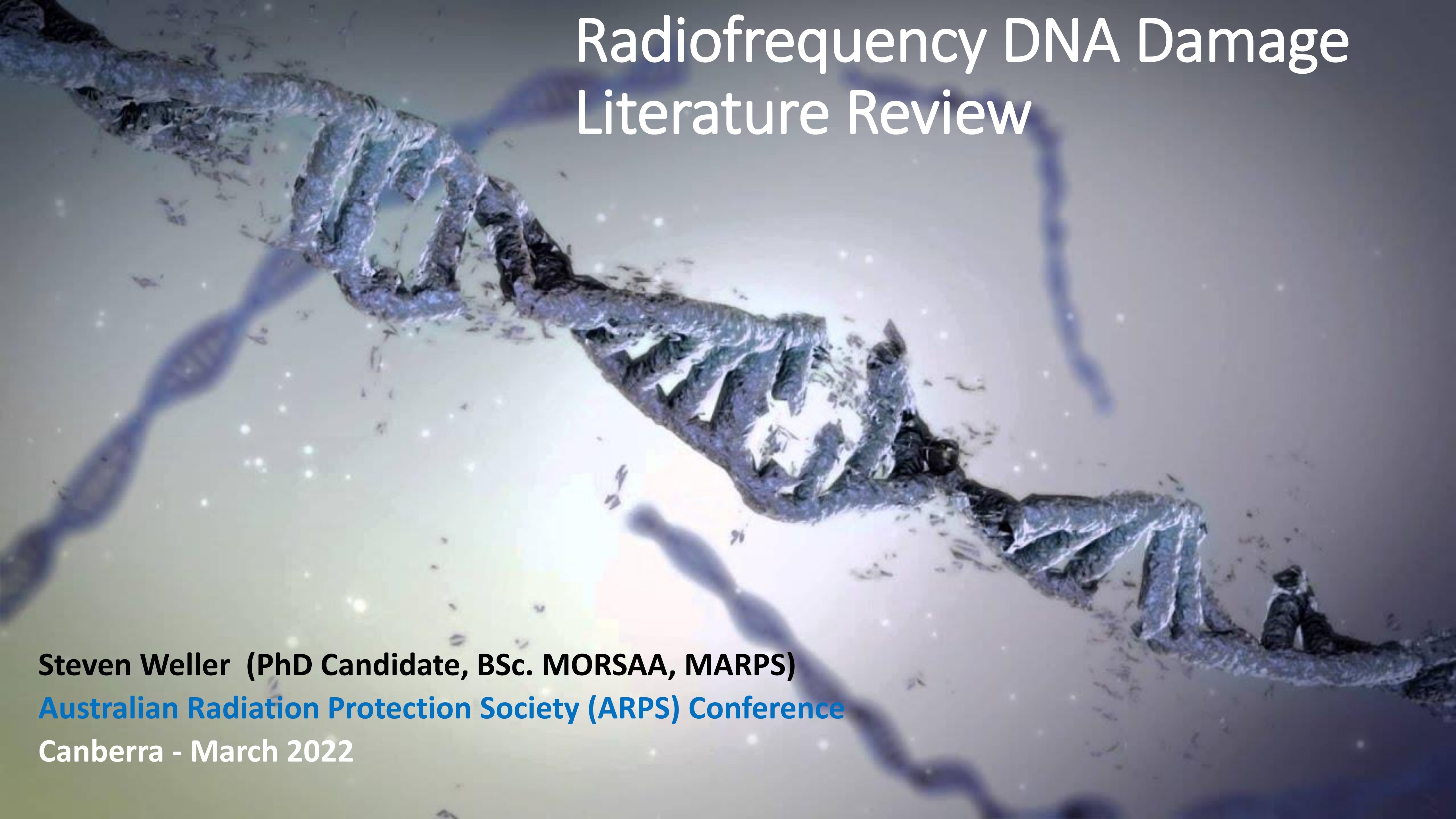


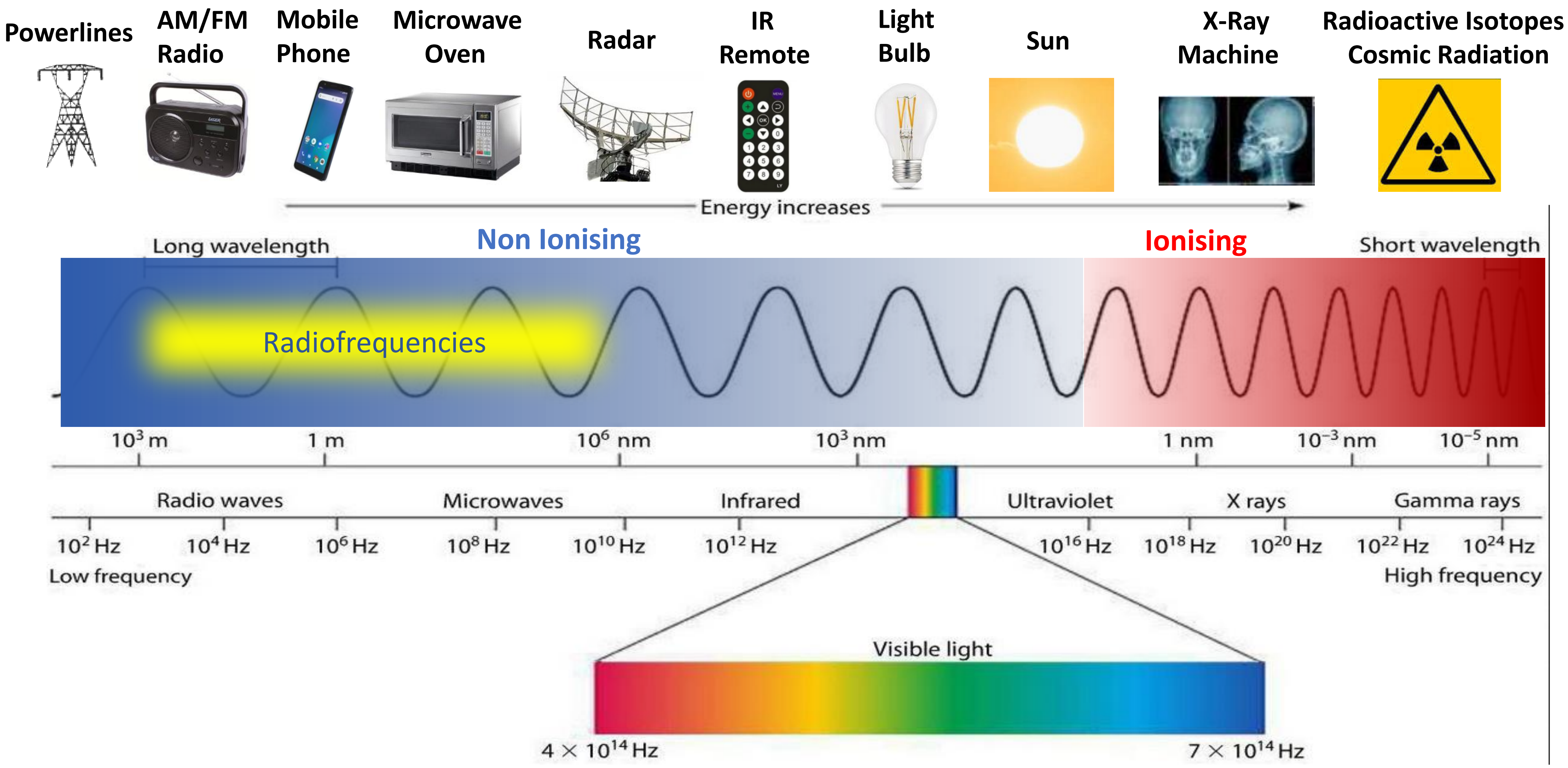
Radiofrequency DNA Damage Literature Review

Steven Weller (PhD Candidate, BSc. MORSAA, MARPS)

