s? The AdViSHE Assessment Tool

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il 2016 of the Assessment of the Validation Status of Health-Economic Decision Models (AdViSHE) models raises a number of issues that the health technology assessment literature has yet to address. The he role of decision models in generating claims that are evaluable and replicable. Unfortunately, this is not checklist which is intended to address the perceived need for a tradeoff between confidence in a decision o allocate resources by developers and payers to validating the model. Irrespective of the degree of er or payers may have in the sufficiency of the model in representing 'reality' unless the model has claims and evidence for those claims in target treating populations, the model fails the standards of normal e absence of a commitment in the AdViSHE checklist to the modeling of claims that are evaluable and on check list makes no allowance for a product pricing strategy that may commits a manufacturer to regular l or semi-annual product price increases. Indeed, product pricing assumptions are conspicuous by their ntary argues that failure to accommodate anticipated pricing behavior renders lifetime cost-per-QALY cation of willingness-to-pay thresholds meaningless. Type: Commentary

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'alidating Imaginary Worlds? The AdViSHE ssessment Tool

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; Imaginary Worlds? The AdViSHE Assessment Tool

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ls raises a number of issues that the health technology assessment literature has yet to address. Th
cision models in generating claims that are evaluable and replicable. Unfortunately, this is not
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levelopers and payers to validating the model. Irrespective of the degree of confidence a develop
ncy of the model in representing 'reality' unless the model has generated evaluable claims and evi
ing populations, the model fails the standards of normal science. Apart from the absence of a comm
e modeling of claims that are evaluable and replicable, the validation check list makes no allowanc
may commits a manufacturer to regular and substantial annual or semi-annual product price incr
ptions are conspicuous by their absence. The commentary argues that failure to accommoda
ers lifetime cost-per-QALY models and the application of willingness-to-pay thresholds meaningles

ViSHE, validation, imaginary worlds, simulations, pricing, thresholds

Vemer et al published details of the Assessment ion Status of Health-Economic Decision Models ol [1]. This tool is a checklist to support the decision models. The objectives are to evaluate odel is a proper and sufficient representation of is intended to represent'. For the authors, a l is one that 'is in accordance with what is known em' while 'sufficient' means that the results of n serve as a 'solid basis' for decision making'. us attempts to set standards for model validity ssessment, the AdViSHE tool focuses on the e-off between building confidence in the model urces to support its validation. The tool presents ist of validation efforts with the objective of e resources yet improving the model's validation eptability for developers and payers.

The purpose of this commentary is to tool kit and its recommendations f priorities from the perspective that the is only meaningful if the model supports outcomes that are credible, evaluable where there is evidence for claims asses fails to support the assessment of claim may be seen as the intrinsic merits c model, then the model fails the standar [4] [5] [6]. As such, it should be considere sharing the stage with intelligent desig selection. If this is the case then regardl 'sufficiency of the 'proper' model, w necessarily entailed, it is difficult to see meaningful input to inform formulary includes providing feedback for the supporting ongoing disease area a reviews. Irrespective, therefore, of the

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builder may have in the model, this n
payers [7 8]. More to the point, payers s
models generating non-evaluable produ

The AdViSHE Toolkit

The toolkif is the outcome of what
exhaustive review process of modified
workshop at the International Society fo
and Outcomes Research (ISPOR) 2014 M
agreed final version of AdViSHE cons
covering the validation of: (i) the conce

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computerized model; and (iv) the behavior and
e model outcomes.

nt checklist is in five parts. Part A addresses the
lidation of the conceptual model and comprises
. The first questions address the question of face
ugh asking experts to judge the models
ss while the second question asks whether the
een compared to other conceptual models to
s validity. Part B comprises two questions on
idation to establish, first, an expert assessment
for the appropriateness of the input data and,
aluation of the fit of the model where the input
re based upon regression models. Part C
our questions on the validation of the
model. These cover: (i) an expert external
model; (ii) model testing for extreme values; (iii)
nent of patient tracking through the model; and
ub-modules in the model. Part D considers, with
s, the operational validity of the model. These
assessment of the face validity of the model
cross validation of the outcomes against those
similar outcomes; (iii) validation against
ng alternative input data; and (iv) validation
aring outcomes to empirical data. A final section,
whether other validation techniques have been

ent checklist is seen as representing a
etween what is feasible and what is necessary in

decision makers. Unfortunately, this po
acceptance in health technology asses
claim to meet validation standards
standards for credible, evaluable and re
seen in the ISPOR-SDMS standards
predictive validation is seen as perhap
test for model credibility as a validation
is considered neither necessary nor su
merits of a model.

