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BONEcheck: A digital tool for personalized bone health assessment

Dinh Tan Nguyen [a, b], Thao P. Ho-Le [a, c], Liem Pham [b], Vinh P. Ho-Van [c], Tien Dat Hoang [c], Thach S. Tran [a, d], Steve Frost [e], Tuan V. Nguyen [a, f, g, *]

[a] School of Biomedical Engineering, University of Technology, Sydney, Australia
[b] Saigon Precision Medicine Research Center, Ho Chi Minh, Viet Nam
[c] Faculty of Engineering and Information Technology, Hatinh University, Hatinh, Viet Nam
[d] Garvan Institute of Medical Research, Sydney, Australia
[e] University of Wollongong, Wollongong, Australia
[f] Tam Anh Research Institute, Ho Chi Minh, Viet Nam
[g] School of Population Health, UNSW Sydney, Australia

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ABSTRACT

Objectives: Osteoporotic fracture is a significant public health burden associated with increased mortality risk and substantial healthcare costs. Accurate and early identification of high-risk individuals and mitigation of their risks is a core part of the treatment and prevention of fractures. Here we introduce a digital tool called 'BONEcheck' for personalized assessment of bone health.

Methods: The development of BONEcheck primarily utilized data from the prospective population-based Dubbo Osteoporosis Epidemiology Study and the Danish Nationwide Registry. BONEcheck has 3 modules: input data, risk estimates, and risk context. Input variables include age, gender, prior fracture, fall incidence, bone mineral density (BMD), comorbidities, and genetic variants associated with BMD.

Results: Based on the input variables, BONEcheck estimates the probability of any fragility fracture and hip fracture within 5 years, subsequent fracture risk, skeletal age, and time to reach osteoporosis. The probability of fracture is shown in both numeric and human icon array formats. The risk is also contextualized within the framework of treatment and management options on Australian guidelines, with consideration given to the potential fracture risk reduction and survival benefits. Skeletal age was estimated as the sum of chronological age and years of life lost due to a fracture or exposure to risk factors that elevate mortality risk.

Conclusions: BONEcheck is an innovative tool that empowers doctors and patients to engage in well-informed discussions and make decisions based on the patient's risk profile. Public access to BONEcheck is available via https://bonecheck.org and in Apple Store (iOS) and Google Play (Android).

1. Introduction

Osteoporosis is a skeletal condition characterized by reduced bone mass and deteriorated bone microstructure, leading to an increased risk of fracture. Globally, osteoporosis affects over 200 million people aged 50 years and older [1], with women being more susceptible than men. In addition, there are 178 million fractures, including 14.2 million hip fractures which is the most severe manifestation of osteoporosis [2]. An existing fracture is associated with an increased risk of further fractures [3] and an increased risk of premature mortality [4]. With the ongoing aging population worldwide, it is expected that the burden and consequences of fractures will be more pronounced in the future.

A significant proportion of osteoporotic fractures and fracture-associated deaths is preventable by either taking a treatment or preventive measures. However, at present, there is a crisis of osteoporosis management in which most patients with a fracture are not treated. Moreover, even among those on treatment, adherence has been poor, with many patients opting out of the treatment program [5]. Therefore, a research priority in osteoporosis is to identify high-risk individuals for treatment and prevention. Over the past 2 decades, fracture risk assessment tools such as the Garvan Fracture Risk Calculator [6] and FRAX [7] have been

* Corresponding author. School of Biomedical Engineering University of Technology, Sydney (UTS) Broadway, Ultimo NSW 2007, Australia.
E-mail address: tuanvan.nguyen@uts.edu.au (T.V. Nguyen).
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developed and implemented in clinical practice. These tools map clinical risk factors to the probability of fractures over 5-year or 10-year for an individual. The implementation of fracture risk calculators represents a significant advance in the field.

Despite the advance, existing fracture risk calculators have a number of limitations in terms of form and communication. First, they use probability as a metric of risk, which is not readily understood by laypeople and doctors alike, especially when the probability is not presented in the context of the treatment [8]. Second, the presentation of risk is in a purely numerical format which is known to be less effective than a frequency format [9]. Third, existing risk calculators do not assess the risk of refracture and mortality, which are highly relevant to an individual. The lack of post-fracture mortality assessment might have led to the underappreciation of osteoporosis as a serious disease. These major limitations call for a more effective and innovative risk assessment tool.

In this paper, we describe the development and implementation of a digital fracture risk assessment tool that addresses the above limitations. The new tool is called 'BONEcheck' and is available free worldwide. It is anticipated that the tool will help facilitate doctor-patient communication about fracture risk, its survival consequences, and interventional options.

2. Methods

BONEcheck includes 3 modules: input data, risk estimates, and risk interpretation or contextualization. The input data are determined from previous studies that have identified relevant and independent risk factors for fracture [10–12]. The output information is designed from patients' perspectives and presented in a format that is meaningful to patients. This output is contextualized in relation to treatment and preventive measures. The language used in the interpretation of risk estimates and risk management is written for individuals whose reading level is at or above 8.

To begin, we conducted a comprehensive review of previous studies and prediction models related to bone health. We carefully examined their methodologies, variables, and parameter settings. Recognizing the variations and potential mismatches across different studies, we sought to reproduce their results while standardizing the variables and addressing discrepancies.

