assignments, as those close together were still poorly corre-
lated. More likely, physicians were taking into account vari-
ables not contained in the MEWS, in assigning a PAR score.

We conclude that the combined use of PAR and MEWS is
more accurate than MEWS alone. A generalizable way to in-
corporate clinical judgment into aggregated weighted scor-
ing systems on the wards may improve detection of clinical de-
terioration and assist with timely mobilization of resources to
address the etiology of clinical deterioration.

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Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Patel, Zadravecz, Edelson.

Critical revision of the manuscript for important intellectual content: Patel,
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Statistical analysis: Zadravecz, Churpek.

Administrative, technical, or material support: Patel, Young, Edelson.

Study supervision: Patel, Churpek, Edelson.

Conflict of Interest Disclosures: None reported.

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Medicine Annual Meeting; May 17, 2013; National Harbor, Maryland.

Methods | To quantify the potential public health importance
of this issue, we examined 2007 to 2012 data from the
National Health and Nutrition Examination Survey to assess how
much metformin nonuse may be attributable to excessive con-
cern about safety in renal insufficiency. Analysis was re-
stricted to participants using oral diabetes drugs. Patients who
reported heart or liver failure, which are also potential con-
traindications to metformin use, were excluded. Sex, age, race/
ethnicity, serum creatinine level, and eGFR6 were examined
as predictors of metformin use. Analysis was conducted using
statistical software (R; http://www.r-project.org/).

Results | In 2011-2012, the rate of metformin use in patients
with an eGFR exceeding 90 mL/min was 90.4% (Figure). At

![Figure. Percentage of Metformin Use Among Patients Taking Oral
Diabetes Medication vs Estimated Glomerular Filtration Rate (eGFR)](image-url)

Metaforin Use Reduction in Mild to Moderate
Renal Impairment: Possible Inappropriate
Curbing of Use Based on Food and Drug
Administration Contraindications

Metformin hydrochloride is the first-line drug for type 2 dia-
betes mellitus (T2DM)1 and is the only oral diabetes drug with
evidence for improved cardiovascular outcomes. Despite this,

half of the patients with T2DM do not take metformin. Even
in patients who are taking other oral T2DM drugs, only about
70% use metformin.2

One likely explanation for this shortfall is the avoidance
of metformin use in renal insufficiency. The drug carries a con-
traindication against use when serum creatinine levels ex-
ceed 1.4 mg/dL in women or 1.5 mg/dL in men based on fears
about lactic acidosis (to convert creatinine level to micro-
moles per liter, multiply by 88.4). This contraindication has
been widely criticized as overly conservative.1,3 Professional
societies support metformin use at estimated glomerular fil-
tration rates (eGFRs), a better measure of renal function than
the serum creatinine level, of 45 or even 30 mL/min (which typi-
cally equates to a serum creatinine level of about 2 mg/dL).1

Because this contraindication may inappropriately discour-
age metformin use in patients with mild renal impairment, US
Food and Drug Administration (FDA) citizen petitions4,5 were
filed in 2012 and 2013, respectively, requesting that the con-
traindication be relaxed and reframed in terms of the more
modern eGFR measure, although the FDA has provided no sub-
stantive response.

Metformin Use, 2011-2012, %

<table>
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<th>eGFR, mL/min</th>
<th>0-29</th>
<th>30-45</th>
<th>46-60</th>
<th>61-90</th>
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<td>10</td>
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<td>10</td>
</tr>
<tr>
<td>&gt;90</td>
<td>40</td>
<td>30</td>
<td>20</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>

Calculated using National Health and Nutrition Examination Survey data from
2011 to 2012.
Abbreviation: NA, not applicable.

Theoretical shortfall is the difference between the observed number of metformin users and the number that would be expected if the 90.4% metformin use rate seen in the highest eGFR category carried over to other categories.

eGFRs greater than 60 to 90 mL/min, at which renal function is mildly impaired but the serum creatinine level is typically below the contraindication cutoff, the rate was 80.6%. At eGFRs of 30 to 60 mL/min, at which metformin use is usually formally contraindicated but professional guidelines support cautious use, rates were 48.6% to 57.4%. At eGFRs below 30 mL/min, at which metformin use is discouraged, the rate was 17.9%.

An estimate of the influence of renal contraindications on metformin use is summarized in the Table. If the 90.4% use rates listed above for an eGFR exceeding 90 mL/min were seen with an eGFR greater than 60 to 90 mL/min, approximately 425,000 additional patients would take metformin. If these rates were extended down to an eGFR of 30 mL/min, the number of patients taking metformin would increase by about an additional 560,000. Most important, these figures do not include patients who are receiving no oral diabetes agents, so they are almost certainly underestimates. However, a lower eGFR may be associated with other factors (eg, undocumented heart failure) that might account for some portion of this shortfall.

Discussion | These findings are relevant to clinical care and health policy because they indicate that exaggerated concerns about the safety of metformin use in renal impairment may unnecessarily prevent its use in hundreds of thousands of patients, even at eGFRs exceeding 60 mL/min. The approximately 50% rate of metformin nonuse in patients with eGFRs between 30 and 60 mL/min has multiple potential causes, but one likely contributing factor is the inconsistency between professional society guidelines and the FDA label. The FDA is overdue to revisit the contraindication to metformin use in patients with renal insufficiency, which may be worsening the care of almost 1 million patients with T2DM in the United States.

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COMMENT & RESPONSE

LESS IS MORE

“Less Is More” and The House of God: Was The Fat Man Right Again?

To the Editor | Set in the early 1970s, The House of God is a semi-autobiographical account of Stephen Joseph Bergman’s (aka, Samuel Shem’s) medical internship in Boston. One of