



Defining and Optimal Standard of Background Medical Care: Insights from VICTORIA

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Canadian **VIGOUR** Centre
Bridging Hearts and Minds



Duke Clinical Research Institute



Disclosures / COI

- Available online: thecvc.ca
- VICTORIA: Executive Committee

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Why measure medication adherence?

- Standard of care (SOC) HFrEF medications such as ACEi/ARB/ARNI, beta-blockers and MRAs modify the outcomes of patients with HFrEF.
- These form the core of HFrEF guidelines.
 - Clinicians encouraged to implement
 - Guideline adherence is suboptimal
 - Measurement of gaps in guideline adherence may highlight areas for interventions
- RCT: The adequacy / dose of SOC therapy may differ across RCTs of new intervention.

Key factors that affect medication adherence



Socioeconomic factors



Health care system-related factors



Concomitant illness



Therapy-related factors



Patient-related factors





Why measure medication adherence?

- A sizable proportion of patients with HF do not receive guideline-directed medical therapy (GDMT) a.k.a. SOC
 - 15381 US outpatients, a **27%** rec'd all GDMT
 - ~57000 UK inpatients **42%** were discharged on triple therapy
 - 3518 US outpatients, **22%** were on triple therapy; 1% @ target dose
- DAPA-HF:
 - **65%** on SOC triple therapy
 - RAS blocker: **38%** \geq 50% target dose
 - Beta-blocker: **52%** \geq 50% target dose





How to measure medication adherence

- Low complexity:
 - **On/off**: measure if a medication class was used or not
 - Pro: Simple to collect, cross-comparable between datasets
 - Con: misses out on if a medication was indicated, the dose, or a c/i





How to measure medication adherence

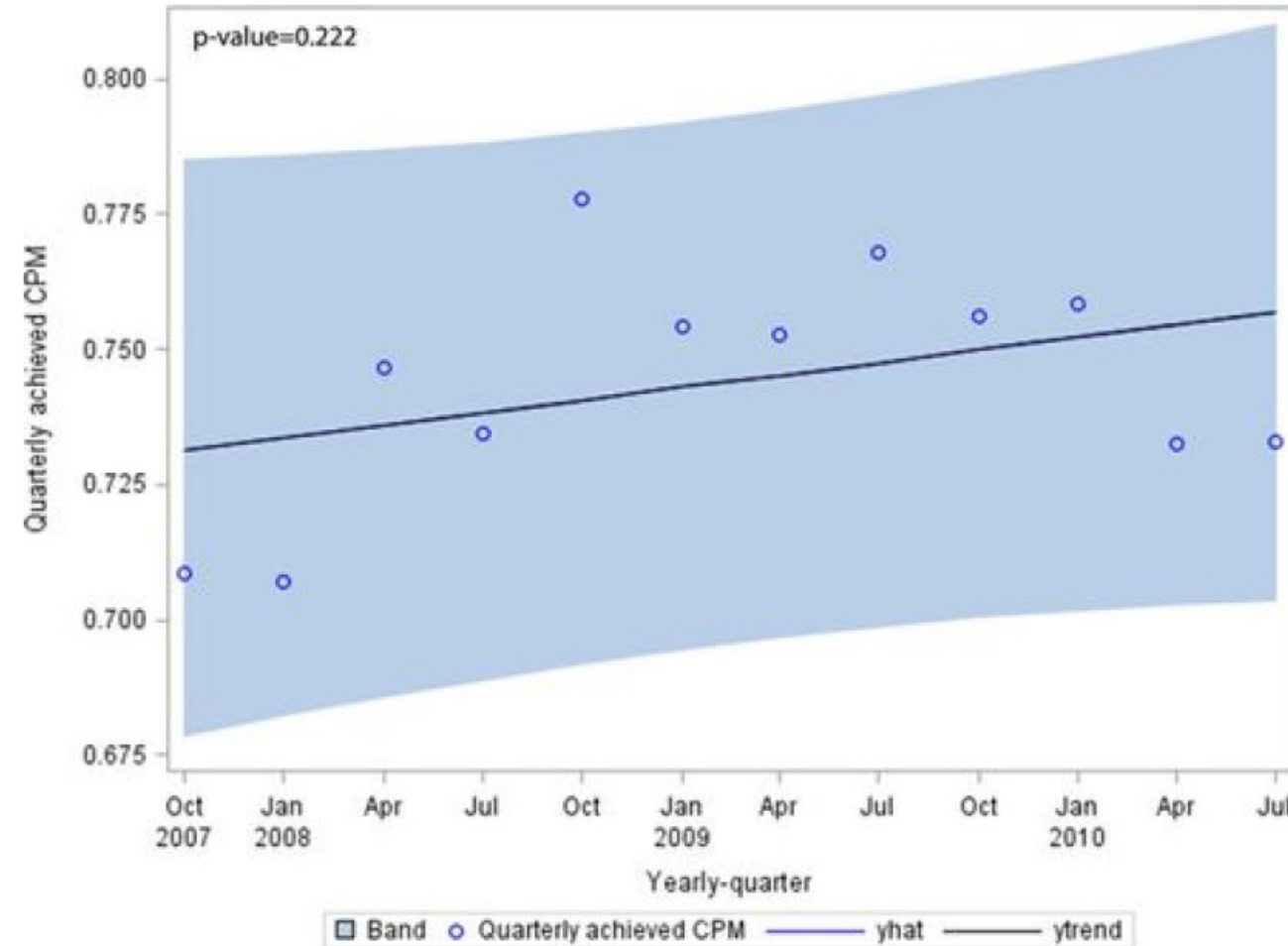
- Medium complexity:
 - All-or-none or opportunistic composite score:
 - Captures a bundle of medications using on/off
 - Aggregates into a single 'score'
 - Pro: data reduction, simple to presentation/interpretation
 - Con: methods may result in dissenting conclusions





