Is glyphosate safe for health and the environment?

The Global Glyphosate Study

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Ramazzini Institute

EU Parliament, September 18, 2023

www.glyphosatestudy.org

GGS: PARTNERS

Boston College, USA

University of California, USA

University of Padua, Italy

Icahn School of Medicine at Mount Sinai, USA

George Mason University, USA

University of Bologna, Italy

University of Copenhagen, DNK

King's College, UK

Federal University Of Parana, BR

GGS: PHASES

PILOT STUDY

1 dose
2 test substances
Limited endpoints

Gather initial information on the potential effects and possible toxicological targets

INTEGRATED STUDY

3 doses
3 test substances
Multiple endpoints

Integrated Experimental design aimed at testing comprehensively major toxicological endpoints: carcinogenicity, reproductive/developmental toxicity, subchronic and long-term toxicity, neurotoxicity, microbiome

GGS
PILOT STUDY

GGS: PILOT STUDY

GROUP	COMPOUND	DOSE
I	Drinking water	Control
II	Glyphosate	US cRfD (1.75 mg/kg bw/day)
III	Roundup	US cRfD (1.75 mg/kg bw/day)

- Animals: Sprague-Dawley rats from CMCRC colony
- Route of Administration: ad libitum in drinking water
- Test Substances: Glyphosate and its formulation Roundup Bioflow (MON 52276)
- Dose: U.S. chronic Reference Dose (cRfD)
- Treatment: 2 WOS (6, 13-week prenatal)

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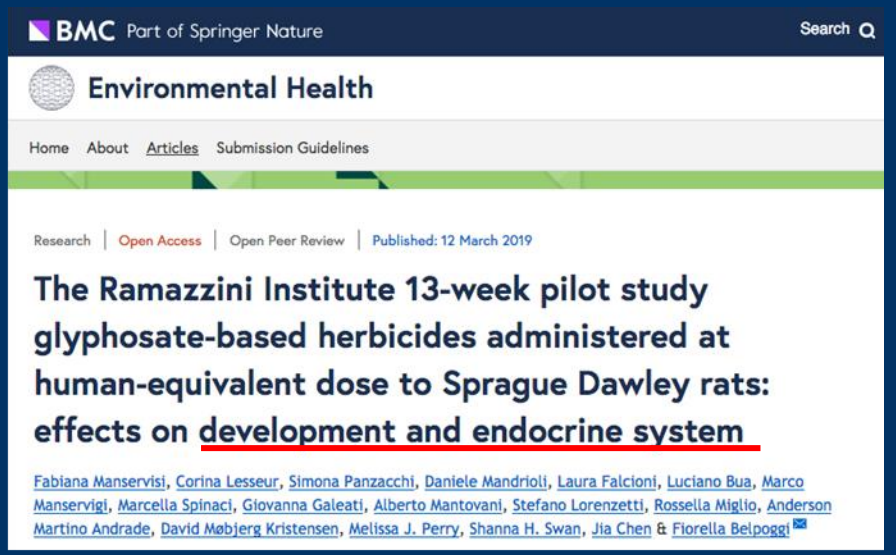
The Ramazzini Institute 13-week pilot study on glyphosate and Roundup administered at human-equivalent dose to Sprague Dawley rats: effects on the microbiome

Qixing Mao, Fabiana Manservisi, Simona Panzacchi, Daniele Mandrioli, Ilaria Menghetti, Andrea Vornoli, Luciano Bua, Laura Falcioni, Corina Lesseur, Jia Chen, Fiorella Belpoggi & Jianzhong Hu



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The Ramazzini Institute 13-week pilot study glyphosate-based herbicides administered at human-equivalent dose to Sprague Dawley rats: effects on development and endocrine system

Fabiana Manservisi, Corina Lesseur, Simona Panzacchi, Daniele Mandrioli, Laura Falcioni, Luciano Bua, Marco Manservigi, Marcella Spinaci, Giovanna Galeati, Alberto Mantovani, Stefano Lorenzetti, Rossella Miglio, Anderson Martino Andrade, David Møbjerg Kristensen, Melissa J. Perry, Shanna H. Swan, Jia Chen & Fiorella Belpoggi

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Conclusion
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Comments

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The Ramazzini Institute 13-week study on glyphosate-based herbicides at human-equivalent dose in Sprague Dawley rats: study design and first in-life endpoints evaluation

