

HOW A BONE DISEASE GREW TO FIT THE PRESCRIPTION (NPR, ALL THINGS CONSIDERED, DEC 21, 2009)

1 *Heard on All Things Considered*

2 *December 21, 2009* - MICHELE NORRIS, host:

3 From NPR News, this is ALL THINGS CONSIDERED. I'm Michele Norris.

4 And today, we have an unusual biography. It's the biography of a box of
5 pills, how it got into a medicine cabinet in Richmond, Virginia, and into the
6 medicine cabinets of millions of women all across America.

7 NPR's Alix Spiegel explains how the marketing of the pills changed the
8 definition of a disease and created a whole new category of people who
9 saw themselves as needing treatment.

10 ALIX SPIEGEL: The box of medicine is very ordinary: a white rectangle
11 covered in writing that spends most of its life in Katie Benghauser's
12 medicine cabinet, sandwiched between a bottle of aspirin and a small army
13 of pet medications.

14 Ms. KATIE BENGHAUSER: We have the flea treatment for the dog, the
15 flea treatment for the cat, heartworm for the cat...

16 SPIEGEL: So the box and its neighbors just sit there, day after day in dark.
17 But then, exactly once a month, Katie comes. She unsticks the door, lifts
18 the box and coaxes a pill from the package.

19 Ms. BENGHAUSER: And press and hold it, then you fold.

20 SPIEGEL: Now, like most people, Katie has no concept of all of the forces
21 that combined to bring these pills into her home. All she knows is that three
22 years ago, she went to her doctor and was told that it was time to take a
23 test. Not that there was anything about Katie that suggested sickness.
24 Katie is 57, but can outrun most 20-year-olds. She's a model of health. Still,
25 she is a little bit thin and she's a woman in her 50s, so her doctor thought it
26 best to be careful.

27 Ms. BENGHAUSER: She felt like because my frame is slight and just the
28 risk factors of being female and white just were at risk for developing
29 osteoporosis.

30 SPIEGEL: Osteoporosis is a disease where bones thin, lose density and
31 can easily fracture. It can be devastating to older women who fall and break
32 a hip. Now, osteoporosis mostly afflicts the elderly. But just to make sure,
33 Katie went in for a test, which measured the density of her bones. Two
34 weeks later, a letter came with an unsettling message.

35 Ms. BENGHAUSER: The results of your bone density show that you have
36 osteopenia and you need to start taking medication.

37 SPIEGEL: Now, let's pause here. Katie's diagnosis was for osteopenia.
38 Osteopenia is different than osteoporosis. In fact, though Katie is very
39 health conscious, she wasn't familiar with it. But then Katie asked around
40 and it turned out that many of her peers had osteopenia. For example,
41 Katie works in an office with seven other women, several of whom had also
42 been diagnosed.

43 Ms. BENGHAUSER: There's four of us that are over 50.

44 SPIEGEL: And three of the four are...

45 Ms. BENGHAUSER: The four are on some type of medication for
46 osteopenia.

47 SPIEGEL: Osteopenia, it turns out, is a slight thinning of the bones, which
48 occurs naturally as women get older and typically doesn't result in disabling
49 bone breaks. In fact, it's a condition that only recently started to be thought
50 of as a problem that required treatment. And to understand its full evolution
51 from non-problem to problem, you need to go back to the beginning, to
52 1992 and a place very far away from Katie Benghauser's suburban
53 Richmond home.

54 Dr. ANNA TOSTESON (Professor of Medicine, Dartmouth College): The
55 meeting took place in Rome, Italy, in a hotel near the top of the Spanish
56 Steps.

57 SPIEGEL: This is Anna Tosteson, professor of medicine at Dartmouth
58 College. In 1992, Tosteson was one of a small group of experts on
59 osteoporosis, invited to Rome for a meeting organized by the World Health
60 Organization. One focus of which was a definition for osteoporosis. You

61 see, for a long time, doctors were only able to diagnose osteoporosis after
62 a woman got a fracture. But bone scanning machines had made it possible
63 to figure out if bones were weak before fractures occurred. The question
64 before the experts then was this: Since after the age of 30, all bones lose
65 density, how much bone loss was normal? And how much put women at
66 risk and so should be categorized as a disease? Anna Tosteson says the
67 experts in the room went back and forth, looking at research and trying to
68 decide where on a graph of diminishing bone loss to draw the line.

