Results of the pilot phase of the validation study of HTE-DLP

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Abstract

Introduction
Atherosclerotic cardiovascular disease (CVD) is the leading cause of death and disability in the world. CVDs place a heavy burden on the economies of the countries. One third of ischemic heart disease is attributable to high cholesterol.

Description
HTE-DLP is a Computerized Decision Support Systems (CDSS) that performs a sequence of clinical decisions including all lipids lowering therapy and shows specific recommendations for each patient using efficiency, safety and cost criteria.

HTE-DLP is the first lipid-lowering therapy CDSS developed in Spain and the first to be validated in Europe.

Results
HTE-DLP has proven to be an efficient, effective, efficient and safe tool that can have a major clinical impact while can mean significant cost savings for the health system.

Conclusion
Using In clinical practice a specific CDSS as HTE-DLP it is possible to improve the management of dyslipidemia with a decrease in coronary heart disease and lowering healthcare costs
Introduction

Every year an estimated 17 million people die of Cardiovascular Disease (CVD), particularly heart attacks and strokes, representing 30% of all global deaths and led to 151 million of years lost due to ill-health, disability or early death (DALYs) (representing 10% of all DALYs).

About 600,000 people in the United States die from heart disease every year—that’s one in four deaths. Every year, 715,000 Americans have a heart attack.

In 2010, the global cost of CVD is estimated at US$ 863 billion and it is estimated to rise to US$ 1.044 billion in 2030.

(Dates from World Health Organization, 2013)

Globally, one third of ischemic heart disease is attributable to high cholesterol. Overall, raised cholesterol is estimated to cause 2.6 million deaths (4.5 per cent of total) and 29.7 million DALYS.

In 2008, the prevalence of raised total cholesterol among adults – defined as total cholesterol of 6.2 mmol/l (240 mg/dl) or higher – was 9.7 per cent. 105 million people in the USA have cholesterol levels a cardiovascular risk. 48 million of American adults with high LDL-C are not treated or not at goal (Fig.1).

(Dates from World Heart Federation, 2008)

Description of HTE-DLP

Computerized Decision Support Systems (CDSS) have been introduced into medical practice and may help physicians tailor recommendations for chronic disease management as dyslipemia, while also obtaining savings in healthcare costs.

HTE-DLP (Effective Hyperlipidemia Treatment CDSS) is an artificial intelligence software developed by researchers from TransLab Research Group of University of Girona, Cardiovascular Research Network of Spain (RIC) and “Corporació de Salut del Maresme y la Selva - Hospital of Blanes-Girona, Spain.

The system offers in terms of cardiovascular risk, patient comorbidities and concomitant drugs, all lipid-lowering treatment options for an individual patient in order from best to worst, valued criteria of effectiveness, safety and cost-efficiency.

http://www.udgmedicina.cat/web/pagina/66/sistemade-apoyo-a-la-toma-de-decisiones-hte-dislipemia
What has it meant HTE-DLP in the treatment of patients at high vascular risk?

<table>
<thead>
<tr>
<th>Category</th>
<th>Observations</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Innovation</strong></td>
<td>- First lipid-lowering therapy CDSS developed in Spain&lt;br&gt;- First lipid-lowering therapy CDSS validated in Europe&lt;br&gt;- HTE-DLP project is a follow-up to the Observatory of Innovation Experiences in ICTs and Health in Catalonia (Foundation TicSalut, Health Department, Government of Catalonia, Spain)</td>
<td>Intellectual Property Registration (RTA 98/09) (Reference 1)&lt;br&gt;Fig. 2</td>
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<td><strong>Effectiveness</strong></td>
<td>- The use of HTE-DLP by vascular risk experts meant additional lowering of LDL-C of 20.5%&lt;br&gt;- When experts in vascular risk using HTA-DLP number of high vascular risk patients reaching lipid targets of LDL-C &lt;70 mg/dl increased by 4.4 times&lt;br&gt;- In general practitioners would increase 5.8 times the patients in LDL-C goal</td>
<td>(Reference 1)&lt;br&gt;Fig. 3</td>
</tr>
<tr>
<td><strong>Efficiency</strong></td>
<td>- Use of HTE-DLP reduced direct costs of lipid-lowering medication, 19% less per 1 mg of LDL-descended&lt;br&gt;- The widespread use in Spain of HTE-DLP would mean in 2020 a decrease in coronary heart disease health costs between 4.7% and 6.4% (between 24 and 32 million Euros savings to the healthcare system)</td>
<td>(Reference 1)&lt;br&gt;Fig. 4&lt;br&gt;(Reference 2)&lt;br&gt;Fig. 5&lt;br&gt;Table 1</td>
</tr>
</tbody>
</table>

