The MAGNIFICAT Study

Assessing the Impact of Cigarette Substitution with E-Cigarettes on the Exposure Profile in Dual Users

Results after 30 days of dual use

Polosa R, Veigl S, Pluym N, Scherer M, Burkhardt T, Belsey J, Russell C, Caponnetto P, Weglarz J, Campagna D

CORESTA PSPT 2025, October 19-23, Annecy, France

Scientific Background

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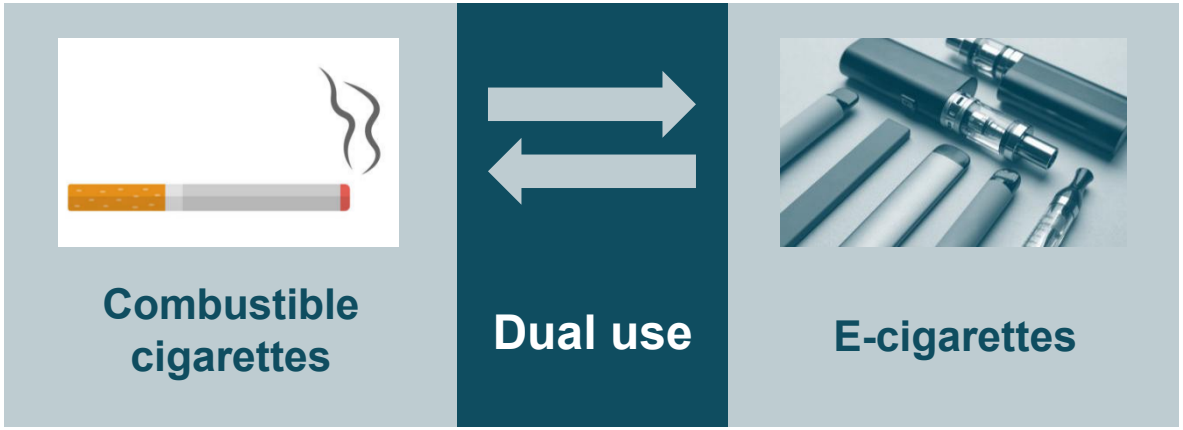
- **Smoking** remains a leading preventable cause for early **death and disability** in the world today

Numbers of early deaths caused by smoking (2021)

- **Significant changes** in tobacco and nicotine products over the past 10 years
- Rise of **e-cigarettes and vaping devices**
- Complete switching to e-cigarettes results in reduced harm



What are the health impacts of dual use?

Services U.S. Department of Health and Human **(2014)**: The Health Consequences of Smoking: 50 Years of Progress. National Library of Medicine Cataloging in Publication. Rockville, MD, USA.
Institute for Health Metrics and Evaluation (IHME) **(2024)**: Anzahl Todesfälle aufgrund von Rauchen in ausgewählten Ländern im Vergleich der Jahre 1990 und 2021 [Grafik]. Online available at: https://de.statista.com/statistik/daten/studie/1172030/umfrage/anzahl-todesfaelle-aufgrund-von-rauchen-in-ausgewaehlten-laendern/ (Accessed : 22.07.2025).
Hajek P. et al. (2014). *Addiction*; 109 (11): p. 1801-10.

Scientific Background

Research Gap

Dual use

Only a few studies have assessed the impact of dual use

Limitations

Dual users treated as homogenous group	Small number of biomarkers investigated	Short-term setting	Studies rely only on self-reported behavior

Well controlled clinical study with multiple endpoints needed

Dual users categorized based on switching behaviour	~ 30 Biomarkers of exposure ~ 6 Biomarkers of potential harm Non-targeted analysis	Longitudinal study over several months	Biomarkers of compliance

Piper M. E. et al. (2019). *Nicotine Tob Res*; 21 (9): p. 1279-84.
McRobbie H. et al. (2015). *Cancer Prev Res (Phila)*; 8 (9): p. 873-8.
Arnold M. J. et al. (2021). *Nicotine Tob Res*; 23 (11): p. 1972-6.
D'Ruiz C. D. et al. (2016). *BMC Public Health*; 16: p. 543.
Shahab L. et al. (2017). *Ann Intern Med*; 166 (6): p. 390-400.

Clinical Study

Clinical Study

Polosa R, Pluym N, Scherer M, Belsey J, Russell C, Caponnetto P, Weglarz J, Campagna D. Protocol for the "magnitude of cigarette substitution after initiation of e-cigarettes and its impact on biomarkers of exposure and potential harm in dual users" (MAGNIFICAT) study. Front Public Health. 2024 Mar 21;12:1348389. doi: 10.3389/fpubh.2024.1348389. PMID: 38584934; PMCID: PMC10996441.

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Study Product

- E-Cigarette: KIWI Pen 2
- Devices and liquids were commercially available on the Polish market
- Disposable e-liquid solution, separated from the E-cigarette device

Nicotine strength: 9 mg/mL

PG/VG ratio: 50 / 50

3 flavors to choose

- Leaf (type: dry tobacco)
- Midway (type: smooth tobacco)
- Glacial (type: tobacco with mint)

Clinical Study - Endpoints and Samples

MEDICAL ENDPOINTS	**Cardiovascular** **Respiratory**
BIOSPECIMENS FOR ANALYTICAL MEASUREMENTS	**Urine (morning)** **Plasma** **Washed erythrocytes** **Exhaled breath**

Clinical Study - Design

Dual users (250 subjects)

Clinical Study - Design

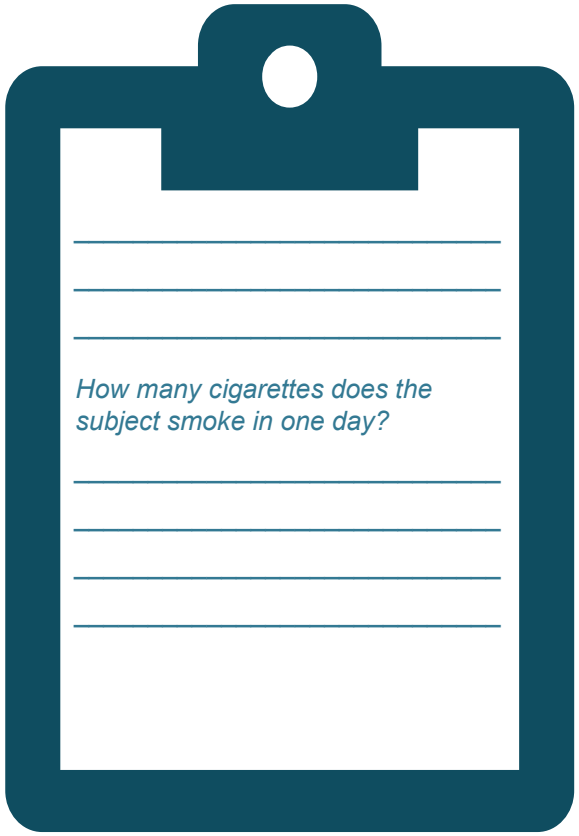
Dual users (250 subjects)

Sub-categories of dual users for every time point

Smoker	Poor Switcher	Moderate Switcher	Intensive Switcher	Quitter

Grouping of Dual-Use Categories

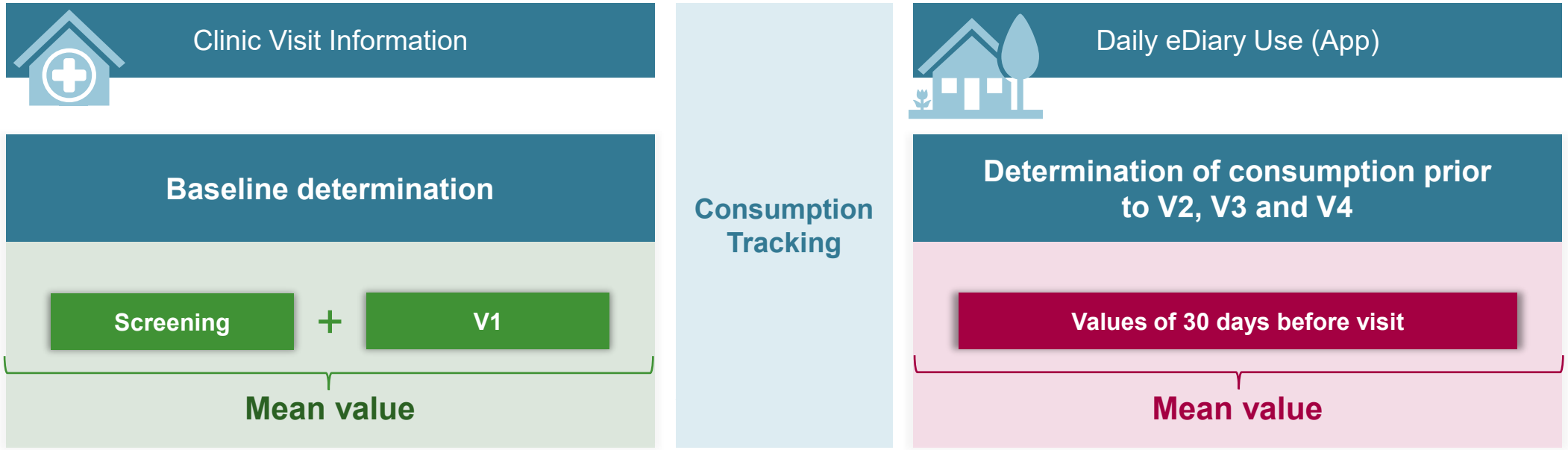
Clinic Visit Information



Consumption Tracking

Daily eDiary Use (App)

Grouping of Dual-Use Categories



Grouping of Dual-Use Categories

Clinic Visit Information

Baseline determination

Screening + V1

Mean value

Consumption Tracking

Daily eDiary Use (App)

Determination of consumption prior to V2, V3 and V4

Values of 30 days before visit

Mean value

Determination of relative CPD reduction [%]

