The Problem of CV Drug Adherence Worldwide

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Disclosure

I do NOT have a financial interest, arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Medication Non-Adherence
...America’s other drug problem

13% of the total US healthcare expenditure!

Nearly 3 out of 4 Americans admit that they do not always take their medication as directed.

194,000 deaths in EU

45% of US population

125,000 deaths in the U.S. each year

Number of Americans affected by a chronic condition requiring medication therapy is expected to grow from 133 million to 157 million by 2020.

300 billion in avoidable costs to the healthcare system annually.

€197 billion in EU
## Medication Non-Adherence

### The Five Dimensions of Non Adherence

<table>
<thead>
<tr>
<th>Social/ Economic</th>
<th>Health Care System</th>
<th>Condition-Related</th>
<th>Therapy-related</th>
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<tr>
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**ADHERENCE TO LONG TERM THERAPIES: EVIDENCE FOR ACTION. WHO 2003**
Importance of Age on Adherence to Cardiovascular Medications

Incidence (%) of Cardiovascular Disease by sex and age

Go A. et al. AHA Statistical Update, Circulation, 2013; 129, 24-292
Direct association between dosing frequency and medication adherence

Physicians usually don’t see adherence as an issue they can address

‘White coat adherence’

Average time spent on outpatient visit: 10-15’

How much time do we spend discussing new prescriptions?
Analysis 181 patients receiving 234 new medication Rx. from 16 family physicians, 18 internists, and 11 cardiologists:
Average time spent by MD explaining role of new medications: 49 seconds.

More than 60 percent of patients misunderstood prescription directions immediately after doctor visits. Forty to 60 percent of patients could not correctly report medication expectations 10 to 80 minutes after physicians provided information

Healthy Adherer Effect

Castellano JM, et al., Global Heart. 2013;8:263
## Medication Non-Adherence
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ADHERENCE TO LONG TERM THERAPIES: EVIDENCE FOR ACTION. WHO 2003
## Prevalence of Good Adherence to CV Medications

**Adherence to cardiovascular therapy: a meta-analysis of prevalence and clinical consequences**

n=1,978,919 (135,627 CVD events and 94,126 cases of all-cause mortality)

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<tr>
<th>Adherence to</th>
<th>No. of Studies</th>
<th>No. of Participants</th>
<th>Proportion (95% CI)</th>
</tr>
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<tr>
<td>any CVD Medication</td>
<td>34</td>
<td>1,230,382</td>
<td>0.60 (0.52-0.68)</td>
</tr>
<tr>
<td>STATINS</td>
<td>12</td>
<td>771,323</td>
<td>0.54 (0.41-0.67)</td>
</tr>
<tr>
<td>ANTIHYPERTENSIVES</td>
<td>11</td>
<td>363,819</td>
<td>0.54 (0.42-0.77)</td>
</tr>
<tr>
<td>ASPIRIN</td>
<td>2</td>
<td>11,068</td>
<td>0.70 (0.49-0.91)</td>
</tr>
<tr>
<td>ANTIDIABETIC AGENTS</td>
<td>2</td>
<td>1,112</td>
<td>0.69 (0.59-0.78)</td>
</tr>
</tbody>
</table>

Relative Risks for ANY CVD in good vs. Poor adherence to major CV medication

n=1978919 (135 627 CVD events and 94 126 cases of all-cause mortality)

<table>
<thead>
<tr>
<th>Adherence to any CVD Medication</th>
<th>No. of Studies</th>
<th>No. of Participants</th>
<th>No. of CVD Events</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>33</td>
<td>1.615.126</td>
<td>135.627</td>
<td>0.80 (0.77-0.84)</td>
</tr>
<tr>
<td>Adherence to STATINS</td>
<td>17</td>
<td>1,055,920</td>
<td>96,216</td>
<td>0.85 (0.81-0.89)</td>
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<tr>
<td>Adherence to ANTIHYPERTENSIVES</td>
<td>13</td>
<td>552,143</td>
<td>36,186</td>
<td>0.81 (0.76-0.86)</td>
</tr>
<tr>
<td>Adherence to ACEI/ARB</td>
<td>4</td>
<td>68,780</td>
<td>4643</td>
<td>0.75 (0.55-1.01)</td>
</tr>
<tr>
<td>Adherence to ASPIRIN</td>
<td>3</td>
<td>15,253</td>
<td>2274</td>
<td>0.60 (0.31-1.16)</td>
</tr>
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Relative Risks for ALL-CAUSE-MORTALITY
good vs. Poor adherence to major CV medication

n=1978919 (135,627 CVD events and 94,126 cases of all-cause mortality)

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<tr>
<th>Medication</th>
<th>No. of Studies</th>
<th>No. of Participants</th>
<th>No. of DEATHS</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adherence to any CVD Medication</td>
<td>23</td>
<td>533,381</td>
<td>94,126</td>
<td>0.65 (0.57-0.67)</td>
</tr>
<tr>
<td>Adherence to STATINS</td>
<td>11</td>
<td>291,864</td>
<td>29,605</td>
<td>0.55 (0.81-0.89)</td>
</tr>
<tr>
<td>Adherence to ANTIHYPERTENSIVES</td>
<td>11</td>
<td>205,598</td>
<td>12,228</td>
<td>0.71 (0.64-0.78)</td>
</tr>
<tr>
<td>Adherence to ACEI/ARB</td>
<td>4</td>
<td>62,196</td>
<td>886</td>
<td>0.74 (0.69-0.80)</td>
</tr>
<tr>
<td>Adherence to ASPIRIN</td>
<td>3</td>
<td>12,980</td>
<td>1573</td>
<td>0.45 (0.16-1.29)</td>
</tr>
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9% of CV deaths EU attributable to poor adherence
Good adherence to CV therapies could be associated with a 20% lower risk of CVD and 35% reduced risk of all-cause mortality

