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CASIDS: CHRONIC ARSENIC INTOXICATION DIAGNOSTIC SCORE IDENTIFICATION SYSTEM

Belo Horizonte
Instituto de Ciências Biológicas
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Dissertation presented to the Graduate Program of Bioinformatics of the Federal University of Minas Gerais in partial fulfillment of the requirements for the degree of master's in bioinformatics.

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Ana Beatriz Delavia Thomasi

Às quatorze horas do dia **25 de novembro de 2019**, reuniu-se, no Instituto de Ciências Biológicas da UFMG, a Comissão Examinadora de Dissertação, indicada pelo Colegiado do Programa, para julgar, em exame final, o trabalho intitulado: **"Casids: Chronic Arsenic Intoxication Diagnostic Score Identification System"**, requisito para obtenção do grau de Mestre em **Bioinformática.** Abrindo a sessão, o Presidente da Comissão, **Dr. Aristóteles Góes Neto**, após dar a conhecer aos presentes o teor das Normas Regulamentares do Trabalho Final, passou a palavra à candidata, para apresentação de seu trabalho. Seguiu-se a arguição pelos Examinadores, com a respectiva defesa da candidata. Logo após, a Comissão se reuniu, sem a presença da candidata e do público, para julgamento e expedição de resultado final. Foram atribuídas as seguintes indicações:

Prof./Pesq.	Instituição	CPF	Indicação
Dr. Aristóteles Góes Neto	UFMG	544348825-20	Aprovada
Dr. Rodrigo Richard Gomes	PUC-Minas	001.536.786-07	APROVADA
Dr. Sergio Ulhoa Dani	INST. MEDAWAR	588.918.036-34	Aprovada

Pelas indicações, a candidata foi considerada: APROVADA

O resultado final foi comunicado publicamente à candidata pelo Presidente da Comissão. Nada mais havendo a tratar, o Presidente encerrou a reunião e lavrou a presente ATA, que será assinada por todos os membros participantes da Comissão Examinadora.
Belo Horizonte, 25 de novembro de 2019.

Dr. Aristóteles Góes Neto ____________________

Dr. Rodrigo Richard Gomes ____________________

Dr. Sergio Ulhoa Dani ____________________

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RESUMO

O arsênio, 33º elemento da tabela periódica, é um metal pesado amplamente encontrado no meio ambiente. O contato com o arsênio pode causar sérias consequências à saúde e tem sido considerada uma substância cancerígena tipo 1 pela Agência Internacional de Pesquisa do Câncer (IARC).

A intoxicação por arsênio é comumente diagnosticada incorretamente devido à semelhança de seus sintomas com outras condições. Para tornar esse procedimento mais preciso, Sergio Dani e Gerhard Franz Walter desenvolveram uma metodologia que dá um diagnóstico assertivo, denominada Chronic Arsenic Intoxication Diagnostic Score (CAsIDS).

Buscando aprimorá-lo ainda mais, este projeto visa utilizar sua metodologia para criar um sistema de identificação que conecte médicos, laboratórios e pacientes. Este sistema fornecerá uma forma de inserir o resultado de um exame que verifica a carga de arsênio ósseo de um paciente e também preencher uma avaliação clínica sistêmica. Ao mesmo tempo, armazenará e mostrará todos os dados adquiridos em painéis para aprimorar estudos futuros.

Palavras-chave: CAsIDS. Envenenamento por Arsênio. Avaliação Clínica Sistêmica.

ABSTRACT

Arsenic, the 33th element of the periodic table, is a heavy metal widely found in the environment. The contact with arsenic may cause serious health consequences and it has been considered carcinogenic substance type 1 by the International Agency for Research on Cancer (IARC).

Arsenic intoxication is commonly misdiagnosed due to its symptom's similarity to other conditions. In order to make this procedure more accurate, Sergio Dani and Gerhard Franz Walter developed a methodology that gives an assertive diagnosis, called Chronic Arsenic Intoxication Diagnostic Score (CAsIDS).

Seeking to improve it even more, this project aims to use their methodology to create an identification system that connects physicians, laboratories and patients. This system will provide a way to insert the result of an exam that verifies bone arsenic load of a patient and also fill a systemic clinical assessment. At the same time, it will store and show all the acquired data in dashboards to improve future studies.

Keywords: CAsIDS. Arsenic Poisoning. Systemic Clinical Assessment.

LIST OF FIGURES

LIST OF TABLES

LIST OF ABREVIATIONS

app-	Aplication
As-	Arsenic
BaaS-	Backend-as-a-Service
BAsL-	Bone Arsenic Load
BW	Body Weight
CAsI -	Chronic Arsenic Intoxication
CAsIDS -	Chronic Arsenic Intoxication Diagnostic Score
DMA-	Di-Methyl Arsenic
eSP	Estimated Skeleton Phosphate
eSW	Estimated Skeleton Weight
IARC-	International Agency For Research On Cancer
iAs	Inorganic Arsenic
MMA-	Mono-Methyl Arsenic Acid
P-	Phosphate
WHO-	World Health Organization

CONTENTS

1 INTRODUCTION

Arsenic, the 33th element of the periodic table, is a heavy metal widely found in the environment. It has the ability to create two forms of components inside the human body: organic and inorganic. Both of these forms are absorbed mainly through oral route, due to water or food contamination, as well as exposure through inhalation as a result of occupational exposure. The ingested arsenic may cause serious health consequences and has been considered carcinogenic substance type 1 by the International Agency for Research on Cancer (IARC).

When acute arsenic poisoning occurs, the first symptoms are: profuse vomiting, diarrhea, cramping, excessive salivation, fever, alterations in the cardiovascular system and central nervous system, which may even cause death. On the other hand, when there is a chronic infection, the symptoms include: changes in the skin with hyperkeratosis, formation of warts and pimples on the palms and soles of the feet. All of these symptoms are very common in other diseases which can be easily confused, leading to a wrong diagnosis.

In order to make this diagnosis process more accurate, Sergio Dani and Gerhard Franz Walter developed a methodology, called Chronic Arsenic Intoxication Diagnostic Score (CAsIDS). It presents a distinctive feature, bone arsenic load as an essential criterion for the individual risk assessment combined with a systemic clinical assessment of 12 multiple choice questions. Each answer has a different weight score and, when summed, it results in the probability of an individual have been poisoned by arsenic.

Although CAsIDS have been tested on many cases and proved precise, it has two main disadvantages: it needs to be done manually and the data gathered is not being recorded for future analysis. Seeking to improve it even more, this project aims to use their methodology to create a monitoring system that connects physicians, laboratories and patients. This system allows a laboratory to insert bone arsenic load exam result of a patient and also help physicians to fill a systemic clinical assessment virtually. At the same time, it will store and show all the acquired data in dashboards to contribute to the academic literature.

This system will be explained throughout this paper, which is divided into four sections: The first one will introduce what is arsenic, how poisoning occurs and affects the body. Next, it will be presented the CAsIDS methodology. In the following section, the process of creation and development of the system prototype will be explained. Finally, the fourth section shows the final considerations and the future works planned.

1.1 Motivation

Helping doctors to deliver a more accurate diagnosis while also improving patients' lives by applying the right treatment.

1.2 The main objective

Create a system to register and monitor patients throughout their Arsenic poisoning diagnosis, improving upon the existing CAsIDS methodology and store and show all the entered data in dashboards to contribute to the academic literature.

1.2.1 The specific objectives

- Create a Mobile Application;
- Create a network among Doctors, Laboratories and Patients;
- Store a database for future studies;
- Contribute with the community with an open source code.

2 ARSENIC POISONING

2.1 What is Arsenic?

Arsenic (As) is the 33rd chemical element of the periodic table and is recognized as a metalloid (Figure 1) (PUBCHEM, 2019).

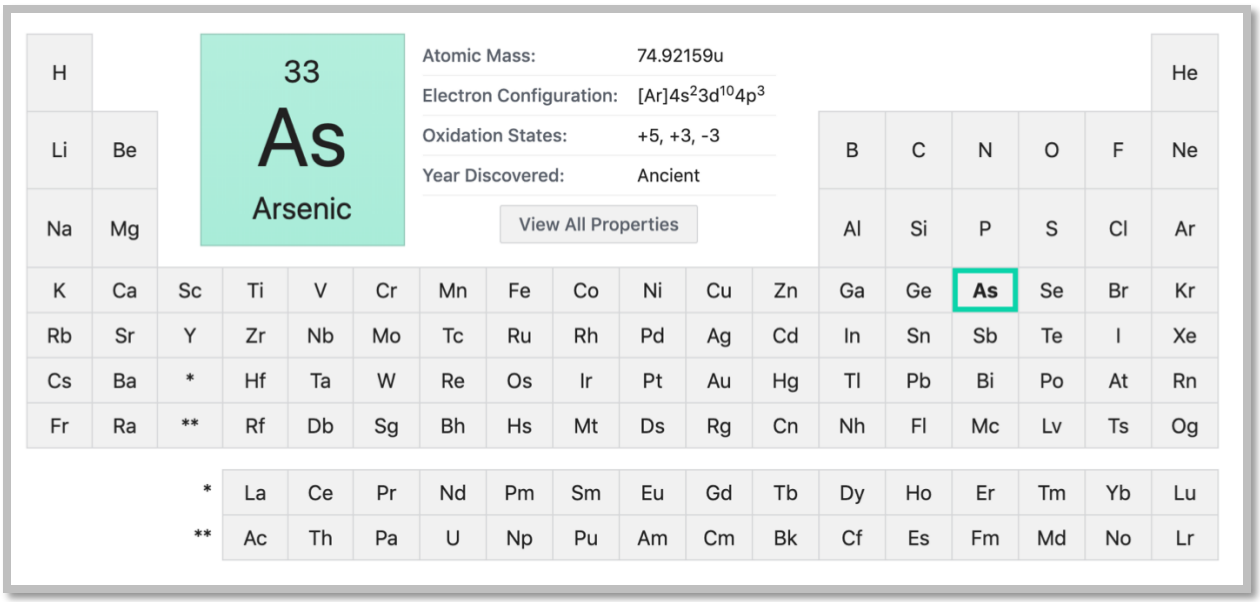


Figure 1. Arsenic in the periodic table (PUBCHEM, 2019)

This element rarely exists in its pure form, being found as organic or inorganic compounds. The organic compounds are not toxic, while the inorganic is extremely dangerous. The latter usually appears in the forms of trivalent (arsenite3+) or pentavalent oxidation (arsenate5+) (Figure 2) (HONG; SONG; CHUNG, 2014).

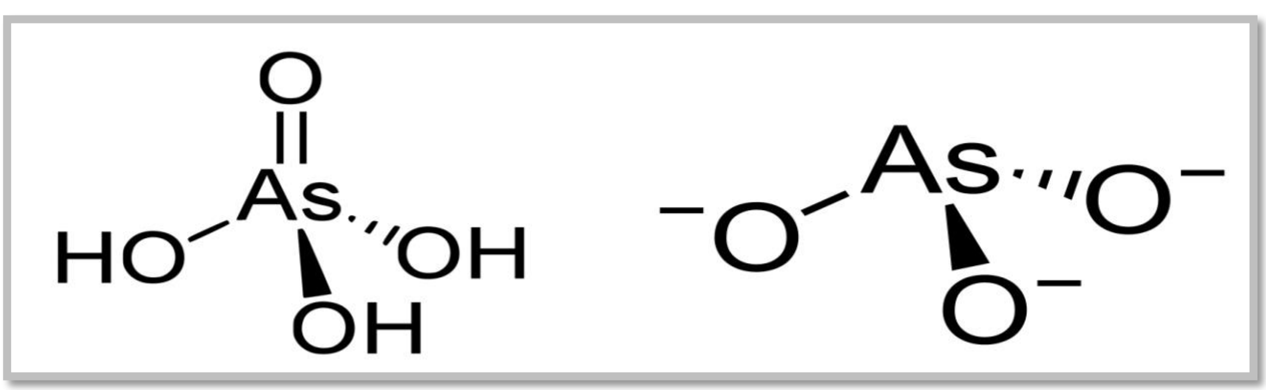


Figure 2. Arsenate x Arsenite (AUTHOR, 2019).

2.2 Where is Arsenic found?

Arsenic is naturally present in the environment, being mostly found in Earth's crust, in its derivates (ex: soil, plants, water, rocks and minerals) and in natural phenomena like volcanism or forest fires. The concentrations of As in each source varies: in crust, it was reported approximately 1.5 mg/kg while in sulphide minerals 10^5mg/kg (BRUNT; VASAK; GRIFFIOEN, 2004).

Being exposed to it is natural but have been recently aggravated by human activities, as it is widely used by industries such as agricultural, technological, among others (Figure 3). The multiple applications of it worldwide have led to a broad contamination of the environment, mainly affecting groundwater (SAHOO; KIM, 2013; TCHOUNWOU et al., 2012).

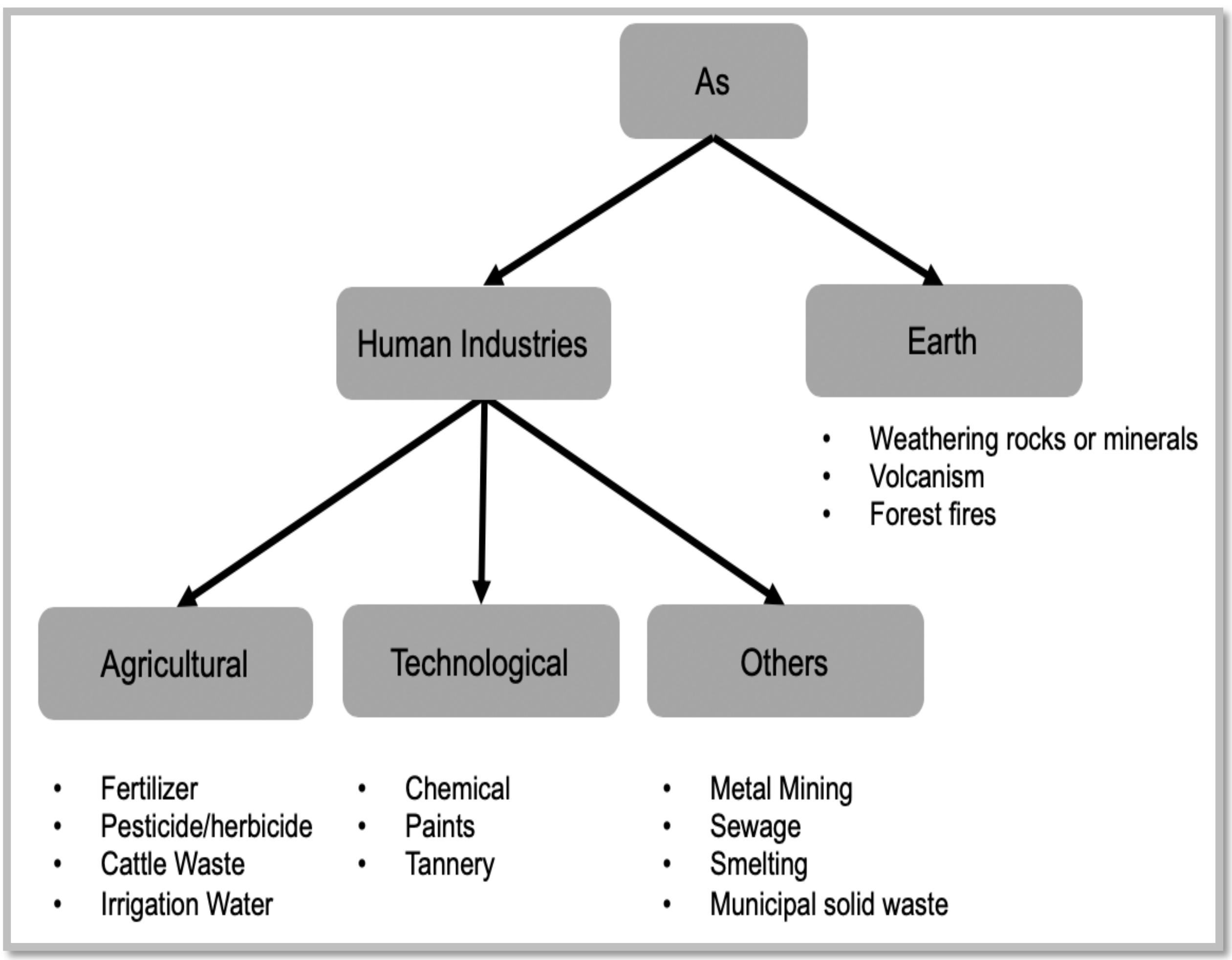


Figure 3. Sources of Arsenic (Adapted from SAHOO; KIM, 2013).

