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CONGRESO NACIONAL
DE LA SOCIEDAD ESPAÑOLA
DE FARMACIA HOSPITALARIA

SEVILLA 17/19 OCT 2019



NUEVOS CONCEPTOS EN LA ERA DE LA POLIFARMACIA EN EL VIH

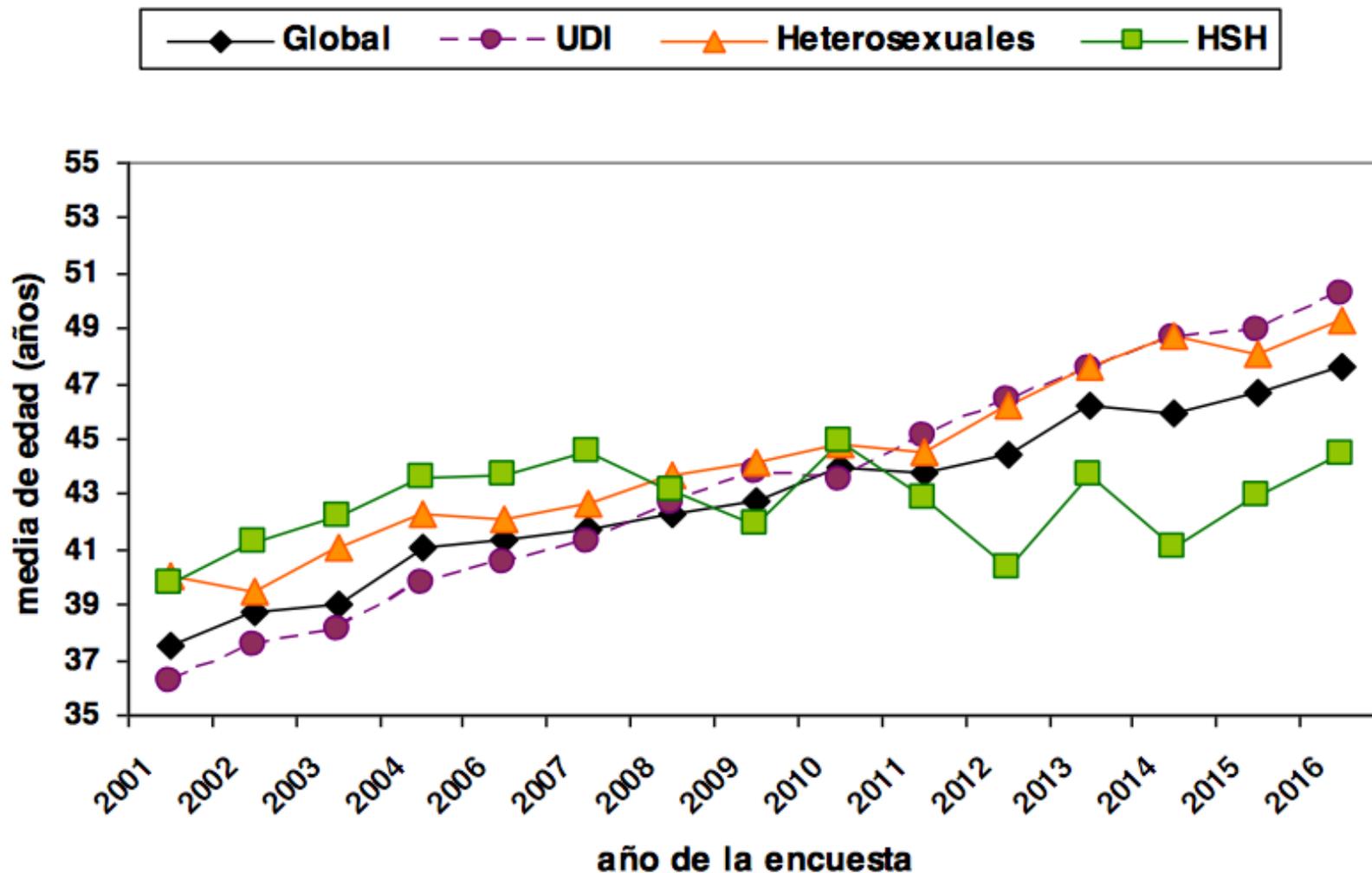
Alfonso Cabello Úbeda
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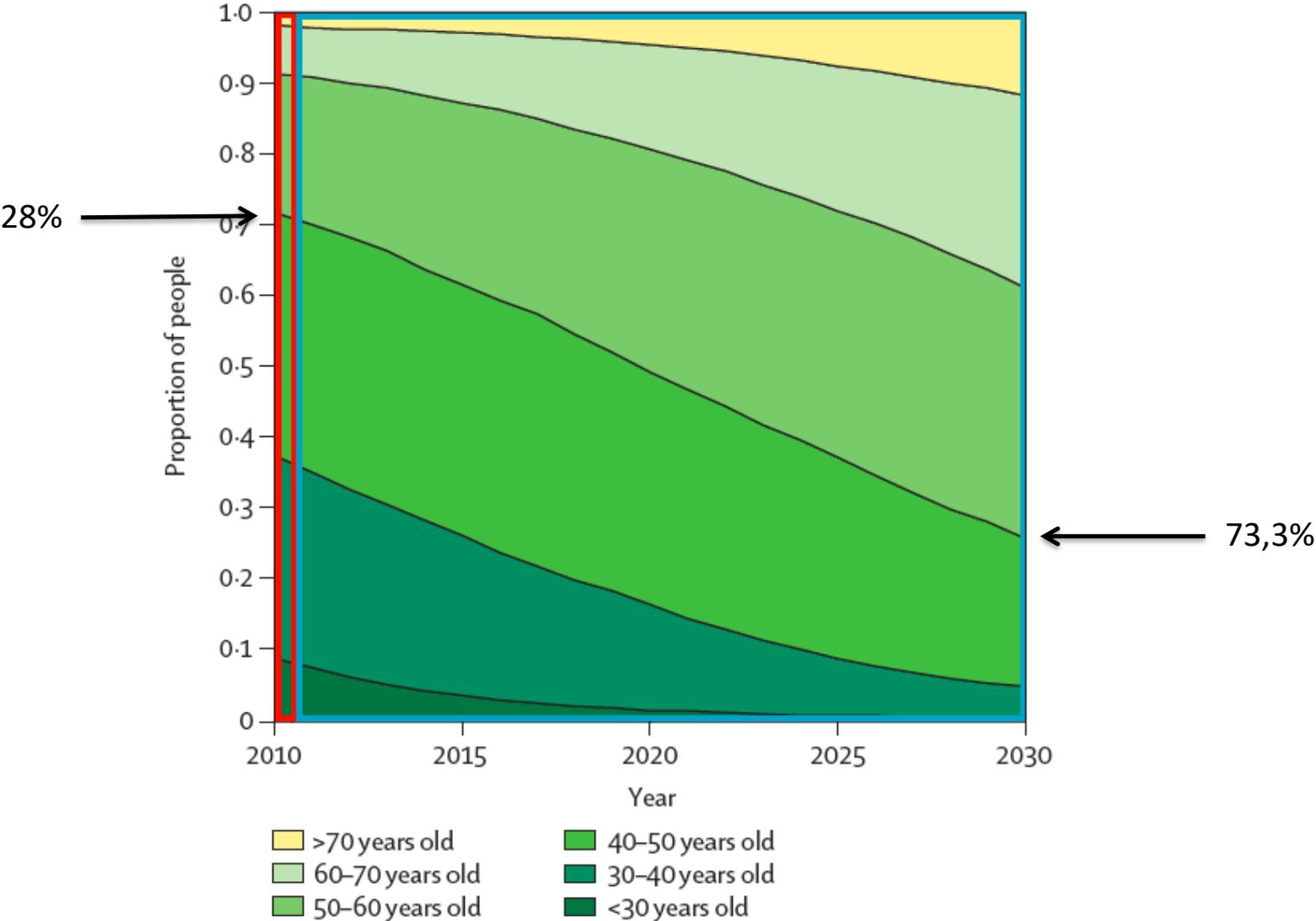
Envejecimiento