One particular challenge we encountered was the variation in variables scales used in different studies. To overcome this, we standardized the variables across all datasets and models to maintain consistency and comparability. Additionally, we ensured that other variables, such as prior fracture, fall incidence, bone mineral density (BMD), comorbidities, and genetic variants associated with BMD, were appropriately standardized and adjusted to match the requirements of the BONEcheck tool. In order to maintain similar performance across models, we carefully adjusted certain parameters to ensure that BONEcheck delivered accurate and reliable risk estimates. This involved fine-tuning the algorithms and calibration to optimize the predictive power of the tool.

In the development of BONEcheck, we utilized several datasets to incorporate relevant information and build the risk prediction algorithm. The datasets were as follows.

- The Dubbo Osteoporosis Epidemiology Study (DOES) [10]: The study was designed as a population-based prospective investigation that has followed more than 3000 men and women aged 50 years and older for up to 30 years. This dataset was used to develop the Garvan Fracture Risk Calculator for predicting the risks of fracture and refracture, which is an algorithm within BONEcheck.
- Danish Nationwide Registry [11] is a comprehensive and population-based registry that contains health-related data on all individuals in Denmark. This dataset was used to estimate the skeletal age for each fracture site.
- DOES [13], Study of Osteoporotic Fractures (SOF) [14], and Osteoporotic Fractures in Men study (MrOS) [12]: These datasets were used to estimate the annual rate of change in BMD, and from which, the time to reach osteoporosis (ie, T-scores ≤ -2.5) in BONEcheck.

2.1. Input data

BONEcheck uses a range of variables that capture the uniqueness of the risk profile for an individual. These variables include anthropometric data (eg, age, gender, height, and weight), lifestyle factors (eg, smoking habit and alcohol consumption), and bone-related data such as femoral neck BMD and a personal history of fracture. We chose to use femoral neck BMD rather than lumbar spine BMD because the former has been shown to be less prone to artefactual errors due to degenerative changes. BMD can be entered either in absolute values (gram per cm^2) or T-score, which is the number of standards deviation from the peak BMD taken as aged between 20 and 30 years. Individuals with a T-score equal to or less than -2.5 is diagnosed to have 'osteoporosis'. The computation, however, uses actual continuous BMD measurement, not T-scores. The personal history of fracture is entered as the number of prior fractures, not a binary value of 'yes' or 'no'.

In addition, BONEcheck also requires input data pertaining to fall history, existing comorbidities, and a genetic profile. The number of falls over the previous 12 months is used for estimating the risk of fracture. Existing comorbidities include a list of 11 chronic conditions (Table 1), with each condition being entered as 'yes' or 'no'. Based on the self-reported comorbidities, BONEcheck calculates the Charlson Comorbidity Index (CCI) [15], which is used as a risk factor for the estimation of post-fracture mortality and skeletal age.

The genetic profile included 34 genetic variants that have been shown to be associated with BMD in a genome-wide association study [16]. Each genetic variant is inputted as the number of minor alleles. Based on the data, an 'Osteogenomic Profile' for each individual is generated as the weighted sum of the number of minor alleles across variants, with the weights being the published regression coefficient associated with each minor allele [17]. This Osteogenomic Profile, which has been shown to be associated with the fracture risk [17] and bone loss [18] in the elderly, is used as an input variable for estimating the risk of fractures.

The flow of input variables and output information is shown in Fig. 1. The web application's input was designed using the web application concept, which does not store or save any input data to keep privacy and confidentiality for users. Additionally, BONEcheck allows users to create accounts to save their results for future comparison and provides the option for users to delete their accounts if desired.

2.2. Output information

Based on the input variables, a series of output information is produced. These outputs are related to (a) the risk of fracture; (b) skeletal age; and (c) bone loss assessment. *The risk of fracture* is presented as the absolute probability of any fracture and hip fracture over the next 5 years. We chose to focus on 5-year window because that is the ideal time for an individual to manage their risk. In addition to numerical probability, we also provide a frequency of human icons to capture the risk visually. For instance, a 10% risk is

Table 1
Input variables and output information in BONEcheck.

