A Mobile-Health Research Framework for Colorectal Cancer Prevention: Coupling Behavioral Change with Biological Evidence

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***Abstract*— Colorectal cancer (CRC) represents a significant global health challenge, ranking among the leading causes of cancer-related morbidity and mortality worldwide. However, despite its high incidence and mortality, CRC is considered a most preventable cancer through a healthy lifestyle adoption that may impede the development of colorectal adenomas and their transition into malignant states. In this regard, although the notions of healthy living and behavioral pathways are well-known, population adherence and awareness in relation to cancer prevention are lacking. Moreover, the evaluation of their impact on biological CRC-related processes and risk via quantifiable biomarkers remains under research. In this regard, this paper presents the design and implementation strategy of a multi-center clinical study investigating the potential of a risk assessment and behavioral change framework for CRC prevention, delivered via a digital solution. Particularly, the DIOPTRA mobile app will integrate accessible risk assessment and personalized behavioral recommendations to empower users in shifting towards healthier lifestyles. Key features of the app will include behavioral questionnaires, risk assessment, personalized suggestions, health literacy, and a diary function to track behaviors and mild symptoms. Upon study enrollment, participants will receive personalized assessment and recommendations, before a follow-up that will investigate adherence, effects, and quality of life. Moreover, a biomarker-based evaluation will be integrated, based on an under-development minimally-invasive screening blood test. Overall, this study aims to highlight the importance of mHealth solutions for CRC prevention on a population level, as well as to establish clinical relevance by seeking to link behavioral change with novel CRC biomarkers.**

Keywords—Colorectal Cancer Prevention, mHealth App, Risk Assessment, Healthy Living, Biomarker-based Screening

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I. Introduction

Colorectal cancer (CRC) is the third most common cancer in men and the second in women, accounting for 10% of all cancers worldwide [1], [2] and ranking second in cancer-related deaths with 9.4%, only below lung cancer. About 1.9 million new cases and 0.9 million deaths occurred in 2020 worldwide, while incidence is projected to rise significantly over the next decade, with 3.2 million new diagnoses annually by 2040 [1]. Moreover, CRC is among the 5 most likely to metastasize cancers. Upon initial diagnosis, 22% of cases are metastatic, while about 70% of patients will eventually develop metastatic relapse [3]. Overall, the state at the time of diagnosis greatly affects the 5-year survival rate, which may reach 90% for stage-I diagnosis (being less than 15% for advanced stages [4]), with screening-based and symptom-based detection bearing a >30% difference for mortality [5].

At the same time, CRC is one of the five most common preventable cancers for both men and women [6], now being regarded as a highly preventable disease with a considerably wide temporal development window [7]. Specifically, the transitional path from normal mucosa to pre-malignant growth and then to malignant lesion might spread over 15 to 20 years, with scientists seeking means for earlier, cost-effective and less taxing detection of pre-malignant states and prevention of further progression [8]. In this regard, the colorectal adenoma constitutes one of the primary precancerous lesions [9], [10] and is tightly linked to risk factors pertaining to both non-modifiable parameters (e.g. age) and behavioral aspects [10], [11], [12]. Specifically, in determining the CRC risk status, factors such as age, BMI, diet, smoking habits and family history [13] have been pinpointed. More importantly, the transition into malignancy is closely linked to dietary habits and overall lifestyle [14], [15], with some of these parameters having been integrated into practice as flagships on risk stratification [2] towards the identification of citizens who should prioritize CRC screening in the context of the aforementioned statistics on screening-based CRC detection and mortality rate. Besides, their documented impact is constantly increasing, with modern lifestyle presumed responsible for the increased CRC incidence in the age group of 40-44 (as shown by Western registry data), considerably lower than the 50-year threshold [16]. More notably, a US study including over 47,000 participants inferred that a resounding 71% of CRC cases were attributed to unhealthy lifestyle choices [17]. These associations are more evident in high-HDI (human development index) nations [18], underscoring the growing issue of modern way of living.