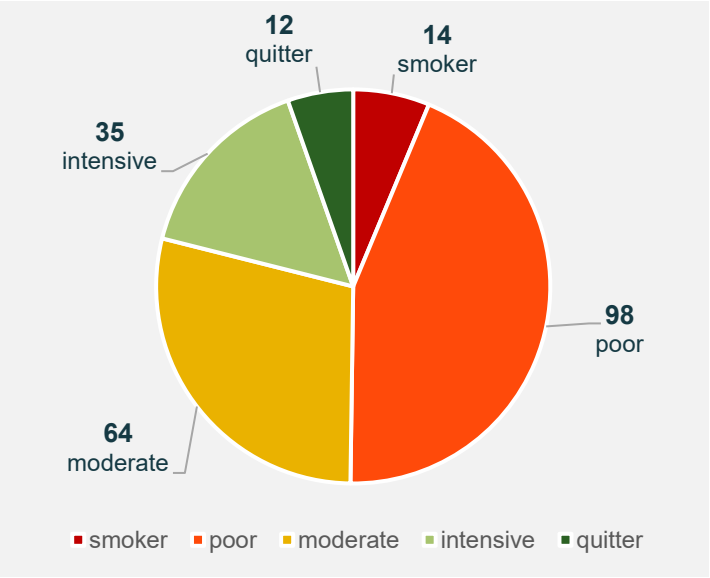
$$\frac{\text{Baseline} - \text{Consumption}}{\text{Baseline}} * 100$$

Smoker	*< 1 %*
Poor Switcher	1 - 50 %
Moderate Switcher	50 - 80 %
Intensive Switcher	80 - 99 %
Quitter	> 99 %

Cigarettes per day reduction

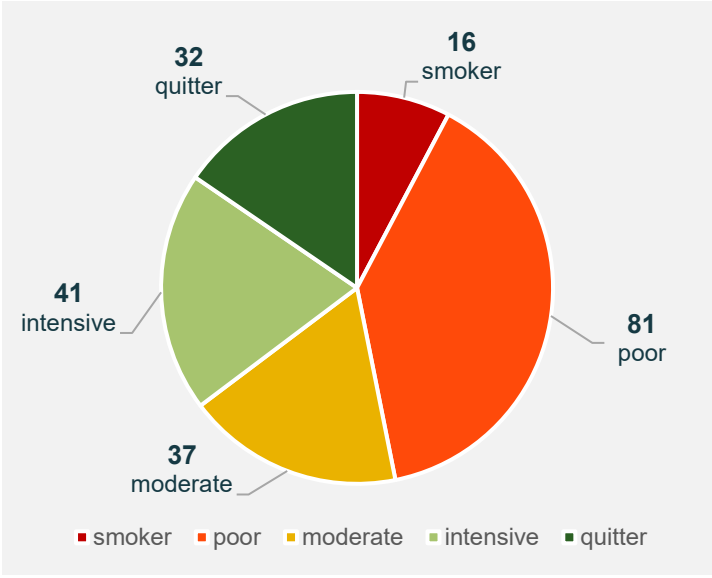
Grouping into dual-use categories - Results

V2 (1 month)



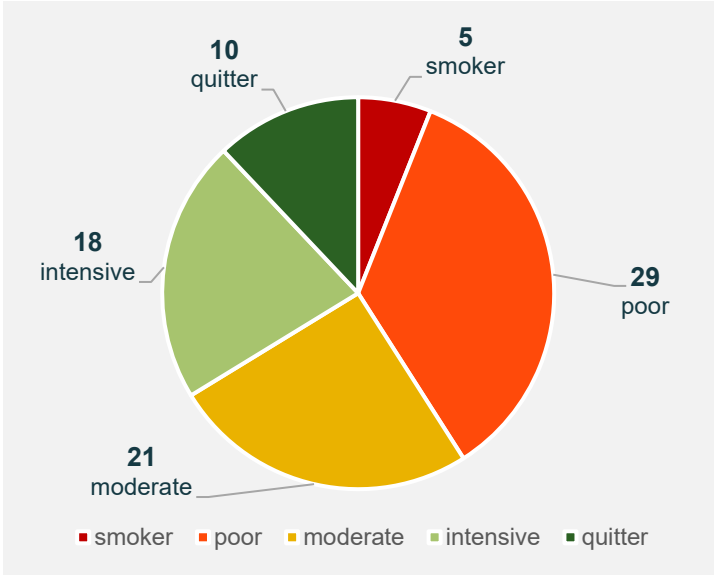
Dual use category	# subjects (N = 223)
smoker	14 (6 %)
poor	98 (44 %)
moderate	64 (29 %)
intensive	35 (16 %)
quitter	12 (5 %)

V3 (3 months)



Dual use category	# subjects (N = 207)
smoker	16 (8 %)
poor	81 (39 %)
moderate	37 (18 %)
intensive	41 (20 %)
quitter	32 (15 %)

V4 (6 months)



Dual use category	# subjects (N = 83)
smoker	5 (6 %)
poor	29 (35 %)
moderate	21 (25 %)
intensive	18 (22 %)
quitter	10 (12 %)

Status of data: 4th sample shipment with recorded visit dates (28-Jul-2025)

Analytical Measurements

Sample Collection and Analysis

Urine

Creatinine
Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. CEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons
3-OH-Benzo(a)pyrene
Aromatic Amines
Eicosanoides
Non-Targeted Analysis

Plasma

sICAM
(Soluble intercellular adhesion molecule-1)
GDF-15
(Growth differentiation factor 15)

Washed Erythrocytes

Hb-Adducts (incl. CeVal)
Non-Targeted Adductomics

Exhaled Breath

Non-Targeted Breathomics

Study Results – Analyzed Samples

2nd visit
1 month

Dual use category	# Subjects (N = 223)
smoker	14 (6 %)
poor	98 (44 %)
moderate	64 (29 %)
intensive	35 (16 %)
quitter	12 (5 %)

Urine

Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
2CyEMA
Tobacco Specific N-Nitrosamines

Washed erythrocytes

Hemoglobin adducts (CeVal)

Dual use category	# Subjects (N = 149)
smoker	8 (5 %)
poor	66 (44 %)
moderate	51 (34 %)
intensive	22 (15 %)
quitter	2 (1 %)

Urine

Mercapturic Acids (incl. 2CyEMA)
OH-Polycyclic Aromatic Hydrocarbons

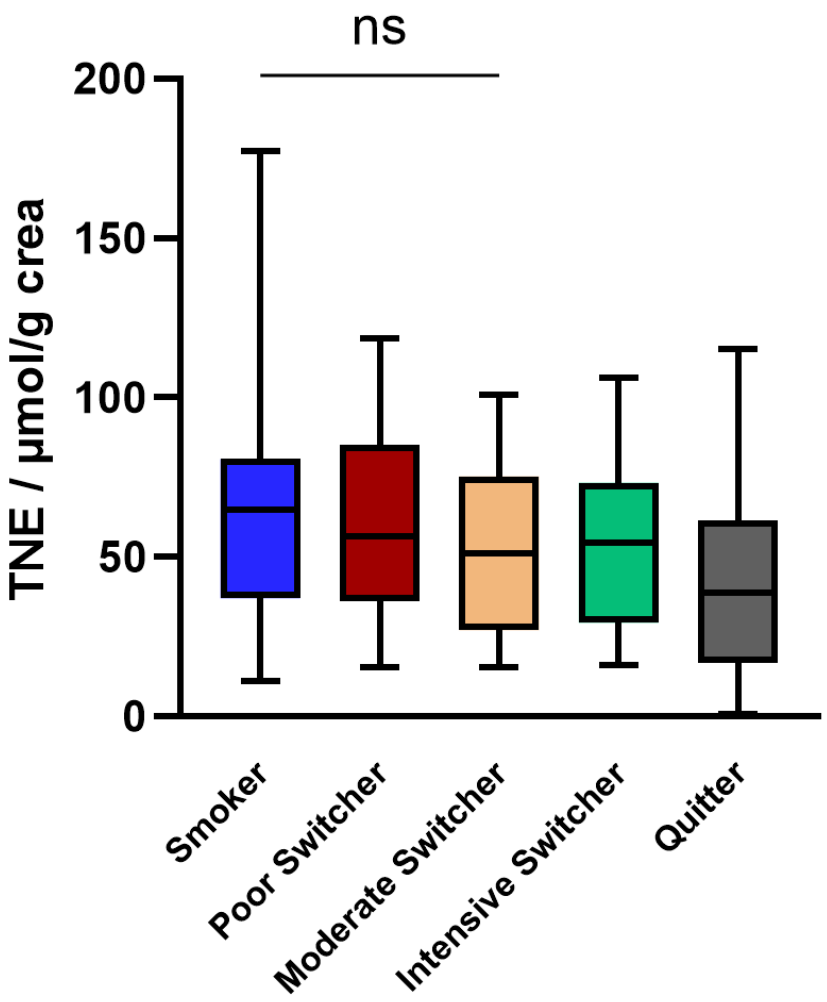
Washed erythrocytes

Hemoglobin adducts (CaEtVal)

