



Fix-dosing ivermectin regimens in mass drug administration activities. Is it time to leave the dosing pole behind?

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INTRODUCTION

Ivermectin (IVM) is a critical tool for the control of different Neglected Tropical Diseases. In mass drug administration (MDA) campaigns it is dosed adjusted to body weight or height. Dosing IVM by weight or height has operational disadvantages. In this study we explored an alternative dosing regimen of IVM for MDA activities.

Key points of evidence that triggered this study:

- Current dosing regimen of ivermectin tends to underdose (1)
- Ivermectin is safe even at higher doses than currently recommended (2)
- Ivermectin appears safe in children with body weight below 15 kg in preliminary data (3)
- Children have an accelerated clearance of IVM, probably requiring higher doses (4)

METHODS

- Study design: Individual participant data metanalysis (IPD MA).
- Registered at International prospective register of systematic reviews: **PROSPERO 2024 CRD42024521610**
- Data search: datasets containing the variables age, sex at birth, weight and height of individual participants were requested to: 1) DHS program; 2) IDDO; 3) Harvard dataverse; 3) Digital Commons@Becker; 4) Individual studies of STH interventions.
- Eligibility: the population groups targeted for STH control in current WHO recommendations were eligible (Pre-School Aged Children –PSAC–, School Aged children –SAC– and Woman of Reproductive Age –WRA–), irrespective of the goals and outcomes of the studies that enrolled the participants.
- Inclusion criteria:
 1. Sites: countries where PC for STH is recommended;
 2. Sex: male and female children and only female adults;
 3. Age group: PSAC (2 to 4 years old); SAC (5 to 15 years old) and WRA (15 to 49 years old).
- Individual data obtained was cleaned from duplicates and missing data and analysed with WHO Anthro and WHO AnthroPlus software to detect inconsistencies between age, weight and height data.
- The dose in µg/Kg of IVM for each participant according to their weight was calculated using three different dosing regimens: 1) Weight-adjusted dose for 200 µg/Kg; 2) Height – adjusted dose (WHO dosing pole); 3) Age based fixed-dose of IVM. See table below for details on dosing regimens.

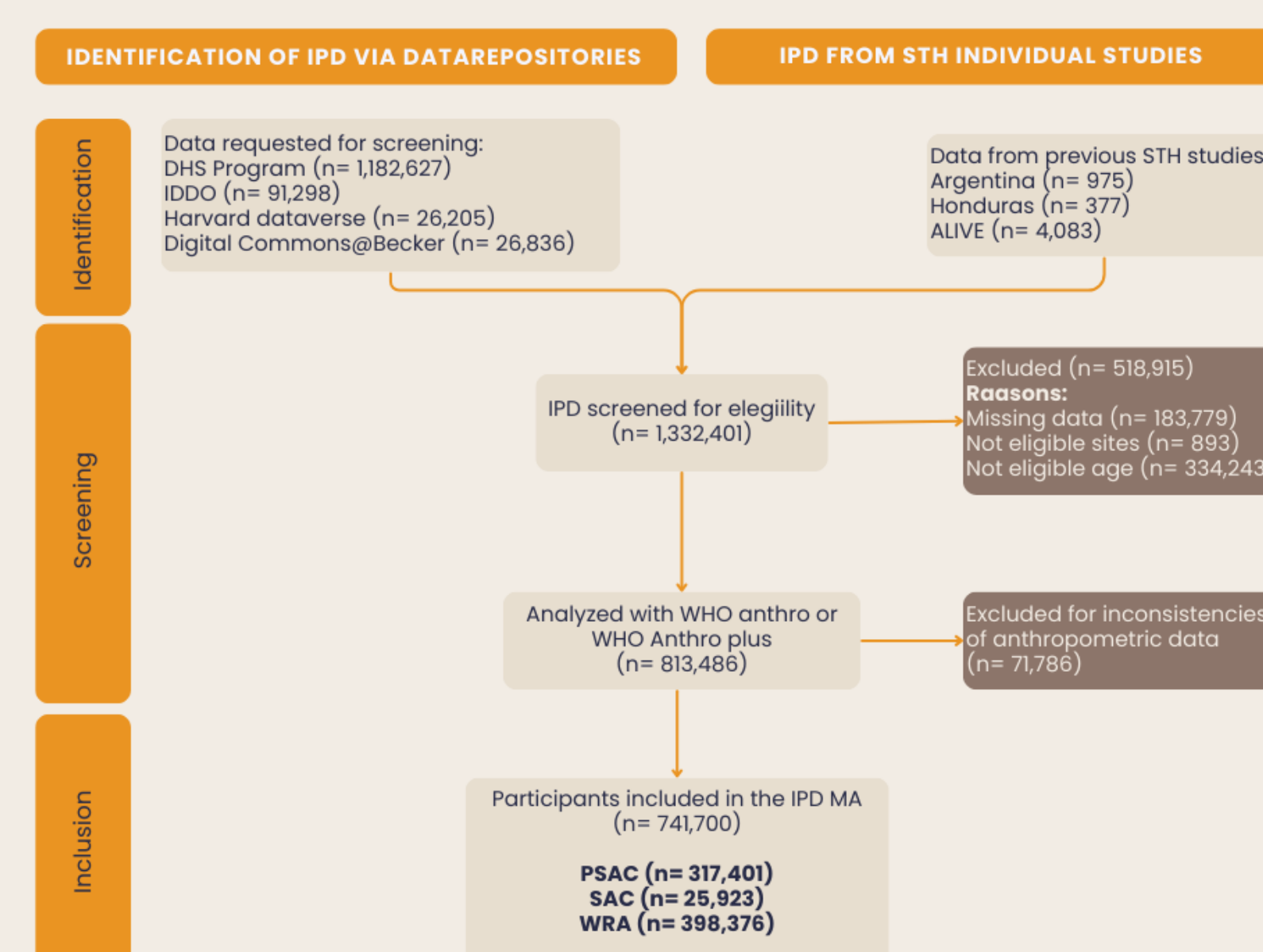
IVM Dosing Regimen	Contraindicated	3 mg	6 mg	9 mg	12 mg	15 mg	18 mg
Weight based	< 15 kg	15 – 24 Kg	25 – 35 Kg	36 – 50 Kg	51 – 65 Kg	66 – 79 Kg	
Height based	< 90 cm	90 – 119 cm	120 – 139 cm	140 – 159 cm	> 159 cm		
Age based fixed dose	None	PSAC (2 to 4 yo)		SAC (5 to 15 yo)			WRA (15 to 49 yo)