However, evidence on a complete risk factor set has not been analyzed in the context of a detailed assessment [19], and despite the long-assumed CRC preventability based on modifiable factors, awareness and exploitation remain low [20]. On exploitation, modifiable risk factors may constitute targets for lifestyle alterations that bear a preventive effect towards colorectal adenomatous polyps [21]. Although the link between CRC and such risk factors has been firmly established and the impact of a healthy lifestyle on CRC risk has been clearly shown, the validation of the preventive effect of behavioral change is yet to be achieved using high-performance screening biomarkers. In view of this reality, the current work describes the design and implementation strategy of a multi-center clinical study that will investigate the CRC prevention potential of a holistic digital solution incorporating accessible and cost-effective risk assessment, together with personalized recommendations for behavioral change. The effect of lifestyle change to CRC risk will be evaluated from a behavioral adherence / personalized profile perspective and by exploiting a quantitative minimally-invasive blood test developed within the DIOPTRA research and innovation (RIA) project (https://www.dioptra-project.eu/, https://cordis.europa.eu/project/id/101096649). This blood test will be developed for screening purposes and will be used within the study as a means to evaluate the CRC risk over the course of a behavioral change strategy. The study is also conducted under this project, as part of a greater clinical study aiming to revolutionize CRC screening.

II. Existing Theories & Previous Work

It is established knowledge that CRC emergence is strongly influenced by behavioral factors which can play a pivotal role in incidence [9], [14], [15], [22]. These modifiable variables have been associated with the development of adenomatous and serrated polyps, both corresponding to major CRC transition candidates [10] (evidence being larger for adenomatous polyps). Namely, the links of diet, weight and exercise to colorectal cancer risk are some of the strongest among all cancer types [23]. Behaviors such as regular physical activity have been associated with a reduced risk of CRC, while on the other hand sedentary behavior and lack of physical activity, such as prolonged sitting, has been acknowledged as a risk factor for CRC, as well as for a few other cancers [14]. Dietary patterns, by the overall effect of ingredients, could also play a crucial role in CRC risk. Healthy patterns feature high consumption of fruits, vegetables, whole grains, and low-fat dairy products and are associated with a lower CRC risk, whereas unhealthy patterns which are characterized by high intake of processed/red meats, sugary beverages and refined grains, are correlated with higher CRC risk [15]. Even cooking-related processes seem to play a part, with very high temperatures (frying, boiling, or grilling) generating chemicals that might raise the associated risk [14]. Additionally, both alcohol consumption and smoking are established risk factors, with even light alcohol intake and smoking being associated with a slight yet statistically significant increase in CRC risk [23]. Furthermore, being overweight increases both the incidence and mortality risk, with a stronger link for men. Anthropometric measurements such as body-mass index (BMI) and waist circumference (WC) are well-established indicators of CRC risk, supported by extensive epidemiological research that shows that both adenomas and CRC bear different dynamics based on BMI [23], [24]. On specific effects, recent systematic reviews have reported a documented decrease of approximately 50% to mortality risk due to a healthy lifestyle adoption [9], [22]. This outcome has been consistent across different populations, albeit adoption by the general population is still low, with less than 6% of the study population of [9] reporting as adhering to all guidelines (smoking, diet, alcohol, physical activity). Utilizing the above knowledge as a baseline, such modifiable factors have the potential to be addressed via lifestyle pathways promoting healthy behaviors including physical activity, BMI control, dietary and other habits (e.g. refraining from smoking or excessive alcohol) [25].

