

Cost- Benefit of treatment in F1 patients

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Cost-Benefits in F1

- Conflicts of interest
- Fees received from AbbVie, Gilead, GSK, Merck

Cost – Benefits in F1

- Cost-effectiveness can be difficult
 - Cost per QALY, discounts, additional costs, additional benefits
- Cost – effectiveness can be easy
 - Compare costs and benefits

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I will take the easy approach

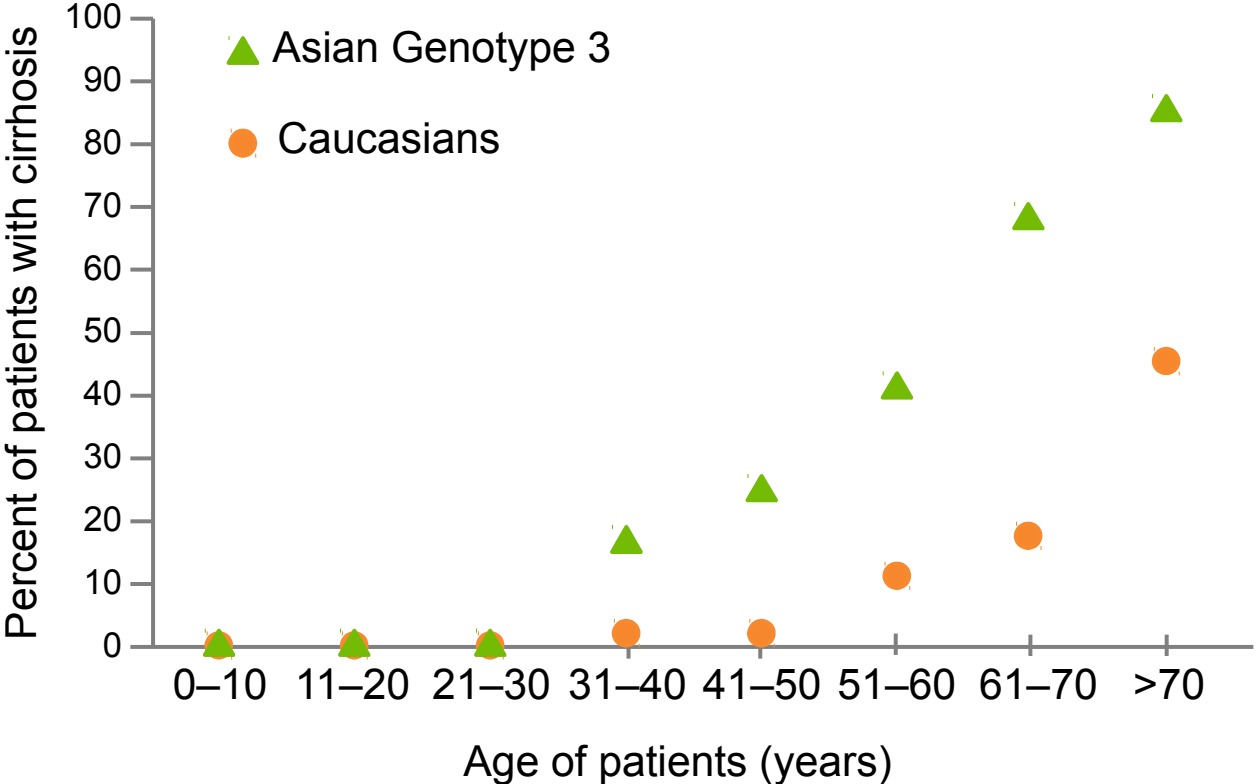
Cost-**benefits** in mild disease

- Avoidance of liver complications
- Avoidance of non-liver complications
- Prevention of transmission

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HCV will eventually cause liver damage



Adapted from D'Souza. Clin Gastroenterol Hepatol 2005;3:910-17

Disease outcomes in a cohort of women in Ireland infected by hepatitis C-contaminated anti-D immunoglobulin during 1970s

Patricia Garvey, Niamh Murphy, Paula Flanagan, Aline Brennan, Garry Courtney, Orla Crosbie, John Crowe, John Hegarty, John Lee, Margaret McIver, Carol McNulty, Frank Murray, Niamh Nolan, Cliona O'Farrelly, Stephen Stewart, Michele Tait, Suzanne Norris, Lelia Thornton