Group	Input and output factors	Valid values	Definition
Baseline data	Age, yr	50–96	Chronological age
	Gender	Man/Woman	Character variable
	Height, cm	100–274	Current height in cm
	Weight, kg	30–150	Current weight in kg
	Smoking	Yes/No	Current smoking status
Bone properties (5 variables)	Previous fragility fractures	0–3	Number of fractures from the age of 50 years
	Falls history	0–3	Number of falls over the last 12 months
	BMD, g/cm^2	0.6–1.4	Femoral neck bone mineral density
	T-score	−5 to +4	Number of standard deviations from the peak bone density
	Densitometer	GE/Hologic	Manufacturer of densitometer
Comorbidity (14 variables)	Cardiovascular disease	Yes/No	Binary variable
	Neuromuscular	Yes/No	Binary variable
	Congestive heart failure	Yes/No	Binary variable
	Dementia	Yes/No	Binary variable
	Chronic obstructive pulmonary disease (COPD)	Yes/No	Binary variable, may include asthma
	Diabetes with chronic complications	Yes/No	Binary variable
	Rheumatologic disease	Yes/No	Binary variable
	Metastatic solid tumor	Yes/No	Binary variable
	Mild liver disease	Yes/No	Binary variable
	Moderate or severe liver disease	Yes/No	Binary variable
	Renal disease	Yes/No	Binary variable
	Hemiplegia or paraplegia	Yes/No	Binary variable
	Any malignancy, including leukemia and lymphoma	Yes/No	Binary variable
	AIDS/HIV	Yes/No	Binary variable
Fracture (15 variables)	Hip	Yes/No	Binary variable
	Pelvis	Yes/No	Binary variable
	Femur	Yes/No	Binary variable
	Vertebrae	Yes/No	Binary variable
	Humerus	Yes/No	Binary variable
	Rib	Yes/No	Binary variable
	Clavicle	Yes/No	Binary variable
	Tibia	Yes/No	Binary variable
	Elbow	Yes/No	Binary variable
	Forearm	Yes/No	Binary variable
	Knee	Yes/No	Binary variable
	Ankle	Yes/No	Binary variable
	Foot	Yes/No	Binary variable
	Hand	Yes/No	Binary variable
	Wrist	Yes/No	Binary variable
Osteogenomic profile	Genetic profile	Selected option	33 genotypes related to fracture risk
Results/output	5-year any fracture risk	1–100	Probability of fracture
	5-year fracture risk with intervention	1–100	Probability of fracture
	5-year hip fracture risk	1–100	Probability of fracture
	5-year hip fracture risk with intervention	1–100	Probability of fracture
	Subsequent fracture risk	1–100	Probability of fracture
	Genetic risk score	1–100	Accumulated number of 'risk alleles'
	Skeletal age	0–10	Years
	Time to reach osteoporosis	0–120	Duration in months

Notes: An overview of the parameter groupings is listed such as demographic factors, fracture history, bone mineral density, comorbidities, and genetic variants associated with BMD. The second column lists the names of each parameter, providing specific details on what each parameter represents. The third column displays the refined validity of the parameter values, indicating the appropriate range or acceptable values for each parameter. The last column provides definitions for each parameter, further clarifying their meaning and interpretation.

presented as 10 red icons in 100 human icons. Because an existing fracture is a signal of further fractures, we also provide the risk of refracture if a fracture has been sustained. The risk of refracture is presented in a numerical probability over the next 2 years using the published model [11]. In addition, any fracture risk is classified as a risk gradient as follows: "high risk" if 5-year fracture probability exceeds 8%; "medium risk" if the probability ranges between 5 and 8%; and "low risk" if the probability is below 5%. When it comes to hip fracture, “high risk” signifies a risk greater than 2%, “medium risk” represents a risk between 1% and 2%, and “low risk” indicates a risk level lower than 1%.

Skeletal age is a new metric of fracture risk assessment. Conceptually, skeletal age is the age of an individual's skeleton because of a fracture or being exposed to risk factors that elevate the risk of fracture [19]. Operationally, skeletal age is defined as the sum of an individual's actual age and the years of life lost associated with a fracture or exposure to risk factors that put an individual at a greater risk of fracture. Years of life lost is based on the comparison between the age of death to the standard life expectancy that is available in a national lifetable [20]. BONEcheck integrates the risk of fracture and the US lifetable to estimate the years of life lost associated with a fracture and then determined the skeletal age.

Bone loss assessment. Using published findings [21,22], BONEcheck estimates the rate of change in femoral neck BMD for those aged 50 years and older stratified by baseline BMD. From the estimated rate of change, the algorithm uses linear regression to determine the time to reach 'osteoporosis' (ie, T-scores ≤ -2.5). There is additional advice that users need to consult with their doctors to determine the time to repeat BMD measurement.