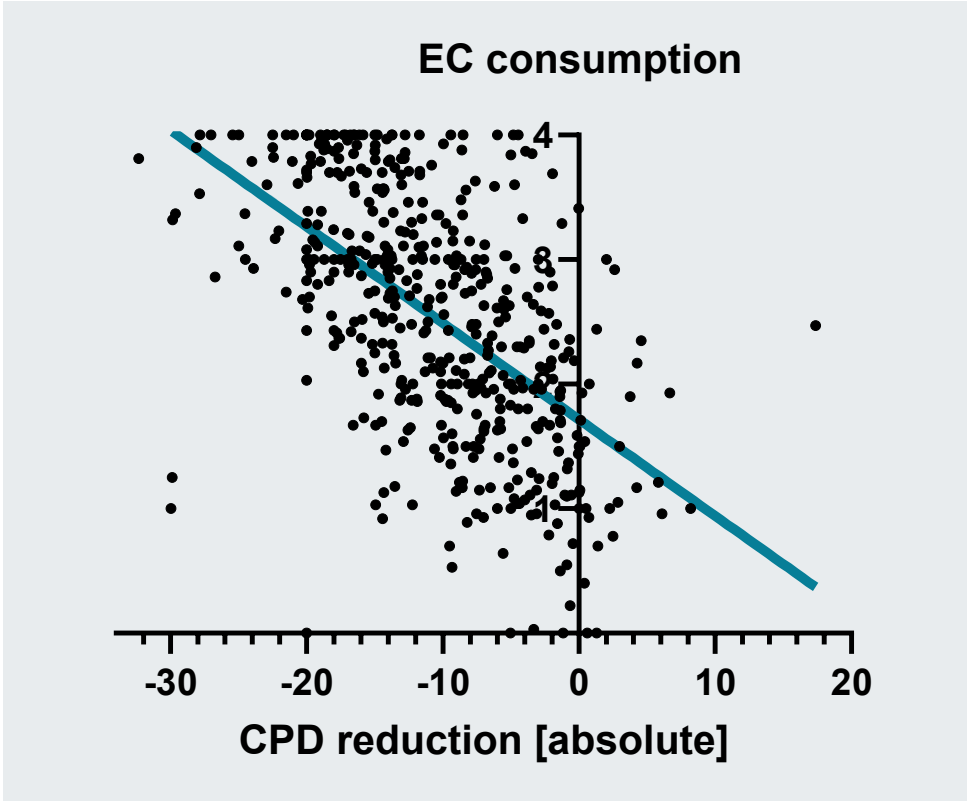
Results – Nicotine exposure

Urine

Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. 2CyEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons



NS = not significant

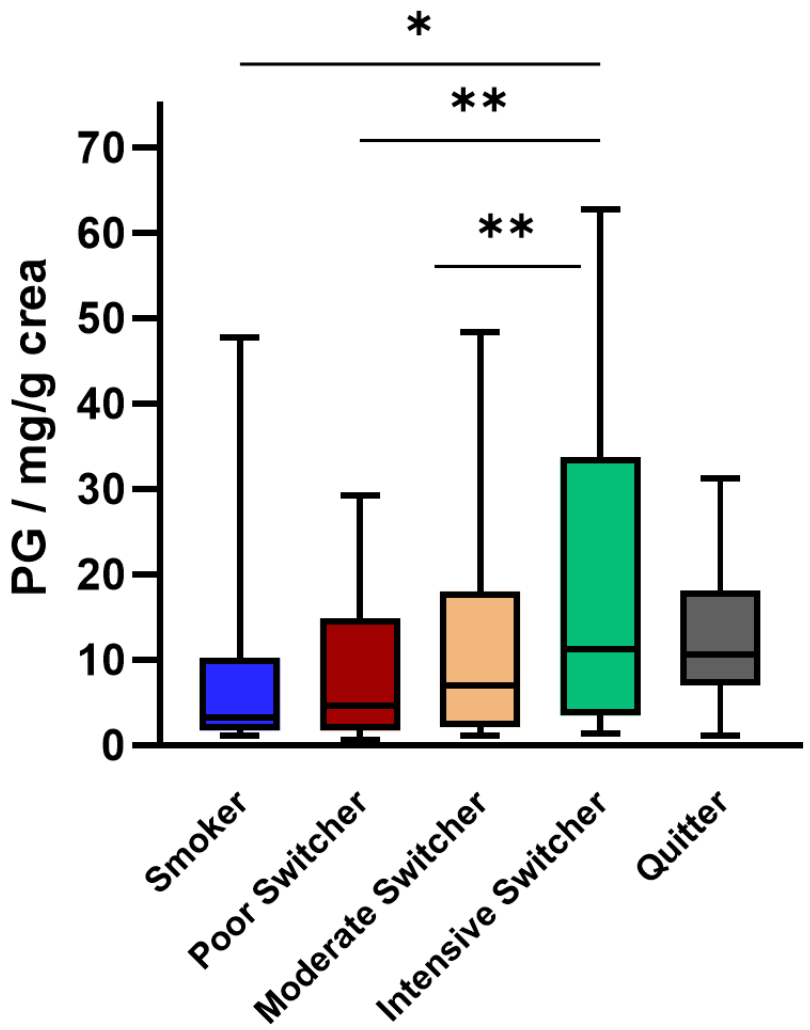


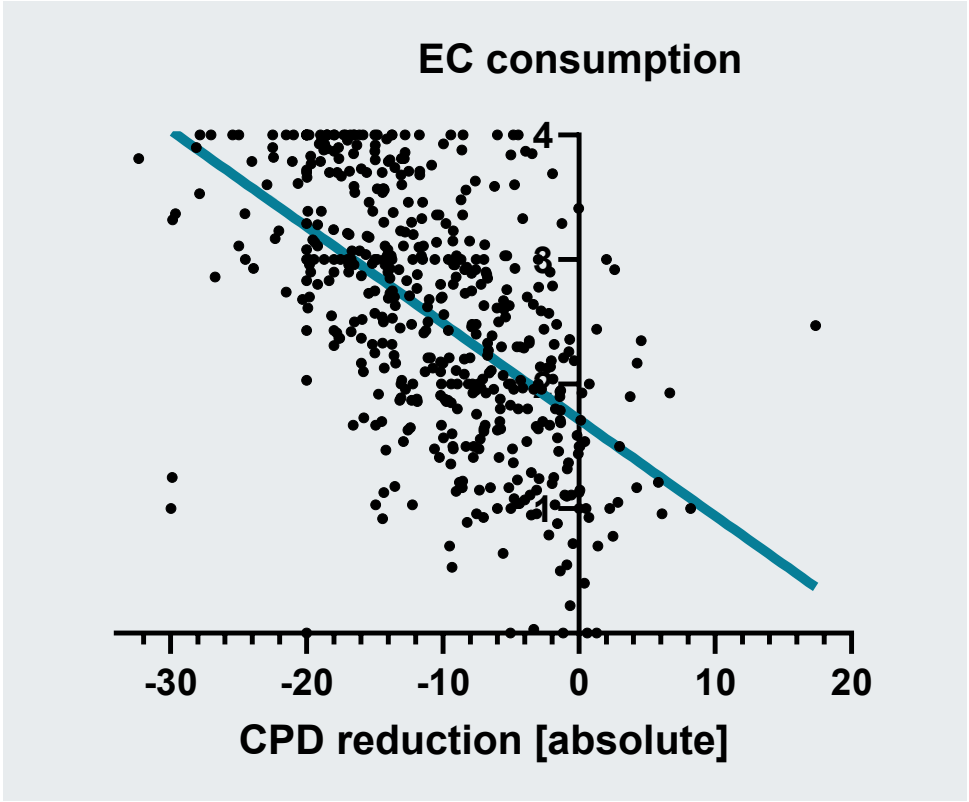
Spearman r = - 0.60
significant (α = 0.05)

Results – PG exposure

Urine

Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. 2CyEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons





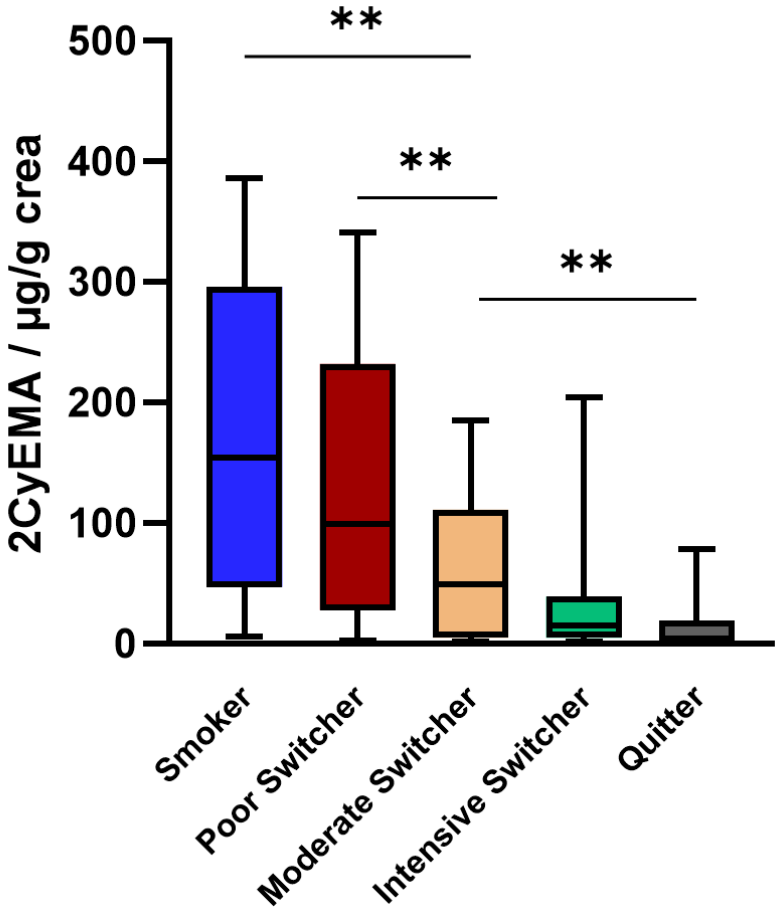
Spearman r = - 0.60
significant (α = 0.05)

