Dr Paddy Mallon
Mater Misericordiae University Hospital, Dublin, Ireland
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<table>
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<tr>
<th>Speaker Name</th>
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<tr>
<td><strong>Dr Paddy Mallon</strong></td>
<td>Dr Mallon and/or his employer has received financial support in the form of honoraria for consultancy services (including advisory boards), speaker services, funding to attend conferences and/or research income from the following companies; Gilead Sciences, ViiV Healthcare, GSK (Ireland), Janssen---Cilag, Merck, Sharpe and Dohme and Bristol Myers Squibb.</td>
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**Date**
October 2014
Life Expectancy
‘living long and well with HIV’

Dr Paddy Mallon

UCD HIV Molecular Research Group
Associate Dean for Research and Innovation
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Evolution of treatment for HIV infection
From mortality to long-term manageability

- Rapidly lethal
- HIV found to be cause of AIDS
- Antibody test
- Zidovudine
- Short Life expectancy
  - PCP ~9 months
  - AIDS ~21 months
  - QoL poor

- Incremental therapeutic advances
- Dual NRTI therapy
- RNA test
- PI-containing HAART
- Entry inhibitors
- Natural life expectancy
  - Good QoL

- Manageable long term
- NNRTI-containing HAART
- Vaccines?

- New drug classes?

Survival trends in HIV with effective ART

Cumulative survival curve for HIV-infected persons (non-HCV co-infected) and persons from the general population.

Survival From Age 25 Years

Probability of Survival

Age (years)

Population Controls
Late HAART (2000-2005)
Early HAART (1997-1999)
Pre-HAART (1995-1996)

n=383,862 (HIV-infected patients, n=3,990; General population controls, n=379,872)

Survival living with HIV on HAART - 2012

- \( N=3280 \) on continuous ART from SMART and ESPRIT trials
- 80% male, 61% MSM (no IDU), 43 years
- CD4 >350 and suppressed HIV RNA
- 62 deaths - mortality rate 5.02/1000 PY (95% CI 3.85, 6.43)
- Standardised mortality ratios (SMR) compared to the Human Mortality Database

<table>
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<tr>
<th>CD4 (cells/mm3)</th>
<th>350-500</th>
<th>&gt;500</th>
</tr>
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<tbody>
<tr>
<td>SMR (95% CI)</td>
<td>1.77</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>(1.17, 2.55)</td>
<td>(0.69, 1.4)</td>
</tr>
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Barriers to achieving CD4+ > 500 cells/mm3

• Later diagnosis
  – Increase HIV testing and detection

• Lower CD4+ count at ART initiation
  – When to start?

• Older age

• Male gender
  – Do we need more personalised treatment guidelines?
HIV – ‘test and treat…..and link into care!’

HIV - ‘test and treat’ - new global direction

90-90-90
An ambitious treatment target to help end the AIDS epidemic

90% 90% 90%
Diagnosed On treatment Virally suppressed

When to Start HIV Treatment

Adapted from Schechter M, *JID* 2004;190:1043-1045

- **Late clinical stages**
  - $< 200$

- **Early clinical stages**
  - $> 500$

- **Any viral load**
  - 200
  - 350

- **High viral load**
  - $> 500$

CD4

DRUG SAFETY

AGE

HMRG
HIV Molecular Research Group
Survival predictions in HIV – effect of ART

Expected age at death* - men

Expected age at death* - women

* Expected age at death for a person aged 35 years with different durations of antiretroviral therapy according to current CD4 count and viral load suppression

Mortality in treated HIV

Causes of death in a **successfully ART-treated** population:

SMART/ESPRIT: causes of death in N=3,280 HIV-infected persons receiving suppressive cART with CD4 counts ≥350 cells/mm³

- **CVD**: 31%
- **Cancer**\(^*\): 19%
- **Unnatural**\(^*\): 18%
- **Infection**: 10%
- **Liver disease**: 8%
- **AIDS**: 3%
- **Unknown**: 2%

\(^*\) = non-AIDS malignancy
\(^*\) = accident, suicide or violent death

## Bone health and HIV

<table>
<thead>
<tr>
<th>Country</th>
<th>N</th>
<th>HIV+ %</th>
<th>% male</th>
<th>Fractures</th>
<th>Association between fracture and HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA¹</td>
<td>119,318</td>
<td>33%</td>
<td>100</td>
<td>1615</td>
<td>HR 1.24 (1.11, 1.39)</td>
</tr>
<tr>
<td>Denmark²</td>
<td>31,836</td>
<td>5,306</td>
<td>76</td>
<td>806</td>
<td>IRR 1.5 (1.4-1.7)</td>
</tr>
<tr>
<td>Canada³</td>
<td>540</td>
<td>138</td>
<td>0</td>
<td>-</td>
<td>OR 1.7 (1.1, 2.6)</td>
</tr>
<tr>
<td>USA⁴</td>
<td>559</td>
<td>328</td>
<td>100</td>
<td>33</td>
<td>No difference in fracture rates</td>
</tr>
<tr>
<td>Spain⁵</td>
<td>1,118,15</td>
<td>2,489</td>
<td>-</td>
<td>24,457</td>
<td>HR 4.7 (2.44, 9.5) hip (HIV+ 49)</td>
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Frailty-related phenotype increases with age, accelerated by HIV infection.

- **MACS cohort study**
  - HIV infected (n = 245)
  - HIV negative (n = 1,905)
  - Compared to HIV- of similar age, ethnicity and education, HIV+ more likely to have frailty phenotype
  - Frailty prevalence increases with longer duration of infection
    - Risk 3–14 fold > in men infected with HIV for 4 to 12 years
  - Frailty prevalence for 55-year-old men infected with HIV for >4 years similar to that of uninfected men >65 years old (3.4%)

Frailty-related phenotype defined as at least 3 of: physical shrinking, exhaustion, slowness, low physical activity level

Reducing risk of MI – what works?

D:A:D - risk of CVD events decreases by nearly 30% after stopping smoking for > 3 years

- 746 CVD events reported during 151,717 person years of follow up, yielding overall crude rates (and 95% CI) per 1,000 person years of 4.92 (4.57, 5.28)

- Compared to current smokers, the risk of CVD among patients who stopped smoking for more than 3 years was reduced by approximately 30% (IRR (95% CI): 0.74 (0.48, 1.15))

Future research in HIV and ageing

‘Pharmacokinetic and Clinical Observations in People over Fifty’

UK and Ireland

The Netherlands