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D2.1. EVIDENCE BASIS REPORT ON EXISTING VALIDATED RISK CALCULATORS AND PREVENTIVE DIGITAL SYSTEMS FOR THE STUDIED CHRONIC CONDITIONS

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DISSEMINATION LEVEL

☒	PU: Public	☐	PP: Restricted to other program participants
☐	RE: Restricted to a group specified by the consortium	☐	CO: Confidential, only for members of the consortium

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1.1	19/03/2021	Ana Maria Wägner	Update on diabetes management
1.2	22/03/2021	Inger Torhild Gram	Update on NCD
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LIST OF ABBREVIATIONS

Abbreviation	Significance
AMI	Acute Myocardial Infarction
APCSC	Asia Pacific Cohort Studies Collaboration
CHD	Coronary Heart Disease
CMCS	Chinese Multi-Provincial Cohort Study
COPD	Chronic Obstructive Pulmonary Disease
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
ERFC	Emerging Risk Factors Collaboration
HCUR	Health Checks Ubon Ratchathani Study in Thailand
MM	Melanoma
NCD	Non-Communicable Disease
PREDICT-CVD	New Zealand Primary Care-Based PREDICT-CVD Cohort
PRS	Polygenetic Risk Score
TLGS	Tehran Lipids and Glucose Study
UVR	Ultraviolet Radiation

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1 INTRODUCTION

The main objective of the WP2 is to provide the blueprint for the development of the preventive WARIFA AI tool that will encompass three main user-directed pillars: to provide a person-centered risk estimation across multiple NCDs, to provide personalized risk-level adapted recommendations for preventive behaviour change, and to help monitoring the risk level changes following successful preventive behaviour change.

Within this main WP2 objective a key specific goal is to define the required input and output variables for the WARIFA AI tool development. The steppingstone towards reaching this specific goal is the first task of the WP2, Task 2.1. Documentation, that consists in performing the scientific literature review focusing on: the interaction between health care systems and the use of preventive mobile apps by the individual citizen; existing digital tools for prevention of the main NCDs, and existing validated risk calculators for the main NCDs, at individual and community level.

The deliverable D2.1. represents the result of the work performed within this task. It provides a succinct overview of the current situation of existent preventing apps and disease risk calculators, supported by scientific evidence. It aims to constitute the evidence base needed to inform the work of the other WPs in developing an innovative AI preventive tool, that goes beyond the state of the art to fill the unmet needs of person-centred prevention in the areas of the major NCDs related with the highest burden of morbidity and mortality in Europe.

2 RISK CALCULATORS

Risk calculators are helpful tools aiming to estimate the individual's risk to develop a specific NCD based on patient's characteristics, family history, clinical variables etc. Based on the information they provide, the physician and patient can tailor their approach to follow evidence-based individual health promotion strategies and lifestyle-change programs to prevent the development of NCDs. We performed a scientific literature overview regarding the available risk calculators for the NCDs associated with the highest morbidity and mortality burden in Europe: Cardiovascular diseases (CVD), Diabetes melitus (DM), Chronic obstructive pulmonary diseases (COPD), and additionally to melanoma, as the skin cancer with the highest mortality burden in Europe.

2.1 MAJOR NCDS

2.1.1 Methodology - Search strategy

The literature search was based on the currently valid recommendations and clinical practice guidelines for use of disease risk predictors and score calculators issued by the European professional associations in the disease areas of CVD, DM and COPD. Variants valid and endorsed by national guidelines in the Consortium countries (i.e., Norway, Spain, Romania) were included if available and different from the European ones. The literature search was supplemented with the analysis of the reviews and systematic reviews published in the last five years on the topic. For multiple versions, the last updated was retained for our review.

2.1.2 Results

Several risk predictors are used in Europe for the studied NCDs, endorsed by European guidelines for prevention in clinical practice (see **Table 1**).

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For CVD there are currently several cardiovascular risk calculators available, based on epidemiological studies, such as the Framingham Heart Study [1]. A very recent review [2] identified twelve validated online tools for MI or CHD risk assessment and one not-validated tool (see **Table 1**). The tools were validated in different countries/regions, inlcuding Germany, the US, Belfast & France, England, Switzerland and other different countries.

The most widely used predictors for the risk of CVD events or for the risk of CVD deaths are the World Health Organization cardiovascular disease risk charts, that estimate the 10-years risk of CVD events, in 21 global regions [3], and the SCORE predictor of 10-years risk of fatal CVD, that comprises 2 versions for low-risk and respectively high-risk European countries [4]. Furthermore, updated recalibrated versions of SCORE have been published for several countries (Belgium, Germany, Greece, the Netherlands, Spain, Sweden, Poland). In Norway the NORRISK 2 CVD risk model is used [5]. The predictors are using between five to eight variables, either clinical or clinical and laboratory-based. Clinical variables include: age, sex, systolic blood pressure, smoking, BMI, personal history of diabetes or CVD, family history of premature CHD. Laboratory variables include total and high-density-lipoprotein serum cholesterol. The models are used to provide a estimated of % risk of CVD or CVD death stratified in five or six levels of risk (seven categoris for NORRISK) (very low to very high). These models are available as online calculators or charts.

For people with diabetes, the Framingham Study- based calculators tend to underestimate risks, since relatively few people with diabetes were included in the study. In addition, they do not account for diabetes-specific features, such as diabetes duration and glycaemic control. The UKPDS Risk Engine is a risk calculator, designed specifically for people with type 2 diabetes, based on the pivotal UKPDS study [6].

For Type 1 Diabetes patients, the Steno diabetes center Copenhagen provides a risk calculator for the ten-year risk of developing CVDs, stratified in three risk levels, including the variables:age, sex, diabetes duration, smoking status, systolic blood pressure, daily exercise level, and laboratory variables HbAc1 levels, albuminuria, eGFR levels, LDL levels.

Eight validated and three non-validated online tools for stroke risk assessment were identified [2]. Of the validated tools, four were designed to estimate also CHD risk (Framingham, RRS, SCORE, PROCAM) and four were stroke-specific, three of them for patients who already experinced cerebrovascular events or atrial fibrillation. The outcome measures included ten-year risk of (first) stroke, ten-year risk of MI, stroke or major CVD two-, seven- and 90-day risk of stroke, annual risk of stroke in patients with atrial fibrillation, and 1-year risk of recurrent stroke.

For the risk of developing DM2, several models of risk predictors exist, validated in different populations like American, Canadian, Australian, European (see **Table 1**). The review by Juchli et al. [2] identified 12 validated and five non-validates online tools for risk assessment of type II diabetes mellitus. These models use the variables: Age, sex, parents/sibbling with DM, HTA, physically active, ethnicity, height & weight/BMI. Additional variables used are: high blood sugar, large baby born, waist circumference, diet, education level. These risk predictors provide a risk score of developing DM2, on one to ten years time span, stratified in three categories (low-medium-high).

