

Marco Borderi
Pierluigi Viale

Web and comorbidities

Infectious Diseases Unit, S. Orsola-Malpighi Hospital, Alma Mater Studiorum Bologna University, Bologna, Italy

Corresponding author:

Marco Borderi
Infectious Diseases Unit - S. Orsola Hospital
Via Massarenti 9, 40138 Bologna, (BO) Italy
Tel.: +39 051 6363355 - E-mail: marco.borderi@aosp.bo.it

As AIDS-related mortality has decreased, a substantial challenge facing practitioners is the increasing prevalence of non-AIDS morbidity and mortality in HIV-infected patients. Diseases that are increasingly common in the HIV-infected population include diabetes, cardiovascular disease, kidney problems, cognitive impairment, osteoporosis, hypogonadism, and frailty.

These conditions, many of which are associated with aging in the general population, appear to occur prematurely or at an accelerated rate in the HIV-infected population.

Goals for the future include more clearly identifying the respective roles of HIV infection and antiretroviral therapy in the risk for developing comorbidities and determining whether these effects are reversible, including whether early institution of antiretroviral therapy is important in this regard. Although some aspects of the management of metabolic and inflammatory dysregulation in HIV-infected patients may differ from the management of risk factors in HIV-uninfected persons, a major component of risk reduction remains a heavy emphasis on reducing standard, modifiable risk factors.

This is a list of principal algorithms free on web that can help HIV-positive persons to calculate their own specific risk of comorbidities.

Framingham

<http://cvdrisk.nhlbi.nih.gov>

Frax

<http://www.shef.ac.uk/FRAX/tool.aspx?country=11>

Qfracture

<http://www.qfracture.org/index.php>

DeFRA

<https://defra-osteoporosi.it/>

BMI

http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm

Waist circumference

http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmi_dis.htm

Calcium intake

<http://www.iofbonehealth.org/calcium-calculator>

Cockcroft-Gault Calculator

<http://nephron.com/cgi-bin/CGSI.cgi>

MDRD Calculator

http://nephron.org/mdrd_gfr_si

CKD-EPI

<http://www.qxmd.com/calculate-online/nephrology/ckd-epi-egfr>

Vacs Index

<http://vacs.med.yale.edu/IC/>

DAD 5 years

<http://hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/aid/0/lid/0/Default.aspx>

EuroSIDA

<http://hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/aid/0/lid/0/Default.aspx>

NNH per ABC

<http://hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/aid/0/lid/0/Default.aspx>

Framingham

<http://cvdrisk.nhlbi.nih.gov>

Cardiovascular disease (CVD) is a leading cause of death and serious illness. In 1948, the Framingham Heart Study - under the direction of the National Heart Institute - embarked on an ambitious project in health research. At the time, little was known about the general causes of heart disease and stroke.

The objective of the Framingham Heart Study was to identify the common factors or characteristics that contribute to CVD by following its development over a long period of time in a large group of participants who had not yet developed overt symptoms of CVD or suffered a heart attack or stroke.

The researchers recruited 5,209 men and women between the ages of 30 and 62 from the town of Framingham, Massachusetts, and began the first round of extensive physical examinations and lifestyle interviews that they would later analyze for common patterns related to CVD development. Since 1948, the subjects have continued to return to the study every two years for a detailed medical history, physical examination, and laboratory tests, and in 1971, the Study enrolled a second generation - 5,124 of the original participants' adult children and their spouses - to participate in similar examinations.

In 1994, the need to establish a new study reflecting a more diverse community of Framingham was recognized, and the first Omni cohort of the Framingham Heart Study was enrolled.

In April 2002 the Study entered a new phase, the enrollment of a third generation of participants, the grandchildren of the Original Cohort. In 2003, a second group of Omni participants was enrolled.

Over the years, careful monitoring of the Framingham Study population has led to the identification of the major CVD risk factors - high blood pressure, high blood cholesterol, smoking, obesity, diabetes, and physical inactivity - as well as a great deal of valuable information on the effects of related factors such as blood triglyceride and HDL cholesterol levels, age, gender, and psychosocial issues. Although the Framingham cohort is primarily Caucasian, the importance of the major CVD risk factors identified in this group have been shown in other studies to apply almost universally among racial and ethnic groups, even though the patterns of distribution may vary from group to group. In the past half century, the Study has produced approximately 1,200 articles in leading medical journals. The concept of CVD risk factors has become an integral part of the modern medical curriculum and has led to the development of effective treatment and preventive strategies in clinical practice.

The Framingham Heart Study continues to make important scientific contributions by enhancing its research capabilities and capitalizing on its inherent resources. New diagnostic technologies, such as echocardiography (an ultrasound examination of the heart), carotid artery ultrasound, magnetic resonance imaging of the heart and brain, CT scans of the heart and its vessels and bone densitometry (for monitoring osteoporosis), have been integrated into past and ongoing protocols.

