another necessary near-term goal.

The usage statistics are favorable indications that the usage of Isabel Pro might become embedded in the practices and used routinely – for the challenging cases, but also to avoid

diagnostic inaccuracy for more common conditions – pneumonia, decompensated congestive heart failure, cancer, acute renal failure, and pyelonephritis. A key element for more extensive usage of Isabel Pro is identifying cases of inaccurate diagnoses where the diagnostician did not use Isabel Pro. These cases could then be analyzed to determine whether Isabel Pro might have helped achieve an accurate diagnosis in those cases. A 2020 article described a possible model for such a process. Entitled “Structured Case Reviews for Organizational Learning About Diagnostic Vulnerabilities: Initial Experiences From Two Medical Centers” (Mathews et al., 2020), the article details the efforts by two healthcare organizations to institute triggered case review programs searching for opportunities for improvement.

The responses to the survey of users are even more encouraging, agreeing or strongly agreeing with all seven of the survey questions to a greater extent than the survey of residents done last spring. The positive responses to consulting Isabel Pro on every encounter and helping in routine clinical practice were particularly encouraging. These are essential pointers to continued usage.

Another significant response was the most typical challenging diagnosis – an unusual combination of symptoms. There could hardly be a challenging diagnosis more suited to computerized diagnostic decision support and producing a well-researched differential. The responses to the survey, albeit a small sample, suggest that challenging diagnostic situations are seen quite regularly – survey respondents reported most often weekly, so the potential for usage of Isabel Pro is not an infrequent occurrence.

Physician acceptance of computerized diagnostic decision support is one of the most significant barriers to embedding Isabel Pro into routine clinical practice. However, the frequent usage of a tool such as UpToDate is a testament to the acceptance of computerized literature

research. Isabel Pro searches a proprietary database composed of medical reference sources to produce a differential diagnosis list arranged in the sequence that the clinical features appear in the database for that condition. It is not the clinical probability but is highly indicative of the condition presenting with those clinical features. This presentation affords the clinician a well-researched list of diagnostic alternatives that should be ruled out or considered for further treatment or testing. Each diagnosis can easily be further researched by merely clicking on the condition to be taken to a medical reference source. In the UHealth application, UpToDate is the first reference source produced by Isabel Pro, with access to the Merck Manual Professional, PubMed, and others by a mouse click. Isabel Pro offers UpToDate as the reference for every diagnosis on the differential merely by clicking the diagnosis. Using UpToDate in this fashion does not limit the reference search to a single diagnostic conclusion, as might be the case in the absence of a differential diagnosis list. A well-researched differential diagnosis will likely improve the diagnostic accuracy of almost any clinician, and Isabel Pro produces that differential in seconds with a minimum of patient information that is readily available at the patient's presentation.

Diagnostic decision support augments and enhances the physician's diagnostic process rather than replacing it. The point is that the clinician and the system are better together than either one alone. Moreover, numerous studies support this contention, with the most recent being published in September 2021, describing the use of Isabel Pro as the computerized diagnostic decision support system (Sibbald et al., 2021). Isabel Pro is in use successfully in several institutional settings, and there is ample reason to believe the incorporation at UTPhysicians will extend beyond this implementation project's duration.

Even among the most confident physicians, awareness of missed diagnostic opportunities is more common in today's medical practice. A UTPhysicians practitioner co-authored the research on the type and frequency of missed diagnostic opportunities in Primary Practice (Singh, Thomas, et al., 2013 & 2014). There could hardly be a more receptive environment for addressing inaccurate diagnoses. The literature on the topic continues to expand – as evidenced by the editorial by Dr. Mark Graber just this past October (Graber, 2021). While a computerized diagnostic decision support system, such as Isabel Pro, will likely reduce diagnostic inaccuracy, the system will be limited in impact unless embedded as an integral part of an organization-wide process to discover cases of diagnostic inaccuracy and learn from them. A paper entitled “Structured case reviews for organizational learning about diagnostic vulnerabilities: initial experiences from two medical centers” describes a possible model for such a process. (Mathews et al., 2020). Key takeaways from this article include the need for non-judgemental, non-punitive forums, clinician agreement on case selection criteria, transparency of the process, and a culture focused on achieving diagnostic excellence.

In the absence of definitive statistics on historical diagnostic errors, a return on investment may not be subject to numerical determination. Still, pre-implementation and follow-on surveys of clinician usage and clinician opinions on the usefulness of the diagnostic differentials and the enhancement of their diagnostic process when using the system may allow clinicians to qualitatively assess the system's effect on patient health and safety. An analysis of specific cases in which the clinicians report the system's effectiveness in a challenging diagnostic encounter can add a more quantitative assessment of the effect on patient outcomes.



The issue with a return on investment for improving diagnostic accuracy is valuing the patient not seen a second or third time for failing to respond to treatment. Some considerations on where does this benefit accrue and where is the investment made are as follows:

- The payor benefits because the insurance company or self-insured employer need not pay for an unnecessary encounter.
- The patient benefits from reduced co-pays and restored good health earlier than otherwise.
- For the provider, though, there is an encounter eliminated and a loss of revenue from the unnecessary encounter. With most practitioners having a backlog of patients, however, the next patient is merely seen sooner than expected, and recognition of the lost revenue occurs at the end of the patient backlog, which for an active practice probably means retirement. The present value of the lost encounter is then de minimis. Accurate diagnosis and better patient outcomes may be at a premium if provider selection becomes based on outcomes. Better outcomes may make the clinician a provider of choice as healthcare moves to a pay-for-performance scheme rather than a fee-for-service system. Many payors are already moving in that direction. Walmart and Amazon are examples of this trend.

From a financial point of view, a diagnostic decision support system offers the prospect of reducing the number of tests necessary to produce an accurate diagnosis, shortening the time required for diagnosis allowing the practice to treat more patients annually, or eliminating the expense of a hospitalization caused by an incorrect or delayed diagnosis. Studies of malpractice claims from Massachusetts revealed that diagnostic decision support systems already in place but

not used could have saved millions of dollars in malpractice settlements by using their information appropriately applied. (Schiff et al., 2013; Zuccotti et al., 2014).

In response to the concerns often expressed about multiple diagnostic alternatives raising the cost of care, several studies address and refute this concern. Two in particular are representative. A 2010 study of decision support in actual hospital use noted: “It may seem paradoxical that evaluating a patient with several diagnoses in mind may be cheaper than doing so with only one until considering how expensive it is to have a single but incorrect diagnosis.” (Elkin et al., 2010). A 2014 study of a pediatric neurological decision support system noted: “Using the software, there was a significant reduction in error, up to 75% for diagnosis and 56% for workup....There was a 6% decrease in the number of workup items accompanied by a 34% increase in relevance. The authors conclude that decision support for a neurological diagnosis can reduce errors and save on unnecessary testing.” (Segal et al., 2014).

## Section 6: Study Limitations

Several limitations apply to this project. First among them is the absence of confirmation that an Isabel Pro differential diagnosis listing led to a correct diagnosis replacing an inaccurate diagnosis. The statistics collected are usage statistics only, and while a rich source of information on the frequency of use and the various patterns of search, the usage by each clinician ceases when the suggestions lead to a diagnosis or when the clinician decides the suggestions are of no help. In neither case is the reason for cessation recorded. An assumption might be that usage alone is enough to conclude that the system was helpful and accurate, especially since the survey responses support that conclusion. Despite the favorable survey responses, the project aimed to implement the usage of the system, not to conclusively prove a reduction in diagnostic inaccuracies by use of the system. There is no baseline of diagnostic accuracy against which to judge improvement in diagnostic accuracy post-usage. A subsequent project designed to find cases of diagnostic inaccuracy and determine whether Isabel Pro was helpful or would have been helpful if used at the initial encounter will be needed.

The responses to the user survey were encouraging, but despite a reasonably representative experience level among the 20 respondents, the response of only 20 out of a possible 73 may not be representative of the potential user group. The fact that roughly one-third of the respondents in both surveys reported a change in their original diagnosis after using Isabel Pro is encouraging since diagnostic decision support offers alternatives to an inaccurate diagnosis. Nonetheless, in the absence of confirmation that the change was an accurate diagnosis, conclusions are hard to draw.

The project did not identify a “clinical champion” who might underscore the system's usefulness and provide an example for other clinicians to see the system's relative advantage.

Interviews with the users might discover a practitioner who, having been faced with a challenging diagnostic situation, discovered that the use of the system was instrumental in arriving at an accurate diagnosis. That practitioner might be the “clinical champion” that could serve as an example for other users.

The project covered a period of 86 days from introduction to the collection of statistics; another limitation of the project since the duration may not be long enough to produce well-supported results from long-term usage. The system usage continues with the system contracted and funded until the end of October 2022. A supplemental program providing for closer contact with users may be forthcoming and, if conducted, will allow addressing some of these limitations.

## Section 7: Conclusions

Diagnostic inaccuracy is a significant patient safety concern in healthcare today. However, systems and techniques for detecting and preventing diagnostic inaccuracy are not widely and systematically employed. Despite any number of articles, research reports, and editorials, there appears little sense of urgency in health care practices or among the practitioners to implement strategies to reduce inaccurate diagnoses.

Computerized diagnostic decision support systems can improve diagnostic accuracy. Many studies support this conclusion, including the most recent study published in September 2021, using Isabel Pro as the diagnostic decision support system. Except for the 2017 study by Dr. Olga Kostopoulou, none of these studies took place in routine clinical practice, and even that study used patient actors in simulated examination rooms. This project appears to be the only study conducted in practicing clinics but relies on survey responses to assess the usefulness and accuracy in the absence of case-specific diagnostic conclusions.

Implementing computerized diagnostic decision support in routine clinical practice is achievable. This project shows that implementation can be accomplished smoothly in a busy academic medical practice and results in continued usage by both faculty and residents. The project did not sustain the implementation, but steady increases in usage in the late weeks of the project are encouraging. A “clinical champion” would be a great help in securing the usage in the practices.

The survey in Spring 2021 with residents and the most recent outpatient and primary care users’ survey demonstrate that clinicians respond favorably regarding the perceived usefulness of the system in practice. The system users reported a more favorable attitude toward the system than those participants furnished with only the differential listing. It remains a project goal to see

this favorable attitude translated into routine usage. A favorable attitude must be reinforced by clinician recognition of relative advantage to the use of the system if usage is to continue and perhaps increase. Instances where clinicians faced a challenging diagnosis and used Isabel Pro to augment the diagnostic process successfully would encourage adoption.

For the three weeks leading to the conclusion of the project data gathering period, usage was trending upwards for both faculty and residents. While not necessarily conclusive, the trend is encouraging because it reversed an earlier trend downward.

The usage trends also underscore the conclusion that communication and dissemination improve usage. An uptick in usage followed the presentations at each Chief Resident's conference. The article in the weekly publication "Inside UTHealth Houston" was followed by increased usage, as was the survey request that went out on February 21. The project did not include clinic presentations to the individual practicing clinicians, but much like the presentations at the Chief Resident's conferences, presentations to the clinics would likely be productive. They would serve as reminders of the systems and allow for questions, discussions, feedback, and presentation of examples of successful system use.

Finally, the author concludes that a computerized diagnostic decision support system, such as Isabel Pro, will reduce diagnostic inaccuracy but will be limited in impact unless embedded as an integral part of an organization-wide process to discover cases of diagnostic inaccuracy and learn from them. The process must be part of a rigorous drive for diagnostic excellence that includes creating a culture of transparency, routinely and diligently searching for cases of missed diagnostic opportunities, studying those cases in a non-judgemental and non-punitive environment, and using the lessons learned to inform the clinicians, moving the practices ever closer to zero diagnostic inaccuracies.

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## Tables

<b>Table 1 Seminal Publications on Diagnosis</b>						
<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Title	Seminal Publication on Diagnosis	Improving Diagnosis in Health Care	Balogh E,	Mil Med. 2016 Mar;181(3):183-5. doi: 10.7205/MILMED-D-15-00562.	2016
The report presented eight detailed recommendations addressing various aspects of diagnostic error, its detection and prevention. The roughly 415-page report led to a wealth of research into diagnostic error that continues to grow dramatically.						
2	Article	Detection and Frequency of Diagnostic Error	Types and origins of diagnostic errors in primary care settings	Singh H	JAMA Intern Med. 2013 Mar 25;173(6):418-25. doi: 10.1001/jamainternmed.2013.2777.	2013
This study is notable because the types of errors were in relatively common conditions, not rare or unusual conditions. The conclusions on the origins of the errors were notable in that the physician-patient exchange during the encounter produced the most significant percentage of failures leading to the diagnostic error. A well researched differential diagnosis listing, such as that produced by Isabel Pro, might improve the physician-patient exchange and reduce the inaccurate diagnoses.						

<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Article	Detection and Frequency of Diagnostic Error	Electronic health record-based surveillance of diagnostic errors in primary care	Singh H	BMJ Qual Saf. 2012 Feb;21(2):93-100. doi: 10.1136/bmjqs-2011-000304. Epub 2011 Oct 13.	2012
This article reports on a program to detect diagnostic error using a trigger algorithm to interrogate the electronic health record for potential error. Cases triggered were reviewed to assess if the presenting information was sufficient to have determined the final diagnosis. Of the 674 cases flagged by the trigger algorithm, 141 were determined to be a missed diagnostic opportunity.						
2	Article	Detection and Frequency of Diagnostic Error	The frequency of diagnostic errors in outpatient care: estimations from three large observational studies involving US adult populations	Singh H	BMJ Qual Saf. 2014 Sep;23(9):727-31. doi: 10.1136/bmjqs-2013-002627. Epub 2014 Apr 17.	2014
This the study takes the frequency of occurrence from earlier studies, together with two studies of chronic conditions, to extrapolate an estimate of diagnostic error prevalence in the entire United States.						

<b>Table 3 Diagnosis Recommendations</b>						
<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Title	Diagnosis Recommendations	Diagnostic error in internal medicine	Graber ML	Arch Intern Med. 2005 Jul 11;165(13):1493-9. doi: 10.1001/archinte.165.13.1493.	2005
This article addressed diagnostic errors in internal medicine and examined 100 cases of known diagnostic error by internists. Of note was that 74% of the cases involved cognitive error, with premature closure being the single most common cause.						
2	Article	Diagnosis Recommendations	Diagnostic errors in primary care: lessons learned	Ely JW	J Am Board Fam Med. 2012 Jan-Feb;25(1):87-97. doi: 10.3122/jabfm.2012.01.110174.	2012
This study surveyed 202 primary care physicians using a one-page questionnaire reporting on a single delayed or missed important diagnosis in their experience. This study bears on the translational project. The study is perhaps the first that included the presenting symptoms as part of the analysis, called for greater use of an expanded differential diagnosis, and confirmed that premature closure represents a significant factor in missed diagnoses.						
3	Article	Diagnosis Recommendations	Primary care closed claims experience of Massachusetts malpractice insurers	Schiff GD	JAMA Intern Med. 2013 Dec 9-23;173(22):2063-8. doi: 10.1001/jamainternmed.2013.11070.	2013
This study is an analysis of malpractice claims against primary care providers in Massachusetts. The pertinent finding in this study is that 72% of the claims were allegations related to a failure to diagnose.						
4	Title	Diagnosis Recommendations	Clinical Decision Support: The Road to Broad Adoption	Greenes R	ISBN: 978-0-12-398476-0	2014
This reference is Dr. Robert Greenes' book, Clinical Decision Support: The Road to Broad Adoption, a classic in diagnostic decision support literature. The book preceded much of the progress made in computerized diagnostic decision support systems but is instructive in defining the path to comprehensive clinical decision support, including diagnostic decision support.						
5	Title	Diagnosis Recommendations	The impact of electronic health records on diagnosis	Graber ML	Diagnosis (Berl). 2017 Nov 27;4(4):211-223. doi: 10.1515/dx-2017-0012.	2017
This article examines the electronic health record as a significant influence in diagnosis, mostly for good, and in many cases the cause of the diagnostic error resulting in serious adverse patient safety outcomes including death.						
6	Article	Diagnosis Recommendations	Two Decades Since To Err Is Human: An Assessment Of Progress And Emerging Priorities In Patient Safety	Bates DW	Health Aff (Millwood). 2018 Nov;37(11):1736-1743. doi: 10.1377/hlthaff.2018.0738.	2018
This article is a commentary on the progress in patient safety in the twenty years following the 1999 publishing of To Err is Human, a watershed treatise on the healthcare system's failure to place patient safety at the top of the priority list. While not explicitly noting computerized diagnostic decision support systems, the emphasis on diagnostic error supports this project's goal.						
7	Article	Diagnosis Recommendations	Tracking Progress in Improving Diagnosis: A Framework for Defining Undesirable Diagnostic Events	Olson APJ	J Gen Intern Med. 2018 Jul;33(7):1187-1191. doi: 10.1007/s11606-018-4304-2. Epub 2018 Jan 29.	2018
The last article in this segment is a perspective article focusing specifically on improving diagnosis by concentrating on those conditions most commonly misdiagnosed and those healthcare areas most vulnerable to diagnostic error. The article proposes a seven-item framework for concentrating improvement efforts in areas where an adverse outcome is most often the result of a diagnostic process breakdown. The authors observe that diagnostic error measurement is difficult, often controversial, and generally inadequate to trigger improvement.						

<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Abstract	DDSS History	Thinking about diagnostic thinking: a 30-year perspective	Elstein AS	Adv Health Sci Educ Theory Pract. 2009 Sep;14 Suppl 1:7-18. doi: 10.1007/s10459-009-9184-0. Epub 2009 Aug 11.	2009
The vast reservoir of the author's diagnostic experience is apparent in this very thoughtful article about the current state and possible future of diagnosis. This project's premise is that early diagnostic suggestions may prevent missed diagnostic opportunities and that almost any physician's diagnostic accuracy improves with a differential diagnosis list						

<b>Table 5 Diagnostic Decision Support Systems</b>						
<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Abstract	Diagnostic Decision Support System	A novel diagnostic aid (ISABEL): development and preliminary evaluation of clinical performance	Ramnarayan, P et al.	Simulation in Healthcare: Journal of the Society for Simulation in Healthcare. 2004;107(Pt 2):1091-5.	2004
This article is one of the first reports on Isabel, a diagnostic decision support system designed initially for pediatric patients. The report follows a two-year development cycle addressing one of the principal issues with previous systems – a knowledge base easily and efficiently updated. The system is fast, the input is relatively simple, and the database's updating is remarkably simple.						
2	Abstract	Diagnostic Decision Support System	Isabel, a clinical decision support system	Vardell E	Med Ref Serv Q. 2011;30(2):158-66. doi: 10.1080/02763869.2011.562800.	2011
This column is a review and introduction of the adult version of the Isabel diagnostic decision support system, beginning with an overview of the database, and notes that Isabel is composed of a database of more than 11,000 diagnoses and 4,000 drugs						
3	Article	Diagnostic Decision Support System	Isabel: A Review	Wood BA	Barbara A. Wood. "Isabel: A Review" Journal of Electronic Resources in Medical Libraries Vol. 11 Iss. 4 (2014) p. 189 - 192 ISSN: 1542-4073 Available at: <a href="http://works.bepress.com/barbara-wood/2/">http://works.bepress.com/barbara-wood/2/</a>	2014
Published as a column in the Journal of Electronic Resources in Medical Libraries, the author reviews the Isabel CDSS to evaluate the product's utility in medical education.						
4	Abstract	Diagnostic Decision Support System	An ontology driven clinical evidence service providing diagnostic decision support in family practice	Corrigan D	AMIA Jt Summits Transl Sci Proc. 2015 Mar 25;2015:440-4. eCollection 2015.	2015
This paper describes a prototype diagnostic decision support system developed during the European project TRANSFoRm. The clinical evidence service allows the presentation of recommendations integrated with an EHR in primary care, using ontology models of evidence. The prototype provides diagnostic support on only three presentations or reasons for encounter.						
5	Article	Diagnostic Decision Support System	Patients could provide initial differential diagnoses	Maude J	Br J Gen Pract. 2015 Mar;65(632):116-7. doi: 10.3399/bjgp15X683893.	2015
Jason Maude is the founder of Isabel Healthcare. This editorial describes the patient's assistance in his diagnosis using the company's system designed for patients.						
6	Article	Diagnostic Decision Support System	Requirements and validation of a prototype learning health system for clinical diagnosis	Corrigan D	Learn Health Syst. 2017 May 31;1(4):e10026. doi: 10.1002/lrh2.10026. eCollection 2017 Oct.	2017
This article attempts to address some of the shortcomings with commercially available diagnostic decision support systems, particularly those relying on a proprietary database, such as Isabel or DXPlain. This decision support tool showed an 8% to 9% improvement in diagnostic accuracy and resulted in more coded data for clinical evidence. The tool was easy to use and quickly learned, but the system described is limited to only three presenting conditions, and the data supporting the system was manually curated. This limitation is no small shortcoming, and the wide use of EHR data is fraught with difficulty not addressed in the article.						

<b>Table 6 Diagnostic Decision Support System Performance</b>						
<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Abstract	Diagnostic Decision Support System Performance	Diagnostic decision support systems	Riesenberg LA	J Med Pract Manage. 2001 Nov-Dec;17(3):163-5.	2001
This study reports on the use of diagnostic decision support systems in a general medical clinic, finding that they could suggest new diagnostic possibilities, focus thinking about clinical problems, and serve as a recertification preparation tool. The study also found diagnostic decision support systems useful for the novice clinician (fourth-year medical students and interns).						
2	Abstract	Diagnostic Decision Support System Performance	Diagnostic decision support systems: how to determine the gold standard?	Berner ES	J Am Med Inform Assoc. 2003 Nov-Dec;10(6):608-10. doi: 10.1197/jamia.M1416.	2003
The editorial lists criteria for evaluating a diagnostic decision support system: 1. Producing the correct diagnosis, 2. The quality of the differential, 3. Appropriate management suggestions, 4. User acceptance. 5. Interaction of the user with the system.						
3	Abstract	Diagnostic Decision Support System Performance	How well does decision support software perform in the emergency department?	Graber MA	Emerg Med J. 2003 Sep;20(5):426-8. doi: 10.1136/emj.20.5.426.	2003
This study sampled 25 patients as they presented to an emergency department. The study audiotaped, transcribed, and together with all written records entered the encounters as input to two diagnostic decision support systems: QMR and Iliad. The final diagnosis of the emergency department attending physician was considered conclusive. The systems displayed approximately the same accuracy in the emergency department as in clinical settings. Neither was sufficiently accurate to rely on as conclusive.						
4	Abstract	Diagnostic Decision Support System Performance	Measuring the impact of diagnostic decision support on the quality of clinical decision making: development of a reliable and valid composite score	Ramnarayan P	J Am Med Inform Assoc. 2003 Nov-Dec;10(6):563-72. doi: 10.1197/jamia.M1338. Epub 2003 Aug 4.	2003
This study aimed to produce a scoring process for comparing the effectiveness of a diagnostic decision support system. The system chosen for the study was Isabel (web-based pediatric version) using six simulated cases subsequently evaluated by 76 physicians, first as presented, and second using the Isabel diagnostic aid. Two experienced physicians assigned scores by conducting an independent assessment of each case. The study did not evaluate the performance of Isabel, but rather the physicians with and without Isabel prompts. The most significant weakness is the involvement of Isabel employees and consultants in the project.						
5	Abstract	Diagnostic Decision Support System Performance	Evaluation of an Internet delivered pediatric diagnosis support system (ISABEL) in a tertiary care center in India	Bavdekar SB	Indian Pediatr. 2005 Nov;42(11):1086-91.	2005
This study aimed to produce an assessment of the sensitivity of the Isabel diagnostic tool in an emergency department setting in a developing country where recent graduates are staffing the public hospitals. The study conducted a retrospective assessment of 200 pediatric patients admitted to a major metropolitan public hospital's emergency department over 18 months. The system yielded an aggregate sensitivity of 80.5%. The study limitations were several, including no ranking of the correct diagnosis.						
6	Abstract	Diagnostic Decision Support System Performance	Validation of a diagnostic reminder system in emergency medicine: a multi-centre study	Ramnarayan P	Emerg Med J. 2007 Sep;24(9):619-24. doi: 10.1136/emj.2006.044107.	2007
The study was the first large-scale evaluation of the Adult version of the Isabel diagnostic decision support system, released in 2005. The study analysed cases from three large academic centers in the UK National Health System. The study aimed to evaluate Isabel's performance, so no results were provided to the clinicians, nor was treatment changed for any patient. The study calculated diagnostic accuracy on 217 discharged patients, 206 cases (95%) correct, with 169 being in the top ten presentations (78%). The study calculated diagnostic utility based on 152 "must not miss" diagnoses, 140 (92%) correct of which 88 were in the top ten (58%). The study is limited by being conducted by researchers with financial relationships with the Isabel developer.						
7	Title	Diagnostic Decision Support System Performance	Performance of a web-based clinical diagnosis support system for internists	Graber ML	J Gen Intern Med. 2008 Jan;23 Suppl 1(Suppl 1):37-40. doi: 10.1007/s11606-007-0271-8.	2008

This 2008 study aimed to evaluate the accuracy and speed of Isabel; an adult patient diagnostic decision support system released in 2005. The study selected 50 consecutive cases describing adult patients from the "Case Records of Massachusetts General Hospital" (New England Journal of Medicine, vol. 350:166–176, 2004 and 353:189–198, 2005). When key factors were input, the system presented the correct diagnosis among the thirty alternatives in 48 of the 50 cases (the knowledge base did not include the two missed diagnoses). Pasting the case history yielded 37 correct. The cases in the NEJM are very complete and likely do not represent routine clinical presentations. The study did not consider the ranking of the diagnosis presentations.						
8	Abstract	Diagnostic Decision Support System Performance	The introduction of a diagnostic decision support system (DXplain™) into the workflow of a teaching hospital service can decrease the cost of service for diagnostically challenging Diagnostic Related Groups (DRGs)	Elkin PL	Int J Med Inform. 2010 Nov;79(11):772-7. doi: 10.1016/j.ijmedinf.2010.09.004. Epub 2010 Oct 14.	2010
The DXplain system was made available to residents. This study aimed to establish the improvement in the cost of treatment of patients when residents availed themselves of the diagnostic suggestions, compared to a control set of similar cases preceding the study. The study addressed 564 diagnostically challenging cases during the study period and 1,173 diagnostically challenging cases during the control period. Total costs were determined to be lower by \$1,281 per case, suggesting annual savings to the institution of roughly \$2 million. The study did not address outcomes, only costs, was conducted at a single hospital and relied on the likelihood that physician experience, case mix, and acuity would be similar during the control and study periods.						
9	Abstract	Diagnostic Decision Support System Performance	Differential diagnosis generators: an evaluation of currently available computer programs	Bond WF	J Gen Intern Med. 2012 Feb;27(2):213-9. doi: 10.1007/s11606-011-1804-8.	2012
The aim of this study was, first, to identify differential diagnosis generators currently available, meeting specific essential criteria for clinical decision support, and second, assess the performance of the systems selected. Of the 23 programs identified, only four met the inclusion criteria: Isabel, DXplain, Diagnosis Pro, and PEPID. The assessment used twenty consecutive diagnosis-focused cases. All the programs missed two diagnoses. Isabel and DXplain were the top performers, each registering 69 points out of 100. The studies do not replicate clinical settings, and the scoring did not include a ranking of the correct diagnosis.						
10	Abstract	Diagnostic Decision Support System Performance	Evaluating online diagnostic decision support tools for the clinical setting	Pryor M	Stud Health Technol Inform. 2012;178:180-5.	2012
This study by New South Wales Clinical was to determine if a commercially available diagnostic decision support system would provide diagnostic assistance. The study found 11 that met the inclusion criteria. The first stage tested all 11 with 3 challenging cases. The second stage compared the 3 top-performing systems (First Consult, Best Practice, and Isabel), using 6 challenging cases. The evaluation ranked the systems from 6 (best) to 18 (worst). Best Practice scored 10, Isabel 11, and First Consult 14. This study made no effort to evaluate patient outcomes or physician improvement in diagnostic accuracy.						
11	Abstract	Diagnostic Decision Support System Performance	The utility of an online diagnostic decision support system (Isabel) in general practice: a process evaluation	Henderson EJ	JRSM Short Rep. 2013 Apr 4;4(5):31. doi: 10.1177/2042533313476691. Print 2013 May.	2013
The study aimed to solicit responses from practicing physicians on their opinions of the usefulness of Isabel in their practice in the UK general practice system. The study employed a focus-group approach and a post-use questionnaire following a three-month survey period. Five practices employed the system on 16 patients. Ten post-use surveys revealed no change in diagnostic decisions using the system. Post-use focus groups suggested the system was not well-tailored to the clinical routine and could be more helpful if better suited. The study was short, involved only a few volunteering practices, and relied heavily on opinions.						
12	Abstract	Diagnostic Decision Support System Performance	Uptake and impact of a clinical diagnostic decision support tool at an academic medical center	Barbieri JS	Diagnosis (Berl). 2015 Jun 1;2(2):123-127. doi: 10.1515/dx-2014-0058.	2015
The study aimed to evaluate the usage and change in treatment requests with the introduction of VisualDX in the academic medical center. VisualDx was made available to the entire system by drop-down menus and mobile applications on phones. The report studied the use of VisualDx for 18 months following its introduction to compare inpatient dermatology consults requested to the number of requests in the preceding 12 months. The study detected no statistically significant difference in dermatology consults following the introduction. The main limitation was the absence of any assessment of the change in patient outcomes.						

13	Article	Diagnostic Decision Support System Performance	The Effectiveness of Electronic Differential Diagnoses (DDX) Generators: A Systematic Review and Meta-Analysis	Riches N	PLoS One. 2016 Mar 8;11(3):e0148991. doi: 10.1371/journal.pone.0148991. eCollection 2016.	2016
This study aimed to conduct a systematic review and meta-analysis seeking diagnostic decision support generators' clinical effectiveness. The study considered four key research questions: 1. Is the system effective at retrieving accurate diagnoses? 2. Does the system perform as well as clinicians? 3. Does the use of the system improve a physician's diagnostic accuracy? 4. What are the enablers and barriers to these systems in clinical practice? This report identifies the evaluation methodology most suitable for validating a diagnostic decision support system.						
14	Abstract	Diagnostic Decision Support System Performance	Assessing the utility of a differential diagnostic generator in UK general practice: a feasibility study	Cheraghi-Sohi S	Diagnosis (Berl). 2020 Feb 14:/dx.doi.org/10.1186/s12916-020-0033-0. doi: 10.1186/s12916-020-0033-0. Online ahead of print.	2020
This study aimed to conduct a process evaluation of Isabel in a UK general practice to assess the tool for routine primary medical care. The study took place in a large inner-city UK general practice in Greater Manchester, England, consisting of approximately 18,000 patients, seventeen general practitioners, and two nurse practitioners. This study indicates that UK physicians see little advantage to Isabel in primary care. The study was over a relatively short period in a single institution with no integration with the EHR. The study is probably a very reasonable assessment of the likelihood of adoption without significant changes.						
15	Article	Diagnostic Decision Support System Performance	Should electronic differential diagnosis support be used early or late in the diagnostic process? A multicentre experimental study of Isabel.	Sibbald, M.	BMJ Quality & Safety. https://doi.org/10.1136/bmjqs-2021-013493	2021
This study used Isabel Pro as a computerized diagnostic decision support system. Participants were in two groups, the first group using Isabel Pro early in the diagnostic process and the second group using Isabel Pro after performing additional tests and accumulating additional diagnostic information. The study reported a 7% improvement in diagnostic accuracy when using the system early and an 8% improvement when using the system later. When using the system later in the diagnostic process, the improvement in diagnostic accuracy applied to all experience levels, from students to faculty.						



<b>Table 7 Physician Diagnostic Accuracy Improvement</b>						
<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Abstract	Physician Diagnostic Accuracy Improvement	Enhancement of clinicians' diagnostic reasoning by computer-based consultation: a multisite study of 2 systems	Friedman CP	JAMA. 1999 Nov 17;282(19):1851-6. doi: 10.1001/jama.282.19.1851.	1999
The study aimed to evaluate the improvement in a physician's diagnostic accuracy when using two diagnostic decision support systems, Iliad and QMR. Each participant evaluated 9 of 36 cases prepared for the study, prepared a differential diagnosis for each case, first without assistance, and then used the system's suggestions. The study reported accurate diagnoses in 39.5% of the cases when not using the system and 45.4% of the cases after consultation. Few cases and the academic setting are limiting.						
2	Abstract	Physician Diagnostic Accuracy Improvement	Comparison of measures to assess change in diagnostic performance due to a decision support system	Maisiak RS	Proc AMIA Symp. 2000:532-6.	2000
This study assessed ten different single measures of diagnostic performance by empirical comparison. The study compared the diagnostic performance of 108 physicians using medical cases of varying diagnostic difficulty and with or without a high level of assistance from a DDSS. The most responsive measures were when the correct diagnoses were within the top 5 to 10 listed diagnoses. Evaluating DDSS performance by examining the correct case diagnosis's rank-order within a restricted number of diagnoses may be responsive but not appropriate since, in the case of challenging diagnostic encounters, lower-ranked diagnoses may well be correct and, therefore, should not be dismissed simply because they do not appear earlier.						
3	Abstract	Physician Diagnostic Accuracy Improvement	Clinician performance and prominence of diagnoses displayed by a clinical diagnostic decision support system	Berner ES	AMIA Annu Symp Proc. 2003;2003:76-80.	2003
This study aimed to examine a clinician's diagnostic accuracy before and after a diagnostic CDSS presentation of alternatives. The subjects were 70 internal medicine residents. The system was QMR (Quick Medical Reference). The study reported two conclusions. First, clinicians who considered the correct diagnosis before the CDSS were more likely to produce the correct diagnosis near the top of the list. Second, physicians are firmly anchored by their initial diagnoses before using the CDSS, and changes in the clinicians' diagnoses are related to the presence or absence of the correct diagnosis in the top 10 diagnoses displayed by the CDSS.						
4	Abstract	Physician Diagnostic Accuracy Improvement	Do physicians know when their diagnoses are correct? Implications for decision support and error reduction	Friedman CP	J Gen Intern Med. 2005 Apr;20(4):334-9. doi: 10.1111/j.1525-1497.2005.30145.x.	2005
This study aimed to examine the agreement between physicians' confidence in their diagnoses and their accuracy. The study aimed to assess clinical experience and its effect on diagnostic confidence. Conducted at three academic medical centers, it involved 72 senior medical students, 72 senior medical residents, and 72 faculty internists. The participants studied synopses of 9 of 36 diagnostically challenging medical cases (each with a correct definitive diagnosis) and generated a differential diagnosis for each case. They indicated their level of confidence in each diagnosis. The study concluded that even experienced clinicians often cannot determine the correctness of their diagnoses. The study was limited to diagnosis only.						
5	Abstract	Physician Diagnostic Accuracy Improvement	Assessment of the potential impact of a reminder system on the reduction of diagnostic errors: a quasi-experimental study	Ramnarayan P	BMC Med Inform Decis Mak. 2006 Apr 28;6:22. doi: 10.1186/1472-6947-6-22.	2006
This study aimed to use a mix of easy and difficult simulated cases to assess the impact of the diagnostic decision support system, Isabel, on clinical decisions made during acute assessment. Participants assessed a balanced set of 24 simulated cases on a trial website, recording clinical decisions such as differential diagnosis, test ordering, and treatment, both in advance and after consultation using Isabel. A panel of two pediatric consultants provided gold-standard responses for each case. The study concluded that the provision of patient- and context-specific reminders might reduce diagnostic omissions altogether. The study is limited by the possibility that prompts or reminders after first assessing the case may be more effective due to the second look at						

the case and less due to the reminders themselves. A further limitation was the relationships of the researchers with the system developer.						
6	Abstract	Physician Diagnostic Accuracy Improvement	Diagnostic omission errors in acute paediatric practice: impact of a reminder system on decision-making	Ramnarayan P	BMC Med Inform Decis Mak. 2006 Nov 6;6:37. doi: 10.1186/1472-6947-6-37.	2006
This study examined the effect of a diagnostic reminder system, Isabel, on clinicians' decisions in an acute pediatric setting during assessments characterized by diagnostic uncertainty. The study assessed junior doctors for five months at four pediatric ambulatory units. The doctors were free to consult the diagnostic aid for diagnostic assistance at any time. Participants recorded their differential diagnosis, test-ordering, and treatment, both in advance of and after system consultation. The study is limited by the inconsistent use of the system by the participants, by the single point choice for performance assessment, and by the possibility that results using a before and after method may be improved simply by a reconsideration of the case. A further limitation was the relationship of the researchers to the developer of the system.						
7	Abstract	Physician Diagnostic Accuracy Improvement	Overconfidence as a cause of diagnostic error in medicine	Berner ES	Am J Med. 2008 May;121(5 Suppl):S2-23. doi: 10.1016/j.amjmed.2008.01.001.	2008
This study aimed to determine: (1) What is the extent of incorrect diagnosis? (2) What percentage of documented adverse events are attributable to diagnostic errors, and, conversely, how often do diagnostic errors lead to adverse events? (3) Has the rate of diagnostic errors decreased over time? The authors conclude that diagnostic error is at least 5%, and perhaps more, that the physicians almost uniformly overestimate the accuracy of their diagnoses and that overconfidence contributes to diagnostic error. In particular application to this project, the authors note that premature closure, getting to a diagnosis too quickly and failing to consider conflicting evidence, is a significant cognitive error in medicine.						
8	Abstract	Physician Diagnostic Accuracy Improvement	Taking steps towards a safer future: measures to promote timely and accurate medical diagnosis	Graber ML	Am J Med. 2008 May;121(5 Suppl):S43-6. doi: 10.1016/j.amjmed.2008.02.006.	2008
This treatise aims to step back from the press of medicine's daily practice to examine whether today's practice of medicine is at the point it should be on the issues of detecting, preventing, and learning about diagnostic error. The article speaks to all the stakeholders in improving diagnosis – physicians, healthcare institutions, researchers, policy-makers, and, last but not least, the patient. In conclusion, the author makes substantive suggestions for improvements to physicians, healthcare institutions, patient safety organizations, and the patient.						
9	Abstract	Physician Diagnostic Accuracy Improvement	Use of diagnostic decision support systems in medical education	Berner ES	Methods Inf Med. 2010;49(4):412-7. doi: 10.3414/ME9309. Epub 2010 Apr 20.	2010
This article addresses diagnostic decision support systems and examines 1) the skills needed in a medical students' clinical experiences, 2) the changes required in the curriculum when introducing the systems into the educational process, and 3) the research issues associated with these systems in educational programs. The study conducts a critical analysis of the literature on diagnostic decision support systems as part of medical education. Students will need specific skills in 1) selecting appropriate system vocabulary and functions, and 2) applying the diagnostic system's suggestions to their particular patient.						
10	Abstract	Physician Diagnostic Accuracy Improvement	The impact of a diagnostic reminder system on student clinical reasoning during simulated case studies	Carlson J	Simul Healthc. 2011 Feb;6(1):11-7. doi: 10.1097/SIH.0b013e3181f24acd.	2011
This study aimed to assess the assistance to diagnostic reasoning provided to students by Isabel PRO, a web-based DRS, using simulated encounters. The study engaged 20 fourth-year medical students to participate in four simulated case scenarios with and without Isabel assistance. The diagnostic accuracy of the students improved after using Isabel PRO. The use of a DRS within the context of a patient case represents a distinct clinical skill set requiring appropriate training. Providing learners with gold standard examples of using such a tool is an essential learning component. Simulated case scenarios offer the most appropriate clinical context.						
11	Abstract	Physician Diagnostic Accuracy Improvement	Impact of a computer-based diagnostic decision support tool on the differential diagnoses of medicine residents	Feldman MJ	J Grad Med Educ. 2012 Jun;4(2):227-31. doi: 10.4300/JGME-D-11-00180.1.	2012

<p>This study aimed to assess the improvement in residents' differential diagnosis or treatment plans when presented with a rank-ordered list of diagnostic possibilities from a medical diagnostic decision support system. The study recruited twenty first-year internal medicine residents at Massachusetts General Hospital. Each participant viewed three actual patient cases (deidentified). The participants entered the differential diagnosis and management plan both before and after seeing the suggested list of diseases in a web-based questionnaire. The study concluded that viewing a rank-ordered list of diagnostic possibilities provided a significant beneficial effect. The study is limited because it was a single site and a small sample, together with the case selection, which maximized the impact of an omitted diagnosis. Also, since participants were interns, the effect may have been more pronounced.</p>						
12	Abstract	Clinician Diagnostic Accuracy Improvement	Use of the Isabel decision support system to improve diagnostic accuracy of pediatric nurse practitioner and family nurse practitioner students	John RM	NI 2012 (2012). 2012 Jun 23;2012:194. eCollection 2012.	2012
<p>This study aimed to assess the use of decision support among Advanced Practice Nurse (APN). The study implemented the Isabel diagnostic decision support system into the curriculum. The study includes 37 PNP and 40 FNP students. All were female except for one FNP student. All had less than five years of RN experience, and more than 90% were between 20-29 years. The assessment of the results is in an assessment follow-up report.</p>						
13	Article	Physician Diagnostic Accuracy Improvement	Differential diagnosis: the key to reducing diagnosis error, measuring diagnosis and a mechanism to reduce healthcare costs	Maude J	Diagnosis (Berl). 2014 Jan 1;1(1):107-109. doi: 10.1515/dx-2013-0009.	2014
<p>This article is an opinion piece by the founder and developer of the Isabel diagnostic decision support system. It is clearly well informed, and proposes that a differential diagnosis would improve the diagnostic accuracy of almost every physician. A differential diagnosis is a feature that his system presents automatically as its diagnostic output.</p>						
14	Article	Physician Diagnostic Accuracy Improvement	Reducing risk with clinical decision support: a study of closed malpractice claims	Zuccotti G	Appl Clin Inform. 2014 Aug 20;5(3):746-56. doi: 10.4338/ACI-2014-02-RA-0018. eCollection 2014.	2014
<p>This study reported on the proportion of malpractice claims potentially preventable by clinical decision support (CDS). In each case, a panel of experts assessed the clinical opportunities to intervene to avert the malpractice event. The expert panel also searched for the presence or absence of CDS that might have prevented the event. The results of this study suggest that, in addition to their known benefits for quality and safety, CDS systems within HIT have a potential role in decreasing malpractice payments. The study concluded that more than half of malpractice events and over \$40 million in indemnity payments were potentially preventable with CDS. The implication for this project is the possibility that this technique might lead to the financial justification for a diagnostic decision support system.</p>						
15	Title	Physician Diagnostic Accuracy Improvement	Early diagnostic suggestions improve accuracy of GPs: a randomised controlled trial using computer-simulated patients	Kostopoulou O	Br J Gen Pract. 2015 Jan;65(630):e49-54. doi: 10.3399/bjgp15X683161.	2015
<p>The study aimed to determine whether providing GPs with early diagnostic suggestions improves accuracy. The study recruited 297 GPs to diagnose nine patient cases, differing in difficulty, in one of three experimental conditions: control, early support, or late support. The participating physicians read initial patient information, along with the Reason for Encounter (RfE). The study concluded that reminding GPs of diagnoses to consider in advance of the diagnostic process can improve diagnostic accuracy regardless of case difficulty, without lengthening information search. The study is limited since the cases relied on diagnostic suggestions from a diagnostic decision system, even though the study did not test a particular system.</p>						
16	Title	Physician Diagnostic Accuracy Improvement	Diagnostic accuracy of GPs when using an early-intervention decision support system: a high-fidelity simulation	Kostopoulou O	Br J Gen Pract. 2017 Mar;67(656):e201-e208. doi: 10.3399/bjgp16X688417. Epub 2017 Jan 30.	2017

<p>The study reported on a prototype Diagnostic Decision Support system and aimed to evaluate the prototype DSS's performance in a high-fidelity simulation. The study recruited 34 GPs to consult with six standardized patients (actors) using their usual EHR. Following that series of encounters, the participants consulted with six other patients using the same EHR but with the integrated DSS. The study noted an 8–9% absolute improvement in diagnostic accuracy when the DSS was used. The study was limited in that the cases did not represent the typical set of daily presentations, and the situation, while well designed to simulate a series of encounters, did not include the noise, interruptions, and other distractions in routine clinical practice.</p>						
17	Abstract	Physician Diagnostic Accuracy Improvement	Structured case reviews for organizational learning about diagnostic vulnerabilities: initial experiences from two medical centers	Mathews BK	Diagnosis (Berl). 2020 Jan 28;7(1):27-35. doi: 10.1515/dx-2019-0032.	2020
<p>This study reports on an effort to establish a detection, prevention, and feedback for improvement program at two large healthcare institutions, based on the premise that an organization's ability to identify and learn from opportunities for improvement (OFI) is key to increasing diagnostic safety. The study describes a five-step process employed to create a review system and provide feedback: (1) identify trigger criteria; (2) establish a review panel; (3) develop a system to conduct reviews; (4) perform reviews; and (5) provide feedback. The study reported three important lessons learned. (1) Peer review of cases provides opportunities to learn and calibrate diagnostic and management decisions at an organizational level. (2) Sharing cases in review groups supports a culture of open discussion of OFIs. (3) Reviews focused on diagnostic safety identify opportunities that may complement other organization-wide review opportunities. The study reported a significant element in acceptance and participation in the process as the subtle reframing of the term "diagnostic error" to "opportunity for improvement." The study attributed much of the increase in self-reporting to this reference change.</p>						

<b>Table 8 Physician Acceptance</b>						
<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Abstract	Physician Acceptance	Internal medicine resident satisfaction with a diagnostic decision support system (DXplain) introduced on a teaching hospital service	Bauer BA	Proc AMIA Symp. 2002:31-5.	2002
The study aimed to determine whether Internal Medicine residents would find using a diagnostic decision support system to be a satisfactory experience. Resident willingness to use the instrument was particularly important because of growing concerns regarding residents' educational experience in the hospital. The study concluded that a significant level of satisfaction with the system existed among residents. Their recognition that it frequently led them to consider novel diagnoses suggests it had a positive educational impact.						
2	Abstract	Physician Acceptance	Diagnostic decision support systems: why aren't they used more and what can we do about it?	Berner ES	AMIA Annu Symp Proc. 2006;2006:1167-8.	2006
This article by Dr. Eta Berner, one of the icons in diagnostic improvement, comments on the reasons behind the limited use of diagnostic decision support systems and describes opportunities to increase their use in routine clinical practice. The author covers many of the issues surrounding objections to the use of systems for diagnostic support and offers a series of opinions on topics to be pursued to increase their use, especially the issue of integration with the EHR.						
3	Abstract	Physician Acceptance	Resources medical students use to derive a differential diagnosis	Graber ML	Med Teach. 2009 Jun;31(6):522-7. doi: 10.1080/01421590802167436.	2009
The study evaluated the usefulness of Isabel, an electronic diagnosis support system. The study recruited 117 third-year medical students to consider a challenging case and to identify and prioritize their top three diagnoses, report the time devoted to the exercise, and list the resources they used and their relative usefulness. The study determined that students who identified the correct diagnosis as their first choice spent significantly more time on the case than other students. Students using Isabel had more success identifying the correct diagnosis (73% for users vs. 53% for non-users), a difference of borderline statistical significance. The study concluded that medical education needs to teach future clinicians how to use these tools to advantage.						
4	Abstract	Physician Acceptance	What can be done to increase the use of diagnostic decision support systems?	Berner ES	Diagnosis (Berl). 2014 Jan 1;1(1):119-123. doi: 10.1515/dx-2013-0014.	2014
This editorial is another commentary by Dr. Eta Berner on topics to increase the use of diagnostic decision support systems. To quote her purposes: "This essay explores the reasons why diagnostic decision support systems are underutilized despite growing concern about diagnostic errors. Factors related to the motivation to use the systems, clinician cognition, system design and implementation, and the absence of feedback in routine clinical care are discussed."						
5	Abstract	Physician Acceptance	Decision support for diagnosis should become routine in 21st century primary care	Delaney BC	Br J Gen Pract. 2017 Nov;67(664):494-495. doi: 10.3399/bjgp17X693185.	2017
This article is an editorial by Dr. Brendan Delaney and Dr. Olga Kostopoulou. Their essential comment is that in this era of time-constrained medical practice and the explosion of research in medicine, computerized diagnostic decision support is essential. The article is a well-founded commentary on the need for diagnostic decision support in primary practice, the factors that have hindered adoption to date, and the encouraging technological developments that point to improvements in the diagnostic process.						
6	Abstract	Physician Acceptance	The impact of a diagnostic decision support system on the consultation: perceptions of GPs and patients	Porat T	BMC Med Inform Decis Mak. 2017 Jun 2;17(1):79. doi: 10.1186/s12911-017-0477-6.	2017
This study concentrated on the opinions of the physicians and the patients following a consultation. The physicians favored the DDS system, 74%, commented that the system improved the diagnostic process by providing diagnoses for consideration and triggering an improved set of questions to the patient. The physicians' coded significantly more symptoms during the consultations, an improvement very much needed to improve the EHR but the physicians accustomed to entering their clinical notes after an encounter expressed their concern with the change in their clinical routine. Patients registered no difference in satisfaction with the encounter.						