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Fig. 4

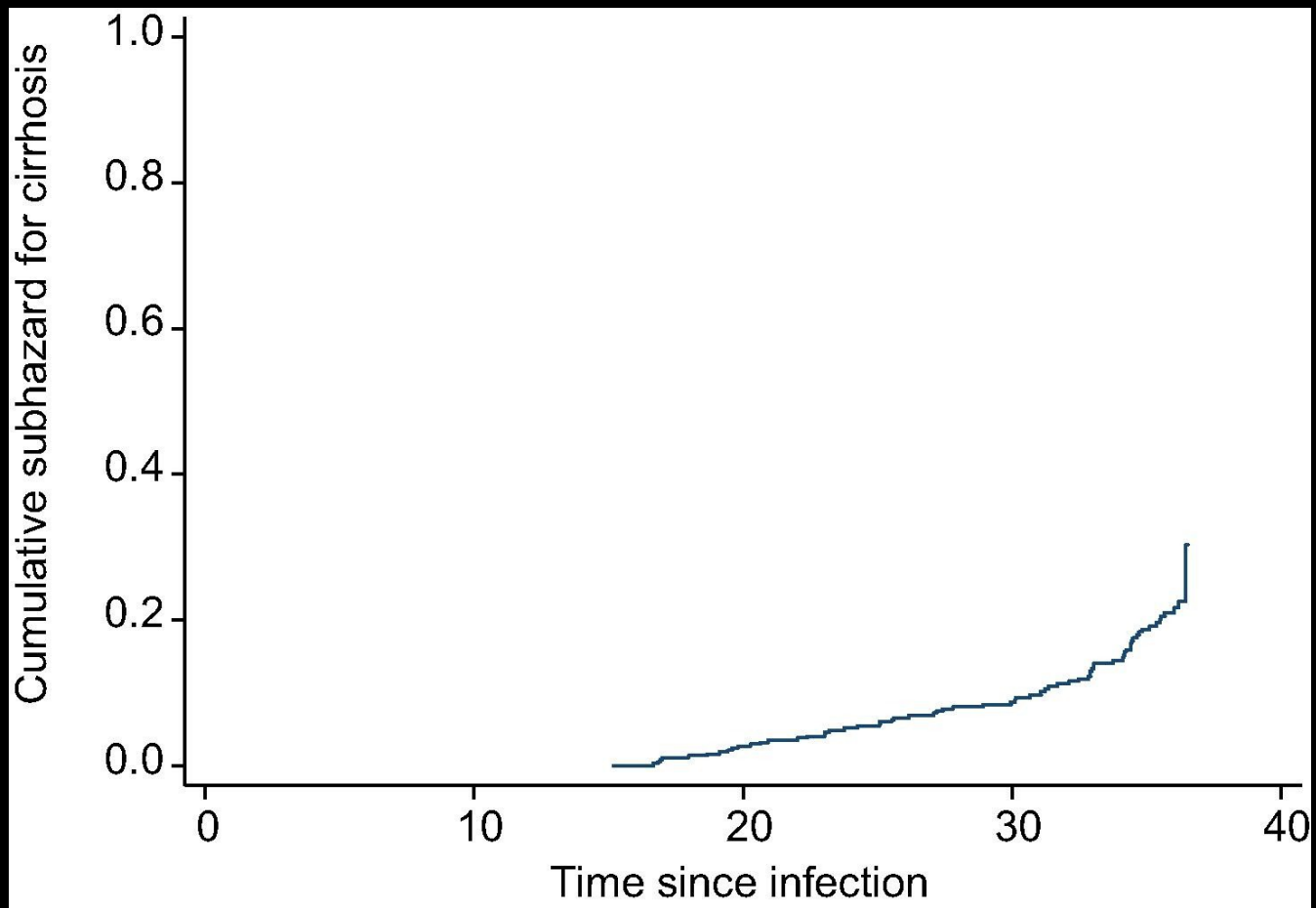


Fig. 4