Cardiovascular Disease (10-year risk):

Outcome

CVD (coronary death, myocardial infarction, coronary insufficiency, angina, ischemic stroke, hemorrhagic stroke, transient ischemic attack, peripheral artery disease, heart failure)

Duration of follow-up

Maximum of 12 years, 10-year risk prediction

Population of interest

Individuals 30 to 74 years old and without CVD at the baseline examination

Predictors

- Age
- Diabetes
- Smoking
- Treated and untreated Systolic Blood Pressure
- Total cholesterol
- HDL cholesterol
- BMI replacing lipids in a simpler model

Regression Coefficients and Hazard Ratios - Primary Model

Men* (10-year Baseline Survival: So(10) = 0.88936)				
Variable	Beta**	p-value	Hazard Ratio	95% CI
Log of Age	3.06117	<.0001	21.35	(14.03, 32.48)
Log of Total Cholesterol	1.12370	<.0001	3.08	(2.05, 4.62)
Log of HDL Cholesterol	-0.93263	<.0001	0.40	(0.30, 0.52)
Log of SBP if not treated	1.93303	<.0001	6.91	(3.91, 12.20)
Log of SBP if treated	1.99881	<.0001	7.38	(4.22, 12.92)
Smoking	0.65451	<.0001	1.92	(1.65, 2.24)
Diabetes	0.57367	<.0001	1.78	(1.43, 2.20)
Women* (10-year Baseline Survival: So(10) = 0.95012)				
Variable	Beta**	p-value	Hazard Ratio	95% CI
Log of Age	2.32888	<.0001	10.27	(5.65, 18.64)
Log of Total Cholesterol	1.20904	<.0001	3.35	(2.00, 5.62)
Log of HDL Cholesterol	-0.70833	<.0001	0.49	(0.351, 0.691)
Log of SBP if not treated	2.76157	<.0001	15.82	(7.86, 31.87)
Log of SBP if treated	2.82263	<.0001	16.82	(8.46, 33.46)
Smoking	0.52873	<.0001	1.70	(1.40, 2.06)
Diabetes	0.69154	<.0001	2.00	(1.49, 2.67)

* The 10-year risk for women can be calculated as $1 - 0.95012^{\exp(\beta X - 26.1931)}$ where β is the regression coefficient and X is the level for each risk factor; the risk for men is given as $1 - 0.88936^{\exp(\beta X - 23.9802)}$

** Estimated regression coefficient

Simple Office-based non-laboratory Predictors of CVD Regression Coefficients and Hazard Ratios

Men* (10-year Baseline Survival: So(10) = 0.88431)				
Variable	Beta**	p-value	Hazard Ratio	95% CI
Log of Age	3.11296	<.0001	22.49	(14.80, 34.16)
Log of Body Mass Index	0.79277	<.0066	2.21	(1.25, 3.91)
Log of SBP if not treated	1.85508	<.0001	6.39	(3.61, 11.33)
Log of SBP if treated	1.92672	<.0001	6.87	(3.90, 12.08)
Smoking	0.70953	<.0001	2.03	(1.75, 2.37)
Diabetes	0.53160	<.0001	1.70	(1.37, 2.11)

Women* (10-year Baseline Survival: So(10) = 0.94833)				
Variable	Beta**	p-value	Hazard Ratio	95% CI
Log of Age	2.72107	<.0001	15.20	(8.59, 26.87)
Log of Body Mass Index	0.51125	<.0609	1.67	(0.98, 2.85)
Log of SBP if not treated	2.81291	<.0001	16.66	(8.27, 33.54)
Log of SBP if treated	2.88267	<.0001	17.86	(8.97, 35.57)
Smoking	0.61868	<.0001	1.86	(1.53, 2.25)
Diabetes	0.77763	<.0001	2.18	(1.63, 2.91)

* The 10-year risk for women can be calculated as $1-0.94833^{\exp(\beta X - 26.0145)}$ where β is the regression coefficient and X is the level for each risk factor; the risk for men is given as $1-0.88431^{\exp(\beta X - 23.9388)}$

**Estimated regression coefficient

Frax

<http://www.shef.ac.uk/FRAX/tool.aspx?country=11>

The FRAX[®] tool has been developed by WHO to evaluate fracture risk of patients. It is based on individual patient models that integrate the risks associated with clinical risk factors as well as bone mineral density (BMD) at the femoral neck.

The FRAX[®] models have been developed from studying population-based cohorts from Europe, North America, Asia and Australia.

The FRAX[®] algorithms give the 10-year probability of fracture. The output is a 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture).

The FRAX[®] charts give fracture probabilities according to the number of risk factors that are found in an individual. Charts are available for:

- men and women aged 50 years or more.
- the 10-year probability of hip fracture or of a major osteoporotic fracture (clinical spine, hip, forearm and humerus fracture)

It can select charts that give fracture probabilities according to body mass index or according to the T-score for femoral neck BMD. When both BMI and BMD are available, better characterisation of risk is provided with BMD. For the purpose of these tables secondary causes of osteoporosis should not be used other than a history of rheumatoid arthritis when using the tables with BMD. Any of the secondary causes of osteoporosis can be used with the BMI charts.

The example below gives the ten-year probability of a major osteoporotic fracture for women aged 65 years from the UK according to the number of clinical risk factors (CRFs) and the T-score for BMD.

Table. Ten-year probability of osteoporotic fractures (%) according to BMD T-score at the femoral neck in women aged 65 years from the UK.

Number of CRFs	BMD T-score (femoral neck)					
	-4.0	-3.0	-2.0	-1.0	0	1.0
0	27	15	9.7	7.1	5.9	5.0
1	37 (33-41)	22 (18-26)	14 (10-18)	10 (7.1-14)	8.5 (5.7-12)	7.3 (4.8-10)
2	49 (42-58)	30 (23-40)	20 (13-29)	15 (8.6-23)	12 (6.8-19)	10 (5.6-17)
3	62 (53-72)	41 (30-55)	27 (17-42)	20 (11-34)	17 (8.7-29)	15 (7.2-26)
4	73 (63-81)	52 (42-65)	36 (26-51)	27 (18-41)	23 (14-36)	20 (11-32)
5	83 (79-87)	64 (58-72)	47 (40-57)	36 (28-47)	31 (22-41)	27 (19-36)
6	89	75	58	46	40	35

Thus a woman aged 65 years with a T-score of -2 SD with no clinical risk factors would have a fracture probability of 9.7%. With two clinical risk factors, the probability rises to 20%. Note that a range is given (13-29% in this example). This is not a confidence estimate. The range arises because the different risk factors have different weights. For example, smoking and excess alcohol consumption are relatively weak risk factors, whereas a previous fracture or a family history of hip fracture are strong risk factors. Thus patients with weak risk factors are likely to have a fracture probability closer to the lower end of the range (i.e. 13%).