Simona Panzacchi †, Daniele Mandrioli †, Fabiana Manservisi, Luciano Bua, Laura Falcioni, Marcella Spinaci, Giovanna Galeati, Giovanni Dinelli, Rossella Miglio, Alberto Mantovani, Stefano Lorenzetti, Jianzhong Hu, Jia Chen, Melissa J. Perry, Philip J. Landrigan and Fiorella Belpoggi

†Contributed equally

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https://doi.org/10.1186/s12940-018-0393-y | © The Author(s). 2018
Received: 2 February 2018 | Accepted: 10 May 2018 | Published: 29 May 2018

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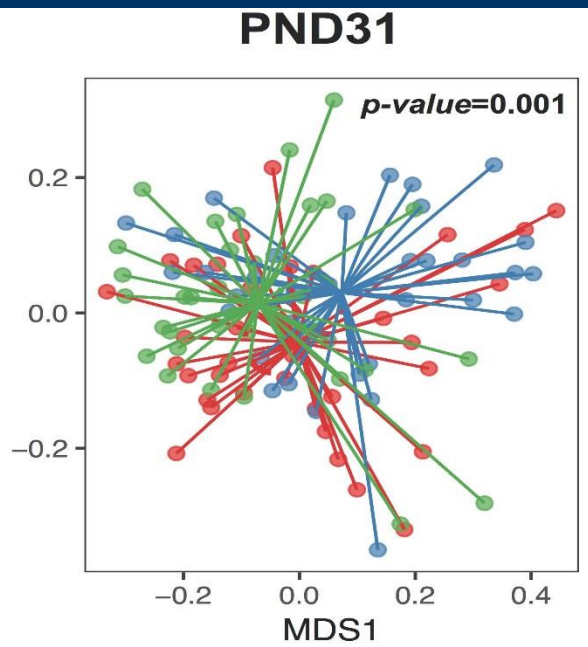
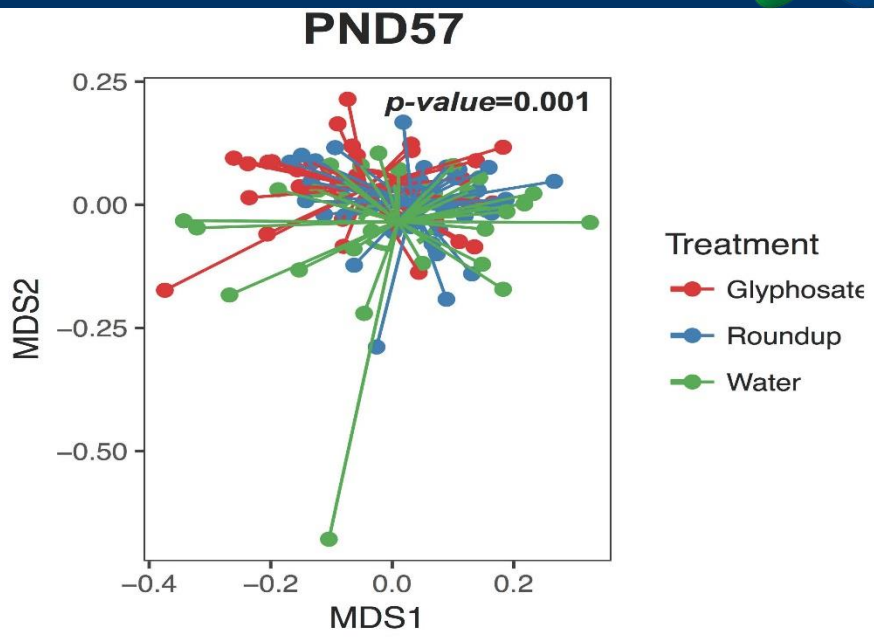
OPEN

