1
00:00:03,830 --> 00:00:07,230
Hello, I'm Dr. Steve
Kopecky a Preventive
2
00:00:07,230 --> 00:00:08,730
Cardiologist
at Mayo Clinic
3
00:00:08,730 --> 00:00:10,125
in Rochester, Minnesota.
4
00:00:10,125 --> 00:00:11,550
It's my pleasure
today to be
5
00:00:11,550 --> 00:00:13,560
speaking with Dr.
Iftikhar Kullo,
6
00:00:13,560 --> 00:00:14,940
who is a Professor
of Medicine
7
00:00:14,940 --> 00:00:16,785
here at Mayo in Rochester.
8
00:00:16,785 --> 00:00:18,840
And one of our
Preventive Cardiologists
9
00:00:18,840 --> 00:00:20,115
will be talking about
10
00:00:20,115 --> 00:00:23,100
genetic testing in
cardiovascular disease.
11
00:00:23,100 --> 00:00:24,390
So Iftikhar welcome.
12
00:00:24,390 --> 00:00:25,050
Thank you, Steve.
13
00:00:25,050 --> 00:00:27,270
A pleasure to
join you today.
14
00:00:27,270 --> 00:00:28,200
I'm really looking
15
00:00:28,200 --> 00:00:29,415
forward to this
conversation.

16
00:00:29,415 --> 00:00:31,380
You know, that the
genetic testing is
17
00:00:31,380 --> 00:00:33,750
really come up about
the last few years,
18
00:00:33,750 --> 00:00:35,970
a large part due
to your research.
19
00:00:35,970 --> 00:00:38,190
Why is genetic
testing needed
20
00:00:38,190 --> 00:00:41,100
for coronary risk
stratification?
21
00:00:41,100 --> 00:00:43,610
Well, Steve, We everyday
22
00:00:43,610 --> 00:00:47,705
use calculators for
risk stratification
23
00:00:47,705 --> 00:00:48,800
and that's a great tool.
24
00:00:48,800 --> 00:00:50,735
We have experimental
cardiologists
25
00:00:50,735 --> 00:00:51,710
and we have to thank
26
00:00:51,710 --> 00:00:54,710
people who kind of develop
those calculators,
27
00:00:54,710 --> 00:00:56,795
particularly the
Framingham investigators,
28
00:00:56,795 --> 00:00:58,280
Dr. Kandel and team.
29
00:00:58,280 --> 00:00:59,405
And that's really a
30
00:00:59,405 --> 00:01:01,295
fantastic resource for us.

31
00:01:01,295 --> 00:01:03,440
And we've used that
and that was dual of
32
00:01:03,440 --> 00:01:04,910
60 years ago and we've been
33
00:01:04,910 --> 00:01:06,500
people into low risk,
34
00:01:06,500 --> 00:01:08,345
intermediate
risk, high risk.
35
00:01:08,345 --> 00:01:10,100
But as you know, and
36
00:01:10,100 --> 00:01:12,230
many of us see
in our practice,
37
00:01:12,230 --> 00:01:13,385
many of these patients,
38
00:01:13,385 --> 00:01:15,125
when they develop an event,
39
00:01:15,125 --> 00:01:16,700
if you had done their risk
40
00:01:16,700 --> 00:01:18,230
estimate the day before,
41
00:01:18,230 --> 00:01:19,910
they would not have
been high risk.
42
00:01:19,910 --> 00:01:23,630
So we do see a lot
of patients that
43
00:01:23,630 --> 00:01:25,190
would not be predicted as
44
00:01:25,190 --> 00:01:27,260
High risk using
these equations.
45
00:01:27,260 --> 00:01:28,610
So there's clearly a need
46
00:01:28,610 --> 00:01:30,230
for us to improve them.