Results – VOC exposure

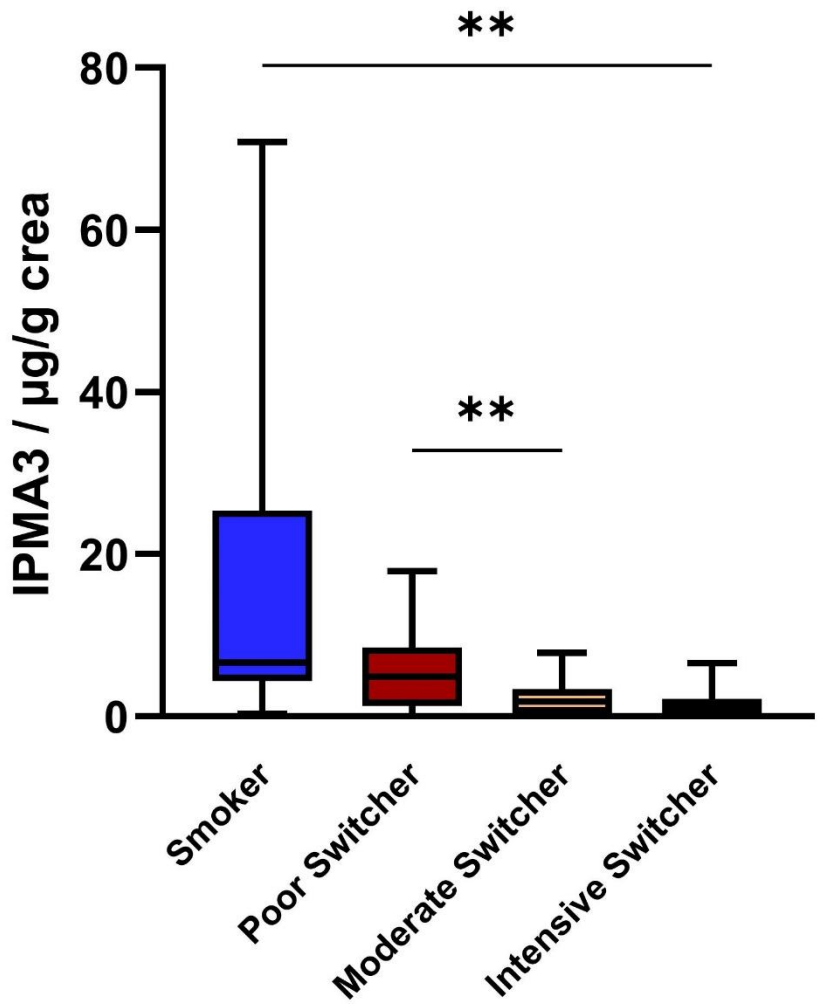
Urine

Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. 2CyEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons

Acrylonitrile



Isoprene

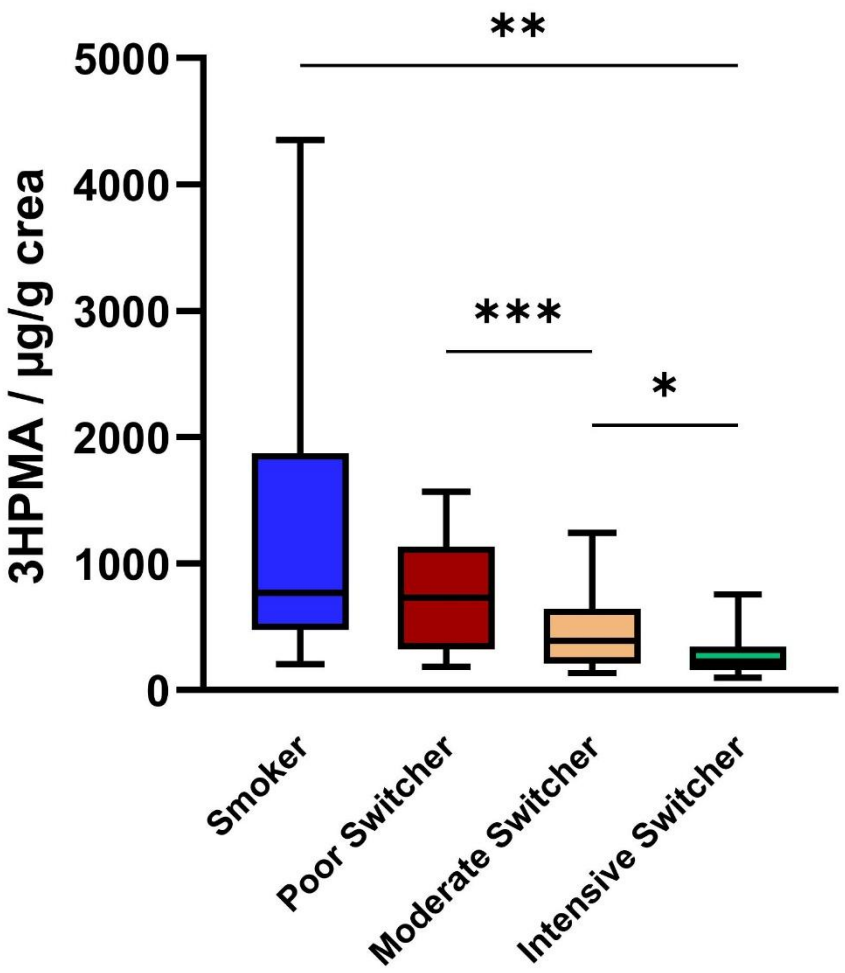


Results – VOC exposure

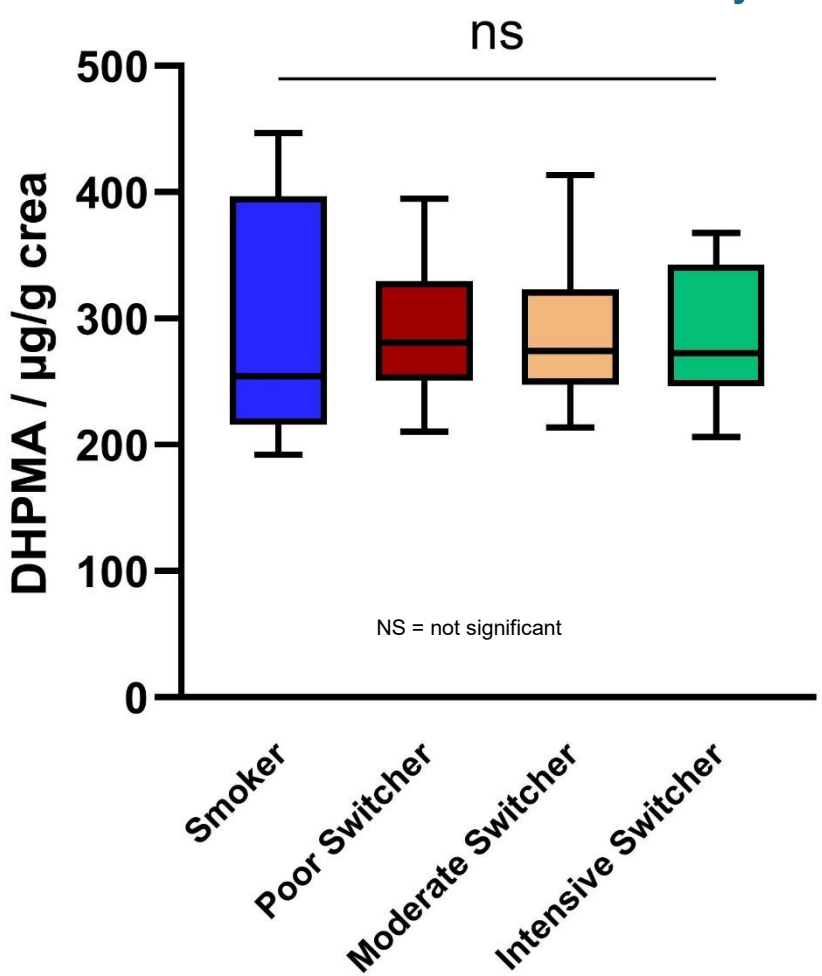
Urine

Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. 2CyEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons

Acrolein



Glycidol

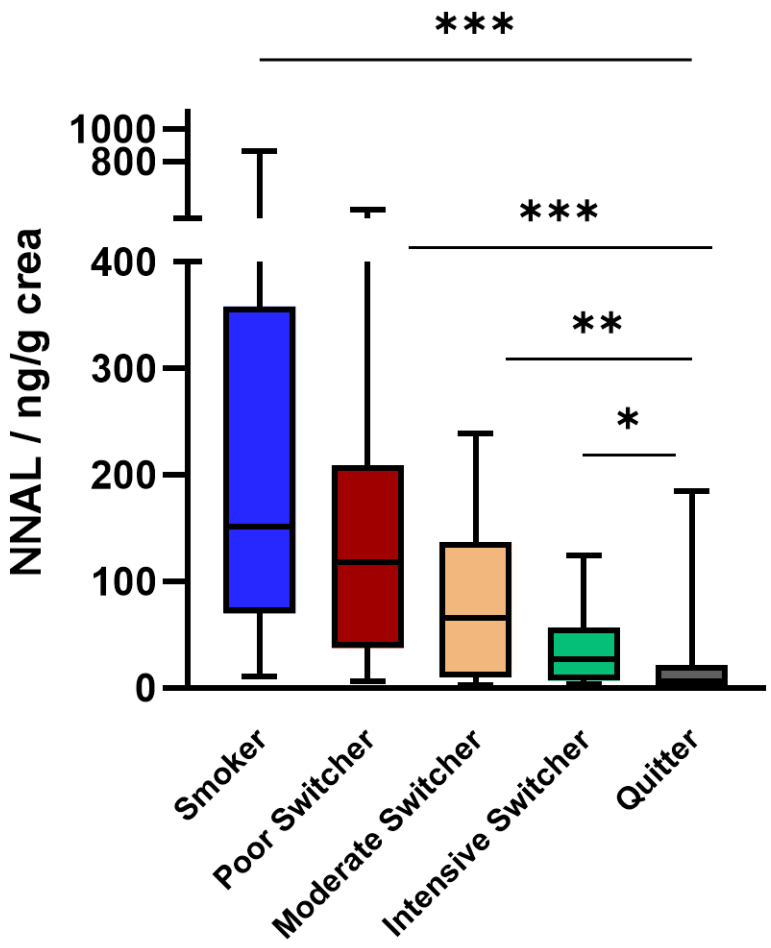


Results – TSNA exposure

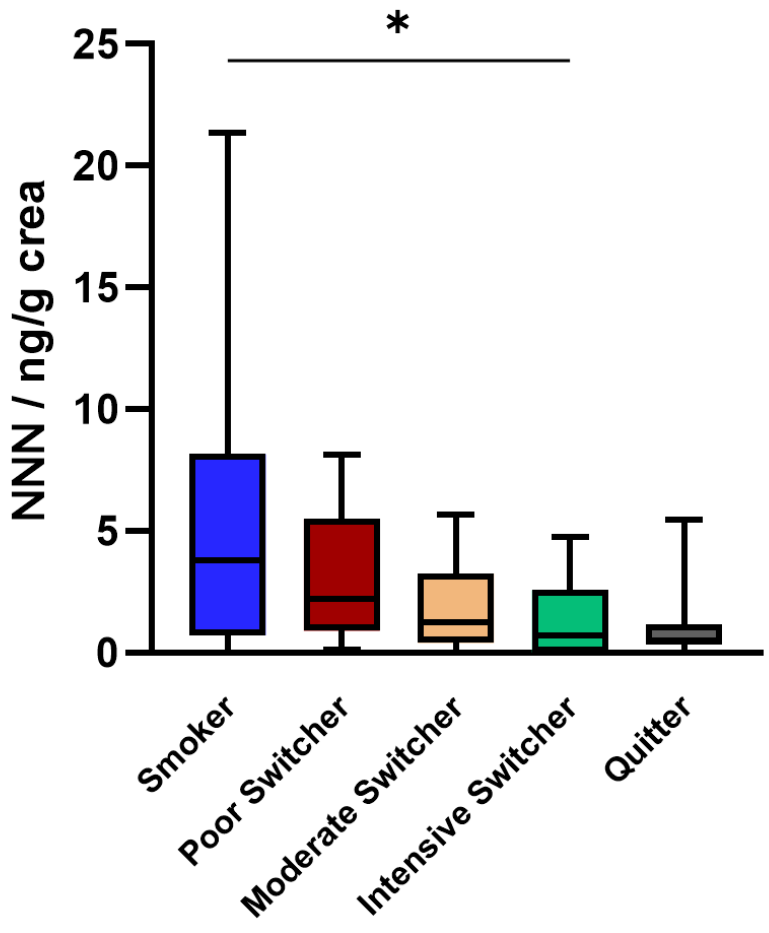
Urine

Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. 2CyEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons

NNK



NNN

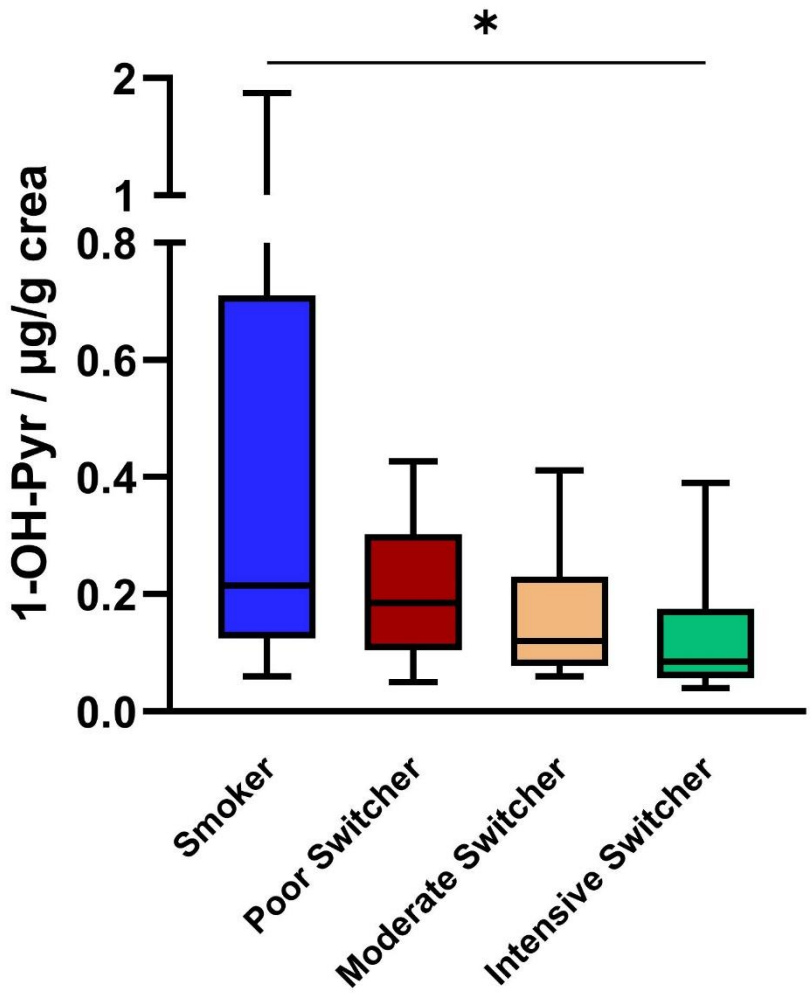


Results – PAH exposure

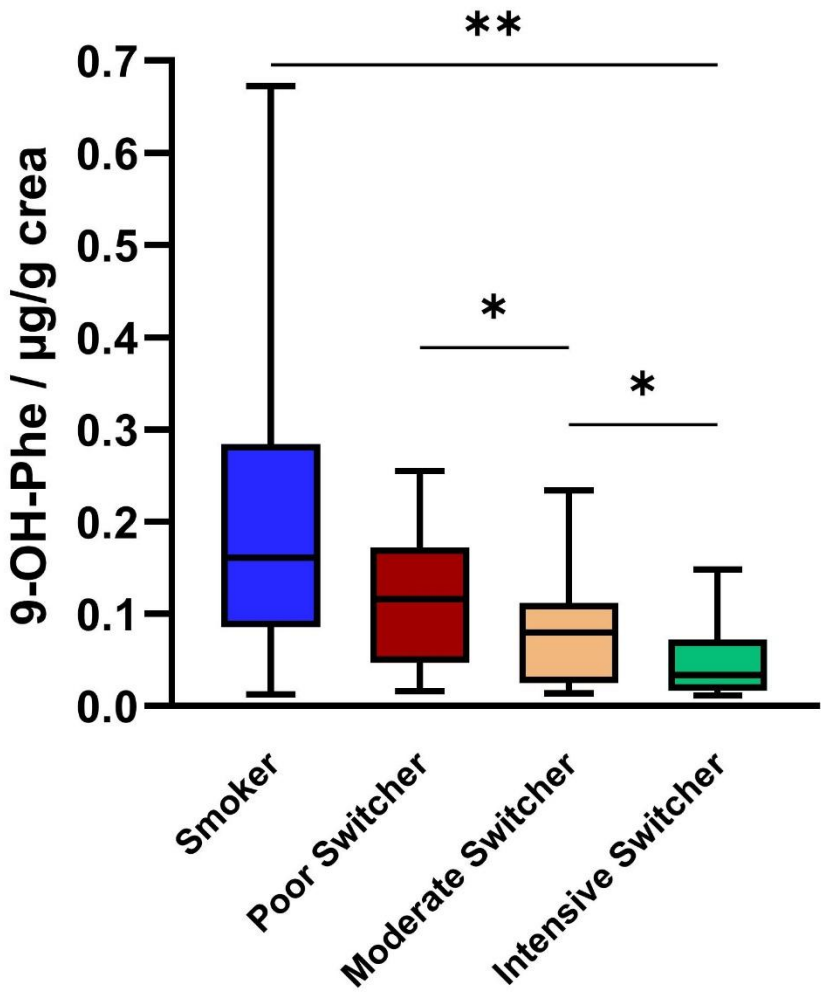
Urine

Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. 2CyEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons

Pyrene



Phenanthrene

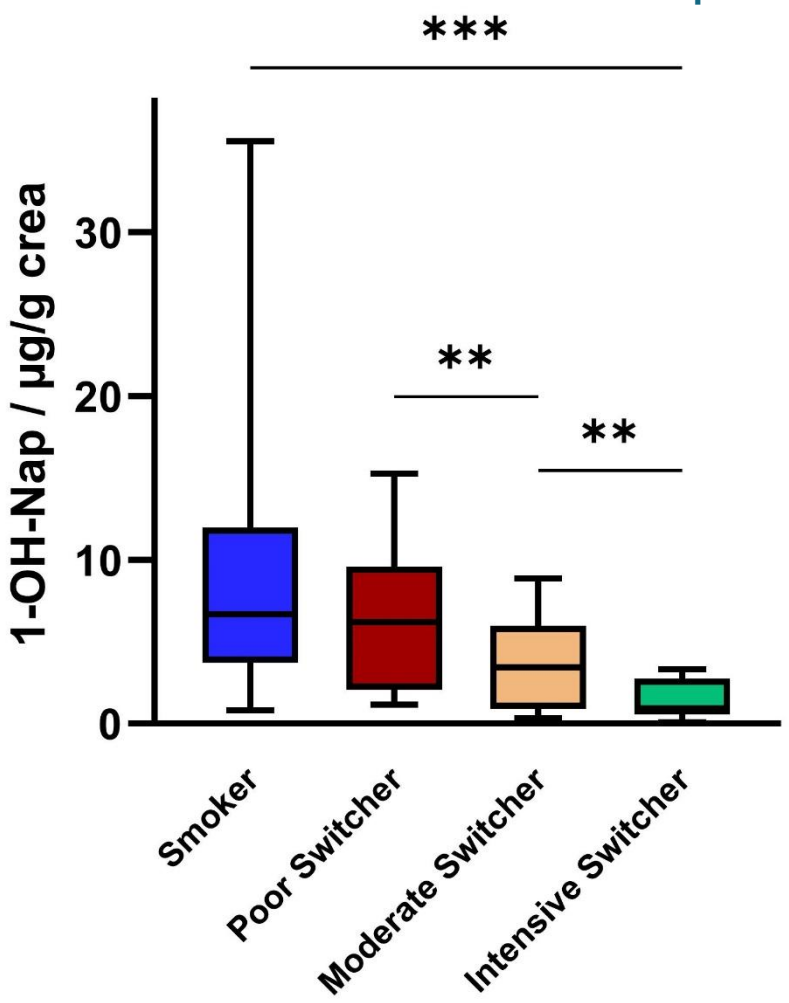


Results – PAH exposure

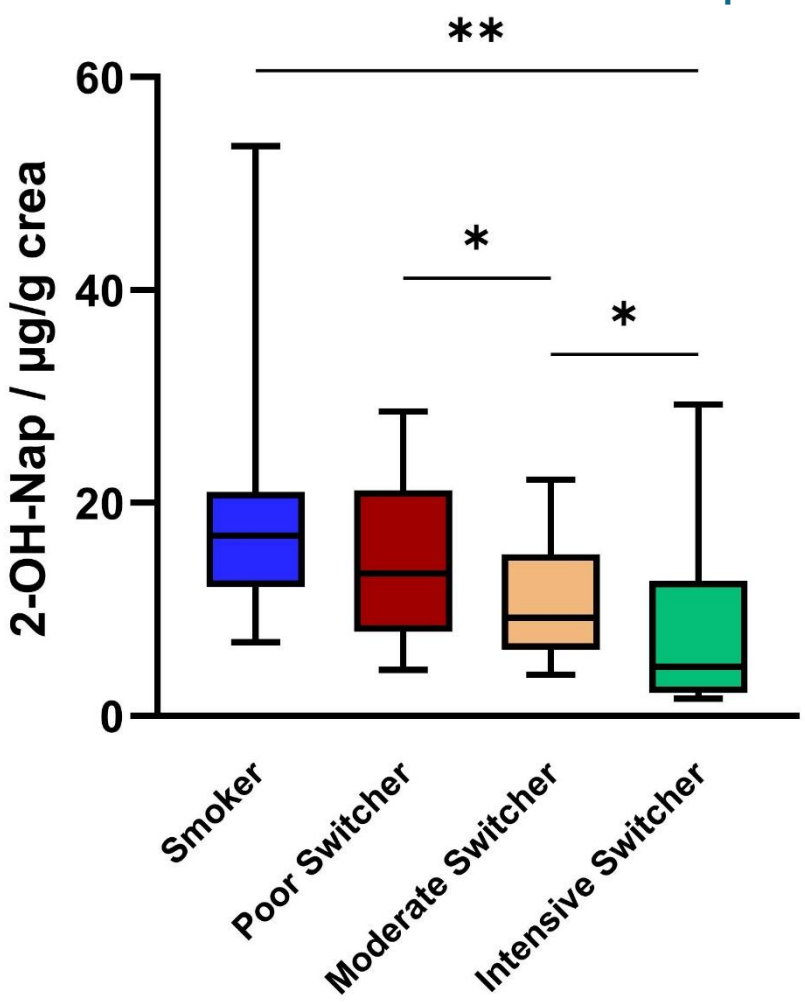
Urine

Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. 2CyEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons

Naphthalene



Naphthalene

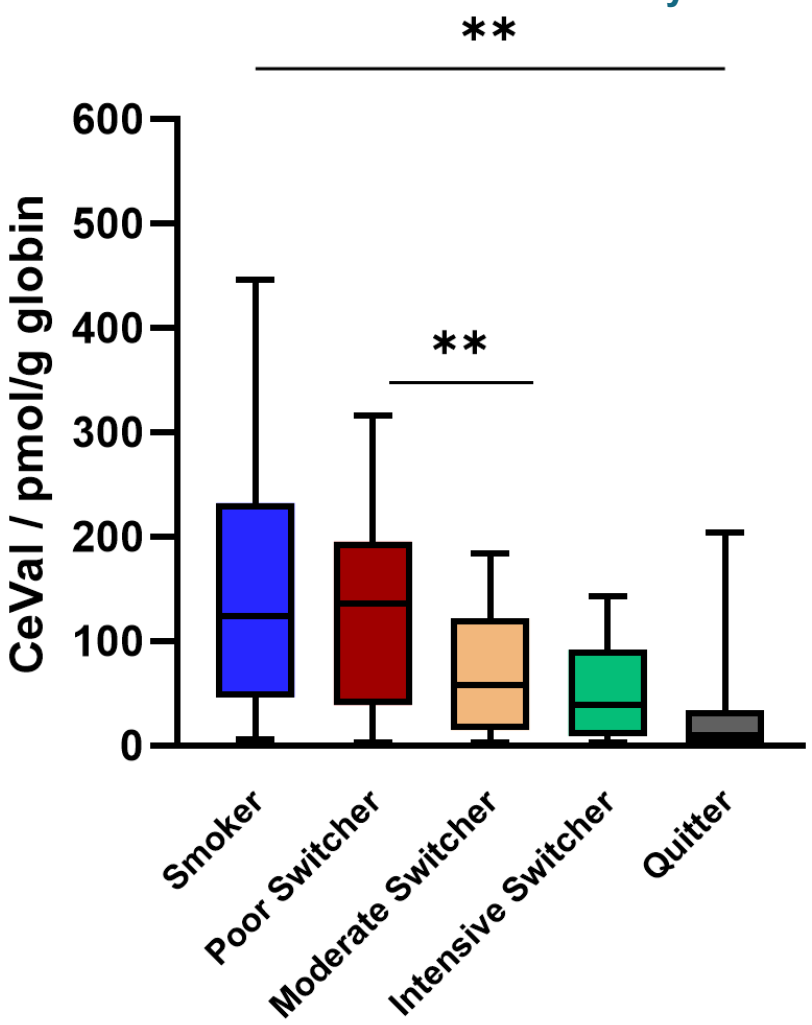


Results – VOC exposure: Hb adducts

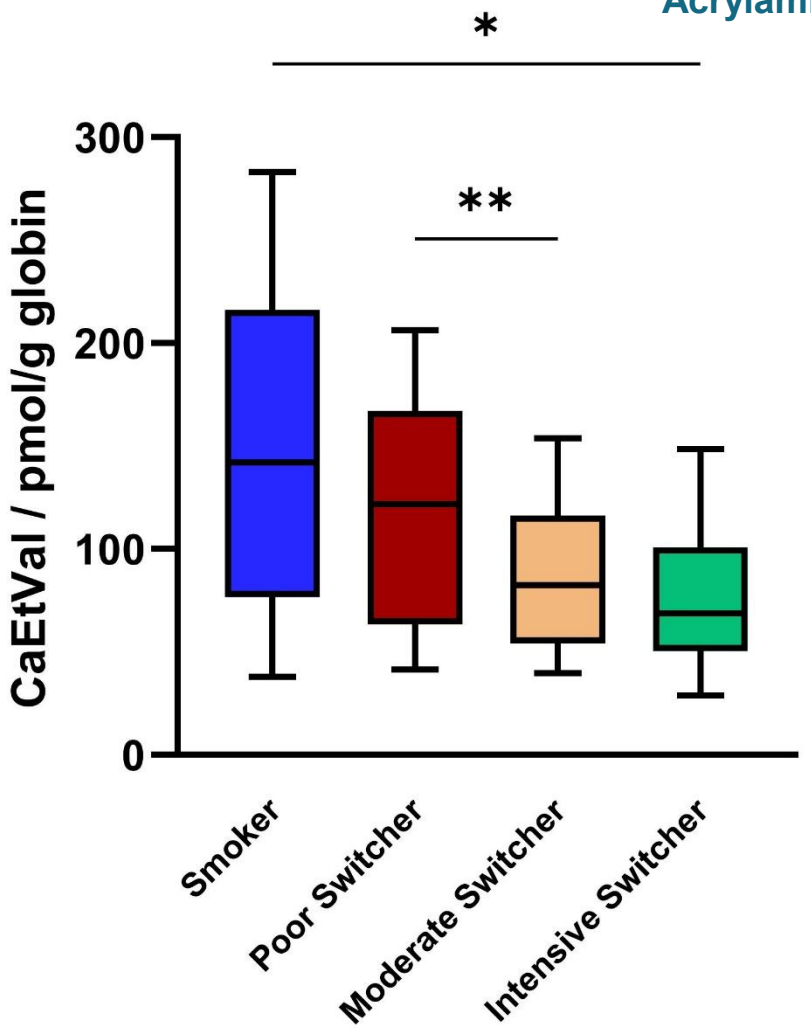
Washed erythrocytes

Hemoglobin adducts (long-term markers)

Acrylonitrile



Acrylamide



Study Results – 3rd Visit (90 days)