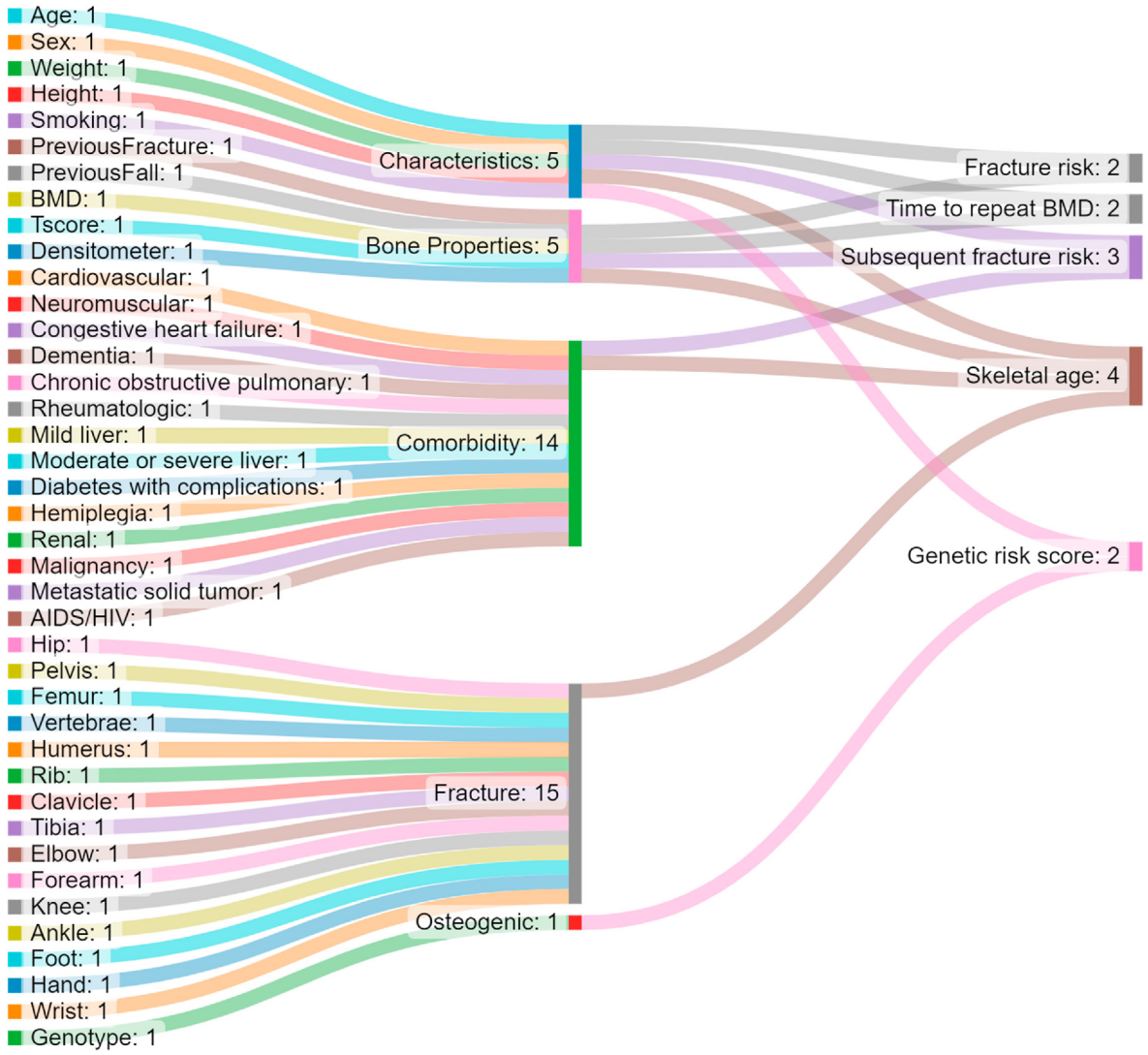

Fig. 1. The flow of input variables and output in the BONEcheck system. The left column shows the input variables and the right column displays the output variables. For instance, the input variables of age, sex, weight, previous fracture, previous falls, and BMD were used to estimate the risk of fracture. The genetic risk score was also used as an option variable to estimate fracture risk.

2.3. Interpretation/contextualization

In addition to risk estimates, BONEcheck provides interpretations of the probability of fracture tailored to an individual's risk profile. The risk is presented in two scenarios: not treatment and on treatment. The interpretation is based on the 'frequentist' school of probability, not subjective probability. Thus, a fracture probability of 10% is interpreted as 10 fractures in 100 men/women like the individual. The reduction of risk was derived from published results of randomized controlled trials [23]. The probability of fracture is then referred to the current Australian Pharmaceutical Benefits Scheme (PBS), which states that individuals with a 5-year fracture probability of 8–13% or higher are eligible for reimbursement.

For skeletal age, it explicitly acknowledges that a fracture is correlated with a reduction in life expectancy, with a corresponding interpretation provided. If an individual's skeletal age surpasses their chronological age, it indicates that the individual is at a greater risk of fracture and mortality when compared to other people of the same age and gender. For those without a fracture, the number of years of life lost is determined as the product of the remaining lifetime risk of fracture and the number of years of life lost associated with a hip fracture, stratified by gender and age. Users are advised that by implementing preventative measures or following a bone specialist's recommended effective treatment, they can decrease their skeletal age.

There is a 'Prevention' tab where users can learn about preventive measures to reduce their risk of fracture and improve their BMD measurement. The advice given in the Prevention tab is based on current guidelines for the treatment and prevention of osteoporosis [24].

3. Results

The web-based graphical interface of BONEcheck is shown in Fig. 2. The tool collects each individual's input data; processes the data; loads the algorithms or training models; calculates the metrics, and displays the results of calculation and interpretation. The risk of fracture is 'individualized' in the sense that each individual has a unique probability of fracture which is calculated from the individual's unique risk profile. This unique profile is defined in terms of the 'Osteogenomic profile' and other clinical parameters.