Australian Radiation Protection Society (ARPS) Conference

Canberra - March 2022

Electromagnetic Radiation Spectrum



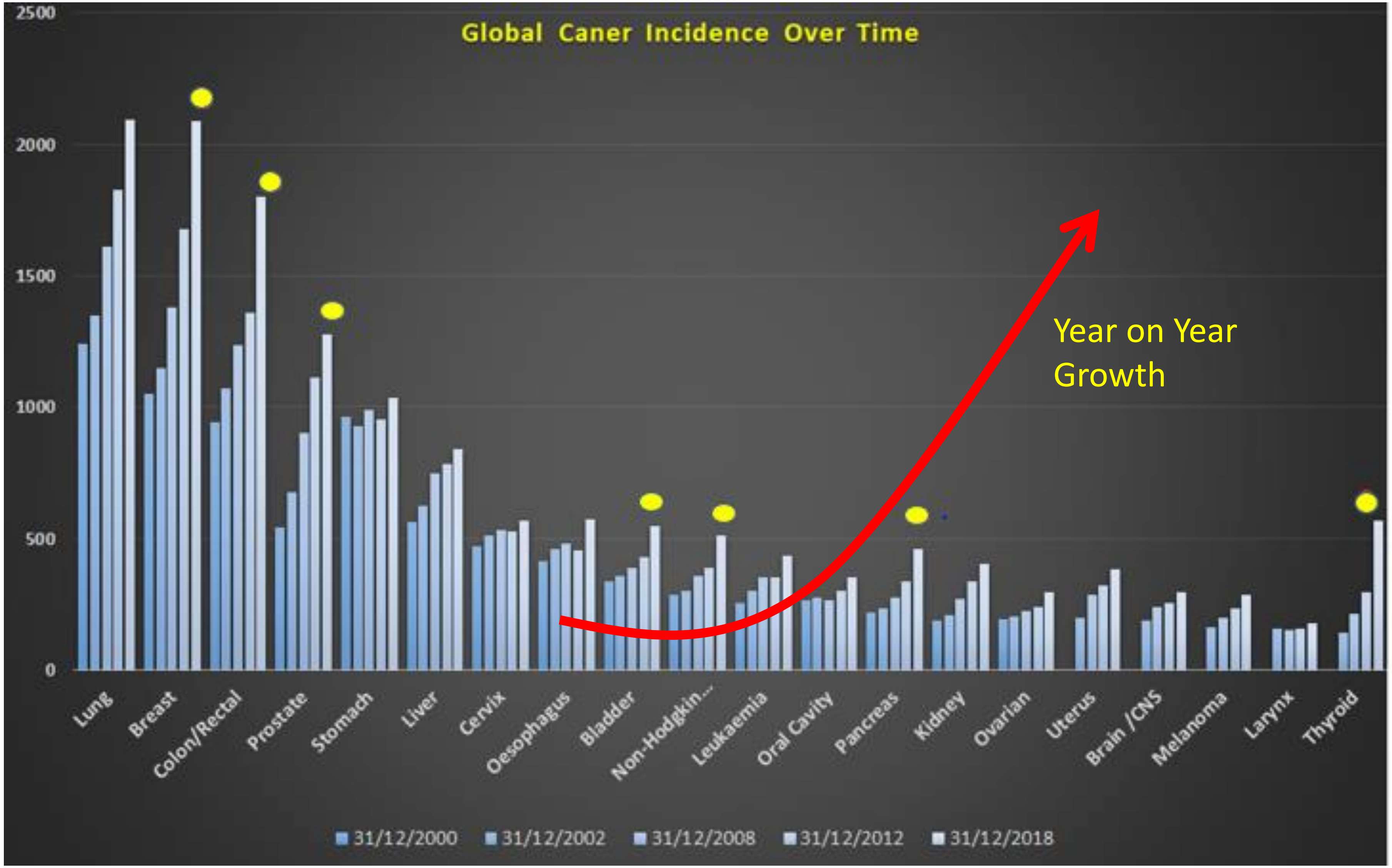
Artist: Ade Stewart

Background

IARC Perspective

- Classified all radiofrequencies (RF) as a Group 2B possible carcinogen (2011)
- Suggested evidence is credible but bias and confounding could not be ruled out
- Mechanism for cancer was unknown
- IARC classification was controversial and downplayed by authorities and industry (comparing RF to pickled vegetables)
- More recently, two important life time exposure studies on rats has provided clear evidence of carcinogenicity (NTP, Ramazzini 2018)
- IARC has nominated RF as a priority for review