In this regard, digital tools such as mobile applications constitute a suitable means for promoting such behavioral changes to the public in the context of CRC risk minimization [26]. To date, several mobile applications focused on CRC have been developed, however they primarily emphasize on educational information about screening techniques [27] by explaining procedures and preparatory measures. With regard to risk assessment and delivery of behavioral suggestions, only one application (provided in Malaysian and no longer maintained, originally designed as a CRC educational tool), has integrated a generic risk assessment functionality [27]. This involves a questionnaire completed by users, addressing factors such as smoking status, family history of CRC, diabetes status, age, and gender. Based on the responses provided, users are prompted to undergo CRC screening tests if deemed necessary. Among the available apps, only a few are freely accessible on the two major application stores (Google Play and Apple App store), tailored towards the individuals' needs rather than specific healthcare facilities [27]. Nonetheless, it can be assumed that all these apps cannot constitute holistic solutions for driving a maintainable healthy lifestyle shift within the general population (with regard both

to CRC and cancer in general), on the basis that they are missing essential usability components to assure user-friendliness and interactivity, therefore long-term adherence and sustainability [27]. Moreover, aspects such as individual navigation, reminders, information on screening procedures, and access to healthcare providers are either fragmentedly provided or missing altogether. Most importantly, risk assessment delivery, provision of behavioral suggestions and self-monitoring are also overlooked, despite the huge evidence showcasing their importance for CRC self-prevention through healthy living.

Furthermore, there is a lack of reported information regarding the empirical testing, efficacy, and effectiveness of these applications. Up to the present day, no mobile application has been developed to assess the personalized risk of users solely based on a self-administered questionnaire, leveraging the results to provide the user with personalized meaningful suggestions that may reduce the risk and contribute to the adoption of a healthier profile, based on current knowledge about CRC prevention factors. Moreover, a recent systematic review identified only ten randomized controlled trials over the past 25 years that have investigated the behavioral change impact of lifestyle recommendations provided to adults after CRC screening [25]. These have showcased behavioral improvements, albeit with varying effect sizes, with the authors reporting a limitation stemming from the between-study heterogeneity as well as the pronounced use of self-report and recall measures, both of which can be addressed via standardized modelling and use of a digital tool across multiple clinical sites.

What is more, there has been no evaluation of efficacy and clinical usefulness of digital tools and behavioral change strategies in terms of CRC-specific biomarkers within the scope of a clinical study [27]. Systematic reviews have reported the lack of large studies to examine the effect of adopting behavioral alterations for healthy living on CRC risk, with cancer bodies such as the World Health Organization (WHO), the American Cancer Society, and the World Cancer Research Fund (WCRF) / American Institute for Cancer Research (AICR) using the current evidence to promote generalized recommendations to citizens and cancer survivors [9], [22]. However, other than the effect of behavioral change on risk factors such as BMI and the overall ground truth of a healthier lifestyle being associated with a lower CRC risk, a true link reflecting the lifestyle alterations' effect on the biological underpinnings of CRC has not been quantitatively established [27]. The only such studies are based on a colonoscopy-based assessment to correlate findings with CRC risk factors [28], or involve the in-situ study of polyps to assess progression as a function of lifestyle variables [29]. Specifically, the latter study involved the detection of polyps that were left in situ to be removed and subjected to histological examination 3 years later for study and control groups, albeit the evaluation was based on medication rather than lifestyle modifications, with the latter only being included in a sub-study of this paper including 29 patients. Furthermore, the above studies utilize biopsy findings, with the non-invasive options mainly featuring the guaiac-based fecal occult blood test (gFOBT), the fecal immunochemical test (FIT), and the multi-targeted stool DNA test (mt-sDNA), with the former being the less relevant today [30]. Such tests have been used to associate CRC findings with risk factors [31], [32], using negative results as the control group. However, these studies that are based on non-invasive screening neither involve the provision and impact assessment of behavioral suggestions based on risk factors, nor exploit digital tools for delivery, self-monitoring and follow-up assessment. Overall, to the best of the authors' knowledge, no app-based study has utilized individual characteristics and accessible screening biomarkers derived from routine blood examinations as an indicator of progress to evaluate the effectiveness of behavioral suggestions.