Where BMD is not available, BMI can be used. An example is given below, again giving the probability of a major osteoporotic fracture for women aged 65 years from the UK according to the number of clinical risk factors.

Table. Ten-year probability of osteoporotic fractures (%) according to body mass index (BMI) in women aged 65 years from the UK.

Number of CRFs	BMI (kg/m ²)						
	15	20	25	30	35	40	45
0	11	9.3	8.6	7.4	6.5	5.6	4.9
1	16 (12-21)	14 (10-18)	13 (9.2-16)	11 (7.9-14)	9.8 (6.9-12)	8.5 (5.9-11)	7.4 (5.1-9.5)
2	24 (16-34)	21 (13-31)	19 (11-29)	17 (9.8-26)	14 (8.4-23)	13 (7.3-20)	11 (6.3-18)
3	35 (24-49)	30 (19-45)	27 (16-43)	24 (14-38)	21 (12-34)	18 (10-30)	16 (8.7-27)
4	48 (35-62)	42 (30-57)	38 (26-54)	34 (22-49)	30 (19-44)	26 (16-39)	23 (14-35)
5	62 (51-71)	56 (45-66)	51 (41-62)	46 (36-56)	41 (32-51)	36 (28-46)	32 (24-41)
6	75	70	65	59	54	48	43

Qfracture

<http://www.qfracture.org/index.php>

QFracture is used to estimate an individual's risk of developing

- hip fracture or
- osteoporotic fracture (hip, spine, wrist or shoulder) over the next 10 years.

The algorithms can be used to identify people at high risk of these fractures so they can be assessed in more detail to reduce their risk.

QFracture has been specifically developed by doctors and academics for use in the UK. The original research was done using the QResearch anonymised medical research database and published in the BMJ.

All medical decisions relating to both scores need to be taken by a patient in consultation with their doctor.

QFracture can be used to assess patients aged between 30 and 99 years unless they have already had an osteoporotic fracture.

The QFracture web calculator can be used to work out the risk of hip or osteoporotic fracture.

The following factors are needed to calculate a QFracture score in men and women:

- Age
- Sex
- Ethnicity
- Smoking status (non smoker, ex smoker, light, moderate, heavy)
- Alcohol use
- Type 1 or Type 2 diabetes
- Parental history of hip fracture/osteoporosis
- Nursing or care home residence
- History of prior osteoporotic (wrist, spine, hip, or shoulder) fracture
- History of falls
- Dementia
- Cancer
- Asthma or COPD
- Cardiovascular disease
- Chronic liver disease
- Chronic kidney disease
- Parkinson's disease
- Rheumatoid arthritis or systemic lupus erythematosus (SLE)
- Gastrointestinal malabsorption (including Crohns disease, ulcerative colitis, celiac disease, steatorrhea, blind loop syndrome)
- Epilepsy or use of anticonvulsants
- Use of antidepressants (at least 2 scripts in last 6 months)
- Use of corticosteroids (at least 2 scripts in last 6 months)
- Body mass index

Additional factors are used for women only:

- Use of oestrogen only Hormone Replacement Therapy
- Endocrine problems (thyrotoxicosis, primary or secondary hyperparathyroidism, Cushing's syndrome)

10 year risk means the risk of someone developing an osteoporotic fracture over the next ten years. If someone has a 10 year score of 10% then in a crowd of 100 people like them, on average 10 people would get an osteoporotic fracture over the next 10 years. Or put another way, they have a 'one in ten' chance of getting a fracture over the next 10 years.

There is no generally agreed threshold, regarding the definition of high risk, equivalent to the 20% intervention threshold used for cardiovascular disease (which is a cost-effectiveness threshold set by NICE). Therefore, thresholds for QFracture are defined based on the risks of patients within the QResearch database for men and women separately.

- For women, the cut off for the top 10% at highest risk is a 10 year risk of 11.1%.
- For men, the cut off for the top 10% at highest risk is 2.6%.

Body mass index is a number calculated from height and weight. It is the weight in kilograms divided by the height in metres squared. Conventionally a person is considered to be obese if they have a body mass index over 30 kg/m². If do not enter a body mass index value on the web calculator it will assume an average value based on patients of the same age and sex.

QFracture-2009 was developed using two thirds of general practices contributing to the QResearch database. Its performance was validated on one third of practices and also directly compared with the FRAX algorithm.

Additional validation of QFracture-2009 has been published by an external team using an independent dataset and the performance was found to be very good. The authors concluded that the QFracture Scores are useful tools for predicting the 10 year risk of osteoporotic and hip fractures in patients in the United Kingdom. The paper can be found here:

- <http://www.bmj.com/content/342/bmj.d3651.full>

Independent validation of QFracture-2012 is currently in progress.

QFracture does not include bone mineral density as it is seldom recorded in GP computer records and it is likely to only be measured in a selected high risk population Also bone mineral density is costly to measure. However QFracture could be used to select high risk patients for bone mineral density measurement as part of their assessment following identification of their high risk status for fracture.