2.3 How does groundwater get contaminated by Arsenic?

In 2001, the World Health Organization (WHO) estimated that about 130 million people around the world were exposed to Arsenic. The affected countries (Figure 4) had concentrations above 50μgL^{-1}in their groundwater (VAN HALEM et al., 2009).

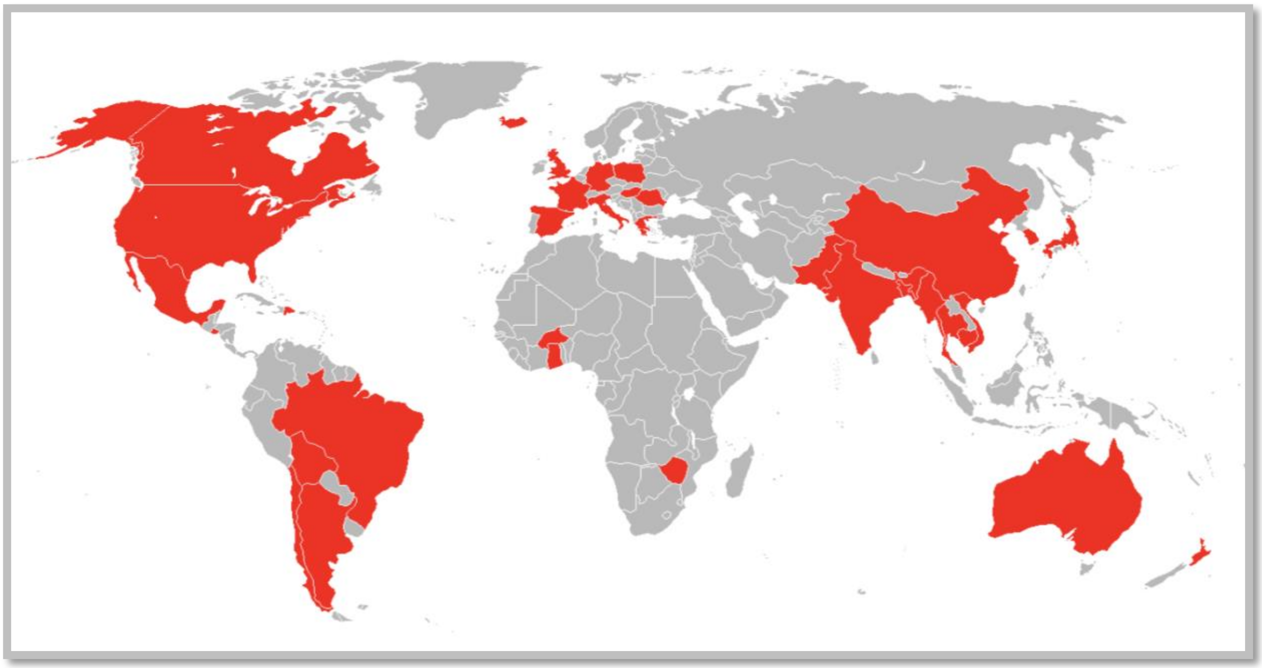


Figure 4. Groundwater Arsenic-affected countries (VAN HALEM et al., 2009).

Arsenic contamination of groundwater is an endless cycle, that as mentioned before can be caused by geogenic and anthropogenic sources (CENTENO et al., 2007; SHAHID et al., 2018).

2.3.1 Geogenic

Geogenic sources can occur through:

- Erosion process of rocks and minerals;
- Volcanism; or
- Forest fires.

The resulting sediments of erosion and volcanism get deposited in the soil, turning to organic matter. This matter, rich in As, is absorbed by groundwater, becoming contaminated. Meanwhile, forest fires produce smoke, releasing As in its volatile form into the air. Clouds are formed partially from this substance and, through precipitation, find its way back to the ground, thus contaminating the groundwater, as previously mentioned (Figure 5) (CENTENO et al., 2007; SHAHID et al., 2018).

2.3.2 Anthropogenic

Man-induced contamination occurs through:

- Industrial waste;
- Agricultural fertilizers and pesticides;
- Livestock.

Industrial waste, fertilizers and pesticides and feces produced by livestock are all rich in As. These sources affect directly the soil, becoming another source of groundwater contamination (Figure 5) (CENTENO et al., 2007; SHAHID et al., 2018).

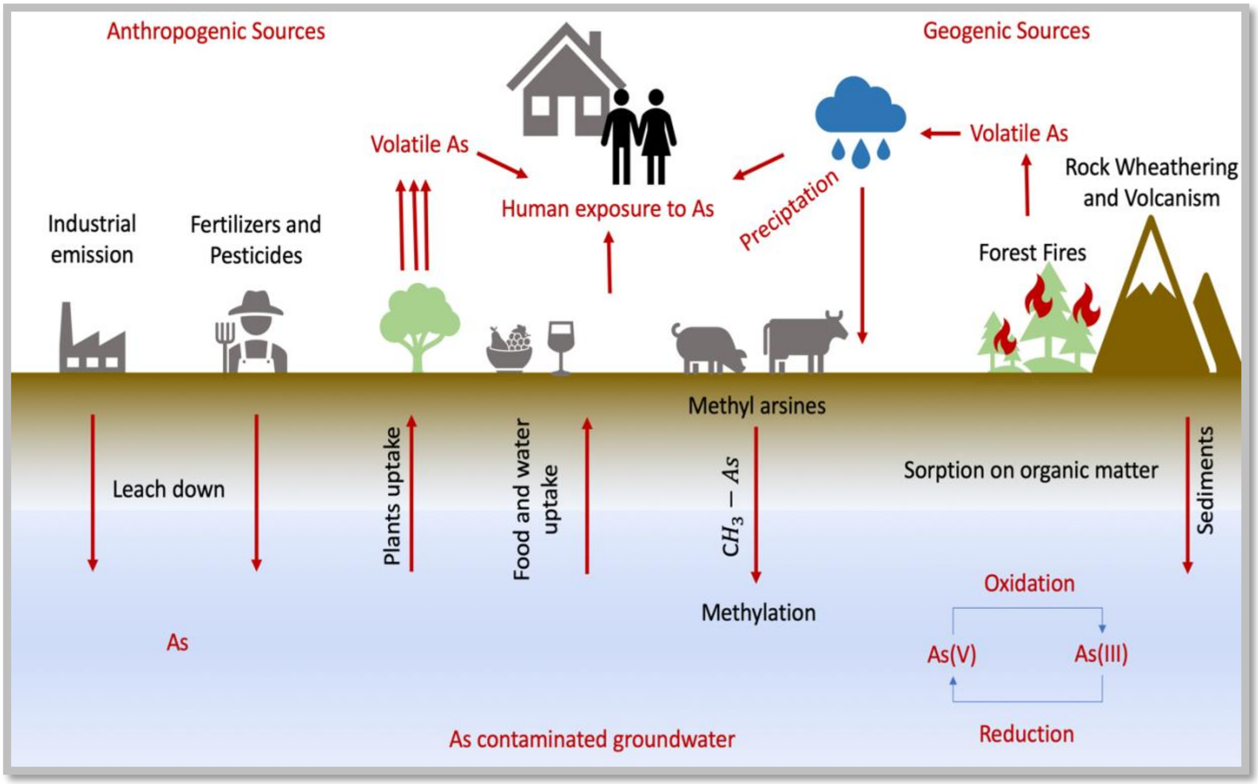


Figure 5. Arsenic cycle (Adapted from SHAHID et al., 2018).

2.4 How humans can be exposed to Arsenic?

Human Arsenic exposure occurs in three main ways, as shown in Figure 6 below:

Figure 6. Arsenic exposure (Autor, 2019).

Inhalation: Plants uptakes As from the contaminated groundwater and releases it into the air in a volatile form throughout photosynthesis or even during natural or induced forest fires. Humans get exposed by inhaling the contaminated air (Figure 5).

Ingestion: Crops as plants uptakes As from the groundwater and also directly from fertilizers and pesticides. Humans get exposed by ingesting their normal diet (Figure 5).

Absorption through skin: Baths, swimming and also occupational exposure can be related to As absorption through skin (RATNAIKE, 2003).

2.4.1 Arsenic exposure standards

In the following Table 1 it is presented the exposure regulations imposed by federal agencies in United States of America for public drinking water, bottled water, air and food (The University of Arizona, 2011).

Source	Federal Agency	Regulation
Public water	US EPA	10 µg/L
Bottled water	US FDA	10 µg/L
Air	US Department of Labor, Occupational Safety & Health Administration	8-hour total weight average permissible exposure limit for general industry of: Inorganic = 10 µg/m; Organic = 0.5 mg/m
Food	US EPA	fruits and citrus at 0.035 ppb
	US FDA	0.05 ppb in eggs and uncooked edible tissues of chickens and turkeys to 0.2 ppb in certain uncooked edible by-products of pigs and others

Table 1. Arsenic standards USA (adapted from The University of Arizona, 2011).

2.5 As inside the body

Arsenic absorbed by the body is stored mainly in the liver, kidney, heart and lungs. Lower amounts are stored in muscles and nervous tissue (Nava-Ruíz and Méndez-Armenta, 2011).

Much of the absorbed arsenate is reduced to arsenite. Biologically, the arsenite (the trivalent substance) is considered the most toxic form of arsenic, which suffers from a primary methylation in the liver and forms mono-methyl arsenic acid (MMA) and di-methyl arsenic (DMA) (Figure 7). These metabolites are excreted rapidly as arsenic through the urine. Although this mechanism of biotransformation was considered a mechanism of elimination, it is now known that these metabolites can be more toxic than inorganic arsenic (Nava-Ruíz and Méndez-Armenta, 2011).

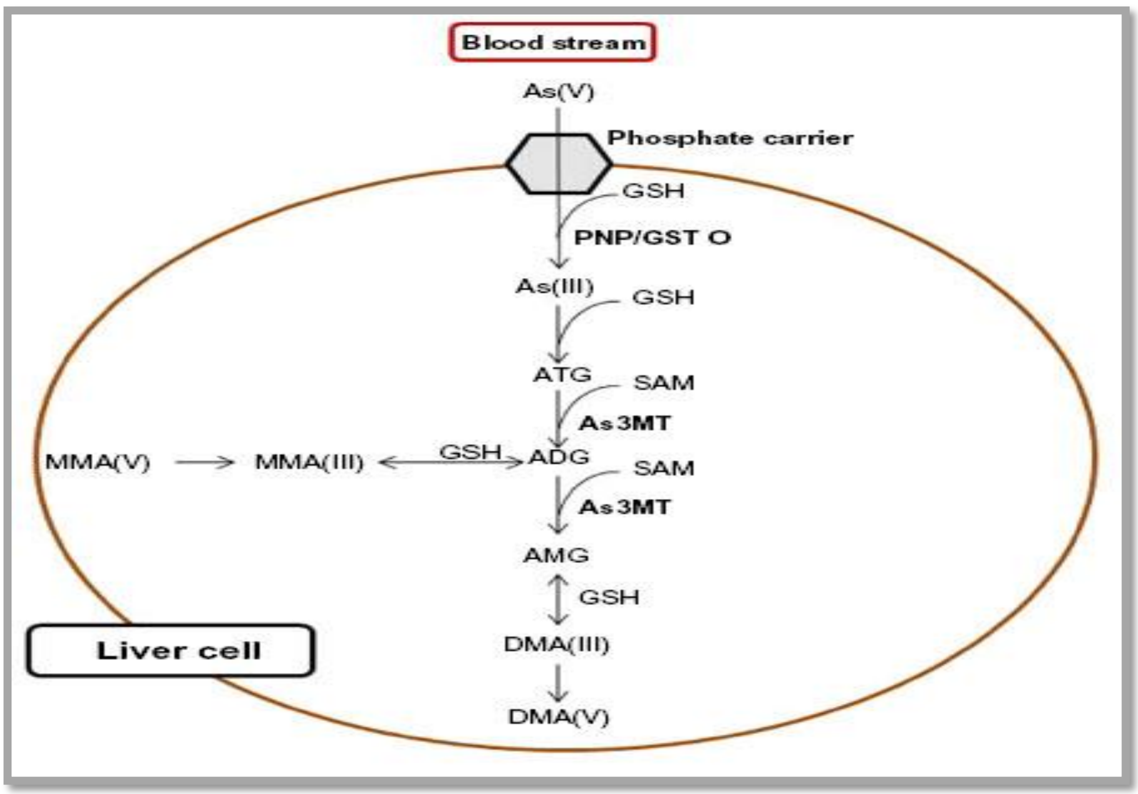


Figure 7. Arsenic inside the Liver cell (GHOSH and SIL, 2015).

The separation and quantification of trivalent and pentavalent inorganic arsenic, as well as that of MMA and DMA, is believed to be the most accurate indicator of a recent arsenic exposure (Nava-Ruíz and Méndez-Armenta, 2011).

2.6 How can arsenic affect our health?

Many factors determine how harmful is As to health, they are:

- Dose: How much arsenic was exposed?;
- Duration: How long have been exposed?;
- Genetic susceptibility: Family traits;
- Route: ingestion, inhalation, or absorption;
- Patient characteristics: Age, lifestyle, etc (The University of Arizona, 2011).

Most of the toxic effects arise from exposure to inorganic arsenic as mentioned before and affects nearly all systems of the body (Figure 8) (SHAHID et al., 2018).