47
00:01:30,230 --> 00:01:31,760
And it's been 60 years
48
00:01:31,760 --> 00:01:32,690
since they were developed.
49
00:01:32,690 --> 00:01:33,770
And as yet, there's
50
00:01:33,770 --> 00:01:35,330
no single biomarker that's
51
00:01:35,330 --> 00:01:37,190
in these pooled
cohort equations.
52
00:01:37,190 --> 00:01:40,880
And I think genetic risk
assessment provides
53
00:01:40,880 --> 00:01:42,920
a very exciting
new avenue for
54
00:01:42,920 --> 00:01:43,940
us to improve these risk
55
00:01:43,940 --> 00:01:45,035
prediction equations.
56
00:01:45,035 --> 00:01:47,210
Very interesting.
So how do you
57
00:01:47,210 --> 00:01:49,595
assess genetic risk
for coronary disease?
58
00:01:49,595 --> 00:01:51,410
Well, everybody,
all of us have
59
00:01:51,410 --> 00:01:53,600
a very simple tool and
that's family history.
60
00:01:53,600 --> 00:01:55,190
We should absolutely never
61
00:01:55,190 --> 00:01:56,900
Miss to ascertain a certain family
62
00:01:56,900 --> 00:01:58,460

history on all our patients.
63
00:01:58,460 --> 00:02:00,140
And as cardiologists, we're
64
00:02:00,140 --> 00:02:02,435
typically
interested in CHD.
65
00:02:02,435 --> 00:02:05,540
And generally any
first-degree relative male,
66
00:02:05,540 --> 00:02:08,150
less than 55, female
less than 65.
67
00:02:08,150 --> 00:02:09,785
We said that's
family history.
68
00:02:09,785 --> 00:02:12,650
And that is very helpful.
69
00:02:12,650 --> 00:02:15,020
It captures not only
some genetic factors,
70
00:02:15,020 --> 00:02:16,610
but also
environmental factors
71
00:02:16,610 --> 00:02:18,620
that the family may
have been exposed to.
72
00:02:18,620 --> 00:02:20,870
That's a very simple, easy,
73
00:02:20,870 --> 00:02:22,760
cheap genomic
tool, I would say.
74
00:02:22,760 --> 00:02:27,095
And the risk
ranges from 1.5 to
75
00:02:27,095 --> 00:02:29,330
twofold higher when you
have a family history
76
00:02:29,330 --> 00:02:30,500
with a first-degree
relative

77
00:02:30,500 --> 00:02:32,255
having premature CHD.
78
00:02:32,255 --> 00:02:34,580
But more interestingly,
recently,
79
00:02:34,580 --> 00:02:35,839
we have this opportunity
80
00:02:35,839 --> 00:02:37,835
to measure genetic
risk scores.
81
00:02:37,835 --> 00:02:40,280
And what those involved is,
82
00:02:40,280 --> 00:02:42,890
we have these, what we
call polymorphisms.
83
00:02:42,890 --> 00:02:46,565
And even though we're
99.9% similar these,
84
00:02:46,565 --> 00:02:48,170
the remaining variation
85
00:02:48,170 --> 00:02:49,280
determines how we look,
86
00:02:49,280 --> 00:02:50,780
how we behave, what
87
00:02:50,780 --> 00:02:52,760
our susceptibility
to disease is.
88
00:02:52,760 --> 00:02:54,950
And that's true
for CHD as well.
89
00:02:54,950 --> 00:02:56,510
And we have done
90
00:02:56,510 --> 00:02:59,119
these large genome-wide
association
91
00:02:59,119 --> 00:03:01,115
studies and they've shown.
92
00:03:01,115 --> 00:03:03,140

Or reveal multiple
93
00:03:03,140 --> 00:03:04,970
susceptibility
genetic variance
94
00:03:04,970 --> 00:03:07,415
up to about 200
nearly at present.
95
00:03:07,415 --> 00:03:09,260
So if we take an
individual and
96
00:03:09,260 --> 00:03:11,180
measured these 200
or so variants,
97
00:03:11,180 --> 00:03:14,090
we can get an assessment of
98
00:03:14,090 --> 00:03:16,460
what the genetic risk
scores simply by
99
00:03:16,460 --> 00:03:17,840
counting the number of risk
100
00:03:17,840 --> 00:03:19,475
variance at each locus.
101
00:03:19,475 --> 00:03:20,600
And if you were really
102
00:03:20,600 --> 00:03:21,935
unfortunate, you'd have to,
103
00:03:21,935 --> 00:03:23,060
400 of them are,
104
00:03:23,060 --> 00:03:23,570
and if you're very
105
00:03:23,570 --> 00:03:25,265
fortunately would
have none of them.
106
00:03:25,265 --> 00:03:30,080
So, so when we do this
in a cohort of people,
107
00:03:30,080 --> 00:03:32,105
the genetic risk
score is bell-shaped.