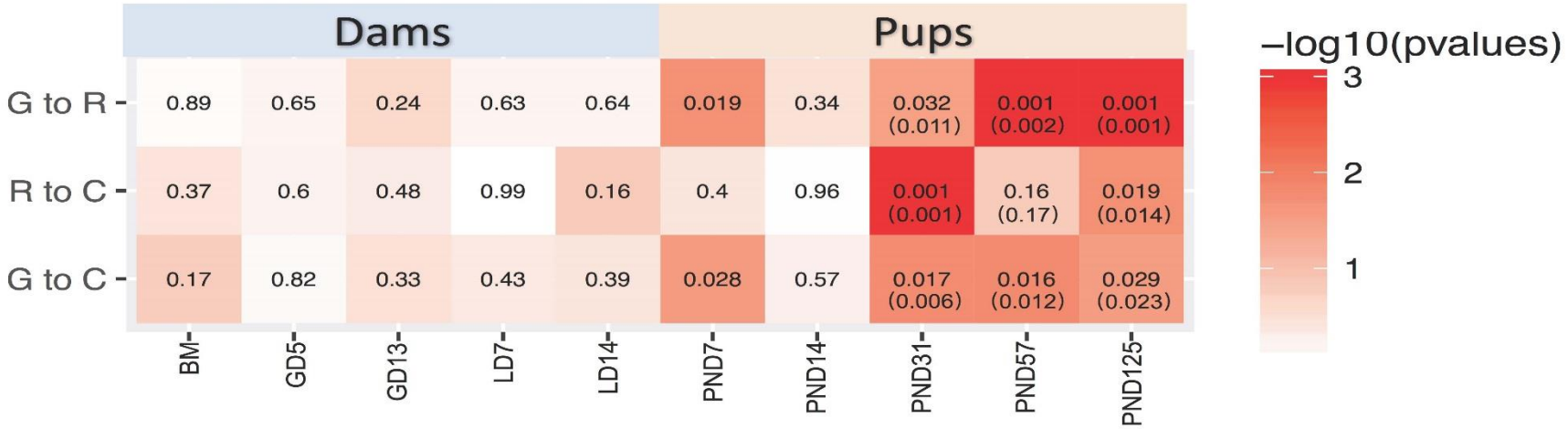
Low-dose exposure of glyphosate-based herbicides disrupt the urine metabolome and its interaction with gut microbiota

Jianzhong Hu, Corina Lesseur, Yu Miao, Fabiana Manservisi, Simona Panzacchi, Daniele Mandrioli, Fiorella Belpoggi, Jia Chen & Lauren Petrick

