

A Telematic Tool to Predict the Risk of Colorectal Cancer in White Men and Women: ColoRectal Cancer Alert (CRCA)

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Abstract Colorectal cancer is an important disease because of its severity and also since it affects much of the population. Nothing helps patients and doctors to determine the risk of suffering from colorectal cancer during their lives, except for medical tests such as the colonoscopy. There have been several studies and research to try to estimate the relative risks of colorectal cancer based on various factors and the applications to calculate the risk of this cancer, but these are not within everyone's research. This project offers a multilingual Web tool, called ColoRectal Cancer Alert (CRCA), to calculate the risk of colorectal cancer for life in men and

women of white race. With this application, doctors can carry out research in a few minutes to explore this risk when they are seeing a patient. The platform is designed in such a way that anyone can use it. It is easy to use and intuitive. We should keep in mind that this tool does not replace diagnostic tests such as the colonoscopy or the sigmoidoscopy. It is designed so that users with the assistance of their doctor know the risk and act accordingly (for example, having more checkups on the disease in case of high risk). To access the tool a computer with Internet connection will be required. Currently, 250 users of white race under the supervision of a specialist have completed the questionnaire.

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Introduction

Cancer of the colon and rectum is also known as colorectal cancer. In the U.S.A. it is the third most common cancer among men and women according to the American Cancer Society. With an early detection it is likely to be cured [1]. The probability of developing colorectal cancer increases with age, but after the age of 50 it is when the risk increases to values of consideration. People are more likely to develop colorectal cancer if they have or have had polyps, if their diet is not very healthy and high in fat, if in their family there are more cases of colorectal cancer, if they have had ulcerative colitis or Crohn's disease, etc. [2].

All those over 50 years old should undergo a study to rule out colorectal cancer. The colonoscopy is a method which your doctor can use to detect the colorectal cancer [3].

This cancer occurs when a healthy cell of the colon or rectum tissue begins to mutate and proliferate uncontrollably, resulting in a mass called tumor. This tumor can be benign or malignant (cancerous). These changes usually take a long time to develop, but also there may be cases in which a person has an inherited syndrome and changes can occur in months or years. The changes may be caused by genetic and environmental factors [4]. For early detection we must be tested for the detection of colorectal polyps and cancer, especially when we are in a risk group. For this we should consult our doctor [5].

In addition, the colorectal cancer is one of the leading cancers in the number of patients and mortality in developed countries. Medicine has evolved into different treatments such as surgery, chemotherapy, radiation, etc. Although as with any disease it is always best to apply the old saying “better safe than sorry” and especially in this case because in this disease. The early detection is a very important factor in curing it. It is advisable to prevent and try to anticipate the onset of the disease going to the doctor regularly for relevant evidence rather than waiting until symptoms appear, and time passes so that the disease develops and produces more complications. These check-ups must be intensified when we are in a risk group including over 50 years old [6].

Within this framework, we can raise some questions: When can we start testing? How many times? What is our risk of developing the disease? Our doctor is the best professional to answer these questions.

In this paper we present the development and evaluation of a web platform, ColoRectal Cancer Alert (CRCA), which can be accessed from any computer with Internet access, in which users, using a questionnaire, can view their risk of developing the disease and compare it with the average population to see if they are in a risk sector and if they should be tested as a preventive way and how often. This work is based on different studies carried out by experts, mainly for the application development we have relied on two studies [7, 8]. By calculation from data obtained in the test, it is able to obtain an estimate of the probability for that patient of suffering from that disease. Risk factors will be explained to the patient through a graph in which he or she will notice the risk based on age. The test will include questions about the main factors (age, family, polyps, etc.) which indicate the probability of suffering from this illness.

The remainder of this paper is organized as follows. “**Related Work**” presents related work. “**Methodology**” describes the methodology to develop the platform while “**Results**” focuses on the results achieved. “**Discussion**” presents a discussion and finally “**Conclusion and Future Work**” shows the conclusions and future work.