7	Article	Physician Acceptance	Reaching 95%: Decision support tools are the surest way to improve diagnosis now.	Graber, M.L.	BMJ Quality & Safety, bmjqs-2021-014033. <a href="https://doi.org/10.1136/bmjqs-2021-014033">https://doi.org/10.1136/bmjqs-2021-014033</a> .	2017
Computerized diagnostic support systems are not universally used or even widely used in routine clinical practice. Dr. Mark Graber, in October 2021, devoted his entire editorial to the issue of the broader use of computerized diagnostic decision support systems and lamented the underutilization of them by clinicians in the real world of patient diagnosis in their practices.						

**Table 9 Diagnostic Decision Support System Integration with the Electronic Health Record**

<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Article	DDSS integration with EHR	Experience with Integrating Diagnostic Decision Support Software with Electronic Health Records: Benefits versus Risks of Information Sharing	Segal MM	EGEMS (Wash DC). 2017 Dec 6;5(1):23. doi: 10.5334/egems.244.	2017
<p>This article does an excellent job of demonstrating the difficulty of integrating a diagnostic decision support system into an electronic health record, the complexity of including the diagnostic process within the EHR, and the opposing positions of physicians using the system as to its usefulness versus the legal liability associated with discoverable interim diagnostic considerations being in the EHR or even in a separate database. The work took place at two large integrated healthcare institutions, Geisinger Health System, and Intermountain Healthcare. The diagnostic decision support system evaluated was SimulConsult, a diagnostic decision support system primarily used in neurology, specifically pediatric neurology. At the end of the effort, the project successfully integrated the diagnostic decision support system with the EHR at Geisinger. However, tension arose from physicians' opposing views regarding the advisability of storing intermediate diagnostic steps in a discoverable format. The study achieved no real reconciliation of these issues.</p>						

Table 10: Summary of Validation Results

<u>Case Identifier</u>	<u>Ultimate Diagnosis Presented ?</u>	<u>Ultimate Diagnosis Ranking</u>	<u>Symptom Literature Match</u>	<u>Ultimate Diagnosis in the Literature Database?</u>	<u>Isabel Pro Diagnosis</u>	<u>Ultimate Diagnosis</u>
<a href="#">52-36001</a>	Y	1	99%	Y	Diabetic Ketoacidosis	Acromegaly (diabetic ketoacidosis)
<a href="#">McGMS Case 1</a>	Y	2	73%	Y	Pyelonephritis	Emphysematous Pyelonephritis, Clinically indistinguishable from severe, acute pyelonephritis
<a href="#">33-36133</a>	Y	2	93%	Y	Megaloblastic Anemias - Pernicious Anemia; Vit B12 Deficiency - Pernicious Anemia; Subacute Combined Degeneration of Spinal Cord	Pernicious Anemia
<a href="#">25-36143</a>	Y	2	88%	Y	Polymyalgia Rheumatica	Polymyalgia Rheumatica
<a href="#">55-36021</a>	Y	2	84%	Y	Carcinoid Syndrome	Carcinoid Syndrome
<a href="#">65-36093</a>	Y	2	91%	Y	Intracranial Hemorrhage - Subarachnoid Hemorrhage	Subarachnoid Hemorrhage
<a href="#">CBD001</a>	Y	3	98%	Y	Polymyalgia Rheumatica	Polymyalgia Rheumatica
<a href="#">45-36053</a>	Y	5	62%	Y	Crohn Disease	Crohn's Disease
<a href="#">64-36072</a>	Y	6	64%	Y	Hemolytic Uremic Syndrome	Hemolytic Uremic Syndrome
<a href="#">KH001</a>	Y	7	54%	Y	Diabetic Neuropathy	Diabetes
<a href="#">23-36113</a>	Y	7	47%	Y	Hemochromatosis	Hemochromatosis
<a href="#">36-36012</a>	Y	8	64%	Y	Liver Neoplasms - Hepatocellular Carcinoma	Metastatic Hepatic Adeno (liver) Cancer
<a href="#">21-36121</a>	Y	9	60%	Y	Myasthenia Gravis	Myasthenia Gravis



<u>Case Identifier</u>	<u>Ultimate Diagnosis Presented ?</u>	<u>Ultimate Diagnosis Ranking</u>	<u>Symptom Literature Match</u>	<u>Ultimate Diagnosis in the Literature Database?</u>	<u>Isabel Pro Diagnosis</u>	<u>Ultimate Diagnosis</u>
<a href="#">13-36043</a>	Y	9	60%	Y	Liver Abscess (Amoebic, Pyogenic)	Amoebic Liver Abscess
<a href="#">61-36042</a>	Y	9	47%	Y	Acute Appendicitis	Appendicitis
<a href="#">24-36063</a>	Y	11	73%	Y	Brucellosis	Brucellosis
<a href="#">McGMS 20200306 Cards Case Conference - Final</a>	Y	14	36%	Y	Myocarditis	lupus myocarditis
<a href="#">11-36052</a>	Y	14	73%	Y	Colorectal Cancer	Colon Cancer
<a href="#">31-36091</a>	Y	18	33%	Y	Guillain-Barre' Syndrome	Guillain-Barre Syndrome
<a href="#">51-36033</a>	Y	18	33%	Y	Thrombotic Thrombocytopenic Purpura	Thrombotic Thrombocytopenic Purpura
<a href="#">54-36092</a>	Y	18	52%	Y	Osteomalacia	Osteomalacia
<a href="#">26-36181</a>	Y	21	43%	Y	Giant Cell Arteritis	Temporal Arteritis (AKA Giant Cell Arteritis)
<a href="#">62-36123</a>	Y	29	26%	Y	Syphilis	Syphilitic Meningitis
<a href="#">McGMS 20200306 Case Conference Pulmonary 3 6 - Final</a>	Y	30	41%	Y	Pancreatitis	Acute necrotizing pancreatitis complicated by recurrent left exudative pleural effusion
<a href="#">McGMS Case 2</a>	N	N/A	N/A	Y	N/A	Warm Autoimmune Hemolytic Anemia
<a href="#">McGMS Case 3</a>	N	N/A	N/A	Y	N/A	Colorectal Cancer
<a href="#">McGMS Case 4</a>	N	N/A	N/A	Y	N/A	Pseudohypoparathyroidism

<u>Case Identifier</u>	<u>Ultimate Diagnosis Presented ?</u>	<u>Ultimate Diagnosis Ranking</u>	<u>Symptom Literature Match</u>	<u>Ultimate Diagnosis in the Literature Database?</u>	<u>Isabel Pro Diagnosis</u>	<u>Ultimate Diagnosis</u>
<a href="#">McGMS Case 5</a>	N	N/A	N/A	N	N/A	PRES [Posterior Reversible Encephalopathy Syndrome] 2/2 to Exchange Transfusion
<a href="#">McGMS Case 6</a>	N	N/A	N/A	Y	N/A	Tubulointerstitial nephritis and uveitis (TINU syndrome) AKA Dobrin syndrome
<a href="#">41-36032</a>	N	N/A	N/A	Y	N/A	Ulcerative Colitis
<a href="#">43-36171</a>	N	N/A	N/A	Y	N/A	Silicosis
<a href="#">53-36062</a>	N	N/A	N/A	Y	N/A	Cryptococcal Meningitis
<a href="#">15-36102</a>	N	N/A	N/A	Y	N/A	Pheochromocytoma
<a href="#">63-36111</a>	N	N/A	N/A	Y	N/A	Mucormycosis
<a href="#">35-36161</a>	N	N/A	N/A	Y	N/A	Porphyria (cutnea tarda)
<a href="#">56-36022</a>	N	N/A	N/A	Y	N/A	Non-Hodgkin's Lymphoma
<a href="#">66-36122</a>	N	N/A	N/A	Y	N/A	Hypokalemic Periodic Paralysis
<a href="#">46-36251</a>	N	N/A	N/A	Y	N/A	Amyloidosis (renal)
<a href="#">16-36083</a>	N	N/A	N/A	Y	N/A	Aortic Dissection
<a href="#">34-36103</a>	N	N/A	N/A	Y	N/A	Cardiac Amyloidosis
<a href="#">44-36082</a>	N	N/A	N/A	Y	N/A	Miliary (disseminated) TB
<a href="#">14-36011</a>	N	N/A	N/A	Y	N/A	Blastomycosis
<a href="#">32-36031</a>	N	N/A	N/A	Y	N/A	Cryoglobulinemia
<a href="#">42-36023</a>	N	N/A	N/A	Y	N/A	Hairy Cell Leukemia
<a href="#">12-36291</a>	N	N/A	N/A	Y	N/A	Gaucher's Disease
<a href="#">22-36112</a>	N	N/A	N/A	Y	N/A	Whipple's Disease

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**Appendix A: Glossary of Terms**

<b>Chief Resident's Conference</b>	Meetings of the Internal Medicine residents at McGovern Medical School conducted by the school's Chief Residents, generally on a weekly or bi-weekly basis
<b>Clinical Champion</b>	A clinician user of Isabel Pro, highly regarded among colleagues for diagnostic capabilities, who found Isabel Pro to be especially helpful in diagnosing a patient with a challenging presentation
<b>Diagnostic Decision Support</b>	Any systematic, typically computerized, means of aiding the clinician in reaching a correct or timely diagnosis
<b>Diagnostic Retrieval Accuracy</b>	With what frequency is the correct diagnosis produced, and where did the correct diagnosis appear in the differential diagnoses' listing
<b>Differential Diagnosis</b>	A listing, in rank order, of the diagnoses that might be indicated by the patient's signs and symptoms
<b>DXplain</b>	A computerized diagnostic decision support system developed at Massachusetts General Hospital
<b>Epic</b>	The electronic health record system produced by Epic Healthcare Systems, 1979 Milky Way, Verona, WI 53593
<b>Gold Standard Diagnosis</b>	A diagnosis of a patient's condition generally accepted as accurate by highly trained clinicians or confirmed by a conclusive test

<b>Inaccurate Diagnosis</b>	A missed opportunity to make a correct or timely diagnosis
<b>Isabel Pro</b>	A computerized diagnostic decision support system produced by Isabel Healthcare, Ltd. of Haselmere, UK, and Ann Arbor, MI, USA
<b>Structured Analysis Methodology</b>	A project management methodology proceeding in phases and described in “Systems Analysis and Design,” Tilley, Scott R., 2020
<b>UpToDate</b>	An evidence-based clinical decision support reference resource produced by Wolters Kluwer Health division of Wolters Kluwer
<b>Visual DX</b>	Diagnostic clinical decision support system designed to enhance diagnostic accuracy, especially in dermatology, including a highly curated medical image library and skin of color atlas

**Appendix B: Project Management Plan**

**Project Management Plan:**

**Evaluation of a Computerized Diagnostic Decision Support System in Primary Practice**

By

Joe M. Bridges

Submitted in fulfillment of the Requirements for

BMI 7360 Advanced Project Management

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April 2, 2021

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## PROJECT OVERVIEW

This project aims to evaluate or validate a commercially available diagnostic decision support system, Isabel Pro, in primary care medical practice using only the patient demographics, chief complaint, symptoms, signs, medications, and medical history available at the outset of the physician-patient encounter. The system searches a well-maintained literature database and produces an evidence-based differential diagnosis list for the physician to review before reaching any diagnostic conclusion about the patient. The project also aims to determine a means of integrating the diagnostic decision support system smoothly into the routine primary care clinical practice at UTPhysicians.

Diagnosis is one of the most, if not the most, complex tasks attempted by humans (Newman-Toker, 2009). A relatively small set of signs and symptoms are common to a great many diseases. There are numerous definitions of diagnostic error, but there is no single, generally accepted definition for diagnostic error, and there exists much disagreement about what constitutes diagnostic error (Olson et al., 2018). Diagnostic errors, or missed diagnostic opportunities, are far more common in primary care medical practice than is generally acknowledged and annually result in cases of patient harm numbering in the millions in the United States alone (Singh et al., 2014). However, unless the diagnostic error results in identifiable patient harm, the diagnostic error typically goes unnoticed, especially in cases of delayed diagnosis of progressive conditions, such as colorectal cancer (Singh et al., 2014).

This study evaluates the diagnostic retrieval accuracy of a diagnostic decision support system, Isabel Pro, using only those signs, symptoms, and medical history elements known at the outset of the patient encounter. The thought behind this effort is the notion that the best way to reduce diagnostic error is to prevent its occurrence in the first place, preventing premature



closure bias. *Isabel Pro* is a web-based differential diagnosis tool designed by Isabel Healthcare, Ltd., a company with head offices in Haslemere, United Kingdom, and Ann Arbor, Michigan. This project aims to determine the answer to four critical questions regarding Isabel Pro's performance in primary care practice (Riches et al., 2016). First, does the system offer accurate and relevant diagnoses? The frequency of the correct diagnosis in the list of diagnostic alternatives, the ranking of the correct diagnosis among the alternatives produced, and the match of the inputs to the scientific literature on each alternative? Second, did the system perform as well as clinicians? Third, did the system suggestions improve the diagnostic accuracy of the physicians using them? Fourth, what are the barriers to using the system in routine clinical practice and integrating it with the electronic health record? The project aims to present a proposal justifying Isabel Pro's use in the primary care practices of UTPhysicians and a process for smoothly incorporating the system into routine clinical practice.

## Problem Statement and Literature Review

A widely cited research study reported the frequency of diagnostic errors in outpatient healthcare (Singh et al., 2014), estimating the annual occurrence of diagnostic errors in primary care to be 12 million instances, 6 million of which were considered likely to result in significant patient harm, including death. A companion study by the same researchers in 2013 (Singh et al., 2013) revealed that commonly seen conditions are the most frequently missed diagnostic opportunities, not the rare or unusual as often thought. This study noted:

1. missed diagnostic opportunities in primary care occur in approximately 5% of cases,
2. in each case of a missed diagnostic opportunity, ample evidence existed at the outset to have made the correct diagnosis, and
3. the most significant failure routinely occurred in the physician-patient encounter.

The literature review in preparation for this report resulted in a robust listing of scholarly articles on several essential topics. The search strategy for article retrieval used the following search string:

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(((diagnostic error* OR diagnostic differential* OR "diagnosis"[Subheading] OR "Diagnosis"[Mesh] OR "Diagnostic Errors"[Mesh] OR diagnostic accura*) AND ("Diagnostic Decision Support" OR "visualdx" OR "Ada dx" OR "isabel healthcare"))))
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A manual review of the 190 articles retrieved during the literature search proceeded in a three-step process:

1. Titles specific enough to exclude an article using the title information alone, which excluded 77 articles,

2. A reading of the abstracts excluded another 14 articles,
3. A full reading of the remaining articles excluded another 43 articles.

The resulting 56 references establish the foundation for the validation study on a diagnostic decision support system covering nine elements (These studies are listed in detail with inclusion criteria in Tables 1 – 9):

- Seminal studies in improving diagnosis (two studies)
- The detection and frequency of diagnostic errors in primary practice (two studies)
- Procedural recommendations for diagnosis from recognized experts in the field (seven studies)
- The history of diagnostic decision support systems (one study)
- The various diagnostic decision support systems developed over the years (six studies)
- Assessments of the diagnostic performance of various diagnostic decision support systems (fourteen studies)
- Assessments of the improvement in physician diagnostic accuracy when using a diagnostic decision support system (seventeen studies)
- Issues of physician acceptance of these systems (six studies), and
- Issues related to integrating a diagnostic decision support system within the electronic health record (one study)

<b>Table 1 Seminal Publications on Diagnosis</b>						
<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>

1	Title	Seminal Publication on Diagnosis	Improving Diagnosis in Health Care	Balogh E,	Mil Med. 2016 Mar;181(3):183-5. doi: 10.7205/MILMED-D-15-00562.	2016
The report presented eight detailed recommendations addressing various aspects of diagnostic error, its detection and prevention. The roughly 415-page report led to a wealth of research into diagnostic error that continues to grow dramatically						
2	Article	Detection and Frequency of Diagnostic Error	Types and origins of diagnostic errors in primary care settings	Singh H	JAMA Intern Med. 2013 Mar 25;173(6):418-25. doi: 10.1001/jamainternmed.2013.2777.	2013
This study is notable because the types of errors were in relatively common conditions, not rare or unusual conditions. The conclusions on the origins of the errors were notable in that the physician-patient exchange during the encounter produced the most significant percentage of failures leading to the diagnostic error.						

**Table 2 Detection and Frequency of Diagnostic Error**

No.	Review Type	Inclusion Exclusion Basis	Title	First Author	Citation	Pub. Year
1	Article	Detection and Frequency of Diagnostic Error	Electronic health record-based surveillance of diagnostic errors in primary care	Singh H	BMJ Qual Saf. 2012 Feb;21(2):93-100. doi: 10.1136/bmjqs-2011-000304. Epub 2011 Oct 13.	2012
This article reports on a program to detect diagnostic error using a trigger algorithm to interrogate the electronic health record for potential error. Cases triggered were reviewed to assess if the presenting information was sufficient to have determined the final diagnosis. Of the 674 cases flagged by the trigger algorithm, 141 were determined to be a missed diagnostic opportunity.						
2	Article	Detection and Frequency of Diagnostic Error	The frequency of diagnostic errors in outpatient care: estimations from three large observational studies involving US adult populations	Singh H	BMJ Qual Saf. 2014 Sep;23(9):727-31. doi: 10.1136/bmjqs-2013-002627. Epub 2014 Apr 17.	2014
This study takes the frequency of occurrence from earlier studies, together with two studies of chronic conditions, to extrapolate an estimate of diagnostic error prevalence in the entire United States.						

**Table 3 Diagnosis Recommendations**

No.	Review Type	Inclusion Exclusion Basis	Title	First Author	Citation	Pub. Year
1	Title	Diagnosis Recommendations	Diagnostic error in internal medicine	Graber ML	Arch Intern Med. 2005 Jul 11;165(13):1493-9. doi: 10.1001/archinte.165.13.1493.	2005
This article addressed diagnostic errors in internal medicine and examined 100 cases of known diagnostic error by internists. Of note was that 74% of the cases involved cognitive error, with premature closure being the single most common cause.						
2	Article	Diagnosis Recommendations	Diagnostic errors in primary care: lessons learned	Ely JW	J Am Board Fam Med. 2012 Jan-Feb;25(1):87-97. doi: 10.3122/jabfm.2012.01.110174.	2012
This study surveyed 202 primary care physicians using a one-page questionnaire reporting on a single delayed or missed important diagnosis in their experience. This study bears on the translational project. The study is perhaps the first that included the presenting symptoms as part of the analysis, called for greater use of an expanded differential diagnosis, and confirmed that premature closure represents a significant factor in missed diagnoses.						
3	Article	Diagnosis Recommendations	Primary care closed claims experience of Massachusetts malpractice insurers	Schiff GD	JAMA Intern Med. 2013 Dec 9-23;173(22):2063-8. doi: 10.1001/jamainternmed.2013.11070.	2013
This study is an analysis of malpractice claims against primary care providers in Massachusetts. The pertinent finding in this study is that 72% of the claims were allegations related to a failure to diagnose.						
4	Title	Diagnosis Recommendations	Clinical Decision Support: The Road to Broad Adoption	Greenes R	ISBN: 978-0-12-398476-0	2014
This reference is Dr. Robert Greenes' book, Clinical Decision Support: The Road to Broad Adoption, a classic in diagnostic decision support literature. The book preceded much of the progress made in computerized diagnostic decision support systems but is instructive in defining the path to comprehensive clinical decision support, including diagnostic decision support.						
5	Title	Diagnosis Recommendations	The impact of electronic health records on diagnosis	Graber ML	Diagnosis (Berl). 2017 Nov 27;4(4):211-223. doi: 10.1515/dx-2017-0012.	2017
This article examines the electronic health record as a significant influence in diagnosis, a great deal of that influence for the good, but not all, and in many cases the cause of the diagnostic error resulting in serious adverse patient safety outcomes including death.						
6	Article	Diagnosis Recommendations	Two Decades Since To Err Is Human: An Assessment Of Progress	Bates DW	Health Aff (Millwood). 2018 Nov;37(11):1736-1743. doi: 10.1377/hlthaff.2018.0738.	2018

			And Emerging Priorities In Patient Safety			
This article is a commentary on the progress in patient safety in the twenty years following the 1999 publishing of <i>To Err is Human</i> , a watershed treatise on the healthcare system's failure to place patient safety at the top of the priority list. While not explicitly noting computerized diagnostic decision support systems, the emphasis on diagnostic error supports this project's goal.						
7	Article	Diagnosis Recommendations	Tracking Progress in Improving Diagnosis: A Framework for Defining Undesirable Diagnostic Events	Olson APJ	J Gen Intern Med. 2018 Jul;33(7):1187-1191. doi: 10.1007/s11606-018-4304-2. Epub 2018 Jan 29.	2018
The last article in this segment is a perspective article focusing specifically on improving diagnosis by concentrating on those conditions most commonly misdiagnosed and those healthcare areas most vulnerable to diagnostic error. The article proposes a seven-item framework for concentrating improvement efforts in areas where an adverse outcome is most often the result of a diagnostic process breakdown. The authors observe that diagnostic error measurement is difficult, often controversial, and generally inadequate to trigger improvement.						

No.	Review Type	Inclusion Exclusion Basis	Title	First Author	Citation	Pub. Year
1	Abstract	DDSS History	Thinking about diagnostic thinking: a 30-year perspective	Elstein AS	Adv Health Sci Educ Theory Pract. 2009 Sep;14 Suppl 1:7-18. doi: 10.1007/s10459-009-9184-0. Epub 2009 Aug 11.	2009
The vast reservoir of the author's diagnostic experience is apparent in this very thoughtful article about the current state and possible future of diagnosis. This project's premise is that early diagnostic suggestions may prevent missed diagnostic opportunities and that almost any physician's diagnostic accuracy improves with a differential diagnosis list						

No.	Review Type	Inclusion Exclusion Basis	Title	First Author	Citation	Pub. Year
1	Abstract	Diagnostic Decision Support System	A novel diagnostic aid (ISABEL): development and preliminary evaluation of clinical performance	Ramnarayan, P et al.	Simulation in Healthcare: Journal of the Society for Simulation in Healthcare. 2004;107(Pt 2):1091-5.	2004
This article is one of the first reports on Isabel, a diagnostic decision support system designed initially for pediatric patients. The report follows a two-year development cycle addressing one of the principal issues with previous systems – a knowledge base easily and efficiently updated. The system is fast, the input is relatively simple, and the database's updating is remarkably simple.						
2	Abstract	Diagnostic Decision Support System	Isabel, a clinical decision support system	Vardell E	Med Ref Serv Q. 2011;30(2):158-66. doi: 10.1080/02763869.2011.562800.	2011
This column is a review and introduction of the adult version of the Isabel diagnostic decision support system, beginning with an overview of the database, and notes that Isabel is composed of a database of more than 11,000 diagnoses and 4,000 drugs						
3	Article	Diagnostic Decision Support System	Isabel: A Review	Wood BA	Barbara A. Wood. "Isabel: A Review" Journal of Electronic Resources in Medical Libraries Vol. 11 Iss. 4 (2014) p. 189 - 192 ISSN: 1542-4073 Available at: <a href="http://works.bepress.com/barbara-wood/2/">http://works.bepress.com/barbara-wood/2/</a>	2014
Published as a column in the Journal of Electronic Resources in Medical Libraries, the author reviews the Isabel CDSS to evaluate the product's utility in medical education.						
4	Abstract	Diagnostic Decision Support System	An ontology driven clinical evidence service providing diagnostic decision support in family practice	Corrigan D	AMIA Jt Summits Transl Sci Proc. 2015 Mar 25;2015:440-4. eCollection 2015.	2015
This paper describes a prototype diagnostic decision support system developed during the European project TRANSFoRm. The clinical evidence service allows the presentation of recommendations integrated with an EHR in primary care, using ontology models of evidence. The prototype provides diagnostic support on only three presentations or reasons for encounter.						
5	Article	Diagnostic Decision Support System	Patients could provide initial differential diagnoses	Maude J	Br J Gen Pract. 2015 Mar;65(632):116-7. doi: 10.3399/bjgp15X683893.	2015
Jason Maude is the founder of Isabel Healthcare. This editorial describes the patient's assistance in his diagnosis using the company's system designed for patients.						

6	Article	Diagnostic Decision Support System	Requirements and validation of a prototype learning health system for clinical diagnosis	Corrigan D	Learn Health Syst. 2017 May 31;1(4):e10026. doi: 10.1002/lrh2.10026. eCollection 2017 Oct.	2017
This article attempts to address some of the shortcomings with commercially available diagnostic decision support systems, particularly those relying on a proprietary database, such as Isabel or DXPlain. This decision support tool showed an 8% to 9% improvement in diagnostic accuracy and resulted in more coded data for clinical evidence. The tool was easy to use and quickly learned, but the system described is limited to only three presenting conditions, and the data supporting the system was manually curated. This limitation is no small shortcoming, and the wide use of EHR data is fraught with difficulty not addressed in the article.						

<b>Table 6 Diagnostic Decision Support System Performance</b>						
No.	Review Type	Inclusion Exclusion Basis	Title	First Author	Citation	Pub. Year
1	Abstract	Diagnostic Decision Support System Performance	Diagnostic decision support systems	Riesenberg LA	J Med Pract Manage. 2001 Nov-Dec;17(3):163-5.	2001
This study reports on the use of diagnostic decision support systems in a general medical clinic, finding that they could suggest new diagnostic possibilities, focus thinking about clinical problems, and serve as a recertification preparation tool. The study also found diagnostic decision support systems useful for the novice clinician (fourth-year medical students and interns).						
2	Abstract	Diagnostic Decision Support System Performance	Diagnostic decision support systems: how to determine the gold standard?	Berner ES	J Am Med Inform Assoc. 2003 Nov-Dec;10(6):608-10. doi: 10.1197/jamia.M1416.	2003
The editorial lists criteria for evaluating a diagnostic decision support system: 1. Producing the correct diagnosis, 2. The quality of the differential, 3. Appropriate management suggestions, 4. User acceptance. 5. Interaction of the user with the system.						
3	Abstract	Diagnostic Decision Support System Performance	How well does decision support software perform in the emergency department?	Graber MA	Emerg Med J. 2003 Sep;20(5):426-8. doi: 10.1136/emj.20.5.426.	2003
This study sampled 25 patients as they presented to an emergency department. The study audiotaped, transcribed, and together with all written records entered the encounters as input to two diagnostic decision support systems: QMR and Iliad. The final diagnosis of the emergency department attending physician was considered conclusive. The systems displayed approximately the same accuracy in the emergency department as in clinical settings. Neither was sufficiently accurate to rely on as conclusive.						
4	Abstract	Diagnostic Decision Support System Performance	Measuring the impact of diagnostic decision support on the quality of clinical decision making: development of a reliable and valid composite score	Ramnarayan P	J Am Med Inform Assoc. 2003 Nov-Dec;10(6):563-72. doi: 10.1197/jamia.M1338. Epub 2003 Aug 4.	2003
This study aimed to produce a scoring process for comparing the effectiveness of a diagnostic decision support system. The system chosen for the study was Isabel (web-based pediatric version) using six simulated cases subsequently evaluated by 76 physicians, first as presented, and second using the Isabel diagnostic aid. Two experienced physicians assigned scores by conducting an independent assessment of each case. The study did not evaluate the performance of Isabel, but rather the physicians with and without Isabel prompts. The most significant weakness is the involvement of Isabel employees and consultants in the project.						
5	Abstract	Diagnostic Decision Support System Performance	Evaluation of an Internet delivered pediatric diagnosis support system (ISABEL) in a tertiary care center in India	Bavdekar SB	Indian Pediatr. 2005 Nov;42(11):1086-91.	2005
This study aimed to produce an assessment of the sensitivity of the Isabel diagnostic tool in an emergency department setting in a developing country where recent graduates are staffing the public hospitals. The study conducted a retrospective assessment of 200 pediatric patients admitted to a major metropolitan public hospital's emergency department over 18 months. The system yielded an aggregate sensitivity of 80.5%. The study limitations were several, including no ranking of the correct diagnosis.						
6	Abstract	Diagnostic Decision Support System Performance	Validation of a diagnostic reminder system in emergency medicine: a multi-centre study	Ramnarayan P	Emerg Med J. 2007 Sep;24(9):619-24. doi: 10.1136/emj.2006.044107.	2007
The study was the first large-scale evaluation of the Adult version of the Isabel diagnostic decision support system, released in 2005. The study analyzed cases from three large academic centers in the UK National Health System. The study aimed to evaluate Isabel's performance, so no results were provided to the clinicians, nor was treatment changed for any patient. The study calculated diagnostic accuracy on 217 discharged patients, 206 cases (95%) correct, with 169 being in the top ten presentations (78%). The study calculated diagnostic utility based on 152 "must not miss" diagnoses, 140 (92%) correct of which 88 were in the top ten (58%). The study is limited by being conducted by researchers with financial relationships with the Isabel developer.						
7	Title	Diagnostic Decision Support System Performance	Performance of a web-based clinical diagnosis support system for internists	Graber ML	J Gen Intern Med. 2008 Jan;23 Suppl 1(Suppl 1):37-40. doi: 10.1007/s11606-007-0271-8.	2008

This 2008 study aimed to evaluate the accuracy and speed of Isabel; an adult patient diagnostic decision support system released in 2005. The study selected 50 consecutive cases describing adult patients from the "Case Records of Massachusetts General Hospital" (New England Journal of Medicine, vol. 350:166–176, 2004 and 353:189–198, 2005). When key factors were input, the system presented the correct diagnosis among the thirty alternatives in 48 of the 50 cases (the knowledge base did not include the two missed diagnoses). Pasting the case history yielded 37 correct. The cases in the NEJM are very complete and likely do not represent routine clinical presentations. The study made no consideration of the ranking of the diagnosis presentations.						
8	Abstract	Diagnostic Decision Support System Performance	The introduction of a diagnostic decision support system (DXplain™) into the workflow of a teaching hospital service can decrease the cost of service for diagnostically challenging Diagnostic Related Groups (DRGs)	Elkin PL	Int J Med Inform. 2010 Nov;79(11):772-7. doi: 10.1016/j.ijmedinf.2010.09.004. Epub 2010 Oct 14.	2010
The DXplain system was made available to residents. This study aimed to establish the improvement in the cost of treatment of patients when residents availed themselves of the diagnostic suggestions, compared to a control set of similar cases preceding the study. The study addressed 564 diagnostically challenging cases during the study period and 1,173 diagnostically challenging cases during the control period. Total costs were determined to be lower by \$1,281 per case, suggesting annual savings to the institution of roughly \$2 million. The study did not address outcomes, only costs, was conducted at a single hospital and relied on the likelihood that physician experience, case mix, and acuity would be similar during the control and study periods.						
9	Abstract	Diagnostic Decision Support System Performance	Differential diagnosis generators: an evaluation of currently available computer programs	Bond WF	J Gen Intern Med. 2012 Feb;27(2):213-9. doi: 10.1007/s11606-011-1804-8.	2012
The aim of this study was, first, to identify differential diagnosis generators currently available, meeting specific essential criteria for clinical decision support, and second, assess the performance of the systems selected. Of the 23 programs identified, only four met the inclusion criteria: Isabel, DXplain, Diagnosis Pro, and PEPID. The assessment used twenty consecutive diagnosis- focused cases. All the programs missed two diagnoses. Isabel and DXplain were the top performers, each registering 69 points out of 100. The studies do not duplicate clinical settings, and the scoring did not include a ranking of the correct diagnosis.						
10	Abstract	Diagnostic Decision Support System Performance	Evaluating online diagnostic decision support tools for the clinical setting	Pryor M	Stud Health Technol Inform. 2012;178:180-5.	2012
This study by New South Wales Clinical was to determine if a commercially available diagnostic decision support system would provide diagnostic assistance. The study found 11 that meeting the inclusion criteria. The first stage tested all 11 with 3 challenging cases. The second stage compared the 3 top-performing systems (First Consult, Best Practice, and Isabel), using 6 challenging cases. The evaluation ranked the systems from 6 (best) to 18 (worst). Best Practice scored 10, Isabel 11, and First Consult 14. This study made no effort to evaluate patient outcomes or physician improvement in diagnostic accuracy.						
11	Abstract	Diagnostic Decision Support System Performance	The utility of an online diagnostic decision support system (Isabel) in general practice: a process evaluation	Henderson EJ	JRSM Short Rep. 2013 Apr 4;4(5):31. doi: 10.1177/2042533313476691. Print 2013 May.	2013
The study aimed to solicit responses from practicing physicians on their opinions of the usefulness of Isabel in their practice in the UK general practice system. The study employed a focus-group approach and a post-use questionnaire following a three-month survey period. Five practices employed the system on 16 patients. Ten post-use surveys revealed no change in diagnostic decisions using the system. Post-use focus groups suggested the system was not well-tailored to the clinical routine and could be more helpful if better suited. The study was short, involved only a few volunteering practices, and was essentially an opinion exercise.						
12	Abstract	Diagnostic Decision Support System Performance	Uptake and impact of a clinical diagnostic decision support tool at an academic medical center	Barbieri JS	Diagnosis (Berl). 2015 Jun 1;2(2):123-127. doi: 10.1515/dx-2014-0058.	2015
The study aimed to evaluate the usage and change in treatment requests with the introduction of VisualDX in the academic medical center. VisualDX was made available to the entire system by drop-down menus and mobile applications on phones. The report studied the use of VisualDx for 18 months following its introduction to compare inpatient dermatology consults requested to the number of requests in the preceding 12 months. The study detected no statistically significant difference in dermatology consults following the introduction. The main limitation was the absence of any assessment of the change in patient outcomes.						
13	Article	Diagnostic Decision Support System Performance	The Effectiveness of Electronic Differential Diagnoses (DDX) Generators: A Systematic Review and Meta-Analysis	Riches N	PLoS One. 2016 Mar 8;11(3):e0148991. doi: 10.1371/journal.pone.0148991. eCollection 2016.	2016
This study aimed to conduct a systematic review and meta-analysis seeking diagnostic decision support generators' clinical effectiveness. The study considered four key research questions: 1. Is the system effective at retrieving accurate diagnoses? 2. Does the system perform as well as clinicians? 3. Does the use of the system improve a physician's diagnostic accuracy? 4. What are the enablers and barriers to these systems in clinical practice? This report identifies the evaluation methodology most suitable for validating a diagnostic decision support system.						
14	Abstract	Diagnostic Decision Support System Performance	Assessing the utility of a differential diagnostic generator in	Cheraghi-Sohi S	Diagnosis (Berl). 2020 Feb 14;/j/dx.ahead-of-print/dx-2019-0033/dx-2019-0033.xml. doi: 10.1515/dx-2019-0033. Online ahead of print.	2020

			UK general practice: a feasibility study			
<p>This study aimed to conduct a process evaluation of Isabel in a UK general practice to assess the tool for routine primary medical care. The study took place in a large inner-city UK general practice in Greater Manchester, England, consisting of approximately 18,000 patients, seventeen general practitioners, and two nurse practitioners. This study indicates that UK physicians see little advantage to Isabel in primary care. The study was over a relatively short period in a single institution with no integration with the EHR. The study is probably a very reasonable assessment of the likelihood of adoption without significant changes.</p>						

<b>Table 7 Physician Diagnostic Accuracy Improvement</b>						
<b>No.</b>	<b>Review Type</b>	<b>Inclusion Exclusion Basis</b>	<b>Title</b>	<b>First Author</b>	<b>Citation</b>	<b>Pub. Year</b>
1	Abstract	Physician Diagnostic Accuracy Improvement	Enhancement of clinicians' diagnostic reasoning by computer-based consultation: a multisite study of 2 systems	Friedman CP	JAMA. 1999 Nov 17;282(19):1851-6. doi: 10.1001/jama.282.19.1851.	1999
<p>The study aimed to evaluate the improvement in a physician's diagnostic accuracy when using two diagnostic decision support systems, Iliad and QMR. Each participant evaluated 9 of 36 cases prepared for the study, prepared a differential diagnosis for each case, first without assistance, and then used the system's suggestions. The study reported accurate diagnoses in 39.5% of the cases when not using the system and 45.4% of the cases after consultation. Little experience and the academic setting are limiting.</p>						
2	Abstract	Physician Diagnostic Accuracy Improvement	Comparison of measures to assess change in diagnostic performance due to a decision support system	Maisiak RS	Proc AMIA Symp. 2000:532-6.	2000
<p>This study assessed ten different single measures of diagnostic performance by empirical comparison. The study compared the diagnostic performance of 108 physicians using medical cases of varying diagnostic difficulty and with or without a high level of assistance from a DDSS. The most responsive measures were when the correct diagnoses were within the top 5 to 10 listed diagnoses. Evaluating DDSS performance by examining the correct case diagnosis's rank-order within a restricted number of diagnoses may be responsive but not appropriate since lower-ranked diagnoses may be correct and, therefore, not dismissed.</p>						
3	Abstract	Physician Diagnostic Accuracy Improvement	Clinician performance and prominence of diagnoses displayed by a clinical diagnostic decision support system	Berner ES	AMIA Annu Symp Proc. 2003;2003:76-80.	2003
<p>This study aimed to examine a clinician's diagnostic accuracy before and after a diagnostic CDSS presentation of alternatives. The subjects were 70 internal medicine residents. The system was Quick Medical Reference. The study reported two conclusions. First, clinicians who considered the correct diagnosis before the CDSS were more likely to produce the correct diagnosis in a prominent position. Second, physicians are firmly anchored by their initial diagnoses before using the CDSS, and changes in the clinicians' diagnoses are related to the presence or absence of the correct diagnosis in the top 10 diagnoses displayed by the CDSS.</p>						
4	Abstract	Physician Diagnostic Accuracy Improvement	Do physicians know when their diagnoses are correct? Implications for decision support and error reduction	Friedman CP	J Gen Intern Med. 2005 Apr;20(4):334-9. doi: 10.1111/j.1525-1497.2005.30145.x.	2005
<p>This study aimed to examine the agreement between physicians' confidence in their diagnoses and their accuracy. The study would assess clinical experience and its effect on diagnostic confidence. The study, conducted at three academic medical centers, involved 72 senior medical students, 72 senior medical residents, and 72 faculty internists. The participants studied synopses of 9 of 36 diagnostically challenging medical cases (each with a correct definitive diagnosis) and generated a differential diagnosis for each case. They indicated their level of confidence in each diagnosis. The study concluded that even experienced clinicians often do not grasp the correctness of their diagnoses. The study was limited to diagnosis only.</p>						
5	Abstract	Physician Diagnostic Accuracy Improvement	Assessment of the potential impact of a reminder system on the reduction of diagnostic errors: a quasi-experimental study	Ramnarayan P	BMC Med Inform Decis Mak. 2006 Apr 28;6:22. doi: 10.1186/1472-6947-6-22.	2006
<p>This study aimed to use a mix of easy and difficult simulated cases to assess the impact of the diagnostic decision support system, Isabel, on clinical decisions made during acute assessment. Participants assessed a balanced set of 24 simulated cases on a trial website, recording clinical decisions such as differential diagnosis, test ordering, and treatment, both in advance and after consultation using Isabel. A panel of two pediatric consultants provided gold-standard responses for each case. The study concluded that the provision of patient- and context-specific reminders might reduce diagnostic omissions altogether. The study is limited by the possibility that prompts or reminders after first assessing the case may be more effective due to the second look at the case and less due to the reminders. The study also suffers from the relationships of the researchers with the system developer.</p>						
6	Abstract	Physician Diagnostic Accuracy Improvement	Diagnostic omission errors in acute paediatric practice: impact of a reminder	Ramnarayan P	BMC Med Inform Decis Mak. 2006 Nov 6;6:37. doi: 10.1186/1472-6947-6-37.	2006



			system on decision-making			
This study examined the effect of a diagnostic reminder system, Isabel, on clinicians' decisions in an acute pediatric setting during assessments characterized by diagnostic uncertainty. The study assessed junior doctors for five months at four pediatric ambulatory units. The doctors were free to consult the diagnostic aid for diagnostic assistance at any time. Participants recorded their differential diagnosis, test-ordering, and treatment, both in advance of and after system consultation. The study is limited by the inconsistent use of the system by the participants, by the single point choice for performance assessment, and by the possibility that results using a before and after method may be improved simply by a reconsideration of the case. The study suffers from the relationship of the researchers to the developer of the system.						
7	Abstract	Physician Diagnostic Accuracy Improvement	Overconfidence as a cause of diagnostic error in medicine	Berner ES	Am J Med. 2008 May;121(5 Suppl):S2-23. doi: 10.1016/j.amjmed.2008.01.001.	2008
This study aimed to determine: (1) What is the extent of incorrect diagnosis? (2) What percentage of documented adverse events are attributable to diagnostic errors, and conversely, how often do diagnostic errors lead to adverse events? (3) Has the rate of diagnostic errors decreased over time? The authors conclude that diagnostic error is at least 5%, and perhaps more, that the physicians almost uniformly overestimate the accuracy of their diagnoses and that overconfidence contributes to diagnostic error. In particular application to this project, the authors note that premature closure, getting to a diagnosis too quickly and failing to consider conflicting evidence, is a significant cognitive error in medicine.						
8	Abstract	Physician Diagnostic Accuracy Improvement	Taking steps towards a safer future: measures to promote timely and accurate medical diagnosis	Graber ML	Am J Med. 2008 May;121(5 Suppl):S43-6. doi: 10.1016/j.amjmed.2008.02.006.	2008
This treatise aims to step back from the press of medicine's daily practice to examine whether today's practice of medicine is at the point it should be on the issues of detecting, preventing, and learning about diagnostic error. The article speaks to all the stakeholders in improving diagnosis – physicians, healthcare institutions, researchers, policymakers, and, finally, the patient. In conclusion, the author makes substantive suggestions for improvements to physicians, healthcare institutions, patient safety organizations, and the patient.						
9	Abstract	Physician Diagnostic Accuracy Improvement	Use of diagnostic decision support systems in medical education	Berner ES	Methods Inf Med. 2010;49(4):412-7. doi: 10.3414/ME9309. Epub 2010 Apr 20.	2010
This article addresses diagnostic decision support systems and examines 1) the skills needed in a medical students' clinical experiences, 2) the changes required in the curriculum when introducing the systems into the educational process, and 3) the research issues associated with these systems in the educational programs. The study conducts a critical analysis of the literature on diagnostic decision support systems as part of medical education. Students will need specific skills in 1) selecting appropriate system vocabulary and functions, and 2) applying the diagnostic system's suggestions to their particular patient.						
10	Abstract	Physician Diagnostic Accuracy Improvement	The impact of a diagnostic reminder system on student clinical reasoning during simulated case studies	Carlson J	Simul Healthc. 2011 Feb;6(1):11-7. doi: 10.1097/SIH.0b013e3181f24acd.	2011
This study aimed to assess the assistance to diagnostic reasoning provided to students by Isabel PRO, a web-based DRS, using simulated encounters. The study engaged 20 fourth-year medical students to participate in four simulated case scenarios with and without Isabel assistance. The diagnostic accuracy of the students improved after using Isabel PRO. The use of a DRS within the context of a patient case represents a distinct clinical skill set requiring appropriate training. Providing learners with gold standard examples of using such a tool is an essential learning component. Simulated case scenarios best offer the appropriate clinical context.						
11	Abstract	Physician Diagnostic Accuracy Improvement	Impact of a computer-based diagnostic decision support tool on the differential diagnoses of medicine residents	Feldman MJ	J Grad Med Educ. 2012 Jun;4(2):227-31. doi: 10.4300/JGME-D-11-00180.1.	2012
This study aimed to assess the improvement in residents' differential diagnosis or treatment plans when presented with a rank-ordered list of diagnostic possibilities from a medical diagnostic decision support system. The study recruited twenty first-year internal medicine residents at Massachusetts General Hospital. Each participant viewed three actual patient cases (deidentified). The participants entered the differential diagnosis and management plan both before and after seeing the suggested list of diseases in a web-based questionnaire. The study concluded that viewing a rank-ordered list of diagnostic possibilities provided a significant beneficial effect. The study is limited because it was a single site and a small sample, together with the case selection, which maximized the impact of an omitted diagnosis. Also, since participants were interns, the effect may have been pronounced.						
12	Abstract	Physician Diagnostic Accuracy Improvement	Use of the Isabel decision support system to improve diagnostic accuracy of pediatric nurse practitioner and family nurse practitioner students	John RM	NI 2012 (2012). 2012 Jun 23;2012:194. eCollection 2012.	2012
This study aims to assess the use of decision support among Advanced Practice Nurse (APN). The study implemented the Isabel diagnostic decision support system into the curriculum. The study includes 37 PNP and 40 FNP students. All are female except for one FNP student. All have less than five years of RN experience, and more than 90% are between 20-29 years. The assessment of the results is in an assessment follow-up report.						
13	Article	Physician Diagnostic Accuracy Improvement	Differential diagnosis: the key to reducing diagnosis error, measuring diagnosis and a mechanism to	Maude J	Diagnosis (Berl). 2014 Jan 1;1(1):107-109. doi: 10.1515/dx-2013-0009.	2014

			reduce healthcare costs			
This article is an opinion piece by the founder and developer of the Isabel diagnostic decision support system. It is clearly well informed and proposes that a differential diagnosis would improve the diagnostic accuracy of almost every physician. A differential diagnosis is a feature that his system presents automatically as its diagnostic output.						
14	Article	Physician Diagnostic Accuracy Improvement	Reducing risk with clinical decision support: a study of closed malpractice claims	Zuccotti G	Appl Clin Inform. 2014 Aug 20;5(3):746-56. doi: 10.4338/ACI-2014-02-RA-0018. eCollection 2014.	2014
This study reported on the proportion of malpractice claims potentially preventable by clinical decision support (CDS). In each case, a panel of experts assessed the clinical opportunities to intervene to avert the malpractice event. The expert panel also searched for the presence or absence of CDS that might have prevented the event. The results of this study suggest that, in addition to their known benefits for quality and safety, CDS systems within HIT have a potential role in decreasing malpractice payments. The study concluded that more than half of malpractice events and over \$40 million in indemnity payments were potentially preventable with CDS. The implication for this project is the possibility that this technique might lead to the financial justification for a diagnostic decision support system.						
15	Title	Physician Diagnostic Accuracy Improvement	Early diagnostic suggestions improve accuracy of GPs: a randomised controlled trial using computer-simulated patients	Kostopoulou O	Br J Gen Pract. 2015 Jan;65(630):e49-54. doi: 10.3399/bjgp15X683161.	2015
The study aimed to determine whether providing GPs with early diagnostic suggestions improves accuracy. The study recruited 297 GPs to diagnose nine patient cases, differing in difficulty, in one of three experimental conditions: control, early support, or late support. The participating physicians read initial patient information, along with the Reason for Encounter (RfE). The study concluded that reminding GPs of diagnoses to consider in advance of the diagnostic process can improve diagnostic accuracy regardless of case difficulty, without lengthening information search. The study is limited since the cases relied on diagnostic suggestions from a diagnostic decision system, even though the study did not test a particular system.						
16	Title	Physician Diagnostic Accuracy Improvement	Diagnostic accuracy of GPs when using an early-intervention decision support system: a high-fidelity simulation	Kostopoulou O	Br J Gen Pract. 2017 Mar;67(656):e201-e208. doi: 10.3399/bjgp16X688417. Epub 2017 Jan 30.	2017
The study reported on a prototype Diagnostic Decision Support system and aimed to evaluate the prototype DSS's performance in a high-fidelity simulation. The study recruited 34 GPs to consult with six standardized patients (actors) using their usual EHR. Following that series of encounters, the participants consulted with six other patients using the same EHR but with the integrated DSS. The study noted an 8-9% absolute improvement in diagnostic accuracy when the DSS was used. The study was limited in that the cases did not represent the typical set of daily presentations, and the situation, while well designed to simulate a series of encounters, did not include the noise, interruptions, and other distractions in routine clinical practice.						
17	Abstract	Physician Diagnostic Accuracy Improvement	Structured case reviews for organizational learning about diagnostic vulnerabilities: initial experiences from two medical centers	Mathews BK	Diagnosis (Berl). 2020 Jan 28;7(1):27-35. doi: 10.1515/dx-2019-0032.	2020
This study reports on an effort to establish a detection, prevention, and feedback for improvement program at two large healthcare institutions, based on the premise that an organization's ability to identify and learn from opportunities for improvement (OFI) is key to increasing diagnostic safety. The study describes a five-step process employed to create a review system and provide feedback: (1) identify trigger criteria; (2) establish a review panel; (3) develop a system to conduct reviews; (4) perform reviews; and (5) provide feedback. The study reported three important lessons learned. (1) Peer review of cases provides opportunities to learn and calibrate diagnostic and management decisions at an organizational level. (2) Sharing cases in review groups supports a culture of open discussion of OFIs. (3) Reviews focused on diagnostic safety identify opportunities that may complement other organization-wide review opportunities. The study reported a significant element in acceptance and participation in the process as the subtle reframing of the term "diagnostic error" to "opportunity for improvement." The study attributed much of the increase in self-reporting to this reference change.						

