ID Week 2025: HIV Highlights

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Disclosures

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Disclaimer

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Objectives

Review highlights of HIV-relevant IDWeek presentations:

- Real World Lenacapavir
- Zoster Vaccination and CV/Cognitive Outcomes
- HIV Primary Care Screening
  - Osteoporosis
  - Colorectal Cancer

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Lenacapavir

Virologic Outcomes with Lenacapavir in Heavily Treatment-Experienced People with HIV: A Multi-Center Real-World Study

- Lenacapavir: first in class HIV capsid inhibitor, approved in treatment as salvage therapy for HIV treatment in combination with optimized background regimen (OBR)
- Data primarily via CAPELLA studies; minimal real-world data

What are real-world outcomes among PWH who start Lenacapavir for salvage therapy?

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Segal-Maurer NEJM 2022

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Virologic Outcomes with Lenacapavir in Heavily Treatment-Experienced People with HIV: A Multi-Center Real-World Study

- Multicenter, observational retrospective cohort study in those initiated on LEN for salvage therapy from November 2020 to June 2025
- Demographic and clinical characteristics were collected including:
  - ART, prior and current OBR
  - RT/PI and INSTI genotypes, Archive genotypes
  - Viral load, CD4
- Survival analysis performed for time to viral load suppression
- Comparison of number of active agents, total agents, and pill burden pre/post LEN

Virologic Outcomes with Lenacapavir in Heavily Treatment-Experienced People with HIV: A Multi-Center Real-World Study

- 70 patients met criteria
  - 54% male, 73% Black
  - 73% on Medicaid or Medicare
  - Avg age at start 53 years; 24 years from HIV diagnosis
  - 54% virally unsuppressed, 4 with VL > 100000 copies/mL

Resistance to 2 or more agents	
NRTI	55 (79%)
NNRTI	52 (74%)
PI	16 (23%)
INSTI	28 (40%)
All 4 Main Classes	5 (7%)
Estimated Number of Active Agents pre-LEN regimen	
Less than 1	8 (11%)
At least 1	17 (24%)
At least 2	43 (61%)
Unknown	2 (3%)

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Virologic Outcomes with Lenacapavir in Heavily Treatment-Experienced People with HIV: A Multi-Center Real-World Study

- INSTI most common OBR medication
- 89% remained on LEN
- 82% of those initially viremic remained suppressed; all those initially suppressed remained so
- ISR common

Table 2: Post-Lenacapavir Initiation	
Medications in OBR	
NRTI	35 (50%)
INSTI	49 (70%)
PI	17 (24%)
NNRTI	22 (31%)
Ibalizumab	7 (10%)
Fostemsavir	8 (11%)
Estimated Number of Active Agents in OBR	
At least 1	38 (54%)
At least 2	30 (43%)
Unknown	2 (3%)
Still prescribed Lenacapavir?	
Yes	62 (89%)
No	8 (11%)
Remain Newly Virally Suppressed with LEN (N=38)	
Yes	31 (82%)
No	5 (13%)
Unknown	2 (5%)
Days Observed on Lenacapavir	
All patients in cohort, median (IQR)	361 (180-546)
Patients with active prescription (n=62), median (IQR)	380 (139-582)
Injection Site Reaction	
Minor	19 (27%)
Moderate (requiring medical visit)	2 (3%)
None	49 (70%)