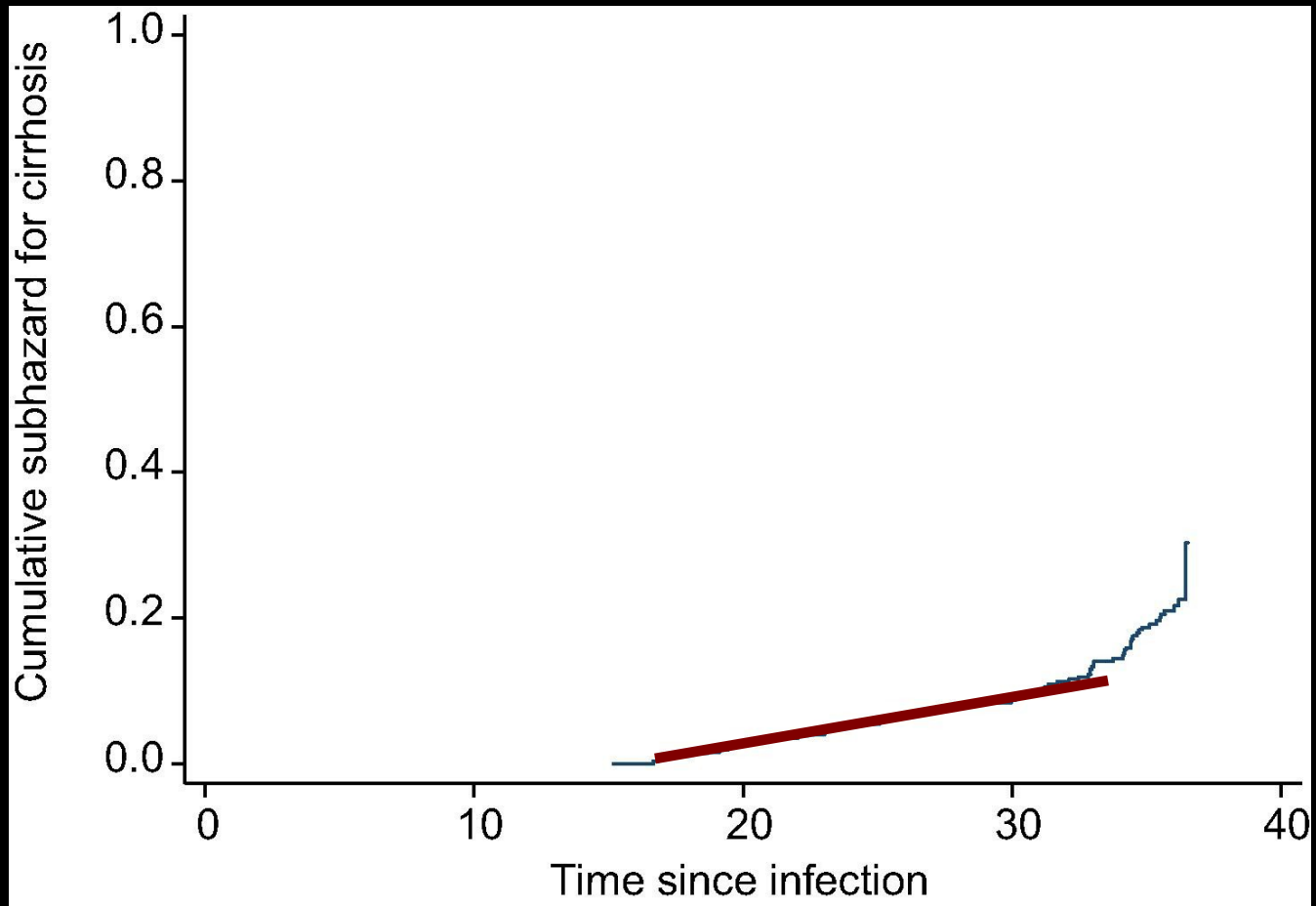
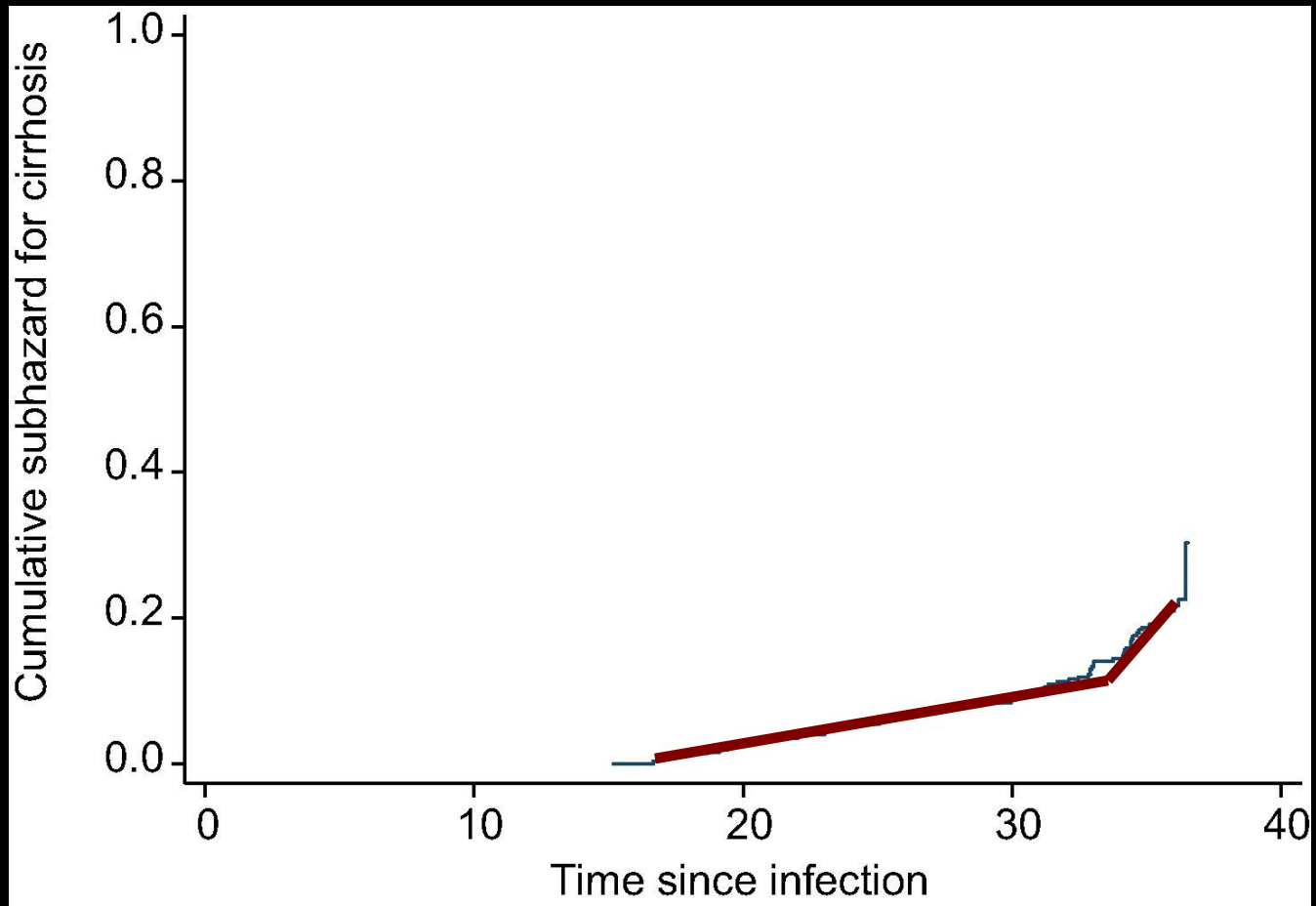
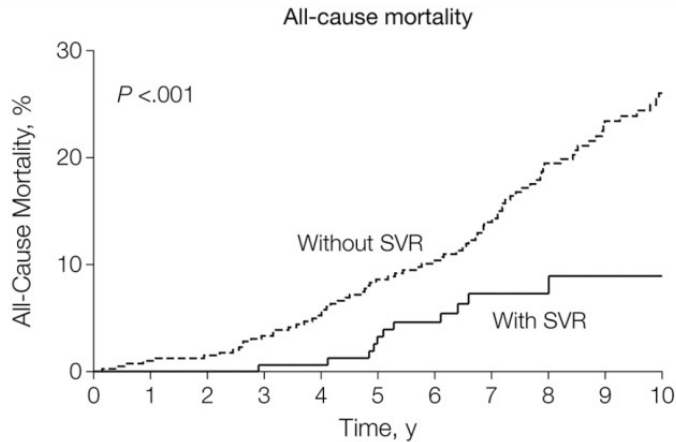