108
00:03:32,105 --> 00:03:33,530
But then there
are people at
109
00:03:33,530 --> 00:03:34,910
the tail end of the
110
00:03:34,910 --> 00:03:36,470
bell-shaped that
are at high risk.
111
00:03:36,470 --> 00:03:37,805
And that's where this
112
00:03:37,805 --> 00:03:40,325
profiling is
really helpful.
113
00:03:40,325 --> 00:03:42,320
Also very interesting and
114
00:03:42,320 --> 00:03:44,120
are these
individual markers,
115
00:03:44,120 --> 00:03:45,575
these markers, you weight
116
00:03:45,575 --> 00:03:47,030
them differently or.
117
00:03:47,030 --> 00:03:48,695
Yes. That's an excellent
point. So
118
00:03:48,695 --> 00:03:50,030
The simplest way is
119
00:03:50,030 --> 00:03:51,425
to just count them, right?
120
00:03:51,425 --> 00:03:52,730
Count how many
risk wheels are.
121
00:03:52,730 --> 00:03:56,450
But you can weight them
by weighting them by
122
00:03:56,450 --> 00:03:58,820
the strength of their
association with
123

00:03:58,820 --> 00:03:59,960
the disease are some snips
124
00:03:59,960 --> 00:04:01,280
are more strongly
associated.
125
00:04:01,280 --> 00:04:02,615
The strongest, as you know,
126
00:04:02,615 --> 00:04:04,820
is the 9P21 locus.
127
00:04:04,820 --> 00:04:06,740
And then there's
a whole host that
128
00:04:06,740 --> 00:04:08,824
are weaker and association.
129
00:04:08,824 --> 00:04:10,400
But the field has actually
130
00:04:10,400 --> 00:04:12,425
moved on Steve now.
131
00:04:12,425 --> 00:04:14,480
So when we say
that or let's say
132
00:04:14,480 --> 00:04:17,375
200 we set a very high bar.
133
00:04:17,375 --> 00:04:18,770
So the p-value has to be
134
00:04:18,770 --> 00:04:20,420
five into ten to
the minus eight.
135
00:04:20,420 --> 00:04:22,025
So that's a
pretty high bar.
136
00:04:22,025 --> 00:04:24,290
And people started looking
137
00:04:24,290 --> 00:04:25,925
at the variance
that we're not,
138
00:04:25,925 --> 00:04:28,460
that were significant
or not significant at

139
00:04:28,460 --> 00:04:29,570
that level and
they found there
140
00:04:29,570 --> 00:04:31,970
was enough additional
information.
141
00:04:31,970 --> 00:04:33,410
So now people what we are
142
00:04:33,410 --> 00:04:35,150
using are called
genome-wide scores,
143
00:04:35,150 --> 00:04:36,170
where we take millions of
144
00:04:36,170 --> 00:04:38,150
snips and take
their p-values.
145
00:04:38,150 --> 00:04:42,140
And it's been shown
that when you calculate
146
00:04:42,140 --> 00:04:43,160
a genome wide risk or
147
00:04:43,160 --> 00:04:44,330
they are actually
stronger than
148
00:04:44,330 --> 00:04:45,380
the ones that you would do
149
00:04:45,380 --> 00:04:47,075
from just a limited set.
150
00:04:47,075 --> 00:04:49,085
So that's where the
field has moved down.
151
00:04:49,085 --> 00:04:51,470
I see. and then this,
152
00:04:51,470 --> 00:04:53,425
so this polygenic
risk score, the,
153
00:04:53,425 --> 00:04:55,805
how do you use it
to assess risk?