http://www.ticsalut.cat/observatori/innova-ticsalut/79/hte-dislipemia
### Acceptance by clinicians

Physicians expressed good agreement with the 1st HTE-DLP recommendation in 86.1% of cases and use was described as *comfortable in 85% of cases* (Reference 1).

### Positive evaluation

Assessing users HTE-DLP by Questionnaire QoE for applications in health was positive (3.89 / 5)

Self-assessment for Distinctive App Healthy of Government of Andalucía (24 /31)

Table 3

Table 4.

### Bibliometric impact


2. Zamora A, et al. Theoretical impact on coronary disease using a computerized system to aid in the prescription of lipid-lowering therapy


### International projection

The clinical validation study of HTE-DLP (1) has been viewed 276 times at Atherosclerosis page in the first year after its publication

Fig. 6
Social impact

The news of the publication of clinical validation study of HTE-DLP (1) appeared in over 30 national newspapers

HTE-DLP Running

HTE-DLP performs a sequence of clinical decisions including all statins and ezetimibe and creates specific recommendations for each patient using efficiency, safety and cost criteria. It is based on European Guidelines for the Management of Dyslipidemia 2011.

Firstly, HTE-DLP applies selection criteria to discard statins which are contraindicated if renal or liver dysfunction or severe drug interactions exist. Secondly, treatments are selected with the necessary power to reduce LDL-C. LDL-C/HDL-C is a secondary target applicable only when user-specified. Following this, HTE-DLP applies order criteria to compare all treatment options in pairs. Drug interactions and market prices are parameterized, prioritizing first safer lipid-lowering therapy and then cheaper products. When HTE-DLP detects a difference, the comparison process ends and the program orders all selected treatments from best to worst. All of these processes are done with a single click on-screen.

The program is configured which allows introducing new order criteria such as genetic factors associated with a higher frequency of adverse effects.

The system also provides a questionnaire on patients’ adherence to Mediterranean Diet. HTE-DLP allows on-line updating.

Clinical Verification, Validation and Evaluation process of HTE-DLP

Clinical Verification process

The software development process has been overseen by an expert clinician in vascular risk to ensure that all recommendations were consistent on the best scientific evidence.

Twelve experts in vascular risk used HTA-DLP for 3 months were asked anonymously about the reliability of the recommendations made.

Clinical Validation process

It was a cluster-randomized trial comparing standard prescriptions with HTE-DLP assistance, conducted by 10 expert physicians (7 specialists and 3 general practitioners) in cardiovascular risk management from 5 different hospitals and primary care centers in Catalonia (Spain). Each physician was asked to recruit 10 patients. The study protocol was approved by local ethics committee. The physicians enrolled consecutive eligible patients with high cardiovascular risk aged >18 years old with LDL-cholesterol (LDL-C) >100 mg/dl and attending participating centers from January to March 2010. Patients gave written informed consent. Included patients were randomly distributed into the intervention or control group by a computer program. HTE-DLP was blocked automatically if a patient was assigned to the control group. Physicians used HTE-DLP in the “real-clinic-world”.

Evaluation process

Twelve experts physicians in the cardiovascular field assessed HTA-DLP by questionnaire QuoE for Measuring the Quality of Experience in mHealth Applications.
Authors evaluated HTE-DLP using criteria of APP certification healthy Government of Andalusia, Spain

The authors self-evaluated HTE-DLP by criteria of certification of “Distinctive App Healthy” of Government of Andalusia, Spain.