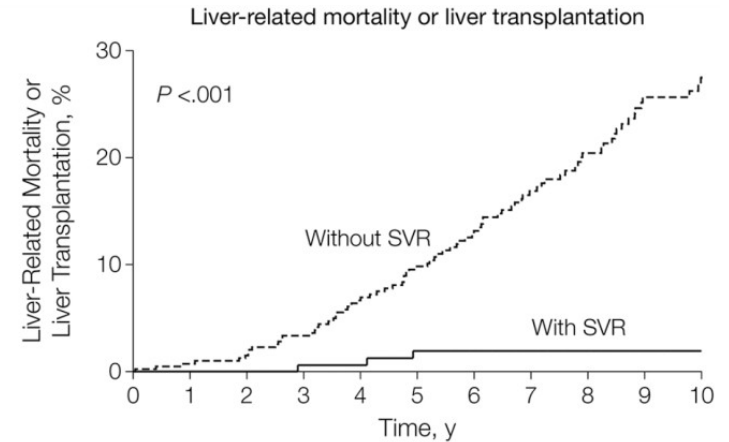
Fig. 4



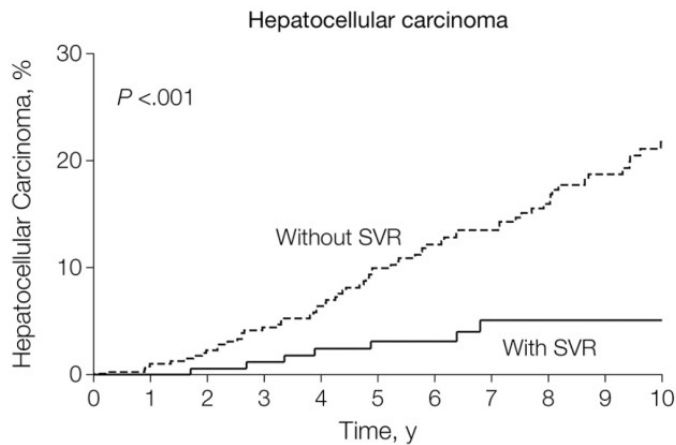
HCV clearance stops liver complications



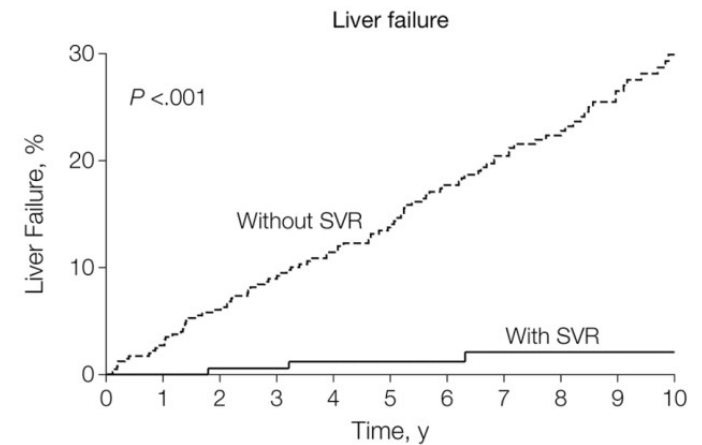
| No. at risk | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Without SVR | 405 | 393 | 382 | 363 | 344 | 317 | 295 | 250 | 207 | 164 | 135 |
| With SVR | 192 | 181 | 168 | 162 | 155 | 144 | 125 | 88 | 56 | 40 | 28 |



| No. at risk | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Without SVR | 405 | 392 | 380 | 358 | 334 | 305 | 277 | 229 | 187 | 146 | 119 |
| With SVR | 192 | 181 | 168 | 162 | 155 | 144 | 125 | 88 | 56 | 40 | 28 |



| No. at risk | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Without SVR | 405 | 390 | 375 | 349 | 326 | 294 | 269 | 229 | 191 | 151 | 122 |
| With SVR | 192 | 181 | 167 | 161 | 152 | 142 | 124 | 86 | 54 | 39 | 27 |