For COPD, public available risk assessment models are not directed to primary prevention, but rather to early detection, as they provide estimates of a person's likelihood of having COPD (see

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Table 1). They assess early symptoms on one hand and smoking history on the other [7] to provide a COPD likelihood score. Other likelihood estimation tools developed as screening method for COPD include variables of medical parameters of the respiratory function like FEV, FVC.

In conclusion, a significant number of online available tools for risk assessment exist for the main NCDs studied. Many of them have been extensively researched and scientifically validated. However, their use for an individual patient must take into account the following caveats: they have been validated for different populations, and their use outside of that population may be misleading, they focus on different groups, such as defiend by certain age, sex, personal or family history; the definition of variables and parameters included vary, the risk estimates are described differently by each tool.

2.2 MELANOMA

2.2.1 Methodology - Search strategy

We have based our literature search for the Warifa project on the recent paper by Kaiser et al [8], a systematic review following up on the systematic reviews of Vuong et al. [9] and Usher-Smith et al. [10]. To this, articles published after January 31st 2020 (end date of search in Kaiser et al. [8]) were added. The results are presented in Table 2.

2.2.2 Results

There are more than 40 papers over the years, and some of the papers include more than 1 model [8]. The studies originate from many countries, most frequent are the US, Australia and Germany. Study designs were mainly case-control. Whether a risk score was calculated is presented in table 2 (“Outcome of the risk calculator”), and here it is also noted whether a cut-off was defined for high risk. In total, 1-16 variables were included in the models. In Kaiser et al. [8], we identified 35 predictors: the most common is nevi, followed by hair color. However, each variable was recorded in different ways in each model/study, e.g., nevi of entire body, only one arm, both arms and/or the back, with different categories in each study. About 1/3 included genetic risk factors. Validation is more common in recent studies. About 50% of the studies used internal validation, and only six external data. To our knowledge only two of the models are available as risk calculators on the web, see table 2 (“Available as app (link/ ref.)”).

3 OVERVIEW OF DIGITAL APPLICATIONS DIRECTED TO PREVENTION

3.1 INTRODUCTION

There is evidence that mobile devices can be used in the personalized management of chronic conditions in individual citizens. In contrast to personal desktop computers, smartphones and tablets are continuously accessible, and are able to interact with web-based health services.

As of 2017, the number of health-related apps already downloaded stood at 3.7 billion [11]. There are estimates that over 100,000 different smartphone Apps for healthcare exist for the Android operating system alone [12]. From sleep apps to those that help individuals self-manage existing chronic conditions like diabetes, these technologies offer an accepted platform that can support tracking risk factors and providing recommendations for preventative measures. In 2019, the WHO released a guideline with recommendations on digital interventions for health system

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strengthening [13]. Despite the promising potential of health apps, there is still insufficient evidence about their effectiveness [13] and uncertainty about their quality control, regulation and certification [11, 14].

3.2 METHODOLOGY- SEARCH STRATEGY

For WARIFA we performed a scientific literature search on existing apps of consumer-directed type, dedicated to improve prevention of main NCDs including CVD, skin cancer, chronic respiratory disease and DM. We based the search on systematic reviews and meta-analyses, including apps for which scientific evidence exists and on the databases previously elaborated by the members of the Consortium. The intention of this section is to provide a broad overview of mobile applications and their functionalities. We therefore included studies on both primary, secondary and tertiary prevention. Information from the European Project MHub [15] has been added.

3.3 APPLICATIONS DEDICATED TO THE PREVENTION OF SKIN CANCERS

Current mobile applications on the market for skin lesions offer functionalities that can be broken into four main categories. Firstly, applications that are aimed as tools to educate and inform users about the risks of UV exposure, and to promote sun safety behaviours as primary prevention. Secondly, applications dedicated to enhance early detection by assisting patients in conducting skin self-examinations; these can offer either functionalities of storing pictures of lesions or total body photography into one accessible place to allow for patients to easily identify new or changing lesions, or functionalities of training and reminding patients to perform skin self-examinations. Thirdly, there are applications that claim to be automatic diagnostic tools for either clinicians or patients themselves, and their methods and performance vary widely. Fourthly, applications to be used to assist medical students in recognising malignant skin lesions was created and trialled and can be extended for early detection education to other non-medical professionals who see skin (massage therapists, nurses, hairdressers, beauticians etc.).

A recent review of the situation of skin cancer dedicated apps [16] identified 43 consumer-directed apps on Android and Apple platforms, with 55.8% new apps compared with 2014. The most common functionality was monitoring/tracking of suspect lesions with 24 of 43 (55.8%) apps performing this. About a third of apps (34.9%) reported clinician, professional or scientific input (increasing from 10% in 2014) but only 5% of them mentioned peer-reviewed evidence along with professional input.

Primary prevention-related functionalities in the analyzed apps included: providing information on melanoma and skin cancers (39.5% of the 43 apps); providing advice on UVR/ sun exposure (23.3%) and risk factors assessment (14%).

Applications aiming to skin cancers primary prevention are dedicated to educate and encourage good sun safety practices. The outcomes of some of these applications have been studied (see Table 3).

An example is Sunface, which is designed as a visual aid that alters a user's photo to highlight the consequences of UV exposure on their skin after a period of time, aimed at informing users of the consequence of excessive sun exposure with a shocking visual medium. There has been moderate success with this application, the results suggesting high levels of engagement with

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adults and children exposed to the application and a high proportion of users being more motivated to increase their sun protection [17, 18].

Applications also exist to provide data on the UV index and sun safety tips tailored to the user`s risk profile in order to encourage better sun safety practices, however, research has only shown moderate success with these apps in changing sun behaviours. A study on the app SolarCell in the USA highlighted only mild improvements in sun protection behaviours, and which were generally negligible in the longer term [19]. This is particularly compounded by the fact that such apps felt like a novelty app that is easily disregarded after first use. This is in line with most mobile applications, with specific strategies that need to be in place in order to encourage long-term engagement, which was not done [20].

The limitations of these applications have been highlighted in the literature. SunSmart, an application that provides data on the UV index and forecasts have highlighted the misconceptions surrounding UV radiation from the sun, which ultimately reduces the impact that these applications have on user behaviour, and the need for concurrent public health messaging resolving these misconceptions for these applications to work effectively [21].

Overall, there has been limited research into applications that aim to prevent malignant skin lesion formation from the outset. There has been a limited number of applications created, and much of the current apps that were studied were hampered by non-ideal app design, that did not allow for longer-term engagement and was limited in the advice they provided.

Ideally these apps would affect longer-term behavioural changes, and this was also not considered beyond 12 weeks after application installation.

There would be benefit in the creation of an application that utilises best practice in long-term user engagement, while also continuing to be interesting for users to use, and that provides relevant and up-to-date information.

The study designs involved with analysing these applications were also mostly poor, with the exception of the US study, with use of study designs that provide a low level of evidence which was generally qualitative.