Related work

This section presents some of the research literature related to online systems to predict colorectal cancer risk. Following are some of these websites:

- Colorectal Cancer Risk Assessment Tool [9]. This tool is published on page <http://www.cancer.gov>, which is freely accessible via the link <http://www.cancer.gov/colorectalcancerrisk/>. This tool tries to give an estimate of our risk of colorectal cancer from a test which takes about 5–10 min. This tool is designed to be used by doctors. In case patients make their own practice, they are advised to show a professional the results. It is only available in English, which makes it a little more complicated for those who do not master this language. Once the test and all the required questions have been answered, the tool will display the results in a bar that goes from 0 to 100 (%) in which a zoom into the area where they are shown. The result will not be a specific value but will be a range (i.e. 3’3–3’6%). It is informed that the results are approximate. This online tool considers next factors: breed (Spaniard or Latin), color skin (white, black or Asian), age, gender, weight, height, feeding (vegetables eaten in the last 30 days), colonoscopy performed and the results obtained, medicines regularly taken including or not aspirin, physical exercise practiced in the last year (of moderate and vigorous intensity), smoke, menstruation and female hormones, and family history.
- Colorectal Cancer Risk Assessment [10]. This application is hosted on <http://www.healthline.com> and again is freely accessible the same as through the link <http://www.healthline.com/sw/rsk-colorectal-cancer-risk-assessment>. In this application we can see a brief text that tells us a little about the extent of colorectal cancer compared with other cancers. We are also reported the trend in the last 15 years to reduce its impact through medical advances. This application, as above, is only in English. It considers next factors: age, gender, physical exercise, weight, height, vegetarian, calories in diet, alcohol consumption, smoker, family history of colorectal cancer or polyps, polyps history, Crohn disease or any other intestinal disease, and breast cancer history.
- Colon cancer [11]. This application is hosted in <http://www.yourdiseaserisk.wustl.edu> and it is freely accessible as the previous two. Note that this website contains tests for the prediction of 12 different cancers (stomach, melanoma, pancreas, etc.) and other diseases such as diabetes, heart disease, osteoporosis and others. It is translated into other languages besides English, including Spanish, making it easier to work with it for non-English speakers. This tool takes into account gender,

age, history of other cancers, family history, weight, height, medicines regularly taken (aspirin), intestinal diseases, diet (red meat weekly eaten, milk products, calcium supplement, multivitamin, and alcohol), exercise (walk), and if any colonoscopy, sigmoidoscopy or fecal occult blood testing (FOBT) has been performed in the last few years.

Methodology

This section will proceed to explain the entire development process which includes both the research and the obtaining of models to calculate the probability of developing colorectal cancer, and the system overview and its architecture.

Colorectal cancer prediction models

Predictive models of colorectal cancer are based on the research carried out by [7, 8]. This research is based on population studies on their relative risk of developing colorectal cancer. These studies are tested on a large number of people to have more accurate data. The studied subjects were grouped by sex and age (in a unit of 5 years). These studies were conducted by different universities in the U.S.A.: Utah (Salt Lake City, UT), Minnesota (Minneapolis, MN), and the Kaiser Permanente Medical Care Program (KPMCP) Northern California (Oakland, CA). The minimum age of individuals is 50 years old as that is when it is estimated that the studied factors begin to have consequences. The cancers are divided into three types: proximal (cecum through transverse colon), distal (splenic flexure, descending and sigmoid colon) and rectal rectosigmoid (rectum).

As we know our lifestyle affects our risk of developing such this disease, so a study on the factors affecting this risk has been carried out [12]. Risk factors that have been studied and that affect the risk of developing some types of colorectal cancer are shown as the following:

- History of colorectal cancer risk (RCC) in first grade. We used the information provided by participants on the number of first-degree relatives (that is to say, father, brothers, mother and children) diagnosed with RCC. We have categorized the number of first-degree relatives with RCC as none, one, two, or more in our analysis [13, 14].
- Fecal occult blood. We have classified participants according to whether they had been informed on a FOBT in the last 10 years before the reference year.
- Sigmoidoscopy/colonoscopy. Participants were also categorized on the basis of whether they underwent a sigmoidoscopy and/or a colonoscopy in the last 10 years before the reference year.
- History of polyps. Among those who reported having had a sigmoidoscopy and/or a colonoscopy, grouping was made based on whether they have been told by a doctor that they had a polyp in the last 10 years before the reference year.
- The use of multivitamins. We have categorized participants as regular users of multivitamins at least three times a week for one month during the year of reference.
- Diet: Red meat, vegetables and fruit intake. We used the information on the number of servings of red meat, vegetables and fruits per week reported by the participants during the reference year, covering [15]. These dietary exposures were obtained during interviews with participants conducted by trained and certified interviewers [16, 17].
- The consumption of alcohol. The weekly intake of servings of red wine, beer and liquor is obtained an estimate of total alcohol consumption per week [18].
- IMC. Weight and Height. Measure defined as weight (kg)/height (m²). We have categorized the body mass index of participants according to classifications based on the World Health Organization (WHO): underweight and normal weight (BMI ≤ 24.9 kg/m²), overweight (BMI 25–29.9 kg/m²) and obesity (BMI ≥ 30 kg/m²).
- Smokers.
- Aspirin and other NSAIDs. We categorized participants as regular users of aspirin. If they were using these drugs for at least three times a week for at least one month during the studied year.
- Physical activity. We evaluated the activity of the current participants in leisure time during the reference year regarding the participants grouped into four categories: 0 h/week, 2 h/week, 2–4 h per week, and more than 4 h/week. Vigorous activities during leisure time are defined as “those activities that make you sweat or get out of breath,” and including racket sports, jogging, running and biking, doing exercise or dance lessons, weight lifting, hiking, swimming vigorously, scrubbing floors or mowing the lawn, gardening and heavy labor.
- State of estrogen. A variable estrogen status has been created, which was classified as estrogen-positive “or” estrogen negative, based on a combination of menopausal status and the use of the hormone replacement therapy (HRT). Premenopausal women and women who had used HRT within 2 years preceding the regarding year were considered estrogen—positive. Postmenopausal women who did not report the use of HRT during the 2 years preceding the year were considered negative concerning estrogen [19].

Most of the factors listed here are used in the platform, but not all of them because some did not show relevance [7].

Different research works have been performed regarding colorectal cancer risk factors. Thus, History of colorectal cancer risk (RCC) is one of the factors more pursued. A conclusion reached in [14] is that cumulative risk of CRC increases at an earlier age in male relatives of probands younger than 60 years of age, than in female relatives. In [20], authors conclude that accurate risk estimates showed how risks vary over time, particularly by pattern of family history and age of individual at-risk.

There are other factors that, although they are not conclusively proved whether they influence the risk of colorectal cancer, it is supposed that they can affect it. One example may be some food in the diet such as coffee [21]. Apart from the diet there are human genes associated with this risk [22].

To calculate the absolute risk estimate the following formula has been used (1):

$$\begin{aligned} AR_i &= 1 - \left(\sum_j Y_{ij} \right)^{-1} \sum_j Y_{ij} / rr_{ij} \\ &= 1 - \left(\sum_j Y_{ij} \right)^{-1} \sum_j Y_{ij} \exp(-x_{ij} \hat{b}) \end{aligned} \quad (1)$$

Where:

- Y_{ij} indicates a status for each case (j) and cancer (i).
- rr_{ij} indicates the relative risk for each cancer case.
- x_{ij} indicates the risk factors for each case and type of cancer.

In the study, 1,599 cases of colon cancer (665 male, 708 female) from 1,974 controls (1,058 male, 916 female) and 664 rectal cancer cases (397 male, 267 female) with 859 controls (478 male, 381 female) were included.

System overview and architecture

The Web platform developed is multilingual, allowing more people access to it. To calculate the probability of developing colorectal cancers, patients are asked to complete a questionnaire asking them about the main factors that make this risk. Based on responses, relevant calculations are made and the

results are shown to the user in a graphical form. The results of the questionnaire will be stored in a database so that they can be accessed by privileged users so they can do further studies and obtain statistics.

In Fig. 1 the architecture of the application is shown. First, the client Web browser launches a request to the server, which processes the request, whereas the required file will (.php) which will generate a file (.html) interpretable by the client browser. The processing of the file is coded in PHP. It is possible that we need to access the database to retrieve data, store them or delete them.

Results

This section shows the developed platform in which the questionnaire to be performed by users, and also the administration section of the platform will be displayed. The results obtained in the surveys so far will be also discussed.