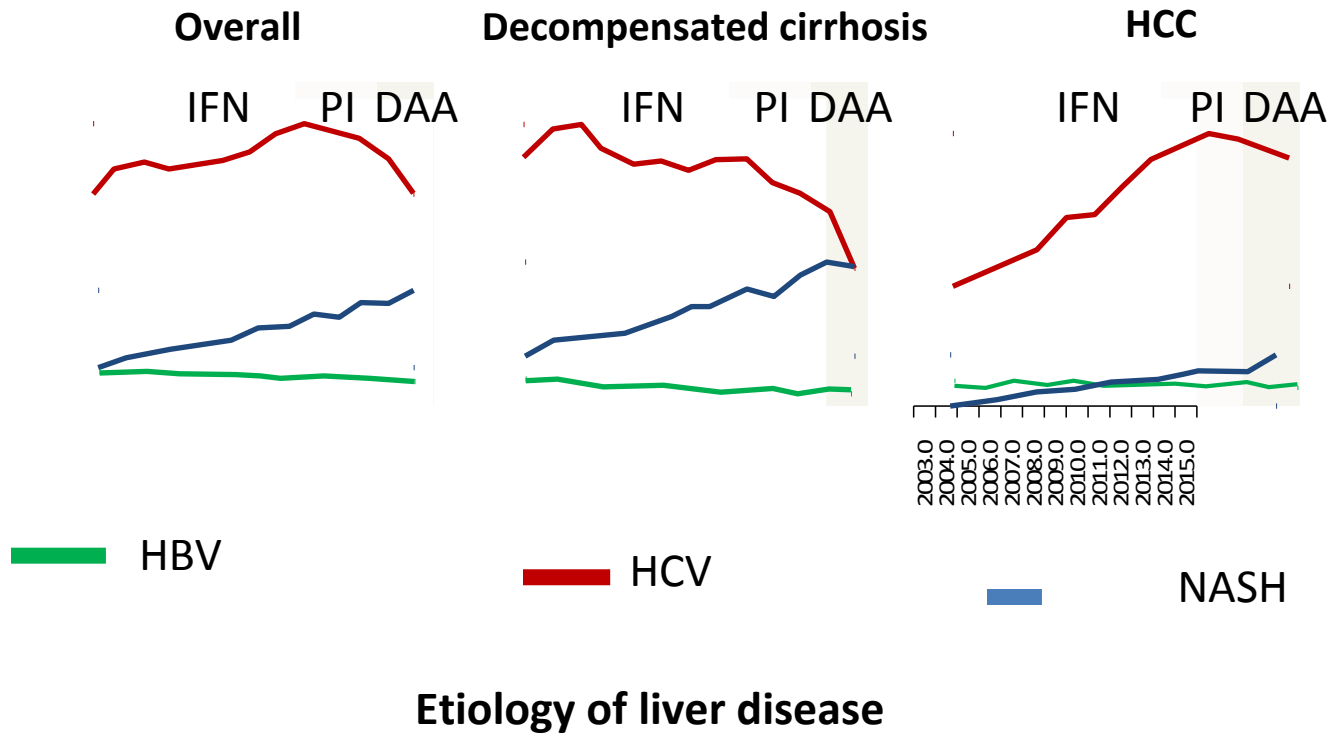


| No. at risk | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|-------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Without SVR | 405 | 384 | 361 | 337 | 314 | 288 | 259 | 216 | 184 | 143 | 113 |
| With SVR | 192 | 180 | 166 | 160 | 152 | 141 | 123 | 88 | 56 | 40 | 28 |

Reduction in liver transplant wait-listing in the era of DAA therapy

Annual standardized incidence rates of LT wait-listing per 100,000 US population
Indication for wait-listing