No.	Review Type	Inclusion Exclusion Basis	Title	First Author	Citation	Pub. Year
1	Abstract	Physician Acceptance	Internal medicine resident satisfaction with a diagnostic decision support system (DXplain) introduced on a teaching hospital service	Bauer BA	Proc AMIA Symp. 2002:31-5.	2002
The study aimed to determine whether Internal Medicine residents would find using a diagnostic decision support system to be a satisfactory experience. Resident willingness to use the instrument was particularly important because of growing concerns regarding residents' educational experience in the hospital. The study concluded that a significant level of satisfaction with the system existed among residents. Their recognition that it frequently led them to consider novel diagnoses suggests it had a positive educational impact.						

2	Abstract	Physician Acceptance	Diagnostic decision support systems: why aren't they used more and what can we do about it?	Berner ES	AMIA Annu Symp Proc. 2006;2006:1167-8.	2006
This article by Dr. Eta Berner, one of the icons in diagnostic improvement, comments on the reasons behind the limited use of diagnostic decision support systems and describes opportunities to increase the interest in their use in routine clinical practice. The author covers many of the issues surround objections to the use of systems for diagnostic support and offers a series of opinions on topics to be pursued to increase their use, especially the issue of integration with the EHR.						
3	Abstract	Physician Acceptance	Resources medical students use to derive a differential diagnosis	Graber ML	Med Teach. 2009 Jun;31(6):522-7. doi: 10.1080/01421590802167436.	2009
The study evaluated the usefulness of Isabel, an electronic diagnosis support system. The study recruited 117 third-year medical students to consider a challenging case and to identify and prioritize their top three diagnoses, report the time devoted to the exercise, and list the resources they used and their relative usefulness. The study determined that students who identified the correct diagnosis as their first choice spent significantly more time on the case than the other students. Students using Isabel had more success identifying the correct diagnosis (73% for users vs. 53% for non-users), a difference of borderline statistical significance. The study concluded that medical education needs to teach future clinicians how to use these tools to advantage.						
4	Abstract	Physician Acceptance	What can be done to increase the use of diagnostic decision support systems?	Berner ES	Diagnosis (Berl). 2014 Jan 1;1(1):119-123. doi: 10.1515/dx-2013-0014.	2014
This editorial is another commentary by Dr. Eta Berner on topics to increase the use of diagnostic decision support systems. To quote her purposes: "This essay explores the reasons why diagnostic decision support systems are underutilized despite growing concern about diagnostic errors. Factors related to the motivation to use the systems, clinician cognition, system design and implementation, and the absence of feedback in routine clinical care are discussed."						
5	Abstract	Physician Acceptance	Decision support for diagnosis should become routine in 21st century primary care	Delaney BC	Br J Gen Pract. 2017 Nov;67(664):494-495. doi: 10.3399/bjgp17X693185.	2017
This article is an editorial by Dr. Brendan Delaney and Dr. Olga Kostopoulou. Their essential comment is that in this era of time-constrained medical practice and the explosion of research in medicine, computerized diagnostic decision support is essential. The article is a well-founded commentary on the need for diagnostic decision support in primary practice, the factors that have hindered adoption to date, and the encouraging technological developments that point to improvements in the diagnostic process.						
6	Abstract	Physician Acceptance	The impact of a diagnostic decision support system on the consultation: perceptions of GPs and patients	Porat T	BMC Med Inform Decis Mak. 2017 Jun 2;17(1):79. doi: 10.1186/s12911-017-0477-6.	2017
This study concentrated on the opinions of the physicians and the patients following a consultation. The physicians favored the DDS system, 74%, commented that the system improved the diagnostic process by providing diagnoses for consideration and triggering an improved set of questions to the patient. The physicians' coded significantly more symptoms during the consultations, an improvement very much needed to improve the EHR but concerned the physicians accustomed to entering clinical notes following the session. Patients registered no difference in satisfaction with the encounter either way.						

<b>Table 9 Diagnostic Decision Support System Integration with the Electronic Health Record</b>						
No.	Review Type	Inclusion Exclusion Basis	Title	First Author	Citation	Pub. Year
1	Article	DDSS integration with EHR	Experience with Integrating Diagnostic Decision Support Software with Electronic Health Records: Benefits versus Risks of Information Sharing	Segal MM	EGEMS (Wash DC). 2017 Dec 6;5(1):23. doi: 10.5334/egems.244.	2017
This article does an excellent job of demonstrating the difficulty of integrating a diagnostic decision support system into an electronic health record, the complexity of including the diagnostic process within the EHR, and the opposing positions of physicians using the system as to its usefulness versus the legal liability associated with discoverable interim diagnostic considerations being in the EHR or even in a separate database. The work took place at two large integrated healthcare institutions, Geisinger Health System, and Intermountain Healthcare. The diagnostic decision support system evaluated was SimulConsult, a diagnostic decision support system primarily used in neurology, specifically pediatric neurology. At the end of the effort, the project successfully integrated the diagnostic decision support system with the EHR at Geisinger. However, tension arose from physicians' opposing views regarding the advisability of storing intermediate diagnostic steps in a discoverable format. The study achieved no real reconciliation of these issues.						

## IT SOLUTION

Information Technology, in the case of this project, must address three key elements.

First, since Isabel Pro is a commercially available system (Isabel Pro is a web-based differential diagnosis tool designed by Isabel Healthcare, Ltd., a company with head offices in Haslemere, United Kingdom, and Ann Arbor, Michigan.), the system's validity must be tested and verified. That validation process begins with primary care cases where the presenting chief complaints, symptoms, signs, medications, and medical history can be input to the Isabel Pro Diagnostic Decision Support System (Isabel Pro). Cases suitable for this validation methodology have two essential components: an initial unknown diagnosis or at least different from the final diagnosis and a conclusive final diagnosis for confirmation. At this point, the validation effort relies on 46 cases, two from UTPhysicians, eight from McGovern Medical School, and 36 from the Learning Health Sciences Department at the University of Michigan Medical School. In applying the validation methodology, the author entered the signs and symptoms from the cases as inputs into the Isabel Pro Differential Diagnosis System. For the 46 cases, Isabel Pro returned the correct diagnosis 24 times (52.2%), with an average ranking of 10 and a range of 1 to 40. To put this in context, for the 36 cases obtained from the University of Michigan Medical School, Isabel Pro returned the correct diagnosis in 19 cases (52.8%). In a study at three Academic Medical Centers (Friedman et al., 1999), 216 physicians (72 Internal Medicine Faculty, 72 Senior Residents, and 72 fourth-year medical students) diagnosed the 36 cases, returning the correct diagnosis 14 times (38.9%). Isabel Pro outperformed the clinicians by nearly 36%. Even if the comparison is limited to diagnoses by only the Internal Medicine faculty, the correct diagnosis was returned 17 times (49.1%). Isabel Pro outperformed the Internal Medicine Faculty by 10%.

A "Diagnostic Challenge," created using the RedCap System with the 46 cases mentioned earlier, allows residents or physicians to diagnose the cases, first without diagnostic suggestions, followed by an opportunity to revisit the case with the Isabel Pro differential diagnosis list and change their initial differential if desired. After each diagnostic pair, a questionnaire assesses the residents' and physicians' opinions regarding the usefulness of the suggestions. The "Diagnostic Challenge" was conducted during Spring 2021 with 120 McGovern Medical School Residents as participants. The challenge results are being analyzed now, with results to be reported in a BMI6002 paper.

Second, Information Technology will be required to develop the process whereby patient admitting information and presentation features may be input to Isabel Pro without requiring a separate and duplicate entry task. This process is essential to minimize any disruption in the clinical setting and to ensure that the differential diagnosis produced by Isabel Pro is available to the physician at the first instant of the physician-patient encounter.

Third, Information Technology is required to incorporate the system as part of the EHR, an outcome highly desirable to make the system as integrated into routine clinical practice as possible. UTPhysicians is currently implementing the Epic electronic health record into the practices, a massive undertaking and one not likely to allow considering incorporating a diagnostic decision support system at this point. The integration feature is unlikely to be part of this DHI translational project other than assessing the requirements for future reference.

## Project Integration

### The Organization

		Giuseppe N. Colasurdo, M.D. President		
		Kevin Dillon, M.B.A., C.P.A. Senior Executive Vice President, Chief Operating Officer		
	Mr. Andrew Casas Medical School MS - MSRDP Administration A&P Senior Vice President, UTHealth and Chief Operating Officer, UT Physicians			Amar Yousif Vice President of Information Technology & Chief Information Officer
Dr Thomas J Murphy Medical School Medical School Reserves A&P Assistant Dean for Community Affairs and Health Policy Medical School Family Medicine Faculty Assistant Professor NTC and Stanley Family Distinguished Chair of Population Health and Community Medicine	Dr Eric Thomas Medical School Internal Medicine, General Div A&P Professor and Associate Dean for Healthcare Quality and Griff T. Ross Professor in Humanities and Technology in Health Care		Dr Babatope Olayinka Fatuyi Medical School MS - Dean A&P Chief Medical Information Officer	Dr James J Griffiths Medical School MS - MSRDP Administration A&P Associate Vice President of Healthcare IT

## Dr. Alter Work System Snapshot (Alter, 2006)

Customers	Products and Services	
Residents McGovern Medical School Primary Care Providers, UTPhysicians	<ul style="list-style-type: none"> <li>• Diagnostic Decision Support, Isabel Pro (Isabel Pro is a web-based differential diagnosis tool designed by Isabel Healthcare, Ltd., a company with head offices in Haslemere, United Kingdom, and Ann Arbor, Michigan.)</li> <li>• RedCap, a secure web platform for building and managing online databases and surveys.</li> </ul>	
Major Activities or Processes		
<ul style="list-style-type: none"> <li>• Validation of the DDSS: All 46 cases have been entered into Isabel Pro and the Differential Diagnosis Produced, compared to the "gold standard" diagnosis for each case, and tabulated the results to the questions: "Was the correct diagnosis presented and what was the ranking?"</li> <li>• Diagnostic Challenge: A "Diagnostic Challenge" was granted a waiver by the Institutional Review Board of the UHealth Committee for the Protection of Human Subjects for a study to assess the performance of clinicians in diagnosing the cases compared Isabel Pro and assessing the improvement in diagnostic accuracy of the clinicians when provided with the diagnostic suggestions from Isabel Pro. This study is presently underway with 120 Residents in Internal Medicine from the McGovern Medical School participating. The initial group of Residents completed the Diagnostic Challenge on February 8, with results being analyzed at this time.</li> <li>• Develop a program for entering the patient's presenting information automatically as inputs to the DDSS. This phase of the project has yet to begin.</li> <li>• Develop a procedure for integrating the DDSS into the Epic EHR to create a smooth process for routine clinical use. This phase of the project has yet to begin and, depending on the priority of Epic-related projects, may not be possible during the DHI program.</li> </ul>		
Participants	Information	Technologies
<ul style="list-style-type: none"> <li>• Residents and physicians participating in the validation process and the diagnostic challenge.</li> <li>• UTPhysicians' practice managers for the primary care units who will judge the outcome of the validation process and approve the implementation.</li> <li>• IT executives who will authorize the data input process for the patient's presenting information.</li> <li>• IT personnel who will design and program the input interface.</li> <li>• DDSS representatives who will propose the licensing requirements and associated costs.</li> <li>• Senior UTPhysicians executives who will review and authorize the project for incorporation in the clinical practice.</li> <li>• Epic personnel who will opine and authorize the inclusion of the DDSS into the Epic EHR.</li> <li>• IT Personnel who will program the interface to the Epic EHR.</li> </ul>	<ul style="list-style-type: none"> <li>• Results of the DDSS validation process, including the responses to the challenge questionnaire.</li> <li>• Assessment of the requirements for automatically capturing the patient's presenting information into the DDSS.</li> <li>• Cost analysis of licensing the DDSS for use in the UTPhysicians clinical practices.</li> <li>• Assessment of the requirements for incorporating the DDSS into the Epic EHR.</li> </ul>	<ul style="list-style-type: none"> <li>• The Isabel Pro Diagnostic Decision Support System (Isabel Pro is a web-based differential diagnosis tool designed by Isabel Healthcare, Ltd., a company with head offices in Haslemere, United Kingdom, and Ann Arbor, Michigan.)</li> <li>• RedCap secure web platform for building and managing online databases and surveys.</li> <li>• The Epic EHR.</li> </ul>

## Project Scope Management

**Scope Statement:** The project scope includes three distinct phases. First, choose the diagnostic decision support system most appropriate to meet the goals of the project. Second, validate the system with actual cases to determine system performance and its performance compared to clinicians. Third, develop the procedure by which the system would automatically incorporate the patient's presenting inputs and produce a differential diagnosis listing for the physician to consider at the first instant of the physician-patient encounter.

The project aims to validate the diagnostic decision support system Isabel Pro, using patient presentation inputs only, by establishing the system's diagnostic retrieval accuracy on 46 cases of varying difficulty, each with a "gold standard" final diagnosis. For each case, determine:

1. Did Isabel Pro produce the correct diagnosis – Yes or No?
2. What was the ranking of the correct diagnosis if produced?

Establish the performance of Isabel Pro compared to clinicians by asking 120 residents of McGovern Medical School to diagnose the cases and produce a differential diagnosis list without awareness of the differential produced by Isabel Pro, comparing their diagnostic accuracy to that of Isabel Pro. Then, establish the performance improvement in the residents' diagnostic accuracy when provided with the differential diagnosis list produced by Isabel Pro for each of the cases.

Develop, in collaboration with UTPhysicians' IT group and the Isabel Healthcare professionals, a procedure for introducing a patient's presentation inputs automatically into Isabel Pro to produce a differential diagnosis list to be viewed by the physician at the first instant of the physician-patient encounter. Isabel Healthcare purports to have Application Program Interface (API) software for several integration levels with the EHR. Request a proposal from



Isabel Healthcare, Ltd. for access to the Isabel Pro Diagnostic Decision Support System for the primary care practices of UTPhysicians.

Produce a proposal to UTPhysicians' executive and physician management teams to acquire Isabel Pro and authorize the necessary IT resources to incorporate it into routine clinical practice.

**Project Charter:** This project aims to address diagnostic errors in primary care practice. Following the findings on the type and frequency of diagnostic error in primary practice (Singh et al., 2013), especially the observation that in most cases of diagnostic error, the information available at the initial encounter was sufficient to have arrived at the correct diagnosis, this project proposes the introduction of a diagnostic decision support system to produce a well-researched differential diagnosis list at the very outset of the physician-patient encounter. The project aims to prevent the bias of premature closure and the subsequent confirmation bias, both issues documented to be all too common in cases of diagnostic error (Graber et al., 2005). The project proceeds in three distinct phases or milestones. First, perform a search of all commercially available diagnostic decision support systems to determine the system best fitted for introduction, including ease of use, speed, scientific quality, and diagnostic retrieval accuracy. Second, validation of the system using actual cases; that is, diagnostic retrieval accuracy (did the system return the correct diagnosis and what was the ranking in the differential produced), does the system perform better than clinicians, and did the diagnostic accuracy of the clinicians improve when furnished with the differential diagnosis listing produced by the system (Riches et al., 2016)? Third, develop a procedure or process whereby the patient's presenting inputs can be entered into the system automatically without duplicating entries, and the

differential diagnosis listing produced made available to the physician at the first instant of the physician-patient encounter.

The key stakeholders begin with UTPhysicians, the academic medical practice of UTHealth, and the physician leaders of the primary care practices (including internal medicine, family medicine, community medicine, and geriatric medicine). Other stakeholders include the IT specialists who deal with those practices and their systems (particularly the EHR), the admissions staff in those practices (including the admitting nurses), and, of course, the business executives who oversee UTPhysicians. The developers of the diagnostic decision support system are essential external stakeholders in the project.

The project concludes when the system, validated, with an approved process for incorporation into the routine clinical practice, has been fully developed. Actual incorporation is unlikely to be achievable due to competing priorities with installing the Epic EHR, a massive project proceeding concurrently with this project.

### Requirements Analysis

Describe (5) system/solution features, capabilities, and functions.

Numbered	Desired Functionality	Existing Functionality	Change / New	Justification for the Desired Functionality	Stakeholders / Business impacted	Priority
1	Enter the clinical features into the DDx Generator manually or the software can integrate with Electronic Medical Records (EMR). The system can be used as a standalone solution or alongside existing software.	N/A	New	Time Constraints	Admissions Staff, IT	1
2	Isabel partners with major medical publishers providing on-click evidence-based knowledge of each disease. Partners	N/A	New	Rapidly Changing Evidence Base	Physicians	1

	include DynaMed® from EBSCO, 5 Minute Consult™ from Wolters Kluwer and Best Practice from the BMJ.					
3	Speed of Response	N/A	New	Time Constraints	Admissions Staff, IT	1
4	Diagnostic Retrieval Accuracy	N/A	New	Avoid Diagnostic Error	Physicians	1
5	Relevance Ranking of Presentations; The DDx Generator covers over 10,000 conditions, all ages, and all specialties. As well as clinical features Isabel utilizes additional algorithms to only present those results relevant to the patient's age, gender, and region.	N/A	New	Avoid Premature Closure Bias	Physicians	1

Describe (5) user requirements based on the interview or literature.

Numbered	Desired Functionality	Existing Functionality	Change / New	Justification for the Desired Functionality	Stakeholders / Business impacted	Priority
1	No Duplicate Entry of Inputs	N/A	New	Time Constraints	Physicians, Admission Staff, IT	1
2	Documented Scientific Foundation; DynaMed® from EBSCO, 5 Minute Consult™ from Wolters Kluwer and Best Practice from the BMJ.	Up-To-Date	Change	Avoid Premature Closure and Confirmation Bias	Physicians	1
3	Automatic Differential Diagnosis Listing	N/A	New	Avoid Diagnostic Error	Physicians	2
4	Diagnostic Retrieval Accuracy	N/A	New	Avoid Diagnostic Error	Physicians	1
5	Incorporation into EHR	N/A	New	Time Constraints	Physicians	2

**Acceptance Criteria:** The system must satisfy several conditions if it is to be accepted and used in routine clinical practice.

1. The system must produce a relevant differential diagnosis listing, scientifically accurate, and current with the latest scientific medical literature. Staying current in today's rapidly changing medical research environment is a challenging,

virtually impossible, task. A diagnostic decision support system offers a solution to this dilemma (Delaney & Kostopoulou, 2017).

2. The system must not require the duplicate entry of the input data. Today's physician is overwhelmed with data entry requirements for the electronic health record systems. Despite their multiple and significant advantages, the transfer of EHR information entry obligations to the physician has resulted in a sharp increase in physician burnout (Graber et al., 2017).
3. The system must offer a rapid return of results to be useful. Earlier systems, and some of the systems available even today, require an hour or more to complete data input (Elkin et al., 2010).
4. The presentation of the diagnostic alternatives must be timely in the context of the physician-patient encounter. In this case, the project contemplates the differential diagnosis listing be available at the first moment of the encounter.
5. The system must demonstrably outperform physicians in the diagnostic process, and the physicians must demonstrably improve their diagnostic accuracy when using the system's diagnostics suggestions. This requirement does not imply that the system replaces the physician but instead operates as an experienced, capable colleague at their side.
6. The system's costs must be offset by better patient outcomes, speedier diagnostic conclusions, an increase in potential patient volumes, and the possibility of higher reimbursements.

**Project Deliverables:** The project deliverables follow the pattern of the three distinct phases of the project generally.

1. A commercially available diagnostic decision support system: Isabel Pro is the system selected for this project. (Isabel Pro is a web-based differential diagnosis tool designed by Isabel Healthcare, Ltd., a company with head offices in Haslemere, United Kingdom, and Ann Arbor, Michigan.)
2. Validation of the system in clinical use (Riches et al., 2016)
  - a. The performance of the system in diagnosing actual cases.
    - i. Did the system return the correct diagnosis?
    - ii. What was the ranking of the correct diagnosis?
  - b. Does the system outperform clinicians (Friedman et al., 1999)?
  - c. Do the clinicians improve their diagnostic accuracy when provided with the diagnostic suggestions produced by the system (Friedman et al., 2005)?
3. Development of a process or procedure for automatically including a patient's presenting inputs to the system and the presentation of the differential diagnosis listing to the physician at the first moment of the physician-patient encounter, which in due course could incorporate the system into the EHR.

## BUSINESS PLANNING SWOT

### Problem Statement

Diagnostic error is far more prevalent than generally assumed; premature closure is one of the most prevalent reasons for diagnostic error. Staying current in medicine is virtually impossible with today's explosion of medical research, much of which modifies or even contradicts earlier research. A diagnostic decision support system that presents at the initial moment of the physician-patient encounter a well-researched differential diagnosis listing compiled from scientific medical literature has the potential to prevent premature closure and reduce diagnostic error in primary practice.

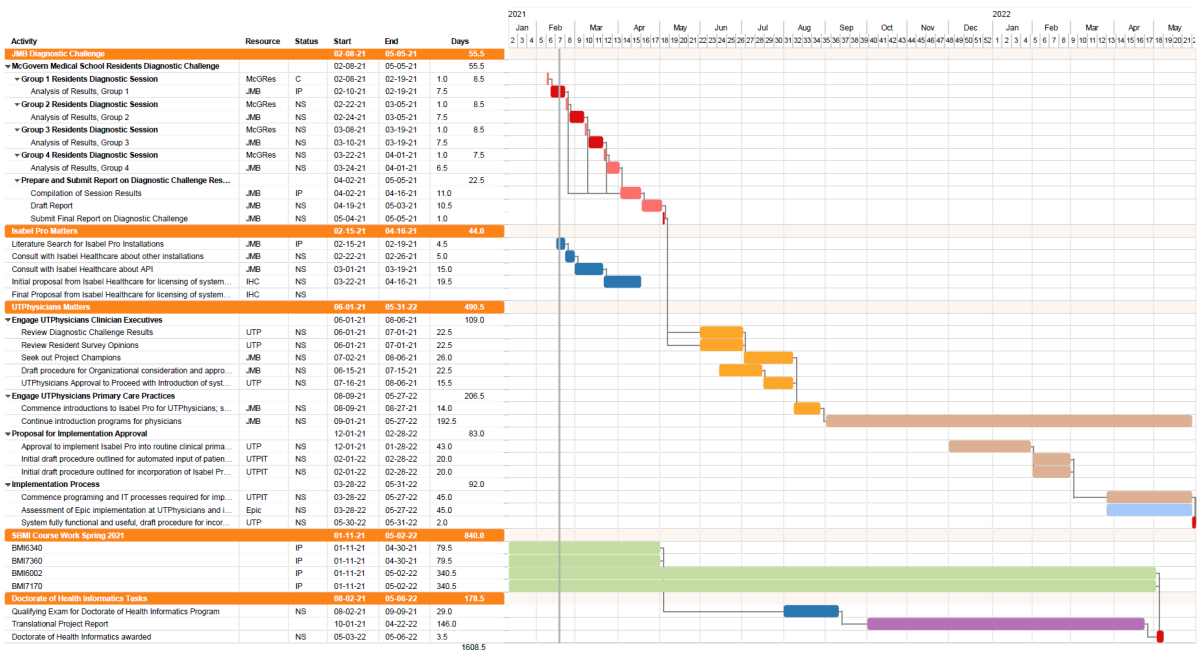
### INTERNAL FACTORS

STRENGTHS (+)	WEAKNESSES (-)
<ul style="list-style-type: none"> <li>Isabel Pro is a commercially available, easy to use, highly accurate diagnostic decision support system.</li> <li>Isabel Pro is currently in use at several institutions in both the UK and the US.</li> <li>Isabel Pro is presently being validated in a diagnostic challenge at UTHealth.</li> <li>Isabel Pro exhibits high diagnostic retrieval accuracy with results presented almost immediately with minimal input.</li> <li>Isabel Pro relies on searches of the most reliable medical literature for its presentations.</li> </ul>	<ul style="list-style-type: none"> <li>Studies show that physicians are highly confident in their diagnostic ability and profess little impetus to seek diagnostic support.</li> <li>The use of diagnostic decision support is not taught in most medical schools, so familiarity is quite low.</li> <li>There are few, if any, programs to detect or prevent diagnostic error in primary practices.</li> <li>Few physicians, after leaving medical school, have time to produce a differential diagnosis listing even though it would almost certainly improve diagnostic accuracy.</li> <li>Most EHRs have no location to store a differential diagnosis listing even if prepared.</li> <li>A discoverable list of diagnostic alternatives considered but rejected is considered a legal liability.</li> </ul>

### EXTERNAL FACTORS

OPPORTUNITIES (+)	THREATS (-)
<ul style="list-style-type: none"> <li>A differential diagnosis listing would almost certainly improve the diagnostic accuracy of almost any physician.</li> <li>Reliable use of the most current evidence-based medical knowledge is virtually impossible without computerized search and retrieval methods.</li> <li>The presentation of well-researched diagnostic alternatives at the first instant of the physician-patient encounter is the most promising means of preventing premature closure.</li> <li>Cutting the annual incidence of diagnostic error in primary care in half would save more than 3 million incidents of patient harm annually.</li> <li>Isabel Pro is imminently scalable to other UT medical institutions if accepted in routine clinical practice at UTPhysicians.</li> </ul>	<ul style="list-style-type: none"> <li>Smooth integration into routine clinical practice without duplication of input is not assured.</li> <li>Integration of Isabel Pro into the Epic EHR is not assured, and examples of past unsuccessful efforts abound.</li> <li>Physician acknowledgement of diagnostic error is often not forthcoming and physician over-confidence is common.</li> <li>Physician acceptance of diagnostic decision support is frequently regarded as an acknowledgement of inability.</li> <li>The legal risks of incorporating diagnostic alternatives into the discoverable record may prevent acceptance.</li> </ul>

## Project Schedule Management Schedule Development - Gantt Chart



**Schedule Control.** The Gantt Chart above depicts the tasks, the task starting and ending dates, the task durations, and identifies the resources responsible for each outlined task, basically the Work Breakdown Structure. Some of the resources are listed in very general terms as they are presently undetermined in specifics at this moment. As Spring 2021 progresses, the emphasis is on identifying resources and updating the chart more specifically. Schedule control for much of the project is the author’s responsibility, but as the project moves into the introduction to the UTPhysicians phase, control of more of the project schedule falls on the organization’s response.

Much of the effort in the task group “Engage UTPhysicians Clinicians Executives” will establish a mutually acceptable schedule for the remaining tasks and a more specific delineation of the individuals involved in each of the remaining tasks. The previous work in validating the system’s performance and its performance compared to clinicians and the improvement in clinician’s performance when using the system suggestions will be essential in substantiating the

potential offered in addressing diagnostic errors and establishing a sense of urgency. The project will generally proceed on a week-to-week basis, and the project schedule will be updated weekly, with time adjustments as needed and additional sub-tasks added as necessary. The weekly process consists of considering each task (Work Breakdown Structure) individually with both adjustments and additions made as needed. The most significant areas for further detail in the Work Breakdown Structure will be when contact with the UTPhysicians Clinician Executives begins, and later, when the UTPhysicians IT group is involved. Neither of these areas is yet fully determinable. The various proposal submission and approval dates are, of course, approximate.



## Project Cost Management

### Cost Estimation

The cost estimate below is very approximate since the author is not yet an employee or otherwise authorized individual at UTPhysicians. However, a few items are reasonably well-known and estimated with some accuracy. The diagnostic decision support system is web-based, including mobile phone access, so the project requires no additional equipment for incorporation into the practices. The subscription cost is \$149 annually without any provision for a volume or institutional discount, which will likely be forthcoming. UTPhysicians has about 15 clinics in the Family Medicine, Geriatric Medicine, and Internal Medicine specialties, employing roughly 100 clinicians. The estimate includes 100 physicians using the standard annual fee, with that fee repeating for five years without escalation. Support fees are \$1,000 daily, with one day allocated for each clinic. Some clinics have as few as two clinicians, while the largest clinics have as many as twenty, but a full day of vendor support for each clinic provides for some shorter sessions and some longer sessions within the overall estimate.

In advance of the project commencement, the estimate includes a visit to an existing institutional user to see the system in action and discuss issues encountered and addressed at that institution. The estimate projects four team members for a two-day on-site visit. The project is estimated to require 19 weeks of elapsed time, with IT at eight hours daily for the entire period, nurses at eight hours for one day each week concentrated near the go-live date. Office staff, primarily admissions personnel, were estimated at the same time as the nurses.

Go-Live estimates were two full days per clinic for the IT personnel, one full day per clinic for the nurse, and two full days for the Super User. The hourly rates for each category are estimates only and can be updated as actual numbers become available.

**Budget:** The budget for this project calls for a five-year total expenditure of \$162,354.43, made up of a Vendor total of \$89,500.00, an Organizational Total of \$60,481.00, and a Tax total of \$12,373.43. Details of the budget, including initial expenditures and annual expenditures by line item, are included in the Cost Excel Spreadsheets below.

**Budget Control:** Most of the project's controllable aspects are related to team makeup and the time spent accomplishing the assigned tasks, much of it in the IT arena. A working team assembled at the project's initial proposal would assess the time required for each element of the project in forming a detailed budget for implementation. Weekly meetings to discuss progress, difficulties, estimate revisions if required and needed changes in the process as indicated by actual events would be the most appropriate method of budget control. This system, commercially available, has existing integration tools, including APIs for various EHRs easily assessed before beginning the project, and can be reviewed with other institutions for lessons learned in their implementations.

## Cost Excel Sheet

<b>UTPhysicians</b>							
<b>Diagnostic Decision Support System</b>							
<b>Proposed 5 Year Total Cost of Ownership (TCO)</b>							
<b>2022-2027</b>							
<b>Vendor Cost</b>	<b>One-time Fees</b>	<b>Year 1</b>	<b>Year 2</b>	<b>Year 3</b>	<b>Year 4</b>	<b>Year 5</b>	<b>Total</b>
Licensed Software	\$ -	\$ 14,900.00	\$ 14,900.00	\$ 14,900.00	\$ 14,900.00	\$ 14,900.00	\$ 74,500.00
Sublicensed Software	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Subscriptions	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Professional Fees	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Remote Hosting Fees	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Installation Fees	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Support/Maintenance Fees	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Go-live Support Fees	\$ 15,000.00	\$ -	\$ -	\$ -	\$ -	\$ -	\$ 15,000.00
Travel/Hotel to Client Site	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
Other Fees	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -	\$ -
<b>Organizational Cost</b>	<b>One-time Fees</b>	<b>Year 1</b>	<b>Year 2</b>	<b>Year 3</b>	<b>Year 4</b>	<b>Year 5</b>	<b>Total</b>
Hardware	\$ -	\$ -					\$ -
Build/Backfill Team	\$ -	\$ 28,600.00					\$ 28,600.00
Go-live Support Team	\$ -	\$ 22,800.00					\$ 22,800.00
Training Materials	\$ -	\$ 3,600.00					\$ 3,600.00
Travel/Hotel to Vendor Site	\$ -	\$ 5,480.00					\$ 5,480.00
Other	\$ -	\$ 1.00					\$ 1.00
<b>Vendor Total</b>	<b>\$ 15,000.00</b>	<b>\$ 14,900.00</b>	<b>\$ 14,900.00</b>	<b>\$ 14,900.00</b>	<b>\$ 14,900.00</b>	<b>\$ 14,900.00</b>	<b>\$ 89,500.00</b>
<b>Organizational Total</b>	<b>\$ -</b>	<b>\$ 60,481.00</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ -</b>	<b>\$ 60,481.00</b>
<b>Taxes</b>	\$ 1,237.50	\$ 6,218.93	\$ 1,229.25	\$ 1,229.25	\$ 1,229.25	\$ 1,229.25	\$ 12,373.43
<b>Grand Total</b>	<b>\$ 16,237.50</b>	<b>\$ 81,599.93</b>	<b>\$ 16,129.25</b>	<b>\$ 16,129.25</b>	<b>\$ 16,129.25</b>	<b>\$ 16,129.25</b>	<b>\$ 162,354.43</b>

<b>Estimated Cost Breakdown</b>			
<b>Hardware</b>	<b>Quantity</b>	<b>Unit Cost</b>	<b>Total</b>
Scanner	0	\$ 10.00	\$ -
Computer	0	\$ 5,000.00	\$ -
Other Device (Work Phone, etc.)	0	\$ 3,000.00	\$ -
<b>Sub Total</b>	<b>0</b>	<b>\$ 8,010.00</b>	<b>\$ -</b>
<b>Backfill/Build Team</b>	<b>No. of Required Build Hrs</b>	<b>Rate per hr</b>	<b>Total</b>
RN	160	\$ 30.00	\$ 4,800.00
IT	760	\$ 25.00	\$ 19,000.00
Office Staff	160	\$ 30.00	\$ 4,800.00
Owner of Home Health Agency	0	\$ 30.00	\$ -
<b>Sub Total</b>	<b>1080</b>	<b>\$ 115.00</b>	<b>\$ 28,600.00</b>
<b>Go-live Support</b>	<b>No. of Support Hrs</b>	<b>Rate per hr</b>	<b>Total</b>
RN	120	\$ 30.00	\$ 3,600.00
IT	240	\$ 30.00	\$ 7,200.00
Home Health Agency Office	0	\$ 30.00	\$ -
Super User	120	\$ 100.00	\$ 12,000.00
<b>Sub Total</b>	<b>480</b>	<b>\$ 190.00</b>	<b>\$ 22,800.00</b>
<b>Training/Materials</b>	<b>No. of Materials</b>	<b>Rate per hr</b>	<b>Total</b>
Training Guide	0	\$ 30.00	\$ -
Other	120	\$ 30.00	\$ 3,600.00
<b>Sub Total</b>	<b>120</b>	<b>\$ 60.00</b>	<b>\$ 3,600.00</b>
<b>Travel/Hotel</b>	<b>No. of Persons/Items</b>	<b>Unit Cost</b>	<b>Total</b>
Airfare	4	\$ 400.00	\$ 1,600.00
Hotel Nights (2 nights, 4 persons)	8	\$ 350.00	\$ 2,800.00
Meals per day (2 days x 4 persons)	8	\$ 65.00	\$ 520.00
Other	4	\$ 140.00	\$ 560.00
<b>Sub Total</b>	<b>24</b>	<b>\$ 955.00</b>	<b>\$ 5,480.00</b>

## Project Quality Management

### Planning

# Evaluation of a Computerized Diagnostic Decision Support System in Primary Practice

<b>Prepared by:</b>	Joe M. Bridges
<b>Date (MM/DD/YYYY):</b>	03/02/2021

1. Deliverables and Acceptance Criteria	
Deliverables	Acceptance Criteria / Applicable Standards
1. A commercially available diagnostic decision support system	Isabel Pro, a web-based diagnostic decision support system, commercially available from Isabel Healthcare, Ltd., Haslemere, UK
2. Validation of the system's performance in clinical application	Results of validation studies showing system performance in diagnostic performance on clinical cases with "gold standard" final diagnoses in three areas: 1. Did the system return the correct diagnosis on each case and what was the ranking of the correct diagnosis in the diagnostic differential listing? 2. Did the system outperform clinicians on the same cases? 3. Did the clinicians improve their performance when using the diagnostic suggestion produced by the system? The system must demonstrably outperform the physicians in diagnostic retrieval accuracy and the physicians must demonstrably improved their diagnostic retrieval accuracy when using the diagnostic suggestions produced by the system.
3. A process or procedure for automatically including a patient's presenting inputs to the system.	The process requires no duplication or re-entry of admitting information to trigger the initiation of the diagnostic decision support process.
4. Production of a differential diagnosis listing for the clinician to consider at the very outset of the physician-patient encounter.	The differential diagnosis listing produced by the system must be available at the instant the physician enters the encounter with the patient.

**Quality Assurance (QA)**

**Quality Control (QC)**

## 2. Quality Assurance Activities

- What steps will you take to ensure that Quality is built into the production processes?

1. The system will produce a differential diagnosis listing using the presentation inputs from 46 clinical cases, each with a difficulty rating and a "gold standard" diagnosis. Diagnostic retrieval accuracy will be measured by whether the correct diagnosis was produced and the ranking of that correct diagnosis.
2. The diagnostic retrieval accuracy of the system will be compared to the diagnostic retrieval accuracy of participating clinicians on the same cases using the same criteria.
3. The improvement of the diagnostic retrieval accuracy of the physicians will be measured by comparing the change in the diagnostic retrieval accuracy of the clinicians on the same cases when provided with the diagnostic suggestions produced by the system.
4. The automatically entered presenting inputs to the system will be manually compared to the presenting inputs in the EHR for a statistically significant number of patients to assure that input information is complete, accurate, and non-duplicative.
5. The availability of the differential diagnostic listing must be immediate at the physician-patient encounter and will be observed for a statistically significant number of patients before acceptance.

- Will the test team work from a Test Plan? Do they understand their responsibilities?

With guidance from the senior physicians at UTPhysicians, an appropriate number of historical cases will be selected for testing of the automated entry of patient presenting inputs, followed by a statistically significant number of admissions to confirm that the automated process is complete and timely.

- How will you ensure that Requirements are correct, complete and accurately reflect the needs of the Customer?

The system is commercially available and presently in use at certain clinical locations. Detailed, on-site visits will be conducted to critically assess the existing performance of the system at those locations and to determine the details of their implementation and integration process, as well as the performance enhancement or changes adopted by those institutions.

- How will you verify that Specifications are an accurate representation of the Requirements?

The system is commercially available and presently in use at certain clinical locations. Detailed, on-site visits will be conducted to critically assess the existing performance of the system at those locations and to determine the details of their implementation and integration process, as well as the performance enhancement or changes adopted by those institutions.

- What steps will you take to ensure that the project plan (e.g. Risk Management Plan, Change Management Plan, Procurement Plan) is followed?

The project plan follows four basic steps: selection of the system, validation of the system, proposal and approval of the system, implementation of the system. The first three steps are basically in the control of and performed by the project manager. The formation of the implementation team will require approval and support of the clinical executives and will involve IT personnel for the automated input programming, admissions staff for the process of patient admission and presentation steps, clinical staff involved in patient admission in advance of the physician encounter, a physician champion to advise and opine on the presentation of the differential diagnosis listing and its helpfulness.

- Describe how *Requirement – Specification – Test Plan* traceability is managed (or provide [Link\\_To\\_Requirements\\_Traceability\\_Matrix](#)):

This traceability matrix will be possible following some of the institutional visits and collaboration with those presently using the system.

- What audits and reviews are required and when will they be held?

<ul style="list-style-type: none"> <li>What steps will you take to ensure that the Vendor is supplying deliverables of adequate quality?</li> </ul>
The validation process described earlier will establish the quality of the system output and performance.
<ul style="list-style-type: none"> <li>What will you measure to determine if the project is out of Scope?</li> </ul>
The system is commercially available, the project scope is very narrow and specific, the clinical practices are known and specific to primary care, so Scope drift is very unlikely.
<ul style="list-style-type: none"> <li>What will you measure to determine if the project is within budget?</li> </ul>
The principal cost variable is IT personnel and the time spent programming. Weekly meetings and time spent should allow ample warning of budget overruns and time extensions.
<ul style="list-style-type: none"> <li>What will you measure to determine if the project is within schedule?</li> </ul>
The principal cost variable is IT personnel and the time spent programming. Weekly meetings and time spent should allow ample warning of budget overruns and time extensions.

3. Project Monitoring and Control	
<i>Define the following:</i>	
<ul style="list-style-type: none"> <li>How will you ensure that adequate testing is done? How do you define “adequate”?</li> </ul>	The other institutions around the country and the world should offer a pattern to be followed in testing and measuring adequacy. Those testing and performance protocols will be adapted to the specific situation at UTPhysicians.
<ul style="list-style-type: none"> <li>How will you report and resolve variances from acceptance criteria?</li> </ul>	The program will be introduced using a receptive clinic with a physician champion. Variances can be observed through usage reviews with the receptive clinic. The pattern in the other institutions presently using the system will be a useful measure of assuring that acceptance criteria are met, as well as providing directions for correcting variances.
<ul style="list-style-type: none"> <li>At what milestones will testing and reviews take place – who and how will they do them?</li> </ul>	Isabel Pro is a commercially available diagnostic decision support system presently in use at several institutions in the United States and the UK. Milestones used by these institutions will provide guidance for this project. Weekly reviews are likely the most effective in assuring successful introduction.
<ul style="list-style-type: none"> <li>What action by the Sponsor constitutes acceptance of deliverables at each phase?</li> </ul>	The local head of each clinic, in conjunction with the practice’s executive physicians will acknowledge acceptance and satisfaction, clinic by clinic.
<ul style="list-style-type: none"> <li>What action by the Sponsor constitutes “full and final acceptance” of final deliverables?</li> </ul>	Acceptance by all clinics in conjunction with the practice’s physician executives will complete the acceptance of the project.