III. Methods

A. Presented study, Research question & Hypothesis

The primary research question of this study is to determine whether a statistically significant difference will be observed as a result of the app use and the provision of personalized suggestions with regard to the attainment of a healthier lifestyle profile (linked to a lower CRC risk) and the effect of such change on the biological profile. The former will be evaluated via self-administered questionnaires, which will be used as inputs to estimate the CRC risk in the form of a wellness and risk profile. On the other hand, the latter will be evaluated via a minimally-invasive biomarker test for CRC screening using blood sampling. As such, baseline assessment will include both steps (performed in parallel with the one not utilizing info derived from the other). Based on the risk assessment results, personalized behavioral recommendations will be provided to the user. After a 1-year time interval, a follow-up evaluation will be completed. All services apart from the biological assessment (risk factor assessment, provision of recommendations, monitoring, etc.) will be administrable via the DIOPTRA mobile application. The overall study design is depicted in Figure 1:

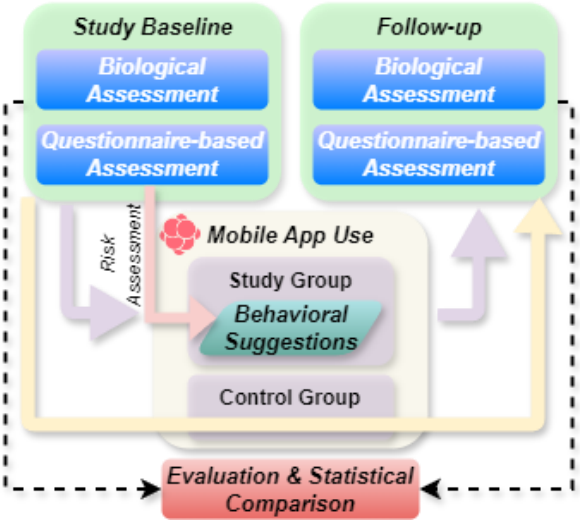

Figure 1: Experimental Design

In general, the study's objectives are multifaceted, aiming to comprehensively address various aspects of personalized CRC risk assessment and behavioral recommendations to enhance CRC prevention among the general population.

B. Applied Research Methods

The key research methods applied for data collection within this study include a) behavioral questionnaires, b) a blood biomarker evaluation test, and c) the DIOPTRA mobile app. Specifically, the behavioral questionnaires play a pivotal role in the study, serving as a foundational tool to generate personalized assessments. They encompass a wide range of dimensions in participants' lives, covering sociodemographic

information, lifestyle habits, dietary patterns, supplement intake, and stress levels. Sociodemographic details, including age, sex, country of birth, residence, education level, income, and occupation, are explored. Transitioning to lifestyle habits, inquiries delve into smoking, alcohol consumption, physical activity, sedentary behavior, and prolonged sitting. Regarding dietary habits, participants are queried about consumption frequency of various food groups such as fruits, vegetables, processed meat, dairy, white meat, whole grains, sugary drinks, sugary desserts, and fast food. Supplement-related inquiries cover omega-3, multivitamin, probiotic, fiber, and folic acid intake. Finally, stress levels are evaluated through questions about feelings of control, confidence, nervousness, and stress experienced over the past two months. During the follow-up assessment, an updated questionnaire will be presented aiming to capture changes compared to the baseline.

The blood biomarker test will be developed as part of a separate phase of the DIOPTRA project utilizing a set of paired tissue & blood samples derived from a population including four subgroups assigned with the following labels [24]: a) healthy, b) non-advanced adenoma, c) advanced adenoma, and d) CRC. Classification will be based on standard clinical diagnostic procedures. The paired samples derived will be analyzed for the development of the biomarker screening test that will be used in the context of baseline & follow-up assessments of the present study.

With regard to the mobile application, this will comprise multiple modules to actively engage users and provide tailored recommendations based on the risk assessment output that will operate on the questionnaire data, with an example shown in Figure 3(a). Recommendations will seek to improve the risk assessment score by modifying users' dietary and physical activity habits ahead of the 1-year follow-up assessment. Furthermore, two additional modules will complement these functionalities within the mobile application (Section III.C).