Global Cancer: A Rising Health Burden for Humanity



Source: World Cancer Reports 2000, 2002, 2008, 2012 and 2018

Rationale for RF genotoxicity review

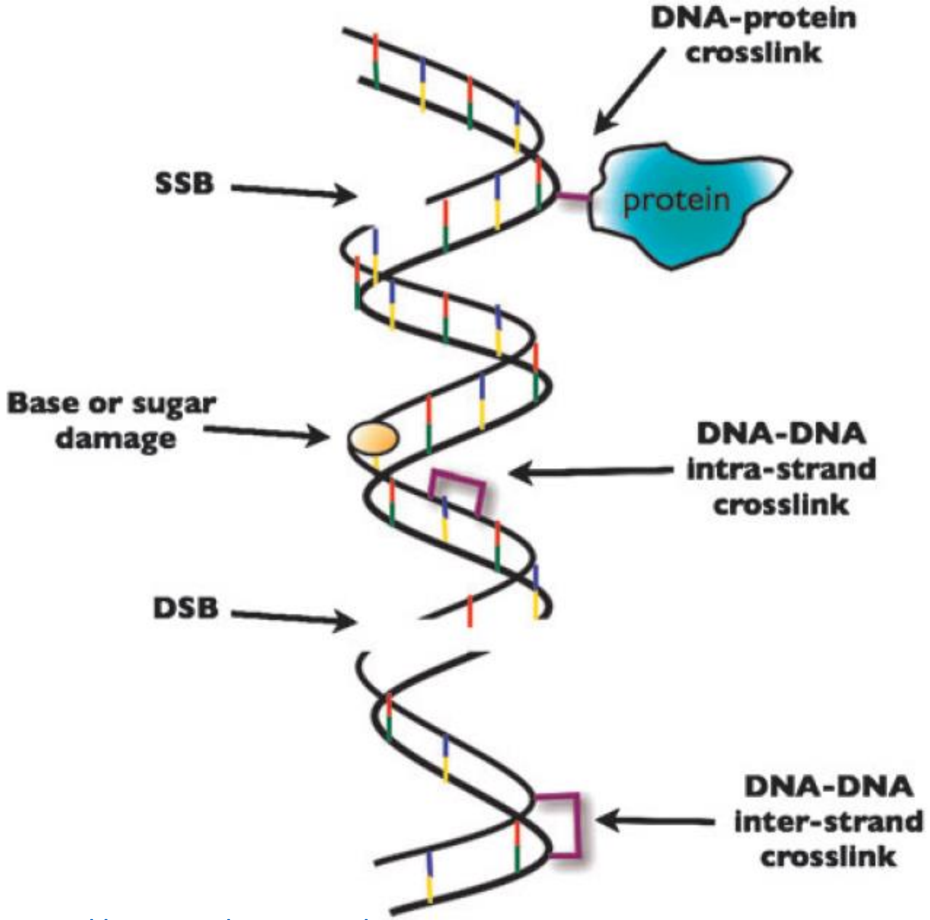
- Genotoxicity (DNA Damage) is a recognised pathway to cancer
- If RF is carcinogenic, evidence of genotoxicity should be present
- Existing literature base is quite substantial but results appear inconsistent
- Past reviews suffer from limitations:
    - Scope is either too narrow (i.e., investigation of in vitro studies only)
    - Too broad (narrative reviews that don't delve into the detail)
    - Some have used biased paper selection methods
    - Do not investigate possible mechanisms in most cases

4 Types of DNA Damage Investigated

Types of DNA Damage

1. DNA Breaks/Fragmentation

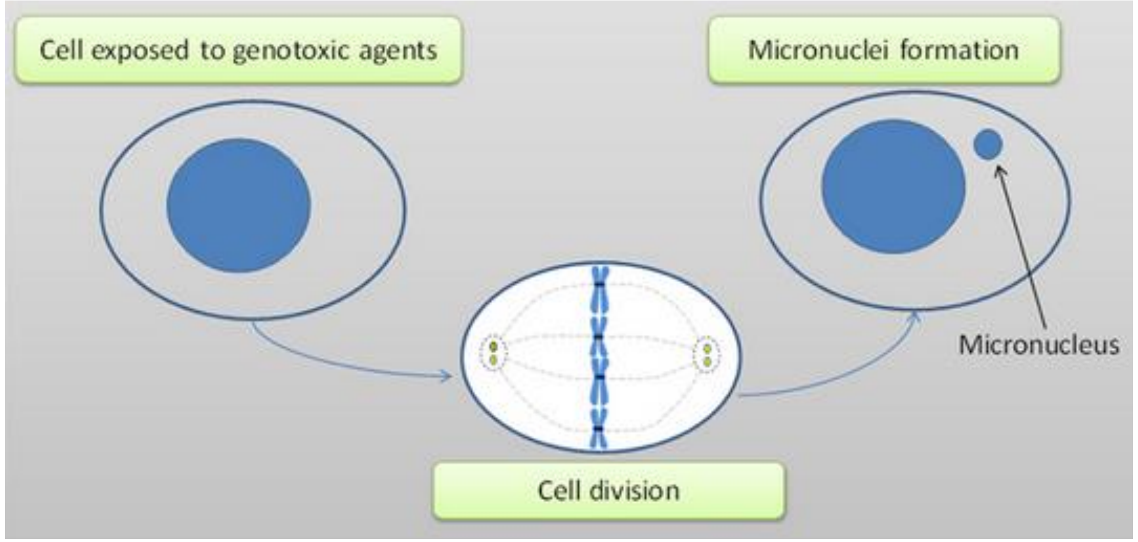
- Appear in the form of single strand (SSB) and double stand breaks (DSB)