154
00:04:55,805 --> 00:04:57,200
To the beauty of these,
155
00:04:57,200 --> 00:05:00,260
Steve is that
they are almost
156
00:05:00,260 --> 00:05:02,780
completely uncorrelated
with the Framingham
157
00:05:02,780 --> 00:05:04,530
or the pool
cohort equations.
158
00:05:04,530 --> 00:05:06,460
So because they're
not correlated,
159
00:05:06,460 --> 00:05:08,635
you can simply multiply
160
00:05:08,635 --> 00:05:11,560
the two together to get
a 10-year estimate.
161
00:05:11,560 --> 00:05:13,870
And so let's
say somebody is
162
00:05:13,870 --> 00:05:15,250
polygenic risk
score puts them
163
00:05:15,250 --> 00:05:17,260
at one point five-fold higher.
164
00:05:17,260 --> 00:05:18,985
And that patient's
165
00:05:18,985 --> 00:05:21,220
predicted 10-year
risk is 7%.
166
00:05:21,220 --> 00:05:24,265
So you can simply
multiply seven into 1.5.
167
00:05:24,265 --> 00:05:26,230
And that puts you, I think,
168
00:05:26,230 --> 00:05:28,495
at ten plus risk.

169
00:05:28,495 --> 00:05:29,860
And that potentially makes
170
00:05:29,860 --> 00:05:31,210
your candidate
for stat mux.
171
00:05:31,210 --> 00:05:33,610
So that's the nice
thing that you
172
00:05:33,610 --> 00:05:36,295
can actually integrate
the two together.
173
00:05:36,295 --> 00:05:38,080
I see. Are these
things are they
174
00:05:38,080 --> 00:05:40,225
starting to creep
into the guidelines,
175
00:05:40,225 --> 00:05:41,920
the polygenic risk scores
176
00:05:41,920 --> 00:05:43,525
or how are they treated?
177
00:05:43,525 --> 00:05:44,770
So at this point,
178
00:05:44,770 --> 00:05:46,420
the ACC AHA guidelines do
179
00:05:46,420 --> 00:05:49,535
not in corporate them.
180
00:05:49,535 --> 00:05:50,825
But if you look at that
181
00:05:50,825 --> 00:05:53,630
HA 2020 statement
on heart disease,
182
00:05:53,630 --> 00:05:56,975
There's a very nice
description of these.
183
00:05:56,975 --> 00:05:59,030
It talks about
family history,
184

00:05:59,030 --> 00:06:01,100
it talks about
polygenic risk scores.
185
00:06:01,100 --> 00:06:02,450
So at this point they're
186
00:06:02,450 --> 00:06:03,560
not in the guidelines,
187
00:06:03,560 --> 00:06:04,580
but I suspect that
188
00:06:04,580 --> 00:06:06,440
eventually they will
be because there's
189
00:06:06,440 --> 00:06:08,090
so much data showing that
190
00:06:08,090 --> 00:06:10,160
these are incremental to
191
00:06:10,160 --> 00:06:12,530
these pool cohort
equations and they're not
192
00:06:12,530 --> 00:06:13,700
correlated so that if
193
00:06:13,700 --> 00:06:14,990
you take the two together,
194
00:06:14,990 --> 00:06:17,840
you get a more refined
risk assessment.
195
00:06:17,840 --> 00:06:19,805
So who, who is your
typical patient?
196
00:06:19,805 --> 00:06:21,095
Now, you use this in,
197
00:06:21,095 --> 00:06:22,550
but if you see a patient,
198
00:06:22,550 --> 00:06:24,020
they come in and
say, I have
199
00:06:24,020 --> 00:06:26,420
My father had a heart
attack at age 50 or

200
00:06:26,420 --> 00:06:28,940
You how do you how
do you factor it in?
201
00:06:28,940 --> 00:06:30,620
Yeah, The
interesting thing, Steve,
202
00:06:30,620 --> 00:06:32,885
is that for some reason
203
00:06:32,885 --> 00:06:34,100
they are not very strongly
204
00:06:34,100 --> 00:06:35,240
correlated with
family history.
205
00:06:35,240 --> 00:06:36,500
Otherwise, you could
make the case well,
206
00:06:36,500 --> 00:06:37,640
if I took the
family history,
207
00:06:37,640 --> 00:06:39,635
why do I need the
polygenic risk score?
208
00:06:39,635 --> 00:06:41,180
But they're not,
they give different
209
00:06:41,180 --> 00:06:42,200
means of information.
210
00:06:42,200 --> 00:06:43,280
So I would say
211
00:06:43,280 --> 00:06:45,185
the best category of
individuals would
212
00:06:45,185 --> 00:06:47,420
be the intermediate risk
213
00:06:47,420 --> 00:06:49,010
are those who have
a family history.
214
00:06:49,010 --> 00:06:50,555
Because intermediate risk,