C. *Research Models and Instruments*

In the direction of fulfilling the current study's needs, the preceding phases of the DIOPTRA project are responsible for providing the risk factor model that is integrated into the corresponding module of the mobile application, as well as the CRC screening test that will be developed through the process of a dedicated biomarker discovery study (outside the scope of the current work). For the development of the risk factor model, Electronic Health Record (EHR) data obtained from participating clinical sites within the project consortium are exploited. Data includes demographic indicators, familial medical history, comprehensive medical records, behavioral patterns, and intricate clinical observations. Variables have been identified based on a filtering process by technical and clinical experts, assessing potential significance of each variable to create a project-specific data template, which utilizes coding systems [33] such as SNOMED, LOINC and ICD and serves as a standardized reference model ensuring uniformity and consistency. This information, coupled with an extensive literature review, constitutes the base input for identifying the most prominent risk factors that will be exploited within the risk factor model. This model is designed to collaboratively operate with a Behavioral Recommendation Engine (BRE) embedded within the corresponding module of the mobile app, as depicted in Figure 3(b). Leveraging the input data, the BRE generates tailored recommendations aimed at cultivating healthier habits associated with CRC risk reduction among users.

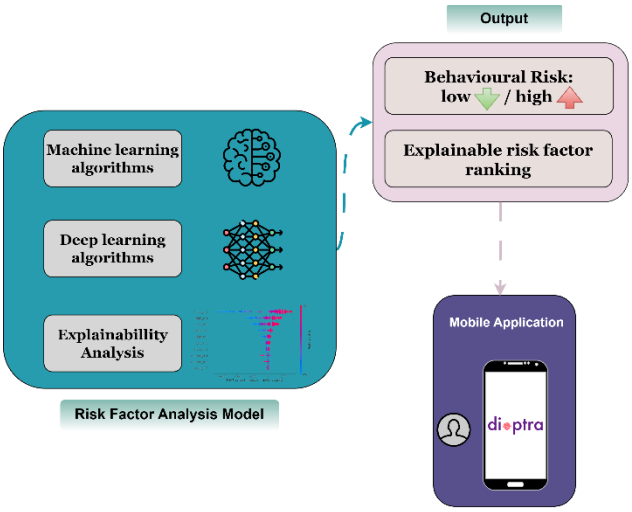

Figure 2: Risk factor model development and integration into the mobile application

On the whole, the DIOPTRA mobile app is built upon three primary modules: a) the Risk Assessment & Personalized Recommendation Module (RAM), b) the Health Literacy Module (HLM), and c) the Diary.

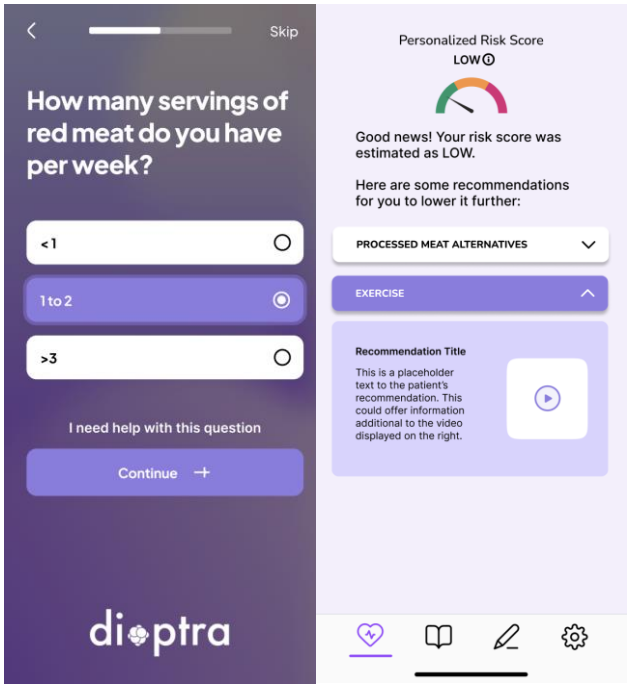

Figure 3: (a) Mock-up showcasing a single question of the baseline questionnaire – (b) Example of the risk assessment results and the personalized recommendations