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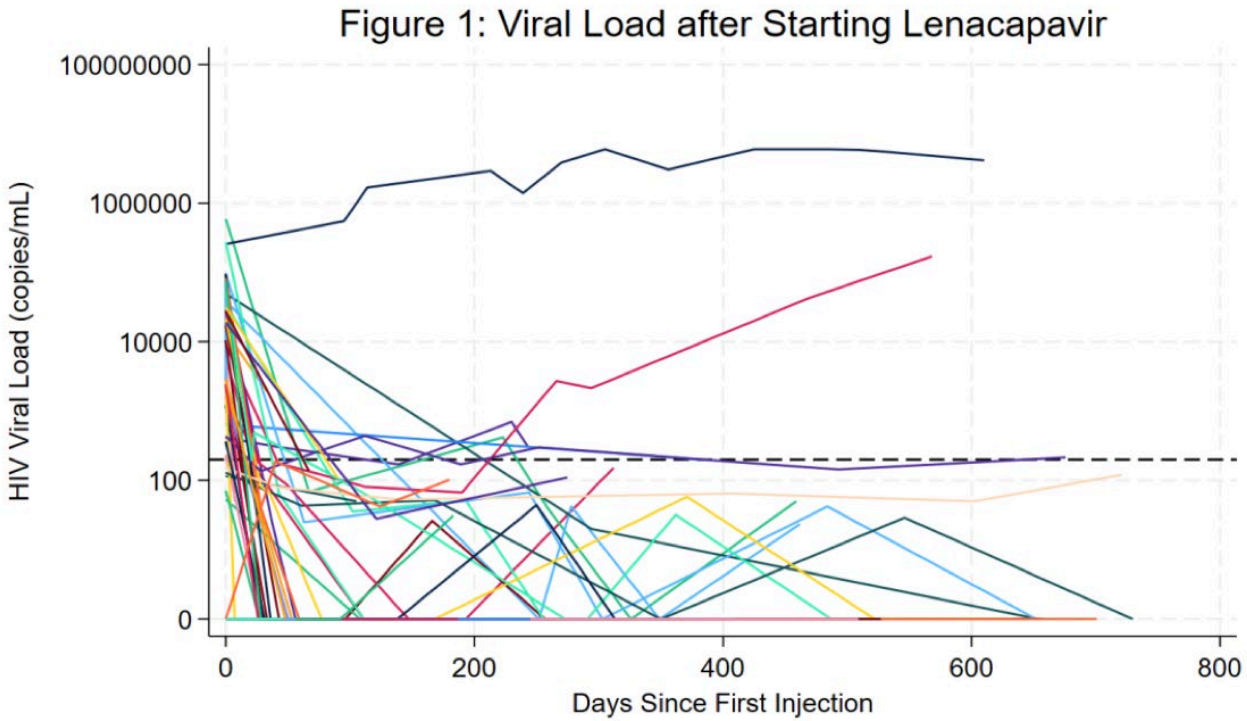
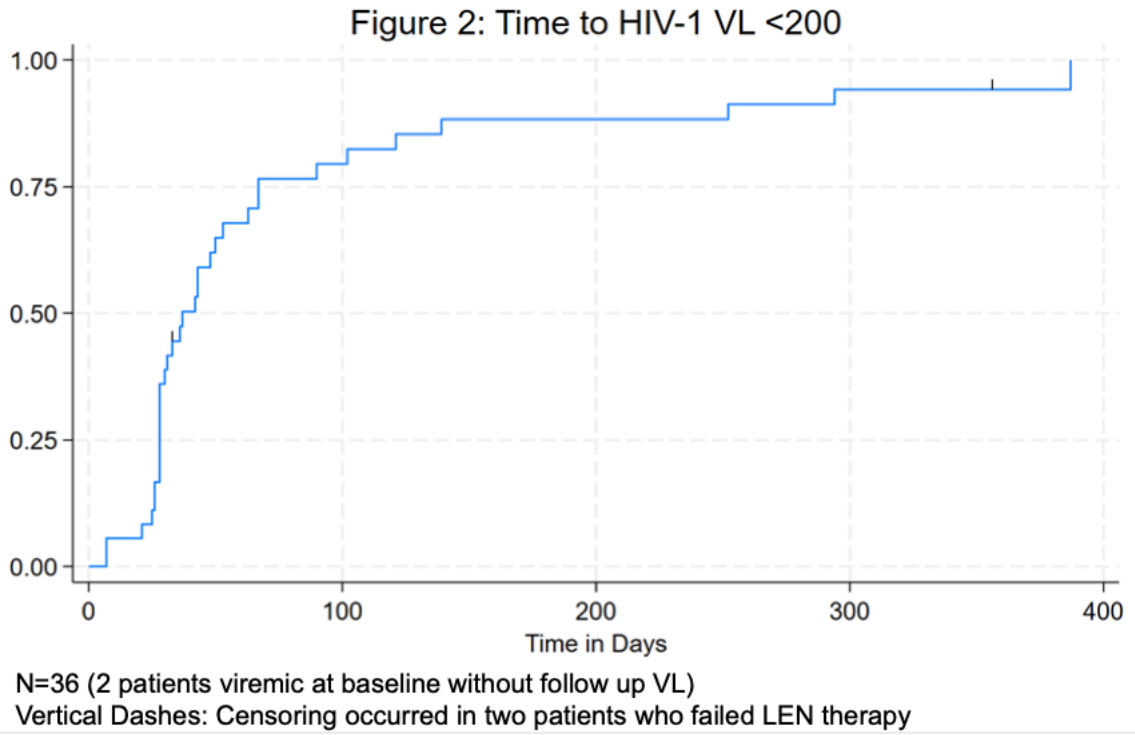
Virologic Outcomes with Lenacapavir in Heavily Treatment-Experienced People with HIV: A Multi-Center Real-World Study





N=36 (2 patients viremic at baseline without follow up VL)
Vertical Dashes: Censoring occurred in two patients who failed LEN therapy