4. Project Quality Plan / Signatures			
<b>Project Name:</b>	Evaluation of a Computerized Diagnostic Decision Support System in Primary Practice		
<b>Project Manager:</b>	Joe M. Bridges		
<i>I have reviewed the information contained in this Project Quality Plan and agree:</i>			
Name	Role	Signature	Date



Name	Role	Signature	Date

*The signatures above indicate an understanding of the purpose and content of this document by those signing it. By signing this document, they agree to this as the formal Project Quality Plan document.*

## Project Resource Management

**Human Resource Management Plan:**

Evaluation and Introduction of a  
 Computerized Diagnostic Decision      Date  
 Project Title: Support System in Primary Practice      Prepared: April 20, 2021

## Roles, Responsibilities, and Authority

Role	Responsibility	Authority
1. Mr. Andrew Casas, UTPhysicians Chief Operating Officer	1. Responsible for operations of UTPhysicians, the academic medical practice of UTHealth	1. Key individual in approving and funding the incorporation of Isabel Pro into routine clinical practice
2. Dr. Eric Thomas, UTPhysicians Associate Dean for Healthcare Quality	2. Senior physician overseeing practice quality, including detection and prevention of diagnostic error	2. Most influential physician- executive in supporting Isabel Pro for reducing the likelihood of diagnostic error.
3. Dr. Thomas J. Murphy, UTPhysicians Assistant Dean for Community Affairs and Health Policy	3. Senior physician overseeing primary and community care practices, oversees the primary care and community clinics	3. Most important physician- executive for incorporation of Isabel Pro into routine clinical practice
4. Dr. James J. Griffiths, UTPhysicians Associate Vice President of Healthcare IT	4. Senior IT executive for UTPhysicians	4. Will oversee and allocate the IT resources necessary to incorporate Isabel Pro into routine clinical practice
5. Mr. Patrick Garrett, Vice President, Isabel Healthcare. Ltd	5. VP for the developer of Isabel Pro and liason to US hospitals presently using Isabel Pro in clinical practice	5. Will be developer liason and implementation executive for incorporation of Isabel Pro into routine clinical practice at UTPhysicians
6. Dr. Jeffrey Chen. Chief Resident, McGovern Medical School	6. Oversees the 120 medical residents participating in the validation study of Isabel Pro	6. Chose the “Diagnostic Challenge” as the weekly assignment for the Residents’ Conference
7. Senior Clinical Admissions Nurse Administrator	7. Will be a key individual in the smooth incorporation of patient presentation information into Isabel Pro	7. In charge of admissions nurses’ processes for

<p>8. Senior Clinical Admissions Staff Administrator</p> <p>9. Clinical Physician Champion</p>	<p>without duplication of entries</p> <p>8. Will be a key individual in the smooth incorporation of patient presentation information into Isabel Pro without duplication of entries.</p> <p>9. Will be a key individual in the acceptance of the system by the practicing physicians</p>	<p>UTPhysicians primary care clinics</p> <p>8. In charge of admissions staff processes for UTPhysicians primary care clinics</p> <p>9. Highly regarded by colleagues and exhibits exceptional influence among clinics and clinicians.</p>
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## Project Communication Management

Project Name:	Evaluation and Introduction of a Computerized Diagnostic Decision Support System in Primary Practice
Project Manager:	Joe M Bridges
Date:	Tuesday, March 30, 2021

#	Recipient	Message	Assumptions	Timeline	Channel	Recipients Response	Responsible	Contact Information
1	Mr. Andrew Casas, UTPhysicians Chief Operating Officer	Key individual in approving and funding the incorporation of Isabel Pro into routine clinical practice	Will review and approve the project and its implementation into routine clinical practice; proposal must be complete, concise, and convincing.	One of the first to see the proposal key individual to get "on-board" early, will need early and continuing support, will need routine updates on project progress	Face-to-Face meeting for project proposal and approval, routine updates by email, regular progress meetings less often, final closure report meeting in one of the clinics to see the system in use.	Approval of project and funding, final approval on fully implemented system s	Joe M. Bridges, Project Manager	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a>
2	Dr. Eric Thomas, UTPhysicians Associate Dean for Healthcare Quality	Most influential physician executive in supporting Isabel Pro for reducing the likelihood of diagnostic error.	Will review and approve the project and its implementation into routine clinical practice; proposal must be complete, concise, and convincing. Will be involved in introducing the program into the clinics, interfacing with the clinicians, and supporting the implementation.	One of the first to see the proposal key individual to get "on-board" early, will need early and continuing support, will need routine updates on project progress, will be routinely involved in implementation steps, especially as to clinician use during encounters, as well as follow-up for improvement in diagnostic accuracy.	Face-to-Face meeting for project proposal preparation, face-to-face meeting for project proposal and approval, routine updates by email, regular progress meetings weekly, regular clinic meetings to see progress and cover schedule and performance issues, final closure report meeting in one of the clinics to see the system in use	Continued support and guidance, assistance in resolving issues, guidance on best practices for system incorporation, hands-on support to engage clinicians and clinic staff.	Joe M. Bridges, Project Manager, Dr. Eric Thomas	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a> , <a href="mailto:Eric.Thomas@uth.tmc.edu">Eric.Thomas@uth.tmc.edu</a>
3	Dr. Thomas J. Murphy, UTPhysicians Assistant Dean for Community Affairs and Health Policy	Most important physician executive for incorporation of Isabel Pro into routine clinical practice	Will review and approve the project and its implementation into routine clinical practice; proposal must be complete, concise, and convincing. Will be involved in introducing the program into	One of the first to see the proposal key individual to get "on-board" early, will need early and continuing support, will need routine updates on project progress, will be routinely involved in	Face-to-Face meeting for project proposal preparation, face-to-face meeting for project proposal and approval, routine updates by email, regular progress meetings	Continued support and guidance, assistance in resolving issues, guidance on best practices for system incorporation, hands-on support to engage	Joe M. Bridges, Project Manager, Dr. Thomas J. Murphy	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a> , <a href="mailto:Thomas.J.Murphy@uth.tmc.edu">Thomas.J.Murphy@uth.tmc.edu</a>

			the clinics, interfacing with the clinicians, and supporting the implementation.	implementation steps, especially as to clinician use during encounters, as well as follow-up for improvement in diagnostic accuracy.	weekly, regular clinic meetings to see progress and cover schedule and performance issues, final closure report meeting in one of the clinics to see the system in use	clinicians and clinic staff.		
4	Dr. James J. Griffiths, UT Physicians Associate Vice President of Healthcare IT	Will oversee and allocate the IT resources necessary to incorporate Isabel Pro into routine clinical practice	Will review and approve the project and the IT aspects of its implementation into routine clinical practice; proposal must be complete, concise, and convincing Will be involved in introducing the program into the IT aspects of the program, interfacing with the clinicians and staff using the system, and supporting the implementation.	One of the first to see the proposal key individual to get "on-board" early, will be deeply involved in the early and continuing IT implementation, will be part of routine updates on project progress, will be routinely involved in implementation steps, especially as to admissions staff and nurses in advance of encounters, as well as follow up on IT matters	Several face-to-face meetings to plan IT implementation and agree on staffing and schedule, regular email contact on issues as they arise, regular progress meetings as IT work progresses, regular meetings with clinic admissions staff, final closure meeting to confirm system functioning as planned.	Continued support and guidance, assistance in resolving issues, guidance on best practices for system incorporation, hands-on support to engage IT staff, clinicians, and clinic staff	Joe M. Bridges, Project Manager, Dr. James J. Griffith	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a> , <a href="mailto:james.j.griffiths@uth.tmc.edu">james.j.griffiths@uth.tmc.edu</a>
5	Mr. Patrick Garrett, Vice President, Isabel Healthcare. Ltd	Will be developer liaison and implementation executive for incorporation of Isabel Pro into routine clinical practice at UT Physicians	Will be developer liaison and implementation executive for incorporation of Isabel Pro into routine clinical practice at UT Physicians, will connect with other institutions for collaboration on "lessons learned" and other implementation guidance, will coordinate with IT and clinical staff	Will be heavily involved in preparation of proposal to implement usage, particularly aware of prior installations, problems, issues, and solutions, vendor liaison during implementation and follow up	Several face-to-face meetings to develop institutional connections for collaboration, also to plan IT implementation and agree on staffing and schedule, regular email contact on issues as they arise, regular progress meetings as IT work progresses, regular meetings with clinic admissions staff, final closure meeting to confirm system functioning as planned.	Regular contact by email and meetings to gauge progress, suggest improvements and adjustments, continued engagement of other institutions for "lessons learned" and other issues to be dealt with as project continues.	Joe M. Bridges, Project Manager, Mr. Patrick Garrett	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a> , <a href="mailto:pat.garrett@isabelhealthcare">pat.garrett@isabelhealthcare</a>

6	Dr. Jeffrey Chen, Chief Resident, McGovern Medical School	Chose the "Diagnostic Challenge" as the weekly assignment for the Residents' Conference and administered the completion of the challenges.	Responsible for choosing the "Diagnostic Challenge" as the format for the weekly Resident conferences, conducted the sessions, confirmed the submission of results.	Agreed to use the "Diagnostic Challenge" in January, implemented the challenge in three sessions of Resident Conferences, total of 120 residents participated, generating over 200 responses to questionnaire and roughly 1,000 diagnostic responses to 24 cases.	Completed "Diagnostic Challenge" on March 22, 2021, data collected and ready for analysis.	Completed.	Joe M. Bridges, Project Manager, Dr Jeffrey Chen	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a> , <a href="mailto:jeffrey.w.chen@uth.tmc.edu">jeffrey.w.chen@uth.tmc.edu</a>
7	Senior Clinical Admissions Nurse Administrator	In charge of admissions nurses' processes for UT Physicians primary care clinics	Will be a necessary conduit for procedures used in clinics for admission and collection of pre-encounter data and medical inputs, will be part of verification effort that data is input to Isabel Pro without duplicate entry	Essential individual in the collection of pre-encounter observations and medical history and medications, will be involved in quality control to assure all information collected appears as inputs to Isabel Pro without reentry of data	Several face-to-face meetings to plan IT and admissions process implementation and agree on staffing and schedule, regular email contact on issues as they arise, regular progress meetings as IT work progresses, regular meetings with clinic admissions staff, final closure meeting to confirm system functioning as planned.	Feedback at outset of issues likely to be encountered, issues already on the horizon anticipated to require special attention, continued feedback on incorporation issues as they arise, suggestions for improvements, encouragement of associates on utility of system	Joe M. Bridges, Project Manager, Dr. James J. Griffith, Dr. Eric Thomas, Dr. Thomas J. Murphy	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a>
8	Senior Clinical Admissions Staff Administrator	In charge of admissions staff processes for UT Physicians primary care clinics	Will be a necessary conduit for procedures used in clinics for admission and collection of pre-encounter data and medical history, medicine lists and other inputs, will be part of verification effort that data	Essential individual in the collection of pre-encounter demographics and medical history and medications, will be involved in quality control to assure all information collected appears as inputs to Isabel	Several face-to-face meetings to plan IT and admissions process implementation and agree on staffing and schedule, regular email contact on issues as they arise, regular progress meetings as IT work progresses,	Feedback at outset of issues likely to be encountered, issues already on the horizon anticipated to require special attention, continued feedback on incorporation issues as they arise, suggestions for improvements, encouragement	Joe M. Bridges, Project Manager, Dr. James J. Griffith, Dr. Eric Thomas, Dr. Thomas J. Murphy	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a>

			is input to Isabel Pro without duplicate entry	Pro without reentry of data	regular meetings with clinic admissions staff, final closure meeting to confirm system functioning as planned.	of associates on utility of system		
9	Clinical Physician Champion	Highly regarded by colleagues and exhibits exceptional influence among clinics and clinicians	Will be well known within the primary practices, well-regarded by peers and associates, respected for opinion, forward-looking in attitude, and known to seek continuous improvements in workflow and outcomes	Key individual in usage of differential diagnoses produced by Isabel, essential as a "change agent" in the primary care practices.	Several face-to-face meetings to plan implementation and agree on clinician usage protocols, on-site visit to institutions using system to see functioning clinics in person, regular email contact on issues as they arise, regular progress meetings as work progresses, regular meetings with clinicians for information and training, training sessions with each individual clinician, final closure meeting to confirm system functioning as planned.	Frank assessments of usage issues to be faced with other clinicians, attendance at training and introduction sessions, assessment of visits to other institutions, suggestions for addressing smooth introduction.	Joe M. Bridges, Project Manager, Dr. James J. Griffith, Dr. Eric Thomas, Dr. Thomas J. Murphy	<a href="mailto:joe.bridges@uth.tmc.edu">joe.bridges@uth.tmc.edu</a>

## Project Risk Management

**Risk Plan Overview:** The project faces three primary risks, each of which must be recognized and addressed to achieve the desired outcome of reducing the occurrence of diagnostic error, or better characterized as “missed diagnostic opportunities.”

First, the diagnostic decision support system selected, in this case, Isabel Pro, must demonstrate validity in practice. The “Diagnostic Challenge” and the steps leading up to that challenge have provided the baseline for this demonstration.

Second, the system must be incorporated in the UTPhysicians’ admissions process smoothly and without requiring duplicate entries, allowing its use in routine clinical practice.

Third, the system needs incorporation into UTPhysicians’ newly installed Epic EHR to ease access and use in routine primary care settings.

The following tables catalog the risks identified in these processes, the schedule for dealing with those risks, the analysis and assessment of those risks, the monitoring of the risks, and the steps anticipated to mitigate and control those risks.

### **Risk Identification:**



Risk	Possible impacts on the project
<ul style="list-style-type: none"> <li>• The use of diagnostic decision support is not taught in most medical schools, so familiarity is relatively low.</li> <li>• After leaving medical school, few physicians have time to produce a differential diagnosis listing even though it would almost certainly improve diagnostic accuracy.</li> <li>• Smooth integration into routine clinical practice without duplication of input is not assured.</li> </ul>	<ul style="list-style-type: none"> <li>• The lack of familiarity with diagnostic decision support systems and the possible subtle prejudices against such systems ingrained in the medical school curriculum are likely impediments to clinicians' acceptance.</li> <li>• There is virtually universal agreement that a differential diagnosis will improve almost any physician's diagnostic accuracy, so a differential automatically prepared without requiring entries by the clinician holds the prospect of acceptance if the system proves effective. However, unless the correct diagnostic alternative appears within the top ten suggestions, the alternative may well be ignored or overlooked.</li> <li>• All the information required for the initial inputs to Isabel Pro is already routinely collected in the admissions process. The challenge will be to capture this information and present the differential diagnosis without requiring duplicate entries.</li> <li>• The smooth integration process is an IT requirement overlaid on implementing the Epic EHR, a project that will almost certainly carry greater priority for IT resources.</li> </ul>
<ul style="list-style-type: none"> <li>• Most EHRs have no location to store a differential diagnosis listing even if prepared.</li> <li>• Integration of Isabel Pro into the Epic EHR is not assured, and examples of past unsuccessful efforts abound.</li> </ul>	<ul style="list-style-type: none"> <li>• Incorporation of programs into Epic that Epic did not develop is notoriously difficult and prone to failure.</li> <li>• There are a few examples of Isabel Pro incorporation into the Epic EHR (a hospital in the UK, for example), but the incorporation often requires a great deal of duplicate input, so the system is not as effective as it might otherwise be.</li> <li>• The current effort in this project is to collaborate with institutions using the system (whether smoothly or not) to develop an implementation process that takes advantage of the lessons learned by those institutions.</li> <li>• Epic is a new installation for UTPhysicians, so resource availability will depend significantly on the successful implementation of that system far enough in advance to allow work on Isabel Pro to take place.</li> </ul>
<ul style="list-style-type: none"> <li>• Studies show that physicians are highly confident in their diagnostic ability and profess little impetus to seek diagnostic support.</li> <li>• Physician acknowledgment of diagnostic error is often not forthcoming, and physician over-confidence is common.</li> </ul>	<ul style="list-style-type: none"> <li>• In practice, the Isabel Pro system must be demonstrably better than the clinicians alone and should offer proof that the clinician is better with the system.</li> <li>• The "Diagnostic Challenge" results will need to produce the proof of this concept in a fashion adequate to encourage usage.</li> <li>• The system should present as "a trusted colleague working at the clinician's elbow" to avoid the perception that the system might replace the clinician.</li> </ul>
<ul style="list-style-type: none"> <li>• There are few, if any, programs to detect or prevent diagnostic error in primary practices.</li> <li>• Often, physician acceptance of diagnostic decision support unfavorably reflects a lack of diagnostic competence.</li> </ul>	<ul style="list-style-type: none"> <li>• The project, so far, has not found an inventory of "missed diagnostic opportunities" in the primary practices of UTPhysicians, so production of an estimate of the benefit of Isabel Pro relies on extrapolation of "Diagnostic Challenge" conclusions.</li> <li>• Positioning the system as a source of the best in evidence-based medicine based on the computerized interrogation of the latest in clinical knowledge accomplishes a task even the most dedicated clinicians cannot possibly achieve given the tidal wave of new findings produced every year.</li> <li>• The issue is not a lack of competence but a lack of time to remain current and still practice in today's demanding environments.</li> </ul>
<ul style="list-style-type: none"> <li>• A discoverable list of diagnostic alternatives considered but rejected is considered a legal liability.</li> <li>• The legal risks of incorporating diagnostic alternatives into the discoverable record may prevent acceptance.</li> </ul>	<ul style="list-style-type: none"> <li>• At least one example exists of the successful incorporation of a diagnostic decision support system in the Epic EHR in a pediatric neurology practice abandoned due to the concerns around the differential diagnosis listing being legally discoverable.</li> <li>• This project's legal implications are yet to be examined and dealt with, but this aspect may well be sufficient to deny incorporation.</li> </ul>

**Risk Management/Schedule:** The project proceeds in three phases.

First, choose the diagnostic decision support system most appropriate to meet the goals of the project.

Second, validate the system with actual cases to determine system performance and its performance compared to clinicians.

Third, develop the procedure by which the system would automatically incorporate the patient's presenting inputs and produce a differential diagnosis listing for the physician to consider at the first instant of the physician-patient encounter.

The First phase completion occurred during the Spring semester of 2020. The completion of the first portion of the second phase occurred during the Fall semester of 2020, and the last portion of the second phase is underway at this moment.

The Gantt Chart depicts the tasks, the task starting and ending dates, the task durations, and identifies the resources responsible (as best known at this time) for each outlined task, basically the Work Breakdown Structure. As Spring 2021 progresses, the emphasis is on identifying resources and updating the chart more specifically.

Schedule control for much of the project is the author's responsibility, but as the project moves into the introduction to the UTPhysicians phase, control of more of the project schedule falls on the organization's response.

The effort in the task grouping "Engage UTPhysicians Clinicians Executives" is establishing a mutually acceptable schedule for the remaining tasks and a more specific delineation of the individuals involved in each of the remaining tasks. The previous work in validating the system's performance and its performance compared to clinicians and the improvement in clinician's performance when using the system suggestions is essential for

substantiating the potential offered in addressing diagnostic errors and establishing a sense of urgency.

The project schedule will be updated weekly, with time adjustments as needed and additional sub-tasks added as necessary. The weekly process considers each task (Work Breakdown Structure) individually with both adjustments and additions made. Greater detail in the Work Breakdown Structure will be forthcoming when contact with the UTPhysicians Clinician Executives begins, and later, when the UTPhysicians IT group is involved. Neither of these areas is yet fully determinable.

The various proposal submission and approval dates are, of course, approximate.

## Risk Analysis:

Risk Level (1–Lowest to 5–Highest)	Probability of Occurrence (%)	Risk	Project Impacts
1	100	The use of diagnostic decision support is not taught in most medical schools, so familiarity is relatively low.	The lack of familiarity with diagnostic decision support systems and the possible subtle prejudices against such systems ingrained in the medical school curriculum are likely impediments to clinicians' acceptance.
3	50	After leaving medical school, few physicians have time to produce a differential diagnosis listing even though it would almost certainly improve diagnostic accuracy.	There is virtually universal agreement that a differential diagnosis will improve almost any physician's diagnostic accuracy, so a differential automatically prepared without requiring entries by the clinician holds the prospect of acceptance if the system proves effective. However, unless the correct diagnostic alternative appears within the top ten suggestions, the alternative may well be ignored or overlooked.
3	50	Smooth integration into routine clinical practice without duplication of input is not assured.	All the information required for the initial inputs to Isabel Pro is already routinely collected in the admissions process. The challenge will be to capture this information and present the differential diagnosis without requiring duplicate entries. The integration process is an IT requirement overlaid on implementing the Epic EHR, a project that will almost certainly carry greater priority for IT resources.
5	100	Most EHRs have no location to store a differential diagnosis listing even if prepared.	Incorporation of programs into Epic that Epic did not develop is notoriously difficult and prone to failure. There are a few examples of Isabel Pro incorporation into the Epic EHR (a hospital in the UK, for example), but the incorporation often requires a great deal of duplicate input, so the system is not as effective as it might otherwise be.
5	100	Integration of Isabel Pro into the Epic EHR is not assured, and examples of past unsuccessful efforts abound.	The current effort in this project is to collaborate with institutions using the system (whether smoothly or not) to develop an implementation process that takes advantage of the lessons learned by those institutions. Epic is a new installation for UTPhysicians, so resource availability will depend significantly on the successful implementation of that system far enough in advance to allow work on Isabel Pro to take place.
5	100	Studies show that physicians are highly confident in their diagnostic ability and profess little impetus to seek diagnostic support.	In practice, the Isabel Pro system must be demonstrably better than the clinicians alone and should offer proof that the clinician is better with the system. The "Diagnostic Challenge" results will need to produce the proof of this concept in a fashion adequate to encourage usage.
5	100	Physician acknowledgment of diagnostic error is often not forthcoming, and physician over-confidence is common.	The system should present as "a trusted colleague working at the clinician's elbow" to avoid the perception that the system might replace the clinician.
5	100	There are few, if any, programs to detect or prevent diagnostic error in primary practices.	The project, so far, has not found an inventory of "missed diagnostic opportunities" in the primary practices of UTPhysicians, so production of an estimate of the benefit of Isabel Pro relies on extrapolation of "Diagnostic Challenge" conclusions.
3	50	Often, physician acceptance of diagnostic decision support unfavorably reflects a lack of diagnostic competence.	Positioning the system as a source of the best in evidence-based medicine based on the computerized interrogation of the latest in clinical knowledge accomplishes a task even the most dedicated clinicians cannot possibly achieve given the tidal wave of new findings produced every year. The issue is not a lack of competence but a lack of time to remain current and still practice in today's demanding environments.
3	50	A discoverable list of diagnostic alternatives considered but rejected is considered a legal liability.	At least one example exists of the successful incorporation of a diagnostic decision support system in the Epic EHR in a pediatric neurology practice abandoned due to the concerns around the differential diagnosis listing being legally discoverable.
3	50	The legal risks of incorporating diagnostic alternatives into the discoverable record may prevent acceptance.	This project's legal implications are yet to be examined and dealt with, but this aspect may well be sufficient to deny incorporation.

## Risk Response and Mitigation:

Risk	Project Impacts	Risk Response	Risk Mitigation
The use of diagnostic decision support is not taught in most medical schools, so familiarity is relatively low.	The lack of familiarity with diagnostic decision support systems and the possible subtle prejudices against such systems ingrained in the medical school curriculum are likely impediments to clinicians' acceptance.	The introduction of the system will recognize the unfamiliarity of the system and plan appropriate training sessions for all personnel, including staff and clinicians.	The system is remarkably easy to use and typically involves little effort to become proficient.
After leaving medical school, few physicians have time to produce a differential diagnosis listing even though it would almost certainly improve diagnostic accuracy.	There is virtually universal agreement that a differential diagnosis will improve almost any physician's diagnostic accuracy, so a differential automatically prepared without requiring entries by the clinician holds the prospect of acceptance if the system proves effective. However, unless the correct diagnostic alternative appears within the top ten suggestions, the alternative may well be ignored or overlooked.	The preparation of a differential diagnosis listing is largely a function of the perceived need and the time required to produce one.	The system produces a differential diagnosis listing automatically. No effort will be required by staff or clinicians for the initial encounter differential diagnosis listing.
Smooth integration into routine clinical practice without duplication of input is not assured.	All the information required for the initial inputs to Isabel Pro is already routinely collected in the admissions process. The challenge will be to capture this information and present the differential diagnosis without requiring duplicate entries. The integration process is an IT requirement overlaid on implementing the Epic EHR, a project that will almost certainly carry greater priority for IT resources.	Close coordination with IT staff and careful choice of resources familiar with the admissions process and technology should identify the key needs that will have to be addressed.	There are institutions that presently use the system or have attempted to incorporate the system. Collaboration with those institutions for lessons learned and best practices will help minimized this risk.
Most EHRs have no location to store a differential diagnosis listing even if prepared.	Incorporation of programs into Epic that Epic did not develop is notoriously difficult and prone to failure. There are a few examples of Isabel Pro incorporation into the Epic EHR (a hospital in the UK, for example), but the incorporation often requires a great deal of duplicate input, so the system is not as effective as it might otherwise be	Early assessment of Epic installations with outside systems incorporated (including Isabel Pro) will alert to necessary interventions.	There are institutions that presently use the system or have attempted to incorporate the system. Collaboration with those institutions for lessons learned and best practices will help minimized this risk.
Integration of Isabel Pro into the Epic EHR is not assured, and examples of past unsuccessful efforts abound.	The current effort in this project is to collaborate with institutions using the system (whether smoothly or not) to develop an implementation process that takes advantage of the lessons learned by those institutions. Epic is a new installation for UTPhysicians, so resource availability will depend significantly on the successful implementation of that system far enough in advance to allow work on Isabel Pro to take place.	Early assessment of Epic installations with outside systems incorporated (including Isabel Pro) will alert to necessary interventions.	There are institutions that presently use the system or have attempted to incorporate the system. Collaboration with those institutions for lessons learned and best practices will help minimized this risk.
Studies show that physicians are highly confident in their diagnostic ability and profess little impetus to seek diagnostic support.	In practice, the Isabel Pro system must be demonstrably better than the clinicians alone and should offer proof that the clinician is better with the system. The "Diagnostic Challenge" results will need to produce the proof of this concept in a fashion adequate to encourage usage.	The recently completed "Diagnostic Challenge" provided some insight into the opinions of clinicians as to the assistance provided by the diagnostic suggestions. These responses will set the priority for addressing the "over-confidence" issue.	Support from key, high-level, and highly regarded clinicians in the UTPhysicians primary care ranks will served to mitigate these risks and overcome the objections.
Physician acknowledgment of diagnostic error is often not forthcoming, and physician over-confidence is common.	The system should present as "a trusted colleague working at the clinician's elbow" to avoid the perception that the system might replace the clinician.	The recently completed "Diagnostic Challenge" provided some insight into the opinions of clinicians as to the assistance provided by the diagnostic suggestions. These responses will set the priority for addressing the "over-confidence" issue.	Support from key, high-level, and highly regarded clinicians in the UTPhysicians primary care ranks will served to acknowledge the issue of "missed diagnostic opportunities" and mitigate these risks and overcome the objections.
There are few, if any, programs to detect or prevent diagnostic error in primary practices.	The project, so far, has not found an inventory of "missed diagnostic opportunities" in the primary practices of UTPhysicians, so production of an	The issue of the frequency (and perhaps even the existence) of diagnostic error or "missed diagnostic opportunities" will be	Absent some assessment of occurrence frequency in the UTPhysicians practice, the need for and economics of the

	estimate of the benefit of Isabel Pro relies on extrapolation of "Diagnostic Challenge" conclusions.	addressed as one of the first items when contacting UTPhysicians executives.	introduction of the system may be weakened.
Often, physician acceptance of diagnostic decision support unfavorably reflects a lack of diagnostic competence.	Positioning the system as a source of the best in evidence-based medicine based on the computerized interrogation of the latest in clinical knowledge accomplishes a task even the most dedicated clinicians cannot possibly achieve given the tidal wave of new findings produced every year. The issue is not a lack of competence but a lack of time to remain current and still practice in today's demanding environments.	The responses of the participants in the "Diagnostic Challenge" will be important points of departure in recognizing the magnitude of this issue.	There is ample research to support the notion that computerized research would improve diagnosis in medicine.
A discoverable list of diagnostic alternatives considered but rejected is considered a legal liability.	At least one example exists of the successful incorporation of a diagnostic decision support system in the Epic EHR in a pediatric neurology practice abandoned due to the concerns around the differential diagnosis listing being legally discoverable.	Early discussions with plaintiff attorneys will shed light on the nature and extent of this issue.	The typical response of the plaintiff attorney to the initial consideration of filing a malpractice claim is looking for a protocol that either did not exist or was not followed.
The legal risks of incorporating diagnostic alternatives into the discoverable record may prevent acceptance.	This project's legal implications are yet to be examined and dealt with, but this aspect may well be sufficient to deny incorporation.	Early discussions with plaintiff attorneys will shed light on the nature and extent of this issue.	Does the malpractice claim originate because the ultimate condition was considered and rejected, or because the ultimate conditions was never considered?

## Risk Monitoring and Control:

Risk	Risk Monitoring	Risk Control
The use of diagnostic decision support is not taught in most medical schools, so familiarity is relatively low.	The Diagnostic Challenge has provided a guide for likely opinions and a blueprint for addressing the training needs.	The system is remarkably easy to use and typically involves little effort to become proficient.
After leaving medical school, few physicians have time to produce a differential diagnosis listing even though it would almost certainly improve diagnostic accuracy.	Once again, the Diagnostic Challenge has provided the guide for showing the improvement in accuracy with a differential. Using actual cases from the UTPhysicians practice during the integrations process may be instructive as well.	The system produces a differential diagnosis listing automatically. No effort will be required by staff or clinicians for the initial encounter differential diagnosis listing. Seeking cases for examples during the implementation process will be helpful.
Smooth integration into routine clinical practice without duplication of input is not assured.	Close coordination with IT staff and careful choice of resources familiar with the admissions process and technology should identify the key needs that will have to be addressed.	There are institutions that presently use the system or have attempted to incorporate the system. Collaboration with those institutions for lessons learned and best practices will help minimized this risk.
Most EHRs have no location to store a differential diagnosis listing even if prepared.	Early assessment of Epic installations with outside systems incorporated (including Isabel Pro) will alert to necessary interventions. Early assessment of the status of the UTHealth Epic installation will be instructive as to these risks.	There are institutions that presently use the system or have attempted to incorporate the system. Collaboration with those institutions for lessons learned and best practices will help minimize and control this risk.
Integration of Isabel Pro into the Epic EHR is not assured, and examples of past unsuccessful efforts abound.	Early assessment of Epic installations with outside systems incorporated (including Isabel Pro) will alert to necessary interventions.	There are institutions that presently use the system or have attempted to incorporate the system. Collaboration with those institutions for lessons learned and best practices will help minimized this risk.
Studies show that physicians are highly confident in their diagnostic ability and profess little impetus to seek diagnostic support.	The recently completed "Diagnostic Challenge" provided some insight into the opinions of clinicians as to the assistance provided by the diagnostic suggestions. These responses will set the priority for addressing the "over-confidence" issue. Frequent contact with UTPhysicians during the process will alert to problems.	Support from key, high-level, and highly regarded clinicians in the UTPhysicians primary care ranks will served to mitigate these risks and overcome the objections.
Physician acknowledgment of diagnostic error is often not forthcoming, and physician over-confidence is common.	The recently completed "Diagnostic Challenge" provided some insight into the opinions of clinicians as to the assistance provided by the diagnostic suggestions. These responses will set the priority for recognizing the "over-confidence" issue.	Support from key, high-level, and highly regarded clinicians in the UTPhysicians primary care ranks will served to acknowledge the issue of "missed diagnostic opportunities" and mitigate these risks and overcome the objections.
There are few, if any, programs to detect or prevent diagnostic error in primary practices.	The issue of the frequency (and perhaps even the existence) of diagnostic error or "missed diagnostic opportunities" will be addressed as one of the first items when contacting UTPhysicians executives.	Absent some assessment of occurrence frequency in the UTPhysicians practice, the need for and economics of the introduction of the system may be weakened.
Often, physician acceptance of diagnostic decision support unfavorably reflects a lack of diagnostic competence.	The responses of the participants in the "Diagnostic Challenge" will be important points of departure in recognizing the magnitude of this issue.	There is ample research to support the notion that computerized research would improve diagnosis in medicine.
A discoverable list of diagnostic alternatives considered but rejected is considered a legal liability.	Early discussions with plaintiff attorneys will shed light on the nature and extent of this issue.	The typical response of the plaintiff attorney to the initial consideration of filing a malpractice claim is looking for a protocol that either did not exist or was not followed.
The legal risks of incorporating diagnostic alternatives into the discoverable record may prevent acceptance.	Early discussions with plaintiff attorneys will shed light on the nature and extent of this issue.	Does the malpractice claim originate because the ultimate condition was considered and rejected, or because the ultimate conditions was never considered?

### **Project Procurement Management**

Project procurement management for this project is straightforward. The Isabel Pro Diagnostic Decision Support System is a commercially available product with clearly advertised prices and availability. There are institutional options noted that are not specified, so a more favorable volume-based pricing is likely in negotiations with the developer. There are integration issues that are generally outlined, such as APIs and other integration modes, so these items and the applicable pricing are also items subject to negotiation. Collaboration with other institutions presently using the system is sure to be informative and helpful on these matters. There should be no additional equipment to be purchased for this installation as the system is web-based, and the IT personnel at UTPhysicians will be necessary only to complete the incorporation of the system inputs without duplication of entries.



## Project Stakeholder Management

### Stakeholder Matrix:

#### EVALUATION OF A COMPUTERIZED DIAGNOSTIC DECISION SUPPORT SYSTEM IN PRIMARY PRACTICE – IDENTIFICATION OF STAKEHOLDERS

Tier 1 Stakeholders		
Senior Leaders and Key Decision Makers		
Ensuring project feasibility	Name of person/group	Why exactly is this person/group important?
<i>UTPhysicians Chief Operating Officer</i>	<i>Mr. Andrew Casas</i>	<i>Responsible for operations of UTPhysicians, the academic medical practice of UTHealth, key individual in approving and funding the incorporation of Isabel Pro into routine clinical practice</i>
<i>UTPhysicians Associate Dean for Healthcare Quality</i>	<i>Dr. Eric Thomas</i>	<i>Senior physician overseeing practice quality, including detection and prevention of diagnostic error, most influential physician in supporting Isabel Pro for reducing the likelihood of diagnostic error.</i>
<i>UTPhysicians Assistant Dean for Eommunity Affairs and Health Policy</i>	<i>Dr. Thomas J. Murphy</i>	<i>Senior physician overseeing primary and community care practices, oversees the primary care and community clinics, most important physician for incorporation of Isabel Pro into routine clinical practice</i>
<i>UTPhysicians Associate Vice President of Healthcare IT</i>	<i>Dr. James J. Griffiths</i>	<i>Senior IT executive for UTPhysicians, will oversee the IT resources necessary to incorporate Isabel Pro into routine clinical practice</i>
<i>UTPhysicians Chief Medical Information Officer</i>	<i>Dr. Babatope O. Fatuyi</i>	<i>Senior executive physician in charge of Epic EHR installation, most important individual in the process of integrating Isabel Pro into the UTPhysicians Epic EHR.</i>

Tier 2 Stakeholders Project Contributors		
Ensuring the quality of deliverables and activity execution:	Name of person/group	Why exactly is this person/group important?
<i>Chief Resident, McGovern Medical School</i>	<i>Dr. Jeffrey Chen</i>	<i>Oversees the 120 medical residents participating in the validation study of Isabel Pro</i>
<i>Chief Executive Officer, Isabel Healthcare, Ltd.</i>	<i>Mr. Jason Maude</i>	<i>CEO for the developer of Isabel Pro and liason to UK hospitals presently using Isabel Pro integrated in Epic EHR</i>
<i>Vice President, Isabel Healthcare. Ltd.</i>	<i>Mr. Patrick Garrett</i>	<i>VP for the developer of Isabel Pro and liason to US hospitals presently using Isabel Pro in clinical practice</i>
<i>Programmer, UTHealth IT Department</i>	<i>TBD</i>	<i>Key resource for implementation of the system</i>
<i>Senior Clinical Admissions Staff Administrator</i>	<i>TBD</i>	<i>Will be a key individual in the smooth incorporation of patient presentation information into Isabel Pro without duplication of entries.</i>
<i>Senior Clinical Admissions Nurse Administrator</i>	<i>TDB</i>	<i>Will be a key individual in the smooth incorporation of patient presentation information into Isabel Pro without duplication of entries.</i>
<i>Clinical Physican Champion</i>	<i>TBD</i>	<i>Will be a key individual in the acceptance of the system by the practicing physicians.</i>

Tier 3 Stakeholders Recipients		
Areas where people/groups may be impacted:	Name of person/group	Why exactly is this person/group important?
<i>Primary Care, Family Care and Community Clinics</i>	<i>All practicing clinicians</i>	<i>Ultimate users of the system</i>
<i>Primary Care, Family Care and Community Clinics</i>	<i>All admissions staff</i>	<i>Ultimate users of the system</i>
<i>Primary Care, Family Care and Community Clinics</i>	<i>All admissions nurses</i>	<i>Ultimate users of the system</i>

## Implementation / Deployment Strategy

Following executive suite approval of the introduction of the Isabel Pro diagnostic decision support system into the routine clinical practices of internal medicine and primary care, the Implementation and Deployment Strategy will assume a stepwise progression to assemble the implementation team, develop the specific steps necessary to incorporate the system, schedule the training of staff and physicians in the use of the system, and commence the usage of the system clinic by clinic, then follow the implementation with a program of assessing and analyzing the results of using the system.

❖ Assemble the implementation team.

- Choose a representative from the developer, Isabel Healthcare, Ltd. to provide system specific guidance on implementation, and lessons learned from other institutions using the system.
- Choose a representative from the developer, Epic Healthcare Systems, to provide specific guidance on the incorporation of the Isabel Pro system with the Epic EHR.
- Choose the IT specialists assigned to the UTPhysicians computerized systems for patient admissions, EHR coordination, and encounter presentations.
- Interview and select a senior admissions staffer overseeing the admissions process for the primary care and internal medicine practices.
- Interview and select a senior admissions nurse overseeing the patients admissions process and pre-encounter observations, and the close coordination with the clinician.

- Interview and select a clinician, highly regarded by other clinicians and interested in diagnostic decision support systems, particularly Isabel Pro.
  - Schedule a team visit to an institution presently using Isabel Pro in clinical practice to allow a “hands-on” assessment of the system in operation and answer implementation questions posed by an implementation program at UTPhysicians.
- ❖ Develop the specific implementation steps necessary for smooth incorporation into the clinical practices of UTPhysicians.
- The project implementation plan will begin with the programming necessary to capture the patient’s presentation inputs needed to produce the differential from Isabel Pro.
    - Collect all the initial admissions information necessary for Isabel Pro to produce an initial differential diagnosis list.
    - The goal will be to capture this information into Isabel Pro without any duplication of entries.
    - IT coordination with the Isabel Healthcare and Epic developer representatives will produce the specific steps required.
  - The project implementation plan will address any specific issues required of the admissions staff, including training on the availability of the system and any system presentation actions.
  - The project implementation plan will address any specific issues required of the admitting nurses, including training on the availability of the system and any

system presentation actions that may be required to present the differential as the clinician begins the encounter.

- The project implementation plan will include awareness training of the clinicians in using the differential as the encounter commences.
  - The project implementation plan will include a “beta test site clinic” for initial go-live testing of the system in practice and correction of any issues that do not go smoothly.
  - The project implementation plan will include a training and introduction program, and a schedule for introducing the system to each clinic sequentially.
  - The project implementation plan will provide for weekly team meetings to report on progress, assess the timetable, report on tasks accomplished and problems encountered, address problems and work out solutions, review the remaining steps and confirm the project timetable.
- ❖ Commence work on the implementation plan, schedule the weekly review meetings, address problems as they occur, jointly determine solutions, and adjust the schedule as needed.
- ❖ Begin training session at the “beta test clinic” as soon as the system development will allow, determine the usability, define problems, and address solutions, smooth the process for wider introduction.
- ❖ Develop a schedule for introduction and training at each clinic, continue to assess issues specific to each clinic and overall issues.

- ❖ Follow up with clinics to assess the use of the system, discover problems or other issues that discourage use.
- ❖ Address the issue of reducing “missed diagnostic opportunities” – how to discover them, did the system help address them, what are the results of having the system available, do the clinicians use the differential to improve their diagnostic accuracy?

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## Appendix C: Return on Investment

In the absence of definitive statistics on historical diagnostic errors, a return on investment may not be subject to numerical determination. Still, pre-implementation and follow-on surveys of clinician usage and clinician opinions on the usefulness of the diagnostic differentials and the enhancement of their diagnostic process when using the system will assess the system's effect on patient health and safety.

The issue with a return on investment for improving diagnostic accuracy is valuing the patient not seen a second or third time for failing to respond to treatment. Where does the benefit accrue, and where is the investment made?

The payor benefits: the insurance company or self-insured employer need not pay for an unnecessary encounter.

The patient benefits: from reduced co-pays and restored good health earlier than otherwise.

For the provider, though, there is an encounter eliminated and a loss of revenue from the unnecessary encounter. With most practitioners having a backlog of patients, however, the next patient is merely seen sooner than expected, and recognition of the lost revenue occurs at the end of the patient backlog, which for an active practice probably means retirement. The present value of the lost encounter is then de minimis. Better outcomes may make the clinician a provider of choice as healthcare moves to a pay-for-performance scheme rather than a fee-for-service system.

In response to the concerns often expressed about multiple diagnostic alternatives raising the cost of care, several studies address and refute this concern. Two, in particular, are representative. A 2010 study of decision support in actual hospital use noted: "It may seem

paradoxical that evaluating a patient with several diagnoses in mind may be cheaper than doing so with only one until considering how expensive it is to have a single but incorrect diagnosis.”

(Elkin et al., 2010). A 2014 study of a pediatric neurological decision support system noted:

“Using the software, there was a significant reduction in error, up to 75% for diagnosis and 56% for workup....There was a 6% decrease in the number of workup items accompanied by a 34% increase in relevance. The authors conclude that decision support for a neurological diagnosis can reduce errors and save on unnecessary testing.” (Segal et al., 2014).

## Appendix D: Quality Improvement Project Charter

**Project Title:** Validate a Diagnostic Decision Support System

**Project Leader:** Joe M. Bridges

**Key Personnel:** Carmel B. Dyer MD, Holly Holmes MD, Haris Kamal, MD

**Performance Sites:** UTPhysicians, McGovern School of Medicine

**Project Duration:** One Year

### General Information

#### **Quality Improvement Project:**

Submitted by Joe M. Bridges, Doctorate of Health Informatics Candidate, School of Biomedical Informatics

#### **Validate a Diagnostic Decision Support System**

- **Theme**
  - Diagnostic error, or rather its prevention, is the theme of this Project.
- **Goal**
  - Validate a diagnostic decision support system, specifically “Isabel”, developed and commercially offered by Isabel Healthcare.
- **Requirement**
  - Physician acceptance of any diagnostic decision support system is critically dependent on proof that the system will provide prompt and valid diagnostic assistance in actual practice.
- **How**
  - Secure approximately thirty (30) complex diagnostic cases for which the ultimate diagnosis is known, selected by three participating UTPhysicians, from the actual practices of UTPhysicians and use those cases to validate the caliber of the initial diagnostic suggestions offered by the system.
- **What**
  - The system to be tested will be the “Isabel” system designed and supported by Isabel Healthcare.
- **Data Inputs**
  - Age Range,
  - Gender at Birth (M or F)
  - Recent travel history by continent (North America, etc)
  - Abnormal clinical features (free text or drop-down selection, negatives)

- **What Next**
  - If validation proves successful, then extend the validation process to additional segments of the UTPhysicians practice.

### **Problem Statement**

The frequency of diagnostic error in today's medical practice is widely acknowledged as a problem of significant size. Estimates of diagnostic error from various studies vary widely, but none are zero. The Institute of Medicine in 2015 reported the results of their 2015 study entitled *Improving Diagnosis in Healthcare*, in which they stated:

“the best estimates indicate that *all of us will likely experience a meaningful diagnostic error in our lifetime.*”

### **Rationale**

There have been a variety of diagnostic decision support systems designed and used to a greater or lesser extent over the years, but none with wide acceptance to date. All of these systems depend to a great extent on rapid and easy access to well-researched evidence-based best practices, no small task given the virtual avalanche of new medical research produced each year. Isabel appears to excel at this retrieval and curation process.

### **Objectives or Goals**

Validate the diagnostic decision support system in augmenting the physician's early diagnostic process. Physician acceptance of any diagnostic decision support system is critically dependent on proof that the system will provide prompt and valid diagnostic assistance in actual practice.

### **Project Design**

The plan is to secure approximately thirty (30) complex diagnostic cases, selected by three participating UTPhysicians themselves, from the actual practices of UTPhysicians and use those cases to determine whether the ultimate diagnosis would have been among the diagnostic alternatives presented by Isabel at the initial encounter.

### **Population**

Complex diagnostic dilemmas chosen by the physicians and for which the ultimate diagnosis is known.

### **Procedures**

Employ the commercially available diagnostic decision support system “Isabel” to provide diagnostic alternatives from each case using the following data inputs.

#### Data Inputs

- Age Range,
- Gender at Birth (M or F)
- Recent travel history by continent (North America, etc)
- Abnormal clinical features (free text or drop-down selection, negatives)

### **Risks and Benefits**

No risks, benefits are accurate diagnoses made more quickly and possible elimination of unnecessary diagnostic tests

**Data Confidentiality**

No personally identifiable information involved in the project

**Statistics**

Case by case assessment of validity of diagnostic prompts provided by the system

**Ethics**

No ethical issues anticipated

**Post Project Plan**

If validation proves successful, then extension of the validation process to cases from other segments of the UTPhysicians practice.

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**ATTACHMENTS (when applicable)**

1. Schematic of Project Design: N/A
2. Consent Document: N/A
3. Data Collection Forms: (from Isabel Pro Diagnostic Decision Support System)
  - **Clinical features**
  - [Age of the patient \\*](#)
  - 
  - Patient's gender at birth
  - FemaleMale
  - Patient's travel history
  - 
  - Enter abnormal clinical features in free text **OR** select from list. **NO** negatives:
    - 
    - [Get Checklist](#) [Clear](#)
    -
4. Surveys and Questionnaires: N/A

## Appendix E: Quality Improvement Project Approval Letter



Office of the Executive Vice President  
for Academic and Research Affairs  
*Committee for the Protection of Human Subjects*

Date: November 12, 2019

Project Leader: Joe Bridges  
School of Biomedical Informatics

Project Title: Validate a Diagnostic Decision Support System

Submission: 2019-489

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Dear Mr. Bridges,

Thank you for registering the above project in the UTHealth Quality Improvement Project Registry. The submission does not meet the regulatory definition of human subjects research and therefore does not need to be submitted to the UTHealth Committee for Protection of Human Subjects (CPHS) for review and approval.

Please submit a follow-up report of this project's progress by **November 12, 2020** in the [UTHealth QI Registry](#).

Please remember that QI findings may be published, but should not be represented or reported as research.

If you have any questions, please contact me at (713) 500-7939 or via email at [Laura.K.Lincoln@uth.tmc.edu](mailto:Laura.K.Lincoln@uth.tmc.edu).

cc: K. Masters  
A. Sarraj

**Appendix F: BMI 6002: Directed Studies, Final Paper, May 1, 2020**

The University of Texas Health Science Center

School of Biomedical Informatics

Submitted in Partial Fulfillment of the Requirements

For

BMI 6002: Directed Studies

Dr. Robert E. Murphy, Associate Professor

Joe M. Bridges, Student, Doctorate of Health Informatics Program

Final Paper

May 1, 2020

### Abstract

Diagnostic error is a topic deserving of further research effort despite considerable discussion in recent years. The goal of this study is to evaluate the performance of a diagnostic decision support system, Isabel Pro, using only those signs, symptoms, and medical history elements known at the initial patient encounter with the physician. A total of ten cases from UTPhysicians and McGovern Medical School patients comprise the suite of cases used in the evaluation. The author entered the signs and symptoms from the cases into the Isabel Pro Differential Diagnosis System, then cataloged the resulting presentation of diagnostic alternatives and compared the results to the actual diagnoses from the cases. The first issue is diagnostic retrieval accuracy, and out of the ten cases, five scored as having returned the case diagnosis. The ranking of the diagnoses is another essential aspect of the usefulness of a diagnostic decision support system. Three cases in the study rank the case diagnosis within the top ten alternatives presented. In two of the cases, the case diagnosis appeared at 14 and 30, respectively. In only one of the cases did the case diagnosis fail to appear in the interrogated literature at all. Ten cases are only a beginning, and the selection bias in these cases is not likely reflective of routine clinical practice. The next phase of this project will be to widen the number of cases evaluated, perhaps employing some form of a computerized search of case records. If achievable, a computerized search would eliminate the imposition on the physicians to select, de-identify, and produce the cases, as well as significantly increase the number of cases available for study.

The author declares no conflicts in the production of this report and no support, financial or otherwise, from Isabel Healthcare, Ltd.



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**Final Paper**  
**BMI6002 Directed Study**  
**Spring Semester 2020**

**Introduction**

Diagnostic error is not a new topic but remains a topic deserving of additional research effort despite considerable discussion in recent years. The goal of this study is to evaluate the performance of a diagnostic decision support system, Isabel Pro, using only those signs, symptoms, and medical history elements known at the initial patient encounter with the physician.

In 2015, the Institute of Medicine produced a 495-page report by its Committee on Diagnostic Error in Health Care entitled “Improving Diagnosis in Health Care,” with the opening comment “The delivery of health care has proceeded for decades with a blind spot: Diagnostic errors...” (Balogh et al., 2015). The report continues with the following conclusion: “the best estimates indicate that all of us will likely experience a meaningful diagnostic error in our lifetime.” (Balogh et al., 2015).

An obvious question might be, just what constitutes a diagnostic error? Several proposed definitions have been used over the years in a variety of study and research contexts. In 2005, Graber and his colleagues used a definition from Australia for their study on diagnostic error in internal medicine:

“Based on a classification used by the Australian Patient Safety Foundation, we defined diagnostic error operationally as a diagnosis that was unintentionally delayed (sufficient information was available earlier), wrong (another diagnosis was made before the correct one), or missed (no diagnosis was ever made), as

judged from the eventual appreciation of more definitive information.” (Graber et al., 2005)

This particular definition is useful, but other forms of diagnostic error involve cognitive errors on the part of the diagnostician – premature closure, for example, or simply being unaware of the existence of a particular diagnostic alternative or the complexities of the presenting symptoms. In their study of the frequency of diagnostic errors, Singh and his co-authors focused on the “missed opportunity” inherent in diagnostic error. In their study, they defined diagnostic errors as follows:

“... diagnostic errors were...defined as missed opportunities to make a timely or correct diagnosis based on available evidence.” (Singh et al., 2014)

The Institute of Medicine’s report considered a wide range of definitions in the course of its study and resolved on what they refer to as a patient-centered definition, recognizing that the patient suffers whatever harm results from the diagnostic error. Their definition is stated as:

“The committee’s patient-centered definition of diagnostic error is: the failure to (a) establish an accurate and timely explanation of the patient’s health problem(s) or (b) communicate that explanation to the patient.” (Balogh et al., 2015)

Another question might be what is the prevalence of diagnostic error. Although complicated by the variety of definitions of diagnostic error, several studies have nevertheless made rigorous efforts to establish just how widespread is the problem of diagnostic error and whether these errors are truly harmful to the patient. In a study to determine the frequency of diagnostic error in outpatient care, Singh and his co-authors made estimates using three large observational studies. As to the prevalence of diagnostic error, the authors made the following conclusion:

“Combining estimates from the three studies yields a rate of outpatient diagnostic errors of 5.08%, or approximately 12 million US adults every year. Based on our previous work, we estimated that about one-half of errors would have the potential to lead to severe harm.” (Singh et al., 2014).

In a more recent study by Matthews et al., designed to offer methods for an organization to identify and make improvements in safety from structured internal analysis of their cases, they noted a similar conclusion as to the prevalence of diagnostic error.