215
00:06:50,555 --> 00:06:52,700
the AHA recommends
adjuncts that
216
00:06:52,700 --> 00:06:57,410
includes calcium
scrolling, LPA or CRP.
217
00:06:57,410 --> 00:06:59,270
But I think the
polygenic risk score
218
00:06:59,270 --> 00:07:01,295
could also be one
such adjunct.
219
00:07:01,295 --> 00:07:03,470
And you would
then reclassify
220
00:07:03,470 --> 00:07:05,150
these intermediate
risk individuals
221
00:07:05,150 --> 00:07:06,575
into high or low risk.
222
00:07:06,575 --> 00:07:08,255
Okay. So just like
anything else,
223
00:07:08,255 --> 00:07:09,350
the intermediate
patients are
224
00:07:09,350 --> 00:07:10,730
the ones you focus on?
225
00:07:10,730 --> 00:07:12,680
I would say that's
where because you know,
226
00:07:12,680 --> 00:07:14,000
if the patient's
high risk based on
227
00:07:14,000 --> 00:07:15,050
conventional risk factors,
228
00:07:15,050 --> 00:07:16,205
you're going to treat them.
229
00:07:16,205 --> 00:07:17,630

So additional
information may
230
00:07:17,630 --> 00:07:18,830
not be all that critical.
231
00:07:18,830 --> 00:07:20,210
But I think in
the intermediate
232
00:07:20,210 --> 00:07:21,425
risk group is
where they met,
233
00:07:21,425 --> 00:07:23,765
there might be the best
utility initially.
234
00:07:23,765 --> 00:07:25,385
And be clear, these,
235
00:07:25,385 --> 00:07:26,750
this polygenic risk score
236
00:07:26,750 --> 00:07:28,070
does not include LPA,
237
00:07:28,070 --> 00:07:30,410
lipoprotein A
or other things
238
00:07:30,410 --> 00:07:31,460
that will code for like
239
00:07:31,460 --> 00:07:32,960
hypertension or
hyperlipidemia.
240
00:07:32,960 --> 00:07:34,370
These are all
separate factors.
241
00:07:34,370 --> 00:07:36,545
That’s a great question,
actually they do.
242
00:07:36,545 --> 00:07:37,880
So if you take all of
243
00:07:37,880 --> 00:07:38,960
these risk factors that
244
00:07:38,960 --> 00:07:40,040
are associated with CHD,

245
00:07:40,040 --> 00:07:41,390
some of them are,
246
00:07:41,390 --> 00:07:42,770
some of the
genetic variance
247
00:07:42,770 --> 00:07:44,420
are associated with CHD
248
00:07:44,420 --> 00:07:46,160
because they're
associated with lipids.
249
00:07:46,160 --> 00:07:48,170
So you might ask well if
250
00:07:48,170 --> 00:07:49,580
the lipids and
blood pressure
251
00:07:49,580 --> 00:07:50,810
and the pool cohort,
252
00:07:50,810 --> 00:07:52,655
why are we adding
these factors?
253
00:07:52,655 --> 00:07:54,500
Well, we've seen that
254
00:07:54,500 --> 00:07:56,030
if you take a blood
pressure measurement,
255
00:07:56,030 --> 00:07:57,470
it's today's
blood pressure.
256
00:07:57,470 --> 00:08:00,110
But the genetic risk for
blood pressure tells
257
00:08:00,110 --> 00:08:02,510
you your accumulated
exposure
258
00:08:02,510 --> 00:08:04,085
to high blood
pressure over time.
259
00:08:04,085 --> 00:08:05,750
And the same is