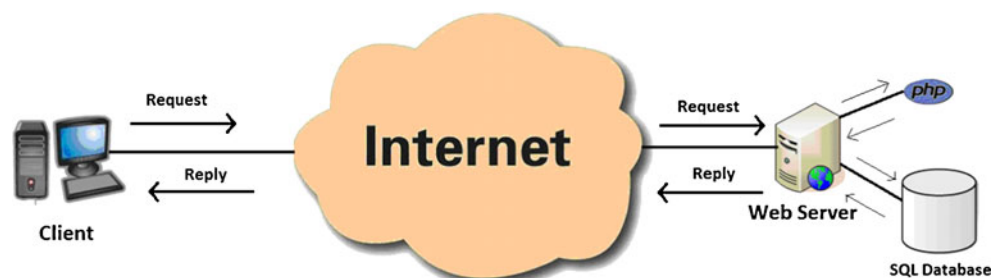
CRCA platform. Web questionnaire

Figure 2 shows the homepage of the platform (accessible via <http://wally.gti.tel.uva.es/cancercolon>). The platform is developed in four languages: Spanish, English, French and Portuguese. On the left of the “language flags” there is a link “Administration” to be used by the platform administrator to access with privileges and to view and modify the database. Beneath the flags we will find the following menu:

- Home: its use leads us to the main screen.
- Questionnaire: its use leads to the beginning of the questionnaire so as to make use of the application.
- Statistics: This section is reserved for the platform administrator and can only be accessed while logged in with necessary.

The questionnaire as well as every page has the same layout as the homepage. In this section 27 questions are shown, although not all the questions have to be answered. Depending on the answers a user gives, subsequent questions will be given. At the end of the questionnaire

Fig. 1 CRCA platform architecture



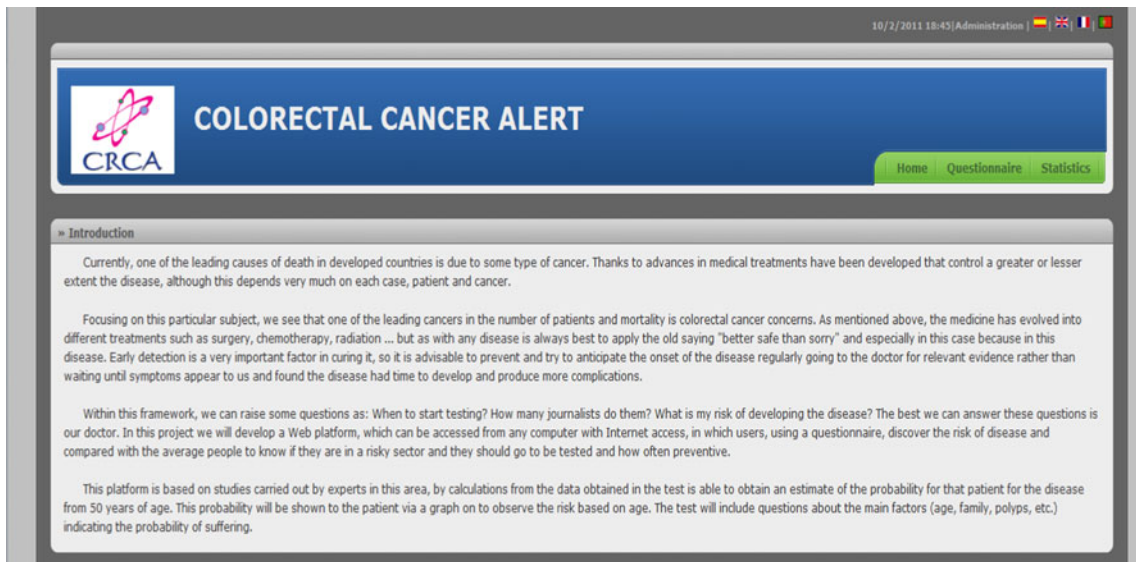


Fig. 2 System’s main screen

there is an area where you are asked for an optional email address in case they would like to receive a copy of the results to our e-mail. Finally, at the end of the page as given in Fig. 3, we have three buttons:

- Calculate: the data processing will begin and the obtained results will be shown.
- Restore: all the results reported in the questionnaire will be deleted. Confirmation before resetting will be asked for.
- Help: it opens a new window which will indicate some aspects of the questionnaire.

Once the questionnaire has been completed correctly, then we click on the button “Calculate” and we will display

the results. Once the page has been loaded correctly we should display a graph (Fig. 4) in which we can observe our risk based on age and compare it with the average white population. Below this chart we can see some tips (usually obvious) if circumstances appear. In case of having indicated an e-mail, you will be informed if it has been sent successfully or if, on the contrary, you have not been able to be sent the results.