- QFracture is similar to FRAX in that both scores can be used to calculate 10 year risk of hip fracture or osteoporotic fracture.
- QFracture is suitable for use in patients aged 30-99 whereas FRAX is suitable for patients aged 30-90 years.
- QFracture was developed and validated on an extremely large and representative primary care population. It has been specifically designed for use in primary care. FRAX was developed and validated on multiple clinical trial cohorts assembled for different studies at different times.
- QFracture includes a more detailed assessment of smoking and alcohol intake than FRAX. This is because the evidence suggests that the effects of smoking and alcohol are dose dependent.
- FRAX has been adapted for international use whereas the current version of QFracture is designed for use in the UK although it could be re-calibrated for international use in due course.
- QFracture has additional factors which are not included in FRAX and therefore may provide a more individualised assessment of risk. These are:
 - Ethnicity
 - Smoking status (non smoker, ex smoker, light, moderate, heavy) has more categories
 - Alcohol use has more categories
 - Type 1 or Type 2 diabetes
 - Nursing or care home residence
 - History of falls
 - Dementia
 - Cancer
 - Asthma or COPD
 - Cardiovascular disease
 - Chronic liver disease
 - Chronic kidney disease

- Parkinson's disease
- Systemic lupus erythematosus (SLE)
- Gastrointestinal malabsorption (including Crohns disease, ulcerative colitis, celiac disease, steatorrhoea, blind loop syndrome)
- Epilepsy or use of anticonvulsants
- Use of antidepressants (at least 2 scripts in last 6 months)

Women only:

- Use of oestrogen only Hormone Replacement Therapy
- Endocrine problems (thyrotoxicosis, primary or secondary hyperparathyroidism, Cushing's syndrome)

These are things to do to lower risk fracture.

- Take regular weight bearing exercise such as walking, jogging, running.
- Stop smoking and reduce alcohol intake
- Make sure to have enough calcium and vitamin D in diet
- Reduce risk of falling by
- Removing loose rugs or small objects that might fall over at home
- Make sure can see properly (get an eye check done if you are worried about your sight)
- Visit GP for a check up if feel dizzy when stand or are unsteady on feet.

There is some evidence that daily supplementation with Vitamin D3 and calcium reduces hip fracture rates amongst high risk older patients in institutional care. Bisphosphonates seem to reduce hip and other fracture rates in community-dwelling older women less than 80 years of age. Hip protectors may reduce the incidence of hip fractures in institutional care provided that compliance/adherence is achieved. There is some evidence from this study and others that HRT reduces overall fracture risk. However, the risks and benefits of HRT for an individual patient need to be taken into consideration and HRT is currently not routinely recommended for prevention of osteoporosis.

Some types of HRT reduce overall fracture risk. The effect is apparent within a year of starting HRT and increases over time. The protective effect appears to wear off once HRT is stopped. Some types of HRT appear to have a greater protective effect than others.

DeFRA

<https://defra-osteoporosi.it/>

BMI

http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm

BMI is a useful measure of overweight and obesity. It is calculated from your height and weight. BMI is an estimate of body fat and a good gauge of risk for diseases that can occur with more body fat. The higher BMI, the higher is the risk for certain diseases such as heart disease, high blood pressure, type 2 diabetes, gallstones, breathing problems, and certain cancers.

Although BMI can be used for most men and women, it does have some limits:

- It may overestimate body fat in athletes and others who have a muscular build.
- It may underestimate body fat in older persons and others who have lost muscle.

Use the BMI Calculator or BMI Tables to estimate body fat. The BMI score means the following:

	BMI
Underweight	Below 18.5
Normal	18.5–24.9
Overweight	25.0–29.9
Obesity	30.0 and Above

Body Mass Index Table 1

To use the table, find the appropriate height in the left-hand column labeled Height. Move across to a given weight (in pounds). The number at the top of the column is the BMI at that height and weight. Pounds have been rounded off.																	
BMI	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
Height (inches)	Body Weight (pounds)																
58	91	96	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167
59	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173
60	97	102	107	112	118	123	128	133	138	143	148	153	158	163	168	174	179
61	100	106	111	116	122	127	132	137	143	148	153	158	164	169	174	180	185
62	104	109	115	120	126	131	136	142	147	153	158	164	169	175	180	186	191
63	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	191	197
64	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	197	204
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210
66	118	124	130	136	142	148	155	161	167	173	179	186	192	198	204	210	216
67	121	127	134	140	146	153	159	166	172	178	185	191	198	204	211	217	223
68	125	131	138	144	151	158	164	171	177	184	190	197	203	210	216	223	230
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	236
70	132	139	146	153	160	167	174	181	188	195	202	209	216	222	229	236	243
71	136	143	150	157	165	172	179	186	193	200	208	215	222	229	236	243	250
72	140	147	154	162	169	177	184	191	199	206	213	221	228	235	242	250	258
73	144	151	159	166	174	182	189	197	204	212	219	227	235	242	250	257	265
74	148	155	163	171	179	186	194	202	210	218	225	233	241	249	256	264	272
75	152	160	168	176	184	192	200	208	216	224	232	240	248	256	264	272	279
76	156	164	172	180	189	197	205	213	221	230	238	246	254	263	271	279	287

Body Mass Index Table 2

To use the table, find the appropriate height in the left-hand column labeled Height.
Move across to a given weight. The number at the top of the column is the BMI at that height and weight.
Pounds have been rounded off.