GGS Pilot Study First Results: Microbiome







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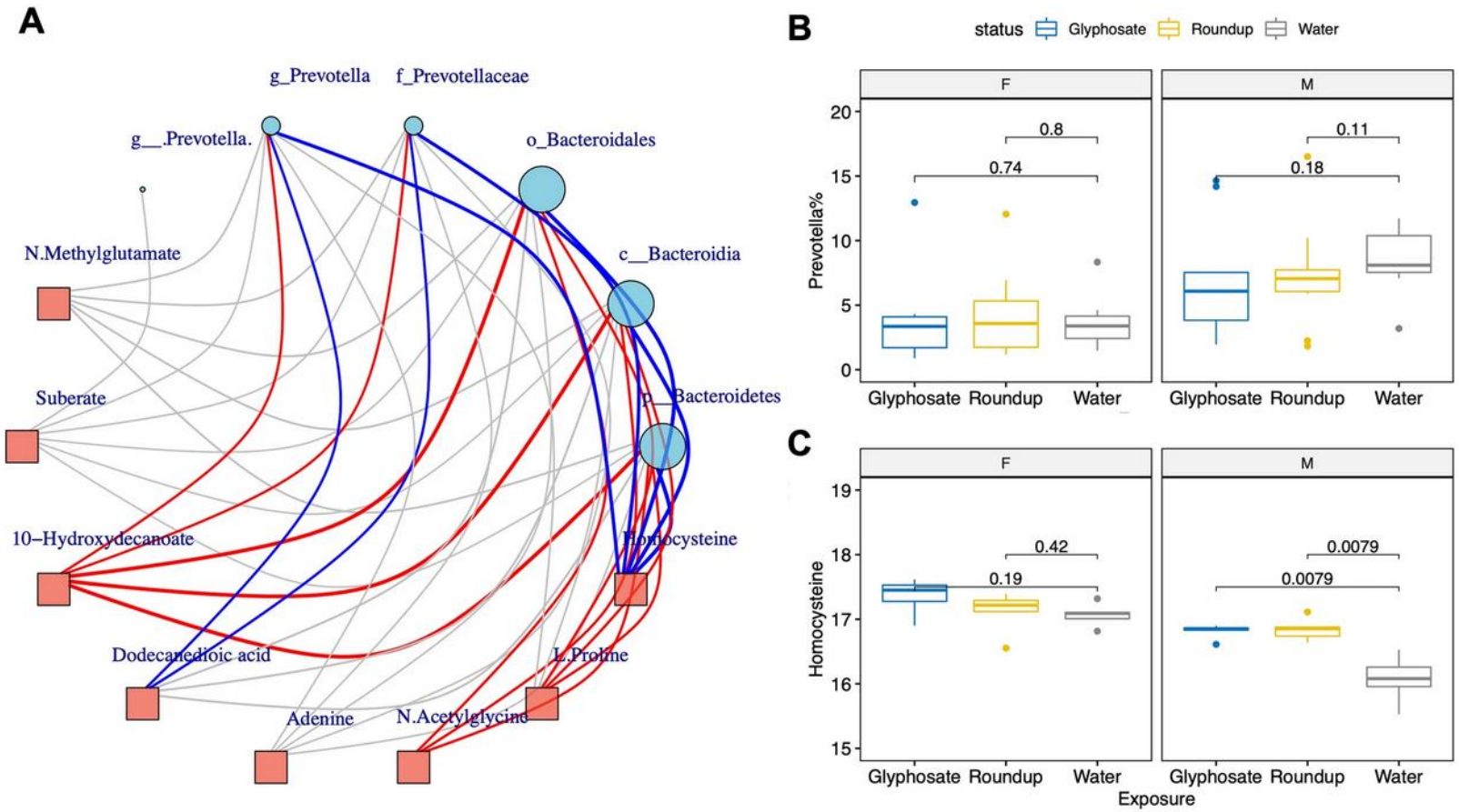
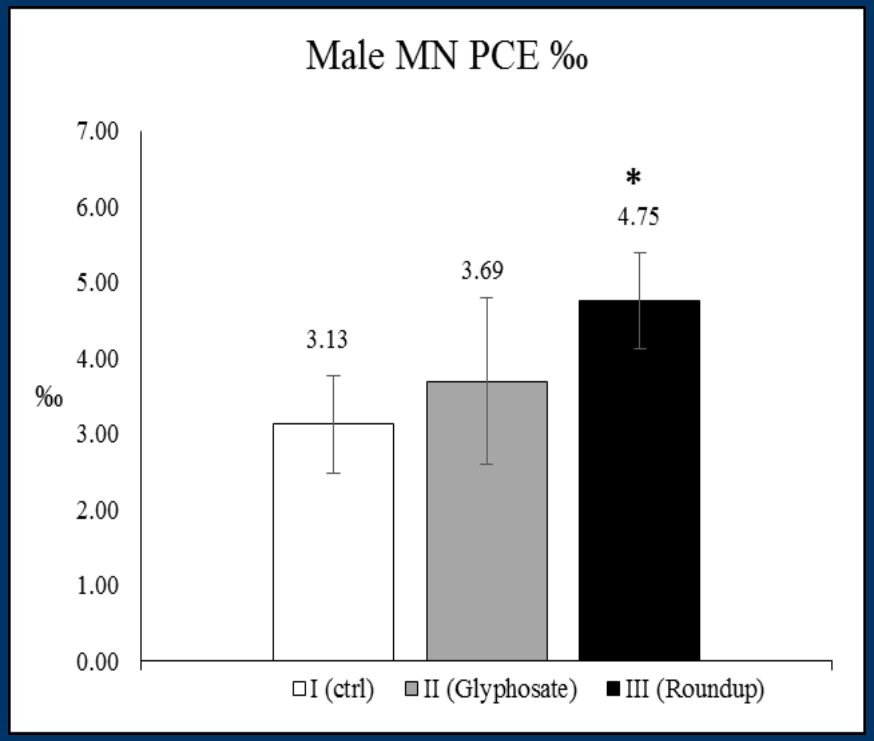
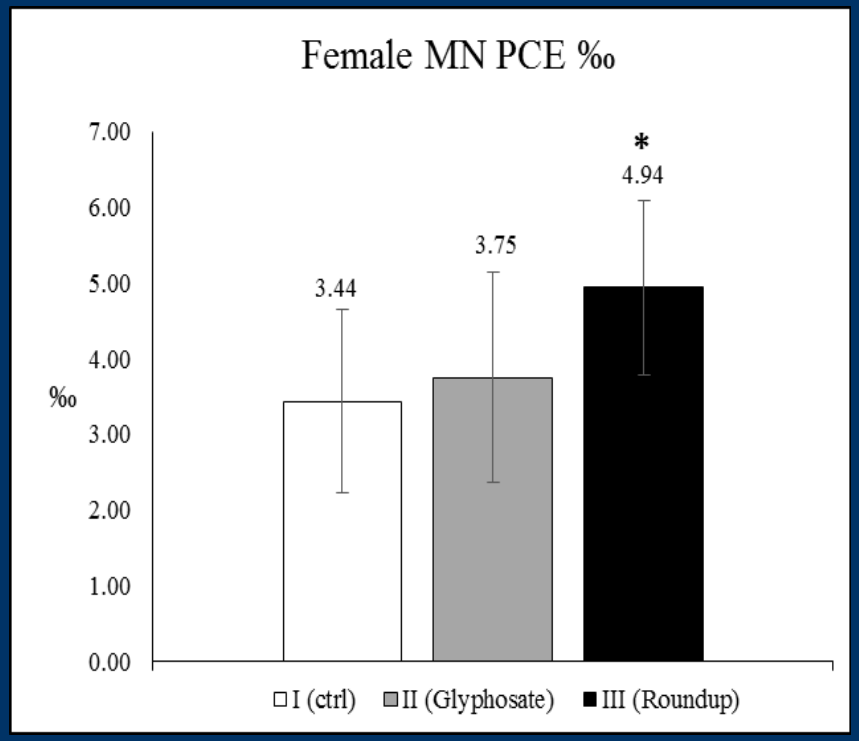