- The proportion of participants with underdose (<200 µg/Kg), recommended dose (200 to 400 µg/Kg), above the recommended dose (401 to 600 µg/Kg) or exceeding dose (> 600 µg/Kg) with each dosing regimen was calculated.

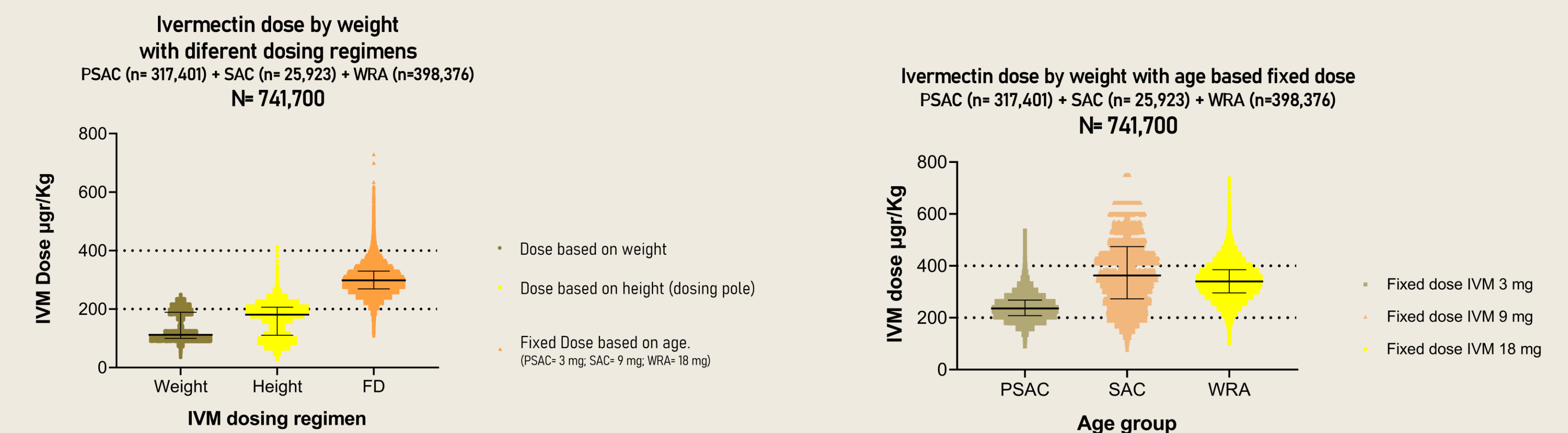
RESULTS

- 1,332,401 subjects from 45 countries were screened for eligibility and 741,700 were finally enrolled.