BMI	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54
Height (inches)	Body Weight (pounds)																		
58	172	177	181	186	191	196	201	205	210	215	220	224	229	234	239	244	248	253	258
59	178	183	188	193	198	203	208	212	217	222	227	232	237	242	247	252	257	262	267
60	184	189	194	199	204	209	215	220	225	230	235	240	245	250	255	261	266	271	276
61	190	195	201	206	211	217	222	227	232	238	243	248	254	259	264	269	275	280	285
62	196	202	207	213	218	224	229	235	240	246	251	256	262	267	273	278	284	289	295
63	203	208	214	220	225	231	237	242	248	254	259	265	270	278	282	287	293	299	304
64	209	215	221	227	232	238	244	250	256	262	267	273	279	285	291	296	302	308	314
65	216	222	228	234	240	246	252	258	264	270	276	282	288	294	300	306	312	318	324
66	223	229	235	241	247	253	260	266	272	278	284	291	297	303	309	315	322	328	334
67	230	236	242	249	255	261	268	274	280	287	293	299	306	312	319	325	331	338	344
68	236	243	249	256	262	269	276	282	289	295	302	308	315	322	328	335	341	348	354
69	243	250	257	263	270	277	284	291	297	304	311	318	324	331	338	345	351	358	365
70	250	257	264	271	278	285	292	299	306	313	320	327	334	341	348	355	362	369	376
71	257	265	272	279	286	293	301	308	315	322	329	338	343	351	358	365	372	379	386
72	265	272	279	287	294	302	309	316	324	331	338	346	353	361	368	375	383	390	397
73	272	280	288	295	302	310	318	325	333	340	348	355	363	371	378	386	393	401	408
74	280	287	295	303	311	319	326	334	342	350	358	365	373	381	389	396	404	412	420
75	287	295	303	311	319	327	335	343	351	359	367	375	383	391	399	407	415	423	431
76	295	304	312	320	328	336	344	353	361	369	377	385	394	402	410	418	426	435	443

Waist circumference
http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmi_dis.htm

Measuring waist circumference helps screen for possible health risks that come with overweight and obesity. If most of the fat is around waist rather than at hips, this is a higher risk for heart disease and type 2 diabetes. This risk goes up with a waist size that is greater than 35 inches for women or greater than 40 inches for men. To correctly measure the waist, stand and place a tape measure around middle, just above hipbones. Measure waist just after you breathe out.

The table Risks of Obesity-Associated Diseases by BMI and Waist Circumference provides with an idea of whether BMI combined with waist circumference increases the risk for developing obesity-associated diseases or conditions.

Classification of Overweight and Obesity by BMI, Waist Circumference, and Associated Disease Risks

	BMI (kg/m ²)	Obesity Class	Disease Risk* Relative to Normal Weight and Waist Circumference	
			Men 102 cm (40 in) or less Women 88 cm (35 in) or less	Men > 102 cm (40 in) Women > 88 cm (35 in)
Underweight	< 18.5		-	-
Normal	18.5–24.9		-	-
Overweight	25.0–29.9		Increased	High
Obesity	30.0–34.9	I	High	Very High
	35.0–39.9	II	Very High	Very High
Extreme Obesity	40.0 +	III	Extremely High	Extremely High

- Disease risk for type 2 diabetes, hypertension, and CVD.
- + Increased waist circumference also can be a marker for increased risk, even in persons of normal weight.

Calcium intake

<http://www.iofbonehealth.org/calcium-calculator>

Calcium is a mineral that is necessary for life. In addition to building bones and keeping them healthy, calcium helps our blood clot, nerves send messages and muscles contract. About 99 percent of the calcium in our bodies is in our bones and teeth. Each day, we lose calcium through our skin, nails, hair, sweat, urine and feces, but our bodies cannot produce new calcium.

That's why it's important to try to get calcium from the food we eat. When we don't get enough calcium for our body's needs, it is taken from our bones.

Too many patients fall short of getting the amount of calcium they need every day and that can lead to bone loss, low bone density and even broken bones.

The daily amount of calcium depends on age and sex.

Women	
Age 50 & younger	1,000 mg* daily
Age 51 & older	1,200 mg* daily
Men	
Age 70 & younger	1,000 mg* daily
Age 71 & older	1,200 mg* daily

*This includes the total amount of calcium you get from food and supplements.

Food is the best source of calcium. Dairy products, such as low-fat and non-fat milk, yogurt and cheese are high in calcium. Certain green vegetables and other foods contain calcium in smaller amounts. Some juices, breakfast foods, soymilk, cereals, snacks, breads and bottled water have calcium that has been added. If drink soymilk or another liquid that is fortified with calcium, be sure to shake the container well as calcium can settle to the bottom.

A simple way to add calcium to many foods is to add a single tablespoon of nonfat powdered milk, which contains about 50 mg of calcium. About two-to-four tablespoons can be added to most recipes.

To determine how much calcium is in a particular food, check the nutrition facts panel of the food label for the daily value (DV) of calcium. Food labels list calcium as a percentage of the DV. This amount is based on 1,000 mg of calcium per day. For example:

- 30% DV of calcium equals 300 mg.
- 20% DV of calcium equals 200 mg of calcium.
- 15% DV of calcium equals 150 mg of calcium.

The amount of calcium is needed from a supplement depends on the amount of calcium got from food. Aim to get the recommended daily amount of calcium is needed from food first and supplement only if needed to make up for any shortfall. If is got enough calcium from the foods, then don't need to take a supplement. In fact, there is no added benefit to taking more calcium in supplements and doing so may even have some risks.

Calcium supplements are available without a prescription in a wide range of preparations (including chewable and liquid) and in different amounts. The best supplement is the one that meets needs based on convenience, cost and availability. When choosing the best supplement to meet needs, keep the following in mind:

- Calcium is absorbed best when taken in amounts of 500 – 600 mg or less. Try to get calcium-rich foods and/or supplements in smaller amounts throughout the day, preferably with a meal. While it's not recommended, taking calcium all at once is better than not taking it at all.
- Take most calcium supplements with food. Eating food produces stomach acid that helps body absorb most calcium supplements. The one exception to the rule is calcium citrate, which can absorb well when taken with or without food.
- When starting a new calcium supplement, start with a smaller amount to better tolerate it. When switching supplements, try starting with 200-300 mg every day for a week, and drink an extra 6-8 ounces of water with it. Then gradually add more calcium each week.
- Side effects from calcium supplements, such as gas or constipation may occur. If increasing fluids in diet does not solve the problem, try another type or brand of calcium. It may require trial and error to find the right supplement, but fortunately there are many choices.