Mediana de edad

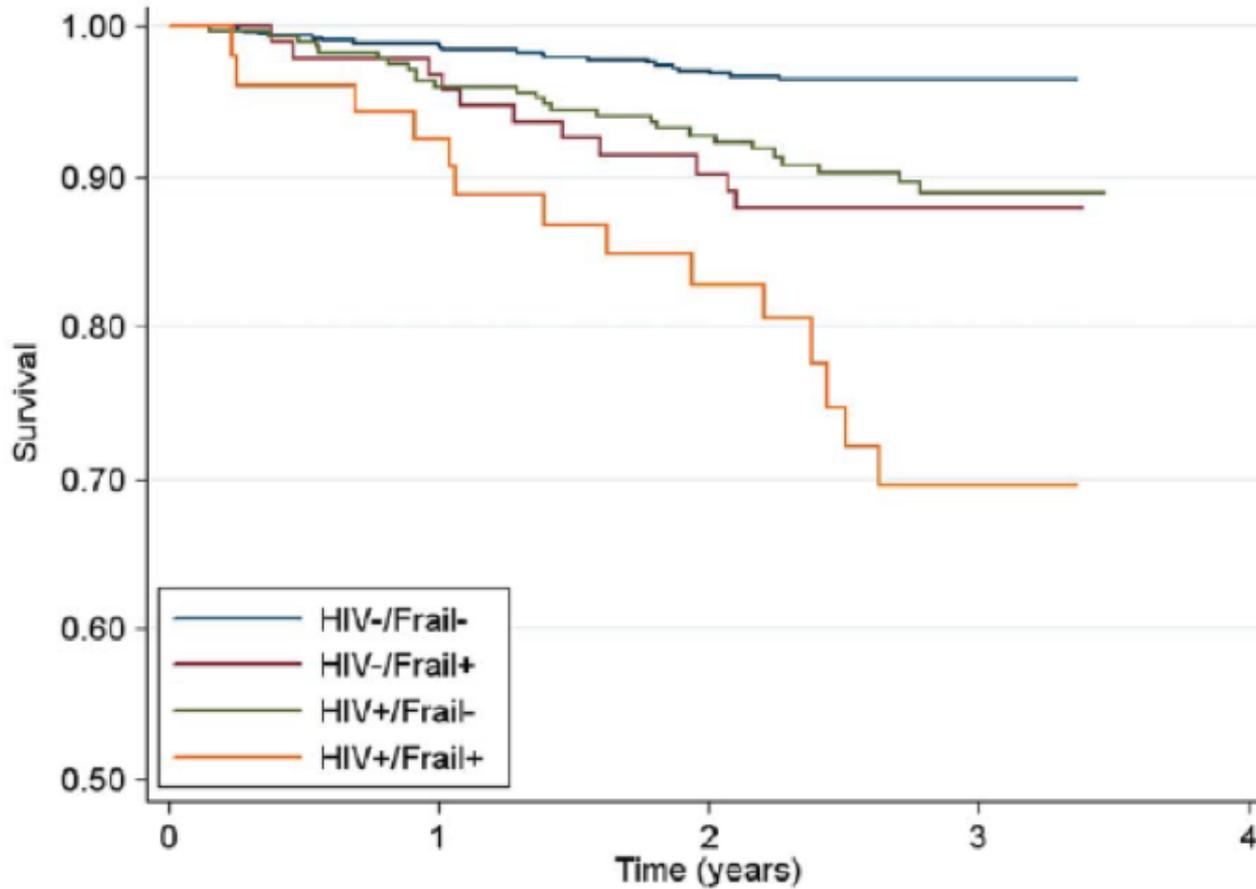


Modelización Cohorte ATHENA



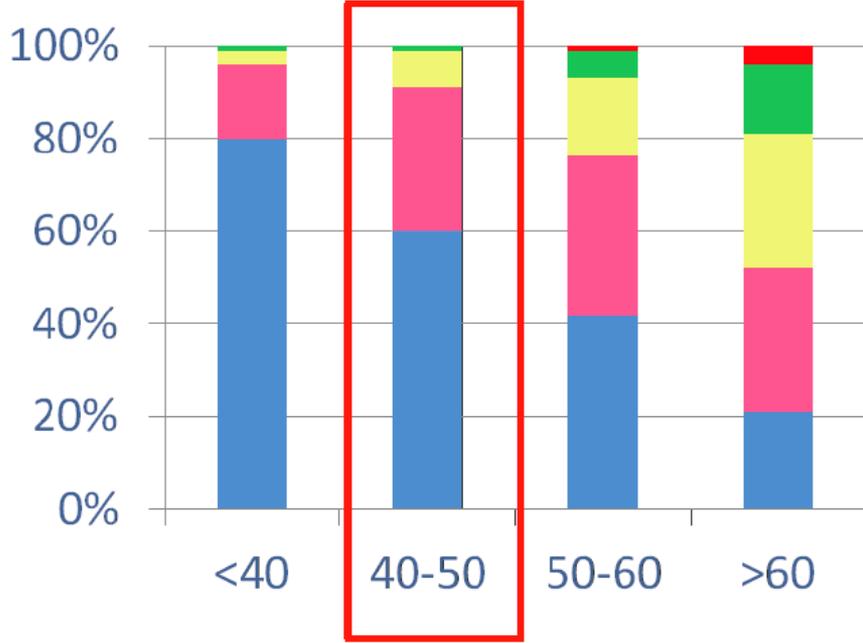
Fragilidad como predictor de eventos adversos en salud