3.4 APPLICATIONS DEDICATED TO THE PREVENTION OF DIABETES

Mobile applications supporting the management of diabetes focus on four major areas: blood glucose monitoring, insulin use, physical activity and diet [22, 23]. In the short term, the applications aim to prevent hypoglycaemia while long term goals focus on quality of life and the prevention of complications of diabetes, in particular CVD. Most studies evaluating diabetes applications investigated clinical impact and usability, while security and privacy were less often analysed [24]. A large number of applications has a functionality to serve as a diary for blood glucose levels. In addition, some apps offer functionalities to assess common factors affecting blood glucose, e.g., food intake or physical activity [23]. There are apps on the market claiming to assist in insulin dosage calculation based on user data [25]. While there is evidence that insulin dosage calculators may provide decision support, there is limited evidence that this works in commercial consumer apps.

Mobile applications may improve diabetes self-management skills in patients with type 1 diabetes. Studies have shown an increase in the frequency of daily blood glucose checks and a significant

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decrease in HbA1c levels during a short follow-up period [26, 27]. Many apps focus exclusively on blood glucose management, and there seems to be a need for more comprehensive functionalities that include other variables relevant for the prevention of both hypoglycaemia and harmful long term effects.

Mobile applications may be effective in reducing lifestyle risk factors in diabetes. In a review Wu found that studies on type 2 diabetes reported significant reductions in HbA1c [28]. For type 1 diabetes the results were mixed. The authors concluded that «there is strong evidence for the efficacy of apps for lifestyle modification in diabetes type 2, and that additional evidence is needed for the other subtypes of diabetes.»

Usability and quality of diabetes apps vary considerably [22, 23, 29]. Brzan tested 65 apps, and 56 of these apps did not meet minimal requirements [29]. Furthermore, very few apps refer to a scientific evidence basis [22]. Experts have asked for better quality control of apps as there are concerns that some apps may have harmful effects [25, 28].

In order to have a preventive effect, citizens and patients need to adhere to app use over time. So far, there is a lack of studies on long term follow-up [26, 28]. Most studies on apps for diabetes provide only short term data, typically for up to 12 months. More research is needed to investigate how adherence may be improved. According to a study by Lee, features that help citizens monitor their health status over time, may improve long term adherence [20].

Several studies have reported a positive effect of mobile applications on quality of life [27, 30].

In addition to self management skills, diabetes also requires long term follow up by the health care system. Patient generated health data such as blood glucose levels and eating habits may be of interest to health personnel in order to improve the quality of medical care [31]. Few studies have investigated the use of patient generated health data in diabetes to improve interaction with health personnel by using mobile applications [32].

3.5 APPLICATIONS DEDICATED TO THE PREVENTION OF OTHER NON-COMMUNICABLE DISEASES

Mobile applications may support patient self-management in both CVD and chronic respiratory disease. The setting can be in primary, secondary or tertiary prevention. The main concept is to reduce the impact of modifiable risk factors by prompting behavioural change and to alert the user in case warning signs appear. This can be achieved by applications offering a variety of monitoring functionalities, e.g., a diary that displays body weight and provides feedback on any changes [14]. In addition, health education and social networking have been concepts used in mobile applications [33]. Many current applications use inbuilt and external sensors to collect clinical data, e.g., on physical activity or blood pressure [34]. The automatic transferral of data from sensors may also reduce the time a user has to spend entering data manually and this may improve long term adherence. The potential of mobile applications to support clinicians has been emphasised [14, 35]. The collection of patient generated data by the use of sensors may help clinicians in assessing a patients current health status and monitor the effect of therapy as well as preventive measures. According to Eapen "clinician engagement is paramount to maximizing the value of any mHealth product because software applications cannot actually treat patients [35]." In a study on physical activity by Middelweerd, self-monitoring, providing feedback on performance, and goal-setting were commonly used techniques to change behaviour [36]. Concepts that provide personalisation, gamification (i.e., use of game-design elements and game

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principles in non-game contexts), rewards, social elements and a simple and clear presentation haven proven beneficial [34].

Regarding modifiable risk factors in CVD, special interest has been in addressing «Life`s simple 7», i.e., physical activity, weight, diet, blood glucose, cholesterol, blood pressure and tobacco use [35]. In chronic obstructive pulmonary disease, researchers have focused on physical activity. The accuracy of physical activity measurements in applications appeared high, although Vorrink identified possible inaccuracies in certain situations, e.g., when the user is sitting on a bus. Only few studies were found reporting effects, which were “modest at best” [33, 37]. Romeo reported that physical activity apps are effective up to 3 months [38]. Obesity interventions have demonstrated short-term success but were ineffective in maintaining weight loss beyond 12 months [33]. Compared with usual care, self-monitoring of blood pressure has shown significant improvements in blood pressure control [33]. The recent Australian tobacco, exercise and diet Messages (“TEXT ME”) randomised clinical trial of 710 patients with coronary heart disease addressed multiple cardiovascular risk factors at the same time. At six-month follow-up, patients allocated to the “TEXT ME” intervention program had lower LDL-cholesterol, blood pressure, body mass index and a greater proportion were physically active and had quit smoking compared to controls [39].

In order to achieve sustainable behavioural change, long term adherence to mobile applications is essential. However, most studies report short term data only, typically from 3 to 12 months.

Furthermore, many studies have mainly focused on secondary and tertiary prevention in patients. The effectiveness of mobile applications for primary prevention in healthy citizens is less well studied. There are still many unanswered questions regarding the effectiveness of mobile applications in the long term.

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Table 1 Risk calculators for NCDs.

Year	Risk calculator OR risk survey	Disease predicted	Ref.	Outcome of the risk calculator	Variables included	Population on which was developed	Internal validation	External validation			Available as app (link/reference)	Additional notes/ observations
								Y/N	Population used	Ref.		
1999	UKPDS Risk Engine	CVD in DM2 patients (coronary heart disease and stroke risk in DM2)	[6]	10 years risk with 95% CI for: CHD, fatal CHD, stroke, fatal stroke	Age, sex, ethnicity, smoking status, presence or absence of atrial fibrillation and levels of HbA1c, systolic blood pressure, total cholesterol and HDL cholesterol	5012 new cases of DM2, 1977-1997, UK				[40]	Https://www.dtu.cx.ac.uk/riskengine/download.php	Better for type2 DM than Framingham
	Steno T1 Risk Engine	CVD in DM1 patients		10 years risk for cvds	Age, sex, diabetes duration, smoking status, systolic blood pressure, daily exercise level, and laboratory variables HbA1c, levels, albuminuria, egfr levels, LDL levels.	4,306 adult type Diabetes patients treated at Steno Diabetes Center Copenhagen, in Denmark, followed 2001-2013.		Yes	2,118 adult type 1 diabetes patients from Denmark.	[40]	Https://steno.shinapps.io/t1riskengine/	
2018	BRAVO risk score	Diabetes complications	[41]	28 different outcomes	Age, ethnicity, sex, HbA1c, age at diagnosis, systolic blood pressure, ldlc, BMI, smoking, history of Myocardial infarction or chronic heart disease,…	10251 US Type 2 diabetes cohort (ACCORD trial)		Yes	ASPEN, ADVANCE and CARDS trial populations	[41]	Http://www.bravo4health.com/demo/	Supplementary material at Https://link.springer.com/article/10.1007/s40273-018-0662-1#Sec9