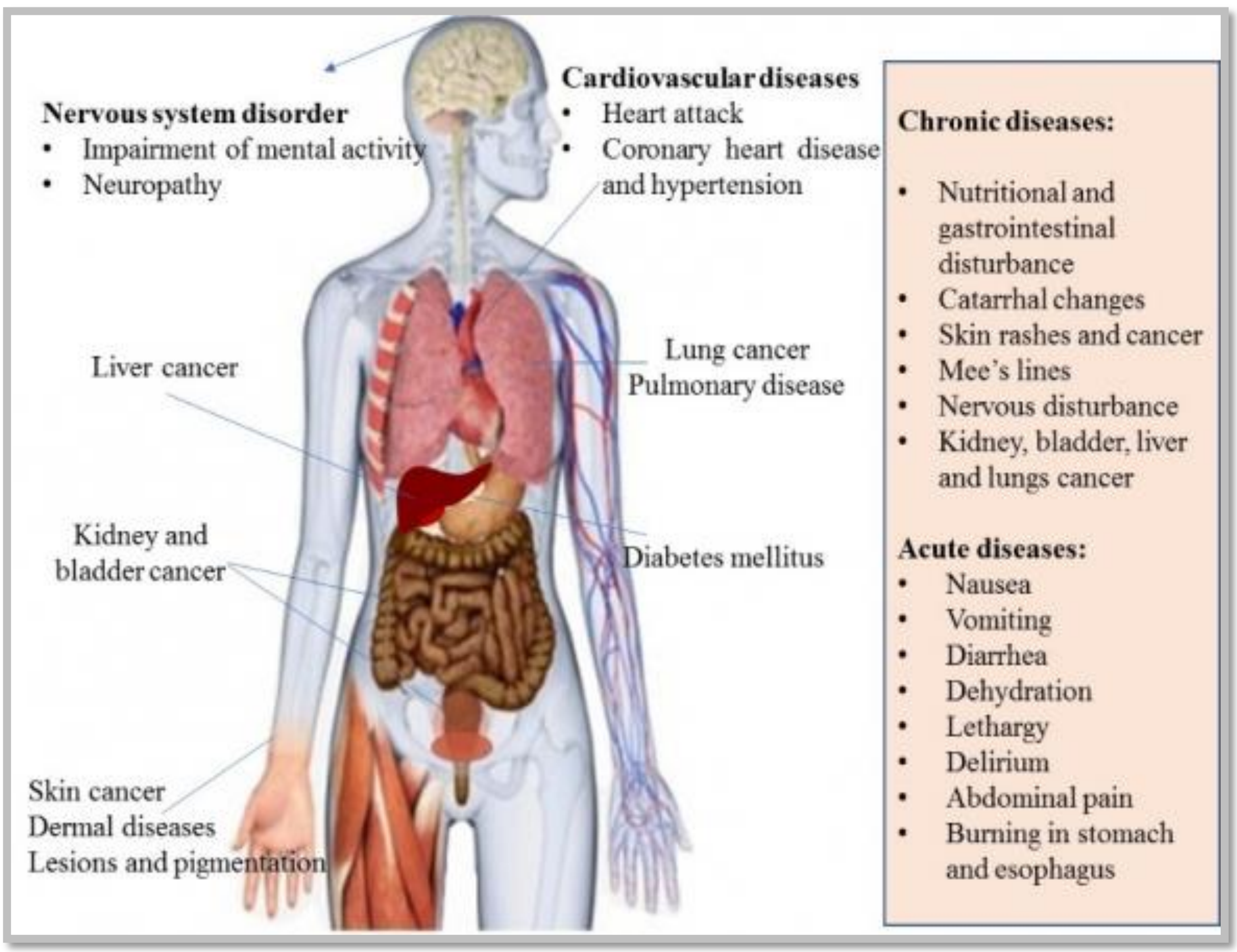


Figure 8. Arsenic poisoning (Adapted from SHAHID et al., 2018).

2.6.1 Symptoms

The development of health problems depends on how much arsenic got into the body and how much it was absorbed. When acute arsenic poisoning occurs, the first symptoms are:

profuse vomiting, diarrhea, cramping, excessive salivation, fever, alterations in the cardiovascular system and central nervous system, which may even cause death. On the other hand, when there is a chronic infection, the symptoms include changes in the skin with hyperkeratosis, formation of warts and pimples on the palms and soles of the feet, with large areas of hyperpigmentation interspersed between small areas of hypopigmentation in the skin. face, neck and back (Figure 9) (Nava-Ruíz and Méndez-Armenta, 2011)..

Figure 9. Arsenic poisoning symptoms (DANI and WALTER, 2017).

3 DIAGNOSTIC OF ARSENIC POISONING, CAsIDS METHODOLOGY

This project will use Sergio Dani and Gerhard Franz Walter study, called Chronic arsenic intoxication diagnostic score published in 2017 in the Wiley Journal of Applied Toxicology. In their study they explored the literature of what is arsenic intoxication and how common it is to misdiagnose this condition and as a solution they proposed a new methodology.

This methodology aims to help physicians to establish a more accurate diagnostic. It presents a distinctive feature, bone arsenic load as an essential criterion for the individual risk assessment combined with a systemic clinical assessment. The latter consists of a form with 12 multiple choice questions, taking into consideration the factors discussed in section 2.6.

3.1 Bone Arsenic Load

Bone arsenic load (BAsL) is estimated using a non-invasive urine test. In order to undertake it, it is required from the patient 3 days of abstinence of rice and fish. The exam consists of two consecutive samples, one in the morning and one in the afternoon.

These samples are then analyzed to determine the concentrations of inorganic arsenic (iAs) and phosphate (P). The iAs:P ratio between the two samples stands for the concentration of As found in the skeleton (since As substitutes P in the bone mineral matrix).

Therefore, to calculate the BAsL we multiply the aforementioned ratio with the estimated skeleton phosphate content (eSP) and divide the result by the estimated skeleton weight (eSW) (DANI and WALTER, 2017).

$$\text{BAsL } (\mu g^{-1}) = \frac{\Delta \frac{iAs}{P} * eSP}{eSW}$$

The eSW consists of a percentage of the individual's body weight (BW, in kilograms) - around 3% in fetus and newborns and around 6–7% in adults and thus it is calculated by:

$$\text{eSW (g)} = 0.03 * \text{BW} * 1000 \text{ (Fetus and newborns)}$$

$$\text{eSW (g)} = 0.07 * \text{BW} * 1000 \text{ (Adults)}$$

The eSP is calculated by the following equation, considering 70% bone mineral matrix and 18.5% phosphate content:

$$\text{eSP (g)} = \text{eSW} * 0.7 * 0.185$$

3.2 CAsIDS Systemic Clinical Assessment

The study postulates that three elements taken together are necessary and sufficient to confirm a suspected chronic arsenic intoxication:

- Diagnosticated or suspected chronic arsenic exposition;
- Presence of arsenic in the bone compartment (taken from the BAsL exam);
- At least one documented subclinical or clinical arsenic toxicity sign or symptom.

This information is obtained through an assessment comprised of 12 multiple choice questions, with each answer having a score. The total score is obtained by the sum of all partial scores. More weight is given to chronic arsenic exposition and BAsL because they are considered as fundamental and essential for diagnosis, respectively. Based on the CAsIDS result, chronic arsenic intoxication is excluded, suspected or confirmed (DANI and WALTER, 2017). The first question evaluates the duration of arsenic exposure (Table 2).

Fundamental condition (must be fulfilled with at least a “1” score)	
1. Known or suspected exposure to inorganic arsenic at concentrations above the reference values for given time periods	Score
100 days	0
3–12 months	1
1–3 years	2
3–26 years	4
3–26 years	8
>50 years	10

Table 2. First question (DANI and WALTER, 2017).

"The concentrations of arsenic in the body reach equilibrium after about 100 days; if the intake of arsenic is suspended then the organ content rapidly falls for all organs except bone – only bone continues to accumulate arsenic throughout life" (DANI and WALTER, 2017). In order to detect bone arsenic load, it is performed a urine test, as mentioned in section 3.1, and its result is scored based on question number 2, shown below (Table 3).

Essential condition (must be fulfilled with at least a “5” score)	
2. Bone inorganic arsenic load (μg g−1)	Score
≤0.060	0
0.061–0.153	5
0.154–1.530	10
1.531–15	20
15.1–150	30
>150	40

Table 3. Second question (DANI and WALTER, 2017).

The third question (Table 4) evaluates if the patient has any dermal diseases.

Typical systemic manifestations of chronic arsenic toxicity	
3. Cutaneous disorders (at least four of the following):	Score
itching;	5
erythema or cutaneous rash;	
conjunctival congestion (it is sometimes observed but not associated with any signs of pain or inflammation in the affected eyes);	
palmo-plantar hyperkeratosis (it is manifested as gradual thickening of soles and palms that leads to cracks and fissures);	
dorsal keratosis (it may appear on dorsum of hands and feet);	
Dupuytren's contracture;	
melanosis (diffuse, abnormal deposition or development of black or dark pigment in the tissues, typically fine spotted melanosis or raindrop pigmentation is found in palms or skin over the chest, back and sometimes on hands and legs);	
leukomelanosis (it can be manifested as simultaneous appearance of pigmented as well as depigmented spots on legs, trunk or other parts of body – The combined features of melanosis with keratosis in palms or soles are the cardinal features of arsenical dermatitis, ASD);	
mucous membrane pigmentation (it is found in some cases on the tongue, inner side of lips, gums or buccal mucous membrane);	
Mee's lines (white lines in the nails).	

Table 4. Third question (DANI and WALTER, 2017).

The next questions 4-11 (Table 5) evaluates if there are any other diseases:

Typical systemic manifestations of chronic arsenic toxicity	Score
4. Hematologic and/or immunologic disorder (at least one of the following): Leukopenia; eosinophilia; anemia including poikilocytic anemia and megaloblastic anemia; splenomegaly and hypersplenism; relapsing infections (chronic infection or more than 2 infections per year); atypical infections (e.g., relapsed tuberculosis).	5
5. Gastrointestinal disorders (at least two of the following): a metallic taste; jaundice; hepatomegaly; hepatic steatosis; liver disease, e.g., non-cirrhotic portal fibrosis with or without portal hypertension with bleeding esophageal varices and splenomegaly and hypersplenism; incomplete septal cirrhosis. Loss of appetite, nausea, vomiting, abdominal pain, diarrhea and increased thirst are common in acute arsenic poisoning but may be also observed in acute-on-chronic arsenic intoxication, as in osteoresorptive arsenic intoxication.	
6. Metabolic, endocrine and reproductive disorders (at least one of the following): Insulin resistance and diabetes mellitus; obesity; low weight; thyroid, parathyroid, gonadal or adrenal dysfunction; osteoporosis; abnormal fecundity; spontaneous abortion.	
7. Chronic pulmonary disease (at least two of the following): Lung function impairment; chronic cough; chronic bronchitis and acute respiratory tract infections; pulmonary nodule; diffuse interstitial lung disease and chronic obstructive pulmonary disease; bronchiectasis; bullous-emphysema.	
8. Cardiovascular disorders (at least two of the following): Peripheral vascular disease (including blackfoot disease); Raynaud's 5 phenomenon and acrocyanosis; non-pitting edema of hands/feet; cardiomyopathy; ventricular tachycardia; QTc interval prolongation; arterial hypertension; ischemic heart disease; stroke.	
9. Renal disorders (at least one of the following): Fanconi syndrome (phosphaturia, glucosuria, aminoaciduria and low-molecular weight proteinuria); albuminuria; chronic kidney disease with progressive deterioration of renal function are clinical characteristics associated with chronic arsenic exposure. Glomerular sclerosis and severe acute tubular necrosis involving all the nephron segments as well as acute tubuleinterstitial nephritis may be observed in acute arsenic poisoning.	
10. Pre-malignancy or malignancy (any pre-cancerous, primary or metastatic neoplasia involving any organ, cell or tissue type including, though not restricted to, skin, bladder and lung).	
11. Neuropathy (at least one of the following): Symmetric neuropathy, polyneuropathy, phrenic paresis, fatigue, hearing loss, blindness, Guillain–Barré syndrome or Guillain–Barré-like syndrome.	

Table 5. 4-11 questions (DANI and WALTER, 2017).

The last question evaluates if there are mental diseases (Table 6).

Typical systemic manifestations of chronic arsenic toxicity	
12. Encephalopathy or mental disease (at least two of the following):	Score
chronic asthenia, insomnia, fatigue, weakness, malaise or dizziness;	5
mental slowing, difficulty concentrating, light-headedness, disorientation or confusion;	
mood and/or behavioral disorder, depression or anxiety;	
delirium, psychosis;	
cognitive impairment, memory impairment or dementia.	
TOTAL	100

Table 6. Twelfth question (DANI and WALTER, 2017).

The final score will be determined by the sum of the scores of each answer and compared with the following Table 7. If the sum is below or equal to 6 Arsenic contamination is excluded with certainty and if it is superior to 51 contamination is confirmed.

Interpretation of CAsIDS results	
	Score
CAsI confirmed with a high degree of certainty	>51
CAsI confirmed	41–50
CAsI highly probable	31–40
CAsI probable	21–30
CAsI cannot be excluded (patient should be re-evaluated)	7–20
CAsI excluded with certainty	≤6

Table 7. CAsIDS Result (DANI and WALTER, 2017).

4 DIGITAL SOLUTION FOR ARSENIC POISONING DIAGNOSTIC

The CAsIDS implementation mentioned in the last section are effective but can result in human error. In order to reduce that, this project created a system that automatizes the process and connect doctors, laboratories and patients.

4.1 App's Flow

The CAsIDS app starts with a Splash screen followed by a Welcome page, that consists of Login, Registration and Dataset features (Figure 10 and 11). Once logged in the user will be redirected to a home screen according to its profile (Patient, Doctor or Laboratory). Which will be discussed in the next sections.

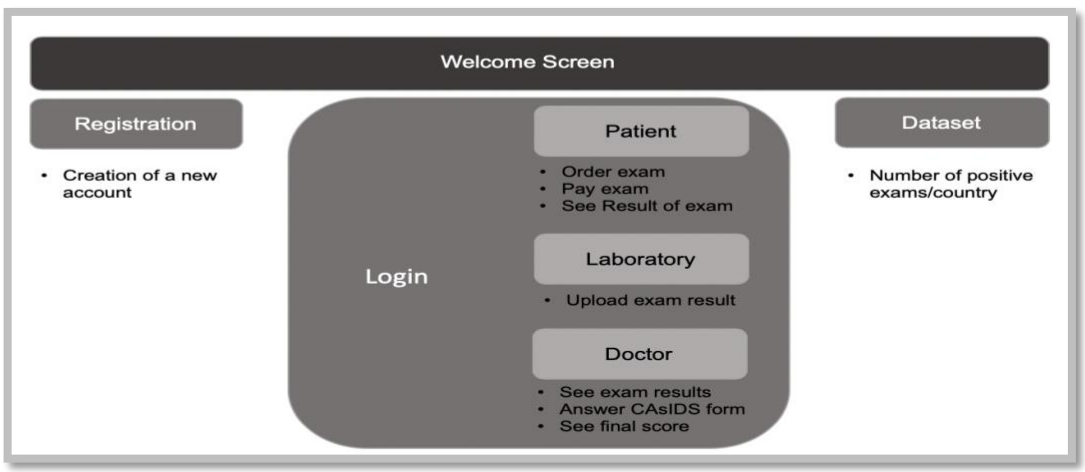


Figure 10. Identification system flow (Author, 2019).

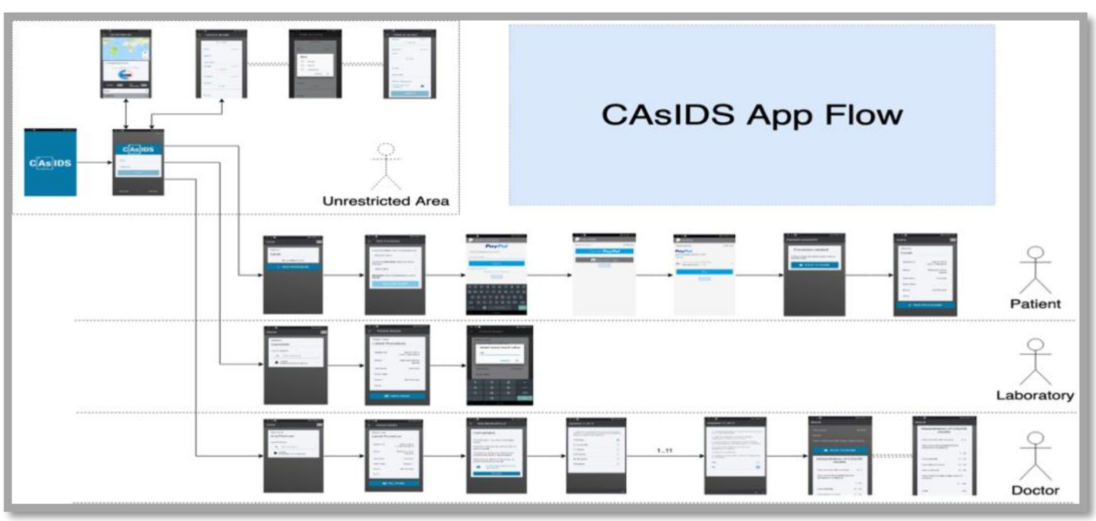


Figure 11. App's flow (Author, 2019).

4.1.1 Splash Screen

The splash screen (Figure 12) is the first element that are presented on application's launch. It consists of a window with a logo.