Mortalidad. Cohorte ALIVE (Fried) – Sinergia fragilidad/VIH

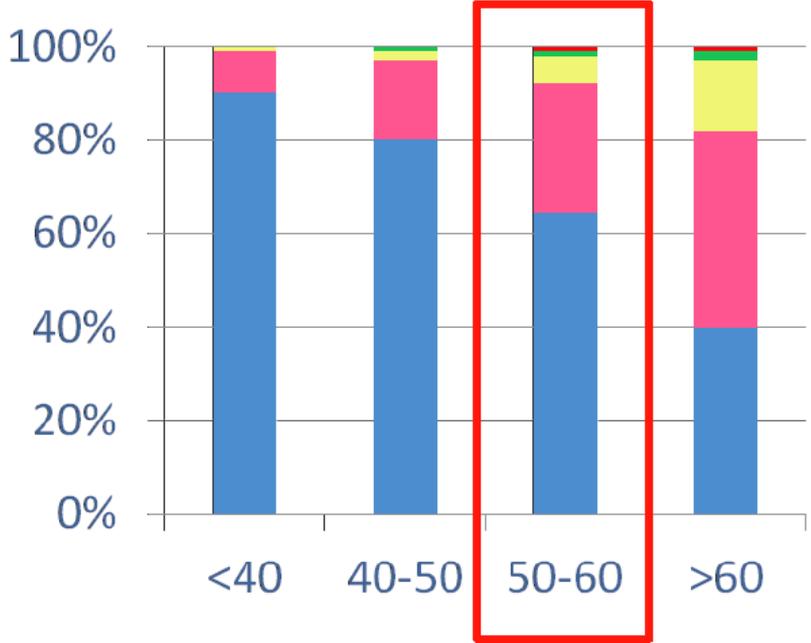


Similares comorbilidades pero con 10 años mas

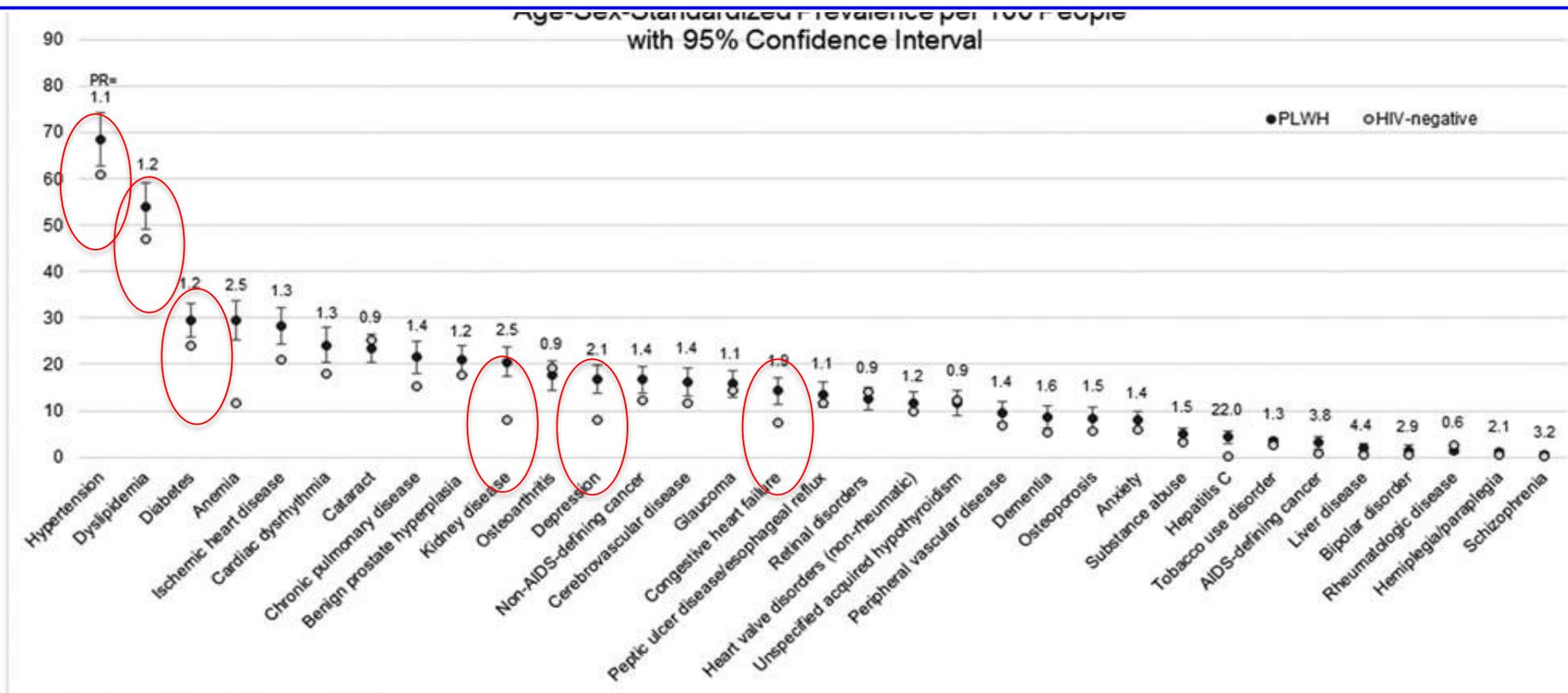
VIH+



VIH-



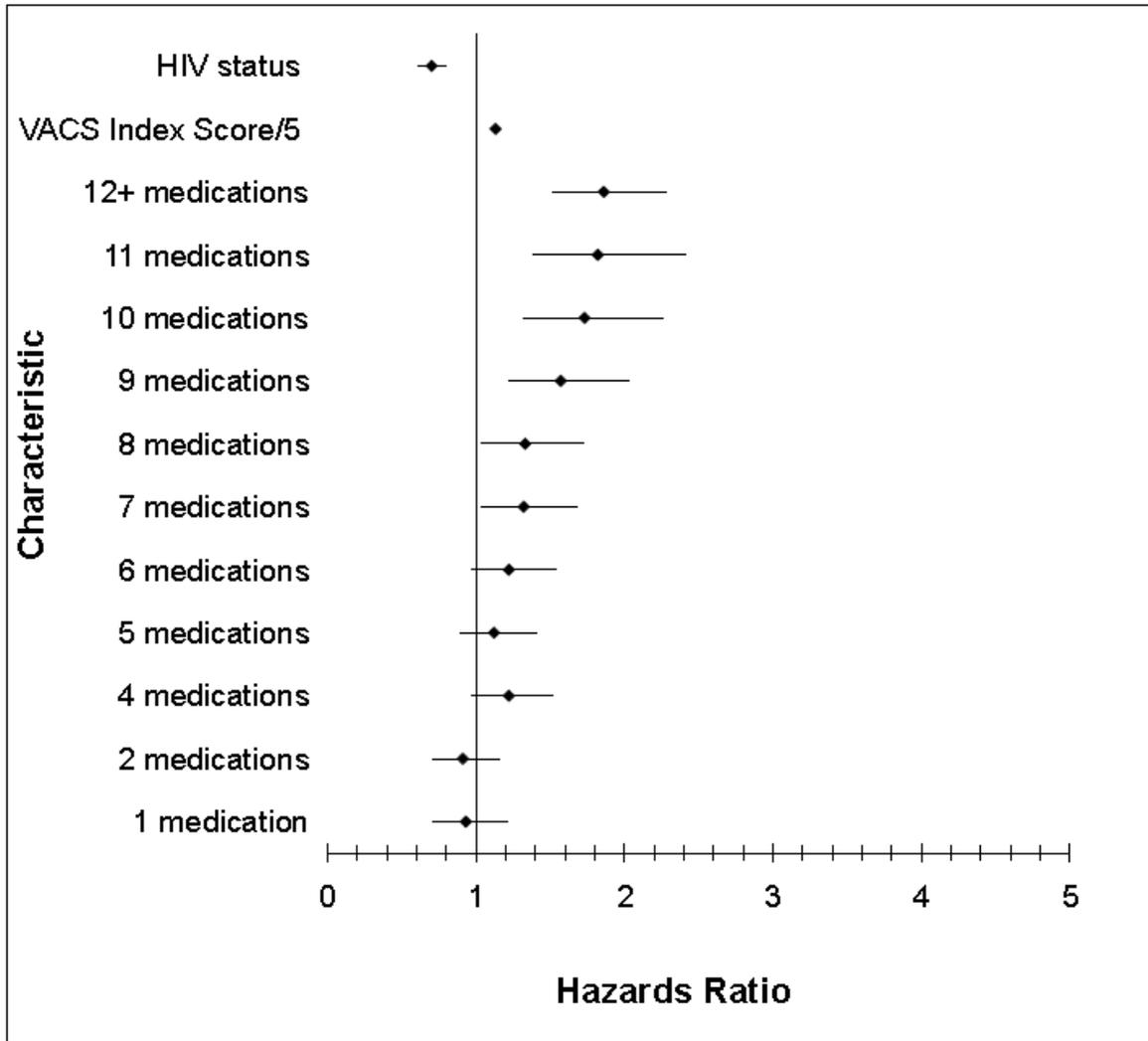
- Ninguna
- 1 comorbilidad
- 2 comorbilidades
- 3 comorbilidades
- 4 comorbilidades