The urine homocysteine levels in pups are associated with sex and glyphosate or Roundup exposure and are strongly correlated with *Prevotella* abundance in gut microbiota. (**A**) Correlation network between exposure associated metabolic features and gut microbiota. *Prevotella* and its belonged *Bacteroidetes* phylum to *Prevotellaceae* family all show strong negative correlation with the urine homocysteine. The links with FDR adjusted *p* value < 0.05 are colored with red (positive correlation) and blue (negative correlation). (**B**,**C**) Boxplots showed that *Prevotella* abundances were lower in female pups than male pups. *Prevotella* was reduced in exposed male pups. In contrast, the female pups have higher homocysteine than the male pups and the homocysteine levels were significantly increased by exposure in male pups.

GGS: PILOT STUDY

- **A statistically significant increase in the micronuclei frequency was observed in male and female rats treated with GBHs**





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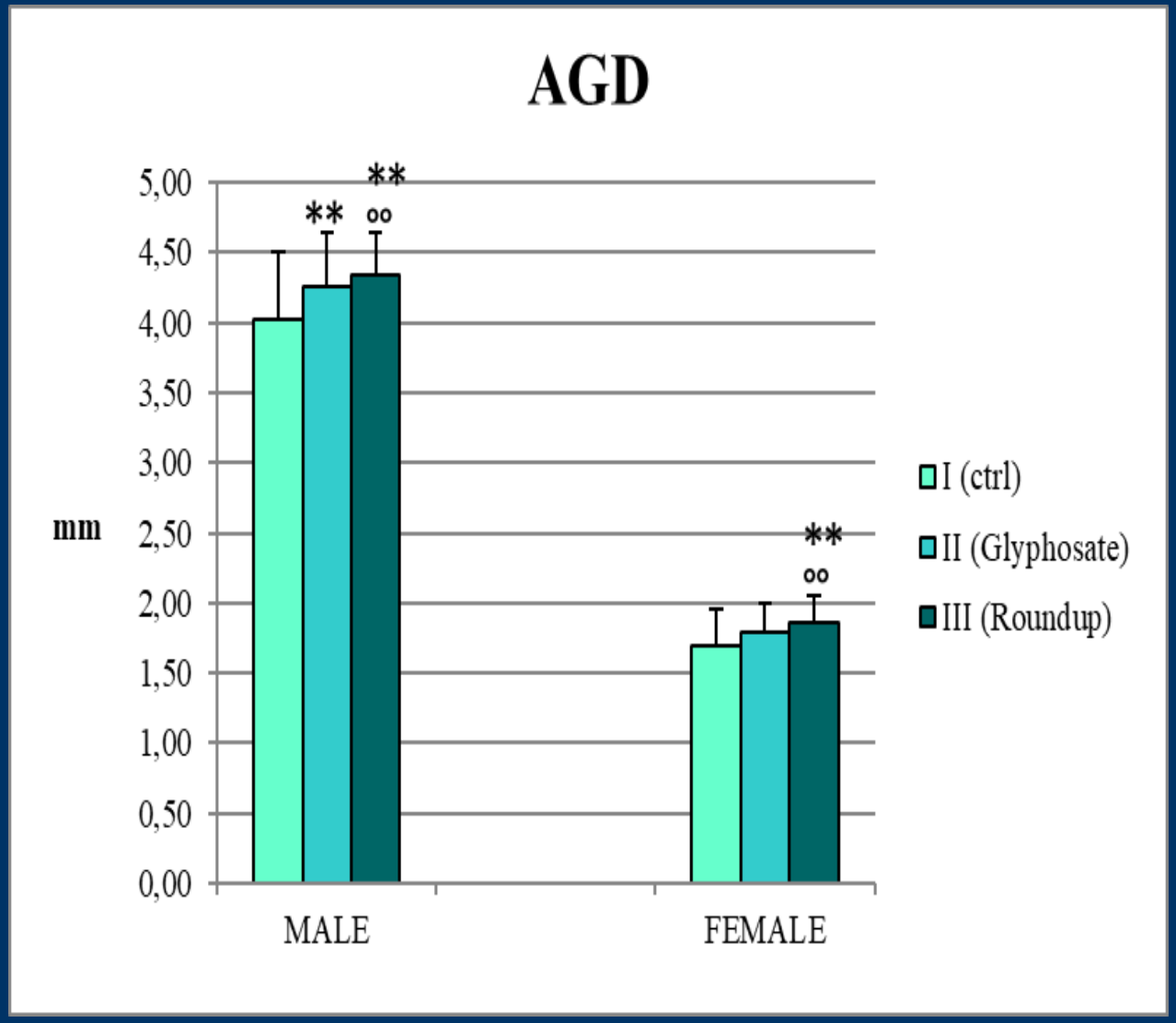

