groups and health care providers with lower rates of recommended medication use. These measures alone may not be sufficient, and investment in other, innovative approaches to promoting evidence-based prescribing practices is warranted. The correlation between use of these therapies and beneficial outcomes in these and other subpopulations also needs further assessment.

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**Coffee Intake and Glucose Homeostasis: Is There a Role for Body Iron?**

Since the original report by van Dam et al, coffee drinking has been associated with a decreased risk of type 2 diabetes mellitus in a number of epidemiological studies. However, body iron has for over a century been known to cause diabetes if in overt excess, manifested as the “bronzed diabetes”—hereditary hemochromatosis. We hypothesize in line with Mascitelli et al in their letter to the editor regarding a study by Pereira et al that the protective effect that coffee shows toward type 2 diabetes mellitus is perhaps, at least partially, explained by the iron absorption inhibitory effect of coffee. If this were so, subjects who consume much coffee should have lower body iron stores and better glucose homeostasis compared with people who drink less or no coffee.

**Methods.** We looked at the association of coffee consumption with body iron and glucose homeostasis in 2682 men, aged 42 to 60 years, in the Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD) in eastern Finland. The KIH study has been approved by the joint research ethics committee of the University of Kuopio and Kuopio University Hospital. Dietary intake of food-stuffs was estimated by a 4-day food record, body iron was assessed as serum ferritin concentration, and glucose homeostasis was studied by the updated homeostasis model assessment (HOMA2) insulin resistance (IR) and pancreatic β-cell function (%B). The steady-state nonlinear HOMA2 models the interplay between hepatic glucose output, body glucose uptake, and insulin secretion and produces computational IR and %B parameters. The model sets the normal IR to 1.0 and the normal %B to 100. Ferritin, glucose, and insulin measurements were carried out in fasting state samples, as previously described.

**Results.** The mean (SD) values for the study subjects was 53.1 (5.1) years for age; 566 (297) mL/d for coffee intake; 168 (152) µg/L for serum ferritin concentration; 1.51 (0.89) for IR; and 112% (39%) for %B.

In an unadjusted linear regression model, IR decreased 2.1% per 100-mL increase in coffee intake and %B decreased 0.8%. Adjustment for ferritin level attenuated the association of coffee intake with IR from −0.843 (P = .001) to −0.009 (P = 0.03) (difference, −54%) and the association of coffee intake with %B from −0.843 (P = .001) to −0.706 (P = .008) (difference, −16%). In the multivariate-adjusted linear regression models, serum ferritin adjustment weakened the age- and body mass index (BMI)-adjusted association of coffee intake with IR markedly (Table, model 2). Multivariate analyses of coffee intake and %B were very resistant to adjustments. Furthermore, serum ferritin concentra-
tion was not associated with %β in these models, probably because adding BMI to our statistical model made the association between iron and B-cell function disappear (regression coefficient, −0.002 [P = .96] with BMI [Table, model 2] vs 0.200 [P < .001] without BMI [model not shown]). Further adjustment for other dietary factors that relate to iron balance, such as intakes of red meats, vegetables, and milk, and for total energy intake did not confound the observed associations significantly (data not shown).

Comment. These results suggest that coffee consumption may be associated with both body iron stores and glucose homeostasis as measured by HOMA2 IR and HOMA2 %β. Furthermore, the results suggest that the association of coffee intake with IR may be partially explained by a decrease in body iron level.

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Table. Multivariate-Adjusted Linear Regression of Coffee Intake With HOMA2 IR and %β

<table>
<thead>
<tr>
<th>Model</th>
<th>HOMA2 IR, Regression Coefficient (95% CI)</th>
<th>P Value</th>
<th>HOMA2 %β, Regression Coefficient (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coffee intake (per 100 mL/d)</td>
<td>-0.010 (-0.020 to -0.000)</td>
<td>.04</td>
<td>-0.579 (-1.073 to -0.081)</td>
<td>.02</td>
</tr>
<tr>
<td>Age, y</td>
<td>0.005 (-0.001 to 0.010)</td>
<td>.11</td>
<td>-0.045 (-0.333 to 0.244)</td>
<td>.76</td>
</tr>
<tr>
<td>BMI</td>
<td>0.140 (0.132 to 0.148)</td>
<td>&lt;.001</td>
<td>3.42 (2.30 to 3.83)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coffee intake (per 100 mL/d)</td>
<td>-0.004 (-0.014 to 0.006)</td>
<td>.43</td>
<td>-0.580 (-1.079 to -0.081)</td>
<td>.02</td>
</tr>
<tr>
<td>Age, y</td>
<td>0.008 (0.002 to 0.013)</td>
<td>.07</td>
<td>-0.045 (-0.336 to 0.245)</td>
<td>.76</td>
</tr>
<tr>
<td>BMI</td>
<td>0.130 (0.122 to 0.138)</td>
<td>&lt;.001</td>
<td>3.42 (2.99 to 3.85)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Serum ferritin concentration (per 10 µg/L)</td>
<td>0.010 (0.008 to 0.012)</td>
<td>&lt;.001</td>
<td>-0.002 (-0.103 to 0.099)</td>
<td>.94</td>
</tr>
</tbody>
</table>

Abbreviations: %β, pancreatic β-cell function; BMI, body mass index; IR, insulin resistance; HOMA2, updated homeostasis model assessment.

1401

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