1) Risk Assessment and Personalised Recommendation Module (RAM): This module is critical for calculating personalized risk assessments based on user responses, as well as for identifying areas that the user may improve in order to shift towards a profile associated with a lower CRC risk. Consequently, the participants are empowered with valuable insights on their behavior, being provided with guidance to set feasible goals through practical and achievable steps for sustainable improvement built on informed decisions. Recommendations are presented in a

user-friendly format, leveraging educational content such as videos, infographics, and text, based on the model's results.

2) Health Literacy Module (HLM): The Health Literacy Module serves as an educational resource designed to enhance public understanding of CRC and healthy behaviors. Curated by clinicians, the module features a diverse range of content, including articles, infographics, and videos, aimed at providing accurate and up-to-date information on CRC. Topics covered include the following:

- Introduction to CRC (definition, significance, prevalence and impact, importance of early detection and prevention)
- Digestive System & CRC (anatomy, pathophysiology of CRC development)
- Causes & Risk Factors (genetic predisposition and hereditary syndromes, lifestyle and age-related factors)
- Symptoms & Warning Signs (common CRC symptoms of CRC, variations based on location/stage, importance of medical evaluation)
- Prevention (role of diet, exercise, and overall lifestyle)
- Screening & Diagnostic Procedures (methods, guidelines, benefits, fears and misconceptions)
- Treatment & Research Advancements

3) Diary: The Diary feature is a user-centric functionality designed to encourage and track individual lifestyle behaviors and mild bowel symptoms. It facilitates the monitoring of behavioral improvements, such as physical activity and nutrition, as well as the identification of any changes or recent trends in these areas. Presented in the form of periodic sets of questions, it enhances user engagement by prompting users to answer before continuing to use the app. Additionally, it helps track mild bowel symptoms, such as chronic constipation or diarrhea, providing valuable insights into user health status and facilitating timely suggestions.

On the design aspects of the application, ensuring a user-friendly interface (e.g. effortless navigation, data entry, comprehension of personalized recommendations) is paramount to enhance user engagement, incorporating active mechanisms like reminders, notifications, and feedback systems to promote proactive health management and enhance user interaction. Compatibility across various mobile platforms, including iOS and Android, is also essential to optimize functionality and performance across a diverse array of devices. Additionally, the inclusion of comprehensive documentation and user support resources into the application facilitates user assistance and issue resolution, thereby ensuring a seamless and uninterrupted user experience.

D. Experiment

The study will be set up in eight European hospitals, that will recruit citizens that visit these sites for standard CRC screening. Upon their enrollment in the study (including verification of eligibility criteria and informed consent), the standard screening process will be carried out based on each hospital's procedures, accompanied by blood sampling for the biomarker screening test. The baseline questionnaire will also be filled on-site by the enrolled participants.

Afterwards, the clinical diagnosis – according to each hospital's standards – will determine the final eligibility for the current study. The diagnostic process should classify the participants either in the "healthy" or in the "non-advanced adenoma" subgroup. Eligible participants will then download the application and be assigned a participant ID. The app will get immediate access to baseline questionnaire responses, which will serve as foundational data for generating the user's personalized risk assessment result.

From that point on, participants will follow a differentiated course based on their assignment to the case or the control group. The case group will receive behavioral suggestions via the application based on the RAM, while the control group will not receive any suggestions. Throughout the year-long study period, the case group will receive app notifications for adherence and will have the option to input new data via the diary module. After this time interval, the follow-up step will include both case and control groups completing a follow-up questionnaire that will assess any changes in behavioral patterns compared to baseline and how these have impacted the personalized profile. Concurrently, participants will revisit their enrollment clinical site for a follow-up blood collection.