Participants flow diagram of the IPD MA

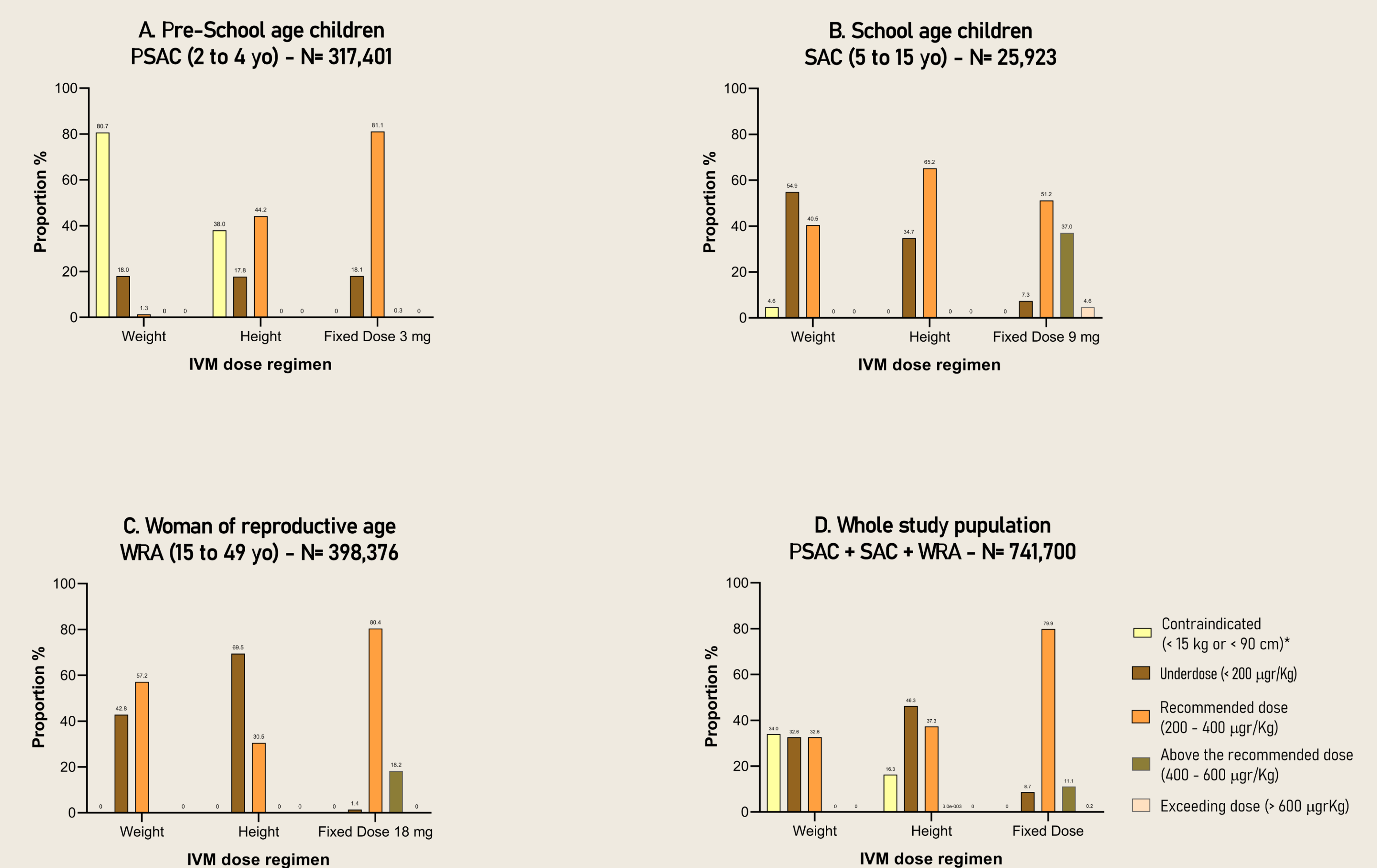


Ivermectin median dose with fixed dose regimen



- The median dose of IVM with the usual dosing regimens was below the recommended dose of 200 µg/Kg: 112 µg/Kg (IQR: 215) with weight-based regimens and 181 µg/Kg (IQR: 384) with height-based regimens. While the median dose achieved with the fixed dose regimen was within the recommended dose: 298 µg/Kg (RIQ: 620).

Proportion of recommended dose achieved with different dosing regimens by age group



* Note: no contraindication criteria was applied for Fixed-dose regimen

- The proportion of individuals of the whole study population that achieved recommended dose of IVM was higher with fixed dose (79.9 %) versus weight (32.6 %) or height (37.2 %) based regimens. The difference was statistically significant in the comparison of FD with both regimens, $p = 0.001$

DISCUSSION

- Implementing a fixed dose IVM regimen based on age would achieve a high proportion of adequate doses, reducing the proportion of underdosing and with little risk of exceeding the recommended dose. Added to the operational advantages of using a single formulation for the entire targeted population.



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<https://stop2030.org/Echazu-et-al-ivm.pdf>

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