“Diagnostic errors are common and dangerous, affecting 5% of United States adult outpatients per year and accounting for 6–17% of hospital adverse events. Over the past decade, there has been an increasing amount of attention paid to these errors.” (Mathews et al., 2020)

Despite the increasing awareness of diagnostic error, one still might question why diagnostic errors remain prevalent. After all, diagnosis is an essential component of medical school training, and physicians engage in diagnosis virtually continuously during their daily patient encounters. Nevertheless, consider this; medical diagnosis is one of the most, if not the most, difficult tasks performed by humans. A relatively small set of signs and symptoms are common to a great many diseases. In a study devoted to analyzing progress in diagnostic improvements, Olson et al., observed:

“Often, a broad array of cognitive and systems-related contributing factors interact in complex ways to make the diagnostic process risk prone. Diagnostic errors include overlapping situations of missed, delayed, and/or incorrect diagnoses, and these three concepts often become hard to disentangle.” (Olson et al., 2018)



In an article published in 2018 in *Health Affairs*, Dr. David Bates and Dr. Hardeep Singh reflected on the two decades that had passed since the publication of the watershed treatise *To Err is Human*, in which they commented on the difficulty of the diagnostic process:

“Errors involve common diseases or conditions, not just infrequent or rare ones, and often result from breakdowns in data gathering and interpretation of patient history and exam or in follow-up of abnormal diagnostic tests.” (Bates & Singh, 2018)

Patients, especially the older ones, rarely have a single presenting condition, with these co-morbidities adding to the complexity of diagnosis exponentially. Couple this with the blistering pace of new research produced every day, much of which disproves, or at least brings into question, earlier research, and the difficulty facing the diagnostician is that remaining abreast of developments in medicine is virtually impossible, even in a narrow specialty.

The need to remain abreast of current developments in evidence-based medicine is where diagnostic decision support systems offer a window of opportunity for accomplishing this important task. Today’s systems use the latest in search technology to interrogate highly-scientific clinical literature sources that are continuously updated to produce diagnostic alternatives that are current and clinically relevant. In a previous study (Bridges, 2020), the author examined

“six studies, each of which, in one way or another, compared the differential diagnosis workup done by a group of physicians without diagnostic decision support, followed by a revised workup after the physicians consulted the support system. Evaluations centered on the improvement of each physician’s differential diagnosis (or lack of improvement) before and after consultation. Cases evaluated

were carefully prepared in advance by experts with the expert's diagnosis acting as the gold standard for the correct diagnosis. In general, the studies showed an improvement in physician diagnostic accuracy with system assistance, especially so in the case of less experienced physicians. The studies also noted that any clinical case likely to challenge an experienced physician would also likely challenge the system.” (Bridges, 2020)

The six studies analyzed evaluate the improvement in diagnostic outcome when a diagnostic decision support system is employed at the outset of the diagnostic process. Today, while writing this report, there are at least three studies funded by the Agency for Healthcare Research and Quality under the Patient Safety Learning Laboratory grant program, each of which focuses explicitly on diagnostic error detection and avoidance. These studies are significant, well-conceived, and conducted by experienced and capable investigators. These and many other studies of diagnostic error are focused on detection, followed by prevention or correction.

This study evaluated the performance of a diagnostic decision support system, Isabel Pro, using only those signs, symptoms, and medical history elements known at the outset of the patient encounter. This paper describes an initial phase using cases from UTPhysicians and McGovern Medical School patients to evaluate the diagnostic retrieval accuracy of Isabel Pro. Isabel Pro is a web-based differential diagnosis tool designed by Isabel Healthcare, Ltd., a company with head offices in Haslemere, United Kingdom, and Ann Arbor, Michigan.

Isabel Healthcare began in 1999 with the illness of founder Jason Maude's three-year-old daughter. She developed Chicken-Pox, which further progressed into undiagnosed Necrotizing Fasciitis and Toxic Shock Syndrome, conditions that proved nearly fatal. Despite the missed

diagnosis, after a month in pediatric intensive care and another month in the hospital, she survived. In an excerpt from the firm's website, the story of Isabel Healthcare is described thus:

“But her suffering could have been avoided had just one of the many doctors asked, “What else could this be?”. Her Chickenpox led her doctors to miss the clear signs of a secondary infection until it was too late.

The idea for a tool to aid clinical reasoning came to Isabel's parents, Jason and Charlotte Maude when, weeks after Isabel's discharge, they visited the hospital responsible for her misdiagnosis. They were told ‘clinical ignorance’ was to blame. If the junior doctors who saw Isabel were lacking the knowledge and experience that Necrotizing Fasciitis was a well-documented complication of Chickenpox, then perhaps technology could give them a helping hand?

Rather than take legal action, Jason Maude then devoted his career to establishing an organization and team to design and build a practical, easy-to-use tool to help clinicians match clinical features to diseases.”

(<https://www.isabelhealthcare.com/about-isabel-healthcare/isabel-story>)

Isabel Pro is built around the search of scientific literature rather than interrogating patient databases. While Artificial Intelligence is promising in seeking clinical insights from patient databases, the simple truth at this point is that there is no patient dataset addressable by any computerized technique that is sufficiently broad and free of bias to permit reliable patient treatment recommendations. A particularly salient comment comes from an article in HealthIT Analytics:

“EHRs are a goldmine of patient data, but extracting and analyzing that wealth of information in an accurate, timely, and reliable manner has been a continual

challenge for providers and developers. Data quality and integrity issues . . . , plus a mishmash of data formats, structured and unstructured inputs, and incomplete records have made it very difficult to understand exactly how to engage in meaningful risk stratification, predictive analytics, and clinical decision support” (Bresnick, J. 2018, April 30).

Isabel Healthcare, Ltd. chooses to perform a search of highly-scientific and rigorously maintained literature sources using the entered signs and symptoms to match diagnoses to those terms. Along with the ranked diagnoses presented, Isabel Pro also presents a listing of the terms matched and the percentage match to the literature. This percentage is not the clinical probability of the diagnosis but is the frequency with which the listed terms and the diagnosis appear together in the literature, as found by the Isabel Pro’s proprietary search algorithm. As noted in the Frequently Asked Questions section of the Isabel Healthcare website:

“Isabel produces a list of relevant diseases, ranked in order of the degree of match between the disease presentations and clinical features, together with age, gender and region, entered by the user. Clinicians can review the Isabel list and access associated evidence-based content to work out which diseases they think are most probable for their patient. Isabel is there to support and assist the clinician in determining the differential and management plan. Isabel is about possibilities while clinical probability is determined by the clinician.”

(<https://www.isabelhealthcare.com/isabel-faqs>)

### **Methodology**

The author applied for and received approval to conduct a Quality Improvement Project from the University of Texas Health Science Center at Houston’s Committee for the Protection

of Human Subjects. Appendix 1 of this report is a copy of the approval request. Receipt of approval for the project occurred on November 12, 2019, included herein as Appendix 2. The original plan was to seek ten cases each from three practicing doctors at UT Physicians referred to as “diagnostic dilemmas,” that is cases from which the ultimate diagnosis was subsequently confirmed, but was not among the diagnoses considered at the outset of the encounter. This case selection and de-identification process proved to be an unreasonable burden on the physicians, who were able to furnish only two such cases. A subsequent request made to the Chief Resident at the McGovern Medical School yielded eight additional cases presented at weekly resident conferences during the medical school curriculum. With those ten cases, the author entered the signs and symptoms from the cases into the Isabel Pro Differential Diagnosis System, cataloged the resulting presentation of diagnostic alternatives, and matched the results to the actual diagnoses that accompanied the cases. The ultimate diagnosis was unknown to the author until after the Isabel Pro presentation. The author entered all signs, symptoms, medical history, and medication lists exactly as presented in the cases. The catalog of data entry items and resulting diagnostic alternatives are attached to this report as Exhibits 1 through 10.

## **Results**

Table 1 presents the results of the analysis. In each case, there was no limit placed on the number of diagnostic alternatives returned by the Isabel Pro system, but for this report, only the top ten are listed in the Exhibits. The validation criteria are those outcomes described in the work of Riches, et al. (2016), an article reviewed in the author’s paper entitled “Validation Methodologies for Diagnostic Decision Support Systems” submitted in BMI6328 (Bridges, April 2020). Of course, diagnostic retrieval accuracy is the highly desired outcome (the presented diagnosis matches exactly the case diagnosis), followed closely by the ranking of the diagnosis

(the higher the ranking, the better in general terms and the more likely to be seriously considered by the diagnostician). The system also returns the entry terms matched in the literature search and the percentage match of those terms as described above. In the cases failing to return a diagnosis match, the author performed a further check to determine whether the case diagnosis even appeared at all in the literature searched by the system by entering the case diagnosis and noting whether the system presented the case diagnosis. The case diagnosis was in the literature in all cases except for one.

Table 1

Case	Ultimate Diagnosis	Isabel Pro Diagnosis	Did IsabelPro Display Correct Diagnosis	IsabelPro Ranking	Degree of Literature Match	Diagnosis in Literature
CBD001	Polymyalgia Rheumatica	Polymyalgia Rheumatica	Y	3	98%	Y
KH001	Diabetes	Diabetic Neuropathy	Y	7	54%	Y
McGMS Case 1	Emphysematous Pyelonephritis, Clinically indistinguishable from severe, acute pyelonephritis	Pyelonephritis	Y	2	73%	Y
McGMS Case 2	Warm Autoimmune Hemolytic Anemia	N/A	N	N/A	N/A	Y
McGMS Case 3	Colorectal Cancer	N/A	N	N/A	N/A	Y
McGMS Case 4	Pseudohypoparathyroidism	N/A	N	N/A	N/A	Y
McGMS Case 5	PRES [Posterior Reversible Encephalopathy Syndrome] 2/2 to Exchange Transfusion	N/A	N	N/A	N/A	N
McGMS Case 6	Tubulointerstitial nephritis and uveitis (TINU syndrome) AKA Dobrin syndrome	N/A	N	N/A	N/A	Y
McGMS 20200306 Cards Case Conference - Final	lupus myocarditis	Myocarditis	Y	14	36%	Y
McGMS 20200306 Case Conference Pulmonary 3_6 - Final	Acute necrotizing pancreatitis complicated by recurrent left exudative pleural effusion	Pancreatitis	Y	30	41%	Y

In reviewing these results, the first issue is diagnostic retrieval accuracy, and out of the ten cases, five scored as having returned the case diagnosis. Two of the cases were unquestionably correct, Case CBD001 and McGMS Case 1. Case KH001 scored in Table 1 as having returned the correct diagnosis, but only because one does not have diabetic neuropathy without having diabetes. The last two cases in Table 1 scored as having returned the correct diagnosis, but a valid question arises in the descriptors around the base diagnosis. For example, is myocarditis an adequate representation of lupus myocarditis? In this case, systemic lupus erythematosus (SLE) was one of the presenting conditions. Since myocarditis in SLE is

uncommon, the appearance of myocarditis as a diagnostic suggestion is likely helpful. Another example, is pancreatitis an adequate representation of acute necrotizing pancreatitis? According to a study on the treatment of necrotizing pancreatitis,

“Acute pancreatitis (AP) is the twelfth most common gastrointestinal presentation to the emergency department (ED) in the United States.... Acute necrotizing pancreatitis accounts for 10% of acute pancreatitis (AP) cases and is associated with a higher mortality and morbidity.” (Boumitri et al., 2017).

So, presenting the diagnosis of pancreatitis, in this case, would likely lead the physician to the ultimate precise diagnosis and subsequent treatment in this case.

The ranking of the diagnoses is another essential aspect of the usefulness of a diagnostic decision support system. In considering the five cases scored as having produced the correct diagnosis among the presented alternatives, it is encouraging that three cases in Table 1 rank the diagnosis within the top ten alternatives presented, in two of the cases within the top three and with each of the three cases showing a literature match exceeding 50%. Two of the cases, however, present a long list of diagnostic alternatives, with the case diagnosis showing rankings of 14 and 30, respectively. While difficult diagnoses are not necessarily highly ranked, the appearance of a diagnostic alternative near the bottom of a lengthy list will no doubt make consideration of the diagnosis unlikely.

As shown in Table 1, five of the cases failed to return the case diagnosis, even though the case diagnosis was in the interrogated literature for four of the cases. The author plans additional study on this point, possibly by taking the case diagnosis and working backward to the initial signs and symptoms which would have corresponded, but were missing from the data entry. Since one does not choose the presenting signs and symptoms, this line of inquiry may or may



not be revealing for future use. As mentioned earlier, in only one of the cases did the case diagnosis fail to appear at all in the interrogated literature. This issue typically occurs in those systems requiring routine manual curation of the diagnosis databases. The author plans more investigation into this matter in a later report as this was a surprising outcome given the scientific breadth of the literature databases accessed by Isabel Pro and the fact they are in a state of continuous, rigorous update.

### **Conclusions**

This study evaluated the Isabel Pro Differential Diagnosis Generator system using cases from the local practices of UT Physicians and Memorial-Hermann Healthcare to assess the performance of the system in diagnostic retrieval accuracy, diagnostic alternative ranking and percentage match of entered signs and symptoms to the interrogated literature. This study seeks to validate the performance of the system by using only those signs, symptoms, and conditions known at the outset of the encounter. Of the ten cases evaluated, five returned a correct diagnosis. Previous studies of the Isabel Pro system noted in the author's earlier report (Bridges, April 2020) showed much higher incidences of diagnostic retrieval accuracy (Graber & Mathew, 2008) (Bavdekar & Pawar, 2005). Ten cases are only a beginning, and the selection bias in these cases is not likely reflective of routine clinical practice. As so often observed in research articles, more study is needed. Nevertheless, diagnostic error is prevalent and begs of attention. In support of the idea that healthcare might find decision support useful, consider the British Medical Journal article which noted:

“One of the primary tasks of the GP is the diagnosis of patients presenting with new symptoms. This is the bedrock on which patient care is founded, particularly in health systems such as the UK NHS, where the GP acts as a ‘gatekeeper’ to

specialist services. Diagnostic error has been defined as *‘a missed opportunity to make a timely or correct diagnosis based on the available evidence*. Over half of litigation claims against GPs are for failure to diagnose. Significant delays have been reported in the diagnosis of common cancers and in conditions such as coeliac disease. Increasing use of standard pathways of care to improve speed of diagnosis, particularly in cancer, means that making a correct initial assessment of the patient is even more important. When we factor in the increasing demands on GPs’ time and workload due to, for example, increasing multimorbidity in older patients, and the multitude of common ‘alternative’ explanations for symptoms, it is clear that we need as much support as possible from technology to provide good-quality and safe patient care.” (Delaney & Kostopoulou, 2017).

In this effort, the next phase of this project will be to widen the number of cases evaluated, perhaps employing some form of a computerized search of case records. If achievable, a computerized search would eliminate the imposition on the physicians to select, de-identify, and produce the cases, as well as significantly increase the number of cases available for study. There might be other avenues to pursue regarding additional cases for evaluation, such as access to the cases from previous research efforts that might be suitable for evaluation using the presenting signs and symptoms in those cases. The selection process will be all-important to assure retrieval of cases that show a definitively confirmed ultimate diagnosis, preferably one that was not among the initial diagnostic considerations

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## Appendix G Form of Diagnostic Challenge

## Diagnostic Challenge Registration Page

Response was added on 11/18/2020 12:37pm.

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Date: 11-18-2020

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Diagnostician Name: (Last, First Middle) Bridges, Joe Mack

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Email Address: joe.bridges@uth.tmc.edu

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Thank you for agreeing to participate in the Diagnostic Challenge.

As you progress through the challenge, you will first be presented with six cases in sequence and be asked to create your own differential diagnosis for each case. The Patient Presentation Summary is the information that would be available at the outset of the physician-patient encounter. Your differential may be as many or as few as you think appropriate up to twenty diagnoses. You will then be presented with the same six cases in the same sequence, but with a list of diagnostic suggestions produced by a commercially available differential diagnosis generator. Your initial differentials will be listed, and you will have the opportunity to replace each of them if you choose. As you complete each case, click on the "Submit" box at the bottom of the page to move to the next case. Following the cases is a short questionnaire seeking your opinion on the diagnostic suggestions. Footnote: The cases may not be downloaded or otherwise retained, including screen shots. We appreciate your understanding and compliance with this request.

## Case 11-36052

Response was added on 11/18/2020 12:39pm.

### Patient Presentation Summary

**Chief Complaints:** This patient is a 60-year-old white male who presented with a three-week history of crampy lower abdominal pain and severe anemia.

**History of Present Illness:** He was in his usual state of health until 2-3 weeks prior to admission when he developed crampy lower abdominal pain which was intermittent and bilateral and not clearly related to eating, bowel movements or position. On the day prior to admission, the pain worsened. He was awakened the morning of admission with pain which increased throughout the day. He presented to an urgent care facility where his hematocrit was found to be 19.3. He denied bright red blood per rectum or melena. He has had increased fatigue and denied any other symptoms, such as vomiting, hematemesis, hematuria, change in urine color, or change in bowel habits or stool. His appetite has been normal. He believed he had lost some weight but could not quantify the amount.

**Past Medical History** was significant for coronary artery disease, S/P bypass grafting, asthma, and eczema. Medications included only acetaminophen. He denied medication allergies.

**Social/Family History:** He was a technical illustrator who has 3-4 beers each week. Family history was unremarkable.

**Physical Examination** revealed a pale man. He was febrile and his pulse was 78, with a respiratory rate of 18 and a blood pressure of 132/68.

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Case 11-36052 Differential Diagnosis #1:	111
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Case 11-36052 Differential Diagnosis #2:	112
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Case 11-36052 Differential Diagnosis #3:	113
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Case 11-36052 Differential Diagnosis #4:	114
Case 11-36052 Differential Diagnosis #5:	115
Case 11-36052 Differential Diagnosis #6:	116
Case 11-36052 Differential Diagnosis #7:	117
Case 11-36052 Differential Diagnosis #8:	118
Case 11-36052 Differential Diagnosis #9:	119
Case 11-36052 Differential Diagnosis #10:	1110
Case 11-36052 Differential Diagnosis #11:	1111
Case 11-36052 Differential Diagnosis #12:	1112
Case 11-36052 Differential Diagnosis #13:	1113
Case 11-36052 Differential Diagnosis #14:	1114
Case 11-36052 Differential Diagnosis #15:	1115
Case 11-36052 Differential Diagnosis #16:	1116
Case 11-36052 Differential Diagnosis #17:	1117
Case 11-36052 Differential Diagnosis #18:	1118
Case 11-36052 Differential Diagnosis #19:	1119
Case 11-36052 Differential Diagnosis #20:	1120

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## Case 12-36291

Response was added on 11/18/2020 12:40pm.

### Patient Presentation Summary

**Chief Complaint:** This 61-year-old white male presented with weight loss and fatigue.

**History of Present Illness:** The patient was in his usual state of health until 3 months prior to admission, when he experienced weakness and fatigue. He complained of being continually tired, spent most of his days at home, and required daily naps. His appetite decreased, and he lost 25 pounds. He experienced diffuse abdominal fullness, without relation to meals. He also experienced frequent arthralgias, and pain in his lower back. He denied fevers, sweats, or chills.

**Past Medical History:** He had a history of hypertension. He also had a history of atrial fibrillation. He had bilateral herniorrhaphies 20 years prior to admission.

**Medications:** Hydrochlorothiazide,

Digoxin, Motrin. **Allergies:** none

known.

**Family History:** No known familial diseases.

**Social History:** The patient is Jewish, of Eastern European extraction. He has smoked 1 ½ packs of cigarettes per day for 40 years. He rarely drinks alcohol.

**Physical Examination:** Thin white male in no acute distress. BP 130/70; pulse 88, irregularly irregular; respirations 16; temperature 98.6oF.

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Case 12-36291 Differential Diagnosis #1:	121
Case 12-36291 Differential Diagnosis #2:	122
Case 12-36291 Differential Diagnosis #3:	123
Case 12-36291 Differential Diagnosis #4:	124
Case 12-36291 Differential Diagnosis #5:	125
Case 12-36291 Differential Diagnosis #6:	126
Case 12-36291 Differential Diagnosis #7:	127
Case 12-36291 Differential Diagnosis #8:	128
Case 12-36291 Differential Diagnosis #9:	129
Case 12-36291 Differential Diagnosis #10:	1210
Case 12-36291 Differential Diagnosis #11:	1211
Case 12-36291 Differential Diagnosis #12:	1212
Case 12-36291 Differential Diagnosis #13:	1213
Case 12-36291 Differential Diagnosis #14:	1214
Case 12-36291 Differential Diagnosis #15:	1215
Case 12-36291 Differential Diagnosis #16:	1216
Case 12-36291 Differential Diagnosis #17:	1217
Case 12-36291 Differential Diagnosis #18:	1218
Case 12-36291 Differential Diagnosis #19:	1219
Case 12-36291 Differential Diagnosis #20:	1220

## Case 13-36043

Response was added on 11/18/2020 12:41pm.

### Patient Presentation Summary

**Chief Complaint:** This 23-year-old Hispanic male migrant worker from Mexico presented with right upper quadrant pain.

**History of Present Illness:** He was admitted to an outside hospital with a two-week history of right upper quadrant abdominal pain. He described his pain as steady and stabbing, worsening with respiration. He had nausea but no diarrhea or constipation. He denied fever. There was no history of hematemesis, hematochezia, or melena. He had no previous episodes of right upper quadrant pain. There was no history of trauma. He had lived in this country for six years, but had traveled in and out of Mexico in the past year including a recent trip three months prior to admission. He admitted to working with animals and drinking water from streams. At the outside hospital he had an abdominal CT scan that showed two cystic lesions in the liver; one 4 cm in diameter located posteriorly in the right lobe adjacent to the diaphragm, the other a 1 cm lesion located anteriorly in the right lobe. His white count was  $14.9 \times 10^9/L$ . The patient transferred to this hospital for further evaluation.

**Past Medical History:** He denied past surgery or medical illness. There had been no previous hospitalization. He had no allergies.

**Physical Examination:** He appeared as a thin, healthy looking man in no distress. The temperature was 98.6 o F (37oC), pulse 76, blood pressure 102/70.

Case 13-36043 Differential Diagnosis #1:	131
Case 13-36043 Differential Diagnosis #2:	132
Case 13-36043 Differential Diagnosis #3:	133
Case 13-36043 Differential Diagnosis #4:	134
Case 13-36043 Differential Diagnosis #5:	135

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Case 13-36043 Differential Diagnosis #6:	136
Case 13-36043 Differential Diagnosis #7:	137
Case 13-36043 Differential Diagnosis #8:	138
Case 13-36043 Differential Diagnosis #9:	139
Case 13-36043 Differential Diagnosis #10:	1310
Case 13-36043 Differential Diagnosis #11:	1311
Case 13-36043 Differential Diagnosis #12:	1312
Case 13-36043 Differential Diagnosis #13:	1313
Case 13-36043 Differential Diagnosis #14:	1314
Case 13-36043 Differential Diagnosis #15:	1315
Case 13-36043 Differential Diagnosis #16:	1316
Case 13-36043 Differential Diagnosis #17:	1317
Case 13-36043 Differential Diagnosis #18:	1318
Case 13-36043 Differential Diagnosis #19:	1319
Case 13-36043 Differential Diagnosis #20:	1320

**Case 14-36011**

Response was added on 11/18/2020 12:43pm.

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Patient Presentation Summary

Chief Complaint: This 53-year-old black male presented with a leg ulcer.

History of Present Illness: The patient developed an ulcer on the right lower leg approximately 1 year prior to admission. The ulcer slowly increased in size, but appeared to worsen over the last 6 months. The ulcer was painless, and exuded foul-smelling pus which would harden and subsequently fall off. The patient also developed a dry hacking cough 6 months prior to admission, and lost approximately 15 lbs. He denied fevers, chills, night sweats, hemoptysis, or shortness of breath.

Past Medical History: Hypertension for several years. No history of diabetes mellitus. Medications: none.

Allergies: none known.

Family History: Noncontributory.

Social History: He has smoked 1 pack of cigarettes per day for 25 years. He drinks alcohol occasionally. He does not use illicit drugs.

Physical Examination: Thin black male in no acute distress. BP 120/80; pulse 80; respirations 18; temperature 98.6oF.

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Case 14-36011 Differential Diagnosis #1:	141
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Case 14-36011 Differential Diagnosis #2:	142
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Case 14-36011 Differential Diagnosis #3:	143
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Case 14-36011 Differential Diagnosis #4:	144
Case 14-36011 Differential Diagnosis #5:	145
Case 14-36011 Differential Diagnosis #6:	146
Case 14-36011 Differential Diagnosis #7:	147
Case 14-36011 Differential Diagnosis #8:	148
Case 14-36011 Differential Diagnosis #9:	149
Case 14-36011 Differential Diagnosis #10:	1410
Case 14-36011 Differential Diagnosis #11:	1411
Case 14-36011 Differential Diagnosis #12:	1412
Case 14-36011 Differential Diagnosis #13:	1413
Case 14-36011 Differential Diagnosis #14:	1414
Case 14-36011 Differential Diagnosis #15:	1415
Case 14-36011 Differential Diagnosis #16:	1416
Case 14-36011 Differential Diagnosis #17:	1417
Case 14-36011 Differential Diagnosis #18:	1418
Case 14-36011 Differential Diagnosis #19:	1419
Case 14-36011 Differential Diagnosis #20:	1420

## Case 15-36102

Response was added on 11/18/2020 12:44pm.

### Patient Presentation Summary

**Chief Complaint/History of Present Illness:** This 49-year-old white professor of history was in an auto accident and suffered a basilar skull fracture. He was admitted to the hospital for observation. His blood pressure was recorded at 132-150/80-98 and his heart rate 84-98/min in the hospital. He then developed lightheadedness particularly upon standing. His BP was then 220/110 and his heart rate 120-150. The episode lasted a matter of minutes and spontaneously subsided.

**Previous Medical History:** His blood pressure had been borderline high for years and in the past year his diastolic pressure was 90 or slightly above. No family history of hypertension was mentioned. He had had a colon biopsy 8 years before but no diagnosis was made.

**Physical Examination:** Vital signs were BP 140/90 supine, 115/84 standing; HR 88 supine, 98 standing. His fundi showed minimal if any changes of hypertension. There were no other abnormalities except deafness in his right ear related to the trauma.

Case 15-36102 Differential Diagnosis #1:	151
Case 15-36102 Differential Diagnosis #2:	152
Case 15-36102 Differential Diagnosis #3:	153
Case 15-36102 Differential Diagnosis #4:	154
Case 15-36102 Differential Diagnosis #5:	155
Case 15-36102 Differential Diagnosis #6:	156
Case 15-36102 Differential Diagnosis #7:	157
Case 15-36102 Differential Diagnosis #8:	158

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Case 15-36102 Differential Diagnosis #9:	159
Case 15-36102 Differential Diagnosis #10:	1510
Case 15-36102 Differential Diagnosis #11:	1511
Case 15-36102 Differential Diagnosis #12:	1512
Case 15-36102 Differential Diagnosis #13:	1513
Case 15-36102 Differential Diagnosis #14:	1514
Case 15-36102 Differential Diagnosis #15:	1515
Case 15-36102 Differential Diagnosis #16:	1516
Case 15-36102 Differential Diagnosis #17:	1517
Case 15-36102 Differential Diagnosis #18:	1518
Case 15-36102 Differential Diagnosis #19:	1519
Case 15-36102 Differential Diagnosis #20:	1520



**Case 16-36083**

Response was added on 11/18/2020 12:45pm.

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**Patient Presentation Summary**

**Chief Complaint:** This 58-year-old black woman presented with shortness of breath.

**History of Present Illness:** The patient had a history of hypertension and had had three weeks of intermittent left sided chest pain. The pain radiated to the back and improved when she leaned forward. There was no change with exertion. Pains lasted for approximately one minute. She also complained of increasing shortness of breath over the previous month. She became dyspneic performing minimum household chores. She denied orthopnea, PND or lower extremity edema. She had an occasional nonproductive cough. She had been seen by a local doctor prior to admission, found to be hypertensive and started on treatment. She complained of night sweats and fever over the previous week but had no weight loss.

**Past Medical History:** Her medications on admission included verapamil 180 mg p.o. q.d., benazepril 10 mg p.o. q.d. and furosemide 20 mg q.d. She had previous trauma to the right eye resulting in blindness. She had a total abdominal hysterectomy and bilateral oophorectomy in the 1970's.

**Social History:** She smoked for ten years, but not any during the previous twenty years. She drinks one beer every six months. She works in the home and lives with her husband.

**Physical Examination:** Her pulse was 90, blood pressure 159/107, temperature 38.3oC and respiratory rate, 22.

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Case 16-36083 Differential Diagnosis #1:	161
Case 16-36083 Differential Diagnosis #2:	162
Case 16-36083 Differential Diagnosis #3:	163
Case 16-36083 Differential Diagnosis #4:	164

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Case 16-36083 Differential Diagnosis #5:	165
Case 16-36083 Differential Diagnosis #6:	166
Case 16-36083 Differential Diagnosis #7:	167
Case 16-36083 Differential Diagnosis #8:	168
Case 16-36083 Differential Diagnosis #9:	169
Case 16-36083 Differential Diagnosis #10:	1610
Case 16-36083 Differential Diagnosis #11:	1611
Case 16-36083 Differential Diagnosis #12:	1612
Case 16-36083 Differential Diagnosis #13:	1613
Case 16-36083 Differential Diagnosis #14:	1614
Case 16-36083 Differential Diagnosis #15:	1615
Case 16-36083 Differential Diagnosis #16:	1616
Case 16-36083 Differential Diagnosis #17:	1617
Case 16-36083 Differential Diagnosis #18:	1618
Case 16-36083 Differential Diagnosis #19:	1619
Case 16-36083 Differential Diagnosis #20:	1620

## Case 11-36052IPD

Response was added on 11/18/2020 12:47pm.

### Patient Presentation Summary

**Chief Complaints:** This patient is a 60-year-old white male who presented with a three-week history of crampy lower abdominal pain and severe anemia.

**History of Present Illness:** He was in his usual state of health until 2-3 weeks prior to admission when he developed crampy lower abdominal pain which was intermittent and bilateral and not clearly related to eating, bowel movements or position. On the day prior to admission, the pain worsened. He was awakened the morning of admission with pain which increased throughout the day. He presented to an urgent care facility where his hematocrit was found to be 19.3. He denied bright red blood per rectum or melena. He has had increased fatigue and denied any other symptoms, such as vomiting, hematemesis, hematuria, change in urine color, or change in bowel habits or stool. His appetite has been normal. He believed he had lost some weight but could not quantify the amount.

**Past Medical History** was significant for coronary artery disease, S/P bypass grafting, asthma, and eczema. Medications included only acetaminophen. He denied medication allergies.

**Social/Family History:** He was a technical illustrator who has 3-4 beers each week. Family history was unremarkable.

**Physical Examination** revealed a pale man. He was afebrile and his pulse was 78, with a respiratory rate of 18 and a blood pressure of 132/68.

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Isabel Pro Differential (Order of Literature Search Match of Symptoms, Not clinical probability)

Churg-Strauss Syndrome  
Conjunctivitis  
Disorders  
Ischemic Heart Disease  
Hemolytic Uremic Syndrome  
Drug Induced Thrombocytopenia  
Thrombotic

Thrombocytopenic Purpura Asthma Cardiogenic Shock Atopic Dermatitis  
Hypertensive Retinopathy Interstitial Nephritis Heavy Metal Intoxication

Iron Deficiency Colorectal Cancer Heart Failure / CHF  
Aortic Aneurysm / Dissection Atypical Hemolytic-Uremic  
Syndrome Food Allergy Myelofibrosis Renal Failure  
Selective IgA Deficiency Myeloma Adrenal Neoplasms  
Antiphospholipid Syndrome

Meningococcal Disease Neoplasms of the Kidney Bladder Neoplasms  
Peripheral Arterial Disease Sideroblastic Anemias Aplastic Anemia Arteriolar  
Nephrosclerosis Lower Urinary Tract Obstruction Diabetic Cardiovascular  
Disease Gaucher Disease Drug Overdose/Poisoning Megaloblastic Anemias  
Sepsis and Shock Aortic Stenosis Heart Neoplasms Left-to-Right Shunt  
Lesions

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Case 11-36052IPD Differential Diagnosis #1: diagnosis: 111	No Change Your previous
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Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #2: diagnosis: 112	No Change Your previous
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Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #3: diagnosis: 113	No Change Your previous
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Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #4: diagnosis: 114	No Change Your previous
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Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #5: diagnosis: 115	No Change Your previous
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Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #6: diagnosis: 116	No Change Your previous
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Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #7:  
diagnosis: 117

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #8:  
diagnosis: 118

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #9:  
diagnosis: 119

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #10:  
diagnosis: 1110

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #11:  
diagnosis: 1111

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #12:  
diagnosis: 1112

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #13:  
diagnosis: 1113

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #14:  
diagnosis: 1114

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #15:  
diagnosis: 1115

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #16:  
diagnosis: 1116

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #17:  
diagnosis: 1117

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #18:  
diagnosis: 1118

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #19:  
diagnosis: 1119

No Change Your previous

Your revised diagnosis if changed:

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Case 11-36052IPD Differential Diagnosis #20:  
diagnosis: 1120

No Change Your previous

Your revised diagnosis if changed:

## Case 12-36291IPD

Response was added on 11/18/2020 12:48pm.

### Patient Presentation Summary

**Chief Complaint:** This 61-year-old white male presented with weight loss and fatigue.

**History of Present Illness:** The patient was in his usual state of health until 3 months prior to admission, when he experienced weakness and fatigue. He complained of being continually tired, spent most of his days at home, and required daily naps. His appetite decreased, and he lost 25 pounds. He experienced diffuse abdominal fullness, without relation to meals. He also experienced frequent arthralgias, and pain in his lower back. He denied fevers, sweats, or chills.

**Past Medical History:** He had a history of hypertension. He also had a history of atrial fibrillation. He had bilateral herniorrhaphies 20 years prior to admission.

**Medications:** Hydrochlorothiazide,

Digoxin, Motrin. Allergies: none

known.

**Family History:** No known familial diseases.

**Social History:** The patient is Jewish, of Eastern European extraction. He has smoked 1 ½ packs of cigarettes per day for 40 years. He rarely drinks alcohol.

**Physical Examination:** Thin white male in no acute distress. BP 130/70; pulse 88, irregularly irregular; respirations 16; temperature 98.6oF.

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Isabel Pro Differential (Order of Literature Search Match of Symptoms, Not clinical probability)

Coronavirus Non-Hodgkin Lymphoma Crohn  
 Disease Brucellosis Interstitial Lung Disease  
 Pituitary Neoplasms Whipple Disease Endocarditis  
 Interstitial Nephritis Heart Failure / CHF Polymyalgia  
 Rheumatica Coccidioidomycosis Liver Neoplasms Neoplasms  
 of the Kidney Aortic Aneurysm / Dissection SLE  
 Glomerulonephritis Celiac Disease Infectious Mononucleosis  
 Microscopic Polyangiitis Churg-Strauss Syndrome Gastric  
 Neoplasms Renal Failure Lyme Disease  
 Peptic Ulcer Disease Substance Abuse Heavy Metal  
 Intoxication Adult Still Disease Giant Cell Arteritis  
 Hyperthyroidism Leptospirosis Rheumatoid Arthritis  
 Granulomatosis with Polyangiitis Megaloblastic Anemias  
 Hemochromatosis Babesiosis HIV / AIDS Hypersensitivity  
 Pneumonitis Pulmonary Hypertension Heart Neoplasms  
 Aortic Arch Syndrome Mesenteric Panniculitis

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Case 12-36291IPD Differential Diagnosis #1: No Change Your Previous  
 Diagnosis: 121

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #2: No Change Your Previous  
 Diagnosis: 122

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #3: No Change Your Previous  
 Diagnosis: 123

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #4: No Change Your Previous  
 Diagnosis: 124

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #5: No Change Your Previous  
 Diagnosis: 125

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #6: No Change Your Previous  
 Diagnosis: 126



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Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #7:  
Diagnosis: 127

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #8:  
Diagnosis: 128

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #9:  
Diagnosis: 129

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #10:  
Diagnosis: 1210

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #11:  
Diagnosis: 1211

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #12:  
Diagnosis: 1212

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #13:  
Diagnosis: 1213

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #14:  
Diagnosis: 1214

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #15:  
Diagnosis: 1215

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #16:  
Diagnosis: 1216

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #17:  
Diagnosis: 1217

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #18:  
Diagnosis: 1218

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #19:  
Diagnosis: 1219

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 12-36291IPD Differential Diagnosis #20:  
Diagnosis: 1220

No Change Your Previous

Your Revised Diagnosis if Changed:

## Case 13-36043IPD

Response was added on 11/18/2020 12:49pm.

### Patient Presentation Summary

**Chief Complaint:** This 23-year-old Hispanic male migrant worker from Mexico presented with right upper quadrant pain.

**History of Present Illness:** He was admitted to an outside hospital with a two-week history of right upper quadrant abdominal pain. He described his pain as steady and stabbing, worsening with respiration. He had nausea but no diarrhea or constipation. He denied fever. There was no history of hematemesis, hematochezia, or melena. He had no previous episodes of right upper quadrant pain. There was no history of trauma. He had lived in this country for six years, but had traveled in and out of Mexico in the past year including a recent trip three months prior to admission. He admitted to working with animals and drinking water from streams. At the outside hospital he had an abdominal CT scan that showed two cystic lesions in the liver; one 4 cm in diameter located posteriorly in the right lobe adjacent to the diaphragm, the other a 1 cm lesion located anteriorly in the right lobe. His white count was  $14.9 \times 10^9/L$ . The patient transferred to this hospital for further evaluation.

**Past Medical History:** He denied past surgery or medical illness. There had been no previous hospitalization. He had no allergies.

**Physical Examination:** He appeared as a thin, healthy looking man in no distress. The temperature was 98.6 o F (37oC), pulse 76, blood pressure 102/70.

Isabel Pro Differential (Order of Literature Search Match of Symptoms, Not clinical probability)

Liver Neoplasms Viral Hepatitis Cholecystitis Leptospirosis

Infectious Mononucleosis Cryptococcus Neoformans Acute  
Appendicitis Yersinia Infection Liver Abscess Pancreatitis  
Cholangitis Biliary Colic

Cholangiocarcinoma Crohn Disease Urinary Lithiasis /  
Nephrolithiasis Urinary Tract Infection Ascariasis Cholelithiasis  
Environmental / Work Exposure Pyelonephritis

Gastroenteritis Intracranial Abscess Peritonitis Adult Still Disease

Diverticular Diseases of the Colon Shigella Infections Toxoplasmosis

Pseudomembranous / Drug-Induced Colitis Cecal Volvulus Cirrhosis Giardiasis

Salmonella Infections

Fluke Infection Diarrheal Disorders Plant Poisoning

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Case 13-36043IPD Differential Diagnosis #1: Diagnosis: 131	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #2: Diagnosis: 132	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #3: Diagnosis: 133	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #4: Diagnosis: 134	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #5: Diagnosis: 135	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #6: Diagnosis: 136	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #7: Diagnosis: 137	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #8: Diagnosis: 138	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #9:  
Diagnosis: 139

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #10:  
Diagnosis: 1310

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #11:  
Diagnosis: 1311

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #12:  
Diagnosis: 1312

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #13:  
Diagnosis: 1313

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #14:  
Diagnosis: 1314

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #15:  
Diagnosis: 1315

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #16:  
Diagnosis: 1316

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #17:  
Diagnosis: 1317

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #18:  
Diagnosis: 1318

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #19:  
Diagnosis: 1319

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 13-36043IPD Differential Diagnosis #20:  
Diagnosis: 1320

No Change Your Previous

Your Revised Diagnosis if Changed:

## Case 14-36011IPD

Response was added on 11/18/2020 12:50pm.

### Patient Presentation Summary

Chief Complaint: This 53-year-old black male presented with a leg ulcer.

History of Present Illness: The patient developed an ulcer on the right lower leg approximately 1 year prior to admission. The ulcer slowly increased in size, but appeared to worsen over the last 6 months. The ulcer was painless, and exuded foul-smelling pus which would harden and subsequently fall off. The patient also developed a dry hacking cough 6 months prior to admission, and lost approximately 15 lbs. He denied fevers, chills, night sweats, hemoptysis, or shortness of breath.

Past Medical History: Hypertension for several years. No history of diabetes mellitus. Medications: none.

Allergies: none known.

Family History: Noncontributory.

Social History: He has smoked 1 pack of cigarettes per day for 25 years. He drinks alcohol occasionally. He does not use illicit drugs.

Physical Examination: Thin black male in no acute distress. BP 120/80; pulse 80; respirations 18; temperature 98.6oF.

Isabel Pro Differential (Order of Literature Search Match of Symptoms, Not clinical probability)

Interstitial Lung Disease COPD Intestinal Ischemia Coronavirus  
Hypersensitivity Pneumonitis Ischemic Heart Disease Cryoglobulinemia  
Intracranial Hemorrhage Obesity-Hypoventilation Syndrome  
Pneumoconioses Tonsillar Neoplasm Lung Neoplasms

Renal Failure Substance Abuse Systemic Sclerosis  
 Neoplasms of the Kidney Pancreatitis Liver Neoplasms  
 Varicose Veins Goodpasture's Syndrome

Hodgkin Disease Antisynthetase Syndrome Non-Hodgkin Lymphoma  
 Atypical Pneumonia Adrenal Neoplasms Alpha-1-Antitrypsin  
 Deficiency Bladder Neoplasms Primary Valve Deficiency Oral Cancer  
 Langerhans Cell Histiocytosis Class 1 Diabetic Nephropathy  
 Hyperthyroidism Chronic Venous Insufficiency Diabetic Neuropathy  
 Pseudoxanthoma Elasticum Gout

Sexual Dysfunction Giant Cell Arteritis Heart Neoplasms  
 Primary Dyslipidemias Rheumatoid Arthritis

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Case 14-3601 IIPD Differential Diagnosis #1: Diagnosis: 141 Your Revised Diagnosis if Changed:	No Change Your Previous
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Case 14-3601 IIPD Differential Diagnosis #2: Diagnosis: 142 Your Revised Diagnosis if Changed:	No Change Your Previous
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Case 14-3601 IIPD Differential Diagnosis #3: Diagnosis: 143 Your Revised Diagnosis if Changed:	No Change Your Previous
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Case 14-3601 IIPD Differential Diagnosis #4: Diagnosis: 144 Your Revised Diagnosis if Changed:	No Change Your Previous
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Case 14-3601 IIPD Differential Diagnosis #5: Diagnosis: 145 Your Revised Diagnosis if Changed:	No Change Your Previous
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Case 14-3601 IIPD Differential Diagnosis #6: Diagnosis: 146 Your Revised Diagnosis if Changed:	No Change Your Previous
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Case 14-3601 IIPD Differential Diagnosis #7: Diagnosis: 147	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #8:  
Diagnosis: 148

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #9:  
Diagnosis: 149

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #10:  
Diagnosis: 1410

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #11:  
Diagnosis: 1411

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #12:  
Diagnosis: 1412

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #13:  
Diagnosis: 1413

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #14:  
Diagnosis: 1414

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #15:  
Diagnosis: 1415

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #16:  
Diagnosis: 1416

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #17:  
Diagnosis: 1417

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #18:  
Diagnosis: 1418

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #19:  
Diagnosis: 1419

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 14-36011IPD Differential Diagnosis #20:  
Diagnosis: 1420

No Change Your Previous

Your Revised Diagnosis if Changed:

## Case 15-36102IPD

Response was added on 11/18/2020 12:51pm.

### Patient Presentation Summary

**Chief Complaint/History of Present Illness:** This 49-year-old white professor of history was in an auto accident and suffered a basilar skull fracture. He was admitted to the hospital for observation. His blood pressure was recorded at 132-150/80-98 and his heart rate 84-98/min in the hospital. He then developed lightheadedness particularly upon standing. His BP was then 220/110 and his heart rate 120-150. The episode lasted a matter of minutes and spontaneously subsided.

**Previous Medical History:** His blood pressure had been borderline high for years and in the past year his diastolic pressure was 90 or slightly above. No family history of hypertension was mentioned. He had had a colon biopsy 8 years before but no diagnosis was made.

**Physical Examination:** Vital signs were BP 140/90 supine, 115/84 standing; HR 88 supine, 98 standing. His fundi showed minimal if any changes of hypertension. There were no other abnormalities except deafness in his right ear related to the trauma.

Isabel Pro Differential (Order of Literature Search Match of Symptoms, Not clinical probability)

Bacterial Meningitis Neurocutaneous Syndromes Renal Failure Systemic Hypertension Disorders

Heavy Metal Intoxication Cerebral Sinus Venous Thrombosis Meniere's Disease Superior Canal Dehiscence Syndrome

Arteriolar Nephrosclerosis Acoustic Neuroma Herpes Zoster Oticus  
Drug Overdose/Poisoning Perilymph Fistula Ischemic Heart Disease  
Polyarteritis Nodosa CVA / Stroke

Transient Ischemic Attack Migraine Otosclerosis Relapsing  
Polychondritis Sarcoidosis Ataxic Disorders Pulmonary  
Hypertension Sensorineural Hearing Loss

Atrial Fibrillation Enlarged Vestibular Aqueduct Ototoxicity Otitis  
Media Complications Susac Syndrome Otitis Media Brain  
Neoplasms Taenia solium

SLE Aortic Arch Syndrome Fibromuscular Dysplasia Vestibulopathy  
Multiple Sclerosis Alport Syndrome Heart Neoplasms  
Antiphospholipid Syndrome Chiari Malformation

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Case 15-36102IPD Differential Diagnosis #1: No Change Your Previous  
Diagnosis: 151  
Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #2: No Change Your Previous  
Diagnosis: 152  
Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #3: No Change Your Previous  
Diagnosis: 153  
Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #4: No Change Your Previous  
Diagnosis: 154  
Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #5: No Change Your Previous  
Diagnosis: 155  
Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #6: No Change Your Previous  
Diagnosis: 156  
Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #7: No Change Your Previous  
Diagnosis: 157  
Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #8: No Change Your Previous  
Diagnosis: 158  
Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #9: No Change Your Previous  
Diagnosis: 159

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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #10: Diagnosis: 1510	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #11: Diagnosis: 1511	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #12: Diagnosis: 1512	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #13: Diagnosis: 1513	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #14: Diagnosis: 1514	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #15: Diagnosis: 1515	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #16: Diagnosis: 1516	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #17: Diagnosis: 1517	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #18: Diagnosis: 1518	No Change Your Previous
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Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #19:  
Diagnosis: 1519

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 15-36102IPD Differential Diagnosis #20:  
Diagnosis: 1520

No Change Your Previous

Your Revised Diagnosis if Changed:

## Case 16-36083IPD

Response was added on 11/18/2020 12:52pm.

### Patient Presentation Summary

**Chief Complaint:** This 58-year-old black woman presented with shortness of breath.

**History of Present Illness:** The patient had a history of hypertension and had had three weeks of intermittent left sided chest pain. The pain radiated to the back and improved when she leaned forward. There was no change with exertion. Pains lasted for approximately one minute. She also complained of increasing shortness of breath over the previous month. She became dyspneic performing minimum household chores. She denied orthopnea, PND or lower extremity edema. She had an occasional nonproductive cough. She had been seen by a local doctor prior to admission, found to be hypertensive and started on treatment. She complained of night sweats and fever over the previous week but had no weight loss.

**Past Medical History:** Her medications on admission included verapamil 180 mg p.o. q.d., benazepril 10 mg p.o. q.d. and furosemide 20 mg q.d. She had previous trauma to the right eye resulting in blindness. She had a total abdominal hysterectomy and bilateral oophorectomy in the 1970's.

**Social History:** She smoked for ten years, but not any during the previous twenty years. She drinks one beer every six months. She works in the home and lives with her husband.