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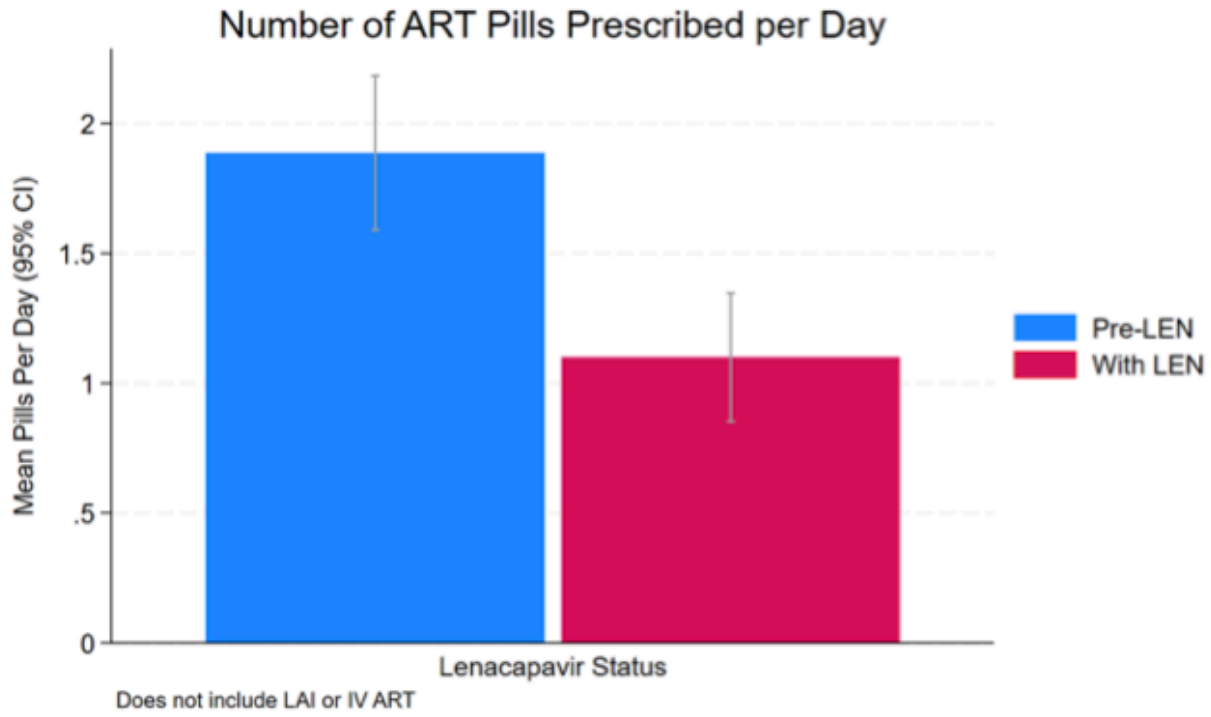
Change in Number of Daily Pills



- Compared using Wilcoxon signed-rank test
- p<0.00005 (z=4.862)

Number of Pills daily in Pre-LEN regimen, median (IQR)	2 (1-2)
0	6 (8.6%)
1	24 (34.3%)
2	23 (32.9%)
3	10 (14.3%)
4	4 (5.7%)
5	2 (2.9%)
6	1 (1.4%)
Number of Pills daily in Post-LEN regimen, median (IQR)	1 (0-2)
0	22 (31.4%)
1	27 (38.6%)
2	16 (22.9%)
3	3 (4.3%)
4	1 (1.4%)
5	1 (1.4%)

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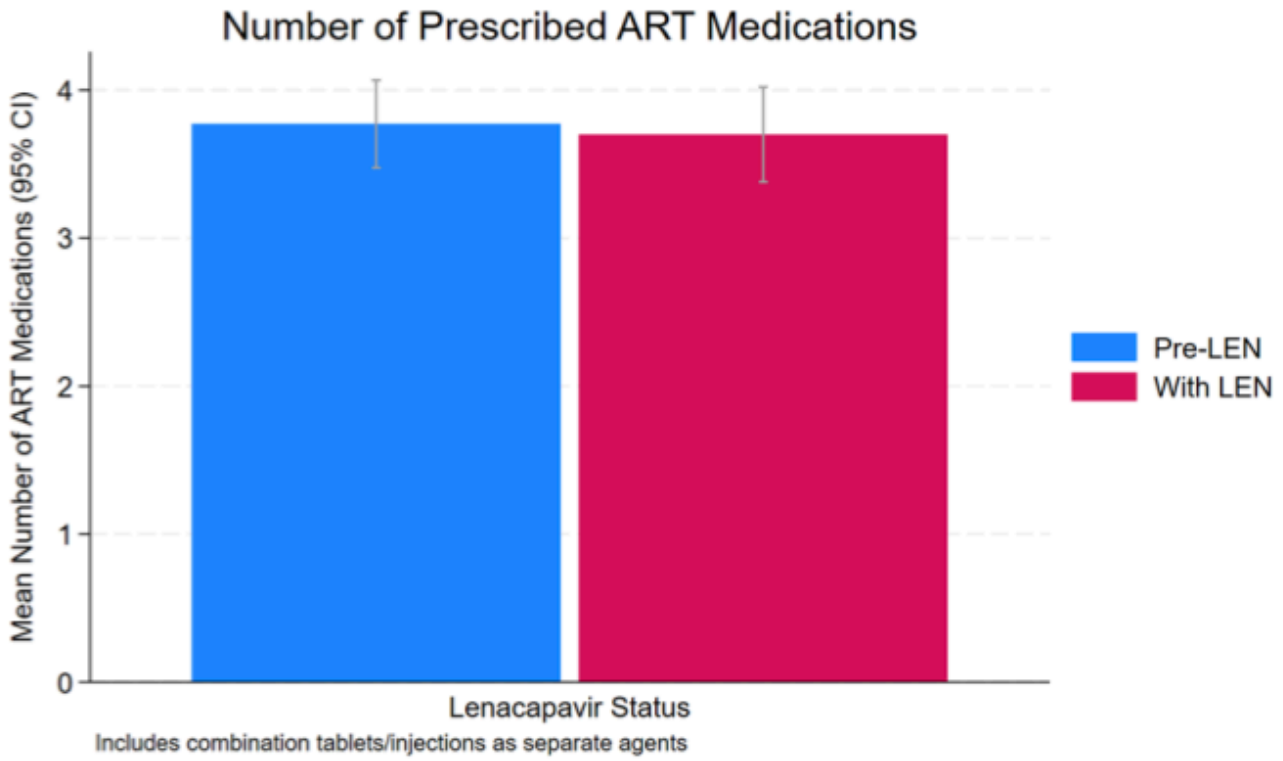
Change in Number of Medications