It is far from clear what the term 'outc
encompass in the AdViSHE checklist. W
D1) are asked to judge the appropria
outcomes, there is no discrimination be
non-evaluable claims. The same critic
validation (Question D2) where the mod
assessed against those of other model
outcomes. There is no requiremen
competing models should be evaluated
no attempt to present evaluable claim
assessment is asked to contrast one
claims against another. This seems to
validation where a more appropriate as
evaluable claims, is to contrast one m
those of another empirically. If this
irrespective of claims for the superiori
another in its structure, assumptions,
decision maker has no idea whether t
even if they are wrong. The same argum
of Question D3 where outcomes a

ling from developer and payer perspectives. It is menting existing validation tools, with particular he ISPOR-SMDM modeling standards, in asking on aspects were tested, how they were tested tcomes are reported [9] [10]. In seeking to avoid idations while identifying unreported validation e benefit of the AdViSHE tool is seen by its llowing model developers to build confidence in through commenting on validations already As such, it reduces overlap between validation of pers and those of model users. The key eing, particularly from a payer perspective, that e relevant to their decision making.

aluation and Replication

AdViSHE framework addresses the issue of re is no attempt to raise the issue of evaluable claims as a criterion for model validation. This is t because it allows the model builder to fall back t if the model is considered sufficient in its n of 'reality' then, because the simulated necessarily entailed, the model can 'inform'

alternative input data. Finally, in valida data (Question D4) there is still confus comparison should take. Information aspects of possible empirical assessm based on summary statistics or patient l differences between model outcomes These comparisons apparently involve (i the data sources on which the model validation) and (ii) a comparison against not used to build the model (independ the latter comparison could be interpret claims in target treating populations, t clear. There is no hint that decision mak that actually generate evaluable claims.

Lifetime Cost-Per-QALY Models

Although not mentioned, the AdViSHE relevant, not only to models that are evaluable and replicable claims for populations, but also for models that 'imaginary worlds'. The failure to ma important because of the popularity c

health technology assessment literature [11] [12] [13] clear from the AdViSHE tool whether there is a thin each disease state, there exists an 'ideal' model that, on the evidence available, can inform ers and justify formulary decisions across erapies. Otherwise, in the absence of any ms, we fall back on a (somewhat pointless) he relative merits of competing models, jostling e with competing manufacturers funding and dels that support their own product.

eference case standards for modeled claims in ealth system does not address the issue of claims her, acceptance of reference case frameworks, ng-term or lifetime modeling of chronic disease, acceptance of modeled imaginary worlds as a formulary decision making. In reference case ocus is on the model itself rather than any the claims generated by the model. In the case

sought by manufacturers is deemed modeled cost-per-QALY falls below a judged cost-effective. Otherwise, the IC discounted price to bring it in line.

A Foot in the Door

Looking back over the past 20 years, it the view that the effort put into deve validation criteria for modeling and stud the perspective of manufacturers wh much of this activity, as nothing more respectable' support for pricing and ma Unfortunately, the AdViSHE tool does belief as pricing assumptions are not con element.