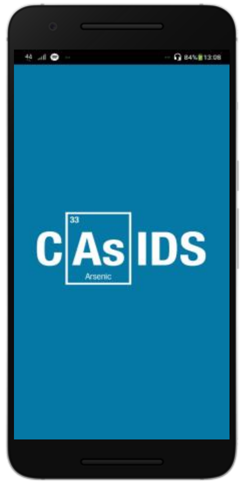


Figure 12. Splash Screen (Author, 2019).

4.1.2 Welcome Page

The welcome page as shown in Figure 13 bellow, has:

- Login card: containing the CAsIDS logo and two fields: email and password;
- Two buttons: Registration and Dataset, each of them redirects to the Registration and Dataset Screens respectively.

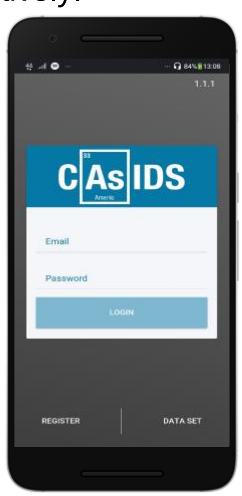


Figure 13. Welcome Page (Author, 2019).

4.1.3 Registration

In order to sign up into the app, (Figure 14 and 15), the user needs to fill a short form with some personal information and accept the terms and conditions involved in using the solution. These informations are:

- **Personal:** Role (Patient, Doctor or Laboratory), name, last name and gender;
- **Contact:** Country of residency and phone;
- **Login:** Email and password.

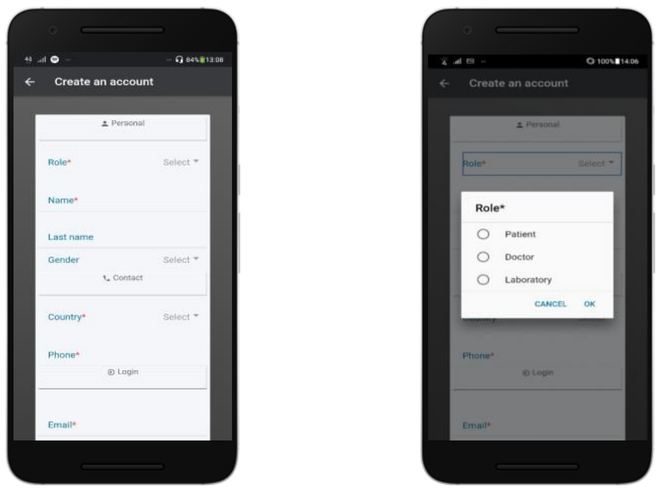


Figure 14. Registration Screen Part 1 (Author, 2019).

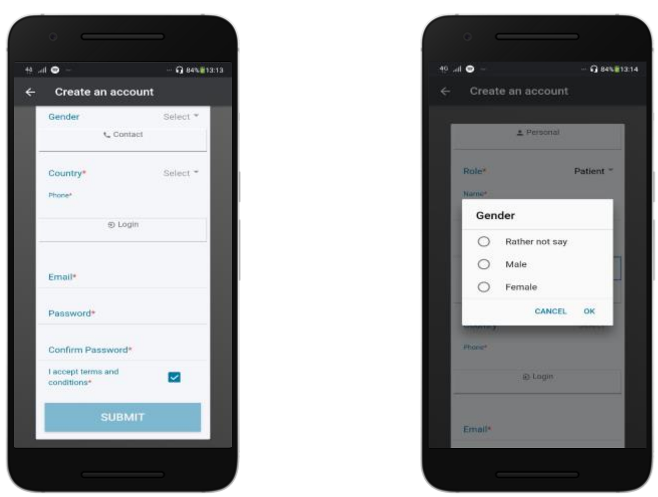


Figure 15. Registration Screen Part 2 (Author, 2019).

4.1.4 Dataset

The dataset screen shows data acquired from procedures done using the app. This information is showed in three forms for any researches who wants to use it. These three forms are: Pizza graph, heat map and list (Figure 16). In the heat map it is possible to zoom in and out. All of these presents the amount of people diagnosed with Arsenic poisoning per country.

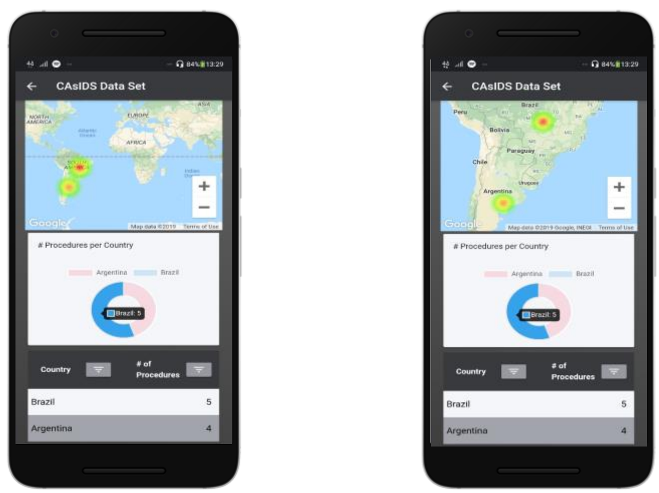


Figure 16. Dataset Screen (Author, 2019).

4.1.5 Profiles

Once logged in successfully, the user will be redirected to a home screen according to its profile (Patient, Doctor or Laboratory). From this point on, the app's flow is different for each profile.

4.1.5.1 Patient's app flow

The patient's home screen contains a card with his name and his latest procedures, if any. There is also a button where it is possible to create a new procedure solicitation.

Figure 20 shows the New Procedure page where the user has to choose a Doctor and a Laboratory that will conduct the analysis. Both had to be registered using the app beforehand. Finally, it's informed the total cost of the exam, which has to be paid through the app using a PayPal account (Figures 17 until 20).

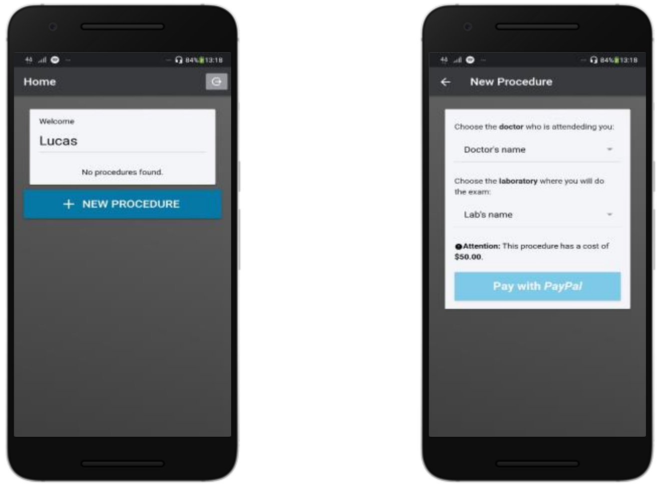


Figure 17. Patient Home Screen (Author, 2019).

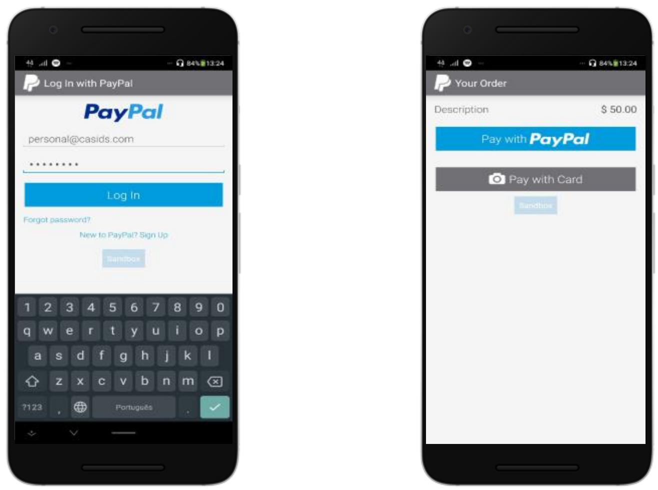


Figure 18. Patient Payment Screens Part 1 (Author, 2019).

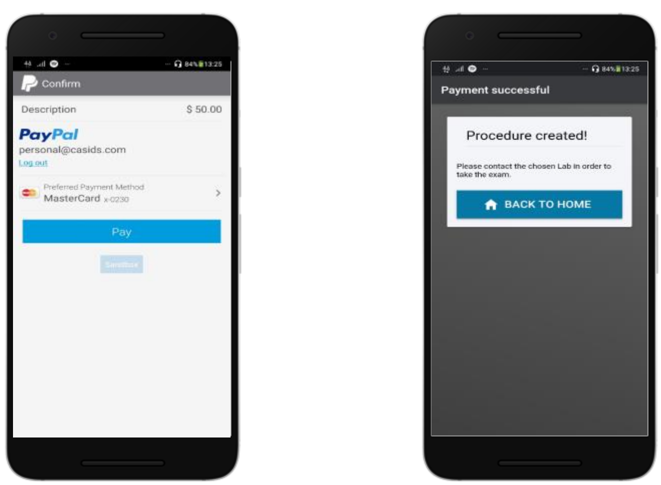


Figure 19. Patient Payment Screen Part 2 (Author, 2019).

After the payment is processed, there is a confirmation message (Payment successful screen) informing the patient to proceed to the chosen Lab. The flow goes back to the home screen with some information of the newly created procedure (Figure 22).

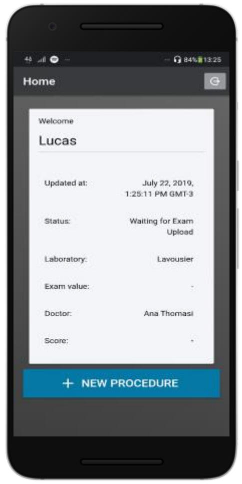


Figure 20. Procedure Screen (Author, 2019).

4.1.5.2 Laboratory app flow

If the logged user is a Laboratory, the home screen will contain a list their patients that have one or more procedures and its status. To make it easier for the user to find the correct entry, it's possible to filter the list by the patient's name. Choosing one patient will open its Detail page, containing information of his latest procedure, similar to the Patient's home page (Figure 21).

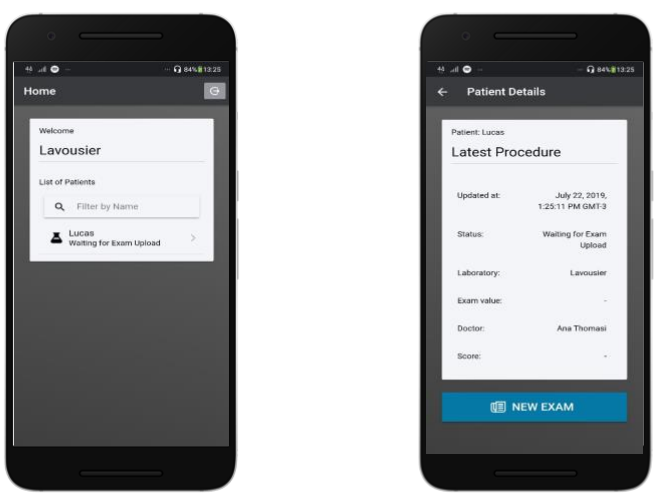


Figure 21. Lab Home Screen (Author, 2019).

There is also a button to upload the result of that patient’s procedure once it’s done (Figure 22). Doing so will automatically update the patient’s procedure status, from “Waiting for Exam Upload” to “Waiting for Form Answers”, which should be conducted by the Doctor.

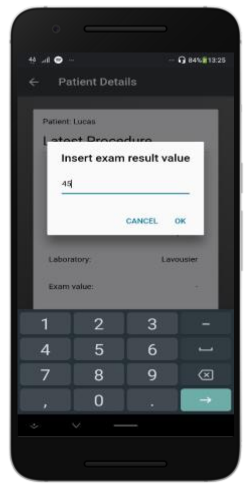


Figure 22. Lab Exam Result Screen (Author, 2019).

4.1.5.3 Doctor’s app flow

The Doctor’s home screen is practically the same as the Laboratory showed in the previous section. Here, the screen contains a card with a list of his patients and choosing an entry will open a Details screen. Instead of uploading an exam result, the Doctor is prompted with a button to fill a form (Figure 23).

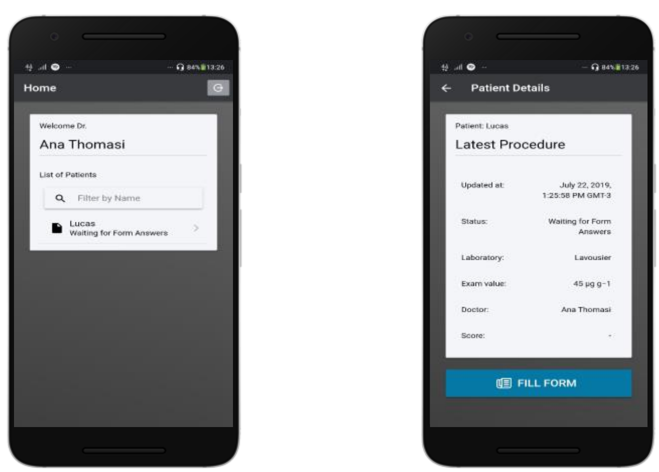


Figure 23. Doctor’s Home Screen (Author, 2019).

This option redirects the user to an Instructions screen, where a short text explaining this part of the procedure and a confirmation box that has to be ticked before continuing. There are 11 multiple choice questions (Figures 24-29), taken from the CAsIDS methodology explained in detail in section 3 of this document – the second question described in the methodology is omitted here once it is automatically evaluated given the Lab's uploaded exam result.

This part should be taken with both Doctor and Patient present: the former can lead by asking the following questions to his patient and marking the chosen answer, or the latter can take the device and fill it on his own, preferable with Doctor's assistance. It is possible to navigate through the questions using the arrows at the bottom of the screen. Each answer has a score, which will be used to sum the final score, showed in the Result screen following the last question (Figure 30). This screen also contains an explanation of each score range according to the CAsIDS study.

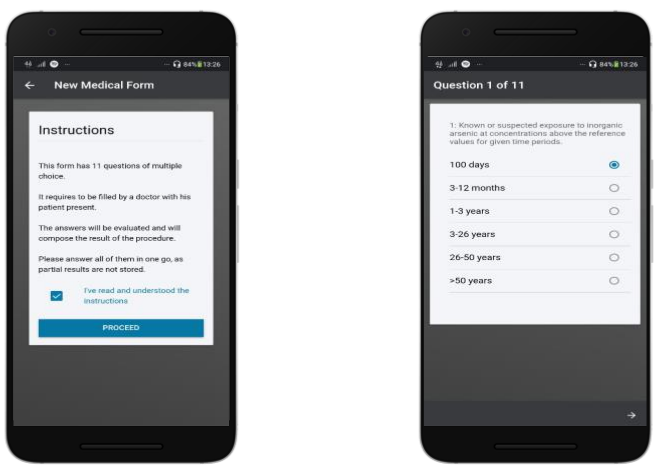


Figure 24. Form Screens (Instruction and Question 1) (Author, 2019).

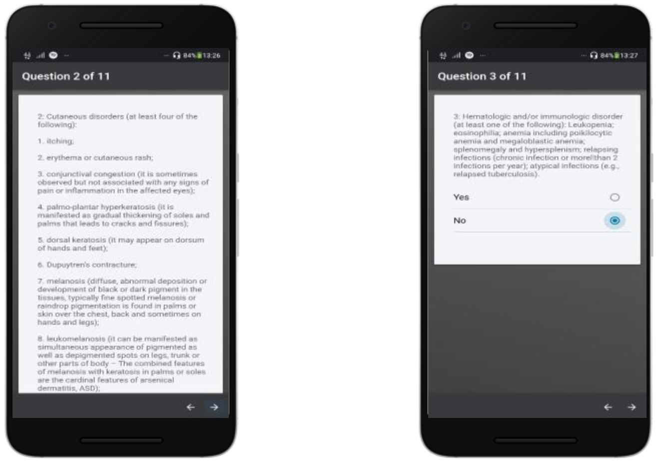


Figure 25. Form Screens (Question 2 and 3) (Author, 2019).