**Physical Examination:** Her pulse was 90, blood pressure 159/107, temperature 38.3oC and respiratory rate, 22.

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Isabel Pro Differential (Order of Literature Search Match of Symptoms, Not clinical probability)

Bacterial Pneumonia Pulmonary Thromboembolism Atypical Pneumonia Pulmonary Hypertension Heart Failure / CHF

Interstitial Lung Disease Asthma Diseases of High Altitudes Coronavirus Pulmonary Edema

Ischemic Heart Disease Sarcoidosis Giant Cell Arteritis Pericardial Effusion / Tamponade Hypersensitivity Pneumonitis

Lung Abscess Q Fever Cardiogenic Shock Systemic Sclerosis, Antisynthetase  
 Syndrome Pulmonary Tuberculosis Non-Hodgkin Lymphoma Hodgkin Disease  
 Endocarditis Aspiration Syndromes Pleurisy  
 Relapsing Fever Esophageal Perforation Myocarditis Castleman's Disease Pericarditis  
 Sepsis and Shock Antiphospholipid Syndrome Adrenal Neoplasms Left-to-Right Shunt Lesions  
 Alpha-1-Antitrypsin Deficiency

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Case 16-36083IPD Differential Diagnosis #1: No Change Your Previous  
 Diagnosis: 161

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #2: No Change Your Previous  
 Diagnosis: 162

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #3: No Change Your Previous  
 Diagnosis: 163

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #4: No Change Your Previous  
 Diagnosis: 164

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #5: No Change Your Previous  
 Diagnosis: 165

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #6: No Change Your Previous  
 Diagnosis: 166

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #7: No Change Your Previous  
 Diagnosis: 167

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #8: No Change Your Previous  
 Diagnosis: 168

Your Revised Diagnosis if Changed:



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Case 16-36083IPD Differential Diagnosis #9:  
Diagnosis: 169

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #10:  
Diagnosis: 1610

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #11:  
Diagnosis: 1611

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #12:  
Diagnosis: 1612

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #13:  
Diagnosis: 1613

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #14:  
Diagnosis: 1614

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #15:  
Diagnosis: 1615

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #16:  
Diagnosis: 1616

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #17:  
Diagnosis: 1617

No Change Your Previous

Your Revised Diagnosis if Changed:

---

Case 16-36083IPD Differential Diagnosis #18:  
Diagnosis: 1618

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #19:  
Diagnosis: 1619

No Change Your Previous

Your Revised Diagnosis if Changed:

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Case 16-36083IPD Differential Diagnosis #20:  
Diagnosis: 1620

No Change Your Previous

Your Revised Diagnosis if Changed:

## Diagnostic Challenge Questionnaire

Please complete the following questionnaire regarding your experience with the Diagnostic Challenge.

Response was added on 11/18/2020 12:52pm.

	Strongly Agree	Agree	Disagree	Strongly Disagree
The Isabel Pro Diagnostic Suggestions are reasonable and helpful.	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The Isabel Pro diagnostic suggestions prompted me to reconsider my original diagnosis.	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>
The Isabel Pro diagnostic suggestions prompted me to change my original diagnosis.	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>
The ranking of the Isabel Pro diagnostic suggestions influenced my diagnostic thinking process.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>
The early presentation of Isabel Pro diagnostic suggestions improved my diagnostic accuracy.	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>
I think the Isabel Pro diagnostic suggestions would be helpful in routine clinical practice.	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>
I would consult the Isabel Pro diagnostic suggestions if they were available at every initial patient presentation.	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

## Exhibit 1

## Translational Project - Diagnostic Decision Support Systems

Validation Project [Results](#)

Case Number CBD001

Diagnosis: Polymyalgia Rheumatica

Isabel Pro Healthcare

Date Entered

2/17/2020

<u>Ranked</u>	<u>% Match</u>	<u>Diagnostic Alternatives</u>	<u>Reasons</u>
1	100%	Osteoarthritis	We matched the terms: shoulder pain   joint
2	100%	Osteoporosis	We matched the terms: osteoporosis   arthritis   hip   chronic   replacement   fract
3	98%	Polymyalgia Rheumatica	We matched the terms: shoulder pain   difficulty raising arms above
4	73%	Osteomyelitis and Septic Arthritis	We matched the terms: shoulder pain   painful joints   painful joint   joint pain   knee   hip
5	71%	Rheumatoid Arthritis	We matched the terms: shoulder pain   painful joints   painful joint   joint
6	61%	Osteomalacia	We matched the terms:
7	56%	Gout	We matched the terms: joint pain   arthritis   arthropathy   knee   hip   chronic   should
8	53%	Giant Cell Arteritis	We matched the terms: shoulder pain   joint
9	50%	Renal Osteodystrophy	We matched the terms:
10	48%	Frozen Shoulder	We matched the terms: shoulder pain   joint pain
			<b>Terms Not Influencing Result:</b> Bimatoprost, simvastatin, reivroxaban, denosumab, tylenol

**Translational Project - Diagnostic Decision Support Systems**Validation Project [Results](#)**Case Number**      **CBD001**      **Diagnosis: Polymyalgia Rheumatica****Isabel Pro Healthcare**      **Date Entered**      **2/17/2020****Age**      Geriatric 65 yrs-over**Gender**      Female**Travel**      North America**Chief Complaints**

- 1      Chronic Pain of Both Shoulders

**Medications**

- 1      Simvastatin 20 mg Oral Daily
- 2      Xarelto (rivaroxaban) 20 mg Oral Daily
- 3      Prolia (denosumab)
- 4      Tylenol Extra Strength 500 mg Oral 4x Daily
- 5      Vitamin D3 5000 unit Oral Every Other Day
- 6      Lumigan (bimatoprost) 0.12% Ophthalmic Solution 1 drop, both eyes, daily

**Medical History**

- 1      History of Arthritis
- 2      History of Osteoporosis
- 3      History of psychiatric treatment
- 4      Bilateral knee replacement
- 5      Bilateral hip fracture

**Allergies**

- 1      Codeine Derivatives

**Immunizations**

- 1      Fluzone High-Dose 0.5 ml

## Exhibit 2

Isabel Pro Healthcare Case KH001 Diagnosis: Diabetes  
 Ranked % Match Diagnostic Alternatives Reasons

Ranked	% Match	Diagnostic Alternatives	Reasons
1	81%	Lyme Disease	We matched the terms: dizziness   low back pain   neck stiffness   stiff neck   neck stiff   back pain   backache   chest pain   throat   cervical   depression   joint   spine   anxiety   hand   bite   face
2	79%	Brucellosis	We matched the terms: dizziness   unsteadiness   weight loss   low back pain   back pain   skin lesion   skin lesions   chest pain   depression   joint   spine   anxiety   cataract   sacroiliac   diarrhea   cough
3	60%	Sjogren's Syndrome	We matched the terms: xerostomia   dry mouth   mouth dry   gastroesophageal reflux disease   gastroesophageal reflux   gerd   sjogren's syndrome   sjogren's   throat   joint   hand   infection   cough   oral
4	59%	Sarcoidosis	We matched the terms: weight loss   skin lesion   skin lesions   chest Pain   cervical   joint   hand   face   infection   cataract   cough   calcium   cirrhosis
5	56%	Meningococcal Disease	We matched the terms: leg weakness   neck stiffness   stiff neck   neck stiff   leg pain   severe leg pain   skin lesion   skin lesions   leg cramp   leg cramps   throat   joint   hand   infection   diarrhea   cough   calcium
6	56%	Osteoarthritis	We matched the terms: low back pain   back pain   hip pain   chest pain   cervical   joint   spine   hand   osteoarthritis   limited
7	54%	Diabetic Neuropathy	We matched the terms: dizziness   lightheadedness   lightheaded   weight loss   leg weakness   hip pain   leg ulcer   leg ulcers   depression   hand   face   diarrhea   extremity
8	50%	Polymyalgia Rheumatica	We matched the terms: weight loss   lower leg weakness   leg weakness   back pain   hip pain   leg cramp   leg cramps   depression   joint   hand
9	46%	Non-Hodgkin Lymphoma	We matched the terms: weight loss   low back pain   back pain   skin lesion   skin lesions   chest pain   joint   face   infection   diarrhea   cough
10	42%	Giant Cell Arteritis	We matched the terms: balance problem   balance problems   weight loss   stiffness in neck   hip pain   throat   depression   joint   face   cough   extremity

We matched the terms: balance problem   balance problems   weight loss   stiffness in neck   hip pain   throat   depression   joint   face   cough   extremity
--

**Age** Geriatric 65yrs-over

**Gender** Female

**Travel** North America

**Chief Complaints**

1 Dizziness; Unintentional Weight Loss, Black Tarry Stools

**Medications**

- 1 Nadolol, 20mg, oral tablet
- 2 Calcium + D tablets
- 3 Biotene Dry Mouth Gentle Throat Liquid

**Medical History**

- 1 Benign essential hypertension
- 2 Breast mass
- 3 Cataract
- 4 Cervical osteoarthritis
- 5 Compensated HCV cirrhosis
- 6 Depression
- 7 Esophageal varices
- 8 Gastroesophageal reflux disease
- 9 History of dry mouth
- 10 Hypothyroidism
- 11 Injury of left lower extremity, sequela
- 12 Injury of right lower extremity, sequela
- 13 Left leg weakness
- 14 Limited scleroderma
- 15 Low back pain
- 16 Neck stiffness
- 17 Iron deficiency anemia
- 18 Pain of back and right lower extremity
- 19 Pain of right sacroiliac joint
- 20 Polyarthralgia 21 Right hip pain
- 22 Seborrheic dermatitis
- 23 Sjogren's syndrome
- 24 Skin lesion
- 25 Stenosis, cervical spine
- 26 Varicose veins
- 27 History of acute diarrhea
- 28 History of Anxiety
- 29 History of Atypical chest pain
- 30 History of cellulitis of hand
- 31 History of colon polyp
- 32 History of cramp in lower leg
- 33 History of dog bite of face

- 34 History of H. pylori infection
- 35 History of acute bronchitis 36 History of cough

**Allergies**

- 1 Sulfa Drugs

**Immunizations**

- 1 Shingrix Injection, 0.5ml



### Exhibit 3

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number McGMS **Emphysematous Pyelonephritis, Clinically indistinguishable**  
Case 1 **from severe, acute pyelonephritis**

Isabel Pro Healthcare **Date Entered 4/6/2020**

<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	99%	Antiphospholipid Syndrome	pain   dizziness   loss of balance   dvt   hypertension   accident   chronic   kidney
2	73%	Pyelonephritis	We matched the terms: nausea   vomiting   nausea and vomiting   vomit   abdominal pain   hypertension   urinary tract infection
3	67%	Renal Failure, Chronic	We matched the terms: nausea   vomiting   vomit   dizziness   hypertension   high blood pressure   chronic   kidney   disease
4	61%	Ischemic Heart Disease	We matched the terms: nausea   vomiting   vomit   abdominal pain   dizziness   lightheadedness   lightheaded   hypertension
5	53%	Polyarteritis Nodosa	We matched the terms: nausea   vomiting   nausea and vomiting   vomit   abdominal pain   hypertension   accident   chronic
6	52%	Pulmonary Hypertension	We matched the terms: nausea   vomiting   vomit   dizzy   deep vein thrombosis   hypertension   chronic
7	51%	Brain Neoplasms	We matched the terms: nausea   nauseated   vomiting   vomit   dizziness   light headed   unsteadiness   light headedness   imbalance   deep vein thrombosis   chronic
8	50%	Pelvic Inflammatory Disease	We matched the terms: nausea   vomiting   nausea and vomiting   vomit   abdominal pain   abdominal discomfort   chronic
9	49%	Heart Failure/ CHF	We matched the terms: nausea   vomiting   vomit   abdominal pain   hypertension   hypertensive   elevated blood pressure   chronic   kidney   disease
10	48%	Escherichia Coli Infections	We matched the terms: nausea   vomiting   vomit   abdominal pain   beta   spectrum   extended
			Please note: Check your spelling. The term/s hemmorrhagic, cebrovascular, gastrostomy, lactamases may not have influenced

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number **from McGMS Case 1** **Emphysematous Pyelonephritis, Clinically indistinguishable  
severe, acute pyelonephritis**

**Isabel Pro Healthcare** **Date Entered 4/6/2020**

**Age** Adult 50-64 yrs

**Gender** Female, not pregnant **Travel**

North America

**Chief Complaints**

- 1 Nausea, 2 days
- 2 Vomiting, 2 days
- 3 Difuse Abdominal Pain
- 4 Vertigo
- 5 Left Eye Pain

**Medications**

- 1 Ertapenem

**Medical History**

- 1 Left Hemorrhagic Cerebrovascular Accident
- 2 Percutaneous Endoscopic Gastrostomy Tube
- 3 T2DM
- 4 Deep Vein Thrombosis, Chronic
- 5 Hypertension
- 6 HLD
- 7 Kidney Disease, Chronic
- 8 Extended Spectrum Beta-Lactamases E coli Urinary Tract Infection

**Allergies**

- 1 NKA

**Immunizations**

- 1 N/A

## Exhibit 4

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number                      McGMS Case 2                      Warm Autoimmune Hemolytic Anemia

Isabel Pro Healthcare                      Date Entered 4/7/2020

<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Heart Failure, CHF	We matched the terms: weakness   fatigue   tired   nausea   vomiting   vomit   shortness of breath   dyspnea   dyspnoea   short of breath   difficulty breathing   pruritus   itching   itch
2	87%	Viral Hepatitis	We matched the terms: weakness   malaise   tiredness   fatigue   tired   nausea   vomiting   nausea and vomiting   vomit   yellow eyes   pruritus   itching   itch   urticaria
3	83%	Cirrhosis	We matched the terms: weakness   malaise   fatigue   lethargy   nausea   vomiting   vomit   yellow eyes   itching
4	73%	Lyme Disease	We matched the terms: weakness   fatigue   lethargy   general fatigue   nausea   vomiting   vomit   shortness of
5	68%	Infectious Mononucleosis	We matched the terms: weakness   malaise   fatigue   nausea   vomiting   vomit   difficulty in breathing   urticaria   pruritic
6	66%	Hyperthyroidism	We matched the terms: generalised weakness   weakness   fatigue   nausea   vomiting   nausea and vomiting   vomit   shortness of breath   dyspnea   itchy   itching   itch   urticaria
7	64%	Ischemic Heart Disease	We matched the terms: weakness   malaise   fatigue   shortness of breath   urticaria   urticarial   asthma   asthma
8	62%	Churg-Strauss Syndrome	We matched the terms: weakness   fatigue   lethargy   general fatigue   nausea   vomiting   vomit   shortness of
9	62%	Anaphalaxis	We matched the terms: nausea   vomiting   emesis   vomit   shortness of breath   dyspnea   dyspnoea   difficulty breathing   pruritus   itchy   itching   itch   urticaria   pruritic   urticarial
10	60%	Coronavirus	We matched the terms: weakness   fatigue   nausea   vomiting   vomit   shortness of breath   dyspnea   difficulty breathing   labored breathing   asthma
			Please note: Check your spelling. The term/s nonsmoker, nondrinker may not have influenced the result.

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number                      McGMS Case 2                      Warm Autoimmune Hemolytic Anemia

**Isabel Pro Healthcare**

**Date Entered 4/7/2020**

**Age**      Adult 30-39 yrs old

**Gender**      Male

**Travel**      North America

**Chief Complaints**

- 1      Weakness, generalized, 4 months
- 2      Fatigue
- 3      Nausea, Vomiting, Intermittent
- 4      Scleral Icterus
- 5      Shortness of Breath
- 6      Itchiness, both wrists

**Medications**

- 1      None

**Medical History**

- 1      None
- 2      Non Smoker
- 3      No Alcohol Use
- 4      Family History of Asthma

**Allergies**

- 1      NKA

**Immunizations**

- 1      N/A

## Exhibit 5

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number                      McGMS Case 3                      Colorectal Cancer

Isabel Pro Healthcare                      Date Entered 4/8/2020

<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Aortic Aneurysm/Dissection	We matched the terms: abdominal pain   low   lower   diabetes   sensation   back   nausea   vomiting   radiating
2	100%	Diabetic Neuropathy	We matched the terms: abdominal pain   low   lower   diabetes mellitus   diabetes   diabetic   burning
3	100%	Ischemic Heart Disease	We matched the terms: chest pain   substernal chest pain   abdominal pain   pain in abdomen   low   shortness of breath   dyspnea   dyspnoea   difficulty breathing
4	100%	Pulmonary Thromboembolism	We matched the terms: chest pain   abdominal pain   low   lower   shortness of breath   dyspnea   burning   back
5	99%	Heart Failure/CHF	We matched the terms: abdominal pain   low   lower   shortness of breath   dyspnea   dyspnoea   short of breath   difficulty breathing   diabetes   sensation   back
6	98%	Pancreatitis	We matched the terms: abdominal pain   low   diabetes   back   nausea   vomiting   eating   radiating   insulin
7	92%	Peptic Ulcer Disease	We matched the terms: chest pain   abdominal pain   low   dyspnea   burning   back   nausea   vomiting   radiating
8	86%	Sarcoidosis	We matched the terms: chest pain   abdominal pain   low   lower   shortness of breath   dyspnea   difficulty breathing   difficult breathing   diabetes   sensation
9	72%	Bacterial Pneumonia	We matched the terms: chest pain   abdominal pain   low   shortness of breath   dyspnea   difficulty in breathing   back   nausea   vomiting   radiating
10	72%	Coronavirus	We matched the terms: chest pain   abdominal pain   abdominal discomfort   low   shortness of breath   dyspnea   difficulty breathing   labored breathing
			Please note: Check your spelling. The term/s amputations may not have influenced the result.

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number                      McGMS Case 3                      Colorectal Cancer

**Isabel Pro Healthcare**

**Date Entered 4/8/2020**

**Age**      Adult 50 - 64 yrs

**Gender**      Male

**Travel**      North America

**Chief Complaints**

- 1      Chest Pain, Several Months, Left Side, Burning Sensation
- 2      Abdominal Pain, Lower, Sharp, Radiating to Back, Five Days Duration
- 3      Nausea/Vomiting, Associated with Abdominal Pain, Worsens with Eating
- 4      Shortness of Breath without exertion

**Medications**

- 1      Insulin

**Medical History**

- 1      Insulin Dependent Diabetes Mellitus Type 2
- 2      Toe Amputations, Right Foot

**Allergies**

- 1      NKA

**Immunizations**

- 1      N/A

## Exhibit 6

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number                      McGMS Case 4                      Pseudohypoparathyroidism

Isabel Pro Healthcare                      Date Entered 4/9/2020

<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	90%	Mitochondrial Encephalomyopathie	We matched the terms: spasm   muscle spasm   muscle spasms   spasms   tiredness   fatigue   tired   fatigability   diabetes   stroke   muscle   weeks
2	81%	Vitamin D Deficiency	We matched the terms: spasm   spasms   cramps   cramp   fatigue   sweating   sweat   diabetes   stroke
3	61%	Endocarditis	We matched the terms: malaise   fatigue   sweating   sweats   sweat   cerebrovascular accident   muscle
4	61%	Parkinson's Disease	We matched the terms: cramps   cramp   fatigue   fatiguable   sweating   sweat   muscle   disease
5	61%	Type 2 Diabetes	We matched the terms: fatigue   diabetes mellitus   dm   diabetes   diabetic   muscle   weeks   disease
6	59%	Renal Failure	We matched the terms: spasm   spasms   cramps   cramp   fatigue   lethargy   exhausted   diabetes
7	54%	Megaloblastic Anemias	We matched the terms: cramps   cramp   tiredness   fatigue   tired   exhaustion   lassitude   fatigability   sweating   sweats   sweat   muscle   disease   twitching
8	52%	Antiphospholipid Syndrome	We matched the terms: spasm   muscle spasm   fatigue   sweat   cva   stroke   muscle
9	49%	Opsoclonus-Myoclonus Syndrome	We matched the terms: spasm   muscle spasm   muscle spasms   spasms   malaise   lethargy   muscle
10	48%	Multiple Sclerosis	We matched the terms: spasm   spasms   fatigue   sweating   sweat   facial numbness   disease
			Please note: Check your spelling. The term/s methimazole, repair, morphine may not have influenced

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number                      McGMS Case 4                      Pseudohypoparathyroidism

**Isabel Pro Healthcare**

**Date Entered 4/9/2020**

**Age**      Adult 30-39 yrs old

**Gender**      Male

**Travel**      North America

**Chief Complaints**

- 1      Muscle Twitching Intermittent One Year
- 2      Muscle Spasms Two Weeks Worsening
- 3      Fatigue
- 4      Sweating
- 5      Facial Numbness
- 6      Suicidal Ideation

**Medications**

- 1      Methimazole

**Medical History**

- 1      Graves Disease
- 2      Rotator Cuff Repair
- 3      Family History of Diabetes Mellitus
- 4      Family History of CerebroVascular Accident

**Allergies**

- 1      Morphine

**Immunizations**

- 1      N/A



## Exhibit 7

## Translational Project - Diagnostic Decision Support Systems

## Validation Project

[Results](#)

## PRES [Posterior Reversible Encephalopathy

## McGMS Case 5 Syndrome] 2/2 to Exchange Transfusion

## Case Number

[Isabel Pro Healthcare](#)[Date Entered 4/9/2020](#)

Ranked	% Match	Diagnostic Alternatives	Reasons
1	100%	Pulmonary Thromboembolism	We matched the terms: leg pain   abdominal pain   productive cough   asthma   pulmonary embolism   pulmonary emboli   pe   pulmonary
2	56%	Sickle Cell Disease / Crisis	We matched the terms: sickle cell   limb pain   abdominal pain   diffuse abdominal pain   pe   pain
3	54%	Heart Failure / CHF	We matched the terms: abdominal pain   chesty cough   asthma   pe   diabetes   pain   deep   venous
4	53%	Churg-Strauss Syndrome	We matched the terms: abdominal pain   asthma   asthma attack   pulmonary embolism   pulmonary
5	50%	Protein C and S Deficiencies	We matched the terms: leg pain   pulmonary embolism   pulmonary emboli   pain   deep   venous
6	49%	Antiphospholipid Syndrome	We matched the terms: abdominal pain   pulmonary embolism   pulmonary emboli   pe   pain   fever
7	49%	Coronavirus	We matched the terms: abdominal pain   abdominal discomfort   productive cough   cough with phlegm
8	45%	Endometriosis	We matched the terms: pain in leg   pain in legs   abdominal pain   pe   cesarean   cesarean section
9	43%	Septic Pelvic Thrombophlebitis	We matched the terms: abdominal pain   pulmonary emboli   pe   cesarean   cesarean section   pain
10	41%	Diabetic Ketoacidosis	We matched the terms: abdominal pain   stomach pain   stomach pains   diffuse abdominal pain   pe

Please note: Check your spelling. The term/s subjective, albuterol, escitalopram, eliquis, folic, hydroxyurea, oxycodone, tramadol, ductus, arteriosis,

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

## PRES [Posterior Reversible Encephalopathy

McGMS Case 5 Syndrome] 2/2 to Exchange Transfusion

## Case Number

Isabel Pro HealthcareDate Entered 4/9/2020Age Young Adult 17-29 yrs oldGender Female, Not Pregnant Travel North America**Chief Complaints**

- 1 Sickle Cell Pain Crisis
- 2 Pain Lower Extremities Bilateral
- 3 Pain Abdominal
- 4 Fever Subjective
- 5 Cough Productive

**Medications**

- 1 Albuterol
- 2 Escitalopram
- 3 Eliquis
- 4 Folic Acid
- 5 Hydroxyurea
- 6 Oxycodone
- 7 Tramadol

**Medical History**

- 1 Sickle Cell Anemia
- 2 Asthma
- 3 Pulmonary Embolism
- 4 Deep Venous Thrombosis
- 5 GastroEsophageal Reflux Disease
- 6 Major Depressive Disorder
- 7 Caesarean Section
- 8 Patent Ductus Arteriosis surgery
- 9 Family History of Sickle Cell Anemia
- 10 Family History of Diabetes Mellitus
- 11 Family History of asthma
- 12 Family History of Rheumatoid Arthritis

**Allergies**

- 1 Augmentin
- 2 Cefepime
- 3 Fentanyl

**Immunizations**

- 1 N/A

## Exhibit 8

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)Tubulointerstitial nephritis and uveitis (TINU  
syndrome) AKA Dobrin syndrome

McGMS Case 6

Case Number

Isabel Pro HealthcareDate Entered 04/08/\*2020

<i>Ranked</i>	<i>% Match</i>	<i>Diagnostic Alternatives</i>	<i>Reasons</i>
1	100%	Osteoarthritis	We matched the terms: weakness   hip pain   shoulder pain   wrist pain   gait   decreased   range
2	64%	Giant Cell Arteritis	We matched the terms: weakness   vision   headache   headaches   head pain   hip pain   shoulder pain
3	57%	Osteomalacia	We matched the terms: weakness   pain in the hips   gait   decreased   range   hips   vitamin
4	53%	Rheumatoid Arthritis	We matched the terms: weakness   general weakness   hip pain   shoulder pain   wrist pain   decreased
5	52%	Greater Trochanteric Pain Syndrome	We matched the terms: hip pain   decreased   range
6	50%	CVA / Stroke	We matched the terms: weakness   sight   vision   headache   unable to raise arm   unable to raise arms
7	45%	Polymyalgia Rheumatica	We matched the terms: weakness   headache   hip pain   shoulder pain   difficulty raising arms above
8	40%	Diabetic Neuropathy	We matched the terms: weakness   vision   hip pain
9	38%	Multiple Sclerosis	We matched the terms: weakness   vision   headache   headaches   gait   decreased
10	37%	Fibromyalgia	We matched the terms: headache   headaches   hip pain   shoulder pain   pain in shoulders   decreased

Please note: Check your spelling. The term/s arthralgia, ibuprophen, ketorolac, shot may not have influenced

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Case Number **McGMS Case 6** **Tubulointerstitial nephritis and uveitis (TINU syndrome) AKA Dobrin syndrome**

**Isabel Pro Healthcare**

**Date Entered 04/08/\*2020**

**Age** \_\_\_\_\_ Adult, 40-49 yrs

**Gender** Female, Not Pregnant **Travel** North America

**Chief Complaints**

- 1 Weakness
- 2 Right eye swelling with discharge and vision change
- 3 Intermittent headaches 4 Arthralgia both hips 5 Gait pain both hips
- 6 Right Shoulder Pain with decreased range of motion
- 7 Wrist pain bilateral

**Medications**

- 1 Ibuprophen
- 2 Ketorolac shot
- 3 Vitamin D2

**Medical History**

- 1 Polycystic Ovary Syndrome

**Allergies**

- 1 NKA

**Immunizations**

- 1 N/A

## Exhibit 9

## Translational Project - Diagnostic Decision Support Systems

Validation Project

[Reference](#)

McGMS

20200306

Cards Case

Conference -

Final

lupus myocarditis

Case Number

[Isabel Pro Healthcare](#)[Date Entered 4/9/2020](#)

Ranked	% Match	Diagnostic Alternatives	Reasons
1	90%	Heart Failure / CHF	We matched the terms: palpitation   palpitations   shortness of breath   dyspnea   dyspnoea   short of breath   difficulty breathing   sle   hypertension   hypertensive   elevated blood pressure   asthma
2	84%	Renal Failure	We matched the terms: palpitation   palpitations   shortness of breath   severe diarrhoea   cardiac arrest   hypertension   nausea   vomiting   nephritis   alcohol
3	77%	SLE	We matched the terms: systemic lupus erythematosus   sle   systemic lupus   hypertension   nephritis   drug   lupus   personality   mycophenolate   rituximab
4	59%	Antiphospholipid Syndrome	We matched the terms: shortness of breath   short of breath   systemic lupus erythematosus   systemic lupus   alveolar haemorrhage   hypertension   nausea   vomiting
5	51%	Asthma	We matched the terms: dyspnea   asthma   asthma attack   asthmatic   prednisone   intravenous   drug
6	51%	Sarcoidosis	We matched the terms: shortness of breath   dyspnea   difficulty breathing   difficult breathing   cardiac arrest
7	49%	Lyme Disease	We matched the terms: palpitation   palpitations   shortness of breath   sle   flat   nausea   vomiting
8	48%	Pulmonary Hypertension	We matched the terms: palpitation   palpitations   heart palpitation   heart palpitations   shortness of breath   dyspnea   breathlessness   breathless   sle   cardiac
9	46%	Substance Abuse	We matched the terms: sle   hypertension   lying   nausea   intravenous   drug   mood   user
10	45%	Churg-Strauss Syndrome	We matched the terms: shortness of breath   alveolar hemorrhage   hypertension   asthma   asthma attack
			Please note: Check your spelling. The term/s torsades, tonsillectomy, recreational, marijuana, borderline, depakote, hydroxyzine, carafate, gabapentin, lisinopril, plaquenil, bactrim, morphine, metoprolol may not have influenced the result.

## Translational Project - Diagnostic Decision Support Systems

Validation Project

[Reference](#)

McGMS

20200306

Cards Case

Conference -

Final

lupus myocarditis

Case Number

Isabel Pro HealthcareDate Entered 4/9/2020Age Young Adult 17-29 yrsGender Female, Unknown if Pregnant Travel North America**Chief Complaints**

- 1 Palpitations Acute
- 2 Shortness of Breath Acute Worsening with walking talking lying flat
- 3 Nausea Vomiting
- 4 chronic diarrhea

**Medications**

- 1 Depakote
- 2 hydroxyzine
- 3 carafate
- 4 gabapentin
- 5 lisinopril
- 6 mycophenolate
- 7 plaquenil
- 8 prednisone

**Medical History**

- 1 fungal esophagitis
- 2 colonic inflammation
- 3 Systemic Lupus Erythematosus
- 4 lupus nephritis
- 5 Diffuse Alveolar Hemorrhage
- 6 torsades with cardiac arrest
- 7 mixed mood disorder
- 8 Hypertension
- 9 asthma
- 10 Tonsillectomy
- 11 recreational marijuana user
- 12 recreational alcohol use
- 13 IntraVenous Drug User
- 14 Family history of borderline personality disorder
- 15 Family history of suicide
- 16 Family history of diabetes mellitus
- 17 family history of hypertension

**Allergies****Immunizations**

- |   |            |     |
|---|------------|-----|
| 1 | Bactrim 1  | N/A |
| 2 | Morphine   |     |
| 3 | rituximab  |     |
| 4 | metoprolol |     |

## Exhibit 10

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

McGMS  
20200306 Case  
Conference  
Pulmonary 3\_6 -  
Final

Acute necrotizing pancreatitis complicated by recurrent  
left exudative pleural effusion

Case Number

Isabel Pro Healthcare

Date Entered

<u>Ranked</u>	<u>% Match</u>	<u>Diagnostic Alternatives</u>	<u>Reasons</u>
1	100%	Aortic Aneurysm / Dissection	We matched the terms: acute abdominal pain   first episode acute abdominal pain   hypertension   high blood pressure   high cholesterol   diabetes   quadrant
2	100%	Heart Failure / CHF	We matched the terms: shortness of breath   dyspnea   dyspnoea   short of breath   difficulty breathing   cough   decreased appetite   hypertension   hypertensive   elevated blood pressure   diabetes   quadrant   back
3	100%	Ischemic Heart Disease	We matched the terms: acute abdominal pain   first episode acute abdominal pain   shortness of breath   dyspnea   dyspnoea   difficulty breathing   cough
4	98%	Coronavirus	We matched the terms: shortness of breath   dyspnea   difficulty breathing   labored breathing   coughing   cough   anorexia   loss of appetite   hypertension
5	79%	Diabetic Ketoacidosis	We matched the terms: acute abdominal pain   first episode acute abdominal pain   shortness of breath   breathing difficulty   difficulty breathing   breathing difficult   labored breathing   loss of appetite
6	69%	Peritonitis	We matched the terms: acute abdominal pain   first episode acute abdominal pain   cough   anorexia
7	63%	Lung Neoplasms	We matched the terms: shortness of breath   dyspnea   coughing   cough   loss of appetite   nausea   vomiting
8	62%	Biliary Colic	We matched the terms: acute abdominal pain   first episode acute abdominal pain   quadrant   back
9	57%	Acute Appendicitis	We matched the terms: acute abdominal pain   first episode acute abdominal pain   anorexia   loss of appetite   reduced appetite   quadrant   back   nausea
10	53%	Bacterial Pneumonia	We matched the terms: shortness of breath   dyspnea   difficulty in breathing   coughing   cough   quadrant
			Please note: Check your spelling. The term/s losartan, pravastatin, metformin may not have influenced the

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

**Case Number** **McGMS**  
**20200306 Case**  
**Conference**  
**Pulmonary 3\_6 -**  
**Final** **Acute necrotizing pancreatitis complicated by recurrent**  
**left exudative pleural effusion**

**Isabel Pro Healthcare****Date Entered****Age** Adult 50-64 years**Gender** Male**Travel** North America**Chief Complaints**

- 1 acute Abdominal pain aching upper left quadrant epigastrium radiating to back
- 2 Nausea vomiting
- 3 shortness of breath with exertion
- 4 cough
- 5 anorexia

**Medications**

- 1 losartan
- 2 pravastatin
- 3 metformin
- 4 aspirin

**Medical History**

- 1 hypertension
- 2 hypercholesterolemia
- 3 non-insulin dependent type 2 diabetes mellitus
- 4 family history of hypertension
- 5 family history of diabetes

**Allergies**

- 1 NKA

**Immunizations**

- 1



## Exhibit 11

## Translational Project - Diagnostic Decision Support Systems

## Validation Project

ResultsGold Standard Diagnosis

Case Number

52-36001

Acromegaly (diabetic ketoacidosis)

Isabel Pro HealthcareDate Entered

<u>Ranked</u>	<u>% Match</u>	<u>Diagnostic Alternatives</u>	<u>Reasons</u>
1	99%	Diabetic Ketoacidosis	We matched the terms: polyuria   excessive thirst   increased thirst   thirst   frequent urination   dry mouth   nausea   vomiting   nausea and vomiting   vomit   weakness   general weakness   hypokalemia   fruity   mouth   odor
2	56%	Hyperthyroidism	We matched the terms: polyuria   polydipsia   nausea   vomiting   nausea and vomiting   vomit   generalised weakness   weakness   weight loss   congestive heart failure   hypokalemia   hypokalemic   eye
3	50%	Type 1 Diabetes	We matched the terms: polyuria   diuresis   polydipsia   increased thirst   thirst   nocturia   xerostomia   nausea   vomiting   nausea and vomiting   vomit   weakness   weight loss
4	46%	Diabetic Neuropathy	We matched the terms: nocturia   nausea   vomiting   vomit   weakness   weight loss   mouth   eye
5	42%	Intersitital Nephritis - Analgesics Nephropathy; Drug and Toxininduced Nephropathy	We matched the terms: polyuria   increased urinary frequency   frequency of urination   nocturia   nausea   vomiting   vomit   weakness   weight loss   mouth
6	37%	Renal Failure - Acute Renal Failure; Chronic Renal Failure	We matched the terms: thirst   nausea   vomiting   vomit   weight loss   congestive heart failure   chf   hypokalemia   mouth   eye
7	35%	Heart Failure/CHF	We matched the terms: polyuria   need to urinate at night   nausea   vomiting   vomit   weakness   congestive heart failure   chf   sudden death
8	32%	Dehydration	We matched the terms: thirsty   extreme thirst   thirst   frequent urination   dry mouth   nausea   vomiting   vomit   weakness   mouth

9	31%	Pyelonephritis	We matched the terms: polyuria   increased urinary frequency   frequency of urination   nocturia   need to urinate at night   nausea   vomiting   nausea and vomiting   vomit   odor
10	30%	Aortic Aneurysm/Dissection - Thoracic Aortic Aneurysm	We matched the terms: dry mouth   nausea   vomiting   vomit   weakness   smoking   sudden cardiac death   mouth

Please note: Check your spelling. The term/s digoxin, nitroglycerine, terbutaline, pilocarpine, drops may not have influenced the result.

**Translational Project - Diagnostic Decision Support Systems****Validation Project****Results****Gold Standard Diagnosis****Case Number** 52-36001 **Acromegaly (diabetic ketoacidosis)****Isabel Pro Healthcare** **Date Entered****Age** 56**Gender** Male**Travel** North America**Chief Complaints**

- 1 Polyuria
- 2 Polydipsia

**Symptoms, Pre-encounter Observations**

- 1 Frequent Urination
- 2 Night Urination
- 3 Thirsty
- 4 Dry Mouth
- 5 Fruity Mouth Odor
- 6 Nausea
- 7 Vomiting
- 8 Generalized Weakness
- 9 Weight Loss
- 10 Elevated Blood Pressure

**Medications**

- 1 Digoxin
- 2 Furosemide
- 3 Potassium
- 4 Nitroglycerine Patch
- 5 Theophylline
- 6 Terbutaline
- 7 Prednisone
- 8 Pilocarpine Eye Drops

**Medical History**

- 1 COPD
- 2 Congestive Heart Failure
- 3 Glaucoma, right eye
- 4 Family History of Myocardial Infarction
- 5 Family History of Glaucoma
- 6 Former Smoker

**Allergies**

- 1

**Immunizations**

- 1

## Exhibit 12

Translational Project - Diagnostic Decision Support Systems  
 Validation Project  
 Case Number 33-36133

Results  
**Gold Standard Diagnosis**  
 Pernicious Anemia

<b><i>Ranked</i></b>	<b><i>% Match</i></b>	<b><i>Diagnostic Alternatives</i></b>	<b><i>Reasons</i></b>
1	100%	Iron Deficiency	We matched the terms: generalised weakness   weakness   malaise   fatigue   tired   exhaustion   tinnitus   pulsatile tinnitus   insomnia   decreased appetite   poor appetite   tingling   anaemia   anemia   low hemoglobin   shortness of breath on exertion   iron deficiency anemia   soreness
2	93%	Megaloblastic Anemias - Pernicious Anemia; Vit B12 Deficiency - Pernicious Anemia; Subacute Combined Degeneration of Spinal Cord	We matched the terms: weakness   depression   fatigue   tinnitus   anorexia   loss of appetite   paresthesia   tingling   paresthesias   numbness   tingling and numbness   hand tingling   constipation   anaemia   anemia   pyrexia   exertional dyspnea   peri
3	65%	Celiac Disease	We matched the terms: weakness   depression   fatigue   lethargy   decreased appetite   numbness   constipation   anemia   iron
4	65%	Crohn Disease	We matched the terms: malaise   fatigue   anorexia   loss of appetite   constipation   anemia   fever   pyrexia   peri   bleeding   bacterial
5	63%	Hypothyroidism	We matched the terms: weakness   depressed mood   depressed   tiredness   fatigue   lethargy   tired   insomnia   poor sleep   poor appetite   paresthesia   paraesthesia   constipation   anemia   dyspnoea on exertion   peri
6	60%	Granulomatosis with Polyangiitis	We matched the terms: weakness   malaise   fatigue   loss of appetite   anemia   fever   shortness of breath on exertion   peri   mouth   middle   pneumonia
7	59%	Heavy Metal Intoxication	We matched the terms: weakness   depression   fatigue   insomnia   loss of appetite   numbness   constipation   anemia   iron deficiency anemia   peri
8	57%	Brucellosis	We matched the terms: weakness   depression   depressed   malaise   fatigue   insomnia   anorexia   loss of appetite   constipation   fever   febrile   fevers   per

9	52%	Myelitis - Transverse Myelitis	<p>We matched the terms:  weakness   depression   malaise   tiredness   fatigue    tired   loss of  appetite   paresthesia   paraesthesia   tingling   par  esthesias   numbness   leg  numbness   parasthesia   constipation   fever   doe</p>
10	49%	Hodgkin Disease	<p>We matched the terms:  weakness   depression   malaise   tiredness   fatigue    tired   anorexia   loss of appetite   appetite  loss   paresthesia   paresthesias   anaemia   anemia    fever   fevers   peri</p>
			<p>Please note: Check your spelling. The  term/s menopausal, radical, mastectomy,  hemithyroidectomy, nortriptyline, epsom, salts may  not have influenced the result.</p>

Translational Project - Diagnostic Decision Support Systems  
Validation Project  
Case Number 33-36133

Results  
**Gold Standard Diagnosis**  
Pernicious Anemia

**Age** 48

**Gender** Female

**Travel** North America

**Chief Complaints**

1 Weakness

**Symptoms, Pre-encounter Observations**

- 1 multinodular goiter
- 2 depression
- 3 breast cancer
- 4 fatigue
- 5 ringing in head
- 6 irregular, profuse vaginal bleeding
- 7 peri-menopausal bleeding
- 8 moodiness
- 9 sleeplessness
- 10 anorexia
- 11 numbness & tingling of hands and feet
- 12 constipation
- 13 anemia
- 14 low hematocrit
- 15 low hemoglobin
- 16 fever
- 17 dyspnea on exertion
- 18 mouth soreness

**Medications**

- 1 Nortriptyline
- 2 Epsom Salts

**Medical History**

- 1 Iron deficiency anemia
- 2 dysfunctional uterine bleeding
- 3 History of Middle lobe pneumonia
- 4 history of bacterial pneumonia
- 5 history of radical mastectomy
- 6 history of hemithyroidectomy

**Allergies**

1

**Immunizations**

1

## Exhibit 13

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

**Gold Standard Diagnosis**

Case Number 25-36143 Polymyalgia Rheumatica

Isabel Pro Healthcare Date Entered

<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Osteoarthritis	We matched the terms: shoulder pain   knee pain   neck pain   cervical spine pain   joint pain   arthritis   pip joint   pip joints   pip   morning stiffness
2	88%	Polymyalgia Rheumatica	We matched the terms: shoulder pain   difficulty raising arms above head   arthralgias   arthralgia   arthritis   morning stiffness   loss of appetite   weight loss   anemia
3	6200%	Rheumatoid Arthritis	We matched the terms: shoulder pain   painful joints   painful joint   joint pain   arthritis   morning stiffness   loss of appetite   weight loss   anemia
4	58%	Adult Still Disease	We matched the terms: knee pain   arthralgia   joint pain   polyarthralgia   arthritis   poor appetite   weight loss   unexplained weight loss   anaemia   decreased red blood cell count
5	54%	SLE	We matched the terms: arthralgia   arthritis   arthropathy   anorexia   weight loss   anaemia   hypertension   renal failure
6	52%	Heavy Metal Intoxication - Lead Toxi	We matched the terms: arthralgias   arthralgia   loss of appetite   weight loss   anemia   hypertension   renal failure
7	51%	Lung Neoplasms	We matched the terms: shoulder pain   joint pain   loss of appetite   appetite loss   weight loss   unexplained weight loss   anemia
8	50%	Cryoglobulinemia	We matched the terms: arthralgias   arthralgia   joint pain   joint ache   arthritis   pip joint   pip joints   pip   weight loss   hypertension   high blood pressure   renal failure
9	49%	Endocarditis	We matched the terms: arthralgia   joint pain   arthritis   anorexia   weight loss   anemia   renal failure
10	49%	Osteomyelitis and Septic Arthritis	We matched the terms: shoulder pain   knee pain   painful joints   painful joint   joint pain   weight loss   unexplained weight loss

Translational Project - Diagnostic Decision Support Systems  
Validation Project [Results](#)

Gold Standard Diagnosis

Case Number 25-36143 Polymyalgia Rheumatica

Isabel Pro Healthcare Date Entered Age 65

Gender Female

Travel North America

**Chief Complaints**

- 1 Shoulder Pain, Bilateral
- 2 Knee Pain, Bilateral
- 3 Neck Pain

**Symptoms, Pre-encounter Observations**

- 1 Arthritis
- 2 Proximal Interphalangeal Joint Pain
- 3 Morning Stiffness
- 4 Anorexia
- 5 Weight Loss
- 6 Hemoglobin Low

**Medications**

1

**Medical History**

- 1 Hypertension
- 2 Multinodular Goiter
- 3 Renal Insufficiency

**Allergies**

- 1 NKA

**Immunizations**

- 1 N/A



<b>Exhibit 14</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
			<b>Gold Standard Diagnosis</b>
<b>Case Number</b>	55-36021		Carcinoid Syndrome
<b>Isabel Pro Healthcare</b>			<b>Date Entered</b>
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Anaphylaxis	We matched the terms: diarrhea   flushing   facial flushing   flush   chest   shortness of breath   dyspnea   dyspnoea   difficulty breathing   respiratory distress   wheezing   neck   pruritic   rash   arms
2	84%	Carcinoid Syndrome	We matched the terms: diarrhoea   flushing   flush   thorax   breathlessness   breathless   wheezing   weight loss   alcohol   pruritic
3	80%	Coronavirus - COVID-19	We matched the terms: diarrhea   dark urine   chest   shortness of breath   dyspnea   difficulty breathing   labored breathing   respiratory distress   wheezing   wheeze   weight loss   rash
4	68%	Non-Hodgkin Lymphoma	We matched the terms: diarrhea   watery diarrhea   chest   shortness of breath   trouble breathing   wheezing   weight loss   neck
5	63%	Lung Neoplasms- Non-Small Cell Lung Cancer; Bronchogenic Carcinoma	We matched the terms: chest   rib   shortness of breath   dyspnea   dyspnoea   breathing problem   breathing problems   wheezing   weight loss   unexplained weight loss   neck
6	58%	Hodgkin Disease	We matched the terms: chest   shortness of breath   breathing difficulty   breathing difficult   wheezing   weight loss   unexplained weight loss   alcohol   neck   rash
7	50%	Whipple Disease	We matched the terms: diarrhea   diarrhoea   clay coloured stool   clay coloured stools   chest   shortness of breath   breathing difficulty   breathing difficult   weight loss   rash
8	45%	Hyperthyroidism	We matched the terms: diarrhea   flushing   flush   chest   shortness of breath   dyspnea   weight loss   neck
9	44%	Salmonella Infections - Typhoid	We matched the terms: diarrhoea   flushed face   flush   flushed   wheeze   wheezes   weight loss   rash   arms
10	43%	Bacterial Pneumonia	We matched the terms: flushing   flush   chest   rib   shortness of breath   labored breathing   respiratory distress   wheezing   weight loss
<b>Age</b>	62		
<b>Gender</b>	Male		
<b>Travel</b>	North America		
<b>Chief Complaints</b>			
1	Diarrhea		
<b>Symptoms, Pre-encounter Observations</b>			
1	Watery Diarrhea		
2	Light tan stool		
3	dark urine		
4	facial flushing		
5	neck flushing		
6	pruritic rash on arms and chest		
7	shortness of breath		
8	wheezing		
9	weight loss		
10	alcohol		
<b>Medications</b>			
1	None		
<b>Medical History</b>			
1	Hyperlipidemia		
2	elevated cholesterol		
3	elevated triglycerides		
<b>Allergies</b>			
1	NKA		
<b>Immunizations</b>			
1			

## Exhibit 15

Translational Project - Diagnostic Decision Support Systems			
Validation Project		Results	
		Gold Standard Diagnosis	
Case Number	65-36093	Subarachnoid Hemorrhage	
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	99%	Intracranial Hypertension - Pseudotumor Cerebri	We matched the terms: blurred vision   nausea   vomiting   vomit   systemic hypertension   hypertension   headache   headaches   neck pain   pulsating   shoulder
2	91%	Intracranial Hemorrhage - Subarachnoid Hemorrhage	We matched the terms: orbital pain   nausea   vomiting   nausea and vomiting   vomit   hypertension   headache   headaches   neck pain   herniation
3	69%	Brain Neoplasms	We matched the terms: nausea   nauseated   vomiting   vomit   headache   headaches   neck pain   shoulder   herniation
4	69%	Ischemic Heart Disease - Non ST Elevation Myocardial Infarction; Myocardial Infarction/Acute Coronary Syndrome; Non ST Elevation Myocardial Infarction; ST Elevation Myocardial Infarction	We matched the terms: nausea   vomiting   vomit   hypertension   neck pain   depression   depressed   shoulder   radiating   disc
5	60%	Headache Disorders - Cluster Headache	We matched the terms: orbital pain   nasal congestion   tearing eye   tearing eyes   nausea   vomiting   vomit   headache   headaches   cephalalgia   cephalalgias   pain head
6	56%	Pancreatitis - Acute Pancreatitis	We matched the terms: nausea   vomiting   vomit   headache   alcohol   shoulder   radiating
7	54%	Postpartum Eclampsia	We matched the terms: blurred vision   nausea   vomiting   vomit   hypertension   high blood pressure   headache   headaches   neck pain
8	53%	Orbital Cellulitis	We matched the terms: eye pain   ocular pain   blurred vision   eye swelling   nausea   vomiting   vomit   headache   disc
9	52%	Fibromuscular Dysplasia	We matched the terms: blurred vision   nausea   high blood pressure   headache   headaches   neck pain   pulsating   disc
10	52%	Neuromyelitis Optica Spectrum Disorders	We matched the terms: eye pain   ocular pain   nausea   vomiting   nausea and vomiting   vomit   headache   headaches   neck pain   disc
Please note: Check your spelling. The term/s suicide, attempt, hysterectomy may not have influenced the result.			
Age	46		
Gender	Female		
Travel	North America		
<b>Chief Complaints</b>			
1	Right Maxillary Sinus Pressure		
<b>Symptoms, Pre-encounter Observations</b>			
1	Right Eye Pop		
2	Sinusitis		
3	Pulsating, spasm-like sinus pressure		
4	blurred vision		
5	eye swelling		
6	eye tearing		
7	nausea		
8	vomiting		
9	fullness in right ear		
10	High blood pressure		
<b>Medications</b>			
1	None		
<b>Medical History</b>			
1	History of headaches		
2	pain in left neck radiating to left shoulder		
3	pain in whole head		
4	depression		
5	attempted suicide		
6	C6 radiculopathy		
7	C5/6 central disc herniation		
8	History of hysterectomy		
9	alcohol		
10	Family History of colon cancer		
<b>Allergies</b>			
1			
<b>Immunizations</b>			
1			