Number of Agents in Pre-LEN regimen, median (IQR)	4 (3-5)
0	1 (1.4%)
1	1 (1.4%)
2	7 (10%)
3	21 (30%)
4	19 (27.1%)
5	16 (22.9%)
6	5 (7.1%)
Number of Agents in Post-LEN regimen, median (IQR)	4 (3-5)
2	15 (21.4%)
3	19 (27.1%)
4	18 (25.7%)
5	10 (14.3%)
6	6 (8.6%)
7	2 (2.9%)

- Compared using Wilcoxon signed-rank test
- p=0.9085 (z=0.119)

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Conclusions

- Most PWH initiated on LEN maintained or achieved new HIV VL suppression
- Active agents in the ART regimens increased; number of daily pills decreased
- No decrease in number of ART agents with LEN initiation

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Zoster Vaccination in PWH and CV/Mortality Risk

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Zoster Vaccination in People Living with HIV is Associated with Reduced Mortality and Cardiovascular Risk: A Real-World Matched Cohort Study

- **Herpes in HIV:**
  - **Common**, even for those on ART
  - HIV worsens VZV specific CD4 T-cell immunity, so zoster episodes are **earlier, recurrent, and more severe** (hence recommendation for earlier vaccination in HIV)
  - Along with rash, inflammation increases with zoster (both vascular and neurologic)
  - Many PWH may have ”silent zoster” and thus inflammation without lesions
  - Stroke, MI risk may rise post zoster
  - PWH already have existing inflammatory burden

- **What about vaccination?**
  - RZV vaccine (Shingrix) restores VZV-specific CD4 immunity

Does zoster vaccination reduce vascular and cognitive complications in HIV?

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Zoster Vaccination in People Living with HIV is Associated with Reduced Mortality and Cardiovascular Risk: A Real-World Matched Cohort Study

- Retrospective, propensity-score matched (for comorbidity, demographics, ART) cohort study from TriNetX Research Network (>100 US healthcare systems) of PWH >= 50 years on ART

Analysis of Effect of Zoster Infection

- People **with uncomplicated zoster infection** vs people **without zoster infection**
- Follow-up: Day 90 to Day 1825 to avoid reverse causation