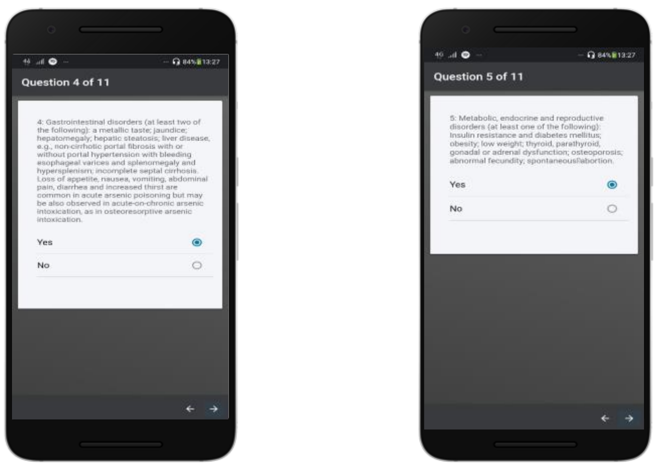


Figure 26. Form Screens (Question 4 and 5) (Author, 2019).

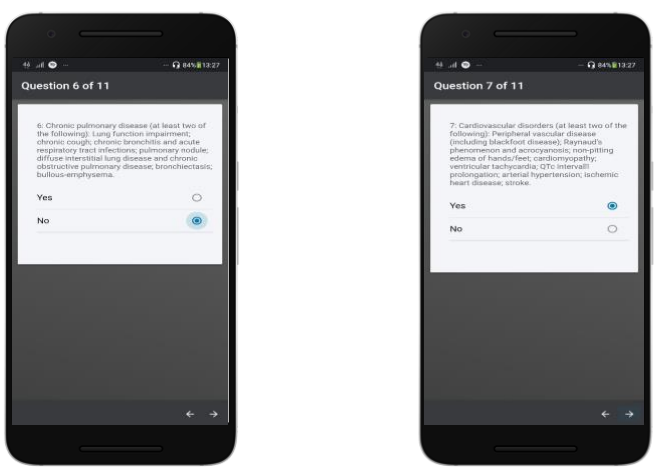


Figure 27. Form Screens (Question 6 and 7) (Author, 2019).

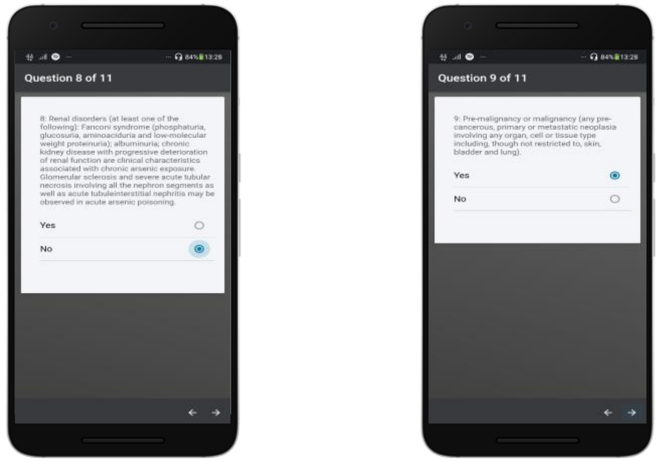


Figure 28. Form Screens (Question 8 and 9) (Author, 2019).

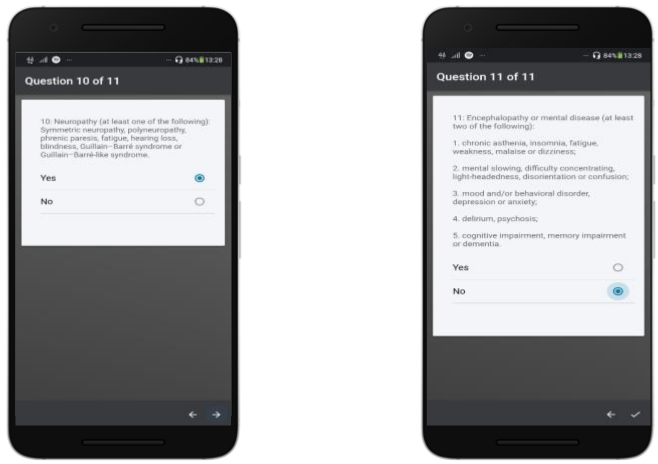


Figure 29. Form Screens (Question 10 and 11) (Author, 2019).

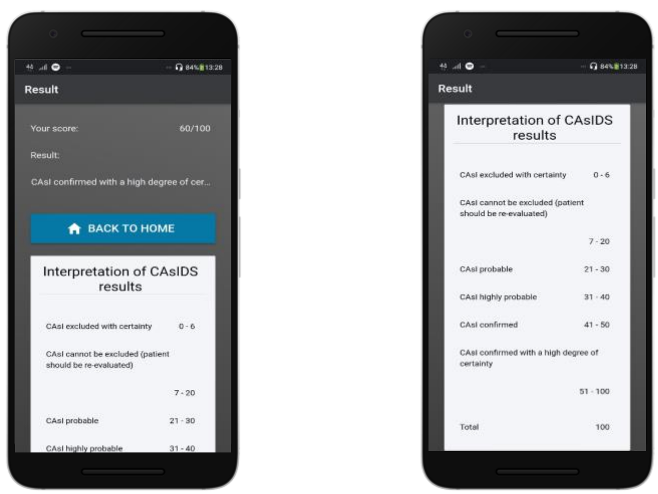


Figure 30. Result Screen (Author, 2019).

At this point, the procedure is considered completed, and its status is automatically updated to "Done" and the Doctor should take proper actions based on his diagnostic. If it's a Chronic Arsenic Intoxication (CAsI) confirmed, it's also included in the Dataset screen, mentioned in section 4.1.3.

4.2 Why a Monitoring System? Which technology?

Nowadays mobile apps have been getting everyone’s attention due to the easy experience and access throughout smartphones. The CAsIDS app was created using Ionic and Firebase (Figure 32).

Figure 31. Ionic and Firebase logos (Author, 2019).

In order to support the main digital platforms used today, Ionic was chosen because it is a mobile app development framework that builds hybrid mobile apps. Hybrid apps are essentially small websites running in a browser shell in an app (Figure 33).

Figure 32. CAsIDS hybrid App (Author, 2019).

4.2.1 Ionic

For this project we used Ionic 4 and its languages HTML5, CSS4 and Typescript to create all the layout and functions. Another option would be using a tool provided by the proper framework, called ionic creator (https://creator.ionic.io/), which is a codeless tool. It allows to create pages by dragging and dropping objects such as a field into a screen while on the background it creates the code automatically (Figure 33). Both ways would work fine, but the first one gives more freedom to personalize the designs.

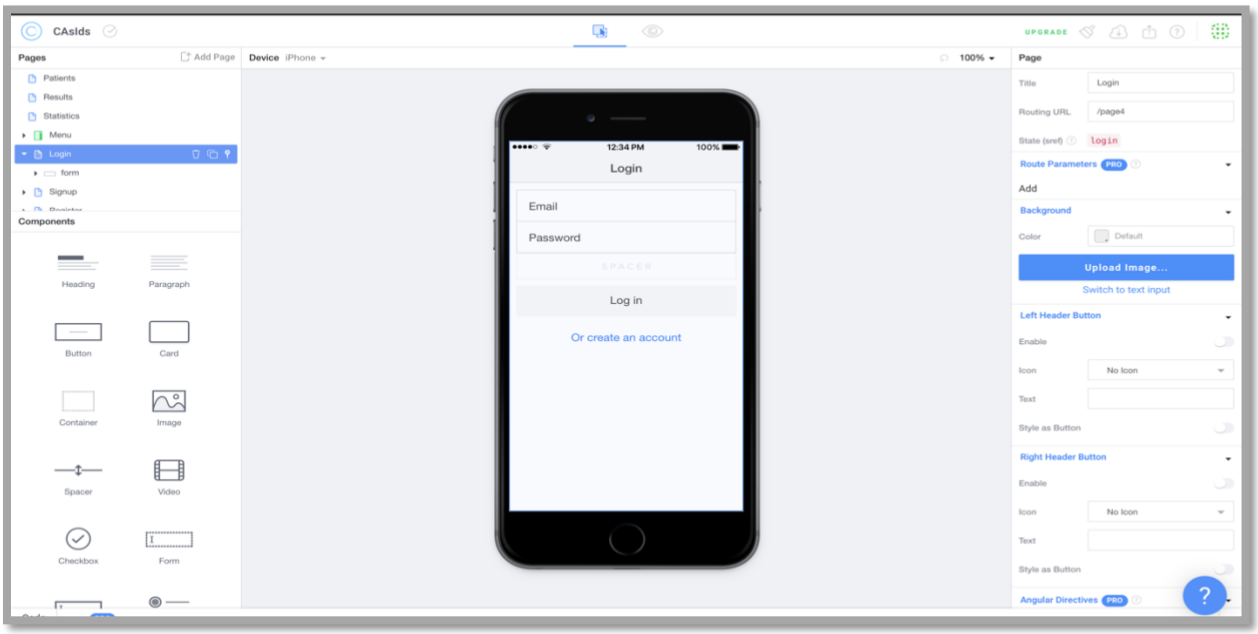


Figure 33. Ionic Creator (Author, 2019).

4.2.2 Firebase

Firebase on the other hand, is a Backend-as-a-Service (BaaS) app development platform that provides hosted backend services such as a real time database, authentication, and hosting for your static files. In this project we used several features from firebase that will be discussed with detail below.

4.2.2.1 Authentication

One of the basic features of most systems is user login and authentication. This feature is important as it takes into consideration aspects such as data security, password encryption, user registration, session control, and more. All of these requirements end up making this feature complex to implement. That's why in this project we resorted to a platform that can solve these problems automatically (Firebase Auth).

CAsIDS app needed to implement data security as its main function is to deal with sensitive medical information. Knowing the user's authentication credentials, in this case e-mail and password, allows the system to securely creates a user UID that connects with the user's profile information stored in the cloud (Figure 34).

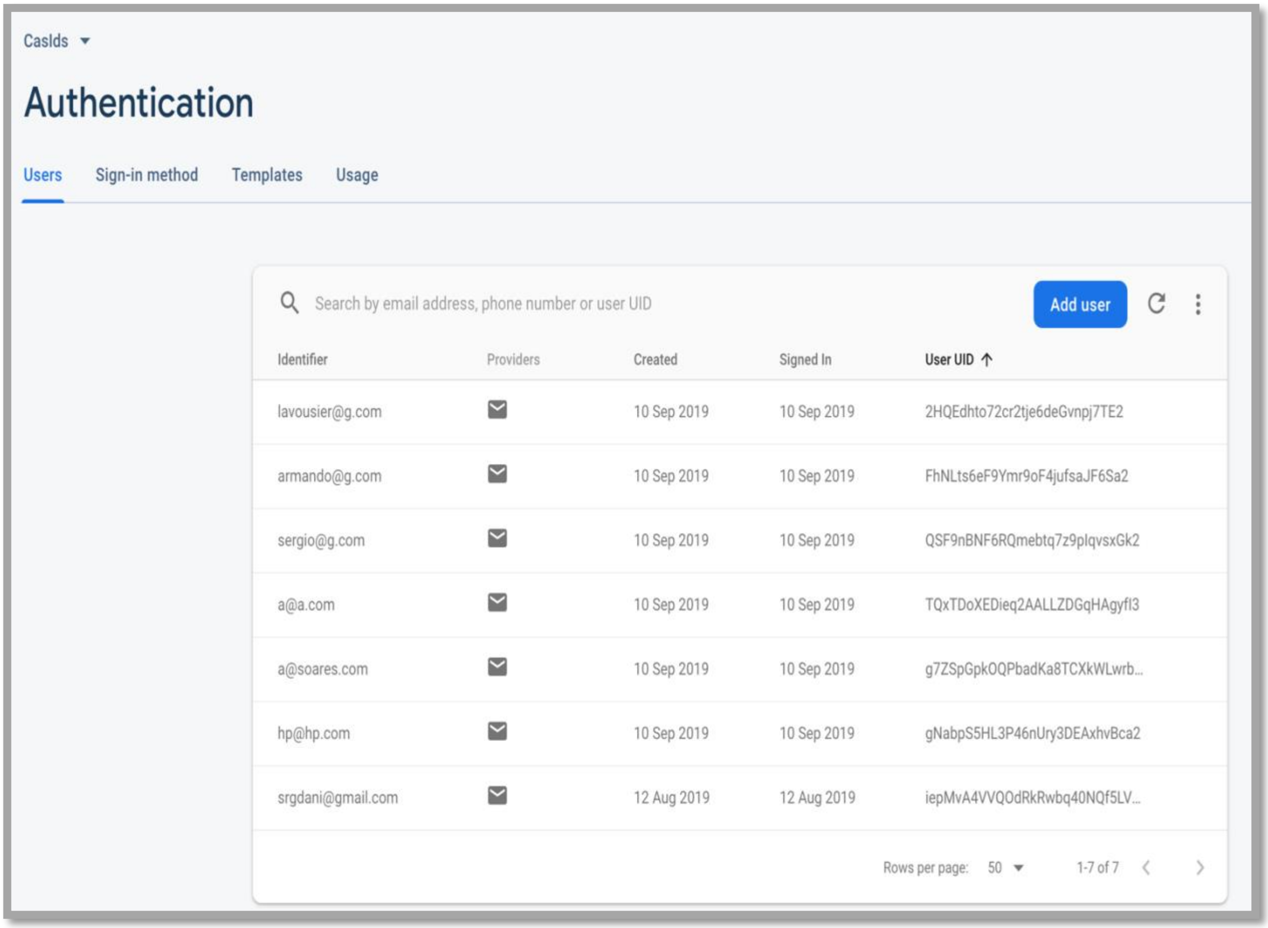


Figure 34. Firebase Authentication (Author, 2019).

It is quite simple to enable Firebase Authentication just need to enable the Email/Password sign-in method on the Authentication menu item (Figure 35).

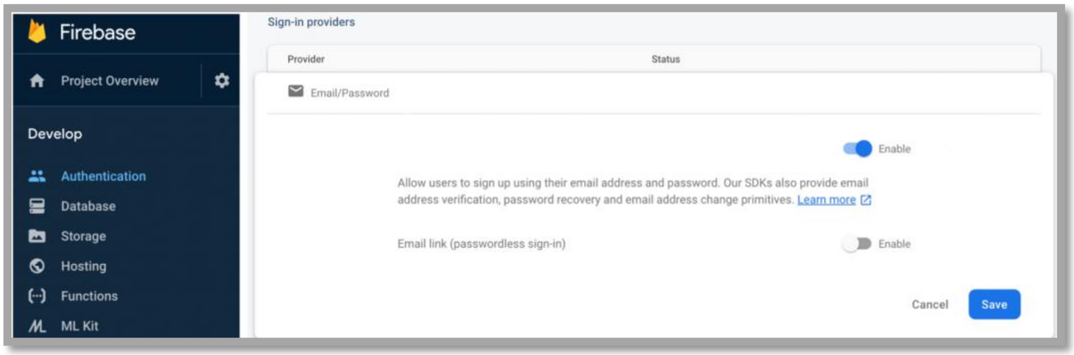


Figure 35. Enabling Authentication (Author, 2019).

4.2.2.2 Database

Cloud computing is the technology that enables the provision of computing services over the internet. Undeniably, it is the current trend, providing differentials such as lower initial investment cost, flexibility, availability, utilization rate, etc.

Firebase also provides a cloud database solution called Cloud Firestore which is fast, fully managed and serverless that simplifies storing, syncing, and querying data. It was used to store all the user's profile information, forms, procedures, scores and heatmap (Figure 36).