Abbreviations: HIV, human immunodeficiency virus; PLWH, people living with HIV; PR, prevalence ratio.

Standardized prevalence of non-HIV conditions and AIDS-defining cancer per 100 people with 95% confidence intervals and prevalence ratios for PLWH versus HIV-negative individuals

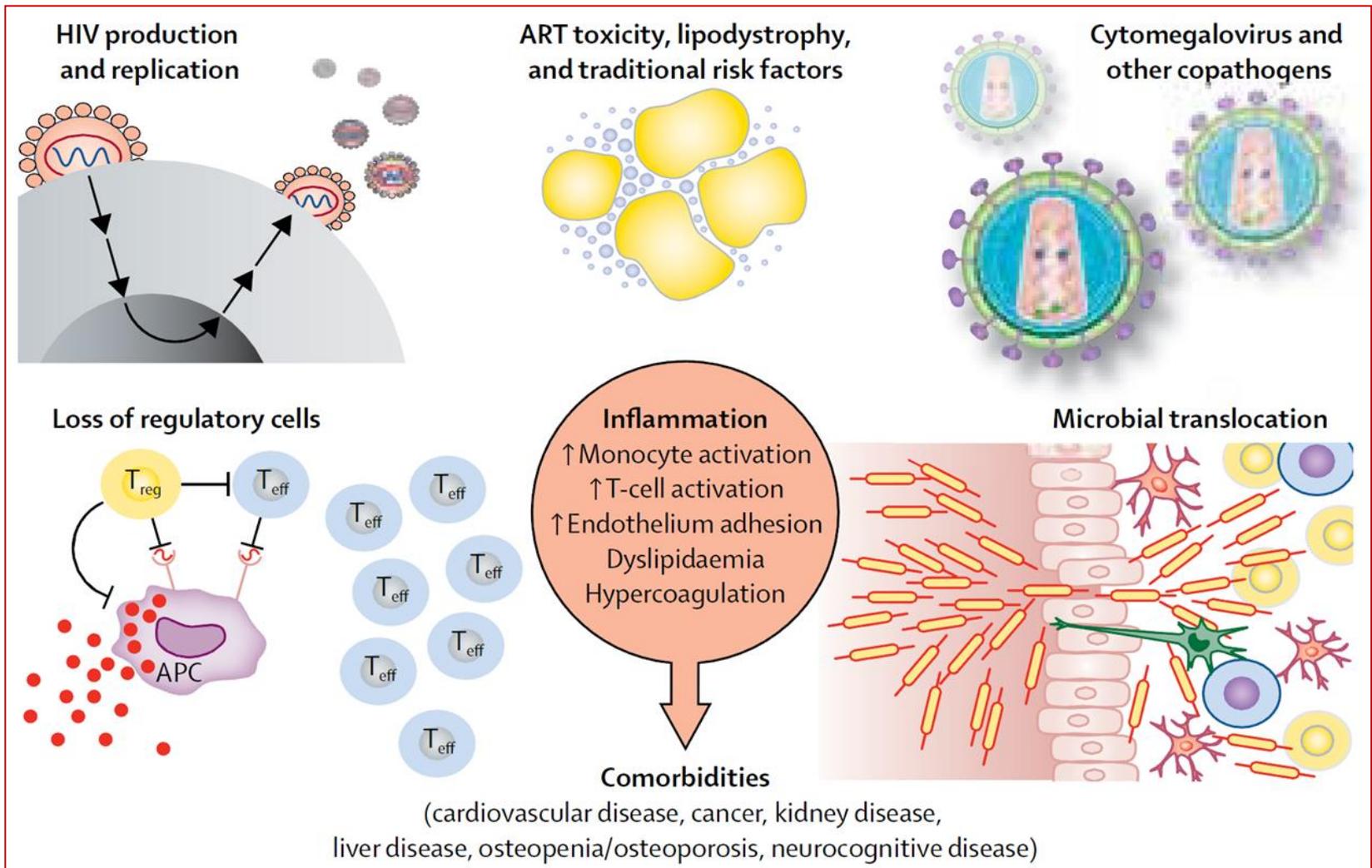
Polimedición y mortalidad (Cohorte VACS)



