# Scale Loss Score (SLoS): a novel measure of drug benefit-risk assessment

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## Introduction

- MultiCriteria Decision Analysis (MCDA) is a popular quantitative method to assess the benefit-risk (BR) **balance** of treatments: it permits to summarize the benefits and the risks of a drug in a **single utility score** ► The utility score is often derived using a linear model which might lead to counter-intuitive conclusions, for example, a recommendation of a non-effective drug
- ► We propose Scale Loss Score (SLoS) as a new tool for benefit-risk assessment: it is based on strong theoretical principles, addresses the issues of the linear MCDA model and can lead to more meaningful recommendations

## Notations

 $\xi_{ij}$ : performance of treatment *i* on criterion *j*,  $j = 1, \ldots, n$ 

$$u_{j}(\xi_{ij}): \text{ linear partial value functions - map}$$
  
the performances on criterion *j* to a (0, 1) scale  
$$u_{j}(\xi_{ij}) = \frac{\xi_{ij} - \xi'_{ij}}{\xi''_{ij} - \xi'_{ij}}, \quad \xi'_{ij} \text{ and } \xi''_{ij} \text{ the worst and best values}$$

 $w_i$  and  $\tilde{w}_i$ : weight reflecting the importance of criterion *j* 

# Linear MCDA

MCDA linear utility score:

$$u(\xi_i, \mathbf{w}) := \sum_{j=1}^n w_j u_j(\xi_{ij})$$
  
Higher utility score  $\rightarrow$  more preferable BR balance

Contours of

## SLoS

Scale Loss Score (SLoS):

$$(\boldsymbol{\xi}_i, \tilde{\boldsymbol{w}}) := \sum_{j=1}^n \left(\frac{1}{u_j(\xi_{ij})}\right)^{\tilde{w}}$$

Lower loss score  $\rightarrow$  more preferable BR balance

#### Contours of



Benefit-risk trade-off is the same for all values of risk / benefit

Drugs with no benefit or extreme risk can be recommended



For a given increase in benefit, a smaller increase in risk is tolerated if benefit is high than if it is low

Drugs with no benefit or extreme risk can never be recommended

Examples

## **Fictive examples**

2 criteria, fixed parameter values and  $w = \tilde{w} = 0.25$ 

### Case study: telithromycin

IMI PROTECT Benefit-Risk Group example

**Proba(telithromycin** >  $\beta$ -lactam antiobiotics)

## Conclusion

**Results of simulations** comparing MCDA and SLoS:

Both are robust to correlations

	Example 1		Example 2		
	Low benefit and risk		High benefit and risk		
	Drug 1	Drug 2	Drug 1	Drug 2	
Benefit	0%	30%	96%	50%	
Risk	9%	20%	100%	85%	
MCDA	0.6825	0.6750	0.2400	0.2375	
SLoS	$+\infty$	2.5334	$+\infty$	5.3381	
$\rightarrow$ SLoS strongly penalizes extremely low					
benefit values and extremely high risk values					

Community Acquired Acute Bacterial				
	Pneumonia (CAP)	Sinusitis (ABS)		
MCDA	59%	71%		
SLoS	51%	55%		

 $\rightarrow$  SLoS results are more in line with the regulatory authorities concerns on ABS indication (CHMP reassessment and FDA removal)

#### between outcomes

- Similar conclusions in many cases
- Clear advantage of SLoS when drugs have no benefit or extreme risk

Scale Loss Score (SLoS) is a novel, simple and valuable tool for BR assessment

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