69 Dr. TOSTESON: Ultimately, it was just a matter of, well, it has to be drawn
70 somewhere. And as I recall, it was very hot in the meeting room.

71 (Soundbite of laughter)

72 Dr. TOSTESON: And people were kind of in shirtsleeves, and it was time to
73 kind of move on, if you will. And I can't quite frankly remember who it was
74 who stood up and drew the picture and said, well, let's just do this.

75 SPIEGEL: So a line is drawn and every woman on one side had
76 osteoporosis, but what about the women just on the other side of that line?
77 Well, for that group, the experts, more or less off the cuff, decided to use
78 the term osteopenia. Anna Tosteson told me that they created the category
79 mostly because they thought it might be useful for public health
80 researchers who like clear categories for their studies. They never
81 imagined, she said, that people would come to think of osteopenia as a
82 condition to be treated, though she does admit that the term sounds a little
83 forbidding.

84 Dr. TOSTESON: Osteopenia sounds like something that, you know, your
85 medicalizing this problem. Low bone mass sounds a little bit less scary.

86 SPIEGEL: Of course, 17 years later in Richmond, Virginia, Katie
87 Benghauser is not only treated for osteopenia, but literally spends her days
88 worried about her diagnosis.

89 Ms. BENGHAUSER: I'm much more aware of making sure I lift my feet up
90 and I don't trip on the sidewalks. And, you know, if I didn't know I had
91 osteopenia, maybe I wouldn't be so cautious.

92 SPIEGEL: So, how does osteopenia change from a category for
93 researchers into a condition that millions of women swallow pills to control?
94 To find out, I drove to the sprawling Pennsylvania home of a man named
95 Jeremy Allen and sat my recording equipment down on his highly polished
96 dining room table.

97 Can you scoot out just a teeny tiny little bit? Okay. So tell me, where are
98 you from originally?

99 Mr. JEREMY ALLEN (President, Bone Measurement Institute): I'm from
100 England.

101 SPIEGEL: Jeremy Allen came to the United States in the 1980s and went
102 to work for a large pharmaceutical company. He had success, much
103 success at various drug and drug research companies. Then in 1995, Allen
104 was approached by the drug company Merck. The pharmaceutical giant
105 had just released a new drug, Fosamax.

106 Mr. ALLEN: Fosamax was the first drug that could credibly make a claim to
107 stop the progress of osteoporosis.

108 SPIEGEL: Now, osteoporosis is a serious problem that affects millions of
109 women, and Fosamax was the first nonhormonal treatment, so the potential
110 market was enormous. But Allen says that after its release, sales of
111 Fosamax were slow. Allen had known the president of Merck America, this
112 guy named David Anstice, for years; they'd worked together at another
113 company. And so, Allen says Anstice came to him with a proposition:
114 Figure out this problem and then fix it.

115 Mr. ALLEN: My job description read: Provide some out of the box thinking.
116 That was a great job description.

117 SPIEGEL: Allen set to work. He talked to doctors, researchers, and soon,
118 the issue with Fosamax sales became clear: In order to get large numbers
119 of women on Fosamax, large numbers of women needed to be diagnosed
120 with osteoporosis by getting their bones scanned. But in America in 1995,
121 there was simply no way to do that.

122 Mr. ALLEN: The only diagnostic procedure was an expensive machine
123 called a bone densitometer that was costing the patient between 200, 250,
124 \$300 per test. And there were only a couple of hundred testing centers in
125 the United States, which meant that almost everybody had a day's ride, or
126 had to go from the suburbs downtown to get the test. It was expensive and
127 it was inaccessible, so lo and behold, nobody did it.

128 SPIEGEL: To sell Fosamax then, Merck and Allen needed to do two things:
129 place machines that could measure bone density in doctors' offices all
130 across America and bring down the price of the tests.

131 But Allen says for him, this wasn't just about selling drugs; it was about
132 helping people. He points out that one in five elderly women will die within a
133 year of a hip break.

134 Mr. ALLEN: Clearly, that's not very good.

135 SPIEGEL: And so, armed with the firm conviction that he was about to do
136 good in the world, and coincidentally sell a ton of drugs for Merck, Jeremy
137 Allen set out to completely rework the way that bone was measured in
138 America.