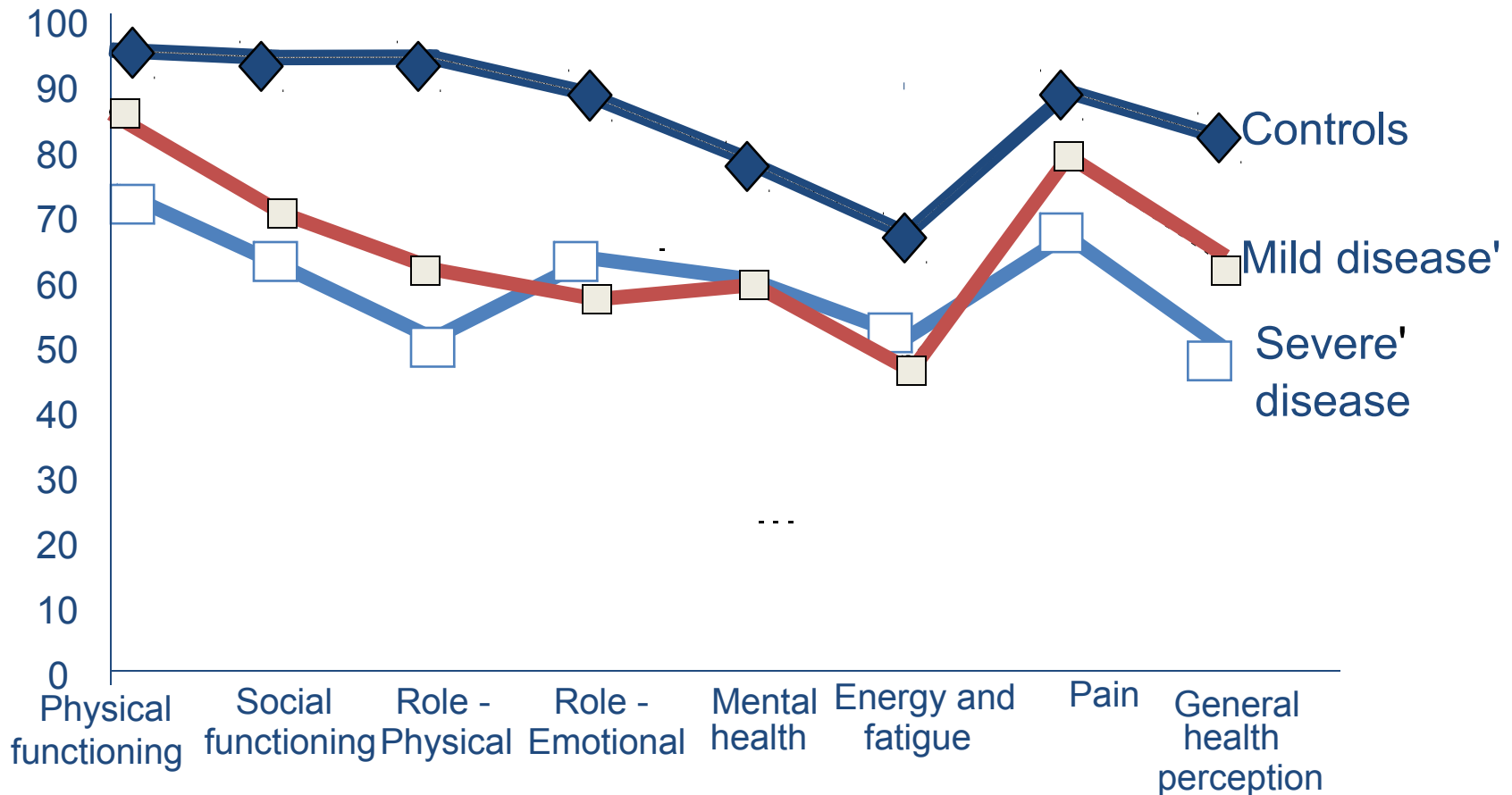
LT WL rate per 100,000 US population



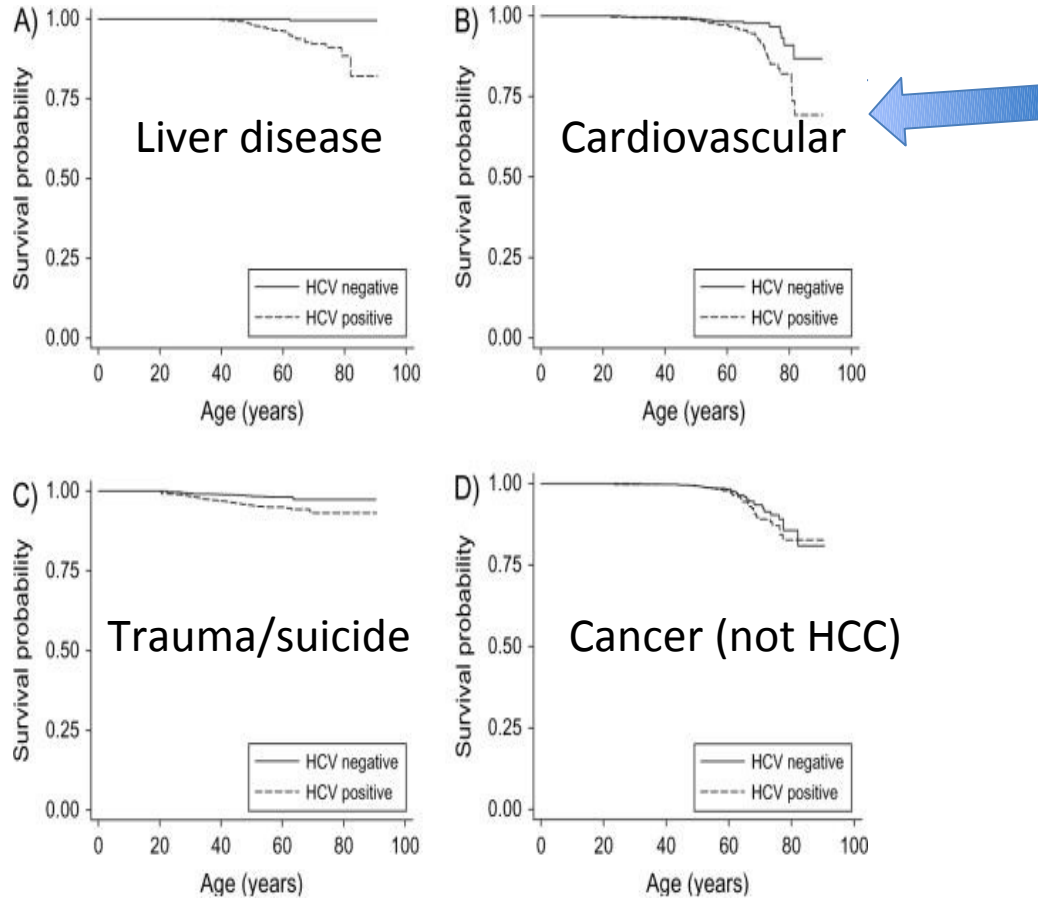
Cost-**benefits** in mild disease

- Avoidance of liver complications
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- Prevention of transmission

Patients with chronic HCV feel unwell



Age specific HCV mortality USA 1991-2003



HCV eradication reduces the occurrence of major adverse cardiovascular events (MACE) in hepatitis C cirrhotic patients

Predictors of MACE (MI, IHD, CVA, Peripheral arterial disease) in 878 patients with compensated HCV-related cirrhosis Multivariate Cox proportional hazards model

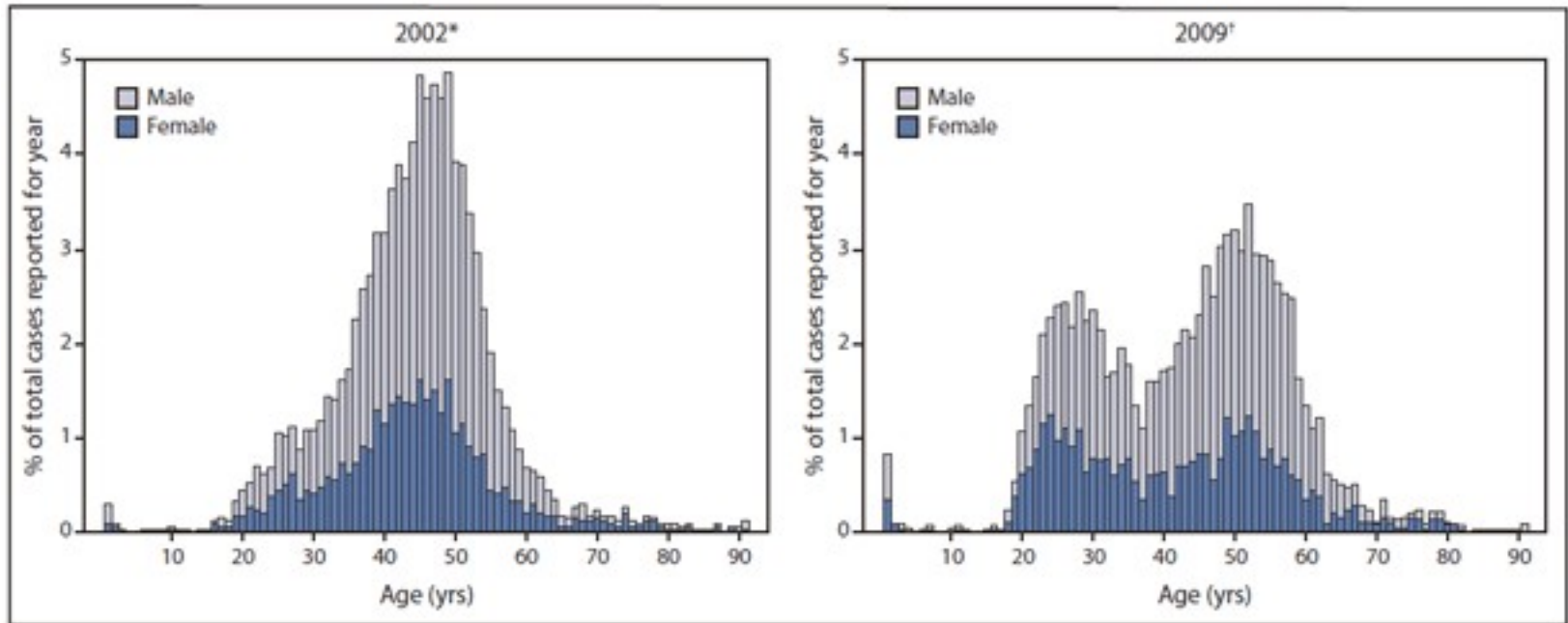
| Features | HR | 95% CI | P-value |
|-----------------------------|------|------------|---------|
| Arterial hypertension | 3.24 | 1.78–5.91 | <0.001 |
| Tobacco consumption | Ref | | <0.001 |
| Never | 1.75 | 0.76–3.91 | 0.18 |
| Past | 4.20 | 2.11–8.64 | <0.001 |
| Ongoing | | | |
| Ethnic origin | | | <0.001 |
| European | Ref | | |
| African | 1.14 | 0.36–2.80 | 0.80 |
| Asian | 9.20 | 2.46–24.95 | 0.003 |
| Serum albumin ≤ 35 g/l | 2.78 | 1.30–5.56 | 0.009 |
| SVR | 0.35 | 0.09–0.97 | 0.044 |