GGS PILOT STUDY RESULTS CONFIRMED IN HUMANS

Environmental Pollution 280 (2021) 117002

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Maternal urinary levels of glyphosate during pregnancy and anogenital distance in newborns in a US multicenter pregnancy cohort☆

Corina Lesseur [a], Patrick Pirrotte [b], Khyatiben V. Pathak [b], Fabiana Manservisi [c, d], Daniele Mandrioli [c], Fiorella Belpoggi [c], Simona Panzacchi [c], Qian Li [a], Emily S. Barrett [e], Ruby H.N. Nguyen [f], Sheela Sathyanarayana [g], Shanna H. Swan [a], Jia Chen [a, *]

GGS: RESULTS IN HUMANS

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Environmental Research

Volume 203, January 2022, 111811

Urinary glyphosate concentration in pregnant women in relation to length of gestation

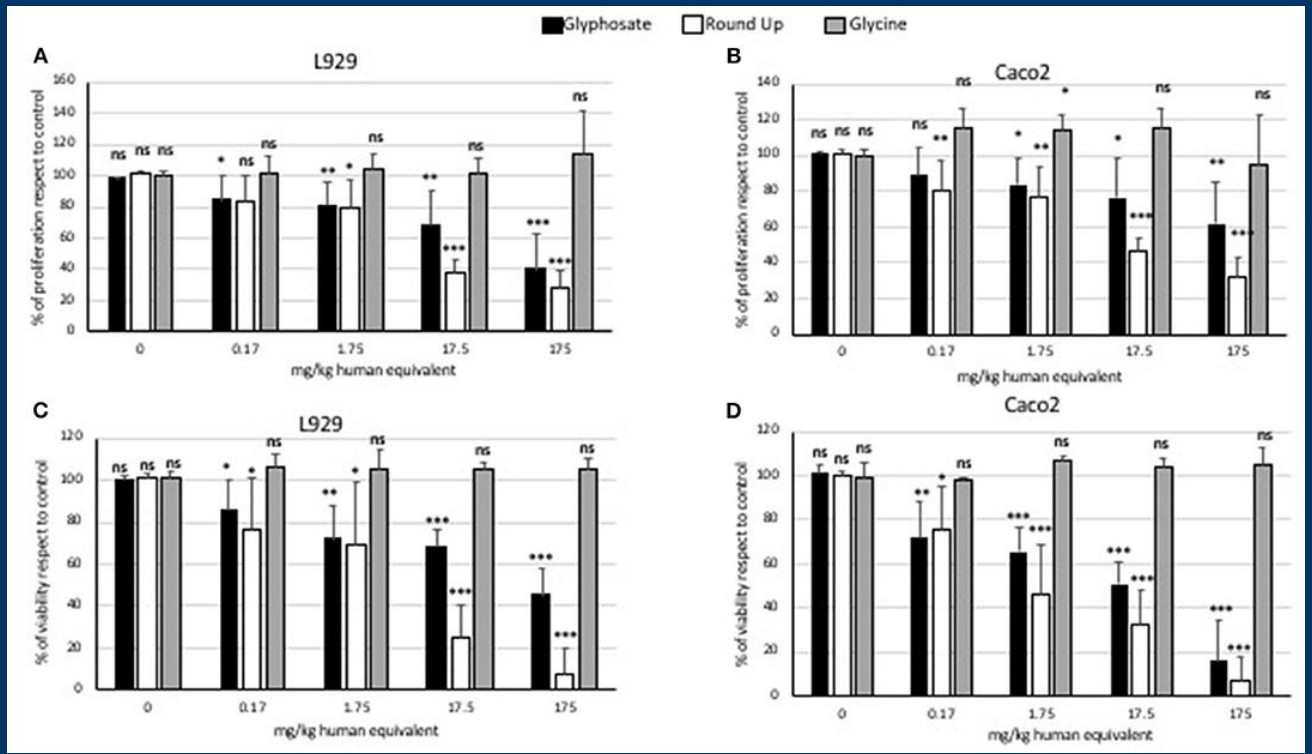
Corina Lesseur [a], Khyatiben V. Pathak [b], Patrick Pirrotte [b], Melissa N. Martinez [b], Kelly K. Ferguson [c], Emily S. Barrett [d], Ruby H.N. Nguyen [e], Sheela Sathyanarayana [f], Daniele Mandrioli [g], Shanna H. Swan [a], Jia Chen [a]