Analyses of Effect of Vaccination

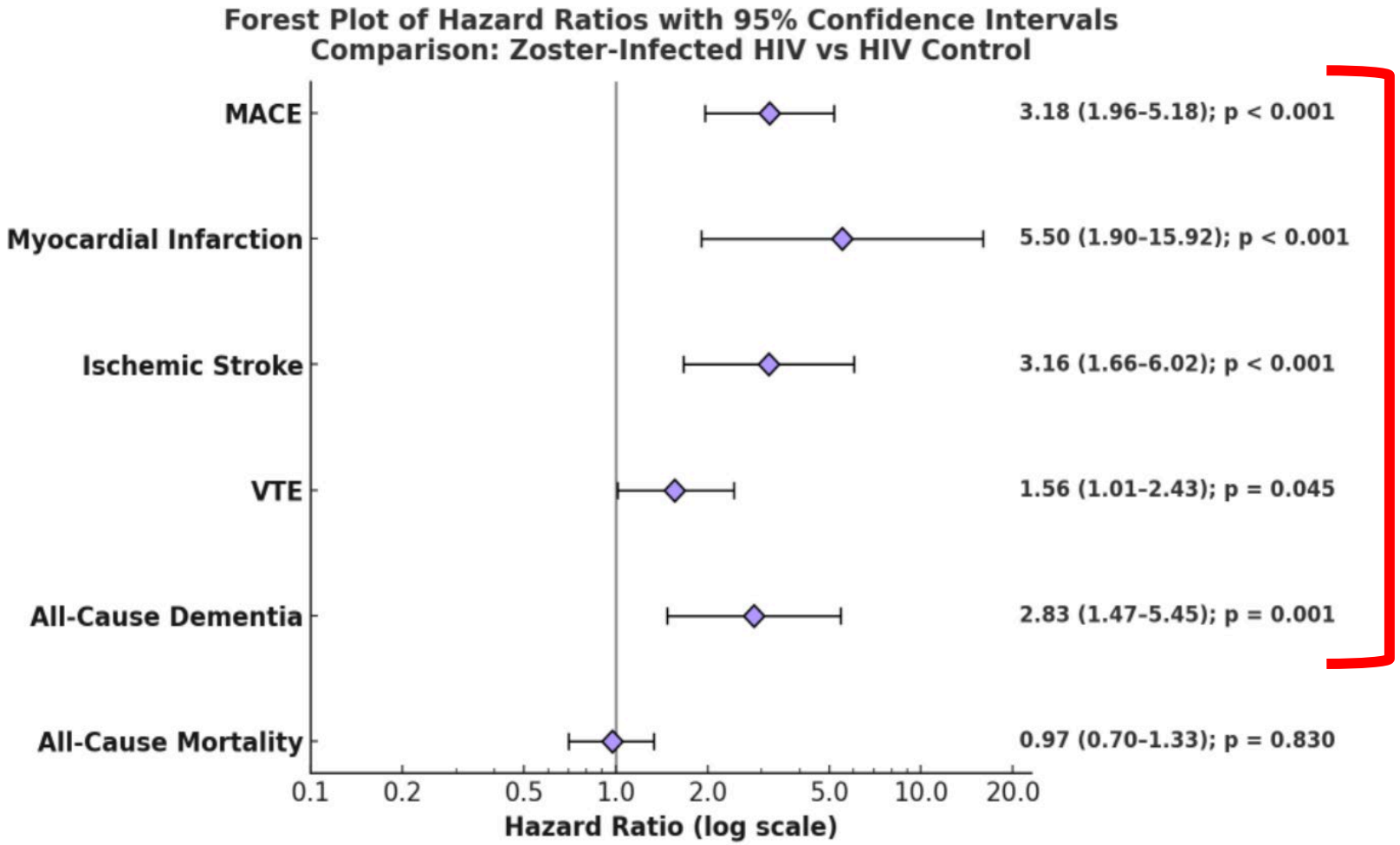
- People who were vaccinated with **RZV** vs **PCV**
  - Excludes people who received live zoster vaccine (ZVL)
- Windows: early (90-540 days), late (540-1460 days), combined (90-1460 days)

- Primary endpoint: MACE
- Secondary endpoints: isolated MI, ischemic stroke, VTE, all-cause dementia, all-cause mortality

Zoster Vaccination in People Living with HIV is Associated with Reduced Mortality and Cardiovascular Risk: A Real-World Matched Cohort Study

Analysis	Per Arm, Post Match, n	Median Follow-up, Yr	Window, Days
Infection **(uncomplicated zoster vs no zoster)**	1347	~5.0	90-1825
Vaccine early **(vaccination with RZV vs PCV)**	2715	~1.5	90-540
Vaccine late **(vaccination with RZV vs PCV)**	2715	~3.0	540-1460
Vaccine combined **(vaccination with RZV vs PCV)**	2712	~3.0	90-1460