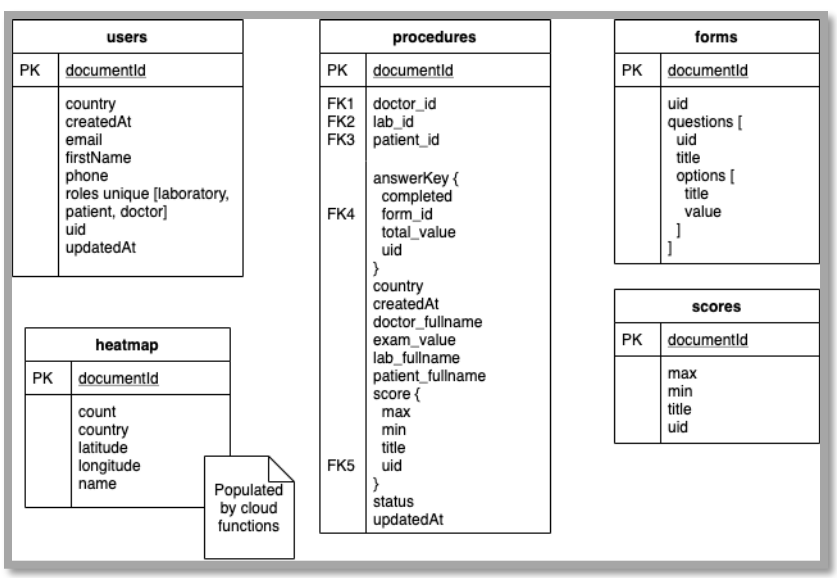


Figure 36. CAsIDs Firestore data diagram (Author, 2019).

The choice of storing them on Firebase (backend) was based on the flexibility of changing data without needing to modify the front-end of the app.

4.2.2.2.1 Forms

As it was mentioned before, forms are one of the data we decided to store in the database. In order to create its collection, was required to give it a name (i.e. forms), and then add a new document that holds all the necessary fields (Figure 37).

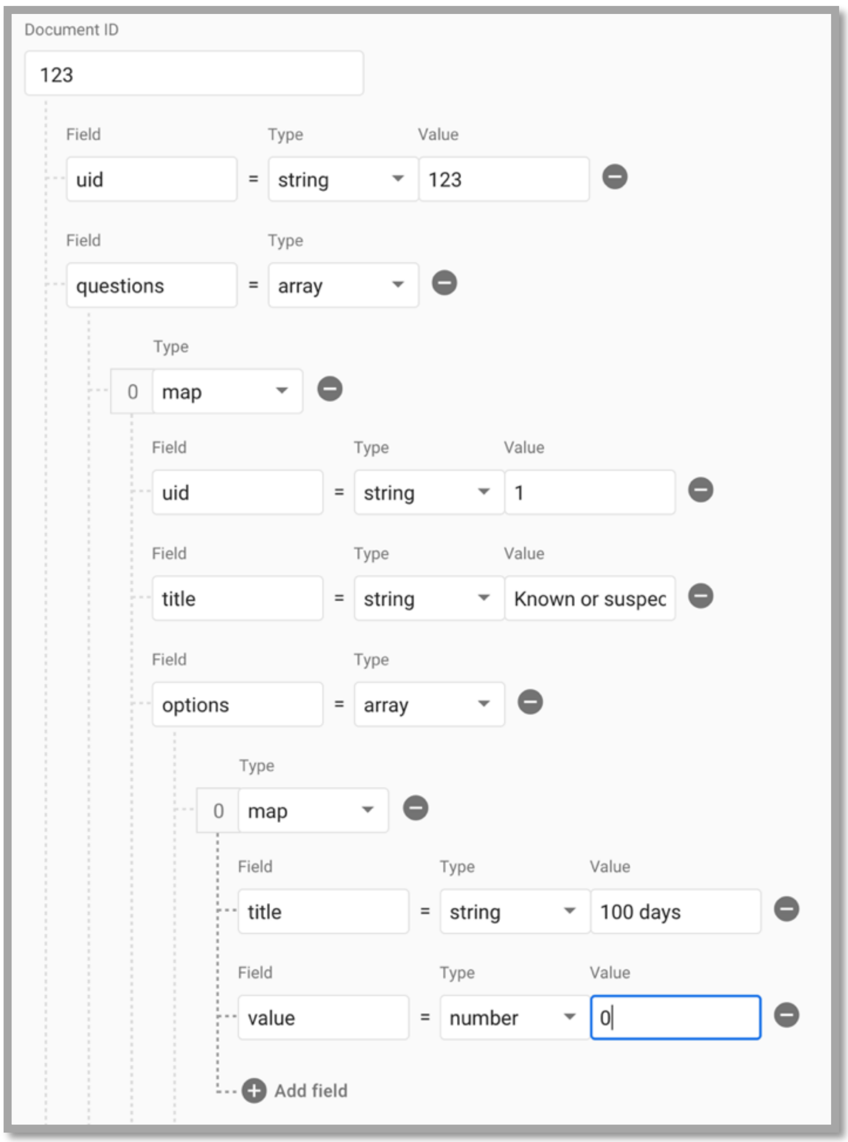


Figure 37. Document fields (question 1, answer option 1) (Author, 2019).

At the top of the document there are two identifiers fields: id and uid. The uid is entirely optional, we only used it to be safe, in case we couldn't access the id.

Next we added a new array, to hold all the 12 questions. Each one of the questions will be a child item (map type), containing an uid field (question identifier) (i.e 1), a title, in this case the text of the question (i.e. *Known or suspected exposure to inorganic arsenic at concentrations above the reference values for given time periods*) and another child array holding the answer options. This new array also has child items (map type), holding the title (i.e. *100 days*) and its respective value or weight (i.e. *0).*

Notice that Firebase automatically generates a hierarchy as more fields are being added to the document. It is only a matter of adding more questions or answer options on the respective array of this hierarchy (Figure 38). It is possible to edit the structure or any defined value later.

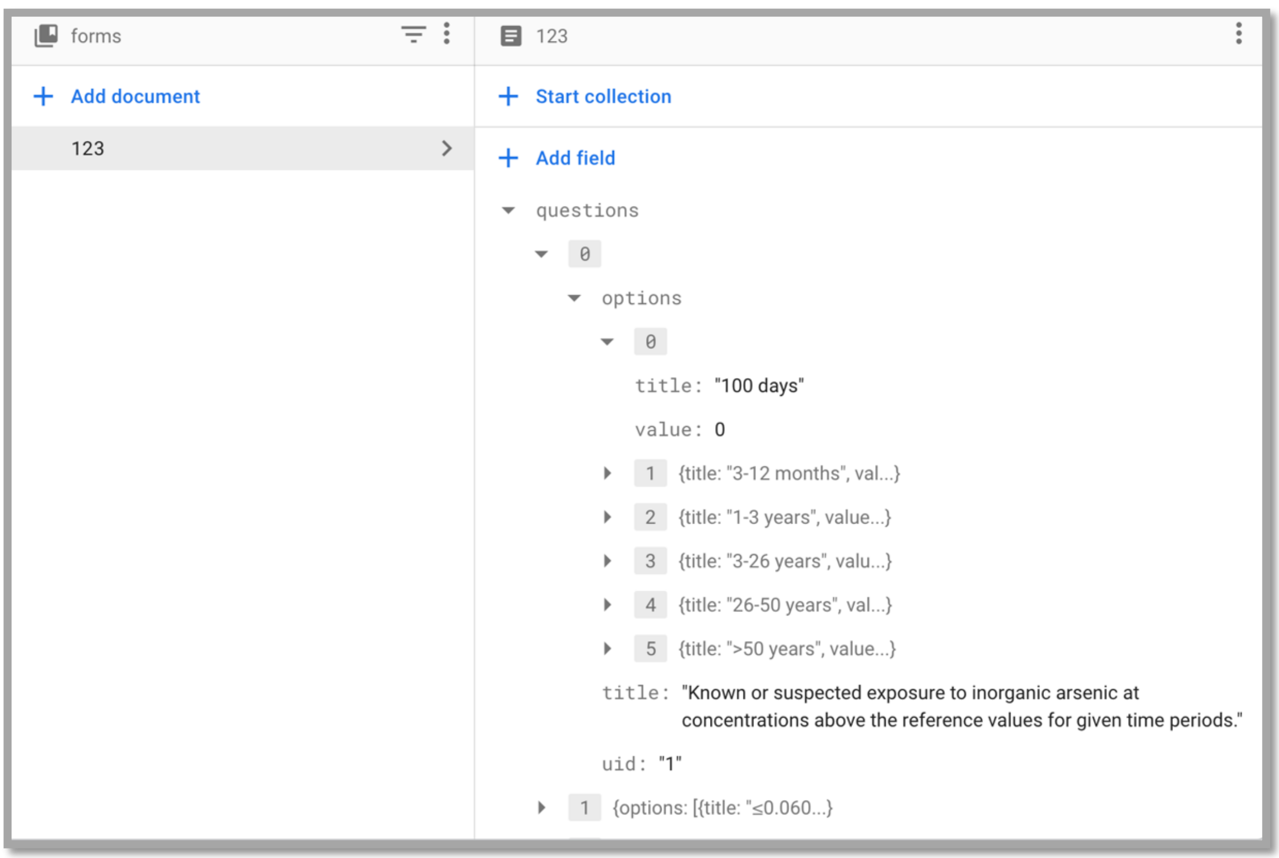


Figure 38. Form (Question 1 an its answer options) (Author, 2019).

4.2.2.2.2 Score

Another similar data we decided to store in the database, for similar reasons, were the scores. The process was pretty much the same. We included another collection (scores), added a document which we identified with an id and uid (i.e. *1*), a title, in this case the description of one of the scores (i.e. *CAsI confirmed with a high degree of certainty.*) and the top and bottom threshold numbers of this score range (i.e. *51* to *100*). The main difference is that in this scenario we need to fabricate new documents (Figure 39 and 40) instead of adding options to a hierarchy within a document.

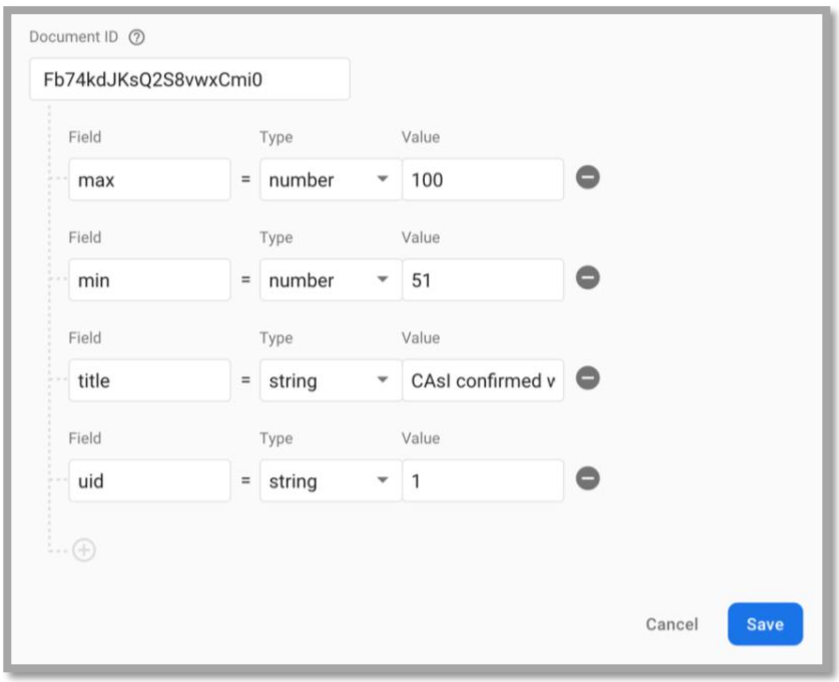


Figure 39. Score (CAsI confirmed with a high degree of certainty) (Author, 2019).

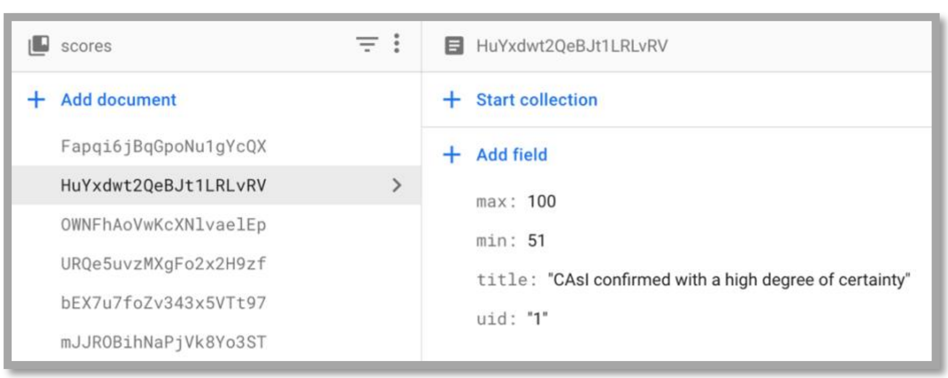


Figure 40. Score document (Author, 2019).

4.2.2.2.3 Other collections

For other collections (and hence documents) that store user information and procedures, it was not needed to create it manually in the Firebase console. The CASIds app handled all the necessary operations and the details will be explained on the next section.

4.2.2.3 CASIds Ionic App – Firebase integration

After having our Firestore collections in place, we needed to implement the app's code responsible for communicating with Firebase. First, based on our data diagram model showed earlier, we created classes composed of variables with their corresponding type (strings for texts, booleans for true or false and numbers for numeric values). Those classes, often called models, stablish a contract between the front-end (app) and the backend (Firestore), avoiding unexpected errors when sending or receiving data. We also took the opportunity to create some useful enums which, in simple terms, are lists of constants.

```
import { firestore } from 'firebase/app';

export class Procedure {
    uid?: string;
    patient_id: string;
    patient_fullname?: string;
    country?: string;
    doctor_id: string;
    doctor_fullname?: string;
    lab_id: string;
    lab_fullname?: string;
    exam_value: number | null;
    answerKey: AnswerKey | null;
    status: number;
    score: Score | null;
    createdAt?: firestore.Timestamp;
    updatedAt?: firestore.Timestamp;
}

export class AnswerKey {
    uid: string;
    form_id: string;
    completed: boolean;
    total_value: number | null;
}

export class Score {
    uid: string;
    title: string;
    min: number;
    max: number;
}
```

```
export enum ProcedureStatus {
    'Waiting for Payment',
    'Waiting for Exam Upload',
    'Waiting for Form Answers',
    'Done'
}

export enum ProcedureStatusIonicons {
    'cash',
    'flask',
    'document',
    'checkmark-circle'
}

export enum UserIdKey {
    'patient_id',
    'doctor_id',
    'lab_id'
}

export class Form {
    uid: string;
    questions: Question[];
}

export class Question {
    uid: string;
    title: string;
    options: Option[];
}

export class Option {
    index: number;
    title: string;
    value: number;
}
```

```
export class Geoloc {
    country: string;
    latitude: number;
    longitude: number;
    name: string;
    count: number;
}

export class User {
    uid: string;
    roles?: Roles;
    email?: string;
    firstName: string;
    lastName?: string;
    gender?: string;
    phone?: string;
    country?: string;
}

export class Roles {
    patient?: boolean;
    doctor?: boolean;
    laboratory?: boolean;
}

export class Patient {
    uid: string;
    name: string;
    numberOfProcedures: number;
    statusOfLatestProcedure: string;
    statusIcon: string;
}
```