GGS: Mechanistic Studies

Front Public Health. 2021 May 7;9:643898. doi: 10.3389/fpubh.2021.643898. eCollection 2021.

Comparative Evaluation of the Cytotoxicity of Glyphosate–Based Herbicides and Glycine in L929 and Caco2 Cells

Francesca Truzzi [1], Daniele Mandrioli [1 2], Federica Gnudi [2], Paul T J Scheepers [3], Ellen K Silbergeld [4], Fiorella Belpoggi [2], Giovanni Dinelli [1]



MTT (proliferation) assay and Trypan Blue (viability) assay: effects of pure glyphosate, Roundup Bioflow, and glycine at the dose range 0–175 mg kg−1 (human equivalent) on cell proliferation of L929 fibroblasts (A), Caco2 cells (B), and on cell viability of L929 fibroblasts (C) and Caco2 cells (D). Data are expressed as mean value (± st. dev.) (% compared to control).

Pairwise comparison based on Anova (Dunnett test). ns, not significant: *P < 0.05; **P < 0.01; ***P < 0.001.

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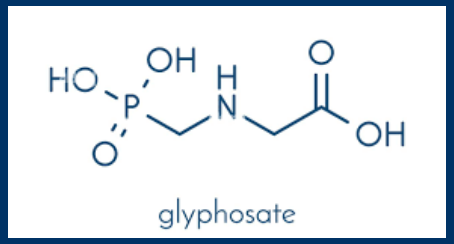
INTEGRATED STUDY

GGS: INTEGRATED STUDY



Active ingredient
Isopropylamine salt of N-(phosphonomethyl)glycine; {Isopropylamine salt of glyphosate}

Composition

COMPONENT	CAS No.	% by weight (approximate)
Isopropylamine salt of glyphosate	38641-94-0	41
Other ingredients		59

The specific chemical identity is being withheld because it is trade secret information of Monsanto Company.

Active ingredient
Isopropylamine salt of N-(phosphonomethyl)glycine; {Isopropylamine salt of glyphosate}

Composition

Components	CAS No.	EC No.	EU Index No. / REACH Reg. No. / C&L ID No.	% by weight (approximate)	Classification
Isopropylamine salt of glyphosate	38641-94-0	933-426-9	015-184-00-8 / - / 02-2119693876-15-0000	41.5	Aquatic Chronic - Category 2; H411; {c} N; R51/53; {b}
Ethoxylated tallowamine			- / - / -	15.5	Xn, N; R22, 41, 51/53; {a}
Water	7732-18-5	231-791-2	- / - / -	43	

The specific chemical identity is being withheld because it is trade secret information of Monsanto Company.

Glyphosate dose (mg/kg bw/day)	
0.5	ADI EU
5	ADI EU 10X
50	NOAEL EU

9 TREATED + 1 CONTROL GROUP

WHAT WE ARE STUDYING

Glyphosate is one of the most used chemicals in the history of mankind and astonishingly its safety has never been comprehensively studied.