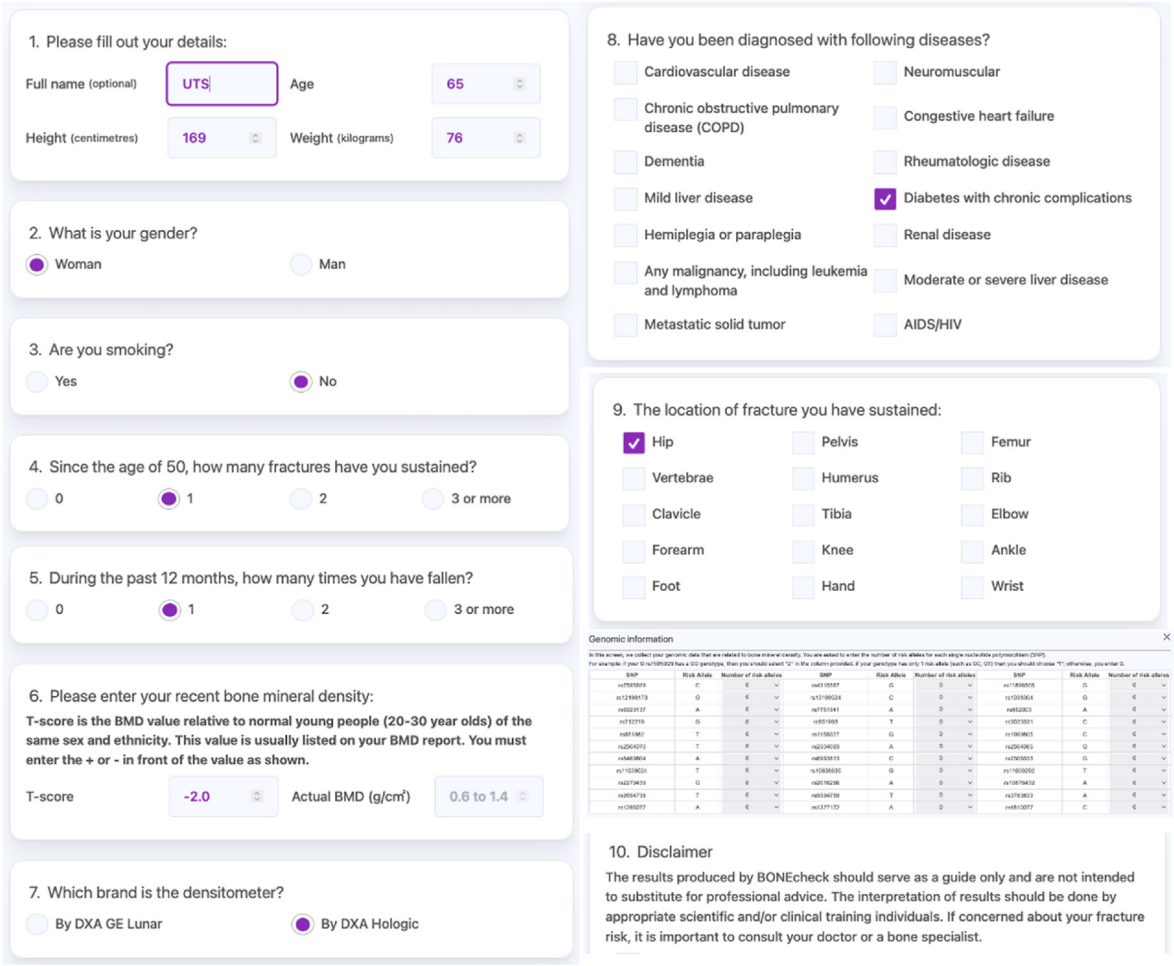

Fig. 2. Input screen of BONEcheck.

For illustration, Table 2 presents the output of BONEcheck for 4 individuals.

- *Individual A*: woman, 65 years old, has sustained a hip fracture, 1 fall over the past 12 months, T-score is −2.0, has type 2 diabetes, no genetic profile data.
- *Individual B*: woman, 65 years old, has no fracture, no fall, T-score is −2.5, has congestive heart failure, genetic profile data.
- *Individual C*: man, 65 years old, has 1 vertebral fracture, 1 fall, T-score is −2.0, has type 2 diabetes mellitus, no genetic profile data.
- *Individual D*: man, 65 years old, has no vertebral fracture, no fall, T-score is −2.5, has COPD, genetic profile data.

As can be seen from Table 2, for the same age and gender, the risk of fracture (any fracture and hip fracture) is inversely associated with femoral neck BMD T-scores, and for the same age and T-score, women, as expected, have a higher risk of fracture than men. For those with an existing fracture, the risk of refracture is relatively high for a shorter duration.

The risk of fracture is also presented in a human icon format (Fig. 3). In this presentation of 100 icons, the ones with a fracture are shown in red color, and the benefit of treatment (in terms of fracture risk reduction) is shown in green color. This is accompanied by an interpretation as follows (for individual A):

"Based on the information you provided, it is estimated that your 5-year risk of any fracture is: 15%. This means that among 100 women like you (eg, the same age and the same risk profile), 15 (red color) will suffer a fracture in the next 5 years, and 85 (grey color) will not. However, with effective treatment, your risk of any fracture within the next 5 years is reduced to 9, resulting in a benefit for 6 (green color) out of every 100 women who receive the treatment."

A similar output and interpretation are also provided for hip fracture risk.

The skeletal age analysis shows that a hip fracture confers a greater impact on the years of life lost and results in a higher skeletal age than a vertebral fracture. A 65-year-old woman who has sustained a hip fracture is predicted to have a skeletal age of 70.3 years (individual A). Moreover, the skeletal age of a 65-year-old man who has sustained a vertebral fracture is estimated to be 70.1 years (individual C). The skeletal age output is also accompanied by a graphical format (Fig. 3) with an interpretation as follows (individual A):

"Based on the information you have provided, given your current age of 65 years old and your estimated skeletal age of 70.3 (the gap is 5.3), it means that you have an increased risk of fracture. More specifically, you are now in the same risk

Table 2
Illustration of BONEcheck with 4 hypothetical cases.