Overall, the aim of the study has been set for a total of 320 participants (accounting for a high dropout rate estimation of 30%), corresponding to a mean contribution of 40 participants per clinical site (8 hospitals in total), equally divided into case/control groups as well as the DIOPTRA study subgroups (i.e. case – healthy, case – non-advanced adenoma, control – healthy, control – non-advanced adenoma). Randomization will be performed to mitigate bias, using appropriate randomization methods such as block randomization and adaptive randomization. Data analysis will encompass the content of the questionnaires, the results of the risk assessment module, as well as the outcomes of the biological test conducted before and after the study interval, using a t-test for paired samples. The goals will be to a) determine if there is a statistically significant change in the profile of the case group participants, b) investigate the existence of any difference in the protein biomarker measurements before and after the behavioral recommendations, and c) evaluate the overall usability and impact of the mobile application. All these points will be studied for each of the two subgroups, referring to healthy and non-advanced adenoma cases.

IV. Discussion

As described based on previous works on the field, the novelty in the comprehensive approach outlined lies in a number of key points. Firstly, the combined integration of personalized risk assessment and behavioral suggestions – with the latter occurring based on the former's findings – builds on the recently-established dose-response relationship between healthy lifestyles and CRC risk. Although evidence linking behavioral aspects and CRC incidence has been demonstrated by a large number of studies, only recently a systematic review and meta-analysis consolidated findings to reveal this dose-response relationship [9]. However, none of these studies have included a pre- and post- assessment to delve into this relationship, thus not advancing beyond correlating CRC and adenoma incidence with the risk factors. The only relevant study has used in-situ polyp analysis to evaluate progression, albeit it used a medication scheme and only engaged a small subset of its participants into a diet-based sub-study. This shortage of relevant research may be

partly attributed to the lack of a quantitative non-invasive (or minimally-invasive) tool that bears high reliability for multi-class classification and is therefore exploitable for a straightforward assessment. Current colonoscopy non-invasive alternatives are either qualitative or lack the concrete evidence to support the quantitative version vs the qualitative one, or they simply bear suboptimal reliability [34], [35], [36]. In any case, the non-invasive (and minimally-invasive) CRC screening is still under active research. As such, this constitutes the second key novelty point of this study, that plans to utilize a new minimally-invasive protein biomarker screening tool for biological profile evaluation before and after the use of the tested solution by the participants. This will allow the combination of behavioral-based assessment with biological findings extracted without the use of an invasive clinical procedure such as colonoscopy.

Furthermore, this will be the first study to incorporate the above into a digital mHealth framework, motivated by the growing literature on the use of mobile apps within clinical studies [37], [38]. The app content (health literacy, recommendations) will be verified through clinical input while the risk factors and model results will occur through the analysis of multidimensional data from different hospitals. This process amounts to the credibility of the application's modules, with the long-term aim to deploy the mobile solution for the general population. The augmentation of the risk assessment and personalized recommendation module with the additional key features of the diary and the health literacy module solidifies the holistic nature of the solution, with the HLM covering a variety of topics to establish the DIOPTRA app as an open knowledge hub on CRC, appealing to both experts and the public. This provision of curated and up-to-date material will promote risk awareness and support behavioral changes. In addition, the incorporation of auxiliary features in the application such as notifications, reminders, customization capabilities, multi-lingual support, compatibility with OS-level accessibility features, as well as incorporation of user feedback for continuous improvement, further adds to the usability and – by extension – to the overall value of the application within the growing mHealth field.

Assuredly, the design and operational principles of the application – as well as the overall study – ensure compliance with the applicable EU data protection laws, fostering transparency and users' control over personal information. Such compliance comprises a principal requirement, since the study and the mobile application appertain to an EU research project, so by default all the project's components and procedures are obliged to abide by the official regulations. Consequently, this increases the target users' trust and therefore enhances penetration prospects.