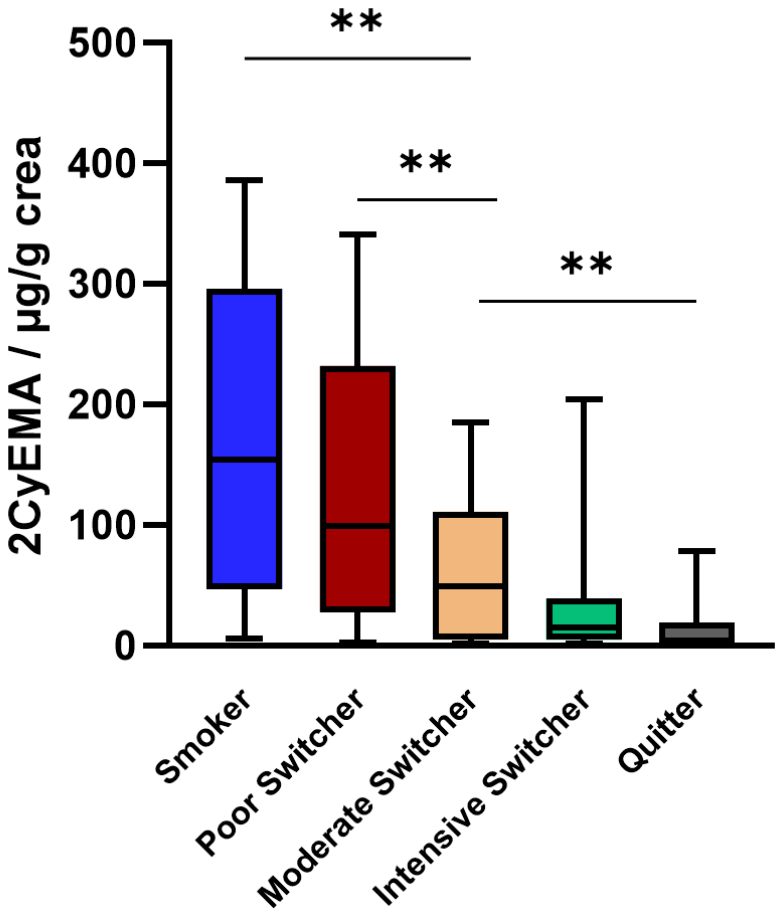
Results – VOC exposure

Urine

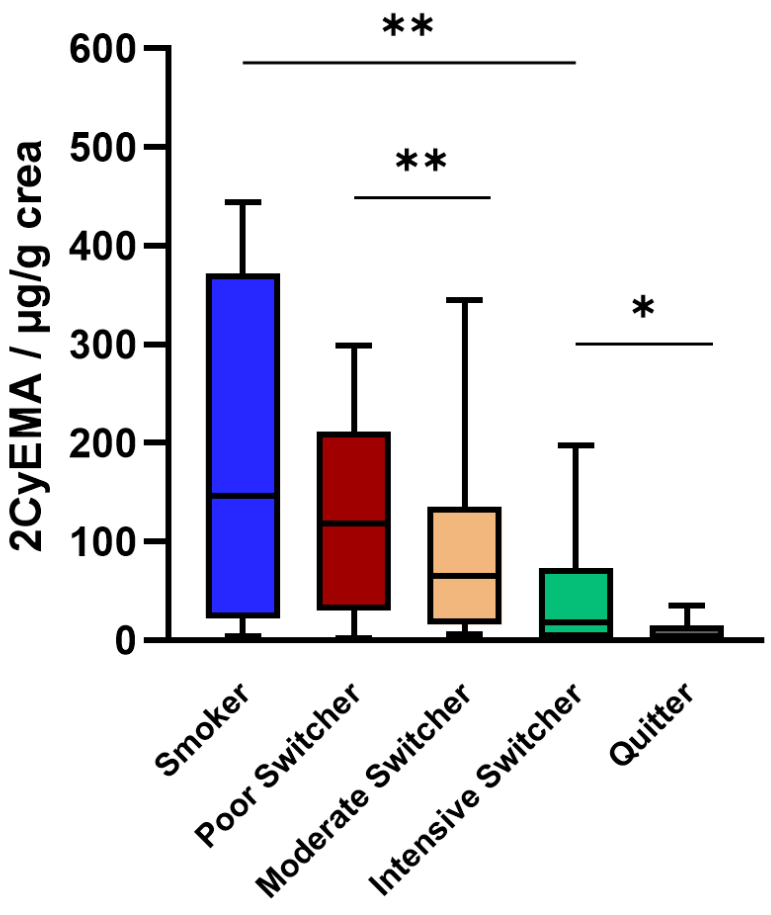
Nicotine, Cotinine, OH-Cotinine
Propylene Glycol
Mercapturic Acids (incl. 2CyEMA)
Tobacco Specific N-Nitrosamines
OH-Polycyclic Aromatic Hydrocarbons

Acrylonitrile

30 days



90 days

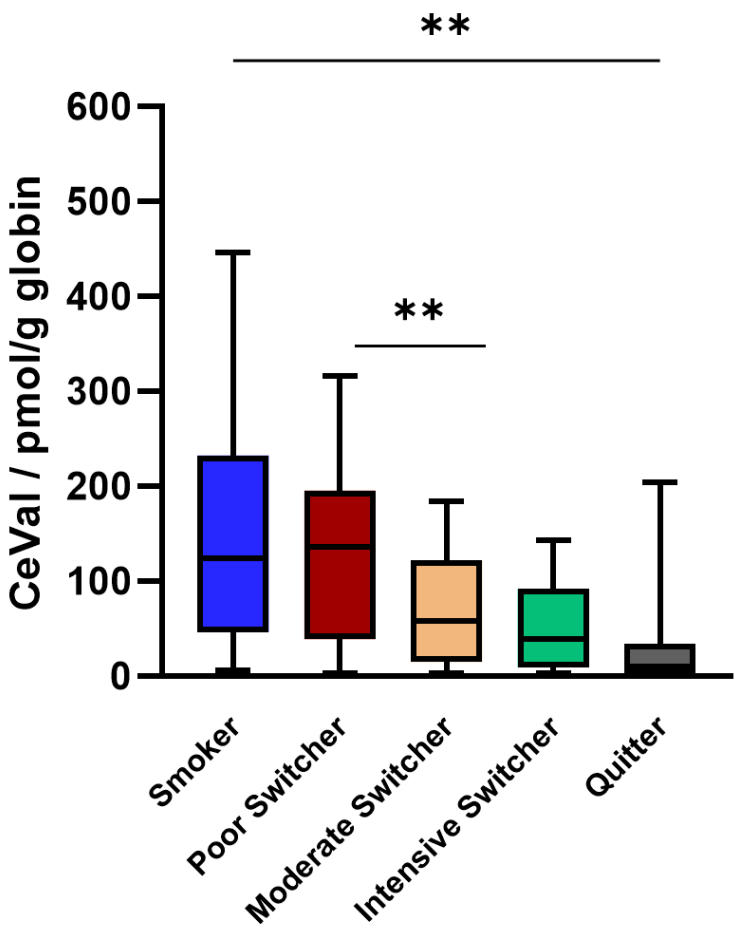


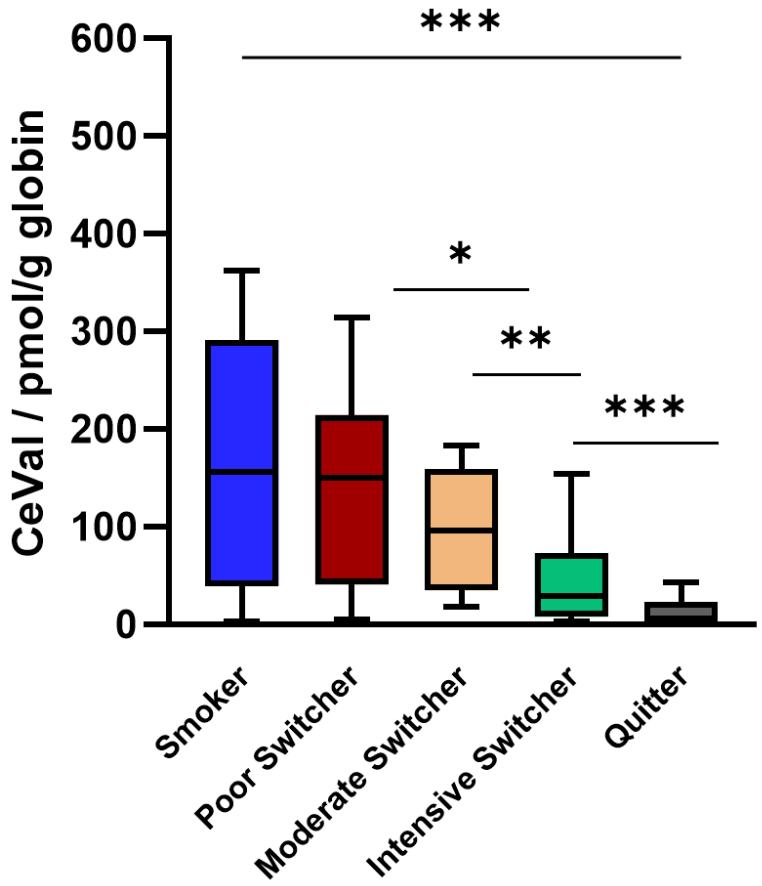
Results – VOC exposure: Hb adducts

Washed erythrocytes

Hemoglobin adducts (long-term markers)