https://doi.org/10.1089/ars.2012.5151

2. Micronuclei Induction

- Are extra-nuclear bodies containing whole or fragmented chromosomes



https://doi.org/10.3389/fgene.2013.00131

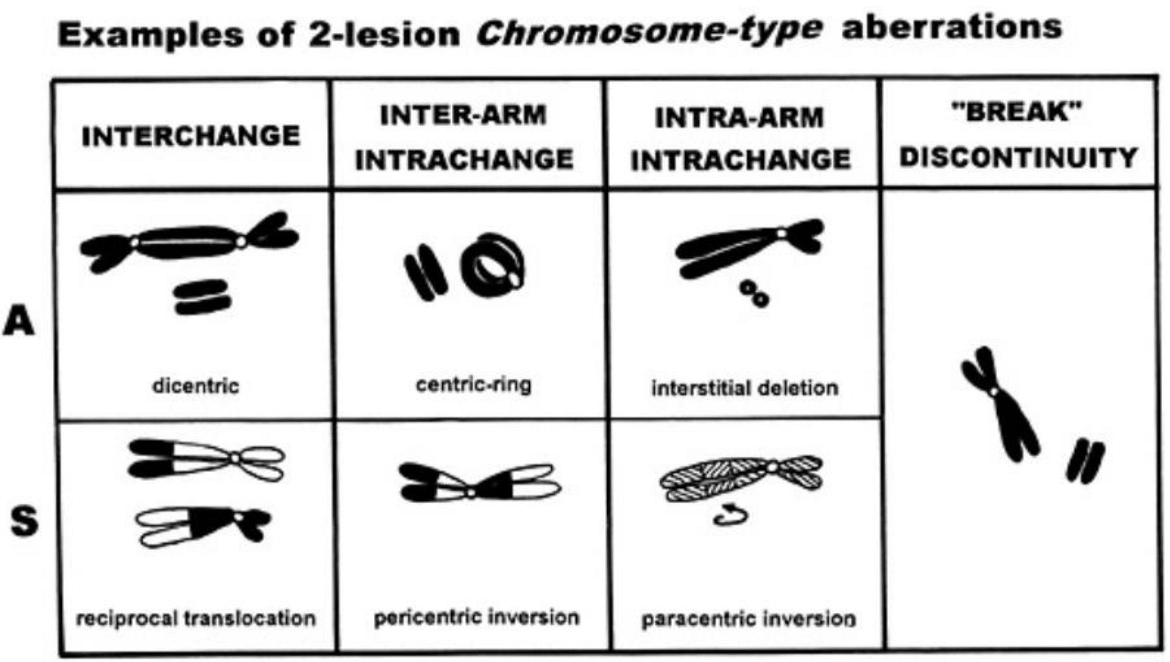
Types of DNA Damage

3. Chromosome Aberrations

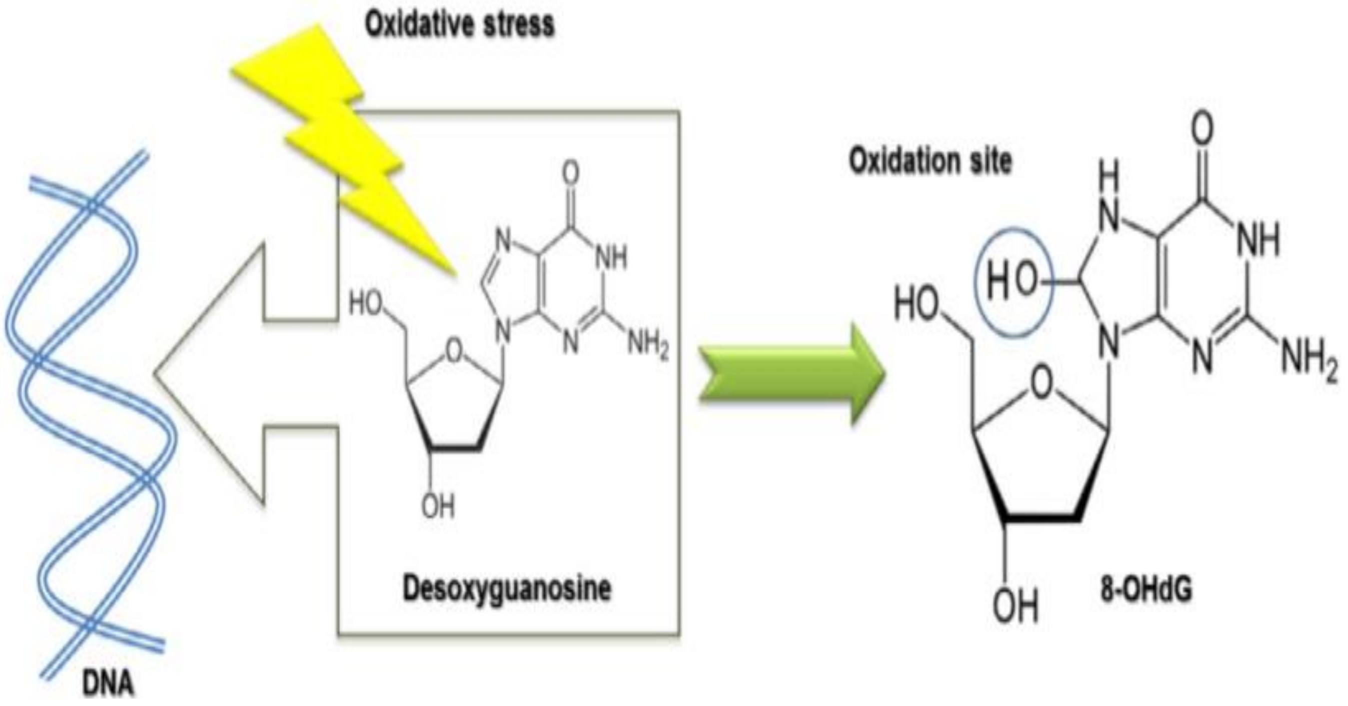
- Structural changes due to chromosome breakage and abnormal reunion of broken chromosomes

4. DNA Base Damage

- DNA base damage can occur from exposure to free radicals



Atlas Genet Cytogenet Oncol Haematol. 1999;3(2):110-115.



https://doi.org/10.1016/B978-0-444-63406-1.00005-2

Research Approach

Radiofrequency DNA Damage Literature Review

- Method: Used specific keywords related to topic and searched International research databases (Medline, EMF-Portal, ORSAA ODEB) + Lai 2021 reference list
- 370 papers were identified
- Included papers published from the 1970's to 2022 covering:
  - DNA Breaks (Single Stranded and/or Double Stranded Breaks) – 199 papers*
  - Micronuclei Induction – 113 Papers
  - Chromosome Aberrations – 89 Papers
  - DNA Base Damage – 37 Papers

- A future paper will include a comprehensive meta-analysis using mixed methods (qualitative and quantitative)