Cardiovascular Risk HIGHER in PWH with Zoster Infection



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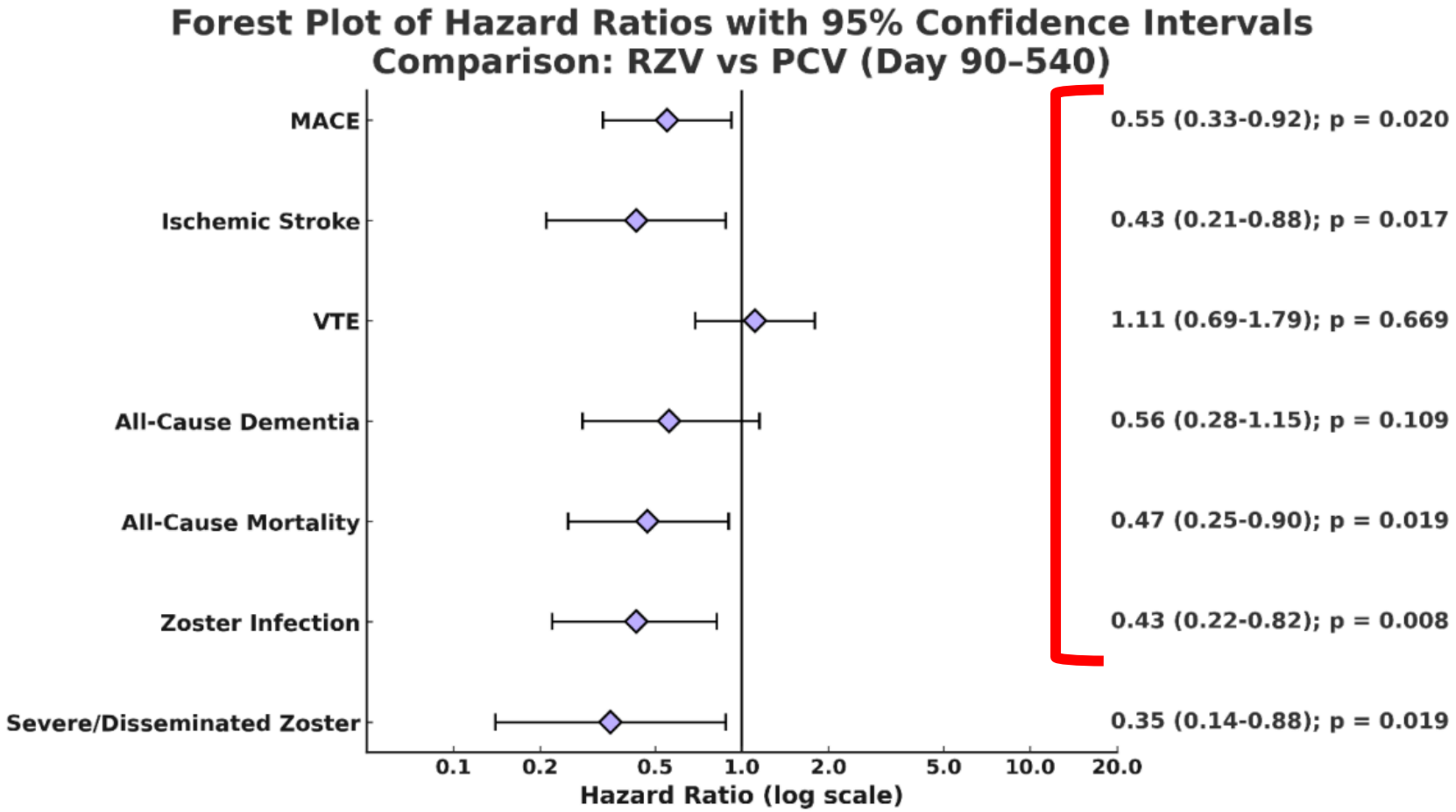
Cardiovascular Risk LOWER in PWH with Zoster Vaccination (Early Window)