**Future directions**

The second version of HTE-DLP on which we are working will incorporate web-oriented-design with automatic data collection from electronic records and databases, last generation of warning systems and treatment adherence and patient’s opinion and experience. It is scheduled to make a *Mobile Medical App* version of HTE-DLP.

HTE-DLP can be a useful tool for businesses of e-health, providers, distributors and hospitals involved in improving the quality and efficiency of healthcare of cardiovascular patients.

**Conclusion**

In the “real-clinic-world” in the cardiovascular field it is possible to improve cholesterol management using CDSS as HTE-DLP.

**Competing interests**

Alberto Zamora and Fernando Fernández de Bobadilla have the rights over intellectual property of HTE-DLP.
References

**Figure 1.** Lipid world atlas

- **Risk factor: lipids**

- **Current recommended lipid levels**
  
<table>
<thead>
<tr>
<th>Lipid Type</th>
<th>European Guideline</th>
<th>US Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>less than 5.0 mmol/l</td>
<td>less than 240 mg/dL (6.0 mmol/l)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>less than 3.0 mmol/l</td>
<td>less than 160 mg/dL (0.8 mmol/l)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>1.0 mmol/l or more</td>
<td>40 mg/dL (1 mmol/l) or more</td>
</tr>
<tr>
<td>Triglycerides (fasting)</td>
<td>less than 1.7 mmol/l</td>
<td>less than 200 mg/dL (2.3 mmol/l)</td>
</tr>
</tbody>
</table>

- **Trends in cholesterol levels in Beijing, China**

- **Cholesterol**
  
  - Average cholesterol levels in women aged 30 and above
  - cholesterol in men
  - data from urban populations only
  
  - 5.0 and above
  - 3.5-5.99
  - 1.0-3.49
  - 3.0-4.99
  - less than 1.0

- **High cholesterol causes among a third of all cardiovascular diseases worldwide.**

- **Fatty deposits along the inside of artery walls lead to atherosclerosis and narrowing of the arteries.**

- **185 million people in the USA have cholesterol levels that are a cardiovascular risk.**
Fig 2. HTE-DLP Interface

Menores y Advertencias

LOS TRATAMIENTOS MOSTRADOS ALCANZAN EL OBJETIVO C-LDL EN Toda SU HORQUILLA DE EFICACIA

ADVERTENCIAS GENERALES:

- Dado que el colonel se tratando en los pacientes con una carga de la deriva, se recomienda la administración nocturna de las estatinas con vida media menor (fluvastatina, torvastatina y rosuvastatina) y durante el día las estatinas con vida media más larga (atorvastatina, pravastatina y simvastatina).

- En el tratamiento hipolipídico se recomienda un control analítico (con fluvastatina y perfil lipídico) previo al inicio de tratamiento, y que 6 semanas tras cada cambio de dosis o al surgir necesidad de efectos secundarios. Si se desea alterar la dosis se debe hacer en intervalos de 3 a 4 meses de que la dosis de referencia valga, disminuyendo la dosis de estatina.

- En caso de infección y si presenta signos de inflamación se debe suspender la terapia hasta que las analíticas sean normales e infección haya desaparecido.

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- En caso de infección y si presenta signos de inflamación se debe suspender la terapia hasta que las analíticas sean normales e infección haya desaparecido.
Figure 3. Percentage of patients achieving goals of LDL-C after 12 weeks of using HTE-DLP
Figure 4 Cost per 1 mg of LDL-C decreased (EUR)