However, on the other side of the above strengths and benefits of the current study and the related outcomes, there exist certain challenges and limitations that must be acknowledged and taken into account during implementation and analysis. Firstly, the participants' engagement and adherence is a major challenge – also reported in other studies implementing behavior change [39] – with regard to both their commitment to the study and the follow-up process and their dedication to the behavioral recommendations that will be presented. In this respect, although the provision and use of the mobile app is by itself a marker of increased adherence [38], the hospitals should maintain close personal contact with the participants [37] to minimize dropout rates and achieve high adherence. Moreover, a plan for incorporating population benchmarks and performance rankings has been discussed, aiming to boost active engagement. Nevertheless, a high expected dropout rate of 30% has been taken into account during the definition of the required sample size for the statistical analysis. Another challenge that should be definitely addressed is the digital literacy of the target population. It should be kept in mind that the participants will arise from a pool of citizens that would typically visit a hospital for CRC screening, i.e. mostly over 50 years old according to EU guidelines [2], [40]. It can be expected that a substantial portion of this population will bear insufficient digital literacy and familiarity with mobile apps. This will be addressed both on the app-design level (incorporating user-friendly interfaces and sufficient documentation) and on the enrollment level, where the hospital personnel will ensure the participants' readiness to reliably use the app for the purposes of the study. Finally, an important limitation lies within the time interval between baseline and follow-up assessments, which is limited by the overall project timeline within its 4-year duration, with the initial phases being dedicated to the design and development of models, tools and infrastructure. As a result, the 1-year interval may not be enough to elicit measurable and statistically significant changes to the biological profile of the participants based on the results of our biomarker test, especially since the transition of polyps to malignant states is a much longer process [8], [41]. If this turns out to be the case, the behavioral findings will be assessed for evidence supporting the continuation of the study beyond the project lifecycle. Most likely, a long-term study will be needed to evaluate the sustained effectiveness of the DIOPTRA application and the overall framework in reducing CRC risk over time.

V. Conclusions and Future Work

In summary, this study outlines a comprehensive approach to colorectal cancer prevention through the development and implementation of a multifaceted mobile application and a related behavioral change strategy. Through an extensive evaluation process, the study seeks to assess the efficacy of behavioral recommendations in influencing CRC risk factors and improving health outcomes. By leveraging existing knowledge on modifiable risk factors and integrating personalized risk assessment tools with recommended behavioral pathways, the application aims to empower users to make informed decisions about their health and reduce their risk of developing CRC. Previous research has established strong links between lifestyle factors and CRC risk, highlighting the importance of recommendations targeting these behaviors and their capacity to impact CRC incidence rates. The digital solution proposed in this study capitalizes on these findings to introduce a framework that bears the capacity to ultimately reduce CRC risk among the general population. Furthermore, the incorporation of biological evaluation exploiting CRC-specific biomarkers extracted via a standard minimally-invasive procedure (blood sampling) contributes both to the novelty of the study and the credibility of the results with regard to the evidence that will be produced.

In addition, user empowerment and active engagement are in the center of the above framework, supported by additional content such as the health literacy module that – in combination with the risk assessment, recommendations and

diary – aims to foster informed decisions towards awareness and long-term adherence. By delivering targeted educational content and facilitating access to screening information, the app serves as a valuable tool for CRC prevention, while also contributing to early detection efforts by promoting increased screening rates among the public.

Moving forward, continued research and evaluation are crucial to refine the effectiveness of the mobile application and ensure its long-term impact on CRC prevention efforts. Longer-term studies are needed to assess the sustained effectiveness in reducing CRC risk and promoting healthy behaviors over time. Additionally, efforts to increase awareness and accessibility of the application among the general population are essential to maximize its public health impact. Overall, the development and implementation of the presented framework represent a significant step towards enhancing CRC prevention and by extension reducing the CRC burden worldwide. Regardless, continuous development and feedback integration via periodic updates with new features or enhancements will be essential for the ongoing evolution of the proposed mobile tool.

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