true for lipids.
260
00:08:05,750 --> 00:08:08,030
So even though these
elements are there,
261
00:08:08,030 --> 00:08:08,660
even if you add
262
00:08:08,660 --> 00:08:10,415
these additional
genetic risk factors,
263
00:08:10,415 --> 00:08:12,380
it doesn't seem to have
264
00:08:12,380 --> 00:08:14,645
too much of a
correlation or overlap,
265
00:08:14,645 --> 00:08:17,810
so it's safe to include
them as well. Okay.
266
00:08:17,810 --> 00:08:19,430
And how how are these
267
00:08:19,430 --> 00:08:20,810
available now
or they widely
268
00:08:20,810 --> 00:08:22,160
available and
how do
269
00:08:22,160 --> 00:08:24,110
you utilize them?
270
00:08:24,110 --> 00:08:25,850
Well, they had
been actually
271
00:08:25,850 --> 00:08:27,110
available for a long time,
272
00:08:27,110 --> 00:08:29,120
but through
direct-to-consumer companies
273
00:08:29,120 --> 00:08:30,590
like Bernicie and Me,
274
00:08:30,590 --> 00:08:32,060
the problem there is that

275
00:08:32,060 --> 00:08:33,830
their genetic risk scores
276
00:08:33,830 --> 00:08:35,180
are somewhat antiquated at,
277
00:08:35,180 --> 00:08:36,680
to my best of my knowledge,
278
00:08:36,680 --> 00:08:39,845
and the way they calculate
them is not clear.
279
00:08:39,845 --> 00:08:41,810
So I wouldn't
really be using
280
00:08:41,810 --> 00:08:43,865
that in clinical practice.
281
00:08:43,865 --> 00:08:46,310
So I think Mayo is
probably one of
282
00:08:46,310 --> 00:08:47,630
the only institution that's
283
00:08:47,630 --> 00:08:49,025
offering this.
284
00:08:49,025 --> 00:08:50,750
We started this
as you know,
285
00:08:50,750 --> 00:08:52,430
after the margin
study and it
286
00:08:52,430 --> 00:08:55,535
includes about 30
risk variants.
287
00:08:55,535 --> 00:08:57,470
And now we're
moving to upgrade
288
00:08:57,470 --> 00:08:58,850
the genetic risk score so
289
00:08:58,850 --> 00:09:00,395
that we are now
290
00:09:00,395 --> 00:09:02,450

offering the
genome wide risk,
291
00:09:02,450 --> 00:09:03,950
polygenic risk score, which
292
00:09:03,950 --> 00:09:06,005
is much, much stronger.
293
00:09:06,005 --> 00:09:08,990
And I'm aware of
many other efforts,
294
00:09:08,990 --> 00:09:12,740
both in England and
the UK and the US.
295
00:09:12,740 --> 00:09:14,120
Other sites are interested
296
00:09:14,120 --> 00:09:15,770
and about to offer these.
297
00:09:15,770 --> 00:09:17,000
And we hope to offer
298
00:09:17,000 --> 00:09:18,530
a genome wide
polygenic risk score
299
00:09:18,530 --> 00:09:20,270
for CHD also in
the near future.
300
00:09:20,270 --> 00:09:21,470
A wonderful, yeah.
301
00:09:21,470 --> 00:09:22,700
And then you mentioned
302
00:09:22,700 --> 00:09:24,425
combining with framingham.
303
00:09:24,425 --> 00:09:26,105
How do you combine
it with the
304
00:09:26,105 --> 00:09:28,370
with the calcium score.
305
00:09:28,370 --> 00:09:30,500
Yeah, so that's, that's
306
00:09:30,500 --> 00:09:32,060