How to measure medication adherence

- Medium complexity:
 - Composite score
 - All or none = $ACE + BB + MRA = 1$;
 $ACE + BB = 0$
 - Opportunistic = $ACE + BB + MRA = 1$;
 $ACE + BB = 0.66$





Effect of Vericiguat in VICTORIA According to Guideline Directed Medical Therapy

Ezekowitz JA, McMullan CJ, Westerhout CM, Piña IL, Lopez-Sendon J, Anstrom KJ, Hernandez AF, Lam CSP, O'Connor CM, Pieske B, Ponikowski P, Roessig L, Voors AA, Koglin J, Armstrong PW, Butler J.

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Objectives

1. Describe the SOC therapy at randomization.
2. Examine the association of the study treatment with the primary outcome according to adherence and dosing of SOC medications at randomization.





Methods: Patients, Trial and Outcomes

- VICTORIA: RCT of 5050 patients with HFrEF
- Key inclusion criteria:
 - NYHA class II–IV*
 - left ventricular EF <45%*
 - On appropriate background therapy for HF*
- Primary outcome: Time to CVD or HFH
- 99.8% (n=5040) patients with data on SOC medications





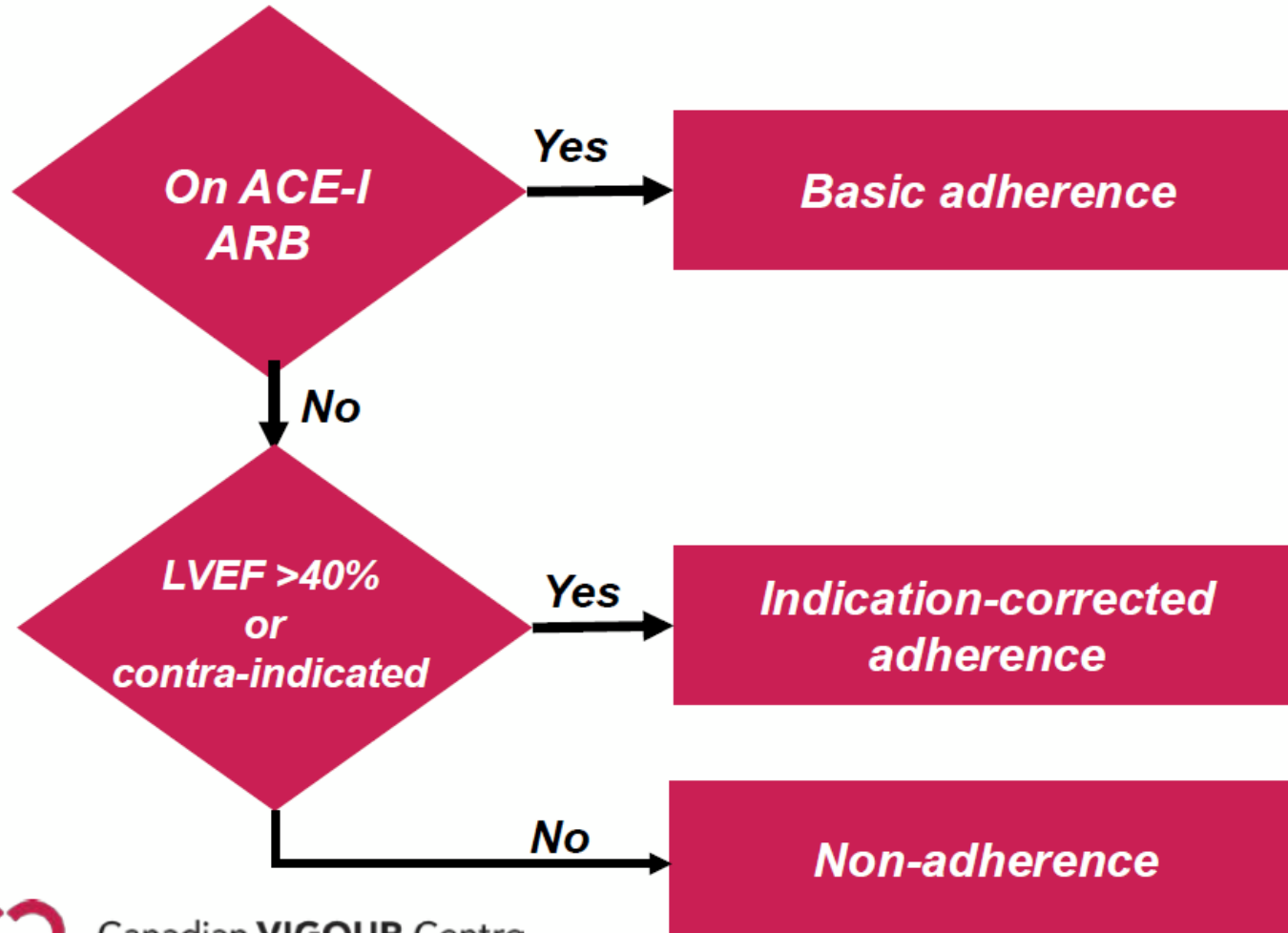
Methods: Adherence Measurement

- Standard of care (SOC) meds were collected at randomization
 - RAS blockers (ACEi/ARB/ARNI), Beta-blockers, MRA
 - This included a prompt for a reason if not on a SOC therapy
 - Further clarifications assessed using data on LVEF, eGFR, potassium, medical Hx.
- Adherence:
 - **Basic** adherence: On/Off medication
 - **Indication-corrected** adherence: Basic + Indication/Clinical data
 - **Dose-corrected** adherence: Dose \geq 50% in indicated patients for meds with evidence-based target doses