Profile	Individual A	Individual B	Individual C	Individual D
Gender	Woman	Woman	Man	Man
Age, yr	65	65	65	65
Weight, kg	45	45	45	45
Prior fracture	Hip	No	Vertebral	No
Number of falls over the past 12 months	1	No	1	No
T-score	−2.0	−2.5	−2.0	−2.5
Comorbidity[1-3]	DM	CHF	DM	COPD
Genetic profile available	No	Yes	No	Yes
Output				
5-year risk of any fracture with BMD	15%	9%	11%	5%
5-year risk of any fracture without BMD	16%	7%	6%	2%
5-year risk of hip fracture with BMD	5%	2%	2%	1%
5-year risk of hip fracture without BMD	2%	1%	2%	1%
Genetic risk score		3.85%		3.57%
Risk of refracture	22%	12.6%	13%	11%
Skeletal age	70.3	67.9	70.1	66.9
Time to reach osteoporosis	22 months	0 months	20 months	0 months

[1] DM, diabetes mellitus.
[2] CHF, congestive heart failure.
[3] COPD, chronic obstructive pulmonary disease.

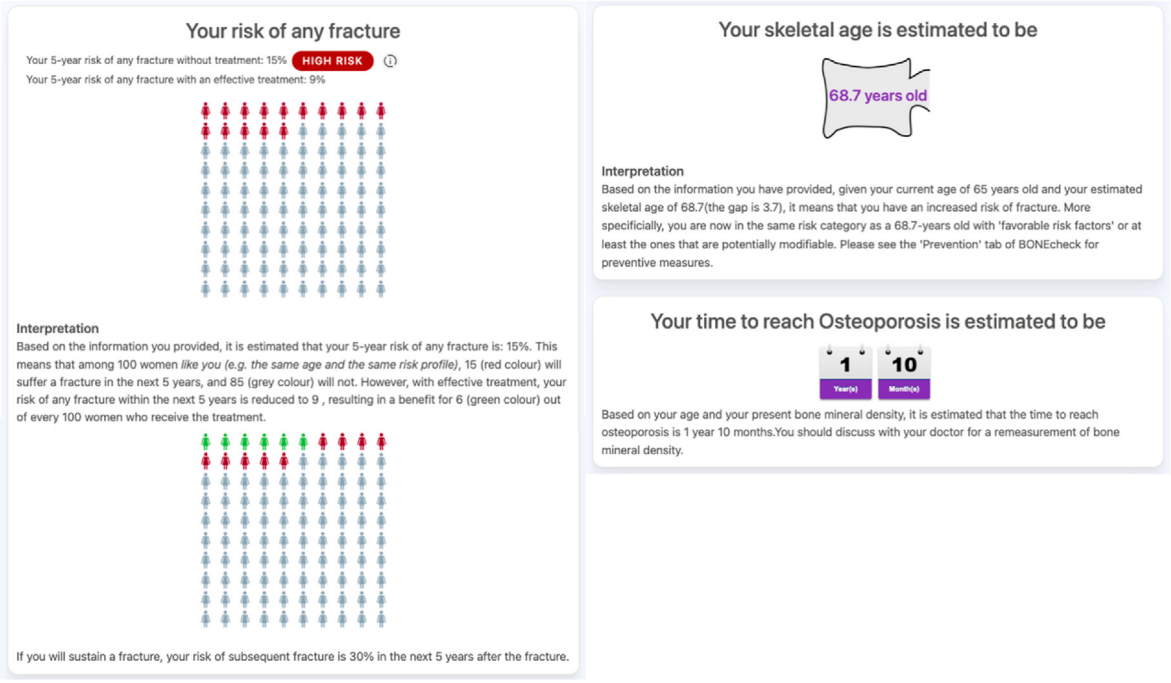

Fig. 3. An example of output screen of BONEcheck.

category as a 70.3-years old with 'favorable risk factors' or at least the ones that are potentially modifiable. Please see the 'Prevention' tab of BONEcheck for preventive measures."

The time to reach osteoporosis (ie, T-scores ≤ -2.5) is estimated based on current age and BMD measurement. Thus, for an individual with a current T-score $= -2.0$, it is estimated that the time to reach osteoporosis ($T < -2.5$) is 22 months (for women) and 20 months (for men). If the current T-score ≤ -2.5, then the output will read "*You are having osteoporosis. You should discuss with your doctor for a treatment option and a repeat bone density measurement.*"

All output information can be saved into a file or an internet link so users can use it to discuss with their doctor. The saved information can also be used for longitudinal comparison for a user.

4. Discussion

Fracture due to osteoporosis remains a significant burden worldwide because it is associated with an increased risk of premature mortality and substantial healthcare costs. An essential effort of fracture prevention focuses on the identification of high-risk individuals for intervention, and a number of risk assessment tools have been developed and implemented for this purpose. However, none of the tools incorporates pre-mature mortality and risk contextualization. Moreover, the majority of osteoporosis patients are not treated or do not adhere to treatment guidelines due in part to poor risk communication. In order to address those

shortcomings, we have developed the BONEcheck system for public use with the hope of contributing to the reduction of the global burden of osteoporosis.