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	Know Your Risk Diabetes UK	DM2		0-10 risk score of having type 2 DM in 3 categories (Low-medium-high)	Age, sex, mother/father/sibbling with DM, HTA, physically active, ethnicity, height, weight						Https://riskscore.diabetes.org.uk/start	NICE endorsed
2006	American Diabetes Association ADA risk test	DM2		0-10 risk score of having type 2 DM in 3 categories (Low-medium-high)	Age, sex, mother/father/sibbling with DM, HTA, physically active, ethnicity, height, weight	1999-2004, NHANES	Yes (ARIC, CHS)				Https://www.diabetes.org/	
	CANRISK	DM2		Risk score of having type 2 DM in 3 categories (Low <25-medium-high >32)	Age, sex, mother/father/sibbling with DM, HTA, high blood sugar, large baby born, physically active, ethnicity, height, weight, waist circumference, diet, education level	40-74y adults					Https://www.healthycanadians.gc.ca/en/canrisk	
2008	Framingham risk score	CVD	[1]	10 year risk of clinical CVD (CAD, stroke, PVD, CHF, cardiac death)	Sex, age (no under 30), total cholesterol, HDL, systolic blood pressure, HTA treatment, diabetic, smoking, previous vascular disease	5209 adults from Framingham (US), 1948-ongoing					Http://static.heart.org/riskcalc/app/index.html#!/baseline-risk	
2016	SCORE	CVD fatal	[4]	% of 10 year risk of fatal CVD in 7	Sex, age, smoking, systolic blood pressure, total cholesterol, region of	12 european cohort studies, 3 million person-y of	Yes	Yes	3554 asymptomatic adults between the ages of 50	[42]	Https://www.heartscore.org	Endoresed by European guidelines of CVD

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				categories (<1%- >15%)	Europe (high vs low risk countries)	observation, 7000 fatal CV events			and 75 years who underwent exercise stress testing as part of an executive health program between October 1990 and December 2002; participants were followed up for a mean of 8 years.			prevention. Different score charts for different countries (low-risk/high-risk). Updated recalibrated versions in Belgium, Germany, Greece, the Netherlands, Spain, Sweden, Poland. Norway uses NORRISK instead). SCORE 2 update submitted
	Reynolds Risk Score	CVD	[43]	10-years risk of CVD	Age, sex, blood pressure, cholesterol levels smoking, blood hscrp family history of premature heart attack			Yes	Validation cohort, n = 8158 initially healthy US >= 45 years followed up for a median of 10.2 years	[43]	Http://www.reynoldsriskscore.org/default.aspx	
	ARIC Coronary Heart Disease Risk Calculator, (n.d.)	CVD	[44]	10 years risk of AMI or fatal CVD	Gender race, smoking, age, diabetes history, systolic blood pressure, blood pressure medication, Total, HDL cholesterol	15,792 persons recruited in 1987-1989 from four U.S. communities,		Yes		[44]	Http://www.cscc.unc.edu/aricnews/riskcalc/html/RC1.html	

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						with follow-up through 1998						
2019	The WHO CVD Risk Chart Working Group (2019)	CVD (fatal/non fatal MI, CHD death, fatal/non-fatal stroke)	[3]	% of CVD risk in 10 years, in 5 categories (very low <5%- very high>30%)	Laboratory based: Age, sex, smoking status, systolic blood pressure, history of diabetes, and total serum cholesterol Non Laboratory based: age, sex, systolic blood pressure, smoking, BMI	376 177 individuals from 85 cohorts, and 19 333 incident cardiovascular events recorded	Yes (ERFC data)	Yes	External cohorts (19 cohorts, 1 096 061 individuals, 25 950 events): APCSC 14 cohorts, 43 735 individuals, 2219 events; CMCS 17 167 individuals, 1613 events; TLGS 4921 individuals, 400 events; PREDICT-CVD 254 680 individuals, 6857 events; HCUR 330 985 individuals, 6409 events; UK Biobank 444 573 individuals, 8452 events	[3]	Https://www.who.int/news/item/02-09-2019-who-updates-cardiovascular-risk-charts	World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions
2014	REGICOR (Registre Gironí del Cor) function	CVD	[45]	10 years risk of coronary events (	Same as Framingham: Sex, age (no under 30), total cholesterol, HDL, systolic BP, HTA treatment, diabetic,			Yes		[46]		Adaptation of Framingham function for Girona, Spain, as example of

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				fatal/non-fatal)	smoking, previous vascular disease							Mediterranean population (Framingham score overestimated the risk)
2017	Risk calculator NORRISK2	CVD (Hospital AMI, CHD Death, hospital stroke, fatal stroke)		% of 10 years risk in 3 categories of range (low/medium/high)	Serum total cholesterol, high-density lipoprotein (HDL) cholesterol, , daily smoking, systolic blood pressure, the present use of antihypertensive drugs and a family history of premature coronary heart disease (CHD). Segregated by sex	10-year follow-up of population-based cohort (CONOR) through linkage to the CVDNOR project - Norway 1994-2009. 31,445 men and 35,267 women aged 40-79 years with 3658 endpoints in men and 2459 in women	Yes	Yes	19,980 men and 19,309 women, of whom 1858 men and 874 women had an endpoint during follow-up	[5]	Http://hjerterisiko.helsedirektoratet.no/	National guidleines for Norway. Valid for 49-79 y old. (SCORE/ SCORE 2 not accepted for Norway)
2008	COPD Population screener	COPD	[7]	Self-scored questionnaire that can identify individuals likely to have COPD (0-10 score of likeliness to	Breathlessness, productive cough, activity limitation, smoking history, age	697 patients, 8-week period in 2004	Yes				Https://www.copdfoundation.org/Screener.aspx https://www.webmd.com/lung/copd/assessment-copd-risk/default.htm	

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				have COPD)								
	Risk calculator	Coronary heart disease		10-year risk of fatal or non-fatal MI	Age, gender, systolic blood presssure, ldlc, hdlc, triglyceride, diabetes, smoking, family history						Https://www.agla.ch/de/rechner-und-tools/agla-risikorechner	
	COPD Causes and Risk factors	COPD		No calculator, list of risk factors	Smoking, Exposure to air pollution, Breathing secondhand smoke, Working with chemicals, dust and fumes, genetic Alpha-1 deficiency, history of childhood respiratory infection						Www.lung.org	
	KOLS Kalkulator	COPD		Probability of COPD diagnosis	Smoking, age, sex, height, weight, respiratory symptoms, previous illness, medical parameters (FEV, FVC)						Https://medguideline.no/kols/	Norway, Norwegian language

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Table 2 Risk calculators for melanoma.

*Code internal validation: 0 = no; 1 = yes, bootstrapping; 2 = yes, cross-validation; 3 = yes, split sample.
**Article does not provide predicted risk for first cutaneous melanoma [8].