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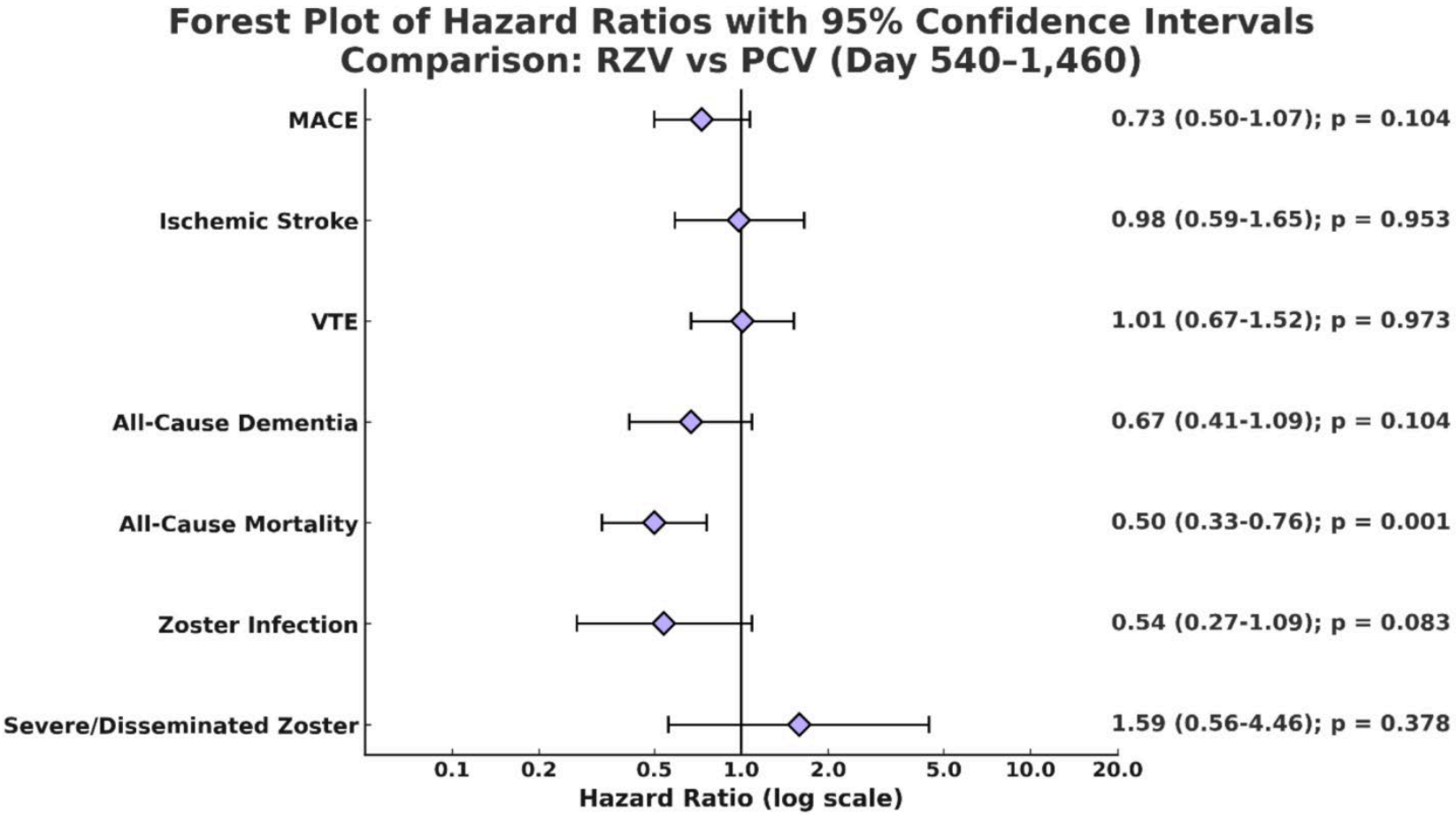
Cardiovascular Risk trends towards lower in PWH with Zoster Vaccination (Late Window), but not as much as Early



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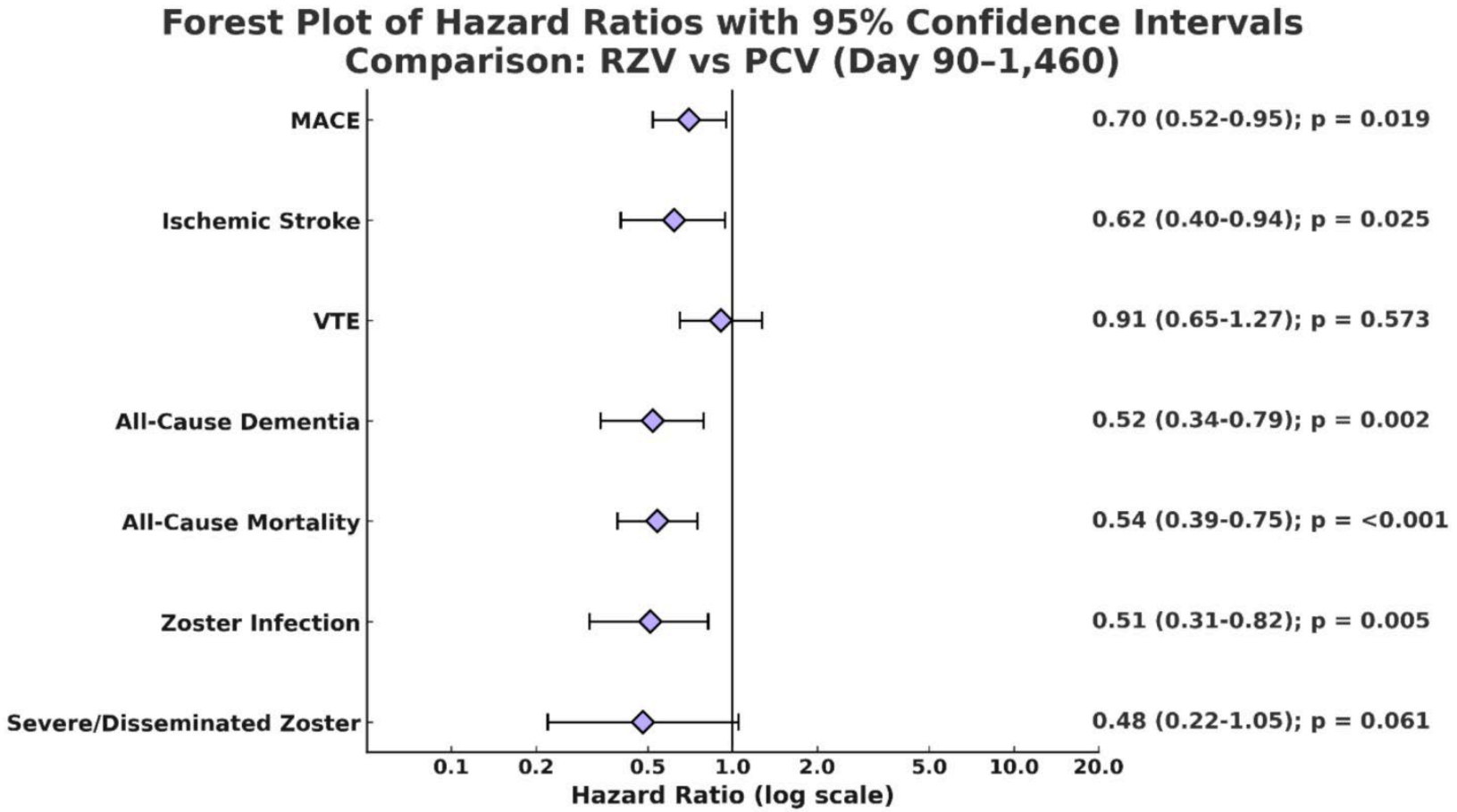
Cardiovascular Risk LOWER in PWH with Zoster Vaccination (Combined)