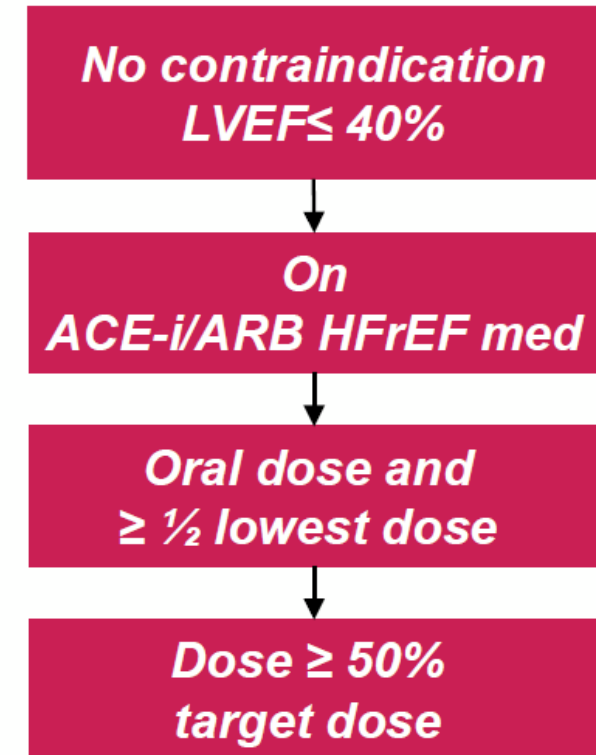




Methods: Example ACEi, ARB



Dose-corrected adherence



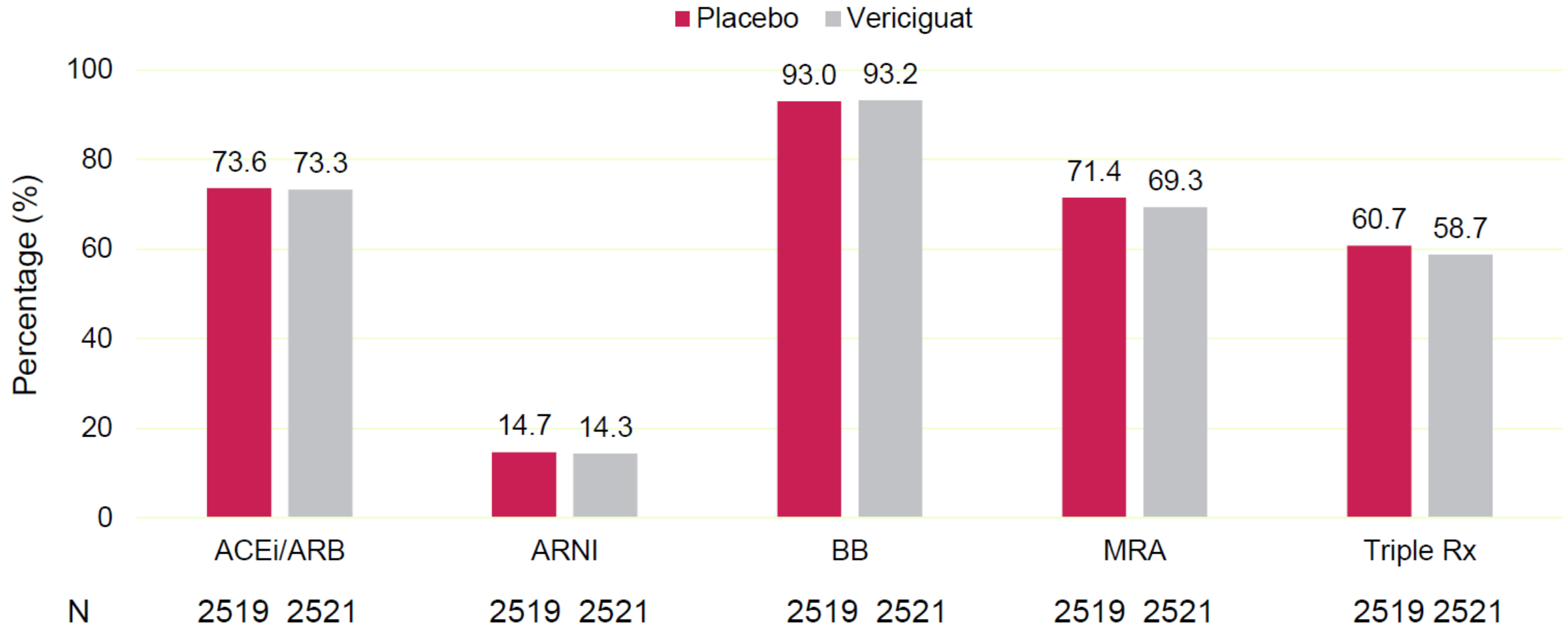


Patient Features by SOC Medications

	0-1 SOC Med (n=431)	2 SOC Meds (n=1600)	Triple SOC Meds (n=3009)
Age (y), median	74.0	71.0	66.0
Male, %	73.3	76.4	76.3
Ejection Fraction <40%, %	80.9	82.4	88.1
Atrial fibrillation, %	51.5	49.5	41.5
Diabetes, %	51.7	50.4	44.4
eGFR (ml/min/1.73m ²), median	39.4	52.2	63.0
NT-proBNP (pg/ml), median	4065	3240	2532



Basic Adherence





Summary/Conclusions

- Methods to measure standard of care vary
- Patients in VICTORIA were
 - On excellent background medical therapy.
 - Doses of SOC medications, for those on triple therapy, was very good.
 - The treatment effect of vericiguat, compared with placebo, on the primary composite endpoint was consistent across SOC medication classes.