SVR is associated with a reduced rate of cardiovascular events

Cost-**benefits** in mild disease

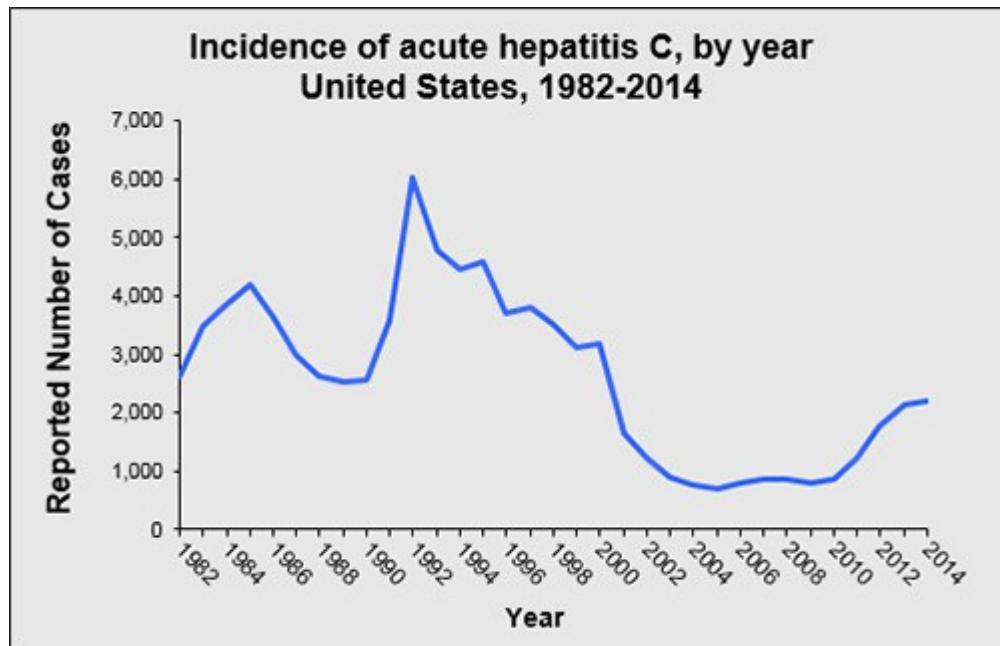
- Avoidance of liver complications
- Avoidance of non-liver complications
- **Prevention of transmission**

What happens if you don't treat early HCV?



Age distribution of newly reported confirmed cases of hepatitis C virus infection --- Massachusetts, 2002 and 2009

HCV is on the rise!



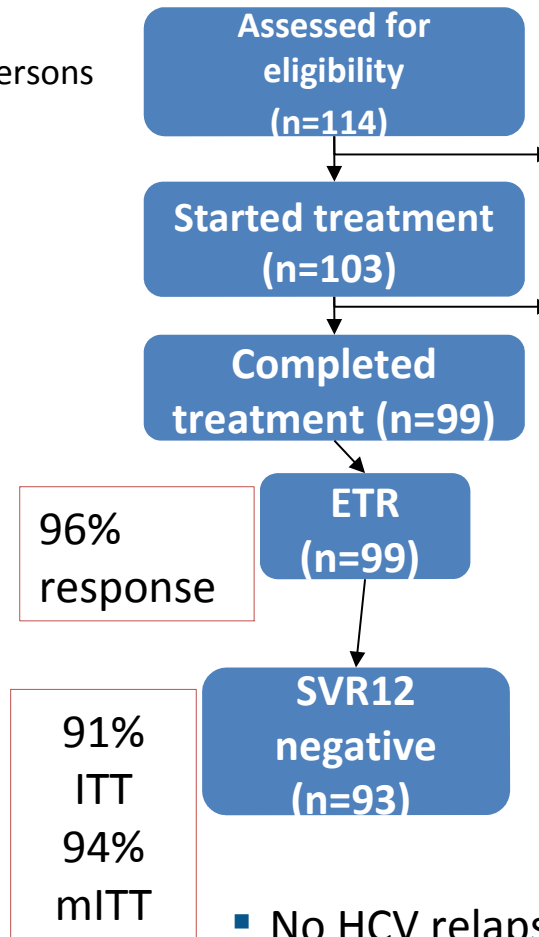
<https://www.cdc.gov/hepatitis/statistics/index.htm>