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Conclusions

- In matched PWH >= 50 years and one uncomplicated zoster episode, there was an **increased (3x higher)** 5-year risk of MACE, MI, ischemic stroke, and dementia
- Those who were vaccinated had lower risk of MACE, ischemic stroke, dementia, and all-cause mortality, most apparent early and persisting through year 4

- Interesting points:
  - Arterial-dominant clinical pattern (perineural travel to peri-arterial tissue during reactivation), thus increased MACE/MI/stroke but not VTE
  - Ongoing priming of endothelium/platelets long after rash

Screening

Missed Opportunities: Gaps in Osteoporosis Screening Among Older Adults Living with HIV

- HIV independently reduces BMD; in PWH, fractures may occur earlier than in those without. Why?
  - Inflammation (Chronic inflammation, immune activation)
  - Immunodeficiency (including reconstitution)
  - ART
  - Associated factors (smoking, low BMI, vitamin D deficiency, hypogonadism)
- HIMVA Primary Care Guidance suggests DXA in post menopausal women and men >= 50 and/or other based on individualized risk factors
- **Study Objectives**
  - Assess adherence to guidelines for BMD screening in PWH in outpatient clinic
  - Identify prevalence of osteoporosis/osteopenia among those screened
  - Determine those with diagnosis prescribed TDF containing regimen

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Missed Opportunities: Gaps in Osteoporosis Screening Among Older Adults Living with HIV

- Single-center retrospective study 1/2024-12/2024, all patients >= 50 years with one visit (856 eligible)
- Results:
  - 26% of eligible female patients, 18% of eligible male patients screened
  - Average age 63 years (M), 65 years (F), high CD4 counts
  - 49% with no prior TDF exposure; high association with low BMD (but ?confounder)
  - 64% had either osteopenia (45%) or osteoporosis (19%)

Need for increased screening and ART optimization strategies

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Who's Being Missed? Baseline Evaluation of Colorectal Cancer Screening in a Ryan White-Funded HIV Clinic

- Cancer is the leading case of death in PWH; CRC screening in all is suboptimal, and unclear whether rates are lower or higher in PWH
- Retrospective review of PWH >= 45 years evaluated in outpatient HIV clinic 7/2023 – 7/2024
  - Need for CRC screening measured by presence of HER "care gap" then manually verified
  - CRC screening (via colonoscopy, FIT, FOBT, and Cologuard) orders and results obtained and manually verified
- 69.7% of 761 patients were up to date; rate was higher than CDC average but lower than target 2030 goal
  - Associations with being not up to date: younger (53 v 56 years), language other than English or Spanish, HIV viremia, those without a PCP

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Who's Being Missed? Baseline Evaluation of Colorectal Cancer Screening in a Ryan White-Funded HIV Clinic

- 157 patients with some form of cancer screening ordered
  - Those who were viremic AND with multiple visits (but two, not three!) during the study year more likely to have colonoscopy rather than non-invasive ordered (78% v 55%)
- Completion rates:
  - Colonoscopy 43%, Cologuard 70%, no reporting of FIT/FOBT
- Disparities: Viral load, language spoken, PCP/retention in care

Despite exceeding national screening rates at one center, CRC screening disparities persist in PWH- think about age, viremia, and language discordance

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Takeaways

- Heavily treatment experienced PWH initiating LEN in the real world largely maintained and/or achieved viral suppression
- As compared to non-zoster infected controls, PWH with herpes zoster infection had significantly higher risk of CV and cognitive conditions
- PWH with zoster vaccination as compared to not had lower risk of poor CV and cognitive outcomes
- Screening for comorbid conditions (i.e. bone mineral density loss, colorectal cancer) in PWH has significant room for optimization

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Thank you!

Questions?

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