## Exhibit 16

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	Gold Standard Diagnosis
Case Number	45-36053		Crohn's Disease
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	90%	Colorectal Cancer - Hereditary Nonpolyposis Colon Cancer	We matched the terms: gastrointestinal bleeding   melena   black stools   black stool   blood in stool   rectal bleeding   lower gastrointestinal bleed   bright red stools   bright red stool   lower abdominal pain   hemoccult positivity   occult bleeding   fecal occult blood test   fecal occult blood testing   fecal occult blood   anemia   fever   blood   colon
2	75%	Ischemic Heart Disease - Myocardial Infarction/Acute Coronary Syndrome; Non ST Elevation Myocardial Infarction; ST Elevation Myocardial Infarction; Angina	We matched the terms: anaemia   fever   aortic regurgitation   hypertension   high blood pressure   blood   aortic   valve   stenosis
3	71%	Peptic Ulcer Disease	We matched the terms: gastrointestinal bleeding   melena   blood in stool   occult blood loss   hemoccult positivity   anemia   fever   gastritis   blood
4	65%	Aortic Stenosis	We matched the terms: fever   left ventricular hypertrophy   blood   aortic   valve   thickened   stenosis
5	62%	Crohn Disease	We matched the terms: gastrointestinal bleeding   bloody stools   hematochezia   rectal bleeding   bloody stool   anemia   fever   pyrexia   leukocytosis   blood
6	49%	Acute Appendicitis	We matched the terms: right lower quadrant pain   rlq pain   lower right quadrant abdominal pain   lower abdominal pain   fever   elevated temperature   elevated temp   leukocytosis   high white cell count   elevated white blood cell count   blood
7	47%	Endocarditis	We matched the terms: anemia   fever   fevers   leukocytosis   aortic regurgitation   blood   aortic   terminal
8	45%	Diverticular Diseases of the Colon - C	We matched the terms: right lower quadrant abdominal pain   rectal bleeding   lower abdominal pain   fever   high white blood cell count   elevated white blood cell count   blood
9	43%	Churg-Strauss Syndrome	We matched the terms: gastrointestinal bleeding   anemia   fever   leukocytosis   gastritis   hypertension
10	43%	Relapsing Polychondritis	We matched the terms: anemia   fever   febrile   leukocytosis   aortic regurgitation   aortic   stenosis
Please note: Check your spelling. The term/s aspirin, caffeine may not have influenced the result.			
Age	30		
Gender	Male		
Travel	North America		
<b>Chief Complaints</b>			
1	Gastrointestinal Bleeding		
<b>Symptoms, Pre-encounter Observations</b>			
1	Lower Right Quadrant Abdominal Pain		
2	Dark Bowel Movement		
3	Bright Red Blood from rectum		
4	lower abdomen cramping		
5	Guaiac positive stool		
6	Hematocrit low (37 to 34)		
7	fever		
8	White Blood Count 17X109/L		
9	blood throughout the colon		
10	blood in the terminal ileum		
11	mild gastritis		
12	thickened aortic valve		
13	sever aortic stenosis		
14	mild aortic insufficiency		
15	concentric left ventricular hypertrophy		
16	high blood pressure		
<b>Medications</b>		<b>Medical History</b>	
1	aspirin	1	
2	acetaminophen	Allergies	
3	caffeine	1	
		<b>Immunizations</b>	
		1	

## Exhibit 17

Translational Project - Diagnostic Decision Support Systems			
Validation Project		Results	
		Gold Standard Diagnosis	
Case Number	64-36072	Hemolytic Uremic Syndrome	
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	99%	Antiphospholipid Syndrome	We matched the terms: anemia   peripheral edema   leg swelling   hypertension   tachypnea   rapid breathing   thrombocytopenia   low platelet count   low platelet   thrombocytopenic
2	88%	Glomerulonephritis - Membranoproliferative	We matched the terms: anemia   hypertension   chronic glomerulonephritis   proteinuria
3	83%	Systemic Sclerosis - Progressive systemic Sclerosis	We matched the terms: anemia   hypertension   hypertensive   hypothyroidism   hypothyroid   pulmonary fibrosis   proteinuria
4	74%	renal Failure - Chronic Renal Failure	We matched the terms: anemia   lower extremity edema   hypertension   high blood pressure   tachypnea   proteinuria
5	70%	SLE - Lupus Nephritis	We matched the terms: anemia   hypertension   thrombocytopenia   proteinuria
6	64%	Hemolytic Uremic Syndrome	We matched the terms: anemia   hypertension   high blood pressure   thrombocytopenia   proteinuria
7	64%	Thrombotic Thrombocytopenic Purpura	We matched the terms: anaemia   anemia   low haemoglobin   hypertension   high blood pressure   thrombocytopenia   decreased platelet count   thrombocytopenic   proteinuria
8	59%	Drug Induced Thrombocytopenia	We matched the terms: anemia   hypertension   thrombocytopenia
9	53%	Pulmonary Edema	We matched the terms: lower extremity edema   hypertensive   rapid breathing   proteinuria
10	51%	Arteriolar Nephrosclerosis	We matched the terms: anemia   hypertension   hypertensive   elevated blood pressure   arterial hypertension   proteinuria
Please note: Check your spelling. The term/s synthroid, ranitidine, verapamil may not have influenced the result.			
<b>Age</b>	65		
<b>Gender</b>	Female		
<b>Travel</b>	North America		
<b>Chief Complaints</b>			
1	Anemia		
<b>Symptoms, Pre-encounter Observations</b>			
1	Low Hematocrit		
2	leg swelling		
3	high blood pressure		
4	elevated respiration rate		
<b>Medications</b>			
1	Synthroid		
2	prednisone		
3	furosemide		
4	ranitidine		
5	verapamil		
<b>Medical History</b>			
1	Thrombocytopenia		
2	Hypothyroidism		
3	Membranous glomerulonephritis		
4	pulmonary fibrosis		
5	proteinuria		
<b>Allergies</b>		<b>Immunizations</b>	
1	NKA	1	N/A

## Exhibit 18

Translational Project - Diagnostic Decision Support Systems			
Validation Project		Results	
		Gold Standard Diagnosis	
Case Number	23-36113	Hemachromatosis	
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	99%	Heart Failure/CHF	We matched the terms: elevated hemoglobin   abnormal liver function tests   abnormal liver function   fatigue   tired   exertional dyspnea   dyspnea on exertion   nonproductive cough   cardiomegaly   hypertension   hypertensive   elevated blood pressure   congestive heart failure   chf   elevated
2	55%	Heart Neoplasms - Cardiac Myxoma	We matched the terms: thrombocytopenia   polycythemia   malaise   fatigue   dyspnea on exertion   arthralgia   joint pain   cardiomegaly   hypertension   congestive heart failure   elevated
3	55%	Interstitial Lung Disease - Idiopathic	We matched the terms: tiredness   fatigue   lethargy   tired   exertional dyspnea   shortness of breath on exertion   dry cough   nonproductive cough   hacking cough   aching joints   cardiomegaly   hypertension   elevated
4	53%	Liver Neoplasms - Hepatocellular Car	We matched the terms: splenomegaly   thrombocytopenia   polycythemia   erythrocytosis   malaise   tired   easy bruising   upper abdominal pain   elevated   cancer
5	51%	Drug Induced Thrombocytopenia	We matched the terms: thrombocytopenia   easy bruising   hypertension   congestive heart failure   cancer   acid
6	49%	Babesiosis	We matched the terms: splenomegaly   enlarged spleen   thrombocytopenia   malaise   fatigue   nonproductive cough   arthralgias   arthralgia   joint ache   elevated   reticulocyte
7	47%	Hemochromatosis	We matched the terms: splenomegaly   abnormal liver function tests   abnormal liver function   lassitude   polyarthritis   arthropathy   enlarged heart   hypertension   congestive heart failure
8	43%	Relapsing Fever	We matched the terms: enlarged spleen   thrombocytopenia   low platelet   low platelets   malaise   fatigue   dry cough   nonproductive cough   arthralgias   arthralgia   joint ache   elevated
9	42%	Endocarditis	We matched the terms: splenomegaly   thrombocytopenia   malaise   fatigue   doe   arthralgia   joint pain   arthritis   congestive heart failure   elevated   acid
10	42%	Viral Hepatitis - Hepatitis C	We matched the terms: low platelet count   low platelet   abnormal liver function tests   abnormal liver function   malaise   tiredness   fatigue   tired   arthralgia   joint pain   epigastric pain   pain epigastric   elevated
			Please note: Check your spelling. The term/s hyperplasia, cholelithiasis, tonsillectomy, inguinal, herniorrhaphy, ranitidine, folic, lasix may not have influenced the result.
Age	50	Chief Complaints	
Gender	Male	1	Splenomegaly
Travel	North America	2	Thrombocytopenia
Symptoms, Pre-encounter Observations		Medical History	
1	Erythroid Hyperplasia	1	Adult onset Diabetes
2	Ring Sideroblasts	2	Hiatal Hernia
3	Cholelithiasis	3	Kidney Stone Removal
4	Fetal Hemoglobin Elevated	4	Tonsillectomy
5	Reticulocyte Elevated	5	Left Inguinal Herniorrhaphy
6	Abnormal Liver function	6	Family History of Pancreatic Cancer
7	Fatigue	7	Family History of Congestive Heart Failure
8	Dyspnea on Exertion	9	Family History of Honeycomb Lung
9	Bruises Easily	Medications	
10	Non-productive Cough	1	Glyburide
11	Arthritis	2	ranitidine
12	Enlarged Heart	3	Folic Acid
13	Suprapubic Pain	4	Lasix
14	Epigastric Pain	Allergies	
15	Sour Taste in Mouth	1	None
16	Blood Pressure High	Immunizations	
		1	None

## Exhibit 19

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	36-36012	Metastatic Hepatic Adeno (liver) Cancer	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	90%	Celiac Disease	We matched the terms: weight loss   unexplained weight loss   abdominal distention   abdominal bloating   bloating   bloat   fatigue   lethargy   lactose intolerance   wasting   anemia   nausea
2	84%	Cirrhosis	We matched the terms: weight loss   abdominal distention   distended abdomen   abdominal swelling   tiredness   fatigue   tired   peripheral edema   swollen legs   swollen leg   muscle wasting   wasting   anemia   nausea
3	79%	Gastritis - Menetrier's Disease	We matched the terms: weight loss   abdominal swelling   peripheral edema   cachexia   anemia   nausea   eating
4	78%	Crohn Disease	We matched the terms: weight loss   unexplained weight loss   abdominal swelling   malaise   fatigue   anemia   nausea   eating
5	72%	Lactose Intolerance	We matched the terms: weight loss   abdominal distention   abdominal bloating   bloating   bloat   lethargy   lactose intolerance   nausea   eating
6	72%	Non-Hodgkin Lymphoma - Burkitt Lym	We matched the terms: weight loss   abdominal distention   abdominal bloating   bloating   bloat   malaise   tiredness   fatigue   tired   swelling leg   legs swelling   swelling legs   anemia   eating
7	69%	Gastroparesis	We matched the terms: weight loss   swollen abdomen   abdominal bloating   bloating   bloated stomach   excess gas   bloated   bloat   fatigue   hypothyroidism   hypothyroid   nausea   eating
8	64%	Liver Neoplasms - Hepatocellular Carcinoma	We matched the terms: weight loss   abdominal distention   abdominal distension   abdominal swelling   swollen abdomen   malaise   tired   cachexia   anemia   nausea
9	62%	Interstitial Nephritis - Analgesics Nephropathy	We matched the terms: weight loss   malaise   tiredness   fatigue   lethargy   tired   hypertension   high blood pressure   peptic ulcer disease   anaemia   anemia   nausea
10	62%	Megaloblastic Anemias - Pernicious Anemia	We matched the terms: loss of weight   weight loss   abdominal bloating   bloating   bloat   fatigue   pedal edema   anaemia   anemia   nausea
			Please note: Check your spelling. The term/s billroth, synthroid, cimetidine may not have influenced the result.
<b>Age</b>	89	<b>Chief Complaints</b>	
<b>Gender</b>	Female	1	Weight Loss
<b>Travel</b>	North America	2	Abdominal Distention
		3	Fatigue
<b>Symptoms, Pre-encounter Observations</b>		<b>Medical History</b>	
1	Nausea when eating	1	Hypothyroidism
2	Lower extremity swelling, bilatera	2	Chronic goiter
3	Lactose intolerance	3	Thyroid mass, stable
4	elevated blood pressure	4	Peptic ulcer disease
5	Cachetic	5	Billroth II surgery
<b>Medications</b>		6	anemia
1	Synthroid	<b>Allergies</b>	
2	Cimetidine	1	None
		<b>Immunizations</b>	
		1	None

## Exhibit 20

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	21-36121	Myasthenia Gravis	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	89%	CVA/Stroke	We matched the terms: diplopia   dysphagia   swallowing difficulty   difficulty swallowing   difficulty swallowing saliva   headache   sore throat   fatigue
2	84%	Motor Neurone Disease - Amyotrophic Lateral Sclerosis	We matched the terms: dysphagia   difficulty swallowing   headache   jaw   fatigue   chewing
3	81%	Antiphospholipid Syndrome	We matched the terms: double vision   headache   headaches   migraine   migraines   hypertension   jaw   fatigue
4	79%	Multiple Sclerosis	We matched the terms: diplopia   double vision   dysphagia   headache   headaches   migraine   migraine headache   fatigue
5	73%	Aortic aneurysm/Dissection - Thoracic Aortic Aneurysm	We matched the terms: dysphagia   dyspnea on exertion   hypertension   jaw   fatigue
6	67%	Lyme Disease	We matched the terms: double vision   headache   headaches   sore throat   jaw   fatigue
7	65%	Guillain-Barre' Syndrome	We matched the terms: diplopia   dysphagia   headache   dyspnea on exertion   fatigue
8	62%	Taenia solium - Cysticercosis	We matched the terms: diplopia   headache   headaches   migraine   migraines   hypertension
9	60%	Myasthenia Gravis	We matched the terms: diplopia   double vision   dysphagia   difficulty in swallowing   difficulty swallowing   difficulty swallowing saliva   fatigue
10	59%	Sleep Apnea - Central Sleep Apnea; Obstructive Sleep Apnea	We matched the terms: difficulty swallowing   headache   headaches   sore throat   high blood pressure   increased blood pressure   fatigue
<b>Age</b>	32	<b>Chief Complaints</b>	
<b>Gender</b>	Male	1	Diplopia
<b>Travel</b>	North America	2	Difficulty Swallowing
<b>Symptoms, Pre-encounter Observations</b>		<b>Medical History</b>	
1	Headache	1	Chondromalacia Patellae
2	Sore Throat	2	Fractured wrist 6 years prior
3	Regurgitation of liquids into nose & mouth	3	Mother had migraine headaches
4	Jaw Fatigue on chewing solids	4	Alcohol user, but quit 5 years ago
5	Mild Dyspnea on exertion	5	Blood Pressure High (134/78)
<b>Medications</b>		6	Pulse Normal (60)
1	N/A	7	Respiration Normal (16)
<b>Allergies</b>		8	Temperature Normal (98.2F)
1	NKA	<b>Immunizations</b>	
		1	N/A

## Exhibit 21

Translational Project - Diagnostic Decision Support Systems				
Validation Project		Results	Gold Standard Diagnosis	
Case Number	13-36043		Amoebic Liver Abscess	
Isabel Pro Healthcare			Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons	
1	90%	Liver Neoplasms	We matched the terms: right upper abdominal pain   right upper quadrant abdominal pain   nausea   liver cancer	
2	87%	Viral Hepatitis	We matched the terms: right upper quadrant abdominal pain   nausea   untreated water	
3	82%	Cholecystitis	We matched the terms: right upper quadrant pain   right upper quadrant abdominal pain   nausea   leukocytosis   elevated white blood cell count	
4	79%	Leptospirosis	We matched the terms: nausea   zoonosis   contaminated water	
5	71%	Infectious Mononucleosis	We matched the terms: right upper quadrant abdominal pain   nausea   elevated white cell count	
6	67%	Cryptococcus Neoformans	We matched the terms: nausea   leukocytosis   zoonosis	
7	66%	Acute Appendicitis	We matched the terms: nausea   leukocytosis   high white cell count   elevated white blood cell count	
8	61%	Yersinia Infection	We matched the terms: nausea   elevated white blood cell count   zoonosis	
9	60%	Liver Abscess (Amoebic, Pyogenic)	We matched the terms: right upper quadrant abdominal pain   nausea   leukocytosis	
10	59%	Pancreatitis	We matched the terms: right upper quadrant abdominal pain   nausea   leukocytosis	
Age	23		Chief Complaints	
Gender	Male		1	Upper Right Quadrant Abdominal Pain
Travel	North America		2	Nausea
<u>Symptoms, Pre-encounter Observations</u>				
1	Space Occupying Liver Lesion Cystic 4cm Posterior			
2	Space Occupying Liver Lesion Cystic 1cm Anterior			
3	White Blood Count High 14.9 x 10 <sup>9</sup> /l			
4	Blood Pressure Normal 102/70			
5	Pulse Normal 76			
6	Temperature Normal 98.6			
Medications	Allergies		Immunizations	
1	None	1 NKA	1	None
<u>Medical History</u>				
1	Works with Animals (Animal Contact)			
2	Drinks from Streams (Untreated Water)			



## Exhibit 22

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	
		Gold Standard Diagnosis	
Case Number	61-36042	Appendicitis	
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	90%	Cystitis/Urethritis	We matched the terms: abdominal pain   right lower quadrant pain   right lower quadrant abdominal pain   left lower quadrant pain   left lower quadrant abdominal pain   microscopic hematuria   pain
2	85%	Urinary Lithiasis/Nephrolithiasis	We matched the terms: abdominal pain   nonspecific abdominal pain   left lower quadrant abdominal pain   microscopic hematuria   pain   lumbar
3	74%	Diverticular Diseases of the Colon - Colon Diverticulitis	We matched the terms: abdominal pain   right lower quadrant abdominal pain   left lower abdominal pain   left lower quadrant abdominal pain   lower left abdominal pain   pain
4	65%	Anterior Cutaneous Nerve Entrapment Syndrome	We matched the terms: abdominal pain   right lower quadrant abdominal pain   left lower quadrant abdominal pain   pain
5	65%	Aortic Aneurysm/Dissection - Abdominal Aortic Aneurysm;	We matched the terms: abdominal pain   right lower quadrant pain   left lower quadrant pain   pain
6	58%	Inflammatory Bowel Disease	We matched the terms: abdominal pain   right lower quadrant pain   left lower quadrant pain   left lower quadrant abdominal pain   pain
7	55%	Testicular Torsion	We matched the terms: abdominal pain   right lower quadrant pain   left lower quadrant pain   pain
8	49%	Ischemic Heart Disease - Angina	We matched the terms: abdominal pain   pain   worsens   walking
9	47%	Acute Appendicitis	We matched the terms: abdominal pain   pain in the abdomen   right lower quadrant pain   rlq pain   lower right quadrant abdominal pain   pain
10	45%	Abdominal Abscess	We matched the terms: abdominal pain   abdominal discomfort   right lower quadrant pain   left lower quadrant pain   pain
<b>Age</b>	48		<b>Chief Complaints</b>
<b>Gender</b>	Male		1 Abdominal Pain
<b>Travel</b>	North America		
<b>Symptoms, Pre-encounter Observations</b>			
1	Right Lower Quadrant Abdominal Pain		
2	Left Lower Quadrant Abdominal Pain		
3	Pain worsens with walking		
<b>Medications</b>			<b>Allergies</b>
1	None		1 NKA
<b>Medical History</b>			<b>Immunizations</b>
1	History of Bell's Palsy		1 None
2	Microscopic hematuria		
3	Lumbar scoliosis		

<b>Exhibit 23</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	24-36063	Brucellosis	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Coronavirus - Covid-19	We matched the terms: weight loss   fever   rigor   rigors   chill   chills   night sweats   sore throat
2	97%	Hodgkin Disease	We matched the terms: weight loss   unexplained weight loss   fever   fevers   night sweats   alcohol
3	91%	Non-Hodgkin Lymphoma - Hepatospl	We matched the terms: weight loss   fever   pyrexia   chill   chills   night sweats
4	87%	Endocarditis	We matched the terms: weight loss   fever   fevers   chill   chills   night sweats   doe
5	87%	Osteomyelitis and Septic Arthritis	We matched the terms: weight loss   unexplained weight loss   fever   rigor   rigors   chill   chills   night sweats
6	81%	Kikuchi Disease	We matched the terms: weight loss   unexplained weight loss   fever   chill   chills   night sweats   sore throat
7	79%	Crohn Disease	We matched the terms: weight loss   unexplained weight loss   fever   pyrexia   chill   chills   night sweats
8	78%	HIV/AIDS - Acute Retroviral Syndrome	We matched the terms: weight loss   fever   rigor   rigors   night sweats   pharyngitis
9	74%	Granulomatosis with Polyangiitis	We matched the terms: weight loss   fever   night sweats   shortness of breath on exertion   tuberculosis
10	73%	Lung Abscess	We matched the terms: weight loss   fever   febrile   rigor   rigors   chill   chills   night sweats
11	73%	Brucellosis	We matched the terms: weight loss   fever   febrile   fevers   chill   chills   night sweats   plant
			Please note: Check your spelling. The term/s cries, meat, packing may not have influenced the result.
<b>Age</b>	38		<b>Chief Complaints</b>
<b>Gender</b>	Male		1 Weight Loss
<b>Travel</b>	North America		
<b>Symptoms, Pre-encounter Observations</b>		<b>Medical History</b>	
1	Fever	1	History of Strep Throat
2	Chills	2	History of Gonorrhea
3	Night Sweats	3	Alcohol
4	Dyspnea with Exertion	4	Family History of tuberculosis
5	Cries Frequently	5	Family History of Sickle Cell Trait
<b>Medications</b>		<b>Allergies</b>	
1	None	1	NKA
		<b>Immunizations</b>	
		1	N/A

## Exhibit 24

Translational Project - Diagnostic Decision Support Systems			
Validation Project		Results	
			Gold Standard Diagnosis
Case Number	11-36052		Colon Cancer
Isabel Pro Healthcare			Date Entered
Ranked	% Match	Diagnostic Alternatives	Reasons
1	100%	Churg-Strauss Syndrome	We matched the terms: anemia   asthma   asthma attack   hypertension
2	97%	Conjunctivitis Disorders	We matched the terms: pallor   asthma   eczema
3	89%	Ischemic Heart Disease	We matched the terms: anemia   cabg   hypertension
4	88%	Hemolytic Uremic Syndrome	We matched the terms: anemia   pallor   pale   hypertension   high blood pressure
5	84%	Drug-Induced Thrombocytopenia	We matched the terms: anemia   acetaminophen   hypertension
6	83%	Thrombotic Thrombocytopenic Purpura	We matched the terms: anaemia   anemia   low haemoglobin   pallor   hypertension   high blood pressure
7	82%	Asthma	We matched the terms: asthma   eczema
8	80%	Cardiogenic Shock	We matched the terms: pale   paleness   coronary artery disease   hypertension
9	77%	Atopic Dermatitis	We matched the terms: pallor   asthma   eczema
10	77%	Hypertensive Retinopathy	We matched the terms: anemia   pallor   hypertension
14	73%	Colorectal Cancer	We matched the terms: lower abdominal pain   anemia   pallor   pale
Age	60		Chief Complaints
Gender	Male		1 Lower Abdominal Pain
Travel	North America		2 Lower Abdominal Cramps
<b>Symptoms, Pre-encounter Observations</b>			3 Severe Anemia
1	Blood Pressure Elevated 132/68		
2	Respiratory Rate Normal 18		
3	Pulse Normal 78		
4	Pale		
5	Hematocrit Low (19.3)		
<b>Medical History</b>			<b>Medications</b>
1	Coronary Artery Disease		1 Acetaminophen
2	Status Post Bypass Grafting		<b>Allergies</b>
3	Asthma		1 NKA
4	Eczema		<b>Immunizations</b>
5	No Family History		1 N/A

## Exhibit 25

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	
		<u>Gold Standard Diagnosis</u>	
Case Number	31-36091	Guillain-Barre Syndrome	
Isabel Pro Healthcare		<u>Date Entered</u>	
<u>Ranked</u>	<u>% Match</u>	<u>Diagnostic Alternatives</u>	<u>Reasons</u>
1	100%	CVA/Stroke	We matched the terms: arm weakness   leg weakness   unable to raise arm   unable to raise arms   hypertensive
2	75%	Osteomyelitis and Septic Arthritis	We matched the terms: hand weakness   lower leg weakness   leg weakness   shoulder pain
3	58%	Lyme Disease - Early Disseminated Lyme Disease	We matched the terms: arm weakness   leg weakness   shoulder pain
4	55%	Intracranial Hematoma - Epidural Hematoma	We matched the terms: arm weakness   leg weakness   hypertension
5	51%	Aortic Arch Syndrome	We matched the terms: arm weakness   lower leg weakness   leg weakness   hypertension
6	49%	Intervertebral Disk Herniation	We matched the terms: interosseous muscle atrophy   lower leg weakness   leg weakness
7	49%	Polymyalgia Rheumatica	We matched the terms: lower leg weakness   leg weakness   shoulder pain   difficulty raising arms above head
8	46%	Rotator Curr Injury	We matched the terms: arm weakness   shoulder pain
9	44%	Thoracic Outlet Syndrome	We matched the terms: arm weakness   hand weakness   shoulder pain   scapular pain
10	40%	Cervical Spondylosis - Cervical Spondylotic Myelopathy	We matched the terms: interosseous muscle atrophy   lower leg weakness   leg weakness
18	33%	Guillain-Barre' Syndrome	We matched the terms: arm weakness   lower leg weakness   leg weakness
<u>Age</u>	67	<u>Chief Complaints</u>	
<u>Gender</u>	Male	1	Arm Weakness, bilateral
<u>Travel</u>	North America	2	Leg Weakness, bilateral
<u>Symptoms, Pre-encounter Observations</u>		<u>Medical History</u>	
1	Unable to sit up	1	N/A
2	unable to move arm or legs	<u>Allergies</u>	
3	Blood Pressure High	1	NKA
<u>Medications</u>		<u>Immunizations</u>	
1	N/A	1	None

Exhibit 26			
Translational Project - Diagnostic Decision Support Systems			
Validation Project		Results	
		Gold Standard Diagnosis	
Case Number	51-36033	Thrombotic Thrombocytopenic Purpura	
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	100%	Sepsis and Shock - Septic Shock	We matched the terms: headache   slurred speech   slurring   shivering   rigor   rigors   chill   chills   shaking chills   dizziness   breathlessness   breathless   lethargy   fever   fevers   high temperature   high temp   hypertension   tachypnea   rapid breathing   fast breathing
2	63%	Coronavirus - COVID-19	We matched the terms: headache   headaches   rigor   rigors   chill   chills   dizziness   shortness of breath   dyspnea   difficulty breathing   labored breathing   respiratory distress   fatigue   fever   hypertension
3	60%	Brucellosis	We matched the terms: headache   chill   chills   dizziness   unsteadiness   dyspnea   difficulty breathing   malaise   fatigue   constipation   fever   febrile   fevers
4	54%	Antiphospholipid Syndrome	We matched the terms: headache   headaches   slurred speech   dizziness   loss of balance   shortness of breath   short of breath   fatigue   fever   hypertension   tachypnea   rapid breathing   occasional
5	51%	Relapsing Fever	We matched the terms: headache   chill   chills   shaking chills   dyspnea   malaise   fatigue   fever   pyrexia   fevers   rapid breathing
6	45%	Adrenal Neoplasms - Pheochromocytoma	We matched the terms: headache   headaches   dyspnea   difficulty breathing   tiredness   tired   constipation   fever   hypertension   high blood pressure   hypertensive   elevated blood pressure   tachypnea
7	45%	Lyme Disease - Early Disseminated Lyme Disease	We matched the terms: headache   headaches   chill   chills   dizziness   shortness of breath   fatigue   lethargy   general fatigue   fever   pyrexia   fevers
8	45%	Non-Hodgkin Lymphoma	We matched the terms: headache   headaches   chill   chills   shortness of breath   trouble breathing   malaise   tiredness   fatigue   tired   constipation   fever   pyrexia
9	44%	Human Granulocytic Anaplasmosis	We matched the terms: headache   headache   headaches   chill   chills   difficulty breathing   malaise   tiredness   fatigue   tired   fever   tachypnea
10	44%	Meningococcal Disease	We matched the terms: headache   headaches   arm weakness   chill   chills   respiratory distress   lethargy   fever   rapid breathing
18	33%	Thrombotic Thrombocytopenic Purpura	We matched the terms: headache   headaches   shortness of breath   respiratory distress   malaise   tiredness   fatigue   tired   fever   hypertension   high blood pressure
Please note: Check your spelling. The term/s marijuana may not have influenced the result.			
Age	20	Chief Complaints	
Gender	Male	1	Headache
Travel	North America	2	Slurred Speech
Symptoms, Pre-encounter Observations		Medications	
1	Weakness in right arm	1	None
2	chills	Medical History	
3	dizziness	1	Marijuana, occasional
4	shortness of breath	Allergies	
5	fatigue	1	NKA
6	constipation	Immunizations	
7	Fever	1	None
8	High blood pressure		
9	elevated respiration rate		

<b>Exhibit 27</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
			<b>Gold Standard Diagnosis</b>
<b>Case Number</b>	54-36092		Osteomalacia
<b>Isabel Pro Healthcare</b>			<b>Date Entered</b>
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	99%	Sleep Apnea - Obstructive Sleep Apnea	We matched the terms: insomnia   sleep disruption   unrefreshing sleep   restless sleep   smoking   weight gain   breathing   abnormal   disease
2	84%	COPD	We matched the terms: smoker   weight gain   breathing   disease   coughing   rib   fracture
3	82%	Heart Failure/CHF	We matched the terms: weight gain   breathing   abnormal   disease   hip
4	73%	Sexual Dysfunction - Erectile Dysfunction	We matched the terms: smoking   abnormal   disease   movement   bowel   prostate
5	72%	Vitamin D Deficiency	We matched the terms: restless sleep   weight gain   disease   hip   rib   joint   acid
6	69%	Pneumoconioses - Asbestosis	We matched the terms: rib pain   sleep disturbance   sleep disturbances   smoker   disease   coughing   rib
7	67%	Osteoarthritis	We matched the terms: disease   fracture   movement   joint   tibia   degenerative   arthroplasty
8	62%	Renal Failure - Chronic Renal Failure	We matched the terms: weight gain   abnormal   disease   acid   potassium
9	61%	Lung Neoplasms - Bronchogenic Carcinoma	We matched the terms: smoker   abnormal   disease   coughing   rib   deeply
10	60%	Chrug-Strauss Syndrome	We matched the terms: disease   bowel   prostate   sneezing
18	52%	Osteomalacia	We matched the terms: abnormal   disease   hip   rib   fracture   tibia
			Please note: Check your spelling. The term/s lithotripsy, resection, morphine, tylenol, nortriptyline, zantac, torecan, azulfidine, synthroid, lasix, chloride, folic may not have influenced the result.
<b>Age</b>	65		<b>Chief Complaints</b>
<b>Gender</b>	Male		1 Severe Right Rib Pain
<b>Travel</b>	North America		
<b>Symptoms, Pre-encounter Observations</b>		<b>Medications</b>	
1	difficulty sleeping	1	Morphine
2	pain with deep breathing	2	Tylenol
3	pain with coughing	3	Nortriptyline
4	pain with sneezing	4	Zantac
5	pain with movement	5	Torecan
6	rib fracture	6	Azulfidine
7	abnormal foci	7	Synthroid
8	smoker	8	Lasix
9	weight gain	9	Potassium Chloride
10	elevated alkaline phosphatase	10	Folic Acid
11	elevated pulse rate		
<b>Medical History</b>		<b>Allergies</b>	
1	Degenerative joint disease	1	
2	arthroplasty of right hip	<b>Immunizations</b>	
3	Nephrolithiasis	1	
4	Lithotripsy		
5	Crohn's Disease		
6	Resection of small bowel		
7	Resection of transverse colon		
8	Transurethral resection of prostate		
9	hypertension		
10	hypothyroidism		

<b>Exhibit 28</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	26-36181	Temporal Arteritis (AKA Giant Cell Arteritis)	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Crohn Disease	We matched the terms: fever   pyrexia   joint pain   arthritis   malaise   fatigue   abdominal pain   pain in abdomen   stomach pain   gastrointestinal bleeding   gastric ulceration   gastric ulcer   stomach ulcer   stomach ulcers
2	81%	Adult Still Disease	We matched the terms: fever   pyrexia   fevers   arthralgia   joint pain   polyarthralgia   arthritis   fatigue   abdominal pain   wrist
3	69%	Polymyalgia Rheumatica	We matched the terms: fever   arthralgias   arthralgia   arthritis   malaise   tiredness   fatigue   tired   wrist   shoulder
4	67%	Lyme Disease	We matched the terms: fever   pyrexia   fevers   arthralgia   joint pain   joint ache   arthritis   arthritic   fatigue   lethargy   general fatigue   wrist   shoulder
5	64%	Churg-Strauss Syndrome	We matched the terms: fever   arthralgias   arthralgia   arthritis   malaise   fatigue   abdominal pain   gastrointestinal bleeding
6	63%	Relapsing Fever	We matched the terms: fever   pyrexia   fevers   arthralgias   arthralgia   joint ache   malaise   fatigue   abdominal pain
7	60%	Whipple Disease	We matched the terms: fever   arthralgia   joint pain   arthritis   polyarthritits   fatigue   abdominal pain   abdominal discomfort   intestinal bleeding
8	59%	Microscopic Polyangiitis	We matched the terms: fever   fevers   arthralgias   arthralgia   joint pain   arthritis   malaise   fatigue   fatigued   abdominal pain   gastrointestinal bleeding
9	57%	Brucellosis	We matched the terms: fever   febrile   fevers   arthralgias   arthralgia   joint pain   malaise   fatigue   abdominal pain
10	54%	Infectious Mononucleosis	We matched the terms: fever   pyrexia   fevers   arthralgias   arthralgia   joint pain   arthritis   malaise   fatigue   abdominal pain
21	43%	Giant Cell Arteritis	We matched the terms: fever   pyrexia   fevers   arthralgias   arthralgia   joint pain   arthritis   malaise   fatigue   abdominal pain
			Please note: Check your spelling. The term/s disalcid, ranitidine may not have influenced the result.
<b>Age</b>	68		<b>Chief Complaints</b>
<b>Gender</b>	Male		1 Fever
<b>Travel</b>	North America		2 Arthralgias
<b>Symptoms, Pre-encounter Observations</b>			<b>Medications</b>
1	Wrist Arthralgia		1 Disalcid
2	Shoulder Arthralgia		2 Ranitidine
3	Fatigue		<b>Medical History</b>
4	Abdominal Pain		1 No prior illnesses or hospitalizations
5	Upper Gastrointestinal Bleed		<b>Allergies</b>
6	Gastric Ulcers		1 NKA
7	Fever		<b>Immunizations</b>
			1 N/A

<b>Exhibit 29</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	<b>Gold Standard Diagnosis</b>
<b>Case Number</b>	62-36123		Syphilitic Meningitis
<b>Isabel Pro Healthcare</b>			<b>Date Entered</b>
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	90%	Lyme Disease	We matched the terms: headache   headaches   dizziness   membranes   erythema   membrane   high   frequency   red   blood   sedimentation   rate   hr   infection   allergic
2	59%	Relapsing Polychondritis	We matched the terms: headache   tinnitus   hearing loss   loss of hearing   sudden loss of hearing   vertigo   unsteadiness   erythema   red   rate   anterior   tenderness   bilateral
3	55%	Iron Deficiency	We matched the terms: headache   headaches   tinnitus   pulsatile tinnitus   dizziness   lightheadedness   lightheaded   membranes   membrane   high   red   blood   sedimentation   rate   hr   infection
4	52%	Renal Failure - Acute Renal Failure; Idiopathic Postpartum Acute Renal Failure	We matched the terms: hearing loss   dizziness   membranes   membrane   high   frequency   red   blood   hr   infection   allergic   tenderness   fluid
5	49%	External Otitis	We matched the terms: headache   tinnitus   hearing loss   decreased hearing   erythema   membrane   red   tenderness   tympanic
6	47%	Otitis Media Complications - Acquired Cholesteatoma	We matched the terms: headache   tinnitus   hearing loss   membrane   high   frequency   red   rate   infection   bilateral   fluid   tympanic
7	42%	Sarcoidosis	We matched the terms: headache   erythema   high   red   blood   sedimentation   rate   hr   anterior   tenderness   bilateral   lesions
8	41%	Herpes Simplex Virus Infection - Genital Herpes	We matched the terms: headache   genital herpes   high   frequency   rate   hr   infection   bilateral   lesions
9	38%	Bacterial Meningitis	We matched the terms: headache   tinnitus   deaf   deafness   vertigo   high   red   blood   infection   bilateral   lesions
10	38%	Otitis Media - Acute Otitis Media	We matched the terms: tinnitus   hearing loss   vertigo   membrane   red   fluid   tympanic
29	26%	Syphilis	We matched the terms: headache   macular rash   hearing loss   balance problem   balance problems   high   red   sedimentation   rate
			Please note: Check your spelling. The term/s bubbles, caesarian, amoxicillin, keflex may not have influenced the result.
<b>Age</b>	25		<b>Chief Complaints</b>
<b>Gender</b>	Female	1	Headaches
<b>Travel</b>	North America	2	Tinnitus
<b>Symptoms, Pre-encounter Observations</b>			
1	Kicked in head		
2	left anterior parietal skull tenderness		
3	fluid and bubbles behind tympanic membranes		
4	Erythema of the left tympanic membrane		
5	faint macular rash on arms		
6	high frequency hearing loss bilateral		
7	Red Blood sedimentation rate of 77 mm/hr		
8	vertigo		
9	flashing lights		
<b>Medications</b>		<b>Allergies</b>	
1	Keflex	1	Amoxicillin
<b>Medical History</b>		<b>Immunizations</b>	
1	History of head trauma	1	N/A
2	history of genital herpes		
3	history of chlamydia infection		
4	smoker		
5	history of caesarian section childbirth		
6	history of herpetic lesions		



## Exhibit 30

Translational Project - Diagnostic Decision Support Systems			
Validation Project		Results	
		<u>Gold Standard Diagnosis</u>	
Case Number	41-36032	Ulcerative Colitis	
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	100%	Crohn Disease	We matched the terms: fever   pyrexia   chill   chills   sweats   sweat   malaise   fatigue   anorexia   loss of appetite   weight loss   unexplained weight loss   bloody stools   hematochezia   rectal bleeding   bloody stool
2	89%	Coronavirus - COVID-19	We matched the terms: fever   rigor   rigors   chill   chills   sweating   sweats   sweat   fatigue   anorexia   loss of appetite   weight loss   hypertension
3	86%	Endocarditis	We matched the terms: fever   fevers   chill   chills   sweating   sweats   sweat   malaise   fatigue   anorexia   weight loss   hands
4	77%	Non-Hodgkin Lymphoma - Burkitt Symphoma	We matched the terms: fever   pyrexia   chill   chills   sweats   sweat   malaise   tiredness   fatigue   tired   anorexia   loss of appetite   decreased appetite   poor appetite   weight loss
5	72%	Brucellosis	We matched the terms: fever   febrile   fevers   chill   chills   sweating   sweats   sweat   malaise   fatigue   anorexia   loss of appetite   weight loss
6	72%	Diverticular Diseases of the Colon - Colon Diverticulitis	We matched the terms: bloody diarrhea   left lower abdominal pain   left lower quadrant abdominal pain   lower left abdominal pain   fever   chill   chills   anorexia   weight loss   rectal bleeding
7	72%	Lung Abscess	We matched the terms: fever   febrile   rigor   rigors   chill   chills   sweating   sweats   sweat   malaise   fatigue   anorexia   loss of appetite   weight loss
8	63%	Coccidioidomycosis	We matched the terms: fever   chill   chills   sweating   sweats   sweat   malaise   tiredness   fatigue   tired   exhaustion   loss of appetite   weight loss
9	63%	Infectious Mononucleosis	We matched the terms: fever   pyrexia   fevers   chill   chills   sweating   sweat   malaise   fatigue   anorexia   loss of appetite   weight loss
10	62%	Bebesiosis	We matched the terms: fever   chill   chills   shaking chills   sweats   sweat   malaise   fatigue   anorexia   weight loss
			Please note: Check your spelling. The term/s osteoarthritis may not have influenced the result.
Age	60	<u>Chief Complaints</u>	
Gender	Male	1	Diarrhea, bloody
Travel	North America	<u>Medications</u>	
<u>Symptoms, Pre-encounter Observations</u>		<u>Medications</u>	
1	abdominal pain, lower left quad	1	Diltiazem
2	Fever	2	Hydrochlorothiazide
3	Chills	<u>Medical History</u>	
4	Sweats	1	Diverticulitis
5	Fatigue	2	Hematochezia
6	anorexia	3	hypertension
7	weight loss	4	Osteoarthritis, hands
Allergies		5	epistaxis
1	N/A	<u>Immunizations</u>	
		1	None

<b>Exhibit 31</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	43-36171	Silicosis	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Heart Failure/CHR	We matched the terms: shortness of breath   dyspnea   dyspnoea   short of breath   difficulty breathing   chesty cough   exertional dyspnea   dyspnea on exertion   leg edema   leg swelling   decreased appetite   hypertension   hypertensive   elevated blood pressure   pulse   rate   increased
2	87%	Cardiogenic Shock	We matched the terms: shortness of breath   dyspnea   exertional dyspnea   peripheral edema   hypertension   coronary artery disease   smoking   tachypnea   rapid breathing   pulse
3	65%	Pulmonary Edema	We matched the terms: shortness of breath   dyspnea   breathing difficulty   breathless   difficulty breathing   breathing difficult   labored breathing   respiratory distress   shortness of breath on exertion   lower extremity edema   loss of appetite   hypertensive   rapid breathing   pulse   increased
4	62%	Pulmonary Thromboembolism - Pulm	We matched the terms: shortness of breath   dyspnea   productive cough   dyspnea on exertion   lower extremity edema   lower limb edema   tachypnea   tachypnoea   rapid breathing   rate   increased
5	56%	COPD	We matched the terms: dyspnea   productive cough   peripheral edema   weight loss   hypertension   smoker   increased
6	51%	Pulmonary Hypertension	We matched the terms: shortness of breath   dyspnea   breathlessness   breathless   exertional dyspnea   dyspnea on exertion   exertional shortness of breath   pedal edema   leg swelling   decreased appetite   hypertension   pulse
7	50%	Iron Deficiency	We matched the terms: shortness of breath   dyspnea   shortness of breath on exertion   pedal edema   decreased appetite   poor appetite   tachypnea   pulse   rate   increased
8	49%	Hodgkin Disease	We matched the terms: shortness of breath   breathing difficulty   breathing difficult   anorexia   loss of appetite   appetite loss   weight loss   unexplained weight loss   alcohol   rate   increased
9	46%	Hypersensitivity Pneumonitis	We matched the terms: shortness of breath   dyspnea   breathlessness   breathless   productive cough   exertional dyspnea   anorexia   loss of appetite   weight loss   hypertension
10	45%	Coronavirus - COVID-19	We matched the terms: shortness of breath   dyspnea   difficulty breathing   labored breathing   respiratory distress   productive cough   cough with phlegm   anorexia   loss of appetite   weight loss   hypertension
<b>Age</b>	71	<b>Chief Complaints</b>	
<b>Gender</b>	Male	1	Shortness of Breath
<b>Travel</b>	North America		
<b>Symptoms, Pre-encounter Observations</b>		<b>Medical History</b>	
1	productive cough	1	transurethral prostatectomy
2	dyspnea on exertion	2	hypertension
3	swelling of the legs	3	coronary heart disease
4	decreased appetiti	4	smoker
5	weight loss	5	alcohol
		6	pulse rate high
		7	respiratory rate high
<b>Medications</b>		<b>Allergies</b>	
1	ampicillin	1	NKA
2	albuterol	<b>Immunizations</b>	
3	theophylline	1	None
4	furosemide		
5	bethanechol	1	None

<b>Exhibit 32</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	53-36062	Cryptococcal Meningitis	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	96%	Hodgkin Disease	We matched the terms: fever   fevers   weight loss   unexplained weight loss   malaise   tiredness   fatigue   tired   anorexia   loss of appetite   appetite loss   white   blood   count   disease   red   sedimentation   rate   decreased   liver   cyst
2	84%	Relapsing Fever	We matched the terms: fever   pyrexia   fevers   headache   confusion   malaise   fatigue   anorexia   chill   chills   shaking chills   hepatosplenomegaly   white   blood   count   rate   line   liver
3	81%	Lyme Disease	We matched the terms: fever   pyrexia   fevers   headache   headaches   fatigue   lethargy   general fatigue   chill   chills   polyneuropathy   hearing   white   blood   count   disease   red   sedimentation   rate
4	78%	Coronavirus - COVID-19	We matched the terms: fever   headache   headaches   weight loss   confusion   fatigue   anorexia   loss of appetite   rigor   rigors   chill   chills   hypertension   disease   red   decreased
5	71%	Human Granulocytic Anaplasmosis	We matched the terms: fever   headache   headache   headaches   weight loss   confusion   malaise   tiredness   fatigue   tired   anorexia   chill   chills   white   blood   red   line   decreased   liver
6	67%	Adult Still Disease	We matched the terms: fever   pyrexia   fevers   weight loss   unexplained weight loss   fatigue   poor appetite   hepatosplenomegaly   white   blood   count   disease   red   line   decreased   liver
7	67%	Brucellosis	We matched the terms: fever   febrile   fevers   headache   weight loss   confusion   malaise   fatigue   anorexia   loss of appetite   chill   chills   hepatosplenomegaly   hearing   decreased   liver
8	64%	Renal Failure - Chronic Renal Failure; Acute Renal Failure	We matched the terms: headache   weight loss   confusion   decreased alertness   fatigue   lethargy   exhausted   anorexia   loss of appetite   ck   hypertension   high blood pressure   white   blood   disease   red   line   decreased   cyst
9	61%	Babesiosis	We matched the terms: fever   headache   weight loss   malaise   fatigue   anorexia   chill   chills   shaking chills   hepatosplenomegaly   count   decreased   liver
10	60%	Infectious Mononucleosis	We matched the terms: fever   pyrexia   fevers   headache   headaches   weight loss   loc   malaise   fatigue   anorexia   loss of appetite   chill   chills   white   count   red   line   decreased   liver
			Please note: Check your spelling. The term/s muffled, hyperplasia, erythroid, granulocytes, precursors, diverticular, albuterol, ipratropium, bromide, inhaler, ranitidine may not have influenced the result.
<b>Age</b>	75	<b>Chief Complaints</b>	
<b>Gender</b>	Male	1	Fever
<b>Travel</b>	North America	2	Headaches
<b>Symptoms, Pre-encounter Observations</b>		3	Weight Loss
1	Fatigue	4	Confusion
2	Loss of Appetite	<b>Medications</b>	
3	Chills	1	Theophylline
4	Muffled Hearing	2	Albuterol
5	White Blood Count 1.6x10 <sup>9</sup> /L	3	Ipratropium bromide inhaler
6	Hyperplasia of the Erythroid line	4	Ranitidine
7	Decreased Granulocytes Precursor	<b>Medical History</b>	
8	Esophageal ulcer	1	Coronary Artery disease
9	hiatal hernia	2	COPD
10	diverticular disease	<b>Allergies</b>	
11	liver cyst	1	NKA
12	polyneuropathy	<b>Immunizations</b>	
13	hepatosplenomegaly	1	None
14	Red Blood Count sedimentation rate 126		
15	CPK 618		
16	TSH 1.85		
17	Elevated Blood Pressure		