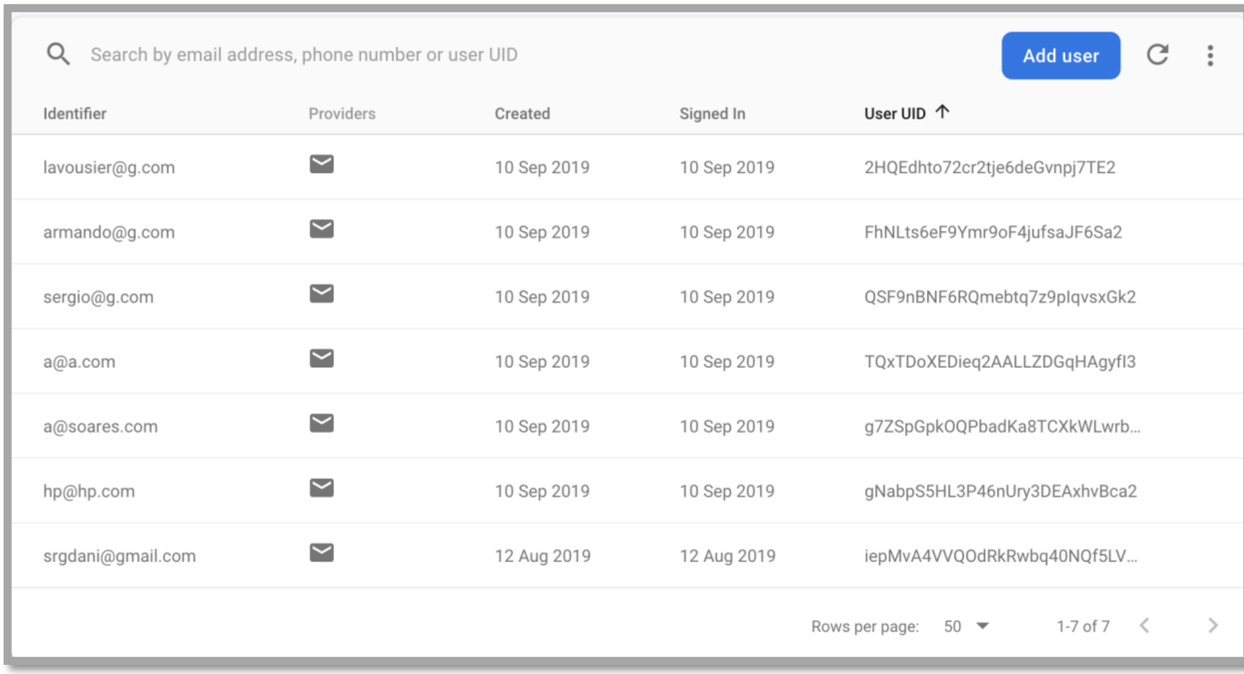
All functions related to authentication operations are in the auth.service.ts file. To facilitate calls to Firebase, we leverage the use of the AngularFire library and its modules for connecting to Auth and Firestore.

```
import { AngularFireAuth } from '@angular/fire/auth';
import { AngularFirestore, AngularFirestoreDocument } from '@angular/fire/firestore';
```

To register a new user, we call the function *createUserWithEmailAndPassword*, passing the email and password the user entered on the form. This will create an entry on Firebase Authentication, navigate the user to the login page and show a success message (Figure 41).

```
onSubmit(values) {
    this.auth.doRegister(values)
    .then(res => {
      // console.log(res);
      this.signup_form.reset();
      this.navCtrl.navigateForward(['login']);
      this.toastController.presentToast('Account created, please log in.', 'success'
);
    }, err => {
      // console.error(err);
      this.toastController.presentToast(err.message, 'error');
    });
  }
```

```
doRegister(values) {
    return new Promise<any>((resolve, reject) => {
      this.afAuth.auth.createUserWithEmailAndPassword(values.email, values.matching_passwords.password)
      .then(res => {
        values.uid = res.user.uid;
        this.createUserData(values);
        resolve(res);
      }, err => reject(err));
    });
  }
```



Search by email address, phone number or user UID

Add user

Identifier	Providers	Created	Signed In	User UID ↑
lavousier@g.com		10 Sep 2019	10 Sep 2019	2HQEdhto72cr2tje6deGvnpj7TE2
armando@g.com		10 Sep 2019	10 Sep 2019	FhNLts6eF9Ymr9oF4jufsaJF6Sa2
sergio@g.com		10 Sep 2019	10 Sep 2019	QSF9nBNF6RQmebtq7z9pIqvsxGk2
a@a.com		10 Sep 2019	10 Sep 2019	TQxTDoXEDieq2AALLZDGqHAgyfI3
a@soares.com		10 Sep 2019	10 Sep 2019	g7ZSpGpkOQPbadKa8TCXkWLwrb...
hp@hp.com		10 Sep 2019	10 Sep 2019	gNabpS5HL3P46nUry3DEAxhvBca2
srgdani@gmail.com		12 Aug 2019	12 Aug 2019	iepMvA4VVQOdRkRwbq40NQf5LV...

Rows per page: 50 1-7 of 7

Figure 41. Registration on Firebase (Author, 2019).

Then, we call *createUserData* to create a new document in the *users* collection in Firestore, using the *uid* of the user created before as the *document id*. This step is essentially to store user related data, such as phone, country, gender and role (Figure 42). Notice that firebase auth manages accounts (email and passwords), while firestore manages data from user's profile)

```
private createUserData(user) {
    // Sets user data to firestore
    const userRef: AngularFirestoreDocument<any> = this.afs.collection('users').doc(`${user.uid}`);

    const data: User = {
      uid: user.uid,
      roles: this.getUserRole(user.role),
      email: user.email,
      firstName: user.name,
      phone: user.country_phone.phone,
      country: user.country_phone.country.iso
    };

    //If Laboratory, the following params should be undefined
    if (user.gender) { data.gender = user.gender; }
    if (user.lastname) { data.lastName = user.lastname; }

    return this.myAfs.set(userRef, data);
  }
```

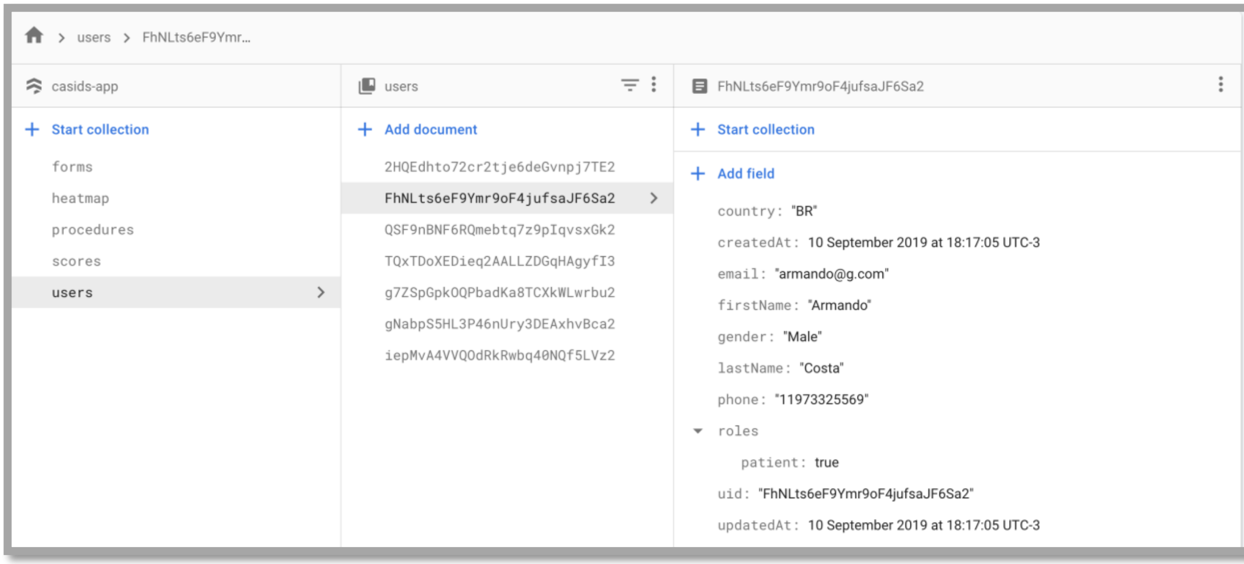


Figure 42. User data (Author, 2019).

Now, to would be able to Login (or Logout) with this newly created user calling the *doLogin* method.

```
doLogin(email, password) {
    return new Promise<any>((resolve, reject) => {
      this.afAuth.auth.signInWithEmailAndPassword(email, password)
      .then(res => {
        // Get user data from firestore database
        const userRef = this.afs.collection('users').doc(`${res.user.uid}`);
        userRef.ref.get().then(function(doc) {
          if (doc.exists) {
              resolve(doc.data());
          } else {
              // doc.data() will be undefined in this case
              reject('User properties not found!');
          }
        }).catch(function(error) {
            reject('Error getting document: ' + error);
        });
      }, err => reject(err));
    });
  }

  async doLogout(): Promise<any>{
    return await this.afAuth.auth.signOut().then(() => this.storage.clear());
  }
```

After successfully authenticating the user with the provided credentials, the app saves the user id and name to the local storage and redirects to the appropriate page based on the role (patient, doctor or lab) associated with the current user.

```
onLogin(values) {
    this.auth.doLogin(values.email, values.password)
    .then((res: User) => {
      // console.log(res);
      // set a key/value
      this.storage.set('userId', res.uid);
      this.storage.set('userName', res.firstName + (res.lastName ? ' ' + res.lastName : '')).then(() => {
        if (this.auth.canCreateProcedure(res)) {
          this.navCtrl.navigateRoot(['home-patient']);
        } else if (this.auth.canCreateForm(res)) {
          this.navCtrl.navigateRoot(['home-doctor']);
        } else if (this.auth.canUploadExam(res)) {
          this.navCtrl.navigateRoot(['home-lab']);
        } else {
          // console.log(res);
          this.toastController.presentToast('You have no permissions for use this app. Please contact support.',
'error');
        }
      });
    }, err => {
      console.error(err);
      this.toastController.presentToast(err.message, 'error');
    });
  }
```

The patient role is allowed to check details of his past procedures and to create a new procedure. The latter involves associating a doctor and a lab, while also paying a fee. For this proof of concept, we`ve opted to integrate the payment options using Paypal. After the payment is successful, the app calls the *createProcedure* method to create a new document in the *procedures* Firestore collection.

```
async createProcedure(userId: string, userName: string, values) {

  // Sets procedure data to firestore
  const procsRef: AngularFirestoreCollection<any> = this.afs.collection('procedures');

  const data: Procedure = {
    patient_id: userId,
    patient_fullname: userName,
    doctor_id: values.doctor.uid,
    doctor_fullname: `${values.doctor.firstName ? values.doctor.firstName : ''} ${values.
doctor.lastName ? values.doctor.lastName : ''}`,
    lab_id: values.lab.uid,
    lab_fullname: `${values.lab.firstName ? values.lab.firstName : ''} ${values.lab.
lastName ? values.lab.lastName : ''}`,
    exam_value: null,
    answerKey: null,
    status: 0,
    score: null,
  };

  const docRef = await this.myAfs.add(procsRef, data);
  console.log(`procId: ${docRef.id}`);
  return this.storage.set('procId', docRef.id);
}
```

Note that, at the moment, the fields *answerKey*, *exam_value* and *score* are *null*, because the form has yet to be answered by the user. The current status is ‘Waiting for Exam Upload’, which can be checked by the field *status*.

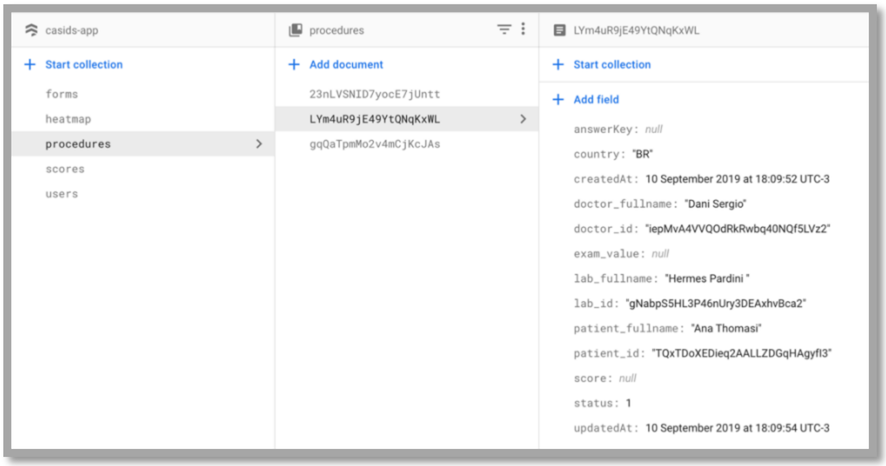


Figure 43. New procedure (Author, 2019).

In order to move it to the next status, the corresponding lab user has to login into the app, choose this procedure and upload the exam value. To get the procedures that the lab is associated to, we query the Firestore collection of *procedures* and filter it to the ones that has the *lab_id* field equals to the logged in user. For a better user experience, we also order the result by the date of its latest update (*updatedAt* value). Each value found is added to a procedures list, which then is retrieved to the screen.

```
getProceduresByLabId(labId: String) {
    return new Promise<any>((resolve, reject) => {
      // Get user data from firestore
      const proceduresCollection: AngularFirestoreCollection<Procedure> = this.afs.collection('procedures');
      const query = proceduresCollection.ref.where(UserIdKey[UserIdKey.lab_id], '==', labId).orderBy(
'updatedAt', "desc");

      query.get().then(function (querySnapshot) {
        const proceduresList: Array<Procedure> = [];
        // console.log(querySnapshot.docs);
        querySnapshot.docs.forEach(function (doc) {
          // console.log(doc);
          const procedure: Procedure = {
            uid: doc.id,
            patient_id: doc.data().patient_id,
            patient_fullname: doc.data().patient_fullname,
            doctor_id: doc.data().doctor_id,
            doctor_fullname: doc.data().doctor_fullname,
            lab_id: doc.data().lab_id,
            lab_fullname: doc.data().lab_fullname,
            exam_value: doc.data().exam_value,
            answerKey: doc.data().answerKey,
            status: doc.data().status,
            score: doc.data().score,
            createdAt: doc.data().createdAt,
            updatedAt: doc.data().updatedAt
          };
          // doc.data() is never undefined for query doc snapshots
          proceduresList.push(procedure);
        });
        resolve(proceduresList);
      })
        .catch(function (error) {
          console.log('Error getting documents: ', error);
          reject(error);
        });
    });
  }
```

Note that, for other queries involving procedures (by patient id, by doctor id, by status, and so on), the method is very similar. The only change is the expression used to construct the *query* constant.