Year	Risk calculator	Ref.	Outcome of the risk calculator	Variables included	Population on which was developed	Internal validation *	External validation			Available as app (link/ ref.)	Additional notes/ observations
							Y/N	Population used	Ref.		
1988	Clinical risk prediction	[47]	Risk score	Clinically assessed: no. of raised nevi (arms); Self assessed: age on arrival in Australia, mean time spent outdoors (summer aged 10–24), family history (melanoma), history of non-melanoma skin cancer	511 cases, 511 controls, 18-80y, 1980-1981, Australia	3					
1989	Clinical risk prediction	[48]	Relative risks	Clinically assessed: no. of melanocytic common nevi, no. of atypical nevi, actinic lentigines; Self assessed: occupational sun exposure, skin type	200 cases, 200 cases, <20-89y, 1987, Germany	0				No	
1989	Clinical risk prediction	[49]	Relative risk (risk groups)	Clinically assessed: benign nevi >2 mm, freckling, atypical nevi >5 mm; Self-assessed: episodes of severe sunburn	280 cases, 280 controls, 11-71+y, 1987, Scotland	0	Yes	629 cases, 535 controls, 32.5±4.9 (age mean±sd),	[50]	No	

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								2001-2005, Australia			
1991		[51]	Relative risks	Skin type, hair color, eye color, total body nevus ≥2 mm count, no. Of dysplastic nevi	121 cases, 379 controls, 30-50y, 1986-1988, Sweden	0					
1992	Self assessed risk prediction	[52]	Relative risk	Self-assessed: hair color, skin reaction to repeated sun exposure, freckle density, nevi density	583 cases, 608 controls, 20-69y, 1984-1986, Canada	0				No	
1994	Clinical risk prediction	[53]	Relative risk estimates (risk groups)	Clinically assessed: no. Of melanocytic common nevi, actinic lentigines, atypical nevi, skin type	513 cases, 498 controls, 56±16y (mean, sd), 1990-1991, Germany	0				No	
1998	Clinical risk prediction	[54]	Risk score (negative score ->low risk)	Clinically assessed: colorimetric variables, Fitzpatrick	150 cases, 546 controls, age not specified, 1992-1995, Italy	2				No	
2001	Clinical risk prediction	[55]	Odds ratios	Clinically assessed: dysplastic nevi, skin color; self-assessed: tanning ability, eye color	183 cases, 179 controls, 17–77y, 1994-1999, Italy	0				No	
2003	Clinical and self assessed risk prediction	[56]	Odds ratios	Both clinical and self-assessed (one model for each): skin type, UV damage, no. of Nevi	202 cases, 202 controls, 57±15y (men) 52±15y (women), 2001, Austria	0				No	
2004	Risk prediction from buccal mucosa	[57]	Odds ratios	Mc1r genotype (buccal mucosa swab), melanin density (skin reflectance at the upper inner arm)	244 cases, 483 controls, 20–59y, 1998-1999, Australia	0				No	

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	swab (mcr1 gene)										
2004	Clinical risk prediction	[58]	Relative risk estimates (high risk: ≥2 (3) risk factors in model 3 (1))	**Model 1:** hair color, eye color, skin type; **model 2:** hair color, eye color, skin type, occupational sun exposure, atypical nevi; **model 3:** skin type, sun exposure, nevi, atypical nevi; **model 4:** skin type, occupational sun exposure, nevi, atypical nevi	100 cases, 200 controls, 18–74y, 2000-2001, Italy	0				No	Clinical assessment: nevi, atypical nevi; self-estimated: hair color, eye color, skin type, occupational sun exposure
2005	Self assessed risk prediction	[59]	Risk score and 10-years-absolute risk	Self-assessed: sex, age, family history, sunburns, no. Of nevi (arms), hair color	535 cases, total 178,155, 25-75y, 1976 1986 1989, US	3	Yes	629 cases, 535 controls, 32.5±4.9 (age mean±sd), 2001-2005, Australia	[50]	No	Health professional (nurses, dentists, veterinarians, pharmacists, optometrists, osteopathic physicians, and podiatrists)
2005	Risk-prediction tool	[60]	10-years-absolute risk	Age, place of residence, number of melanocytic nevi (upper limbs), skin color, mc1r genotype	Not specified, multiple countries	0				No	Absolute risks estimated for each combination of risk factors based on relative risks derived from published case-control studies, no information

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											about clinical or self-assessed data
2006	Clinical risk prediction	[61]	5-years-absolute risk (high risk: p≥0.15%)	Clinically assessed: skin color, freckling, no. Of moles (≥5 mm for men; ≥2 mm for women); self-assessed: sex, sunburns, severe sun damage (only men), tanning ability (only women)	718 cases, 945 controls, 20-79y, 1991-1992, US	0	Yes	629 cases, 535 controls, 32.5±4.9 (age mean±sd), 2001-2005, Australia	[50]	No	
2007	Clinical risk prediction	[62]	Risk score (high risk: score 4–5)	Sex, regular dermatologist, history of previous melanoma, mole changing, age (+/- 50y)	3329 cases, total 362,804, 18-100y, 2001-2005, US	0				No	
2010	Clinical risk prediction	[63]	Individual risk score (high risk: risk score ≥ 3)	Clinically assessed: no. Of common nevi; self assessed: freckles in childhood, skin color, hair color, sunburns in childhood	304 cases, 305 controls, age 53y for cases and 51y for controls (mean), 2001-2003, Italy	0	Yes	66 cases, 53 controls, age 57y for cases and 58y for controls (mean) , 2005-2008, brezil; + 629 cases, 535 controls, 32.5±4.9 (age mean±sd), 2001-2005, Australia	Same + [50]	No	
2011	Population specific clinical risk	[64]	5-year-absolute risk	Clinically assessed: common nevi, atypical nevi, freckles, hair color,	Not specified, Australia	0	Yes	629 cases, 535 controls,	[50]	No	Prediction for 3 Australian states using ar

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	assessment tool			family history, non-melanoma skin cancer, personal melanoma history				32.5±4.9 (age mean±sd), 2001-2005, Australia			and paf published from 1990 to 2006
2011	Self assessed risk prediction	[65]	Hazard ratios for each risk factor	Self-assessed: family history, no. Of nevi (left arm), hair color, sunbathing vacations, sunbed use	215 cases, total 29,520, 25-64y, 1990-1992, Sweden	0				No	Women only, anatomical subgroup analysis
2011	Self assessed risk prediction	[66]	Risk score	**Gail method:** sunburn in childhood, family history, no. Of common nevi (arms), density of freckles, skin type, recalled total sun exposure; **logistic regression and combinatorial analysis:** sex, age, skin type, presence of freckles, no. Of nevi (arms), severe blistering sunburn in childhood, life in a country at low latitude, family history	171 cases, 1390 controls, 18-70y , 2007, France	1				No	
2011	Self assessed risk prediction	[67]	Risk score (high risk: top 15%)	Sex, age, no. Of severe sunburns (age 2-18), hair color (age 15), freckles (arms, before age 20), no. Of raised moles (both arms), non-melanoma skin cancer history	386 cases, 727 controls, 35-74y, 1997, us	3	Yes	629 cases, 535 controls, 32.5±4.9 (age mean±sd), 2001-2005, Australia	[50]	No	75% training set, 25% validation
2012	Clinical risk prediction	[68]	Risk score (high risk: >0.0034)	Age, hair color, personal history of melanoma,	250 cases, total 108,281, -21-65+y,	1	Yes	629 cases, 535 controls,	[50]	No	