The difference in output between BONEcheck and existing algorithms is shown in Table 3. Existing fracture risk assessment tools such as the Garvan Fracture Risk Calculator [6], FRAX [7], and Qfracture [25] provide 5-year [6] or 10-year [6,7] risk of any fracture or osteoporotic fracture and hip fracture. The present BONEcheck utilizes the Garvan Fracture Risk Calculator algorithm to estimate 5-year risk of fracture. The performance of the Garvan Fracture Risk Calculator has been extensively validated through external studies and reviewed elsewhere [26]. The results of these validation studies [27–29] have indicated that the Garvan model performed as well as or usually better than the FRAX model in terms of fracture discrimination and accuracy.

The predicted risk of fracture is different between algorithms due largely to underlying statistical models and input variables. Although FRAX's predicted risk is adjusted to account for the competing risk of mortality, the method of adjustment has not been disclosed. On the other hand, the Garvan model was created using data from the Dubbo Osteoporosis Epidemiology Study, where each individual's sequential events of fracture, refracture, and death were directly observed. As a result, the predicted risk inherently represents the likelihood of experiencing a fracture among those who are at risk for the remainder of their specific lifespan. In a study of hip fracture prediction among old women (average age 83) of Chinese background, the Garvan model performed better than FRAX and Qfracture [29]. In the Geelong Osteoporosis Study [27], the Garvan model underestimated fracture risk by around 25% in women and 19% in men, whereas FRAX underestimated it by 55% in women and 66% in men. In contrast, in the New Zealand cohort, the Garvan model predicted nearly 100% of fracture cases but overestimated hip fracture risk by 50%, while FRAX underestimated fracture risk by 50% [28]. However, the Garvan model's overestimation has no negative clinical impact since high-risk individuals would be recommended for treatment regardless. There is evidence suggesting that the Garvan model's predicted risk is consistent with the clinical decision-making [30,31].

At present, the management of osteoporosis is in a crisis of an ‘osteoporosis treatment gap’ characterized by low treatment uptake among those at high risk. Hip fracture is the most serious consequence of osteoporosis because patients suffering from the fracture are at increased risk of mortality. There are treatments that have been shown to reduce the risk of refractures and mortality [32,33]. However, few patients with hip fractures were on treatment. In 2001, 40% of hip fracture patients were on treatment, and this proportion decreased to only 21 in 2011 [5]. Moreover, among those on treatment, adherence has been poor [34]. There are many reasons for the treatment gap, including the problem of risk communication. According to a qualitative study, patients who believed that osteoporosis was a natural part of aging, that treatment was ineffective, and that fractures were not serious chose not to pursue or discontinue treatment [35–37]. Moreover, patients were more likely to accept treatment if they were presented with the benefit of treatment in terms of absolute risk reduction rather than relative risk reduction [38]. Taken together, the research evidence indicates the necessity for innovative approaches to risk communication in order to enhance the adoption and compliance with anti-osteoporosis treatment.

Table 3
Comparison between existing fracture risk assessment tools.

Tool functions	FRAX	Garvan	QFracture	BONEcheck
5-year fracture risk	−	−	+	+
10-year fracture risk	+	+	+	−
Subsequent fracture risk	−	−	−	+
Polygenic risk score	−	−	−	+
Skeletal age	−	−	−	+
Time to reach osteoporosis	−	−	−	+
Risk contextulization	−	−	−	+
Interpretation	−	−	+	+

Currently, patients are presented with fracture probabilities over a specific time frame without any quantitative information about the consequences of a fracture. Additionally, there is no clear indication of the survival advantages of treatment. To address these issues, BONEcheck was developed. BONEcheck not only offers absolute fracture risk assessments but also frames the absolute risk reduction and the survival benefits of treatment. This information can be valuable for facilitating productive discussions between doctors and patients regarding risk, treatment, and benefits. The risk information and treatment benefits are shown in the human icon array rather than in numerical format [39].

In addition to offering a predicted risk of fracture, BONEcheck capitalizes on recent research to provide information on the skeletal age [19]. Skeletal age is a way to understand the risk of fracture and its consequence of premature mortality. An individual's risk of fracture may be higher if the individual's skeletal age is greater than their chronological age. In this context, if an individual is 60 years old but has a skeletal age of 65, it implies that the individual's fracture risk matches that of a 65-year-old person with a 'healthy' risk profile or at least ones that can be modified. Previous studies suggested that conveying risk using biological age indicators, such as heart age, vascular age, lung age, and skeletal age, could potentially have a favorable influence on patient behavior [40]. Since most fractures occur outside the high-risk (osteoporosis) group [41], risk communication using skeletal age ('older than I actually am') can help raise awareness of the mortality consequence of fracture in those groups.

In addition to risk communication (eg, risk probability and skeletal age), BONEcheck also presents data on the estimated duration it would take for individuals who are currently not classified as having osteoporosis to develop the condition. This information can be especially useful for facilitating discussions between doctors and patients regarding the appropriate timeframe for repeating BMD measurements.