Of course, as noted, in single payer syste on pricing subsequent to market entry. the US. There is abundant evidence for

d the Netherlands, to give two examples, the
e is the standard [16] [17] [18]. As long as the model
erence case criteria and receives, in the case of
of approval from the external review group and
endorsement, the issue of claims evaluation is
ndeed, as pointed out in previous reviews of the
n framework, the reference case is not actually
enerate evaluable claims. Rather, it is a pricing
allocation exercise. If, the final version of the
ts cost-per-QALY claims below a lifetime or long
QALY willingness to pay threshold then the price
a manufacturer is accepted. If not, negotiations
wer price, discounts or some form of risk
ssue. Manufacturers are on notice, therefore,
to submit a modeled reference case submission
pproval within the National Health Service.
adjust their target price to meet a willingness-
old or opt to argue for a premium 'above
e is their choice. The model, irrespective of how
judged is immaterial as it makes no pretensions
evaluable claims.

in the US and in other non-single payer health
newhat different. While the view that reference
lar standards are nothing more than a pricing
te of passage' is echoed in the US in the reports
the Institute for Clinical and Economic Review
appears to be little support for cost-per-QALY
willingness-to-pay thresholds [20] [21]. The ICER
rors that of NICE in the application of the
e cost-per-QALY framework with willingness-to-
s. Applying threshold values for cost-per-QALY
framework to judge whether or not the price

see as a long term strategy by manufac
increases over the patent life of the p
coupon discount policies to maintain ma
is difficult (if not impossible) to find li
models that factor in long term pricing
their long term modeled cost-per-QALY
case of multiple sclerosis drugs wher
Hartnung et al, provides estimates of th
costs for nine of the disease modifying t
1993 to 2014 [22]. Apart from the fact th
to three time bigger in the US than
principal finding is that DMT costs h
beyond inflation and substantially ab
observed in a similar biologic class. Anr
cost of the DMTs ranged from 35.7% (
7.9% for fingolimod. Four of the DMT
increases above 20% and four with annu
between 13.0% and 16.8%. Nataliz
although being withdrawn briefly from
February 2005 and June 2006, increased
in 2004 to $64,233 in 2013 or an annuali

If long-term pricing strategies are put to
assumption that the market entry WAC
maintained over its patent lifetime, the
what possible justification there is for
support claims for cost-effectiveness.
'sufficient' nor 'proper'. Attempts to
'purity' through advocating models th
course of a disease, willingness-to-pay
advocacy (at least in the US) for cost-per
misplaced. The AdViSHE tool makes
advisability of incorporation models th

part of the model. Indeed, pricing is not
a discretionary variable that can be adjusted to
s for comparative cost-effectiveness.

uld not be unreasonable to make the case that
lude potential long-term pricing strategies in
per-QALY or cost per life year saved models,
stantial element of bias in favor of claims for a
s product. After all, if we consider the case of

of the model and not, as has been a
number of previous occasions, on
hypotheses to support evaluation and
and cost-effectiveness claims, makes it u
committees and other payers will pay it
the AdViSHE checklist is intended as a
the validity of a model that is submitte
and pricing claims, the absence of cr
credibility, evaluation and replication

ysis and consider a pricing strategy that increases by 10% per annum over a ten-year time frame C will have increased by 135%. This does not urse, potential price increases for other direct . Given this, it seems a little odd to apply a standard is 3%) to future costs based on the direct medical costs, to include, drug prices nged.

erm models were modified to accommodate ng scenarios, the fact remains that such models ded to generate evaluable predictions. Until pers accept the premise that health decision e claims that can be validated in a meaningful uch models may be intended to inform but are accepted. In these circumstances it is difficult to the AdViSHE tool can accomplish in bringing the ther.

alidation tool is probably best seen as a checklist cing justification models. The fact that the focus validating the core structure and assumptions oversight

From this perspective of claims evaluat manufacturers to underwrite lifetime should be seen as simply an exercis strategy. Formulary committees are ask model justifies a price consistent wit position and, if possible, a premium pric term a strategy of regular price increa modeling redundant is beside the poin supporting pricing negotiations and for position which is apparently accepte recognized, by academic groups and org Academy of Managed Care Pharmacy together with journal editors. Presum argued that, as long as the cost-per-QA for peer review and publication, the ma any interest in the intrinsic merits of the not it adheres to the AdViSHE validatio bottom line is achieving formulary accep consistent with a manufacturer's long-te share strategy.

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