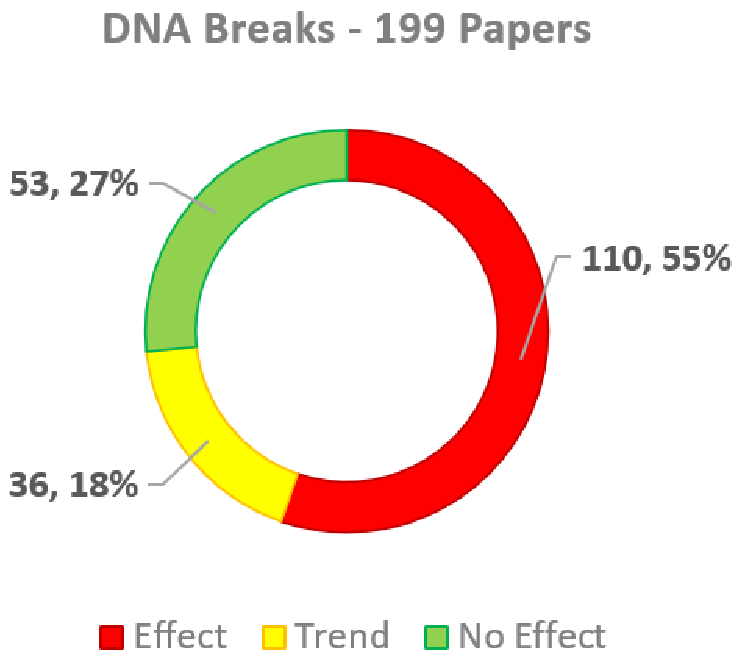
*Covered in detail in this presentation

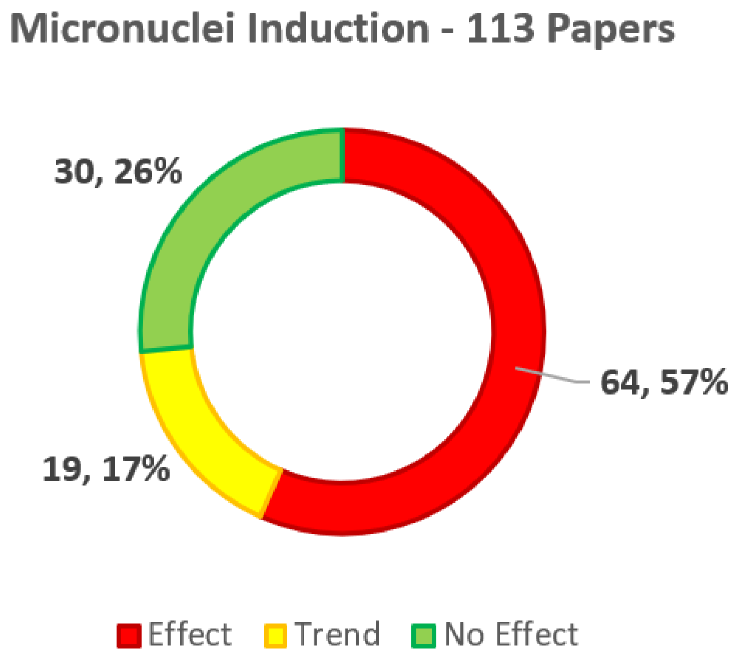
Assumptions

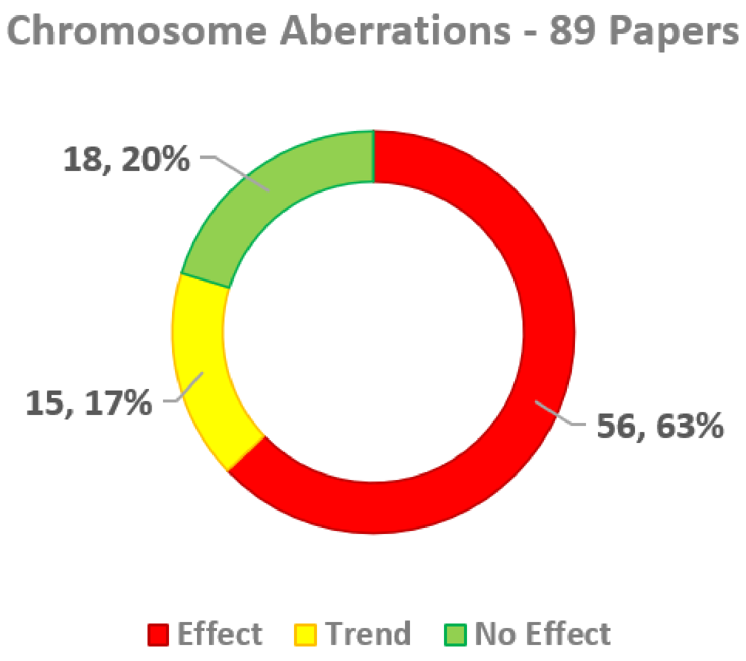
- All papers reviewed contain legitimate findings (no false data)
- All experimental findings were published, no data withheld
- Recorded measurements are accurate
- Funding sources when declared are fully disclosed