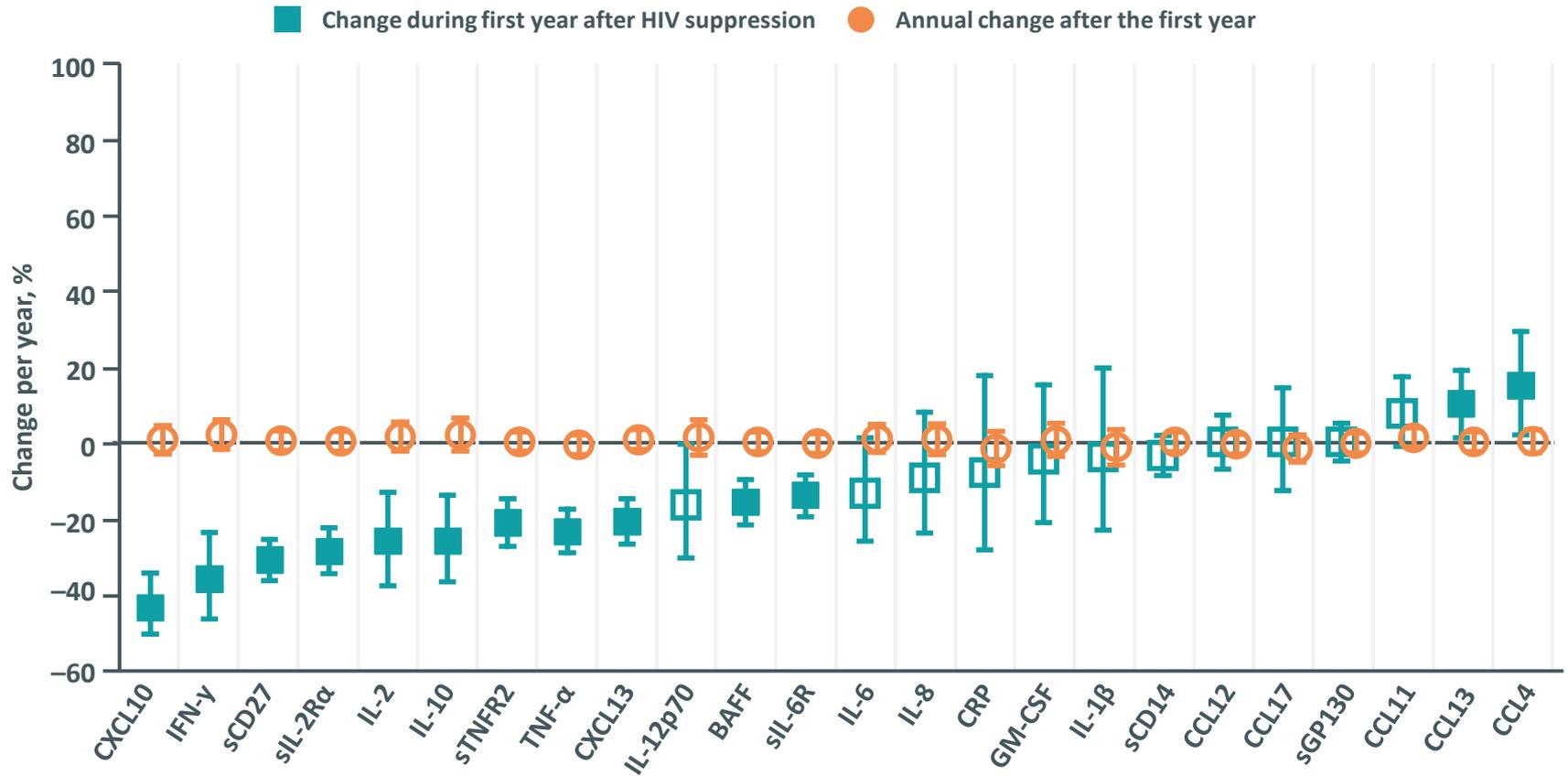
Seven or more medications is associated with an increased risk of mortality after adjusting for HIV status and disease severity.

*Note: reference is 3 medications

| Non-ARV drugs | ATV/r | DRV/c | DRV/r | LPV/r | EFV | ETV | NVP | RPV | MVC | DTG | EVG/c | RAL | ABC | FTC | 3TC | TDF | ZDV | |
|----------------------|-------------------------|----------------------|-----------------|-----------------|---------------------|-------------------|------|--------|-----------------|-----|-------------------|----------------|------|-----|-----|-----|-----|-----------------|
| Cardiovascular drugs | atorvastatin | ↑ | ↑ | ↑ | ↑490% | ↓43% | ↓37% | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | fluvastatin | ↔ | ↑ | ↔ | ↔ | ↑ | ↑ | ↔ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | pravastatin | ↔ | ↑ | ↑81% | ↔ | ↓44% | ↓ | ↔ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | rosuvastatin | ↑213% | ↑ | ↑48% | ↑107% | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↑38% | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | simvastatin | ↑ | ↑ | ↑ | ↑ | ↓68% | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | amlodipine | ↑ ⁱⁱⁱ | ↑ | ↑ | ↑ ⁱⁱⁱ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | diltiazem | ↑ ⁱⁱⁱ | ↑ | ↑ | ↑ ⁱⁱⁱ | ↓69% | ↓E | ↓ | E | E | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | metoprolol | ↑ ⁱⁱⁱ | ↑ | ↑ | ↑ ⁱⁱⁱ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | verapamil | ↑ ⁱⁱⁱ | ↑ | ↑ | ↑ ⁱⁱⁱ | ↓ | ↓E | ↓ | E | E | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | warfarin | ↑ or ↓ | ↑ | ↓ | ↓ | ↑ or ↓ | ↑ | ↑ or ↓ | ↔ | ↔ | ↔ | ↑ or ↓ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | CNS drugs | diazepam | ↑ | ↑ | ↑ | ↑ | ↓ | ↑ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ |
| midazolam (oral) | | ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| triazolam | | ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| citalopram | | ↑ ⁱⁱⁱ | ↑ | ↑ | ↑ ⁱⁱⁱ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| mirtazapine | | ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| paroxetine | | ↑↓? | ↑↓? | ↓39% | ↑↓? | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑↓? | ↔ | ↔ | ↔ | ↔ | ↔ | |
| sertraline | | ↓ | ↑ | ↓49% | ↓ | ↓39% | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| bupropion | | ↓ | ↔ | ↓ | ↓57% | ↓55% | ↔ | ↓ | ↔ | ↔ | ↔ | ↑? | ↔ | ↔ | ↔ | ↔ | ↔ | |
| pimozide | | ↑ ⁱⁱⁱ | ↑ | ↑ | ↑ ⁱⁱⁱ | ↑ | ↓ | ↓ | ↔ ^{iv} | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| carbamazepine | | ↑D | ↑D | ↑ | ↑D | ↓27%D36% | D | ↓D | D | D | D | D | D | ↑ | ↔ | ↔ | ↔ | ↑ ^{ix} |
| lamotrigine | | ↓32% ⁱ | ↔ | ↓ ⁱⁱ | ↓50% | ↓ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| phenytoin | ↓D | D | ↓D | ↓D | ↓D | D | ↓D | D | D | D | D | D | D | ↔ | ↔ | ↔ | ↓ | |
| Anti-infectives | clarithromycin | ↑ ⁱⁱⁱ | ↑ | ↑ | ↑ ⁱⁱⁱ | ↓ | ↓E | ↓ | E | E | ↔ | ↑E | ↔ | ↔ | ↔ | ↔ | ↔ | D |
| | fluconazole | ↔ | ↑? | ↔ | ↔ | ↔ | E86% | E100% | E | ↔ | ↔ | ↑? | ↔ | ↔ | ↔ | ↔ | ↔ | E74% |
| | itraconazole | ↑E | ↑E | ↑E | ↑E | ↓ | ↓E | ↓61% | E | E | ↔ | ↑E | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | rifabutin | ↑ | ↑D | ↑E50% | ↑ | ↓38% | D37% | ↑17% | D | * | ↔ | ↑D | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | rifampicin | D72% | D | D | D | D26% | D | D58% | D80% | D | D54% ^x | D | D40% | D | ↔ | ↔ | ↔ | D47% |
| | voriconazole | ↓ | ↑E | ↓ | ↓ | ↓E | ↑E | ↓E | E | E | ↔ | ↑E | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | antacids | D | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | D | ↔ | D | D | D | ↔ | ↔ | ↔ | ↔ | ↔ |
| PPIs | D | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | D | ↔ | ↔ | ↔ | E | ↔ | ↔ | ↔ | ↔ | ↔ | |
| H2 blockers | D | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | D | ↔ | ↔ | ↔ | E | ↔ | ↔ | ↔ | ↔ | ↔ | |
| Miscellaneous | alfuzosin | ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | beclometasone inhal. | ↑? ^v | ↑? ^v | ↓11% | ↑? ^v | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ ^v | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | buprenorphine | ↑67% | ↑ | ↑ ^{vi} | ↔ | ↓50% | ↓25% | ↔ | ↔ | ↔ | ↔ | ↑35% | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | budesonide inhal. | ↑ | ↑ | ↑ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | ergot derivatives | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↓ | E | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | ethinylestradiol | ↓ ^{vii} | ↑ | ↓ | ↓ | ↔ ^{viii} | ↔ | ↓ | ↔ | ↔ | ↔ | ↓ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | fluticasone inhal. | ↑ | ↑ | ↑ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | methadone | ↓ ^{ii, iii} | ↑? | ↓16% | ↓53% ⁱⁱⁱ | ↓52% | ↑6% | ↓≈50% | ↓16% | ↔ | ↔ | ↔ | ↔ | ↓ | ↔ | ↔ | ↔ | E29-43% |
| | salmeterol inhal. | ↑ ⁱⁱⁱ | ↑ | ↑ | ↑ ⁱⁱⁱ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | sildenafil (erec. dys.) | ↑ | ↑ | ↑ | ↑ | ↓ | ↓37% | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | St John's wort | D | D | D | D | D | D | D | D | D | D | D | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| varenicline | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | |



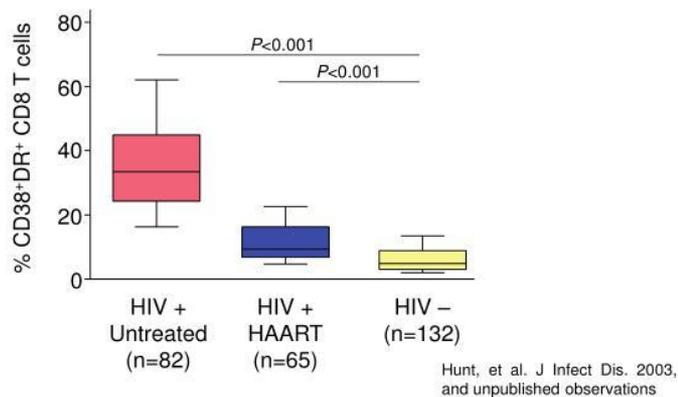
Different effect of HIV on circulating markers of inflammation and immune activation



Filled markers represent differences that were statistically significant after Bonferroni adjustment ($p < 0.002$)

¿Persistencia de activación inmune residual?

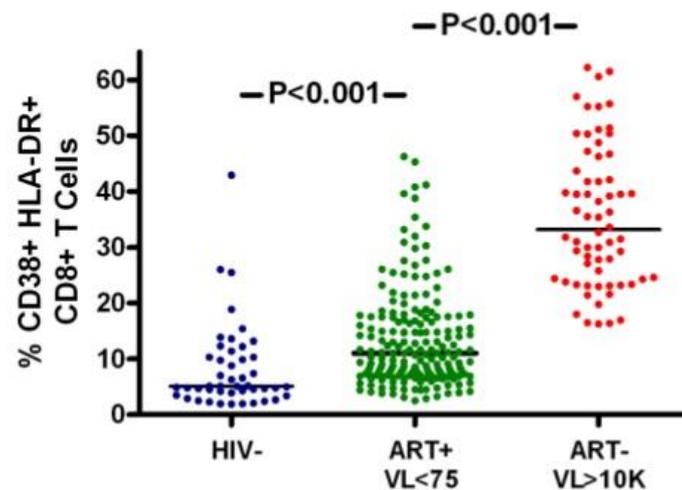
ART and T Cell Immune Activation ^{Slide 9 c}



T cell activation declines during long-term ART, but remains elevated, even after many years of viral suppression

From DC Douek, MD, at San Francisco, CA: March 24, 2013, IAS-USA.

But Remains Abnormally High During ART-mediated Viral Suppression



Hunt et al, JID, 2003; PLoS One, 2011

¿PERSISTE ACTIVACIÓN INMUNE RESIDUAL?

Nuevos diagnósticos VIH

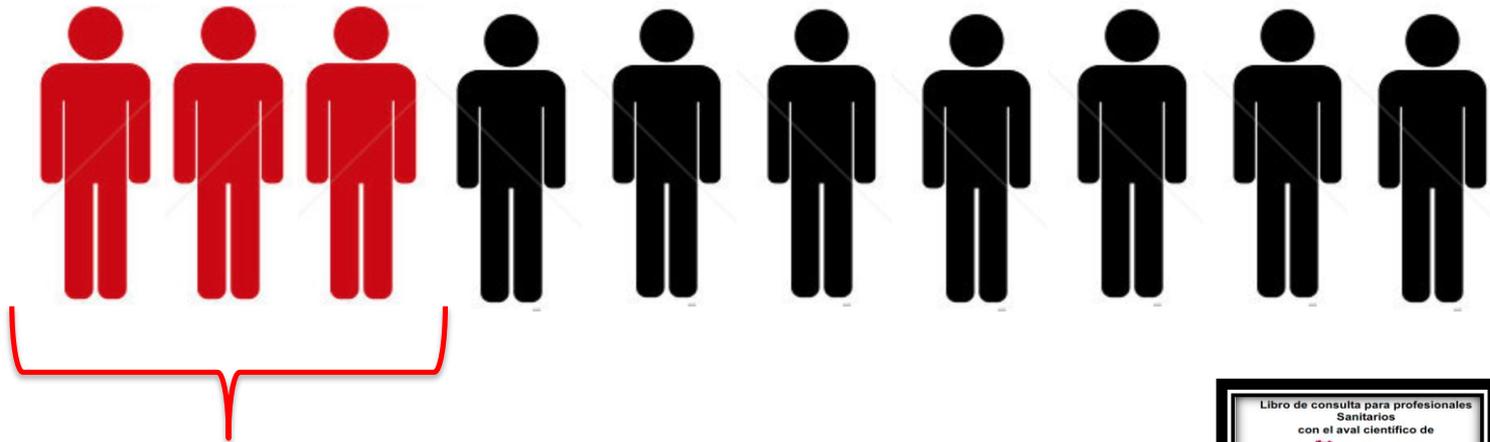
Estimación de la prevalencia de personas con el VIH en la población general 0,4%