Note: Total Cost of lipid lowering in Spain: 2.339 million of EUR on year
Figure 5. Reduction in expected cases per 100,000 inhabit of fatal and nonfatal coronary events using (Dark line) or not HTE-DLP (Clear line)
**Figure 6.** Views of clinical validation article of HTE DLP in the first year of its publication (October 2013- November 2014)
Table 1. Effect of using HTA-DLP on the incidence and numbers of fatal and non-fatal coronary events in the population of Spain aged 35 to 74 years extrapolated to 2020 (Methodology Cassandra Regicor)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>HTE-DLP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated male population at 35 to 74 years</td>
<td>12.502.843</td>
<td>12.951.521</td>
</tr>
<tr>
<td>Estimated female population 35 to 74 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence rate of 100.00 inhabitants in males aged 35 to 74</td>
<td>234.5-238.4</td>
<td>220.5-220.7</td>
</tr>
<tr>
<td>Incidence rate of 100.00 inhabitants in females aged 35 to 74</td>
<td>50.3-50.5</td>
<td>49.4-49.5</td>
</tr>
<tr>
<td>Expected number of cases of coronary heart disease in males aged 35 to 74</td>
<td>29.139-29.807</td>
<td>27.569-27.594</td>
</tr>
<tr>
<td>Expected number of cases of coronary heart disease in females aged 35 to 74</td>
<td>6515-6541</td>
<td>6398-6411</td>
</tr>
<tr>
<td>Estimated cost of coronary artery disease in females aged 35-74 years (millions of EUR)</td>
<td>91.659.535 - 92.035.329</td>
<td>90.013.462 - 90.196.359</td>
</tr>
</tbody>
</table>

+Numbers of prevented coronary events in males aged 35 to 74

1570-2213

+Numbers of prevented coronary events in females aged 35 to 74

117-130

+Decreased costs to secondary coronary events avoided in male population of 35-74 years

22.088.330 - 30.815.343 (millions of EUR)

+Decreased costs to secondary coronary events avoided in female population of 35-74 years

1.646.073 - 1.838.970 (millions of EUR)
<table>
<thead>
<tr>
<th>Nº</th>
<th>Questions</th>
<th>SCORE Mean (DE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Perceived quality of the content of the application</td>
<td>4,08 (0,36) / 5</td>
</tr>
<tr>
<td>2</td>
<td>Level of security provided by the application</td>
<td>3.75 (1.05) / 5</td>
</tr>
<tr>
<td>3</td>
<td>Usability of the application</td>
<td>4.16 (0.38) / 5</td>
</tr>
<tr>
<td>4</td>
<td>Guarantee access to the application at any time</td>
<td>3.91 (1.16) / 5</td>
</tr>
<tr>
<td>5</td>
<td>Ease learning program operation</td>
<td>3.91 (0.51) / 5</td>
</tr>
</tbody>
</table>

**TOTAL POINTS**

3.89 (0.48) / 5

<table>
<thead>
<tr>
<th>FUTURE TRENDS</th>
<th>SCORE Mean (DE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Would you use the application if it will develop in app format?</td>
</tr>
<tr>
<td>2</td>
<td>Do you think that in the future this application can be used widely in clinical practice?</td>
</tr>
<tr>
<td>3</td>
<td>Do you think you can improve the quality of life of users if generalized?</td>
</tr>
<tr>
<td>4</td>
<td>Do you think that in the future this application can help in the treatment of disease?</td>
</tr>
</tbody>
</table>
### Table 3. Self-assessment for the design, use and evaluation of health apps
Distinctive App Healthy. Evaluation of HTE-DLP

<table>
<thead>
<tr>
<th>Category</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design and relevance</td>
<td>4 / 4</td>
</tr>
<tr>
<td>Quality and safety information</td>
<td>11 / 11</td>
</tr>
<tr>
<td>Delivery service</td>
<td>3 / 5</td>
</tr>
<tr>
<td>Confidentiality and privacy</td>
<td>6 / 11</td>
</tr>
<tr>
<td><strong>TOTAL SCORE</strong></td>
<td><strong>24 / 31</strong></td>
</tr>
</tbody>
</table>

http://www.calidadappsalud.com/listado-completo-recomendaciones-app-salud/
Appendix: Researchers (in alphabetical order)

A- TransLab Research Group

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