another very
interesting question.
307
00:09:32,060 --> 00:09:33,845
If you have the
calcium score,
308
00:09:33,845 --> 00:09:36,455
where does a polygenic
risks come in?
309
00:09:36,455 --> 00:09:38,210
Well, Steve, the way I
310
00:09:38,210 --> 00:09:39,860
see it is that, you know,
311
00:09:39,860 --> 00:09:41,210
this is going to be a very
312
00:09:41,210 --> 00:09:43,055
cheap tests where you can,
313
00:09:43,055 --> 00:09:44,450
let's say genotype somebody
314
00:09:44,450 --> 00:09:45,380
and you can calculate
315
00:09:45,380 --> 00:09:48,620
the risk of many
diseases, not just CHD.
316
00:09:48,620 --> 00:09:50,360
And therefore there's
so much utility
317
00:09:50,360 --> 00:09:52,070
you can extract so
much information,
318
00:09:52,070 --> 00:09:53,630
you can do a colon
cancer risk,
319
00:09:53,630 --> 00:09:55,100
breast cancer
risk assessment
320
00:09:55,100 --> 00:09:56,675
from the same chip.
321
00:09:56,675 --> 00:09:58,775
So my sense is that

322
00:09:58,775 --> 00:10:00,965
in the future this
will become routine.
323
00:10:00,965 --> 00:10:03,380
And you can actually
measure this risk
324
00:10:03,380 --> 00:10:05,810
at age 20 or in teens.
325
00:10:05,810 --> 00:10:07,520
And it will project
326
00:10:07,520 --> 00:10:08,840
your lifetime genetic
327
00:10:08,840 --> 00:10:10,385
risk for that condition.
328
00:10:10,385 --> 00:10:13,910
And and it could
potentially be just
329
00:10:13,910 --> 00:10:15,185
incorporated into the
330
00:10:15,185 --> 00:10:16,685
routine risk calculators
331
00:10:16,685 --> 00:10:18,380
because it's going to
be cheap and available.
332
00:10:18,380 --> 00:10:20,270
And then you can use
that combined rest
333
00:10:20,270 --> 00:10:21,320
to determine what to do.
334
00:10:21,320 --> 00:10:23,330
For example, should
we do a CT scan
335
00:10:23,330 --> 00:10:24,410
earlier in this patient or
336
00:10:24,410 --> 00:10:26,090
put them on Staten earlier?
337
00:10:26,090 --> 00:10:27,860
Or should I do a

colonoscopy of
338
00:10:27,860 --> 00:10:29,840
that colon cancer
risk is high earlier,
339
00:10:29,840 --> 00:10:32,090
so I would say that the two
340
00:10:32,090 --> 00:10:33,170
would be adjunct and
341
00:10:33,170 --> 00:10:34,910
not necessarily competing.
342
00:10:34,910 --> 00:10:36,575
I see. Yeah. So say
343
00:10:36,575 --> 00:10:38,480
Iftakar you see two
patients one day the,
344
00:10:38,480 --> 00:10:40,430
first patient comes
in, you do the,
345
00:10:40,430 --> 00:10:42,005
the risk score and here
346
00:10:42,005 --> 00:10:43,505
they have nothing, right?
347
00:10:43,505 --> 00:10:46,250
The next patient you see
all 400 are positive.
348
00:10:46,250 --> 00:10:48,050
How do you do you
tell the first one?
349
00:10:48,050 --> 00:10:49,190
Go do whatever you want.
350
00:10:49,190 --> 00:10:50,300
Don't worry, you're
not going to get
351
00:10:50,300 --> 00:10:51,620
disease and the second one.
352
00:10:51,620 --> 00:10:53,420
And you say, Oh
my gosh, this is
353

00:10:53,420 --> 00:10:55,670
a fait accompli or how
do you approach them?
354
00:10:55,670 --> 00:10:56,960
Yeah, I think that's
355
00:10:56,960 --> 00:10:58,430
a great question
because people,
356
00:10:58,430 --> 00:11:00,290
patients had that concept
357
00:11:00,290 --> 00:11:01,730
that genetics
is determinism.
358
00:11:01,730 --> 00:11:04,295
It's not, it's something
you can change.
359
00:11:04,295 --> 00:11:06,200
And so the person that
360
00:11:06,200 --> 00:11:07,970
had a low genetic
risk score,
361
00:11:07,970 --> 00:11:10,490
if you went out and eat
burgers and smoked,
362
00:11:10,490 --> 00:11:12,410
he's going to get
CHD at some point,
363
00:11:12,410 --> 00:11:14,015
it's going to be high risk.
364
00:11:14,015 --> 00:11:16,010
And the person who
has a very high risk
365
00:11:16,010 --> 00:11:17,690
if he or she
366
00:11:17,690 --> 00:11:20,435
modulates their
lifestyle and
367
00:11:20,435 --> 00:11:21,980
if needed, takes a statin.
368