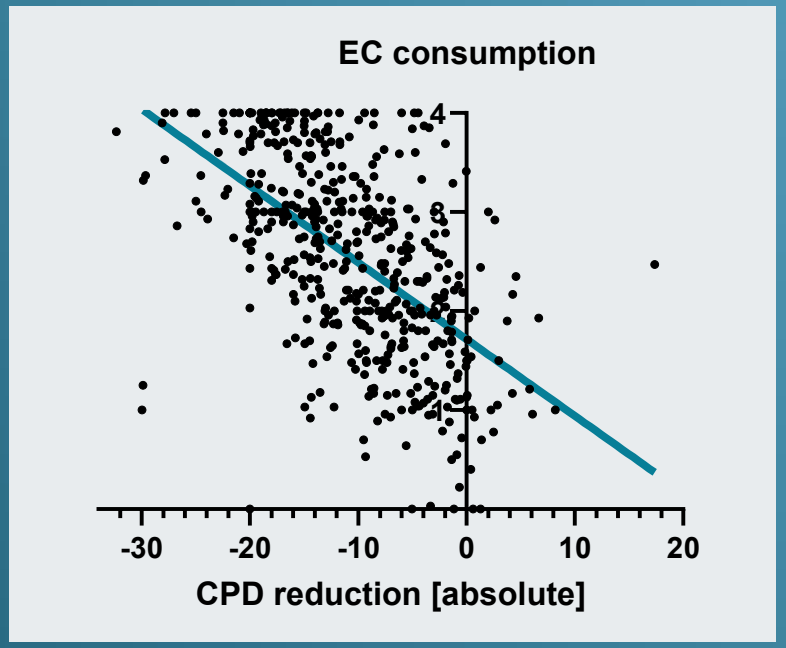
30 days | CeVal | 90 days

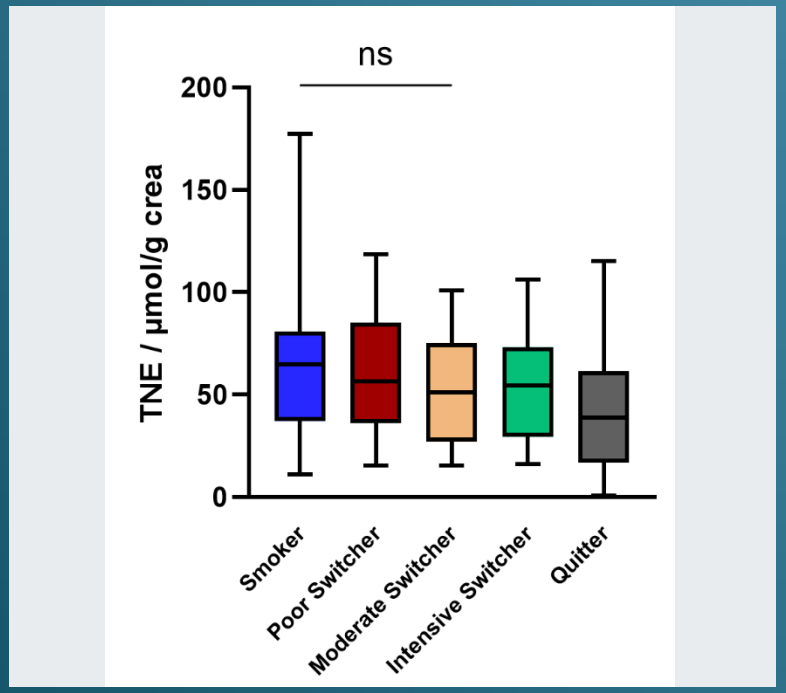




Conclusion

- **Detailed characterization of dual users**
  - Stratification of dual users by use patterns
  - Extensive biomarker panel covering exposure and potential harm
- **Nicotine Compensation**
  - Reduction in CC strongly correlates with increase in EC
  - Dual Users compensate Nic intake with vaping





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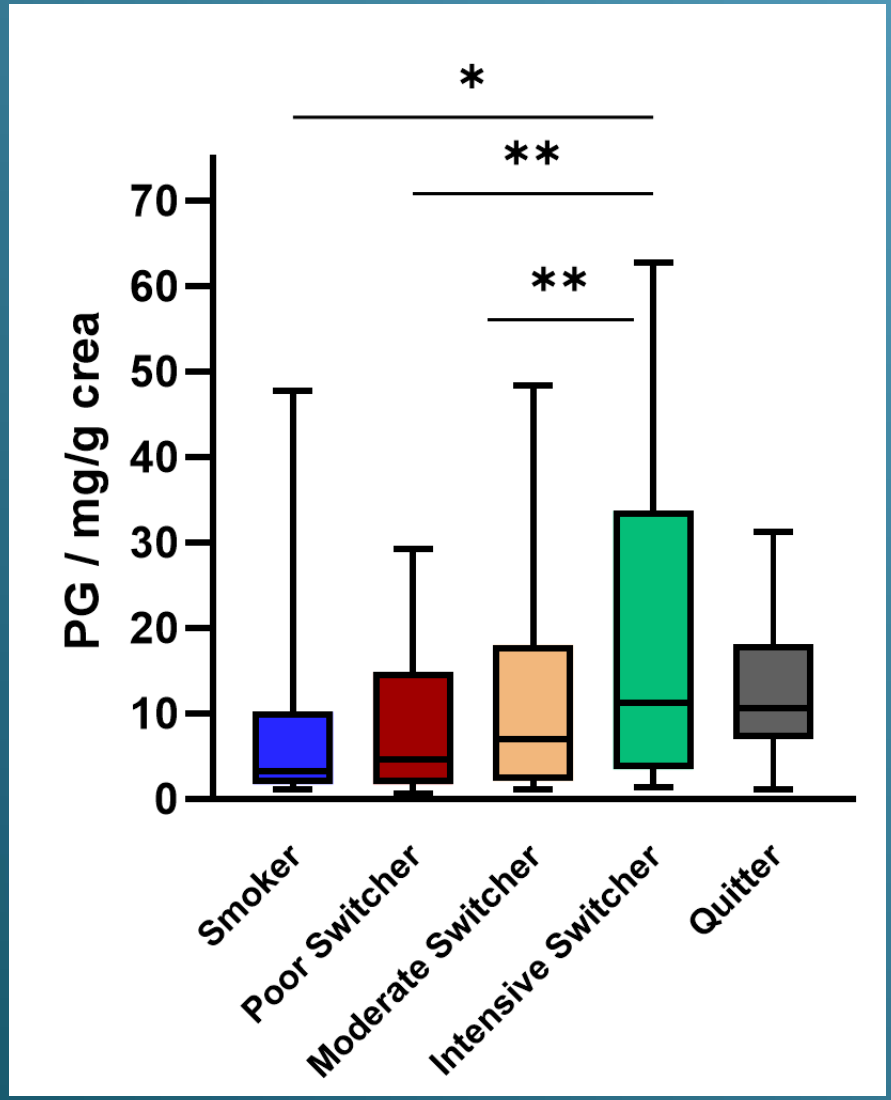
- **Urinary PG indicative of EC vaping**
  - Intensive switching results in significant increase of PG



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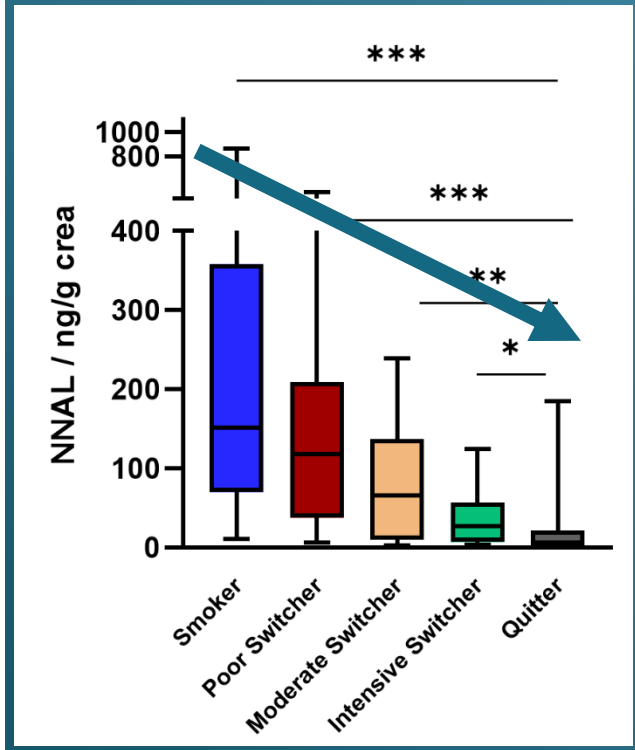
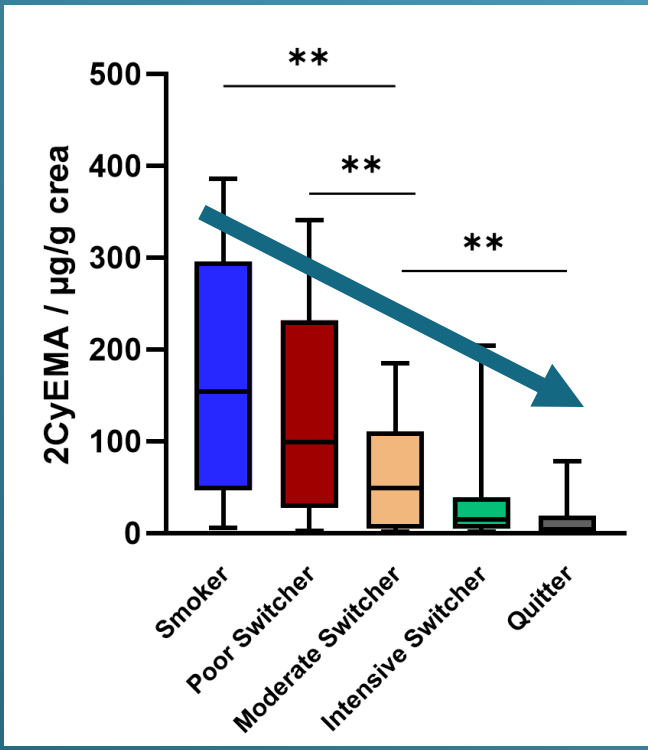
  - Clear trend towards lower BoE levels with reduction in CPD accompanied by increase in EC vaping
  - Substitution of CC with EC leads to lower toxicant exposure





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  - Clear trend towards lower BoE levels with reduction in CPD accompanied by increase in EC vaping
  - Substitution of CC with EC leads to lower toxicant exposure

- EC **vaping** does not contribute to exposure to tobacco-related toxicants
- No increase in **glycidol exposure** due to vaping
- Substantial **reduction** in **exposure** to **HPHCs** like **TSNAs, VOCs, PAHs** driven by **reduction** in **CPD**
- **CC use main contributor to toxicant exposure in Dual Users**

Acknowledgment

ABF Team: Simona Veigl, Janina Mütze, Carmen Tiwald, Veronika Spindler, Marta Latawiec, Richard Kanis, Johanna Lehocky, Roman Tögel

Pratia – MTZ Clinical Research Warsaw

CoEHAR Center of Excellence for the Acceleration of HArm Reduction

Riccardo Polosa
Jakub Weglarz
Jonathan Belsey

GLOBAL ACTION TO END SMOKING | Accelerating Research & Education to Save Lives

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