

In this subgroup, the MI rate ran 2.5% in women randomized to calcium supplement treatment, and 2.0% among women in the placebo arm, a 22% relative increased MI rate with the calcium supplement that was statistically significant. The rate of MI or stroke ran a relative 16% higher among the women taking the calcium supplement, which was also statistically significant. The results showed no significant effect of calcium supplementation on stroke rate. "We saw the same effect as in the meta-analysis," Dr. Reid said.

But if Dr. Reid's analysis did not start

with a prior hypothesis, this finding can only be considered hypothesis generat-



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DR. REID

ing, not hypothesis testing, Dr. Manson said in an interview. "Many subgroups

were tested in the WHI, and some would be expected to show significant effect modification by chance," she pointed out. In addition, randomization made background levels of calcium use similar in the two treatment arms and thereby neutralized background calcium use as a possible confounder. Dr. Manson also noted that if supplemental calcium posed a risk, the event rates should have been highest among women taking both the study calcium dose and an additional dose on their own.

When the Auckland researchers added the results from the WHI subanalysis to

their previously reported meta-analysis, they "just reinforced the trends and made them more significant," Dr. Reid said in an interview.

When data from the WHI subgroup that did not use personal calcium supplements at baseline were added to the meta-analysis, the results showed that those who did take supplements had a 24% relative excess of MIs, a 15% relative excess of stroke, and a 16% relative excess of MI or stroke, he reported.



There are concerns about 'whether omitting the subgroups with favorable results is appropriate.'

DR. MANSON

"What we now have is six or seven very large trials, and [the results they show] for myocardial infarction all line up very consistently, without significant heterogeneity. When you look at risk vs. benefit, the evidence for an increased risk of myocardial infarction is stronger than the evidence that calcium supplements prevent bone fractures. It's hard to justify continuing calcium supplements," Dr. Reid said. ■

Indications for Use

The CGMS *iPro* Digital Recorder is intended to continuously record interstitial glucose levels in persons with diabetes mellitus. This information is intended to supplement, not replace, blood glucose information obtained using standard home glucose monitoring devices. The information collected by the digital recorder may be downloaded and displayed on a computer and reviewed by healthcare professionals.

This information may allow identification of patterns of glucose-level excursions above or below the desired range, facilitating therapy adjustments which may minimize these excursions.

The CGMS *iPro* Digital Recorder:

- Is intended for prescription use only.
- Will not allow readings to be made available directly to patients in real time.
- Provides readings that will be available for review by physicians after the recording interval (72 hours).
- Is currently intended for occasional rather than everyday use.
- Is to be used only as a supplement to, and not a replacement for, standard invasive measurement.
- Is not intended to change patient management based on the numbers generated, but to guide future management of the patient based on response to trends noticed. That is, these trends or patterns may be used to suggest when to take fingerstick glucose measurements to better manage the patient.

The glucose sensor, tester, charger, and CGMS *iProWand* are intended for use with the CGMS *iPro* Digital Recorder. The Sen-serter® device is indicated only for insertion of the Medtronic MiniMed glucose sensor.

Important Safety Information

Contraindication

Do not use magnetic mattress pads while wearing the CGMS *iPro* Digital Recorder.

Warning

Product contains small parts and may pose a choking hazard for young children.

Important Safety Information, continued

Sensor

The glucose sensor should be removed if redness, bleeding, pain, tenderness, irritation, or inflammation develops at insertion site, or if you experience unexplained fever. An optional occlusive dressing should be removed if irritation or reaction to the tape develops.

The glucose sensor may create special needs regarding your patients' medical conditions or medications. Healthcare professionals should discuss this with their patients before they use the glucose sensor.

Wait 5 minutes after glucose sensor insertion before setting up the CGMS *iPro* Digital Recorder with Solutions CGMS *iPro*.

- Make sure that the site is not bleeding before connection.
- If bleeding occurs, apply steady pressure with a sterile gauze or clean cloth at the insertion site until bleeding stops. After bleeding stops, attach the digital recorder to the glucose sensor.
- If bleeding persists after 3 minutes, remove the glucose sensor and discard. Insert a new glucose sensor in a different location.

Contact the 24 Hour HelpLine if you experience any adverse reactions associated with the digital recorder or glucose sensor.

Precautions

If performing multiple CGMS *iPro* Digital Recorder studies on the same patient, establish a rotation schedule for choosing new glucose sensor sites. Avoid sites that are constrained by clothing, have scar tissue, or are subject to rigorous movement during exercise.

For additional information, please consult the *iPro* CGM user guides.

iPro™ is a trademark of Medtronic MiniMed, Inc. Sen-serter® is a registered trademark of Medtronic MiniMed, Inc.

References

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Bone Changes Precede RA Symptoms

Bone metabolism appears to change before patients show clinical signs of rheumatoid arthritis and could ultimately serve as an early marker of disease, based on a study of 79 patients.

"There appears to be an alteration in bone metabolism parallel to inflammation and autoimmunity in the asymptomatic preclinical phase of RA, which may reflect the beginning of joint destruction," according to Dr. Dirkjan van Schaardenburg, a rheumatologist at Jan van Breemen Institute in Amsterdam, and his coinvestigators.

They found significantly increased average levels of only P1NP (procollagen type I intact N-terminal propeptide) and osteoprotegerin in the group of preclinical RA patients, compared with a control group of healthy individuals. Specifically, P1NP increased by 5 ng/mL and osteoprotegerin increased by 4 pmol/L (*Ann. Rheum. Dis.* 2010 Oct. 18 [doi:10.1136/ard.2010.135723]).

Three blood samples taken 1, 2, and 5 years prior to the onset of symptoms were identified for 47 patients with RA; two samples were collected from 18 patients and one sample was collected from 14 patients. The individuals had been blood donors prior to developing the disease.

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—Kerri Wachter