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				suspicious melanocytic lesions	2005-2006, Germany			32.5±4.9 (age mean±sd), 2001-2005, Australia			
2012		[69]		**Model a:** sex, age, hair color, eye color, mole count, freckling, family melanoma history (clinical model?) **Model b:** model a + outdoor UV, indoor UV, mc1r	923 cases, 813 controls, 25-59y, , us	0				No	Not found
2013	Clinical risk prediction	[70]	Risk score (high risk: >3)	Clinically assessed: skin color, eye color, hair color; self-assessed: presence of freckles in childhood, sunburn episodes throughout life	53 cases, 66 controls, 57y (mean), 2005-2008, Brazil	0				No	105 models were constructed combining the summary coefficients of different risk factors derived from the meta-analysis
2013	Blood (mcr1 gene) + clinical and self-assessed risk prediction	[71]	Odds ratios	**Base model:** age, sex, city, European ancestry **self-reported model:** mc1r genotype, nevi (body), pigmentation score (2), sun and sunbed exposure (3), family history, non-melanoma skin cancer **physician-measured model:** nevi (30 body sites), mc1r genotype, non-melanoma skin cancer, solar lentigines	413 cases, 263 controls, 19-39y, 2000-2002, Australia	1	Yes	841 cases, 452 controls, 18-76y, 2000-2005, UK	Same	No	(2) score calculated from the variables: tanning ability, propensity to sunburn, skin color, eye color, hair color and freckles. (3) term for the individual variables total

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				(upper back), family history, pigmentation score (4)							childhood sun exposure, blistering sunburns and lifetime sunbed sessions. (4) score was calculated from the following variables: hair color, eye color, skin reflectance, tanning ability, propensity to sunburn and freckles.
2013	Blood (spns) risk prediction	[72]	Odds ratios	Model 1: single snp; model 2: prs (5); model 3: sex + age; model 4: sex + age + pigmentation; model 5: sex + age + pigmentation + prs	2298 cases, 6652 controls, 52±15y (cases) 51±13y (controls), 1998-2008, US	0	Yes	494 cases, 5628 controls, 30-75y, 1973 1986, US	Same	No	(5) comprised of 11 snps that demonstrated association with melanoma risk in previous studies self-assessed pigmentation; blood sample for snps; other data extracted from patients records external validation: Harvard nurse

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											health study (women) and Harvard health professionals follow-up (men)
2013	Blood (snps) + clinical assessed risk prediction	[73]	Odds ratios	**Model a:** eye color, hair color, skin color, skin type, tanning, sunburns; **model b:** (model a) + 3 strongest snps; **model c:** (model a) + all snps (34 snps)	284 cases, 284 controls, 18-85y, 2003-2009, Greece	2				No	Blood sample for snps; clinical assessment: eye color, hair color, skin color, skin type; self-assessed: tanning, sunburns
2014	Clinical risk prediction	[74]	Absolute risk	Clinical assessment: Fitzpatrick, hair color, eye color, no. Of common nevi (body), no. Of dysplastic nevi, congenital nevi, solar damage of skin (shoulders and back); self-assessed: level of education, intermitted exposure, use of sunbeds, hct	341 cases, 356 controls, 19-87y, 2001–2012, Serbia	2				No	
2014	Mouthwash specimens (mc1r gene) + self assessed risk prediction	[75]	Odds ratios	**Base model:** age, sex, hair color, eye color, skin color, freckles, mole phenotype; **full model:** base model + sunburns, indoors tanning, mc1r genotype	875 cases, 765 controls, 25-59y, 2004-2007, US	3				No	Same group as smith et al. 2012

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2014	Self-assessed risk prediction	[76]	5-year-absolute risk	**Women:** skin color, 1st degree relative with large or unusual moles, no. Of moles (right arm), personal history of nonmelanoma skin cancer; **men:** no. Of moles (right arm), personal history, age at diagnosis, occupation, birthplace	368 cases, 270 controls, 20-79y, 1992-1994, New-Zealand	1	Yes	629 cases, 535 controls, 32.5±4.9 (age mean±sd), 2001-2005, Australia	[50]	No	
2015	Self-assessed risk prediction	[77]	Risk score (with risk categories)	Self-assessed: hair color, skin type, freckles, family history, nevi distribution, no. Of large nevi, sunburn	5700 cases, 7216 controls, , 1979-1999, several countries	1	Yes	960 cases, 513 controls, 18-76y, 2000-2005, UK; **+** 629 cases, 535 controls, 32.5±4.9 (age mean±sd), 2001-2005, Australia	Same + [50]	No	Pooled of 16 case-control studies from Europe, north America, Australia and Hawaii
2016	Blood (snps) risk prediction	[78]	Odds ratios for snps	Genetic risk score (6), age, sex, eye color, hair color, skin color, phototype, tanning ability	800 cases, 800 controls, median age: 53 for cases and 41 for controls , 2000-2004, Greece	2				No	6) based on snps that showed genome-wide significant association with melanoma in previous studies. Blood sample for snps + questionnaire

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											was filled out by all participants under the supervision of a certified dermatologist who performed the clinical examination.
2016	Self-assessed risk prediction	[79]	20-year-absolute risk	Self-assessed: hair color, nevi density, family history, personal history of non-melanoma skin cancer, sunbed use	629 cases, 535 controls, 18-39y, 2000-2002, Australia	0	Yes	4 independent population-based studies, The western Australia melanoma study (511 case-control pairs, 10-80y, 1980-1981, Australia), leeds melanoma case-control study (960 case, 513 controls, 18-76y, 2000-2005, UK),	Same	https://melanomarisk.org.au/	

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								epigene-qskin study (766 cases, total 44 544, 18-79y, 2007-2010, Australia), and Swedish women's lifestyle and health cohort study (273 cases, total 49 259 women, 30-50y, 1991-1992, Sweden)			
2018	(snps) risk prediction	[80]	Odds ratios and hazard ratios for snps score	Genetic risk score (7)	422/289 cases (lifetime/incident), total 19,102, median age 67y, us	0				No	7) calculated using 21 genome-wide association study—significant snps postmenopausal women not specified from which biologic sample they measures snps