The chart below will help to estimate the amount of calcium got from food on a typical day.

Product	Servings Per Day	Calcium (mg)	Total
Milk (8 oz.)		X 300	=
Yogurt (6 oz.)		X 300	=
Cheese (1 oz. or 1 cubic inch)		X 200	=
Fortified Foods & Juices		X 80 - 1,000	=
Estimated total from other foods Note: Increase this amount if you get more than 250 mg of calcium from other foods.			= 250
Total Daily Calcium Intake, in mg			=

How to Estimate Your Daily Calcium Intake

Step 1: Estimate the number of servings on a typical day for each type of food. One serving is equal to approximately:

- 8 oz. or one cup of milk
- 6 oz. of yogurt
- 1 oz. or 1 cubic inch of cheese

The amount of calcium in fortified foods and juices ranges from 80 - 1,000 mg. Some examples are juices, soymilk and cereals.

Step 2: List the estimated number of servings of each food item under “Servings Per Day.”

Step 3: Multiply the number of “Servings Per Day” by the number of milligrams (mg) under “Calcium.”

Step 4: After calculated the total amount of calcium for each product, add these totals to get Total Daily Calcium Intake.

Step 5: Subtract final total daily calcium intake from the recommended amount of calcium that is needed each day. This number is the additional calcium needed each day, by adding calcium-rich foods to diet and/or by taking a calcium supplement.

Cockcroft-Gault Calculator
<http://nephron.com/cgi-bin/CGSI.cgi>

MDRD Calculator
http://nephron.org/mdrd_gfr_si

Because mild and moderate kidney injury is poorly inferred from serum creatinine alone, NKDEP strongly encourages clinical laboratories to routinely estimate glomerular filtration rate (GFR) and report the value when serum creatinine is measured for patients 18 and older, when appropriate and feasible. An estimated GFR (eGFR) calculated from serum creatinine using the Modification of Diet in Renal Disease (MDRD) Study equation is a simple and effective way in which laboratories can help health care providers detect CKD among those with risk factors—diabetes, hypertension, cardiovascular disease, or family history of kidney disease. Providers also may use eGFR to monitor patients already diagnosed with CKD.

The following is the IDMS-traceable MDRD Study equation (for creatinine methods calibrated to an IDMS reference method)

$$\text{GFR (mL/min/1.73 m}^2\text{)} = 175 \times (S_{\text{cr}})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$$

The equation does not require weight or height variables because the results are reported normalized to 1.73 m² body surface area, which is an accepted average adult surface area.

Laboratories should program their information systems to use the MDRD Study equation to automatically estimate and report GFR for patients ages 18 and older, when appropriate and feasible.

There are several reasons for using the MDRD Study equation to estimate GFR, including:

- The normal serum creatinine reference interval does not necessarily reflect a normal GFR for a patient. Because the MDRD Study equation employs age, gender, and race, providers may observe that CKD is present despite a serum creatinine concentration that appears to fall within or just above the normal reference interval.
- The MDRD Study equation is the most thoroughly validated equation. The equation has been validated extensively in Caucasian and African American populations between the ages of 18 and 70* with impaired kidney function (eGFR < 60 mL/min/1.73 m²) and has shown good performance for patients with all common causes of kidney disease.
- The MDRD Study equation is currently superior to other methods of approximating GFR. Direct comparison of the MDRD to other equations such as Cockcroft-Gault, and to creatinine clearance measured from 24-hour urine collections has demonstrated this superiority. Note that creatinine clearance should be considered when the patient's basal creatinine production is very abnormal. This may be the case with patients of extreme body size or muscle mass (e.g., obese, severely malnourished, amputees, paraplegics, or other muscle-wasting diseases), or with unusual dietary intake (e.g., vegetarian, creatine supplements).
- Measurement of kidney function (eGFR or creatinine clearance) is essential once albuminuria is discovered.

CKD-EPI

<http://www.qxmd.com/calculate-online/nephrology/ckd-epi-egfr>

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is a new equation, published in 2009, to estimate glomerular filtration rate (GFR) from serum creatinine, age, sex, and race for adults age ≥ 18 years. The National Kidney Disease Education Program has not made a recommendation on general implementation of this equation. The equation is still being validated and, while offering some improvement for eGFR between 60 and 120 mL/min/1.73 m², it is not clear that implementing CKD-EPI in place of the Modification of Diet in Renal Disease (MDRD) equation would alter clinical detection or management of patients with CKD. However, a laboratory that reports eGFR numeric values > 60 mL/min/1.73 m² should consider using the CKD-

EPI equation. Although the CKD-EPI equation is, on average, more accurate for values > 60 mL/min/1.73 m² than is the MDRD Study equation, the influence of imprecision of creatinine assays on the uncertainty of an eGFR value is greater at higher eGFR values and should be considered when determining the highest eGFR value to report.

The equation is based on the same four variables as the MDRD Study equation but uses a 2-slope “spline” to model the relationship between GFR and serum creatinine, age, sex, and race. The equation is given in the following table for creatinine in mg/dL. The equation can be expressed in a single equation or as a series of equations for different race, sex, and creatinine conditions.