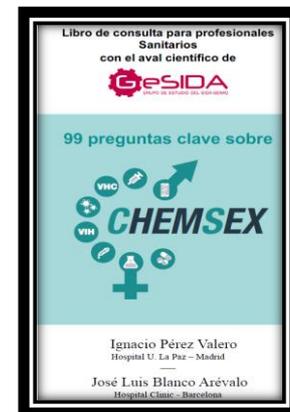
Fuente: SINIVIH 2016

Utilización de drogas en HSH

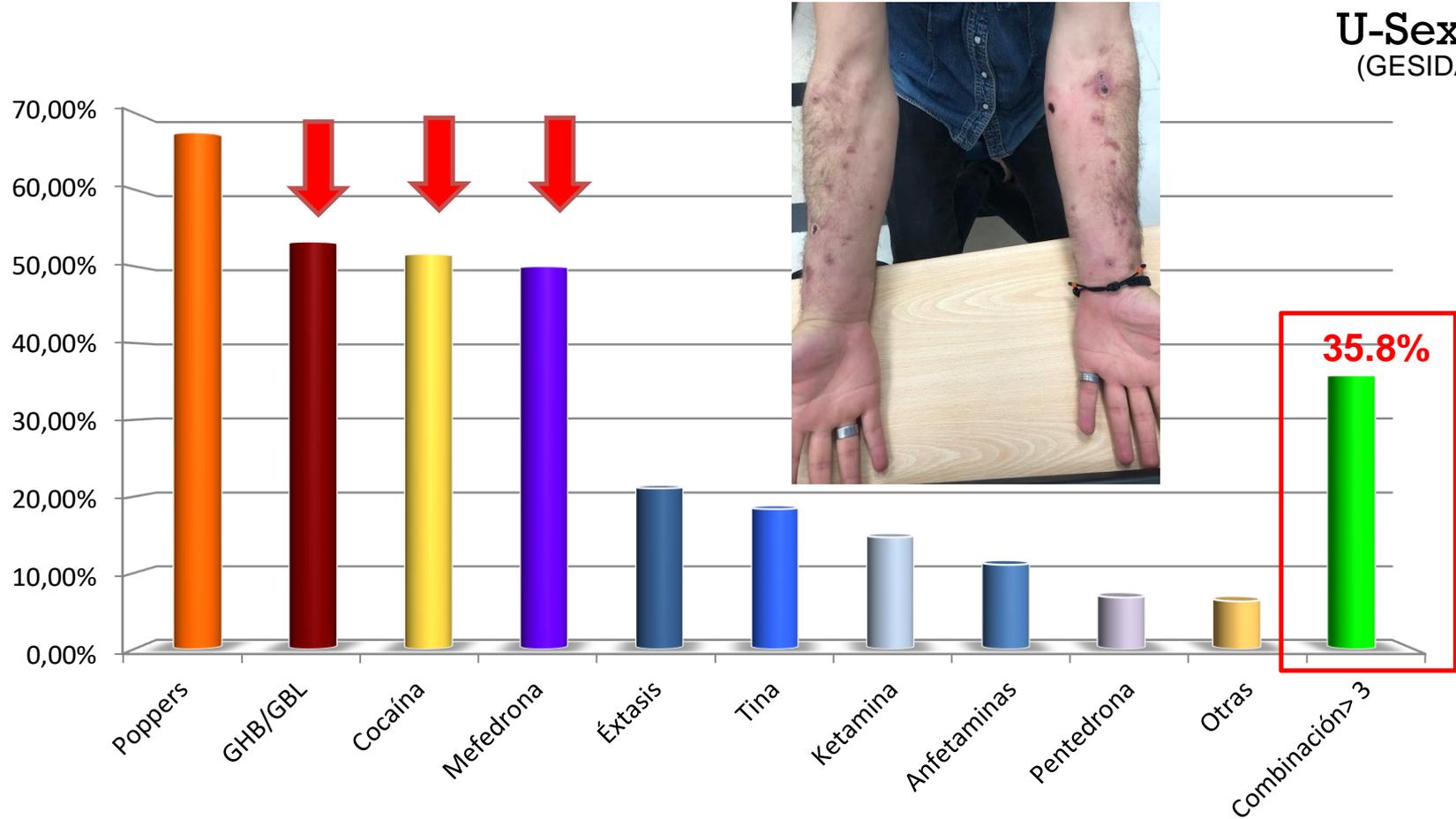
Hombres que tienen sexo con hombres infectados por el VIH



29,1% utilizan drogas de forma intencionada para potenciar y facilitar las relaciones sexuales (Chemsex).



Consumo durante relaciones sexuales en el último año



TARV y sus interacciones con drogas recreativas

| Droga | Mefedrona | Metanfetamina | GHB | Éxtasis | Cocaína | Agentes disfunción eréctil | Ketamina |
|----------------|-----------|---------------|--------|---------|---------------------|----------------------------|----------|
| Vía Metabólica | CYP2D6 | CYP2D6 | CYP2D6 | CYP2D6 | Esterasas CYP3A4 | CYP3A4 | CYP3A4 |

| CYP450 IC50 (µM) | 1A2 | 2B6 | 2C8 | 2C9 | 2C19 | 2D6 | 3A |
|------------------|-----|-----|-----|-----|------|-----|------|
| COBI | >25 | 2.8 | >25 | >25 | >25 | 9.2 | 0.15 |
| RITO | >25 | 2.9 | 5.5 | 4.4 | >25 | 2.8 | 0.11 |

-  Moderado riesgo de interacción
-  Riesgo de interacción
-  Alto riesgo de interacción