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2018	Blood (prs) and self-assessed risk prediction	[81]	Odds ratios for snps score	**Base model:** family history, hair color (age 18), nevi, personal history of non-melanoma skin cancer, sunburns in childhood, sunbed sessions, freckles, eye color, sun exposure; **full model:** (base model) + prs (8)	578 cases, 457 controls, 18-39y, 2000-2002, Australia + 964 cases, 496 controls, 18-82y, 2000-2005, UK	2				No	(8) derived from 21 gene regions (41 snps) associated with melanoma Australia and Leeds studies
2018	Blood (snps for prs) and self-estimated risk prediction	[82]	10- and 20-year-absolute risk	**Model 1:** age, sex, country; **model 2:** (mod 1) + eye color, hair color, skin type, common nevi; **model 3:** (mod 1) + prs (9); **model 4:** (mod 2) + prs	3102 cases, 2301 controls, 18-78+y, 1998-2014, melanostrum study (Italy, Spain and Greece)	2				No	(9) combines 204 common snps, based on results from melanoma meta-analysis consortium (15,976 cases, 25,504 controls) blood sample: polygenic risk scores (prs); self-estimated: age, sex, country, eye color, hair color, skin type, common nevi
2018	Clinical risk prediction	[83]	Odds ratios	Sex, age, personal melanoma history, family history, multiple common nevi (≥40), atypical nevi (≥1), congenital nevi (≥1)	585 cases, total 354,635, 20-65+, 2003-2004, Germany	0				No	

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2018	Self assessed risk prediction	[84]	Hazard ratios and 1-, 2- 3-year-absolute risk	**Model 1** (invasive melanoma): age, sex, tanning ability, moles at age 21, hair color, no. Of previous skin lesions treated destructively, sunscreen use; **model 2** (all melanoma): (mod 1) + ethnicity, private health insurance, family history, past history of excisions for skin cancer, skin checks in past 3 years	655 cases, total 41,954, 40-69y, 2011-2014, Australia	3				https://publications.qimrberghofer.edu.au/custom/qskinmelanomarisk	2/3 for prediction model, 1/3 to assess performance
2018	Clinical risk prediction	[85]	Risk score	**Not specified**	17,246 cases, total 9,531,408, 67y±13 (cases) 52y±22 (non cases) , 2011-2017, US	3				No	Compare sensitivity, specificity, auc results from logistic regression, decision tree, and random forest models to predict melanoma risk but don't specify which covariates are used
2018	Blood or buccal cells (mcr1 gene) + clinical risk prediction	[86]	Odds ratios	**Base model:** age, sex, sunburns, no. Of common nevi (>30), rh-phenotype; **base model** + mc1r genotype	3830 cases, 2619 controls, not specified, several countries	0				No	International collaboration: the m-skip project (7 melanoma case-control studies from Netherlands,

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											Italy, UK, USA and Italy) mc1r genotype estimated from blood or buccal cells
2019		[87]**	Short-term sun protection behaviours	Absolute remaining lifetime risk of melanoma (to 85y), relative remaining lifetime risk and risk category based on self-reported melanoma risk factor	134 personalized risk group 46y±16, 138 generic risk group 45y±16, 2016, Australia	0				No	Randomized controlled trial, effect on short-term melanoma-prevention behaviours of web-based, real-time, model-generated personalized melanoma risk information
2020	Clinical risk prediction	[88]	Relative risks	Clinically assessed: naevi ≥ 2 mm (whole body), solar lentigines (upper back); self-assessed: hair colour (age 18) and history of keratinocyte cancer	421 cases, 329 controls, 18-39y, 2000-2002, Australia	1	Yes	960 cases, 513 controls, 18-76y, 2000-2005, UK	Same	No	Both clinical and self-assessment
2020	Clinical risk prediction	[89]**	Risk score group derived from probability scores		8 cases, 507 participants, -45-66+, 2019, Australia					No	To assess the clinical utility of risk assessment tools to identify individuals with prevalent skin cancers in a volunteer-based

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											screening clinic, based on derived risk stratification tools from qskin study to predict melanoma risk over a 3.5-year period (Olsen et al. 2018)
2020	Blood assessed risk prediction	[90]**	Predicted risk and 1-, 5- and 10-year absolute **risks of new primary melanoma**	Blood sample: polygenic risk score, cdkn2a functional mutation; Self-assessed: sex, age (1st primary melanoma), previous keratinocyte cancer, history of melanoma 1st-degree relatives), skin colour, mole density, ability to tan, recreational sun exposure (beach and water activities from age 15), anatomical site of primary melanoma, histological subtype of primary melanoma and composite risk scores (10)	1266 melanoma patients, (2613 primary melanoma), median age 59y±15, 2000-2003, Australia	0				No	Melanoma cases only, investigate risk of new primary melanoma (10) the composite risk score comprises all 12 other risk factors
2021	Blood (prs) assessed risk prediction	[91]	Odds ratios	Blood sample: polygenic risk score; Self-assessed: age, sex, family history (skin cancer), dysplastic moles, presence of large	3994 cases, 98906 controls, 30-90y, 2016-2017, USA	3					Participants from 23andme research cohort

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				moles, no. Of moles (right arm), actinic keratosis (before the age of 40), skin, eye, and hair colors, no. Of freckles (face and body), no. Of blisters caused by sunburns, sun hair lightening, skin response to 3-4h of sun exposure, skin response tosun exposure without sun protection sunbathing frequency (before age 30), tanning bed usage, childhood and adulthood latitude, elevation, typical sun exposure (per week), outdoor job, and physical activity, bmi, weight, smoking, alcohol consumption, seasonal allergies, being a 'morning person' and preference for keeping a 'clean desk'							

Note: The information in Table 2 was particially extracted from [8].

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Table 3 Apps for NCD prevention.

App	URL/company/ reference	App's Objective	Disease/ condition targeted	Target population (users)	Variables included	Scientific Validation yes/no (ref)	Additional comments/ observations
Diacert		Improve physical activity	Diabetes	General public	Steps walked HbA1C	Yes	
Diabetesdagboka (The Diabetes diary)	https://play.google.com/store/apps/details?id=no.telemed.diabetesdiary&hl=gsw&gl=US	Improve blood sugar control	Diabetes	General public	Blood glucose Food intake Physical activity	Yes	
Figwee	www.figwee.com	Healthy eating Weight control	General health	General public	Food calories		
Myfitnesspal	https://apps.apple.com/us/app/myfitnesspal/id341232718	Healthy eating Weight control	General health	General public	Food calories	Yes	
MySugr	https://www.mysugr.com/en/diabetes-app	Glucose control, dose calculation, diary	Diabetes (mostly type 1)	People with diabetes	Glucose, insulin dose, carbohydrate intake, exercise	CE Health product certification	Was bought by Roche
Social Diabetes	https://www.socialdiabetes.com	Glucose control, dose calculation	Diabetes (mostly type 1)	People with diabetes	Glucose, insulin dose, carbohydrate intake, insulin per carbohydrate ratio, exercise	CE Health product certification	Previous versions intrusive
ABC4D (Advanced bolus calculator for diabetes)	http://www.imperial.ac.uk/bio-inspired-technology/research/metabolic/abc4d/	Dose calculation	Diabetes	People with diabetes	Glucose, glucose target, insulin-to carbohydrate ratio, total daily carbohydrates, sensitivity factor (glucose reduction per unit insulin)	In progress https://clinicaltrials.gov/ct2/show/NCT02053051	Developed by Imperial College London