<b>Exhibit 33</b>				
<b>Translational Project - Diagnostic Decision Support Systems</b>				
<b>Validation Project</b>		<b>Results</b>		
		<b>Gold Standard Diagnosis</b>		
<b>Case Number</b>	15-36102	Pheochromocytoma		
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>		
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>	
1	100%	Bacterial Meningitis	We matched the terms: vertigo   hypertension   high blood pressure   hypertensive   deaf   deafness	
2	88%	Neurocutaneous Syndromes	We matched the terms: dizziness   balance problem   balance problems   hypertension   high blood	
3	82%	Renal Failure	We matched the terms:	
4	79%	Systemic Hypertension Disorders	We matched the terms: dizziness   hypertension   high blood pressure   hypertensive   elevated blood pressure	
5	78%	Heavy Metal Intoxication	We matched the terms: vertigo   hypertension   deaf   deafness   hearing	
6	70%	Cerebral Sinus Venous Thrombosis	We matched the terms:	
7	69%	Munier's Disease	We matched the terms: vertigo   dizziness   lightheadedness   lightheaded   balance disturbance   hearing loss	
8	69%	Superior Canal Dohisence Syndrome	sensation   whirling sensation   dizziness   lightheaded   disequilibrium   balance problem   imbalance   hearing loss   hearing	
9	66%	Arteriolar Nephrosclerosis	We matched the terms: dizziness   hypertension   hypertensive   elevated blood	
10	65%	Acoustic Neuroma	We matched the terms: vertigo   dizziness   loss of balance   hearing loss   decreased hearing	
<b>Age</b>	49	<b>Chief Complaints</b>		
<b>Gender</b>	Male	1	Basilar Skull Fracture.	
<b>Travel</b>	North America	2	Lightheadedness on standing	
<b>Symptoms, Pre-encounter Observations</b>				
1	High Blood Pressure, Fluctuating			
2	Hearing Loss in right ear			
<b>Medications</b>		<b>Allergies</b>		
1	N/A	1	NKA	
<b>Medical History</b>		<b>Immunizations</b>		
1	Hypertension	1	N/A	

<b>Exhibit 34</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	63-36111	Mucormycosis	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Heart Failure/CHF	We matched the terms: fatigue   tired   increased abdominal girth   hypertension   hypertensive   elevated blood pressure   polyuria   diabetes   end stage renal disease   cri   kidney failure   pain   rapid   pulse   previous
2	80%	Type 2 Diabetes	We matched the terms: fatigue   hypertension   polyuria   polydipsia   diabetes mellitus   dm   diabetes   diabetic   cri   rapid   previous
3	74%	Langerhans Cell Histiocytosis Class 1	We matched the terms: fever   malaise   polyuria   polydipsia   thirst   diabetes   smoker   pain   rapid
4	64%	Cardiogenic Shock	We matched the terms: fatigue   lethargy   hypertension   diabetes   cri   smoking   pain   rapid   pulse   previous
5	64%	Coronavirus - COVID-19	We matched the terms: fever   sore throat   fatigue   nasal congestion   hypertension   diabetes mellitus   diabetes   pain
6	61%	Granulomatosis with Polyangiitis	We matched the terms: fever   facial pain   facial nerve palsy   malaise   fatigue   sinus pain   chronic renal failure   pain   rapid
7	60%	Sinusitis	We matched the terms: fever   sore throat   facial pain   fatigue   nasal congestion   hypertension   smoker   pain   previous   maxillary
8	59%	Pancreatitis - Acute Pancreatitis; Chronic Pancreatitis	We matched the terms: fever   fevers   fatigue   lethargy   tired   swollen abdomen   bloating   bloat   alcohol   pain   rapid   pulse
9	58%	Hyperthyroidism	We matched the terms: fever   fatigue   hypertension   high blood pressure   polyuria   polydipsia   pain   rapid   pulse
10	58%	Renal Failure - Acute Renal Failure; Chronic Renal Failure	We matched the terms: fever   fatigue   hypertension   high blood pressure   polyuria   polydipsia   pain   rapid   pulse
			Please note: Check your spelling. The term/s prazosin, trifluoperazine, benzotropine, amitriptyline may not have influenced the result.
<b>Age</b>	36	<b>Chief Complaints</b>	
<b>Gender</b>	Male	1	Fever
<b>Travel</b>	North America	2	Sore throat
<b>Symptoms, Pre-encounter Observations</b>		3	facial pain
1	facial drooping, right side	<b>Medical History</b>	
2	lethargic	1	polyuria
3	nasal congestion	2	polydipsia
4	maxillary pain, right	3	alcoholic cirrhosis
5	abdominal swelling	4	diabetes mellitus
6	elevated blood pressure	5	hypertension
7	rapid pulse	6	chronic renal insufficiency
<b>Medications</b>		7	schizophrenia
1	Furosemide	8	smoker
2	spironolactone	9	alcohol
3	prazosin	10	Previous IV heroin
4	trifluoperazine	11	Previous IV cocaine
5	benztropine	<b>Allergies</b>	
6	amitriptyline	1	NKA
		<b>Immunizations</b>	
		1	None

## Exhibit 35

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	35-36161	Porphyria (cutnea tarda)	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Pancreatitis - Acute Pancreatitis; Chro	We matched the terms: abdominal pain   diffuse abdominal pain   epigastric pain   upper abdominal pain   pain below ribs   difficulty concentrating   radiating   back   worsens
2	94%	Viral Hepatitis - Hepatitis C; Hepatitis A; Hepatitis B; Hepatitis D	We matched the terms: abdominal pain   stomach pain   stomach pains   dark urine   epigastric pain   pain epigastric   right upper quadrant abdominal pain   aching   rash
3	84%	Cholelithiasis	We matched the terms: abdominal pain   dark urine   epigastric pain   nocturnal epigastric pain   right upper quadrant abdominal pain   radiating   back
4	80%	Peptic Ulcer Disease - Duodenal Ulcers	We matched the terms: abdominal pain   epigastric pain   epigastric tenderness   right upper quadrant abdominal pain   radiating   back   relieved
5	79%	Biliary Colic	We matched the terms: abdominal pain   stomach ache   epigastric pain   right upper quadrant abdominal pain   radiating   back
6	78%	Cholangiocarcinoma	We matched the terms: abdominal pain   abdominal discomfort   dark urine   epigastric pain   right upper quadrant pain   right upper quadrant abdominal pain
7	76%	Cirrhosis - Primary Biliary Cirrhosis	We matched the terms: abdominal pain   abdominal discomfort   dark urine   abdominal pain upper   upper abdominal pain   right upper abdominal pain   back
8	75%	Cholecystitis - Chronic Cholecystitis	We matched the terms: abdominal pain   dark urine   epigastric pain   nocturnal epigastric pain   right upper quadrant pain   right upper quadrant abdominal pain   radiating   back
9	72%	Coronavirus - COVID-19	We matched the terms: abdominal pain   abdominal discomfort   dark urine   back   rash
10	70%	Aortic Aneurysm/Dissection - Abdom	We matched the terms: abdominal pain   upper abdominal pain   radiating   back
			Please note: Check your spelling. The term/s prone, penicillin may not have influenced the result.
<b>Age</b>	43	<b>Chief Complaints</b>	
<b>Gender</b>	Male	1	Abdominal Pain
<b>Travel</b>	North America	2	Dark Urine
<b>Symptoms, Pre-encounter Observations</b>		<b>Medications</b>	
1	Dull, Aching Abdominal Pain	1	None
2	Occasionally Sharp, Stabbing Abdominal Pain		
3	Radiating to back	<b>Medical History</b>	
4	radiating to Upper right quadrant	1	Syphilis, treated with penicillin
5	Worsens when lying down	2	smoker, heavy
6	relieved when sitting up	3	alcohol, heavy
7	hand rash, non-tender, no-pruitic	4	IV drug user
8	Facial darkening	5	high blood pressure
9	Difficulty concentrating	<b>Immunizations</b>	
<b>Allergies</b>		1	N/A
1	None		

<b>Exhibit 36</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
			<b>Gold Standard Diagnosis</b>
<b>Case Number</b>	56-36022		Non-Hodgkins Lymphoma
<b>Isabel Pro Healthcare</b>			<b>Date Entered</b>
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Cytomegalovirus - CMV Disease in the Immunocompromised Host	We matched the terms: anemia   hiv   hiv infection   malaise   fatigue   lethargy   imbalance   hypotension   herpes   simplex   cd   count   pneumonia
2	65%	Hodgkin Disease	We matched the terms: anaemia   anemia   recurrent fever   recurrent fevers   relapsing and remitting fever   relapsing and remitting fevers   malaise   tiredness   fatigue   tired   nausea   splenomegaly   enlarged spleen   hypersplenism   count   lymphadenopathy
3	61%	Iron Deficiency	We matched the terms: anaemia   anemia   low hemoglobin   malaise   fatigue   tired   exhaustion   nausea   splenomegaly   dizziness   lightheadedness   lightheaded   blood in stool   count
4	56%	HIV/AIDS	We matched the terms: anemia   hiv   hiv infection   malaise   fatigue   cd   count   pneumonia   lymphadenopathy   pharyngitis
5	52%	Hematologic HIC Manifestations	We matched the terms: anemia   hiv   hiv infection   cd   count   lymphadenopathy
6	49%	Viral Hepatitis - Hepatitis C	We matched the terms: recurring fever   hiv   tiredness   fatigue   tired   nausea   enlarged spleen   muscle wasting   wasting
7	48%	Infectious Mononucleosis	We matched the terms: malaise   fatigue   nausea   splenomegaly   count   lymphadenopathy   pharyngitis
8	47%	Babesiosis	We matched the terms: anemia   periodic fever   malaise   fatigue   nausea   splenomegaly   enlarged spleen   count
9	45%	Relapsing Fever	We matched the terms: anaemia   anemia   low hemoglobin   recurrent fever   relapsing fever   recurrent fevers   malaise   fatigue   nausea   enlarged spleen   count
10	45%	Salmonella Infections - Typhoid	We matched the terms: anaemia   hiv   malaise   nausea   splenomegaly   hypotension   count   pneumonia
			Please note: Check your spelling. The term/s candidal, aortocaval, portahepatic, trazodone, pcp may not have influenced the result.
<b>Age</b>	37		<b>Chief Complaints</b>
<b>Gender</b>	Male		1 Severe Anemia
<b>Travel</b>	North America		2 Recurrent Fevers
<b>Symptoms, Pre-encounter Observations</b>			<b>Medications</b>
1	HIV Infection		1 pentamidine
2	Candidal Pharyngitis		2 trazodone
3	Herpes Zoster		<b>Medical History</b>
4	Herpes Simplex Proctitis		1 Non PCP Pneumonia
5	Malaise		2 syphilis
6	Nausea		<b>Allergies</b>
7	Hematocrit low and declining		1 NKA
8	CD4 count 40		<b>Immunizations</b>
9	Splenomegaly		1 None
10	Aortocaval		
11	Portahepatic Lymphadenopathy		
12	Lightheaded		
13	hematochezia		
14	cachectic		
15	low blood pressure		

## Exhibit 37

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	Gold Standard Diagnosis
<b>Case Number</b>	66-36122		Hypokalemic Periodic Paralysis
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<u>Ranked</u>	<u>% Match</u>	<u>Diagnostic Alternatives</u>	<u>Reasons</u>
1	90%	Hyperthyroidism - Graves Disease; Thyroid Storm	We matched the terms: hyperthyroidism   palpitation   palpitations   anxiety   nervousness   stress   depression   heat intolerance   heat sensitivity   frequent bowel movements   low tsh   low serum tsh   high   radioiodine   uptake
2	57%	Aortic Aneurysm/Dissection - Thoracic Aortic Aneurysm	We matched the terms: limb pain   leg pain   severe leg pain   back pain   chest pain   palpitation   palpitations   anxiety   dysphagia   hypertension   high
3	51%	Necrotizing Fasciitis	We matched the terms: limb pain   pain in leg   pain in arm   fever   palpitation   palpitations   high   erythema   site   wound
4	48%	Ischemic Heart Disease; Myocardial Infarction/Acute Coronary Syndrome - Non ST Elevation myocardial Infarction; ST Elevation Myocardial Infarction; Angina; Prinzmetal's Variant Angina	We matched the terms: back pain   chest pain   substernal chest pain   arm pain   fever   palpitation   palpitations   anxiety   stress   hypertensive   high
5	45%	Pulmonary Thromboembolism - Pulmonary Embolism and Infarction	We matched the terms: leg pain   back pain   chest pain   arm pain   fever   apprehension   high
6	43%	Lyme Disease - Early Disseminated Lyme Disease	We matched the terms: back pain   backache   chest pain   pain in arm   fever   pyrexia   fevers   palpitation   palpitations   anxiety   panic   severe anxiety   depression   high   erythema   limbs   site
7	40%	Acute Porphyria - Variegate Porphyria; Acute Intermittent Porphyria	We matched the terms: limb pain   leg pain   back pain   chest pain   fever   palpitation   palpitations   heart palpitation   heart palpitations   anxiety   depression   hypertension   high blood pressure   high
8	37%	Pituitary Neoplasms - Thyrotropinoma	We matched the terms: hyperthyroidism   palpitation   palpitations   heart palpitation   heart palpitations   anxiety   nervousness   heat intolerance   frequent bowel movements   high blood pressure   high   free
9	35%	Osteomyelitis and Septic Arthritis	We matched the terms: lower leg weakness   leg weakness   leg pain   back pain   fever   tibia   high   erythema   site   fracture
10	34%	Myelitis - Transverse Myelitis	We matched the terms: back pain   chest pain   fever   anxiety   depression
Please note: Check your spelling. The term/s seized, thyroidal, hrs, figety, prozac, atenol may not have influenced the result.			
<b>Age</b>	30		<b>Chief Complaints</b>
<b>Gender</b>	Male		1 Leg weakness, bilateral
<b>Travel</b>	North America		2 leg pain, bilateral
<b>Symptoms, Pre-encounter Observations</b>		<b>Medical History</b>	
1	difficulty standing	1	hyperthyroidism
2	pain in legs	2	left tibial fracture
3	weakness in legs	3	fevers
4	pain in back, chest, and arms	4	erythema at tibial fracture site
5	unable to climb stairs	5	palpitations
6	Seized up	6	anxiety
<b>Medications</b>		7	depression
1	prozac	8	heat intolerance
2	Atenol	9	frequent bowel movements
3	I-131	10	TSH less than 0.003
<b>Allergies</b>		11	Free T4 greater than 6
1	NKA	12	Thyroidal radioiodine uptake 61.4% in 24 hrs
<b>Immunizations</b>		13	dysphagia
1	None	14	high blood pressure
		15	figety
		16	tremulous



## Exhibit 38

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	Gold Standard Diagnosis
Case Number	46-36251		Amyloidosis (renal)
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	100%	Heart Failure/CHF	We matched the terms: leg edema   leg swelling   exertional dyspnea   dyspnea on exertion   weight gain   hypertension   hypertensive   elevated blood pressure   swelling
2	74%	Pulmonary Edema - Cardiogenic Pulmonary Edema	We matched the terms: lower extremity edema   swollen hand   swollen hands   shortness of breath on exertion   weight gain   hypertensive
3	73%	Spinal Infections - Epidural Abscess	We matched the terms: leg edema   leg swelling   iv drug use   intravenous drug abuse   iv drug user   swelling   arm   user
4	70%	Nehrotic Syndrome	We matched the terms: pedal edema   oedema lower limb   oedema lower limbs   swollen hand   swollen hands   weight gain   hypertension   swelling
5	68%	Systemic Sclerosis - Localised Scleroderma	We matched the terms: swollen hand   swollen hands   exertional dyspnea   pulmonary fibrosis   hypertension   hypertensive   swelling
6	61%	Cardiogenic Shock	We matched the terms: peripheral edema   exertional dyspnea   hypertension   arm   cocaine
7	57%	Pulmonary Hypertension	We matched the terms: pedal edema   leg swelling   exertional dyspnea   dyspnea on exertion   exertional shortness of breath   hypertension   swelling
8	55%	Complex Regional Pain Syndrome	We matched the terms: leg swelling   foot swelling   hand swelling   swollen hand   swollen hands   swelling   arm
9	49%	Glomerulonephritis - Membranous Glomerulonephritis	We matched the terms: feet edema   hand swelling   hand edema   high blood pressure   swelling
10	49%	Rheumatoid Arthritis	We matched the terms: feet swelling   swollen hand   swollen hands   pulmonary fibrosis   swelling   arm
<b>Age</b>	44		<b>Chief Complaints</b>
<b>Gender</b>	Male		1 Swelling of the arms
<b>Travel</b>	North America		2 Swelling of the legs
<b>Symptoms, Pre-encounter Observations</b>			<b>Medications</b>
1	Swelling of the hands		1 None
2	Swelling of the genitalia		<b>Medical History</b>
3	Dyspnea on exertion		1 Elevated Blood Pressure
4	Weight gain		2 IV drug abuse cocaine
5	pulmonary fibrosis		3 IV drug abuse heroin
<b>Allergies</b>			<b>Immunizations</b>
1	NKA		1 None

## Exhibit 39

Translational Project - Diagnostic Decision Support Systems				
Validation Project		Results		
		Gold Standard Diagnosis		
Case Number	16-36083	Aortic Dissection		
Isabel Pro Healthcare		Date Entered		
Ranked	% Match	Diagnostic Alternatives	Reasons	
1	100%	Bacterial Pneumonia	breath   dyspnea   difficulty in breathing   shortness of breath on exertion   chest pain radiating   dry	
2	78%	Pulmonary Thromboembolism	breath   dyspnea   breathlessness   short of breath   breathless   shortness of breath on exertion   radiating chest pain   dry	
3	70%	Atypical Pneumonia	breath   dyspnea   dyspnoea   breathlessness   b reathless   respiratory distress   exertional dyspnoea   night sweats   low-grade fever   tachypnea   tachypnoea	
4	66%	Pulmonary Hypertension	We matched the terms: shortness of breath   dyspnea   breathlessness   breathless   exertional dyspnea   dyspnea on exertion   exertional shortness of	
5	64%	Heart Failure/CHF	breath   dyspnea   dyspnoea   short of breath   difficulty breathing   exertional dyspnea   dyspnea on exertion   nonproductive cough   hypertension   hypertensive   elevated	
6	59%	Interstitial Lung Disease	breath   dyspnea   breathlessness   breathless   exertional dyspnea   shortness of breath on exertion   dry cough   nonproductive cough   hacking cough   hypertension	
7	57%	Asthma	We matched the terms: dyspnea   exertional dyspnea   nonproductive	
8	56%	Diseases of High Atitudes	breath   dyspnea   dyspnea on exertion   shortness of breath on exertion   dry cough   low-grade fever   tachypnea	
9	55%	Coronavirus	breath   dyspnea   difficulty breathing   labored breathing   respiratory distress   dry cough   night sweats   hypertension	
10	49%	Pulmonary Edema	breath   dyspnea   breathing difficulty   breathless   difficulty breathing   breathing difficult   labored breathing   respiratory distress   shortness of	
Please note: Check your spelling. The term/s verapamil, benazepril, hysterectomy,				
Age	58	Chief Complaints		
Gender	Female	1	Shortness of Breath, with exertion	
Travel	North America	2	Chest Pain, Left Side Moving to Back	
Symptoms, Pre-encounter Observations		3	Occasional Non-Productive Cough	
1	Very High Blood Pressure 159/107	4	Night Sweats	
2	Fever 100.9	5	Fever	
3	Respiratory Rate High 22	Medical History		
4	Pulse Normal 90	1	Hypertension	
Medications		2	Total Abdominal Hysterectomy	
1	Verapamil, 180 mg, p.o., q.d.	3	Bilateral Oophorectomy	
2	Benazepril 10 mg p.o. q.d.	Immunizations		
3	Furosemide 20 mg q.d.	1	N/A	
Allergies				
1	NKA			

<b>Exhibit 40</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
			<b>Gold Standard Diagnosis</b>
<b>Case Number</b>	34-36103		Cardiac Amyloidosis
<b>Isabel Pro Healthcare</b>			<b>Date Entered</b>
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Myocarditis	We matched the terms: congestive heart failure   anorexia   malaise   fatigability   jugular venous distention   rales   rale   cardiomegaly   mitral regurgitation   tricuspid insufficiency   pericardial effusion   tachypnea   pulmonary   wave   flattening   atria
2	62%	Cardiomyopathy - Dilated Cardiomyopathy; Hypertrophic Cardiomyopathy	We matched the terms: congestive heart failure   fatigue   third heart sound   ventricular gallop   enlarged heart   tricuspid regurgitation   apical impulse   pulmonary   wave   atria   veins   enlarged
3	61%	Heart Failure/CHF	We matched the terms: congestive heart failure   chf   decreased appetite   fatigue   tired   elevated jvp   raised jugular venous pressure   crackles   crepitations   rales   rale   crep   crepitation   third heart sound   cardiomegaly   exertional dyspnea   dyspnea on exertion   atria   veins
4	46%	Pulmonary Edema	We matched the terms: loss of appetite   fatigue   wheezing   jugular venous pressure increased   crackles   rales   rale   mitral regurgitation   shortness of breath on exertion   rapid breathing   pulmonary   atria
5	45%	Pulmonary Hypertension	We matched the terms: decreased appetite   tiredness   fatigue   tired   elevated jugular venous pressure   tricuspid regurgitation   exertional dyspnea   dyspnea on exertion   exertional shortness of breath   pulmonary   wave   atria
6	42%	Tricuspid Insufficiency/Regurgitation	We matched the terms: congestive heart failure   fatigue   cardiomegaly   tricuspid insufficiency   tricuspid regurgitation   pulmonary   wave   atria   veins
7	40%	Pulmonary Thromboembolism - Pulmonary Embolism and Infarction	We matched the terms: wheezing   jugular venous pressure increased   rales   rale   dyspnea on exertion   tachypnea   tachypnoea   rapid breathing   pulmonary   wave   atria
8	35%	Lung Neoplasms - Non-Small Cell Lung Cancer; Bronchogenic Carcinoma	We matched the terms: loss of appetite   fatigue   wheezing   pericardial effusion   doe   pulmonary   veins   lobe
9	33%	Cardiogenic Shock	We matched the terms: fatigue   lethargy   jugular venous distention   crackles   mitral regurgitation   exertional dyspnea   tachypnea   rapid breathing   pulmonary
10	29%	Hypothyroidism	We matched the terms: congestive heart failure   poor appetite   tiredness   tired   cardiomegaly   pericardial effusion   wave
			Please note: Check your spelling. The term/s enalapril, hydrochlorothiazide, diazepam may not have influenced the result.
<b>Age</b>	74		<b>Chief Complaints</b>
<b>Gender</b>	Female		1 Congestive Heart Failure
<b>Travel</b>	North America		<b>Medications</b>
<b>Symptoms, Pre-encounter Observations</b>			1 Enalapril
1	Loss of Energy		2 Hydrochlorothiazide
2	Decreased appetite		3 Vitamin B-12
3	Tires easily		4 Diazepam
4	Wheezing when prone		<b>Medical History</b>
5	Distended Neck Veins		1 History of Pernicious Anemia
6	Bibasilar Rales		2 History of Mitral Valve Prolapse
7	S3 Gallop		
8	Cardiomegaly with prominence of the upper lobe pulmonary veins		
9	T-Wave Flattening		
10	Long QT Interval		<b>Allergies</b>
11	Enlarged Left & Right Atria		1 NKA
12	Mitral regurgitation		<b>Immunizations</b>
13	Tricuspid regurgitation		1 None
14	Pericardial effusion		
15	Shortness of breath with exertion		
16	Laterally displaced PMI		
17	Respiratory rate elevated		

<b>Exhibit 41</b>			
<b>Translational Project - Diagnostic Decision Support Systems</b>			
<b>Validation Project</b>		<b>Results</b>	
		<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	44-36082	Miliary (disseminated) TB	
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>
1	100%	Renal Failure - Chronic Renal Failure; Acute Renal Failure	We matched the terms: fatigue   lethargy   exhausted   pleural effusion   anemia   diabetes   hypertension   high blood pressure   ecchymosis   protein   total   red   peritoneal   fat   cysts   kidney   syndrome   insulin
2	85%	Arteriolar Nephrosclerosis	We matched the terms: weakness   anemia   hypertension   hypertensive   elevated blood pressure   arterial hypertension   protein   total   red   fat   kidney   syndrome   indices   albumin   benign   cortical
3	82%	Coronavirus - COVID-19	We matched the terms: weakness   fatigue   ldh   lactate dehydrogenase   diabetes mellitus   diabetes   hypertension   red   fat   kidney   syndrome   albumin   congestion
4	66%	Cytomegalovirus - CMV Disease in the immunocompromised Host	We matched the terms: malaise   fatigue   lethargy   leukocyte   leukocytes   anemia   pancytopenia   fat   kidney   syndrome   dependent   hepatic   factor   neut   granulocyte
5	66%	Nephrotic Syndrome	We matched the terms: malaise   fatigue   pleural effusion   pleural effusions   hypertension   protein   total   dl   red   fat   kidney   syndrome   dependent   albumin   extremities   hepatic
6	66%	SLE	We matched the terms: malaise   fatigue   anemia   cytopenia   hypertension   protein   fat   kidney   syndrome   cbc   mono   urinalysis   factor
7	63%	Heart Failure/CHF	We matched the terms: weakness   fatigue   tired   lactate dehydrogenase   pleural effusion   pleural effusions   diabetes   hypertension   hypertensive   elevated blood pressure   red   fat   kidney   extremities
8	58%	Cirrhosis	We matched the terms: weakness   tiredness   fatigue   tired   pleural effusion   anemia   pancytopenia   red   fat   syndrome   albumin   hepatic
9	52%	Infectious Mononucleosis	We matched the terms: weakness   malaise   fatigue   axillary lymph node enlargement   lactate dehydrogenase   protein   red   fat   mono
10	52%	Mitochondrial Encephalomyopathies	We matched the terms: weakness   tiredness   fatigue   tired   fatigability   diabetes   fat   syndrome   insulin   dependent   cortical   extremities
			Please note: Check your spelling. The term/s inguinal, hernia, hct, lymphs, wnl, packed, stapholococcus, epidermis, myelodysplastic, colony, stimulating, verapamil, pericolace may not have influenced the result.
<b>Age</b>	62	<b>Chief Complaints</b>	
<b>Gender</b>	Male	1	Fevers daily
<b>Travel</b>	North America	2	generalized weakness
<b>Symptoms, Pre-encounter Observations</b>		3	fatigue
1	diffuse ecchymosis of the extremities		
2	right inguinal hernia		
3	right axillary mass		
4	CBC Hct 27 (with normal indices) 42-52%		
5	WBC 1.4 X10 <sup>9</sup> 4-10 X 10 <sup>9</sup> /L		
6	Neut 10 50-75 %	<b>Medications</b>	
7	lymph's 50 20-50 %	1	Granulocyte colony-stimulating factor
8	mono 11 3-10 %	2	verapamil
9	bands 29 0-15%	3	pericolace
10	protein total 7.2 6.0-8.3 g/dl	<b>Medical History</b>	
11	albumin 3.6 3.5-4.9 g/dl	1	
12	LDH 318 60-200 U/L	<b>Allergies</b>	
13	Urinalysis WNL	1	NKA
14	right pleural effusion	<b>Immunizations</b>	
15	refractory anemia	1	None
16	packed red blood cell transfusions		
17	pancytopenia		
18	Stapholococcus epidermis		
19	congestion of mesenteric and peritoneal fat		
20	benign hepatic cysts		
21	benign cortical calcification of the left kidney		
22	myelodysplastic syndrome		
23	non-insulin dependent diabetes mellitus		
24	hypertension		
25	high blood pressure		

## Exhibit 42

Validation Project		Results		
			<b>Gold Standard Diagnosis</b>	
<b>Case Number</b>	14-36011		Blastomycosis	
<b>Isabel Pro Healthcare</b>			<b>Date Entered</b>	
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>	
1	100%	Interstitial Lung Disease	We matched the terms: dry cough   nonproductive cough   hacking	
2	81%	COPD	We matched the terms: weight	
3	78%	Internal Ischemia	We matched the terms: weight	
4	77%	Coronavirus	We matched the terms: dry cough   weight	
5	75%	Hypersensitivity Pneumonitis	We matched the terms: dry cough   nonproductive cough   weight	
6	71%	Ischemic Heart Disease	We matched the terms: high blood	
7	70%	Cryoglobulinemia	We matched the terms: leg ulcer   leg ulcers   weight loss   hypertension   high	
8	70%	Intracranial Hemorrhage	We matched the terms:	
9	68%	Obesity-Hypoventilation Syndrome	We matched the terms: weight	
10	68%	Pneumoconioses	We matched the terms: dry cough   weight	
<b>Age</b>	53		<b>Chief Complaints</b>	
<b>Gender</b>	Male		1	Ulcer, Right Lower Leg
<b>Travel</b>	North America		2	Cough, Dry Hacking
<b>Symptoms, Pre-encounter Observations</b>			3	Weight Loss
1	Blood Pressure Elevated 120/80		<b>Medical History</b>	
2	Pulse Normal 80		1	Hypertension
3	Respiration Rate Normal 18		2	Smoker
4	Temperature Normal 98.6		3	Alcohol in Moderation
<b>Medications</b>			<b>Immunizations</b>	
1	N/A		1	None
<b>Allergies</b>				
1	NKA			

## Exhibit 43

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	
		Gold Standard Diagnosis	
Case Number	32-36031	Cryoglobulinemia	
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	100%	Nephrotic Syndrome	We matched the terms: facial swelling   pedal edema   oedema lower limb   oedema lower limbs   swollen hand   swollen hands   hypertension   weight gain   fever
2	78%	Hemolytic Uremic Syndrome	We matched the terms: swelling of the face   swollen hand   swollen hands   hypertension   high blood pressure   fever   brown
3	57%	Heart Failure/CHF	We matched the terms: leg edema   leg swelling   hypertension   hypertensive   elevated blood pressure   weight gain   brown
4	55%	Endocarditis	We matched the terms: leg edema   iv drug abuse   fever   fevers   brown
5	50%	Cardiomyopathy - Dilated Cardiomyopathy	We matched the terms: peripheral oedema   swollen feet   swollen legs   leg swelling   swollen leg   hypertension   weight gain   fever
6	50%	Erythromelalgia	We matched the terms: face swelling   swollen face   swollen feet   swollen foot   swollen hand   swollen hands   increased temperature
7	50%	Glomerulonephritis - Rapidly Progressive	We matched the terms: feet edema   hand swelling   hand edema   high blood pressure   fever   elevated body temperature
8	46%	Pulmonary Edema	We matched the terms: lower extremity edema   swollen hand   swollen hands   hypertensive   weight gain
9	43%	Cellulitis	We matched the terms: facial edema   foot edema   lower extremity edema   leg swelling   swollen leg   fever
10	42%	Non-Hodgkin Lymphoma	We matched the terms: face swelling   swelling leg   legs swelling   swelling legs   fever   pyrexia
Age	38	Chief Complaints	
Gender	Male	1	Facial Swelling, painless
Travel	North America	2	Extremities Swelling, painless
Symptoms, Pre-encounter Observations		Medical History	
1	Intravenous Drug Abuse	1	IV Cocaine
2	Methodone Maintenance	2	IV Brown Heroin
3	Hypertension	3	Shares Needles
4	Weight Gain	Allergies	
5	Blood Pressure Very High	1	NKA
6	Fever	Immunizations	
Medications		1	None
1	Methodone		
2	Hydrochlorothiazide		

## Exhibit 44

## Translational Project - Diagnostic Decision Support Systems

Validation Project		Results	
Case Number		42-36023	<u>Gold Standard Diagnosis</u> Hairy Cell Leukemia
Isabel Pro Healthcare			<u>Date Entered</u>
Ranked	% Match	Diagnostic Alternatives	Reasons
1	100%	Coronavirus - COVID-19	We matched the terms: shortness of breath   dyspnea   difficulty breathing   labored breathing   respiratory distress   chest pain   productive cough   cough with phlegm   fever   rigor   rigors   chill   chills   hypertension   diabetes mellitus   diabetes
2	75%	Bacterial Pneumonia	We matched the terms: shortness of breath   labored breathing   respiratory distress   chest pain   productive cough   cough with expectoration   fever   pyrexia   chill   chills   tachypnea   tachypnoea   rapid breathing
3	72%	Pulmonary Thromboembolism - Pulmonary Embolism and Infarction	We matched the terms: shortness of breath   dyspnea   chest pain   productive cough   fever   tachypnea   tachypnoea   rapid breathing
4	67%	Hypersensitivity Pneumonitis	We matched the terms: shortness of breath   dyspnea   breathlessness   breathless   chest pain   productive cough   fever   febrile   fevers   chill   chills   hypertension
5	66%	Viral pneumonia - Herpes Simplex Virus Pneumonia	We matched the terms: shortness of breath   chest pain   productive cough   fever   chill   chills   shaking chills   increased respiratory rate   rapid breathing
6	65%	Sepsis and Shock	We matched the terms: breathlessness   breathless   fever   fevers   high temperature   high temp   shivering   rigor   rigors   chill   chills   shaking chills   tachypnea   rapid breathing   fast breathing   hypertension
7	59%	Cardiogenic Shock	We matched the terms: shortness of breath   dyspnea   chest pain   substernal chest pain   tachypnea   rapid breathing   hypertension   diabetes   depression
8	56%	Antiphospholipid Syndrome	We matched the terms: shortness of breath   short of breath   chest pain   fever   tachypnea   rapid breathing   hypertension   depression
9	56%	Brucellosis	We matched the terms: dyspnea   difficulty breathing   chest pain   fever   febrile   fevers   chill   chills   depression   depressed
10	56%	Lung Abscess	We matched the terms: shortness of breath   dyspnea   chest pain   productive cough   fever   febrile   rigor   rigors   chill   chills
Please note: Check your spelling. The term/s amitriptyline, premarin, provera may not have influenced the result.			
<u>Age</u>	67		<u>Chief Complaints</u>
<u>Gender</u>	Female		1 Shortness of Breath
<u>Travel</u>	North America		<u>Medications</u>
<u>Symptoms, Pre-encounter Observations</u>			1 Amitriptyline
1	Chest pain		2 Premarin
2	cough with yellow sputum		3 Provera
3	deep inspiration		<u>Medical History</u>
4	fever		1 diabetes
5	chills		2 depression
6	rapid pulse		3 Family History of Diabetes
7	respiratory rate elevated		<u>Allergies</u>
8	high blood pressure		1 NKA
			<u>Immunizations</u>
			1 None

## Exhibit 45

Translational Project - Diagnostic Decision Support Systems			
Validation Project		Results	
Case Number		Gold Standard Diagnosis	
Isabel Pro Healthcare		Date Entered	
Ranked	% Match	Diagnostic Alternatives	Reasons
1	100%	Coronavirus	We matched the terms: weight loss   fatigue   anorexia   loss of
2	100%	Non-Hodgkin Lymphoma	We matched the terms: weight loss   malaise   tiredness   fatigue   tired   anorexia   loss of appetite   decreased appetite   poor appetite   abdominal fullness   joint pain   low back pain
3	84%	Crohn Disease	loss   malaise   fatigue   anorexia   loss of appetite   abdominal fullness   early satiety   joint pain   arthritis   af
4	68%	Brucellosis	We matched the terms: weight loss   malaise   fatigue   anorexia   loss of
5	65%	Interstitial Lung Disease	We matched the terms: weight loss   tiredness   fatigue   lethargy   tired   anorexia   loss of appetite   aching joints   hypertension
6	64%	Pituitary Neoplasms	We matched the terms: weight loss   fatigue   decreased appetite   arthralgias   arthralgia   high blood pressure   atrial fibrillation   irregular heartbeat
7	63%	Whipple Disease	We matched the terms: weight loss   fatigue   loss of appetite   arthralgia   joint
8	61%	Endocarditis	We matched the terms: weight loss   malaise   fatigue   anorexia   arthralgia   joint pain   arthritis   af   bilateral
9	59%	Interstitial Nephritis	loss   malaise   tiredness   fatigue   lethargy   tired   joint pain   arthritic   low back pain   hypertension   high blood pressure   af
10	55%	Heart Failure/CHF	We matched the terms: fatigue   tired   decreased appetite   hypertension   hypertensive   elevated blood pressure   atrial fibrillation   af   bilateral
			Please note: Check your spelling. The term/s digoxin, ibuprophen, herniorrhaphy, jewish may not have
<b>Age</b>	61		<b>Chief Complaints</b>
<b>Gender</b>	Male		1 Weight Loss
<b>Travel</b>	North America		2 Fatigue
<b>Symptoms, Pre-encounter Observations</b>			3 Tiredness
1	Blood Pressure High 130/70		4 Loss of Appetite
2	Pulse Normal 88		5 Abdominal Fullness
3	Respiratory Rate Normal 16		6 Arthralgias
4	Temperature Normal 98.6		7 Lower Back Pain
<b>Medications</b>		<b>Medical History</b>	
1	Hydrochlorothiazide	1	Hypertension
2	Digoxin	2	Atrial Fibrillation
3	Ibuprofen (Motrin)	3	Bilateral Herniorrhaphy
<b>Allergies</b>		4	Smoker
1	NKA	5	Jewish
<b>Immunizations</b>		6	No Family History
1	N/A		



<b>Exhibit 46</b>				
<b>Translational Project - Diagnostic Decision Support Systems</b>				
<b>Validation Project</b>		<b>Results</b>		
		<b>Gold Standard Diagnosis</b>		
<b>Case Number</b>	22-36112	Whipple's Disease		
<b>Isabel Pro Healthcare</b>		<b>Date Entered</b>		
<b>Ranked</b>	<b>% Match</b>	<b>Diagnostic Alternatives</b>	<b>Reasons</b>	
1	100%	Crohn Disease	We matched the terms: diarrhea   diarrhoea   weight loss   unexplained weight loss   foul smelling stool   foul smelling	
2	70%	Celiac Disease	We matched the terms: diarrhea   weight loss   unexplained weight loss   foul-smelling	
3	47%	Intestinal Obstruction - Fecal Impaction	We matched the terms: diarrhea   weight loss   fecal incontinence   nausea   sick	
4	41%	Renal Failure - Acute Renal Failure; C	We matched the terms: diarrhea   diarrhoea   weight	
5	40%	Intestinal Ischemia - Chronic Mesente	We matched the terms: diarrhea   weight loss   nausea   vomiting   vomit   smoking	
6	39%	Giardiasis	We matched the terms: diarrhea   weight loss   foul-smelling	
7	38%	Irritable Bowel Syndrome	We matched the terms: diarrhea   loose stools   weight	
8	36%	Diarrheal Disorders - Acute Diarrhea	We matched the terms: diarrhoea   loose stools   weight loss   nausea   vomiting   nausea	
9	34%	Pancreatitis - Chronic Pancreatitis	We matched the terms: diarrhea   diarrhoea   weight loss   foul smelling	
10	33%	Pseudomembranous/Drug-Induced C	We matched the terms: diarrhea   diarrhoea   faecal	
			Please note: Check your spelling. The term/s supplements, appendectomy may not have	
<b>Age</b>	36		<b>Chief Complaints</b>	
<b>Gender</b>	Male		1	Diarrhea
<b>Travel</b>	North America		2	Weight Loss
<b>Symptoms, Pre-encounter Observations</b>				
1	Foul smelling, greasy, non-bloody diarrhea			
2	Fecal Incontinence		<b>Medical History</b>	
3	Nausea		1	Mild mental retardation
4	Vomiting		2	Microcytic, hypochromic anemia
5	Volume depletion		3	Status post cholecystectomy
<b>Medications</b>			4	Status post appendectomy
1	Iron supplements		5	Smoker
<b>Allergies</b>			<b>Immunizations</b>	
1	NKA		1	N/A

## Vita

### Joe M. Bridges

#### Executive

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Founded, managed, and disposed of two private oil & gas companies

Founded, managed, and disposed of a private oil & gas contract drilling company

Evaluated, negotiated, and completed acquisition of 1,400-acre ranch

Founded, managed IPOs, managed exchange listings for two public oil & gas companies

Served as CFO, managed public filings, oversaw property acquisitions, banking relationships and ultimate sale of a public oil & gas company

Served as Executive Vice President & Division Manager of a Major Houston Bank

Served as Vice President & Lending Officer of a Major Houston Bank

Served as Reservoir Engineering Manager of District Office for a Major Oil Company

#### Skills

Executive Management

Financial Management

Engineering Management

Real Estate & Agricultural Management

#### Work History

1992-01 - **Managing General Partner**

Current Bridges Family Partnership, Ltd., Houston, TX

Investment Portfolio Management, Ranch Management, Oil & Gas Property Management, Real Estate Property Management, Financial Reporting and Banking

- 2004-07 - **President**  
Current Bridges Family Petroleum, Inc., Houston, TX  
Oil & Gas Property Acquisition Analysis, Reservoir Engineering and Geological Analysis, Financial Reporting and Banking
- 1989-05 - **President**  
Current Greystone Ranch, Inc., Houston, TX  
Ranch Management, Cattle Management, Wild Game Management, Real Estate Property Management, Financial Reporting and Banking
- 2005-01 - **Founder, Managing Director**  
2008-06 Greystone Drilling, LP, Houston, TX  
Executive responsibilities for all aspects of oil & gas contract drilling company
- 2004-05 - **Founder, Managing Partner**  
2008-06 Greystone Oil & Gas, LLP, Houston, TX  
Executive Responsibilities for all aspect of oil and gas drilling, production, property acquisition and dispositions, financial reporting, and financings
- 1995-01 - **Founder, Chairman & Chief Executive Officer**  
2004-05 Greystone Petroleum, Inc., Houston, TX  
Executive responsibilities for all aspects of oil & gas activities: property acquisitions and dispositions, drilling of wells, construction of pipeline systems, marketing of natural gas, financial reporting, and financing
- 1983-08 - **Founder, President & Chief Operating Officer**  
1994-12 Kelley Oil Corporation, Houston, TX  
Executive responsibilities for all aspects of oil & gas operations, drilling, production, financial and banking, equity offerings
- 1980-10 - **Senior Vice President & Chief Financial Officer**  
1983-08 McRae Consolidated Oil & Gas, Inc., Houston, TX  
Financial responsibilities for all aspect of oil & gas operations, gas pipeline operations, property acquisitions, banking, and public filings

- 1975-07 - **Executive Vice President**  
 1980-09 Houston National Bank, Houston, TX  
 Executive Manager of Banking Division including Energy, International, National and Correspondent Banking Departments; Senior Vice President in charge of Energy Department
- 1971-01 - **Vice President, Lending Officer**  
 1975-06 First City National Bank, Houston, TX  
 Lending Officer in Petroleum & Minerals Department; Bank loans to oil & gas production companies, drilling companies, other energy-related businesses
- 1966-08 - **Reservoir Engineering Manager, Reservoir Engineer**  
 1970-12 Humble Oil & Refining Company, Rosenberg, Katy, TX  
 Reservoir Engineering Manager, Rosenberg District; Reservoir Engineer, Katy District

### Education

- 1960 -1965 **Bachelor of Science: Mechanical Engineering**  
 University of Texas At Austin - Austin, TX
- 1965 -1966 **Master of Science: Mechanical Engineering**  
 University of Texas At Austin - Austin, TX
- 1973 -1975 **Certificate of Completion: Banking**  
 School of Banking of The South at Louisiana State University - Baton Rouge, LA
- 2019-08 - **Doctorate of Health Informatics: Biomedical Informatics**  
 Current Doctoral Candidate Enrolled in DHI Program, Graduation Ceremony May 13, 2022  
 University of Texas Health Science Center at Houston, School of Biomedical Informatics - Houston, TX

### Affiliations

- University of Texas Health Science Center at Houston
- 2011 to Present: Member Development Board

2012 to Present: Member, Advisory Council, School of Nursing

2012 to Present: Member, Advisory Council, School of Biomedical  
Informatics

2012: Member, Interview Committee, Dean, School of Biomedical  
Informatics

2016 - Present: Member, UTHHealth Campaign Cabinet

2018 to 2021: Chairman, Advisory Council School of Biomedical  
Informatics

2019: Member, Interview Committee, Chief Medical Information Officer,  
UTHealth

2019 - Present: Member, External, Audit Committee, UTHealth

Member, Legion of Honor, Society of Petroleum Engineers

Member, American Medical Informatics Association

Member, Healthcare Information Management Systems Society

Member, Society to Improve Diagnosis in Medicine

### **Publications**

Atkins, S. J., & Bridges, J. M. (1977, January 1). Project Financing. Society of Petroleum  
Engineers. doi:10.2118/6334-MS

### **Unpublished Reports**

Bridges, Joe M. (December 9, 2019) "Module 14 Informatics Specialties, Critical Review" Paper

Submitted in Partial Fulfilment, BMI5300 Introduction to Biomedical Informatics, Fall

2019 <https://uth.instructure.com/courses/47156/assignments/132050>

- Bridges, Joe M. (April 12, 2020) “Validation Methodologies for Diagnostic Decision Support Systems” Final Paper Submission, BMI 6328 Healthcare Delivery in EHR Enabled Environment, Spring 2020 <https://uth.instructure.com/courses/49820/assignments/132215>
- Bridges, Joe M. (May 1, 2020) “Final Paper Submission”, BMI 6002 Directed Studies Spring 2020,  
[https://uth.instructure.com/courses/49202/assignments/145153?module\\_item\\_id=585021](https://uth.instructure.com/courses/49202/assignments/145153?module_item_id=585021)
- Bridges, Joe M. (August 10, 2020) “A Literature Review to Compile a List of Commonly Misdiagnosed Conditions in Ambulatory Care Practices in the United States” Final Paper Submission, BMI 7350 Scholarly Foundations of Advanced Health Informatics Practice, Summer 2020  
<https://uth.instructure.com/courses/53646/assignments/147248/submissions/56346>
- Bridges, Joe M. (Draft November 30, 2020) “Evaluation of a Computerized Diagnostic Decision Support System in Primary Practice” Draft Final Report Submission, BMI6002 Directed Studies, BMI7170 Project Advisement, Fall 2020,  
<https://uth.instructure.com/courses/56459/assignments/161248/submissions/56346?download=3554355>
- Bridges, Joe M. (April 2, 2021). “Project Management Plan: Evaluation of a Computerized Diagnostic Decision Support System in Primary Practice” Final Paper Submission, BMI 7360, Advanced Project Management,  
<https://uth.instructure.com/courses/58510/assignments/170608/submissions/56346?download=3876779>
- Bridges, Joe M. (June 2, 2021). “Diagnostic Challenge: Validate a Diagnostic Decision Support System” Submission to the Journal DIAGNOSIS, Publication declined June 17, 2021,

<https://uth.instructure.com/courses/62444/assignments/194064/submissions/56346?download=4185732>

**Field of Study**

Health Informatics