WP-2
Update Jan 2019

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Deliverables planning

Focus today on DICE modelling tool:

1. Validation of the technique against existing methods
2. Publicly accessible platform to allow direct modelling by Health Technology Assessment (HTA) agencies
3. Speeding up execution of the DICE Simulation macro
4. Training modules and manuals for HTA staff, reviewers and modelers

Other deliverables pertain to:

Review of methods used to extrapolate randomized controlled trial (RCT) outcomes using Real World Data (RWD).
DICE - Activities to date

- Survey regarding features of full platform desired by HTA agencies drafted
- Six published models identified by NICE for piloting
  - Breast cancer prevention model rebuilt using DICE
  - Two working session with NICE completed
  - Next model in progress
- Training
  - On-line modules produced
  - Template, build guides and sample models completed
  - Training of ERGs being scheduled
- Python software chosen for platform
  - Piloting at HTAi in Cologne
### Timeline

<table>
<thead>
<tr>
<th>Preparatory work: Prepare protocol</th>
<th>Apr-18</th>
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</thead>
<tbody>
<tr>
<td><strong>Task 1: Extrapolation of health benefits</strong></td>
<td></td>
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<tr>
<td><strong>Task 2: Treatment costs</strong></td>
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<tr>
<td>Milestone: Methods for Extrapolating Treatment Costs</td>
<td>Apr-19</td>
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<tr>
<td>Review methods and Guidance on matching data from RCTs &amp; RWD</td>
<td>Jan-20</td>
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<tr>
<td><strong>Task 3: Development of DICE for HTA</strong></td>
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<tr>
<td>Validation of the DICE model against industry standard models</td>
<td>Apr-20</td>
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<tr>
<td>Enhanced, ready to use DICE Simulation Model</td>
<td>Jun-20</td>
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<tr>
<td><strong>Task 4: Pilot DICE model and apply to NICE Guideline</strong></td>
<td></td>
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<tr>
<td>NICE clinical guideline or segment of guideline selected</td>
<td>Jun-20</td>
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<tr>
<td>Design and implement model using DICE</td>
<td>Sep-20</td>
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<tr>
<td>Training modules and manuals</td>
<td>Sep-20</td>
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</tbody>
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Collaborations foreseen or required

• DICE modules will be posted on line and IMPACT members strongly encouraged to try them out and provide feedback
• Integration of data produced by other WPs into the DICE platform should be discussed and included in WP-2 plan
• Suggestions of who to include from HTAs in the feature survey are welcomed
BRIEF “WORKSHOP”
DICE simulation: Two basic concepts

Start:
- Alive: Y N
- Sex: M F
- Age: 40
- BsAge: 40
- Time: 0
- oLY: 0

Update:
- Age: 3 yrs
- BsAge: 43

Dynamic Condition:
- Alive: Y N
- Sex: M F
- Age: 43
- BsAge: 40
- Time: 3

Death:
- Alive: Y N
- Sex: M F
- Age: 85
- BsAge: 40
- oLY: 40
- Time: 45

End:
- Report results (value of output conditions)
- Terminate this part of the simulation
What is DICE?

A modeling technique that conceptualizes the decision-analytic problem in terms of two fundamental aspects:

**Conditions**
- Bits of information
- Persist over time
- Have levels, which can change
- For some, interested in time spent at a given level because it has value

**Events**
- Points in time where Conditions change
- Have no duration
- Have consequences
- For some, interested in counting them and recording when they happen
# Simple concept, but very flexible...

<table>
<thead>
<tr>
<th>DICE component</th>
<th>Survival partition</th>
<th>Cohort Markov</th>
<th>Microsimulation</th>
<th>DES</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condition(s)</td>
<td>PFS, PPS, OS</td>
<td>- Transition probabilities - State memberships</td>
<td>- Profiles - Current state - Transition probabilities</td>
<td>- Profiles - Equation parameters</td>
<td>- Valuations - Discount rates - Time - Time horizon</td>
</tr>
<tr>
<td>Events (Main)</td>
<td>Partition</td>
<td>Transition</td>
<td>Transition</td>
<td>- Real world Modeling (e.g., Update)</td>
<td>- Start - End - (Valuate)</td>
</tr>
<tr>
<td>Purpose</td>
<td>- Read PFS, OS curves</td>
<td>- Apply transition probabilities</td>
<td>- Test transition probability against random number</td>
<td>- Simulate disease process</td>
<td>- Handle simulation execution</td>
</tr>
<tr>
<td>Outcomes</td>
<td>- Survival curves</td>
<td>- Markov trace</td>
<td>- Dwell times</td>
<td>- Event counts</td>
<td>- Accrue QALY, costs</td>
</tr>
</tbody>
</table>

[IMPACT HTA Logo]
Example Model

- Compare 3 agents for chemoprevention to none
  - Postmenopausal women
  - 2 risk strata
  - 4 age groups
- Annual probabilities of
  - breast cancer depends on age and risk stratum
  - adverse effects, constant, no risk factors
    - Endometrial cancer
    - TE (thromboembolism)
    - Fractures (hip, wrist, vertebral, or other site)
  - death depends only on age (NOT on breast ca or tmt)

- Chemoprevention effects represented as RR
- Costs
  - Annual for treatment and monitoring
  - Per event for breast cancer
  - Nil for no chemoprevention
- Treatment discontinuation
  - 50% at 1 year, all effects lost
  - Planned 100% at 5 yrs
    - Lose endometrial cancer and TE
    - Retain fracture risk for 5 years
    - Retain breast cancer benefit lifetime
What to think about

• What are the things that should happen in my model?

• For each item,
  – When?
  – So what?

• Should any of them be grouped?
What should happen & when?

- Start chemoprevention
- Onset of breast cancer
- Endometrial cancer
- TE (thromboembolism)
- Fractures
- Death
- Monitoring
- Treatment discontinuation

- At start of simulation
- Depends on risk
- Depends on risk
- Depends on risk
- Depends on risk
- Twice a year, DEXA at start if Ana
- 1 yr, 5 yr
VIEW MODEL
## Comparison

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Traditional</th>
<th>DICE</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 tmts, 2 risk strata, 4 age grps</td>
<td>32 Markov models (18 mb)</td>
<td>Single model, run for 8 profiles &amp; 4 tmts</td>
</tr>
<tr>
<td>Annual probabilities</td>
<td>210x32 formulas like: =AR5*(1-VLOOKUP(MIN (AP5,100),'Life table'!$B$5:$C$105,2,FALSE))+AQ5*VLOOKUP(AP5,'Life table'!$F$5:$K$130,2,FALSE)</td>
<td>5 expressions apply prob</td>
</tr>
<tr>
<td>Tmt effects</td>
<td>1032 RR applied to age-dependent rates</td>
<td>4 expressions apply RR</td>
</tr>
<tr>
<td>Costs</td>
<td>2,240 Cases x cost/case</td>
<td>4 expressions apply cost/case</td>
</tr>
<tr>
<td>Treatment discontinuation</td>
<td>Weighted averages applied in various columns</td>
<td>3 events for early non-adherence</td>
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<tr>
<td></td>
<td></td>
<td>5 yr treatment stop</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 yr end fx risk</td>
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</table>
Questions & Next steps

• Do you find the approach simple and transparent?
• Are the advantages of this approach clear to you?
• Is it useful for **HTA** purposes?
  – Do you see this tool being widely implemented within HTA agencies?
  – What road blocks do you envisage which may prevent this?
• How can it be improved?
• How should we make the DICE platform available to you?
• SURVEY coming soon!