SIMPLIFY: Efficacy and safety of SOF/VEL in people with chronic HCV infection and recent injecting drug use

- International study of SOF/VEL for 12 weeks in persons with recent IDU (< 6 months)
- 19 sites (Australia/New Zealand, NA, Europe)

| Characteristics, n (%) | SOF/VEL (12 wks) n=103 |
|--|------------------------|
| Age <40 years | 25 (24) |
| Female sex | 29 (28) |
| OST and injecting drug use (in last month) | |
| No OST, no injecting | 12 (12) |
| No OST, injecting | 33 (32) |
| OST, no injecting | 15 (15) |
| OST, injecting | 43 (42) |
| HCV genotype | |
| 1 | 36 (35) |
| 2 | 5 (5) |
| 3 | 60 (58) |
| 4 | 2 (2) |
| Fibrosis stage (METAVIR) | |
| F0–F1 | 59 (62) |
| F2–F3 | 27 (28) |
| F4 | 9 (9) |

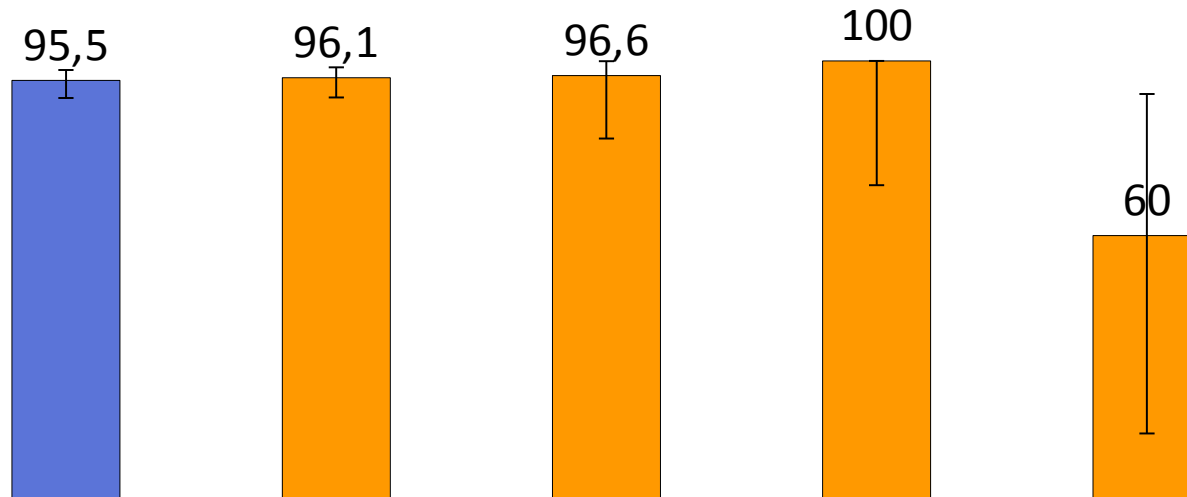
Grebely



- No HCV relapse or re-infection to date

SOF/VEL for 12 weeks was effective in persons with recent IDU
Additional follow-up is needed to define risk of reinfection

Trial of Grazoprevir/Elbasvir in Injecting drug users



| | All GT ⁺ | GT1a* | GT1b | GT4 | GT6 |
|--|---------------------|---------|-------|-------|-----|
| | 189/198 | 147/153 | 28/29 | 11/11 | 3/5 |
| Failures | | | | | |
| Relapse | 7 | 4 | 1 | 0 | 2 |
| Discontinuation | 2 | 2 | 0 | 0 | 0 |
| Reinfection – counted as success | | | | | |
| | 5 | 3 | 0 | 0 | 2 |
| LTFU or discontinued unrelated to Virologic Failure – excluded from mFAS analysis | | | | | |
| | 2 | 1 | 1 | 1 | 0 |

*Includes one subject with mixed infection (GT1a and GT1b) who achieved SVR12

Incidence of reinfection

Through FW12

Through
>FW48

Through
FW24

From End of Treatment Through Observation Visit 1

- 8 reinfections
- 197.5 person years
- 4.0 reinfections per 100 person years (95% CI: 1.7, 8.0)

From End of Treatment Through Observation Visit 1 (Includes only those patients with persistent HCV RNA)

- 5 reinfections
- 199.0 person years
- 2.5 reinfections per 100 person years (95% CI: 0.8, 5.9)

Cost-**benefits** in mild disease

- Avoidance of liver complications PROVEN
(and avoids long term follow up costs)
- Avoidance of non-liver complications PROVEN
- Prevention of transmission DATA SUPPORTED

Cost-benefits in mild disease

Costs of therapy (drugs /admin) MINUS costs of follow up

Costs vary by country but in ALL countries drug price should no longer be rate limiting

Cost – benefits of treating mild disease

- Treating mild disease is always cost-effective
- Is it affordable?
- If treating mild disease is not affordable in your country then a focus on severe disease may be necessary

Cost – Benefits in Mild Disease

- Therapy in mild disease is always cheaper, easier and avoids long term follow up costs
- For most countries the drugs are priced so that therapy in mild disease is affordable
- If the drugs are not affordable then a focus on severe disease may be required