When a lab user chooses the corresponding procedure, and it is on status 'Waiting for exam upload', the option to upload a new value is enabled. After the upload confirmation, the procedure is updated with the new data: *exam_value*, *updatedAt* and *status*.

```
async updateProcedure(procId: string, data: any) {
    // Sets procedure data to firestore
    const procsRef: AngularFirestoreDocument<any> =
this.afs.collection('procedures').doc(procId);
    await this.myAfs.update(procsRef, data);
  }
```

The procedure status now would be 'Waiting for Form Answers'. Now, the doctor user associated with this procedure has to log in, choose this procedure and start to answer the form. It is recommended that this step should be accomplished by a doctor and the patient together. The question, answers and values corresponding to the form will be retrieved from the Firestore collection *forms*, which was registered earlier in the Firebase console.

```
getFormById(formId: string) {
  return new Promise<any>((resolve, reject) => {
    // Get user data from firestore
    const formRef: AngularFirestoreDocument<Form> = this.afs.collection('forms').doc(formId);
    formRef.ref.get().then(function(doc) {
      if (doc.exists) {
        resolve(doc.data());
      } else {
        // doc.data() will be undefined in this case
        reject('Form not found!');
      }
    }).catch(function(error) {
      reject('Error getting document: ' + error);
    });
  });
}
```

The user will be prompted to answer the questions in one go, as the app keeps answers in memory to save data transfers. When the user completes the questionnaire, the values of each answer is summed up, and the result is used to query the corresponding score range. The answerKey containing the form id, the answers index for each question, the status ‘completed’ and the sum result, is then updated in the procedure, along with the new status ‘Done’ and the score range found.

```
createScoreInProcedure(procId: string, formId: string, t: number) {
    return new Promise<any>((resolve, reject) => {
      // console.log('Total value: ' + t);
      const scoresRef = this.afs.collection('scores').ref.where('max', '>=', t);
      scoresRef.get().then((querySnapshot) => {
        resolve(this.findScore(querySnapshot, procId, formId, t));
      }).catch(function(error) {
        reject('Error getting document: ' + error);
      });
    });
  }

  findScore(querySnapshot, procId: string, formId: string, t: number) {
    if (!querySnapshot.empty) {
      // console.log('Number of values with min <=: ' + doc.size);
      let score: Score;
      querySnapshot.docs.forEach((element) => {
        // console.log('Looking for element: ');
        if (t >= (element.data() as Score).min) {
          // console.log("Found it in");
          // console.log(element.data() as Score);
          score = (element.data() as Score);
        }
      });
      if (isUndefined(score)) {
        throw 'Score not found in range!';
      } else {
        const procRef: AngularFirestoreDocument<any> = this.afs.collection('procedures').doc(procId);
        const answerKeyUid = this.afs.createId();
        const data: AnswerKey = {
          uid: answerKeyUid,
          form_id: formId,
          completed: true,
          total_value: t
        };
        return this.myAfs.update(procRef, {
          'score': score,
          'answerKey': data,
          'status': 3
        });
      };
    } else {
      // doc.data() will be undefined in this case
      throw 'Score not found!';
    }
  }
```

4.2.2.4 Hosting

Another feature needed was to host the website on the web. Firebase Hosting did the job as it is a fully managed hosting service for static and dynamic content. Using this service, we automatically received a Firebase subdomain (casids-app.web.app) (Figure 45). However, you can choose to display your own content on a custom domain for a charge.

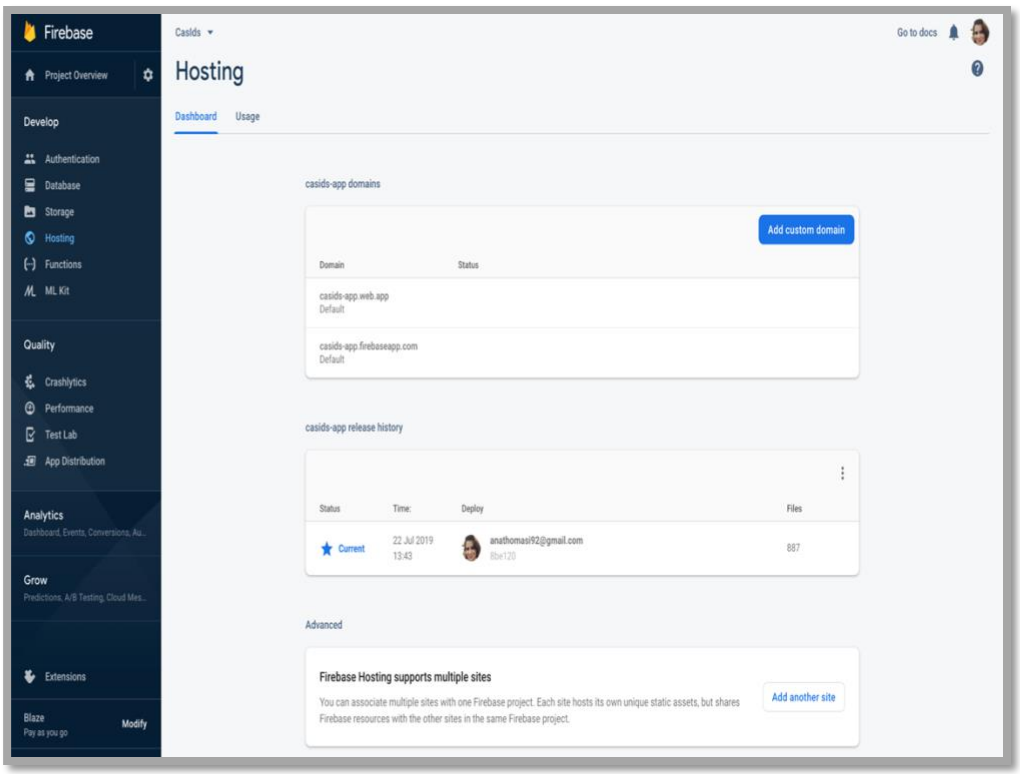


Figure 45. Firebase hosting (Author, 2019).

4.2.2.5 Functions

Cloud Functions for Firebase offers a way to extend platform behavior and integrate available resources by adding server code. It was identified an opportunity to leverage this feature for building the data sample for the heatmap (Figure 46). Once a user completes one procedure, cloud functions automatically increment the number of patients diagnosed with CAsI confirmed with a high degree of certainty, on that user’s country.

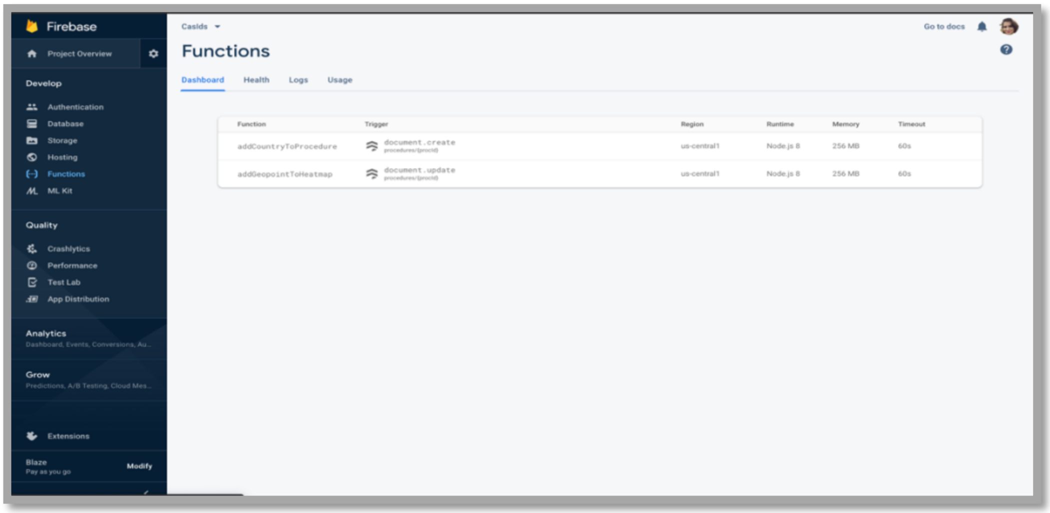


Figure 46. Firebase Functions (Author, 2019).

To build the map with the number of cases around the world, we’ve used Cloud Functions to automatically update the heatmap once a procedure is completed.

To get the location of that procedure, we’ve opted to create a function that queries the user data of the patient, get the country field and copy it to the procedure data. This process will facilitate the next function, which is described below.

```
exports.addCountryToProcedure = functions.firestore
    .document('procedures/{procId}')
    .onCreate((snap, context) => {
        // Get an object representing the document
        // e.g. {'name': 'Marie', 'age': 66}
        const newValue = snap.data();

        if (newValue !== undefined && newValue !== null &&
            newValue.patient_id !== undefined && newValue.patient_id !== null) {

            // console.log("user id: " + newValue.patient_id);
            // access a particular field as you would any JS property
            return admin.firestore().collection('users').doc(newValue.patient_id).get()
            .then((doc) => {
                const data = doc.exists ? doc.data() : null;
                if (data) {
                    const userCountry = data.country;
                    // console.log("country found: " + userCountry);
                    return snap.ref.set({ country: userCountry }, {merge: true});
                } else {
                    // console.error("user not found");
                    throw new Error("user not found");
                }
            })
            .catch((err:any) => console.error(err));
        }
        // console.error("error: snap data is null");
        // console.log(newValue);
        return null;
});
```

The second Cloud Function triggers every time a procedure status changes to ‘Done’. The code evaluates the score of this procedure and, if it is in the range of confirmed CAsI, it updates the *heatmap* collection in the Firestore database (Figure 47). The *documentID* for each document in this collection corresponds to the patient’s country of that procedure. Each document has a *count* field, which is incremented each time a new procedure of the same country is found by this Cloud Function. The document also has a latitude and longitude pair of fields, with identifies the location of that country in the map. To save time, we’ve imported a JSON file containing the latitude and longitude for every country in the world.

```
exports.addGeopointToHeatmap = functions.firestore
    .document('procedures/{procId}')
    .onUpdate((change, context) => {
        // Get an object representing the document
        const newValue = change.after.data();
        const previousValue = change.before.data();

        if (newValue !== undefined && newValue !== null &&
            previousValue !== undefined && previousValue !== null &&
            newValue.status !== previousValue.status && newValue.status === 3) {

            const countryObj = jsonData.countries.find((c: any) => c.country === newValue.country);
            // console.log(countryObj);

            if (countryObj) {
                return admin.firestore().collection('heatmap').doc(countryObj.country).get()
                .then((doc) => {
                    const data = doc.exists ? doc.data() : null;
                    if (data) {
                        return admin.firestore().collection('heatmap').doc(countryObj.country).set({
count: data.count + 1}, {merge: true});
                    } else {
                        countryObj['count'] = 1;
                        return admin.firestore().collection('heatmap').doc(countryObj.country).create(
countryObj);
                    }
                })
                .catch(err => console.error(err));
            }
        }
        return null;
});
```

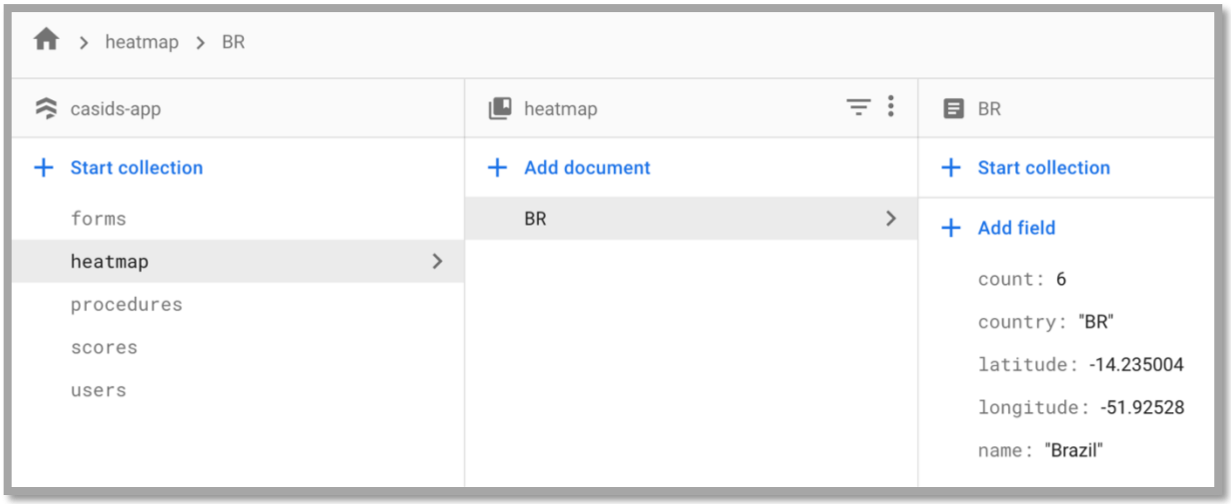


Figure 47. Dataset actualization (Author, 2019).

5 CONCLUDING REMARKS AND FUTURE WORKS

CAsIDS methodology is usually applied following 5 steps (Figure 48):

1. Patient goes into a Doctor's appointment and the symptoms described makes the doctor suspect of As contamination;
2. Doctor asks a urine test to confirm his suspicion;
3. The patient does the test and returns to the doctor with results in hand;
4. Doctor fills the 12 questions form of CAsIDS with the patient;
5. Doctor calculates CAsIDS final score, to be certain of the Arsenic contamination diagnostic.

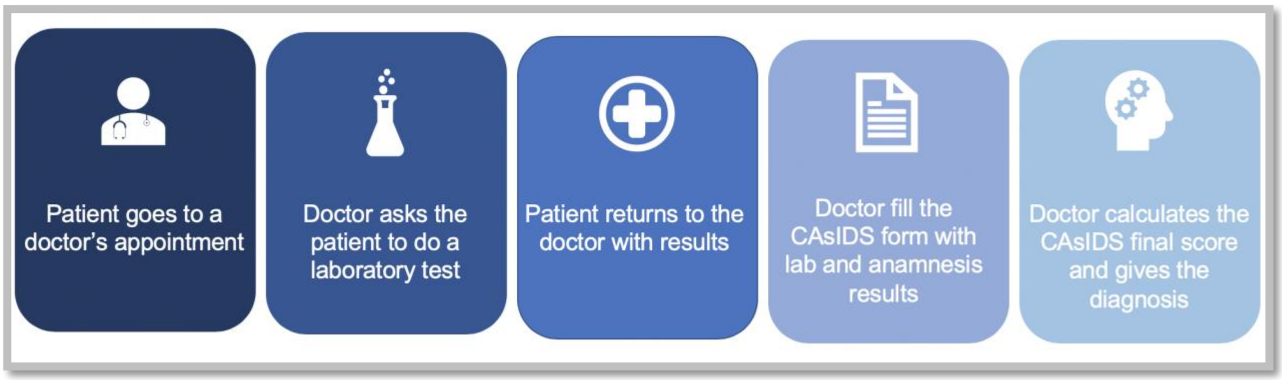


Figure 48. CAsIDS step-by-step (Author, 2019).

Conducting the same procedure using the CAsIDS mobile app will take the following steps (Figure 49):

1. Users download the app or access it through the web application;
2. Patient logs in and creates a new procedure by selecting a registered doctor and laboratory and paying the fee through the app;
3. Patient goes to the chosen lab and undertake the exam. Laboratory logs in, chooses the correct patient from the list and uploads the result;
4. Patient goes to a Doctor's appointment. Doctor logs in, chooses the correct patient from the list and fill the CAsIDS form;
5. After the last question is answered, the app calculates the final score and shows it on screen. Doctor may take the necessary precautions.

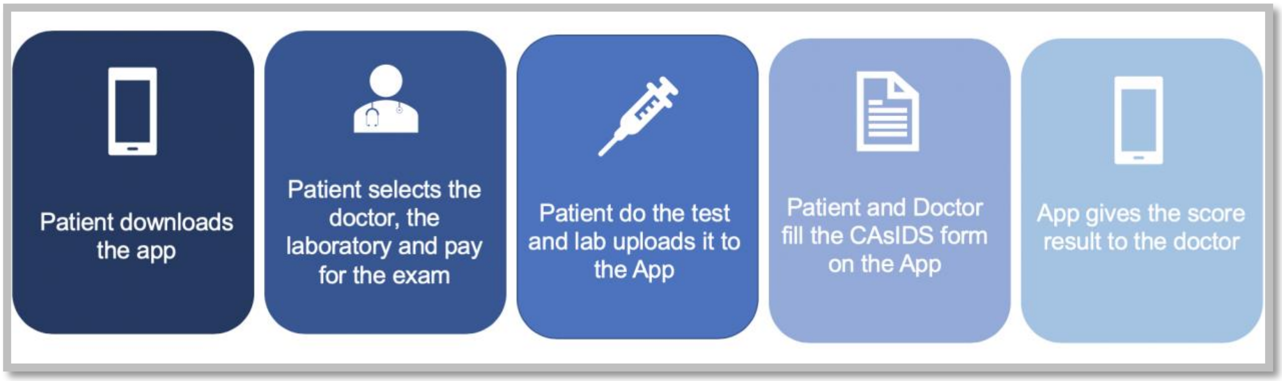


Figure 49. Digital CAsIDS step-by-step (Author, 2019).

In conclusion, the app allows the diagnostic score to be obtained with a minor degree of error if compared to the manual process as it automates certain key steps of the procedure. It may also seem more trustworthy by the same reasons.

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