139 Now, to do this, he figured, the first thing he needed was an institution, an
140 entity whose mission was not to sell drugs, but to serve the public good. So
141 he decided to create one. In 1995, Allen convinced Merck to establish a
142 nonprofit called the Bone Measurement Institute. On its board were six of
143 the most respected osteoporosis researchers in the country. But the
144 institute itself had a rather slim staff: Allen, you see, was its only employee.

145 Mr. ALLEN: There was no payroll, there was no building, there was no
146 office with the name Bone Measurement Institute.

147 SPIEGEL: It was literally like your desk at Merck?

148 Mr. ALLEN: Yes, I was it.

149 SPIEGEL: Now, once this institute was established, Allen sought some
150 alternative to the usual way that bone was measured in America. Instead of
151 machines that were big and expensive, he wanted machines that were
152 cheap and small, and soon, he found them.

153 Mr. ALLEN: You could use what was called peripheral machines, measure
154 bone density at the forearm or at the heel, rather than the hip and spine.

155 SPIEGEL: Allen felt these smaller machines were the perfect solution. The
156 problem he says was that few companies produced them.

157 Mr. ALLEN: So we went very strongly to the six or seven manufacturers
158 who were either in this business or wanted to get into this business and
159 said, we will fund your development of these other machines.

160 SPIEGEL: But several of the machine companies weren't as enthusiastic
161 as Allen had hoped. In fact, according to Allen, two of the dominant players
162 were downright hostile.

163 Mr. ALLEN: Because it wasn't as profitable. I was a threat to their business
164 model. Their business model was to sell just a few machines at a very, very
165 high price. And I wanted them to sell a lot of machines at a much lower
166 price.

167 SPIEGEL: And you were going to their competitors and help subsidize their
168 competitors if they didn't change their model?

169 Mr. ALLEN: Yes.

170 SPIEGEL: Jeremy Allen, though, isn't the only person with a version of this
171 story.

172 Dr. RICHARD MAZESS (Founder, Lunar Corporation): We had a - not a
173 very comfortable relationship with Jeremy Allen and his so-called Bone
174 Measurement Institute.

175 SPIEGEL: This is Richard Mazess, founder of the Lunar Corporation, one
176 of the largest producers of bone density machines. Now, Mazess does
177 remember Allen's proposal, but says his resistance had absolutely nothing
178 to do with money. The problem with peripheral machines, Mazess says, is
179 that taking a measurement of someone's finger or forearm isn't going to tell
180 you what you need to know about the bones in the part of the body which, if
181 fractured, actually threaten a woman's health: the spine and the hip. And
182 therefore, Mazess says, the machines could only lead to bad medicine.

183 Dr. MAZESS: We were not about to go ahead and tell physicians to use
184 inadequate diagnostic equipment simply because Merck wanted that. And
185 we were threatened, basically, that we will support your competitors and
186 that we will tell the people that are working with Merck not to use Lunar
187 machines. They were going to make sure that we paid the price.

188 SPIEGEL: And Lunar wasn't the only company put on notice. Jeremy Allen
189 says that to encourage other companies to take seriously Merck's goal of
190 dropping the price of measuring machines, Merck actually purchased a
191 bone measurement business.

192 Mr. ALLEN: We bought one of the companies and showed how low the
193 price could become purely to get everybody's attention. And we got
194 everybody's attention. And subsequently, when everybody else moved, we
195 let it go, and the company closed. And we cheered its demise.

196 SPIEGEL: Now, there is a third version of this story. Paul Strain is a lawyer
197 who represents Merck's corporate office. And though he wasn't able to
198 comment on many of the particulars of Jeremy Allen's story, he did confirm
199 the broad outline: that the Bone Measurement Institute worked to spread
200 the number of machines. However, Strain completely rejects this idea that
201 the smaller machines Merck promoted were inferior, that a scan of the wrist
202 or forearm doesn't provide good information about the risk of hip fracture.

203 Mr. PAUL STRAIN (Attorney): Oh, I think there definitely is a clear
204 correlation, and I think there are many, many studies that have shown that.

205 SPIEGEL: But others disagree. In fact, according to Sanford Baim, former
206 president of the International Society for Clinical Densitometry, smaller
207 machines should only rarely be used in diagnosis. Nevertheless, Allen says
208 Merck helped to get the smaller machines through the FDA process by
209 funding trials and assisting with submissions. He says pamphlets from each
210 company were sent out with a Fosamax sales force. Merck even created a
211 leasing program so that doctors could finance the purchase of a machine,
212 big or small.