Antiretrovirals and Recreational Drugs

Charts produced October 2014. Full information available at www.hiv-druginteractions.org and www.hiv-druginteractionslite.org

| | ATV/r | DRV/r | FPV/r | IDV/r | LPV/r | SQV/r | EFV | ETV | NVP | RPV | MVC | DTG | EVG/c | RAL | ABC | FTC | 3TC | TDF | ZDV |
|----------------------|----------------------------------|-----------------|----------------|----------------|----------------|-------------------|--------------------|----------------|----------------|----------------|-------------------|-----|----------------|----------------|-----|-----|-----|-----|-----|
| Stimulants | Amyl nitrate (Poppers) | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Cocaine | ↑ ^{ab} | ↑ ^a | ↑ ^a | ↑ ^a | ↑ ^{ab} | ↑ ^{ab} | ↑ ^c | ↑ ^c | ↑ ^c | ↔ ^b | ↔ | ↔ | ↑ ^a | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Ecstasy (MDMA) | ↑ ^d | ↑ ^d | ↑ ^d | ↑ ^d | ↑ ^d | ↑ ^d | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ ^d | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Mephedrone | ↑ ^e | ↑ ^e | ↑ ^e | ↑ ^e | ↑ ^e | ↑ ^e | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ ^e | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Methamphetamine | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ |
| Depressants | Alcohol | ↔ | ↔ | ↔ ^f | ↔ | ↔ ^f | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ |
| | Alprazolam | ↑ ^g | ↑ ^g | ↑ ^g | ↑ ^h | ↑ ^g | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Codeine | ↑ ⁱ | ↑ ⁱ | ↑ ⁱ | ↑ ⁱ | ↑ ⁱ | ↑ ⁱ | ↓ ⁱ | ↓ ⁱ | ↓ ⁱ | ↔ | ↔ | ↔ | ↑ ⁱ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Diazepam | ↑ | ↑ | ↑ | ↑ ^h | ↑ | ↑ | ↓ | ↑ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | GHB (gamma hydroxybutyrate) | ↑ ^j | ↑ ^j | ↑ ^j | ↑ ^j | ↑ ^j | ↑ ^j | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↑ ^j | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Heroin (Diamorphine) | ↔ ^k | ↔ ^k | ↔ ^k | ↔ ^k | ↔ ^k | ↔ ^k | ↔ ^k | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ ^k | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Hydrocodone | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Hydromorphone | ↓ | ↓ | ↓ | ↓ | ↓ | ↓ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Ketamine | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Pethidine (Meperidine) | ↓ ^l | ↓ ^l | ↓ ^l | ↓ ^m | ↓ ^l | ↓ ^l | ↓ ^l | ↓ ^l | ↓ ^l | ↔ | ↔ | ↔ | ↑? | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Methadone | ↓ ^b | ↓16% | ↓18% | ↓ | ↓53% ^b | ↓19% ^{bm} | ↓52% | ↑6% | ↓~50% | ↓16% ^b | ↔ | ↔ | ↑7% | ↔ | ↓ | ↔ | ↔ | ↔ |
| | Midazolam (oral) | ↑ ⁿ | ↑ ⁿ | ↑ ⁿ | ↑ ⁿ | ↑ ⁿ | ↑ ⁿ | ↓ ⁿ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ ⁿ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Morphine | ↓ ^o | ↓ ^o | ↓ ^o | ↓ ^o | ↓ ^o | ↓ ^o | ↑ | ↔ ^o | ↔ | ↔ | ↔ | ↔ | ↔ ^o | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Oxycodone | ↑ | ↑ | ↑ | ↑ | ↑ | ↑ | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Temazepam | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| Triazolam | ↑ ⁿ | ↑ ⁿ | ↑ ⁿ | ↑ ⁿ | ↑ ⁿ | ↑ ⁿ | ↓ ⁿ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ ⁿ | ↔ | ↔ | ↔ | ↔ | ↔ | |
| Hallucinogens | Cannabis | ↓ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ | ↔ |
| | Lysergic acid diethylamide (LSD) | ↑ ^p | ↑ ^p | ↑ ^p | ↑ ^p | ↑ ^p | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ ^p | ↔ | ↔ | ↔ | ↔ | ↔ | |
| | Phencyclidine (PCP, angel dust) | ↑ ^q | ↑ ^q | ↑ ^q | ↑ ^q | ↑ ^q | ↑ ^q | ↓ | ↓ | ↓ | ↔ | ↔ | ↔ | ↑ ^q | ↔ | ↔ | ↔ | ↔ | |

Colour Legend

- No clinically significant interaction expected.
- These drugs should not be coadministered.
- Potential interaction which may require a dosage adjustment or close monitoring.
- Potential interaction predicted to be of weak intensity (<2 fold ↑AUC or <50% ↓AUC). No a priori dosage adjustment is recommended.

Herbolario

| | Darunavir | Dolutegravir | Efavirenz | Elvitegravir/Cobi/FTC/TAF | Raltegravir | Rilpivirine |
|--|-----------|--------------|-----------|---------------------------|-------------|-------------|
| Aloe vera | ◆ | ◆ | ◆ | ◆ | ◆ | ◆ |
| Cubeb pepper (Piper cubeba) | ◆ | ◆ | ◆ | ■ | ◆ | ▲ |
| Echinacea | ◆ | ◆ | ◆ | ◆ | ◆ | ▲ |
| Eucalyptus globulus | ◆ | ◆ | ◆ | ◆ | ◆ | ◆ |
| Garlic | ■ | ■ | ■ | ■ | ◆ | ■ |
| Ginger (Zingiber officinale) | ◆ | ◆ | ◆ | ◆ | ◆ | ▲ |
| Ginkgo biloba | ◆ | ▲ | ■ | ◆ | ◆ | ▲ |
| Goldenseal root (Hydrastis canadensis) | ◆ | ◆ | ◆ | ◆ | ◆ | ◆ |
| Grapefruit juice | ◆ | ◆ | ◆ | ◆ | ◆ | ▲ |
| Hops (Humulus lupulus) | ■ | ■ | ■ | ■ | ◆ | ■ |
| Liquorice (Glycyrrhiza glabra) | ◆ | ▲ | ◆ | ■ | ▲ | ▲ |
| Menthol | ◆ | ◆ | ◆ | ◆ | ◆ | ▲ |
| Milk thistle | ◆ | ◆ | ◆ | ◆ | ◆ | ◆ |
| Saw palmetto (Serenoa repens) | ◆ | ◆ | ◆ | ◆ | ◆ | ◆ |
| Seville orange juice | ◆ | ◆ | ◆ | ◆ | ◆ | ▲ |
| St John's Wort | ● | ● | ● | ● | ■ | ● |

● Do Not Coadminister
 ■ Potential Interaction
 ▲ Potential Weak Interaction
 ◆ No Interaction Expected

La polifarmacia en pacientes VIH: mayor riesgo de interacciones entre medicamentos

Prevalence of polypharmacy⁵

61%



Of patients <50 years of age, 61% were found to take co-medications (n=1020)

82%

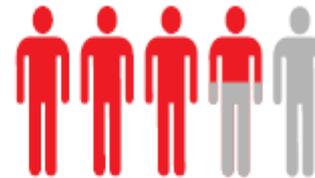


Of patients ≥50 years of age, 82% were found to take co-medications (n=477)

Adapted from Marzolini C, et al. 2011.

Prevalence of potential drug interactions⁵

35%



About 3.5 in 10 patients <50 years of age were found to be at risk of drug interactions (n=1020)

51%



About 5 in 10 patients ≥50 years of age were found to be at risk of drug interactions (n=477)

Adapted from Marzolini C, et al. 2011.