CRCA platform. Statistics and evaluation

Finally the statistics section, as seen in Fig. 5, depicts some of the results about colorectal cancer relative risk stored in the database. To access statistics, we have to repeat the steps described previously. The administrator will be

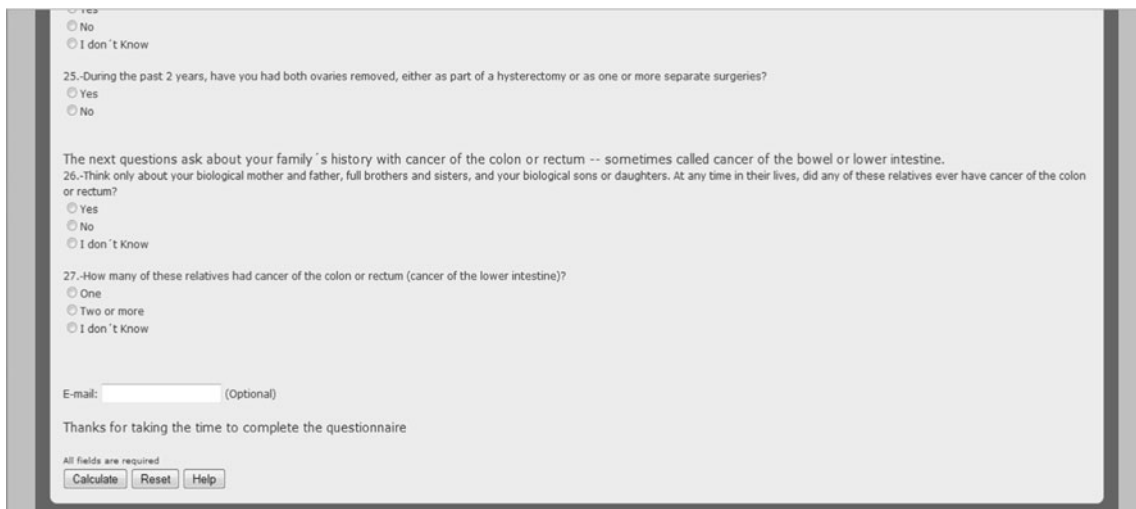


Fig. 3 Questionnaire

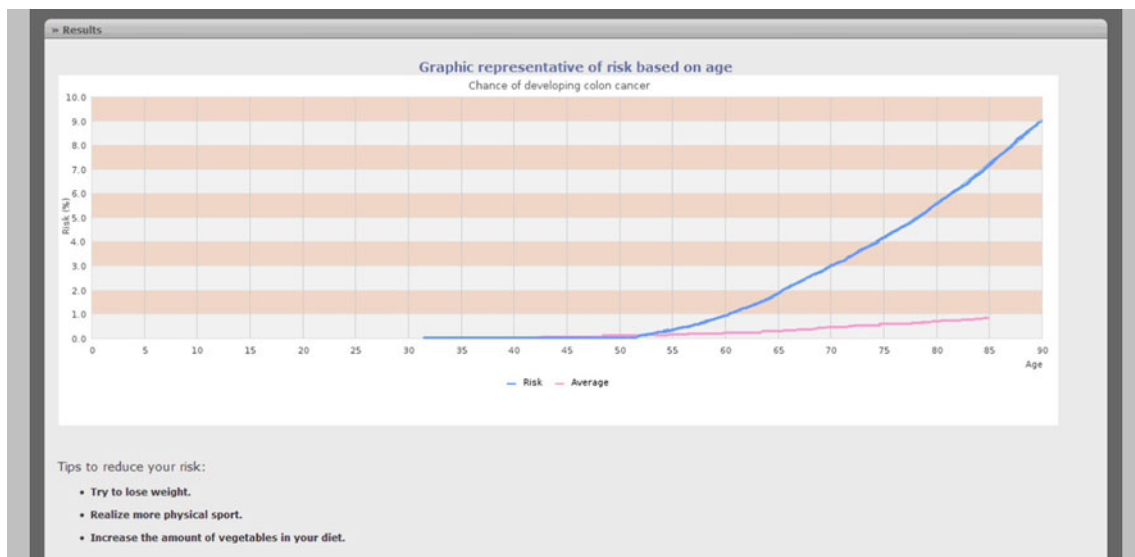


Fig. 4 Representative graphic of risk based on age

allowed deleting specific records in this database if it is appropriate or directly deleting the entire database. So far, 250 surveys have been conducted among white men and women over 50 and reviewed by a specialist, in which a large percentage of users (in this case 70%) has a risk above the average. Most users utilized the platform in Portuguese and Spanish (a total of 240 users); remainder users employed French (5 users) and English (5 users) languages.