213 More importantly, Merck worked to change the very economics of
214 measuring bone by getting bone scans reimbursed by Medicare.

215 Now, Jeremy Allen actually left the Bone Measurement Institute before
216 much of this work took place. But in 1997, the institute and several other
217 interested organizations successfully lobbied to pass the Bone Mass
218 Measurement Act, which changed Medicare reimbursement rules. Several
219 of those other organizations, by the way, also got funding from Merck. And
220 according to Steve Cummings, director of clinical research at California
221 Pacific Medical Center Research Institute, and a major bone researcher
222 who's followed these issues for years, it is impossible to overemphasize
223 just how important this legislation was.

224 Dr. STEVE CUMMINGS (Former Director of Clinical Research, California
225 Pacific Medical Center Research Institute): Up to that point, patients
226 needed to pay for bone densitometry out of their own pocket. Now that it's
227 reimbursed, clinicians can now be reimbursed if they buy the machines.
228 They get paid for making measurements of bone density. And in the 1990s
229 and into the early 2000s, measuring bone density is a profitable thing to do.

230 SPIEGEL: Now, as Cummings points out, 1997 was also the year that
231 Merck got clearance from the FDA for a new version of its drug.

232 Dr. CUMMINGS: Merck developed a dose of Fosamax, a five-milligram,
233 lower dose that was intended for use by women who had osteopenia.

234 SPIEGEL: And here is where we get back to this question of how
235 osteopenia, Katie Benghauser's diagnosis, ultimately became a widely
236 treated condition.

237 Cummings says that in order to understand how come so many women
238 today are treated for osteopenia, what you need to do is look more closely
239 at all of the machines - big and small - that Merck helped to place in
240 doctors' offices.

241 Dr. CUMMINGS: I think the critical event in turning osteopenia into a
242 condition that people believe needs treatment is the report that comes from
243 the bone density machine that says osteopenia.

244 SPIEGEL: See, when these tests are done, the machines produce a report,
245 or chart, really. Recently, my producer Gisele Grayson and I went to a
246 doctor to get tested at the Fairfax Radiology Center in Fairfax, Virginia. A

247 technician named Jasmine Wilson(ph) loaded Gisele onto a large machine
248 that measured the hip and spine.

249 Ms. JASMINE WILSON (Technician, Fairfax Radiology Center): Have you
250 ever had a bone density before? Super easy. I'm just going to ask you to lie
251 down on your back for me, head at the pillow.

252 SPIEGEL: A button was pushed, and two minutes later, Wilson was holding
253 a paper with a clear, color-coded chart at the bottom.

254 Ms. WILSON: We have a color graph: green, yellow and red. Green
255 indicates normal bone density. Yellow is osteopenia, and then red is
256 osteoporosis.

257 SPIEGEL: Now, Gisele is 38 years old, the mother of two. And I know she
258 often says this about herself, so I feel comfortable saying it. Pretty much
259 everything about her screams perky, except apparently her bone density.

260 Ms. WILSON: So according to the color graph here, you're in the yellow,
261 which indicates osteopenia.

262 SPIEGEL: Now, it's highly unlikely that a doctor would medicate Gisele.
263 She's too young. But Steve Cummings argues that the very existence of
264 this word osteopenia on these medical reports has this incredible impact.

265 Dr. CUMMINGS: When millions of women are getting the word osteopenia
266 from the bone density test that they're getting in their 50s and 60s, they get
267 worried. When a clinician sees the word osteopenia on a report, they think
268 it's a disease. They want to know: What should I do?

269 SPIEGEL: Now, Merck, and eventually other companies, are running
270 commercials advertising drugs to prevent osteoporosis. And those
271 commercials don't feature humped grannies but young-looking women.
272 And, says Cummings, at a certain stage, it simply reaches this tipping
273 point.

274 Dr. CUMMINGS: Bone densitometry becomes increasingly available. And
275 women start wanting it, and they hear their friends have had a
276 measurement of bone density, and their friend was told that they have

277 osteopenia, and they want to know whether they should be treated. And so,
278 it's almost viral.

279 SPIEGEL: And through this process of testing, at least 1.5 million tests by
280 1999, and advertising, eventually a cultural consensus takes hold.
281 Osteopenia simply becomes a condition that should be seriously
282 considered for treatment. And for many people, particularly Jeremy Allen,
283 this is all for the good. Everyone has won.