00:11:21,980 --> 00:11:23,720
And there are studies
showing that,
369
00:11:23,720 --> 00:11:26,825
that genetic risk is
significantly reduced.
370
00:11:26,825 --> 00:11:28,130
So I think it's a really
371
00:11:28,130 --> 00:11:29,240
important point to make
372
00:11:29,240 --> 00:11:30,590
that genetics is not
373
00:11:30,590 --> 00:11:32,210
your destiny necessarily.
374
00:11:32,210 --> 00:11:34,130
You can alter it by
375
00:11:34,130 --> 00:11:36,620
lifestyle
modification or by
376
00:11:36,620 --> 00:11:38,225
treatment of risk factors.
377
00:11:38,225 --> 00:11:39,215
Okay.
378
00:11:39,215 --> 00:11:41,360
Well, that's fascinating
information.
379
00:11:41,360 --> 00:11:43,490
Anything else we
need to discuss?
380
00:11:43,490 --> 00:11:45,740
Well, I just wanted
to mention that
381
00:11:45,740 --> 00:11:47,540
this polygenic
risk scores are
382
00:11:47,540 --> 00:11:49,610
just one facet of
genetic testing.
383
00:11:49,610 --> 00:11:51,950

There's a lot of other
interesting things
384
00:11:51,950 --> 00:11:53,750
coming down the road.
385
00:11:53,750 --> 00:11:56,585
You know, epigenetics
is one of them.
386
00:11:56,585 --> 00:11:59,585
And then there's a
phenomenon called chip,
387
00:11:59,585 --> 00:12:02,210
which is clonal
hematopoiesis of
388
00:12:02,210 --> 00:12:03,725
indeterminate potential
389
00:12:03,725 --> 00:12:06,680
and then expression
profiles.
390
00:12:06,680 --> 00:12:08,120
And I shouldn't, of course,
391
00:12:08,120 --> 00:12:10,640
forget to mention
our favorite disease
392
00:12:10,640 --> 00:12:12,980
FH, which is monogenic.
393
00:12:12,980 --> 00:12:14,930
And we should not, should
394
00:12:14,930 --> 00:12:16,820
be aware of that
condition in people who
395
00:12:16,820 --> 00:12:18,350
have early disease or have
396
00:12:18,350 --> 00:12:20,630
high cholesterol and we shouldn’t
397
00:12:20,630 --> 00:12:21,980
forget that there's
genetic testing
398
00:12:21,980 --> 00:12:23,900
available for that as well.

399
00:12:23,900 --> 00:12:26,450
So I think that message
400
00:12:26,450 --> 00:12:28,205
would be there are
some patients who,
401
00:12:28,205 --> 00:12:31,310
whose disease is probably
related to page,
402
00:12:31,310 --> 00:12:33,680
particularly if they
had it early on,
403
00:12:33,680 --> 00:12:35,330
had high cholesterol,
our family history.
404
00:12:35,330 --> 00:12:36,860
So in those
cases, we should
405
00:12:36,860 --> 00:12:39,920
certainly consider
genetic testing for FH.
406
00:12:39,920 --> 00:12:41,300
Well, yeah, very true.
407
00:12:41,300 --> 00:12:41,600
That's
408
00:12:41,600 --> 00:12:43,610
a very important disease
to genetic test.
409
00:12:43,610 --> 00:12:45,830
Well, this has been a
fascinating discussion
410
00:12:45,830 --> 00:12:46,940
today with Dr. Iftakar Kullo.
411
00:12:46,940 --> 00:12:48,710
One of our
genetic experts here in
412
00:12:48,710 --> 00:12:51,005
cardiology and
cardiovascular prevention.
413
00:12:51,005 --> 00:12:52,625

Thank you Iftakar
for joining us.
414
00:12:52,625 --> 00:12:54,870
Thank you, Steve.
It was a pleasure.