BONEcheck is the first tool that incorporates the polygenic risk score (PRS) to predict fracture risk. Several PRSes have been formulated [42–44] based on the identification of genetic variants linked to BMD or fracture, in addition to our own [17]. These PRSes utilize different genetic variants, but each has been validated as an independent predictor of fracture risk beyond clinical risk factors. Our PRS, which was created from 33 genetic variants associated with BMD, can replace family history as a fracture risk factor. Assessing the likelihood of fracture, or any disease risk, should be personalized because no "average individual" exists in the population, and each person is unique. An individual's distinctiveness can be characterized in terms of clinical risk factors, as well as PRS.

Nevertheless, a number of potential weaknesses should be acknowledged. The algorithms used to create BONEcheck were derived from data obtained from Caucasian populations which may have a higher fracture risk compared to Asian populations. Thus, the extrapolation of risk from BONEcheck to non-Caucasian requires certain adjustments. Comorbidity or concomitant diseases

Table 4
Brief definition of comorbidity included in BONEcheck.

Comorbidity	Definition
Cardiovascular disease	Diseases of the heart and blood vessels.
Neuromuscular disease	Encompasses a range of conditions affecting the nerves and muscles.
Chronic pulmonary disease	Includes chronic conditions that affect the lungs and airways, such as chronic obstructive pulmonary disease (COPD) and asthma.
Congestive heart failure	Refers to a chronic condition where the heart is unable to pump blood efficiently.
Rheumatologic disease	Encompasses various conditions that affect the joints, muscles, and connective tissues, such as rheumatoid arthritis or systemic lupus erythematosus.
Dementia	Refers to a decline in cognitive abilities, memory loss, and other symptoms that significantly impact daily functioning.
Mild liver disease	Generally refers to mild liver dysfunction or liver abnormalities that do not severely impact liver function.
Diabetes with chronic complications	Includes diabetes cases where there are long-term complications resulting from the condition, such as kidney disease, nerve damage, or eye complications.
Hemiplegia or paraplegia	Hemiplegia refers to paralysis of one side of the body, while paraplegia refers to paralysis of the lower body.
Renal disease	Refers to diseases or conditions affecting the kidneys.
Any malignancy including leukemia and lymphoma	Encompasses all types of cancer, including leukemia and lymphoma.
Moderate or severe liver disease	Refers to liver dysfunction or abnormalities that significantly impact liver function.
Metastatic solid tumor	Refers to cancerous tumors that have spread to other parts of the body from the primary site.
AIDS/HIV	Refers to the human immunodeficiency virus (HIV) infection and the resulting acquired immunodeficiency syndrome (AIDS).

(Table 4) are largely based on self-report, and misclassification is a potential issue. Furthermore, there is a lack of evidence from randomized controlled trials indicating that intervening in individuals at high risk of fracture results in a decrease in fracture risk. Despite this, the output provided by BONEcheck can be beneficial for promoting discussions between doctors and patients regarding the prevention of osteoporotic fractures.

5. Conclusions

In conclusion, we have developed and implemented a digital tool called 'BONEcheck' for fracture risk assessment which is now available free worldwide. The tool can help facilitate doctor-patient discussion about fracture risk, clinical consequences, and treatment benefits so that an informed decision can be reached.

CRediT author statement

Dinh Tan Nguyen: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Thao P. Ho-Le: Conceptualization, Methodology, Software, Supervision, Validation.

Liem Pham: Funding acquisition, Project administration, Resources, Software, Visualization.

Vinh P. Ho-Van: Data curation, Software.

Tien Dat Hoang: Data curation, Software.

Thach S. Tran: Formal analysis, Investigation, Methodology, Supervision, Validation, Writing – review & editing.

Steve Frost: Conceptualization, Data curation, Investigation, Project administration.

Tuan V. Nguyen: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Availability

BONEcheck is now accessible to users through multiple platforms. Users can access it directly from our website or download the app from the Apple Store or Google Play. Please click on the links below to start utilizing the BONEcheck tool:

Website: https://bonecheck.org.

Apple Store: https://apps.apple.com/app/bonecheck/id6447424513.

Google Play: https://play.google.com/store/apps/details?id=org.saigonmec.bonecheck.

Auto access: https://onelink.to/8cjb7m.

QR code:

Conflicts of interest

Thach Tran, Thao Ho-Le, Dinh Nguyen, Vinh Ho-Van, Tien Hoang and Steve Frost have no competing interests to declare. Dinh Nguyen is supported by a grant from the Medical Research Future Fund (grant number APP1176600). Tuan Van Nguyen has received grants from Australian National Health and Medical Research Council and Amgen Competitive Grant Program; fees for lectures from Amgen, Bridge Health Care (VN), DKSH Pharma, MSD and VT Health Care (VN); and support from Amgen for attending the annual meeting of APCO and from VT Health Care (VN) for attending the Vietnam Osteoporosis Society Annual Scientific Meeting. Dr. Nguyen is also Chair of the Research Committee for the Australian and New Zealand Bone and Mineral Society, a Senior Advisor for the Vietnam Osteoporosis Society, and an Executive Member of the Asia Pacific Consortium on Osteoporosis.

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0000-0002-6454-124X. Steve Frost: 0000-0002-8879-0486. Tuan V. Nguyen: 000-0002-3246-6281.

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