284 Mr. ALLEN: Fosamax became a successful drug, and there are a lot less
285 women dying of hip fractures or stooped over than there were a couple of
286 generations ago.

287 SPIEGEL: Well, maybe. Yes, there is a scientific consensus that it's
288 beneficial to give Fosamax to women with osteoporosis, especially older
289 women and any woman who has already had a fracture.

290 Paul Strain, the lawyer from Merck, argues that Fosamax also is good for
291 women with osteopenia. He says it builds bones and therefore prevents
292 fractures in osteopenic women.

293 Mr. STRAIN: It's well-established that there is a clear correlation between
294 bone mineral density and fracture risk. And by preserving and maintaining
295 bone mineral density, Fosamax lowers their risk of fracture.

296 SPIEGEL: But increasingly, bone scientists say Fosamax is not necessarily
297 a win for women with osteopenia.

298 Both Steve Cummings and Susan Ott, professor of medicine at the
299 University of Washington, say studies in women with osteopenia show that
300 while very rare spinal fractures are reduced, the types of bone fractures
301 most common among women with osteopenia are not affected. Susan Ott.

302 Professor SUSAN OTT (Medicine, University of Washington): There was
303 no difference in how many fractures you had, whether you took the
304 medicine or a placebo. It does make your bone density go up higher, but
305 the number of fractures is what really matters, and that didn't really change.

306 SPIEGEL: And what about the long-term? Among women with osteopenia
307 who start Fosamax, say, at age 50 and continue to 60 and beyond in the

308 hopes of preventing old-age fractures. Well, there are no studies of what
309 happens to those women more than 10 years out, and none are planned.

310 So Steve Cummings says treatment should start only when risk is
311 significant or a woman already has a spine fracture. Susan Ott even
312 worries that taking these medications long-term - over 10 years or more -
313 might actually make bones brittle.

314 Ott points to a very small number of case reports about spontaneous
315 breaks in the upper leg, which - though rare - could be important, she says,
316 given what's at stake.

317 Prof. OTT: Instead of preventing fractures, you might get fractures. But it
318 certainly doesn't happen in the first five years.

319 SPIEGEL: So among specialists, there is still controversy about when
320 women with osteopenia should get this medication. But what is clear is that
321 getting that box of pills into Katie Banghauser's medicine cabinet wasn't a
322 simple matter. Jeremy Allen told me it just took a huge amount of work,
323 work he loved because from his perspective, he helped save lives.

324 Mr. ALLEN: I get a great sense of satisfaction that I was able to re-jigger
325 the marketplace so that women could be treated for osteoporosis before it
326 got them. That was a good episode of my life.

327 SPIEGEL: But Richard Mazess from the Lunar Corporation doesn't see it
328 that way.

329 Dr. MAZESS: He was complicit in a plot to misdiagnose American women.

330 SPIEGEL: From Mazess' perspective, millions of women with osteopenia
331 are now needlessly exposed to the risks of a medication that may not
332 ultimately help them.

333 And the paradox of our health care system is that both of these men are
334 probably right. That is, drug companies produce these incredible drugs that
335 greatly relieve suffering. But one way they profit from those drugs is to
336 extend their use so that medications are used in populations with milder
337 and milder versions of a disease, and the risks of medicating can come to
338 outweigh the benefits. I've told you a story about osteoporosis and

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339 osteopenia. But there are versions of this story about a lot of diagnoses.
340 Caleb Alexander is a pharmacoepidemiologist at the University of Chicago,
341 and he says the dynamic is well understood:

342 Mr. CALEB ALEXANDER (Pharmacoepidemiologist, University of
343 Chicago): Whether you consider treatments for osteoporosis or treatments
344 for depression or treatments for high cholesterol - in all of these settings -
345 pharmaceutical firms stand to benefit if the therapies for these diseases are
346 broadly used, even if they're being used among people that have very mild
347 forms of these diseases.

348 SPIEGEL: So, tonight before bed, open your medicine cabinet. There you
349 will see a shelf of pillboxes, many with complicated biographies.

350 Alix Spiegel, NPR News, Washington.

351 (Soundbite of music)

352 NORRIS: At our Web site, you can see an image from a bone density scan
353 and find a chart of Fosamax sales over the years. You can find that at
354 npr.org.

355 (Soundbite of music)

356 NORRIS: You're listening to ALL THINGS CONSIDERED from NPR News.

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