Although the sample is too small to take decisions, in this case we can see that the risk of developing colorectal cancer was slightly higher (about 10%) in men, and especially in

smokers. Moreover, we can see in Fig. 5 that the colorectal cancer relative risk increases with the age.

Discussion

The application is designed on studies carried out on white population can work for other races (black, Asian, Oceanic, etc.) [7, 8], although these results may not have sufficient accuracy. Age is also another constraint because after 90 years old no data on the risk are reported, that is because no studies have been conducted with people of that age, although it is known that after 50 years old the risk increases significantly every year. It is unknown if from some age this risk stabilizes and stops growing. The platform is translated into four languages but there must be people interested in using this tool who does not know any of these languages.

Approximately 250 users have already used this tool. Most of these people are covered between the ages of 40 and 60. Many of these people and especially those who are over 50 years old, since that's when the risk is public knowledge, have more risk than the average and they were probably unaware of this fact. Maybe from now onward these people decide to take this disease (in particular) more seriously and to live a healthier life and to take a test for prevention and detection in case of suffering from it. It is worth mentioning that, as mentioned earlier, this disease can be cured if detected early enough, while too late can be fatal. For this reason it is advisable to have a checkup, especially when the risks are too great.

Keep in mind that many of the factors that determine the risk can be modified with lifestyle (exercise, diet, medi-

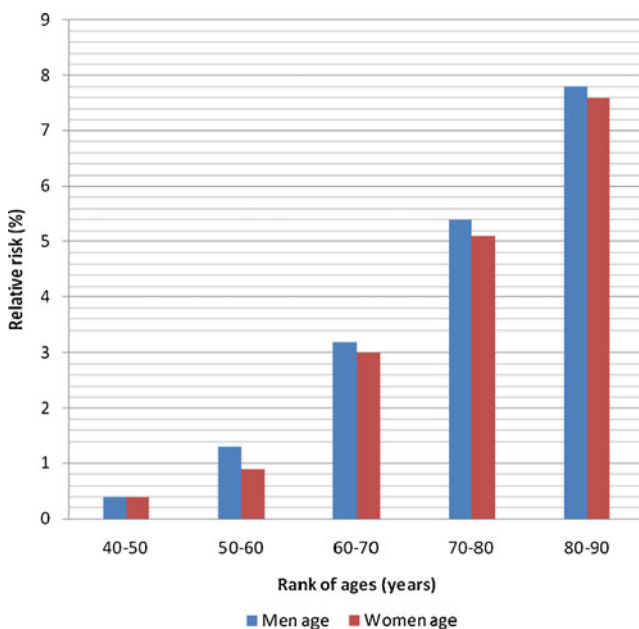


Fig. 5 Statistics

cations, etc.), while others do not (family, polyps, menstruation, etc.), it is advisable to lead a healthy life and reduce this risk as possible [23–28].

Conclusion and future work

Web platforms in the field of e-health are an efficient solution since neither their display nor their maintenance are very expensive.

In this work, in a first stage, a research on scientific articles about colorectal cancer published by specialists has been carried out to find the reasons and factors that may determine the likelihood of developing this disease.

The developed platform has the following advantages in relation to the platforms discussed in Related Work:

- Fully committed: this platform has been designed exclusively for the purpose of predicting the risk of suffering from colorectal cancer while on other platforms this is not their main objective, which can not be efficient enough.
- Better display: this platform dedicates entirely the whole screen while others open a popup window in a corner of the screen which makes it harder to display the contents especially when you see the results. Besides there is no advertising on the page so viewers do not have unnecessary distractions.
- Accurate and complete results: this application displays results for each year in life (up to 90 years old) while others give only average results indicating the risk only for a specific year.
- Convenience: If you want the results are sent automatically to our e-mail so that we can view these results any time while other applications need to print the results with the troubles that it entails.

Although the platform is completed and in operation several improvements, can be carried out, we include:

- Translation: The platform is translated in four languages (English, Spanish, French and Portuguese), but more translations should be done to other languages to provide greater accessibility to it.
- Delivery of Multimedia Messaging System (MMS): an operating system is in charge of sending e-mails to users who require their results, but a system to send the results to mobile phone using MMS should be developed.
- Adaptation to mobile phones: Web design is intended to be viewed on computer screens so if you try to make a connection to the platform from a mobile terminal with Internet access some pages may not be displayed properly, so an adjustment of the platform

should be made to access from a mobile device without renouncing to quality.

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