Assessing the Impact of Medication Adherence on Long-term Outcomes Post Myocardial Infarction

S. Bansilal, JM. Castellano, HG. Wei, EG. Vinado, A. Freeman, CM. Spettell, FG. Alonso, G. Steinberg, G. Sanz, V. Fuster

European Society Of Cardiology Congress 2014

Presented ESC 2014 Registry Hotline Aug 31, 2014
Adults following MI between 1/1/2010 - 2/28/2013: 14,119

- Adults following MI & ACEI and statin fill in 6 months: 7,107
  - Fully adherent: 1,761 (43%)
  - Partially adherent: 1,263 (31%)
  - Non-adherent: 1,031 (26%)
- Adults following MI & ACEI and statin fill in 6 months with a pre-period of 6 months: 5,776
- Adults following MI & ACEI and statin fill in 6 months with no pre-period: 1,761

7,012 No fill of both ACEI and Statin during the 6 months after the MI

1,331 excluded (diagnostic codes)
- 29% mental disease
- 1% maternity or delivery
- 10% hospice or respite care
- 23% nursing facility
- 33% ARB fill during 6 months post-MI
- 4% MI as a subsequent episode
Time to Major cardiac Event by Adherence Levels

Cumulative Incidence

Time in Months

Number at Risk:
4015  3541  2421  1510  871  438  99  0

Log-Rank p-value=.0002
Medication Non-Adherence
Impact on Health Care Costs

- Poor Medication Adherence
  - Costs passed on to patient
  - Increased Health Care Costs
  - Increased Service Utilization
  - Poor Health Outcomes

Costs passed on to patient

Increased Health Care Costs

Increased Service Utilization

Impact of Medication Adherence in Chronic Vascular Disease on Health Services use (2005-2008)

Strategies to Improve Adherence
Strategies to Improve Adherence

Medico Pak makes medication perfectly clear

See-through blister packs with the right dose, for the right time of day, so you don't forget to take your medication even if you're away from home.
Strategies to Improve Adherence
What Is Effective in Helping Chronic Non-Adherence: Sobering Findings

Annals of Internal Medicine Systematic Review 2012 and the Cochrane Review:

- 36 of 83 interventions in 70 RCTs improved adherence, but only 25 led to clinical improvement
- Almost all were complex interventions but led to only modest improvements—case management and patient education with behavioral support
- Cost effectiveness needs to be studied
- Policy interventions aimed at co-payment costs or drug coverage were also effective

Strategies to Improve Adherence

S — Simplify the regimen
I — Impart knowledge
M — Modify patient beliefs and behavior
P — Provide communication and trust
L — Leave the bias
E — Evaluate adherence

Polipíldora para prevención Cardiovascular: del Concepto a la Realidad

- Reducción del número de componentes para simplificar el tratamiento
- Favoreciendo la Adherencia
- Estrategia Coste Efectiva
- Favoreciendo la asequibilidad
- Favorece la accesibilidad global al tratamiento farmacológico
RCTS USING A POLYPILL TO STUDY THE EFFECT ON ADHERENCE

**KANYINI GAP**
RR = 1.49

**IMPACT**
RR = 1.75

**UMPIRE**
RR = 1.33

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Improving accessibility through the use of a polypill strategy

<table>
<thead>
<tr>
<th>CV drug</th>
<th>High (%)</th>
<th>UMI(%)</th>
<th>LMI(%)</th>
<th>Low (%)</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelets</td>
<td>62.0</td>
<td>24.6</td>
<td>21.9</td>
<td>8.8</td>
<td>25.3</td>
</tr>
<tr>
<td>BB</td>
<td>40.0</td>
<td>25.4</td>
<td>10.2</td>
<td>9.7</td>
<td>17.4</td>
</tr>
<tr>
<td>ACEI / ARBs</td>
<td>49.8</td>
<td>30.0</td>
<td>11.1</td>
<td>5.2</td>
<td>19.5</td>
</tr>
<tr>
<td>BP-lowering</td>
<td>73.8</td>
<td>48.4</td>
<td>37.4</td>
<td>19.2</td>
<td>41.8</td>
</tr>
<tr>
<td>Statins</td>
<td>66.5</td>
<td>17.6</td>
<td>4.3</td>
<td>3.3</td>
<td>14.6</td>
</tr>
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Prospective Urban Rural Epidemiology (PURE)

Cost of Cardiovascular Disease

Forecasting the Future of Cardiovascular Disease in the United States
A Policy Statement From the American Heart Association

Projections of Prevalence

Projections of Cost

Heidendreich P. et al, Circulation 2011; 123:933-944
Medication Non-Adherence

“Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments”

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