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Tidepool	https://www.tidepool.org	Interoperability platform. Intelligently displays glucose and insulin for easy dose adjustment	Diabetes (type 1)	People with diabetes, health professionals	Glucose meters and sensors, as well as insulin pump information can be downloaded. Also manual entry for notes.		User-friendly overview of treatment and its effect
Loop		Semi-automatic insulin infusion	Type 1 diabetes	People with diabetes,	CGM (Continuous Glucose Monitoring) data, rough carbohydrate estimates including glycemic index, insulin dosing	FDA approval requested	Hybrid closed loop
OpenAPS		Semi-automatic insulin infusion	Type 1 diabetes	People with diabetes,	CGM data, carbohydrate estimates, insulin dosing		Hybrid closed loop
AndroidAPS		Semi-automatic insulin infusion	Type 1 diabetes	People with diabetes,	CGM data, carbohydrate estimates, insulin dosing		Hybrid closed loop
Diabeloop	https://www.dbl-diabetes.com/dblg1-system	Semi-automatic insulin infusion	Type 1 diabetes	People with diabetes,	CGM data, carbohydrate estimates, insulin dosing	https://www.thelancet.com/pdfs/journals/landig/PIIS2589-7500(19)30003-2.pdf	Hybrid closed loop. Commercially available with Roche's Insight pump
CamAPS	https://camdiab.com	Semi-automatic insulin infusion	Type 1 diabetes	People with diabetes,		YES https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)31947-0/fulltext	Hybrid closed loop

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						https://www.nejm.org/doi/10.1056/NEJMoa1509351	
Dottli	https://dottli.com/www/	WhatsApp for health data. Share your selected data with peer support groups automatically.	Type 1 diabetes, also many other chronic conditions	People with diabetes, people with chronic conditions, generic population	Location, documents, meals, activities, glucose, fever symptoms, HbA1c, insulin, exercise, mood, fruits, vegetables, water, coffee, weight, height, body temperature, sleep time, sleep quality, cholesterol, ketones, alcohol, smoking, steps, distance, awake times, blood pressure, heart rate, oxygen saturation, other medicine, illness, CGM – all though manual entries or though integrations to various data sources		
Balansio	https://www.balansio.com/				Glucose, carb estimates	CE marked medical device	Class IIb medical device and a bolus calculator. Also AI supported coaching.

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Glucostratus	https://gsbalance.com/personal/?lang=en	Automated data transfer from devices, especially for assisted living scenarios	People with diabetes, people with chronic conditions, especially elderly people	People with diabetes, people with chronic conditions, generic population, healthcare profesionals	Glucose, blood pressure	CE marked medical device	Glucostratus also has glucose meters with built-in cellular data connections
Sensotrend	https://www.sensotrend.com/	Combine data from medical devices and wellness trackers for actionable insights	Diabetes	People with diabetes, healthcare professionals, peers	Glucose, CGM, insulin, nutrition, activity, exercise, blood pressure, HbA1c	CE marked medical device	Sensotrend participates in the WARIFA project
UnderMyFork	https://undermyfork.com/	Combine meal photos and glucose, learn the effects of different kind of meals	Diabetes	People with diabetes, healthcare professionals	CGM, meals, meal photos	CE marked medical device (soon)	
MealLogger	https://www.meallogger.com/	AI assisted meal diary, focused on group support	Obesity, diabetes, all issues with nutrition	General population, people with diabetes, weight loss, healthcare professionals	Meals, nutrition information, meal photos		
Wellmo	https://www.wellmo.com/	Manual data tracking and aggregation of data from many data sources	Chronic conditions, wellness	General population	All data from Google FIT and Apple Health, and many more data sources, also manual tracking		Can be easily customized and is available as a white-label product. Ideal at least for early prototyping in WARIFA?

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xDrip	https://github.com/NightscoutFoundation/xDrip	Open source integration to many glucometers and CGMs	Type 1 diabetes	People with type 1 diabetes	CGM data, glucose, nutrition info, steps, heart rate		Implemented by the open source development community Nightscout

Table 4 Apps for skin cancer prevention.

App	URL/company/ reference	App's Objective	Disease/ condition targeted	Target population (users)	Variables included for primary prevention	Scientific Validation yes/no (ref)	Additional comments/ observations
Sunsmart	https://www.sunsmart.com.au/	Improve sun protection behaviour	All skin cancers	General public	UV index Sun protection times UV and sunprotection alerts, sunscreen calculator, weather and UV forecast	Yes	
Solar Cell		Improve sun protection behaviour	All skin cancers	General public	UV index Sun protection advice, sunscreen application alert	Yes	
Be Skin Smart	https://www.beskinsmart.co.za/ Meda Pharma	UVR and sunprotection advice Risk factor assessment	All skin cancers	General public	estimating skin type, sun-protection timer		

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BeWare of the Sun	Portuguese Cancer League (LPCC)	UVR and sun protection advice Image analysis, Monitoring/tracking	All skin cancers	General public	UV Index Sun protection advice		
Fotoskin	https://fotoskin.en.uptodown.com/android	UVR and sun protection advice Risk factors assessment SSE techniques, monitoring/tracking	All skin cancers	General public	Estimates skin phototype UV index Sun protection advice	Dermatologist advisory board	
Know Your Own Skin	LEO Pharma A/S	UVR and sun protection advice SSE techniques, monitoring/tracking	All skin cancers	General public	General sun protection advice		
Melanoma Test- Risk Calculator for Skin Cancer	Pears Health Cyber	Skin cancer Information Risk factors assessment			Assess melanoma risk (risk score) on patient's questionnaire	No info	
Melanoma Watch		Information on skin cancers UVR/sun safety advice SSE					
Miiskin		Information on skin cancers UVR/sun safety advice SSE Tracking/monitoring				Dermatologist advisor	
Molexplore		Information on skin cancers UVR/sun safety advice SSE Risk factors assessement Tracking/monitoring		General public	UV index real time	Dermatologist advisor	

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Mollie's fund		Information on skin cancers UVR/sun safety advice SSE					
Skinvision	https://www.skinvision.com/de/	Detect skin cancer	All skin cancers	General public	Diagnostic accuracy	Yes	See review of papers
UM Skin Check		Information on skin cancers UVR/sun safety advice SSE Risk factors assessement Tracking/monitoring					
'Min soltid' My solar time	https://play.google.com/store/apps/details?id=se.stralsakerhetsmyndigheten.minsoltid&hl=sv≥=US	Limit time in the sun	Sun safety	General public	GPS location, UV index, self assessed sun skin sensitivity	Strålsäkerhetsmyndigheten (Swedish Radiation Safety Authority)	Strålsäkerhetsmyndigheten (Swedish Radiation Safety Authority)
UV index	https://www.cancer.dk/solkampagnen/	Information on UV index and estimated time to sunburn (in Denmark and abroad)	Avoid sunburn	General public	GPS		Kræftens bekæmpelse and TrygFonden

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