The Global Glyphosate Study is covering a truly comprehensive group of endpoints in what is being described as one of the largest ever studies on a single chemical:

- Carcinogenicity
- Short-term and long-term toxicty
- Prenatal developmental toxicity
- Neurotoxicity
- Multi-generational toxicity
- Endocrine disruption
- Microbiome

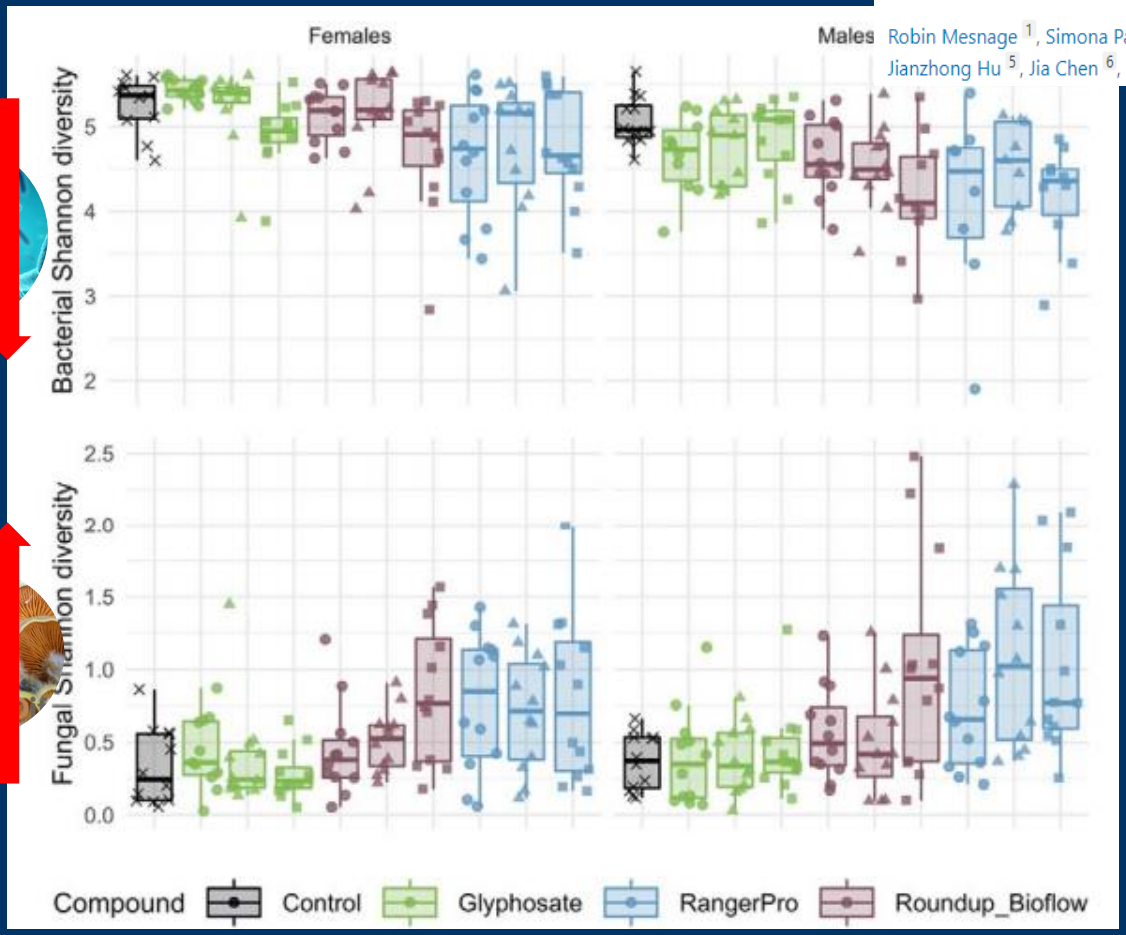
We are studying both glyphosate alone and two different full formulations of glyphosate-based herbicides as sold in the U.S. and the EU respectively.

GGS: INTEGRATED STUDY

› Front Microbiol. 2022 Oct 5;13:888853. doi: 10.3389/fmicb.2022.888853. eCollection 2022.

Glyphosate and its formulations Roundup Bioflow and RangerPro alter bacterial and fungal community composition in the rat caecum microbiome

Robin Mesnage [1], Simona Panzacchi [2], Emma Bourne [3], Charles A Mein [3], Melissa J Perry [4], Jianzhong Hu [5], Jia Chen [6], Daniele Mandrioli [2], Fiorella Belpoggi [2], Michael N Antoniou [1]



Glyphosate alone altered bacterial alfa diversity

Alteration of both bacterial and fungal flora in the formulations

GGS: INTEGRATED STUDY

- **Doses considered "safe" in the EU (ADI) caused statistically significant effects on different endpoints**
- **First endocrine disrupting effects observed in the pilot study have been confirmed in human cohorts**
- GBHs induced dose-dependent alterations of the **microbiome**
- **Liver and kidney** are target organs of GBHs
- Carginogenicity study results will be presented in late October 2023
- Urgent need for support to finalize the Integrated Study

Thank you