Table 1: CKD EPI Equation for Estimating GFR Expressed for Specified Race, Sex and Serum Creatinine in mg/dL

Race	Sex	Serum Creatinine, S _{cr} (mg/dL)	Equation (age in years for ≥ 18)
Black	Female	≤ 0.7	$GFR = 166 \times (S_{cr}/0.7)^{-0.329} \times (0.993)^{Age}$
Black	Female	> 0.7	$GFR = 166 \times (S_{cr}/0.7)^{-1.209} \times (0.993)^{Age}$
Black	Male	≤ 0.9	$GFR = 163 \times (S_{cr}/0.9)^{-0.411} \times (0.993)^{Age}$
Black	Male	> 0.9	$GFR = 163 \times (S_{cr}/0.9)^{-1.209} \times (0.993)^{Age}$
White or other	Female	≤ 0.7	$GFR = 144 \times (S_{cr}/0.7)^{-0.329} \times (0.993)^{Age}$
White or other	Female	> 0.7	$GFR = 144 \times (S_{cr}/0.7)^{-1.209} \times (0.993)^{Age}$
White or other	Male	≤ 0.9	$GFR = 141 \times (S_{cr}/0.9)^{-0.411} \times (0.993)^{Age}$
White or other	Male	> 0.9	$GFR = 141 \times (S_{cr}/0.9)^{-1.209} \times (0.993)^{Age}$

CKD-EPI equation expressed as a single equation:

$$GFR = 141 \times \min(S_{cr}/\kappa, 1)^\alpha \times \max(S_{cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if black]}$$

where:

S_{cr} is serum creatinine in mg/dL,

κ is 0.7 for females and 0.9 for males,

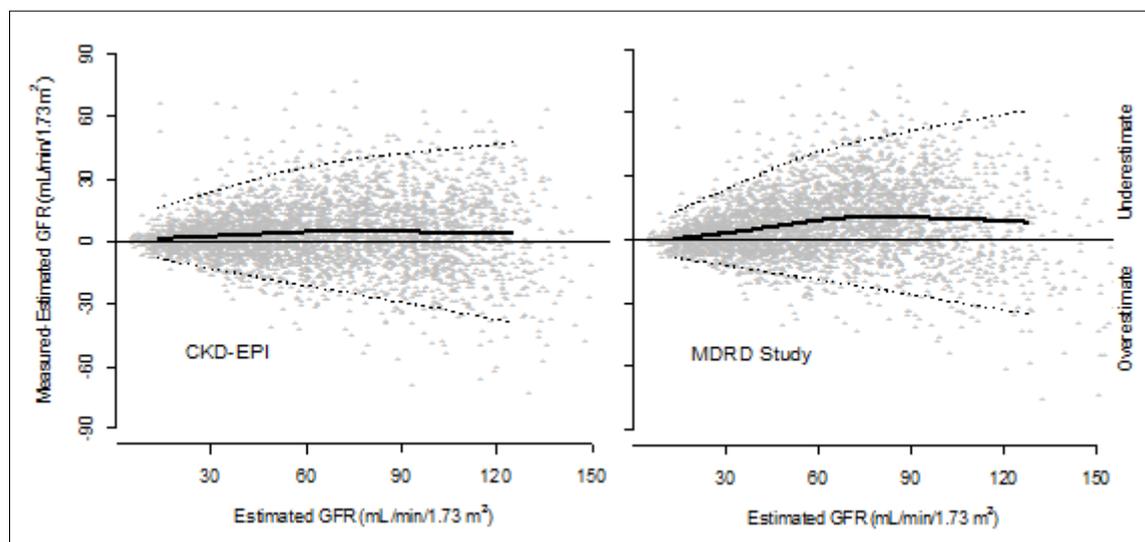
α is -0.329 for females and -0.411 for males,

min indicates the minimum of S_{cr}/ κ or 1, and

max indicates the maximum of S_{cr}/ κ or 1.

As shown in the figure below, the CKD-EPI equation was as accurate as the MDRD Study equation in a subgroup with estimated GFR (eGFR) less than 60 mL/min/1.73 m² and more accurate in a subgroup with eGFR between 60 and 120 mL/min/1.73 m². However, the receiver operator curves (ROC) for detecting GFR categories less than 90, 75, 60, 45, 30 and 15 mL/min per 1.73 m² did not differ between the CKD-EPI and MDRD Study equations

Figure 1. Accuracy of the CKD-EPI and MDRD equations to estimate GFR for the validation data set (N=3896). Both panels show the difference between measured and estimated (y-axis) vs. estimated GFR (x-axis). A smoothed regression line is shown with the 95% CI for the distribution of results, using quantile regression, excluding the lowest and highest 2.5% of estimated GFR.



VACS Index

<http://vacs.med.yale.edu/IC/>

The Veterans Aging Cohort Study Index (VACS Index) creates a score by summing pre-assigned points for age, routinely monitored indicators of HIV disease (CD4 count and HIV-1 RNA), and general indicators of organ system injury including hemoglobin, platelets, aspartate and alanine transaminase (AST and ALT), creatinine, and viral hepatitis C infection (HCV). This score is specifically weighted to indicate increasing risk of all-cause mortality with increasing score. The score can be used to estimate risk of all-cause mortality using a conversion factor.

The VACS Index predicts all cause and cause specific mortality and other outcomes in those living with HIV infection and mortality among those without HIV infection. It responds to important changes in risk related to treatment and health behaviors. It improves upon the accuracy of provider assessment (clinical judgment) of mortality risk.

- *It predicts mortality among those in treatment with HIV infection:* The Index was developed in veteran patients and its reproducible accuracy has been validated in other patient populations in North America and Europe. It discriminates risk of mortality more effectively than an index restricted to CD4 count, HIV-1 RNA and age (Restricted Index) especially among those with undetectable HIV-1 RNA and those 50 or more years of age. The accuracy of the Index for predicting mortality among HIV infected individuals in treatment meets or exceeds the accuracy reported for indices currently used in clinical practice. Further, its accuracy is independent of length of antiretroviral treatment and is robust among important patient subgroups including women, people of color, those with HCV coinfection, and those over 50 years of age. It is also highly predictive of mortality among young active duty military relatively free of comorbid disease and among those initiating salvage antiretroviral therapy after becoming resistant to at least two classes of antiretroviral therapy.

- *It predicts mortality among uninfected individuals:* If you assume that those without HIV infection have no HIV-1 RNA (i.e. 0 points) and a CD4 cell count above 500 cells/mm³ (i.e., 0 points), the VACS Index also predicts mortality among those without HIV infection. This has been demonstrated for 30-day mortality from MICU admission and for long term (median of 5 years) mortality.
- *It predicts 30 day mortality, length of stay, and readmissions after bacterial pneumonia among HIV infected and uninfected older (50+ years) veterans (Barakat, IDSA 2013).*
- *It is associated with frailty:* frailty is defined as decreased ability to recover from additional injury¹⁰. It is associated with increased risk for a number of adverse outcomes including mortality, hospitalization, geriatric syndromes (falls, fragility fractures, and cognitive decline) and is strongly associated with chronic inflammation. The VACS Index is correlated with markers of chronic inflammation, microbial translocation, and hypercoagulability (IL-6, soluble CD14, D-dimer) with measures of functional performance and sarcopenia, and with multiple measures of neuro cognitive performance. The VACS Index predicts morbidity including hospitalization, medical intensive care unit admission, and fragility fractures. It is also associated with autonomic neuropathy. It is likely an excellent measure of physiologic frailty. Of note, the approach to frailty employed by the VACS Index is more attuned to the Rockwood conceptualization of frailty as accumulation of deficits than that of Fried which describes a clinical syndrome.
- It responds to important changes in health and health behaviors: VACS Index scores change in response to antiretroviral initiation and interruption, and discriminate among levels of ART adherence. VACS Index scores differ by level of smoking, alcohol consumption and hypertension. When levels of alcohol consumption change among HIV infected subjects, the index score also changes. Similarly, when HIV infected subjects in treatment for substance abuse have positive urine toxicology screens, their scores are higher than when the same subjects have negative toxicology screens.
- *It is accurate in a wide range of patient population:* VACS Index is strongly predictive of all-cause mortality in a wide range of HIV infected populations including those first initiating ART, after the first year of ART, among highly treatment experienced patients and among young military recruits. It predicts well among men and women, older and younger subjects, those with and without HCV co infection, and those with and without HIV-1 viral suppression.
- *It predicts cause specific mortality:* VACS Index predicts both HIV and non HIV associated mortality better than an index restricted to CD4 count, HIV-1 RNA, and age. It predicts cardiovascular mortality as accurately as it predicts all cause mortality.
- *It improves accuracy of provider assessment of risk among HIV+/- individuals:* Despite the fact that providers have results of the routine clinical biomarkers included in the VACS Index available at the time of assessment, provider assessments do not accurately incorporate the implications of these tests for risk of mortality among those with or without HIV infection. For both veterans with and without HIV infection, provider assessments of severity of illness (“How sick is this patient?”) and risk of 10 year mortality were substantially less accurate than estimates based upon the VACS Index and were considerably improved when combined with the VACS Index. Thus, the VACS Index adds important insight to provider assessment of severity of illness and risk of mortality.

Over the course of the first 12 months of ART, CD4 and HIV-1 RNA change dramatically, but so does level of hemoglobin, FIB 4, and, to a lesser extent, eGFR. Similarly, values differ by level of adherence to ART, by smoking, by alcohol, by HCV status, by number of non ARV medications, and by physical function. As mentioned above under responsiveness to changes in health and health behaviors, VACS Index scores rise during negative health behaviors (alcohol and substance use) and fall when these behaviors are diminished or extinguished. It is likely that successful interventions in any or all of these domains would alter the VACS Index Score.

Potential applications of the VACS Index include research and clinical care.

Research applications include risk adjustment, risk stratification and as an intermediate outcome. For example, observational studies frequently struggle with issues around confounding by indication when studying post marketing treatment effects. The VACS Index could be used as a powerful adjustment either directly or as part of a propensity score. Randomized trials often need to insure that the arms of the trial are equally at risk for the observed outcome (i.e., that the randomization worked), the VACS Index offers a means of making this determination taking into account a number of important predictors of major clinical outcomes). Conversely, randomization could be stratified by VACS Index score. Finally, change in VACS Index score could be used as a response measure for a number of diverse interventions, thereby allowing assessment of their comparative effectiveness.

Clinical care applications include estimating short and long term risk of morbidity and mortality, estimating life expectancy, mapping response to interventions, and detecting HIV and non HIV treatment toxicity. For example, the VACS Index might help inform medical decision making regarding hospitalization, admission to the Medical Intensive Care Unit, the timing of discharge, and discharge planning. The index might also inform decisions regarding frequency of clinical follow up, elective surgical procedures, nursing home placement, and other case management issues.

The index may also be useful in motivating behavior change and prioritizing treatment. While the index does not include all potentially important targets for intervention (smoking, CVD risk factors, alcohol intake, ART adherence, etc.), it responds to differences in these factors and therefore reflects their effects.

DAD 5 years

<http://hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/aid/0/lid/0/Default.aspx>

EuroSIDA

<http://hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/aid/0/lid/0/Default.aspx>

NNH per ABC

<http://hivpv.org/Home/Tools/tabid/91/ctl/ExamView/mid/500/aid/0/lid/0/Default.aspx>