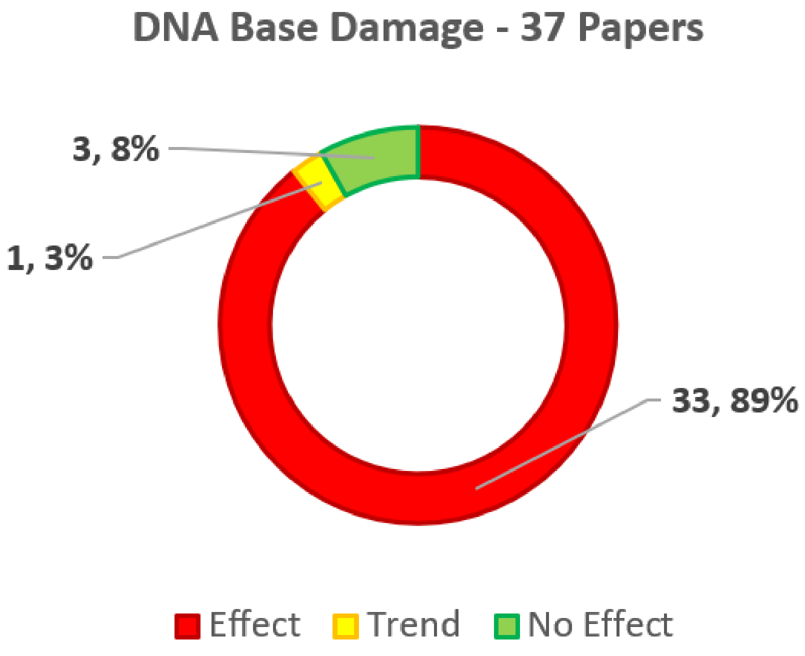
Overall Summary Findings

Balance of Evidence – Paper Level









A significant effect is recorded when p value < 0.05

Exposure duration - A factor for DNA damage

Exposure Time	DNA Breaks # Papers Effect	DNA Breaks %	Micronuclei Induction #Papers Effect	Micronuclei Induction %	Chromosome Aberrations # Papers Effect	Chromosome Aberrations %	DNA Base Damage #Papers Effect	DNA Base Damage %
<1 Minute	1	100.0	1	100.0	3	60.0	0	0.0
1 - 5 Min	2	100.0	1	100.0	2	40.0	0	0.0
6 -15 Min	5	100.0	8	80.0	7	53.8	0	0.0
16 -30 Min	7	35.0	9	60.0	11	55.0	1	50.0
31 - 40 Min	4	80.0	2	66.7	0	0.0	0	0.0
41- 60 Min	12	46.2	8	66.7	9	50.0	2	66.7
61 min - 2 Hours	17	34.0	5	27.8	11	52.4	6	85.7
3 - 4 Hours	9	40.9	7	46.7	13	76.5	3	75.0
5 - 8 Hours	8	38.1	2	28.6	6	75.0	6	85.7
9 - 16 Hours	8	61.5	4	33.3	3	60.0	1	50.0
17 - 24 Hours	10	28.3	8	30.8	5	38.5	3	100.0
25 -48 Hours	4	33.3	8	57.1	3	75.0	2	66.7
49 - 96 Hours	12	70.6	10	58.8	4	66.7	4	100.0
97 Hours - 7 Days	8	80.0	3	100.0	1	100.0	3	100.0
7 Days - 2 Weeks	4	80.0	2	100.0	1	50.0	1	50.0
2 Weeks - 4 Weeks	5	100.0	1	33.3	0	0.0	5	83.3
4 Weeks - 8 Weeks	3	75.0	4	100.0	2	66.7	2	66.7
8 Weeks - 3 Months	3	100.0	1	100.0	1	50.0	1	100.0
3 Months - 1 Year	3	100.0	1	50.0	2	66.7	1	100.0
>1 Year	12	100.0	13	86.7	7	77.8	1	100.0

Key

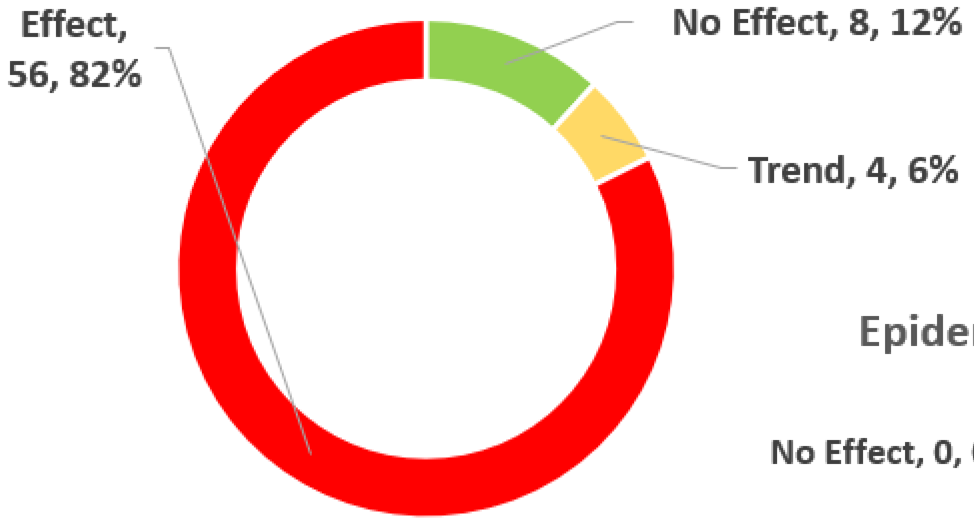
- No papers
- 70% > Effect
- 55 - 69% Effect
- 45 - 54% Effect
- 30 - 44% Effect
- < 29 % Effect

Findings

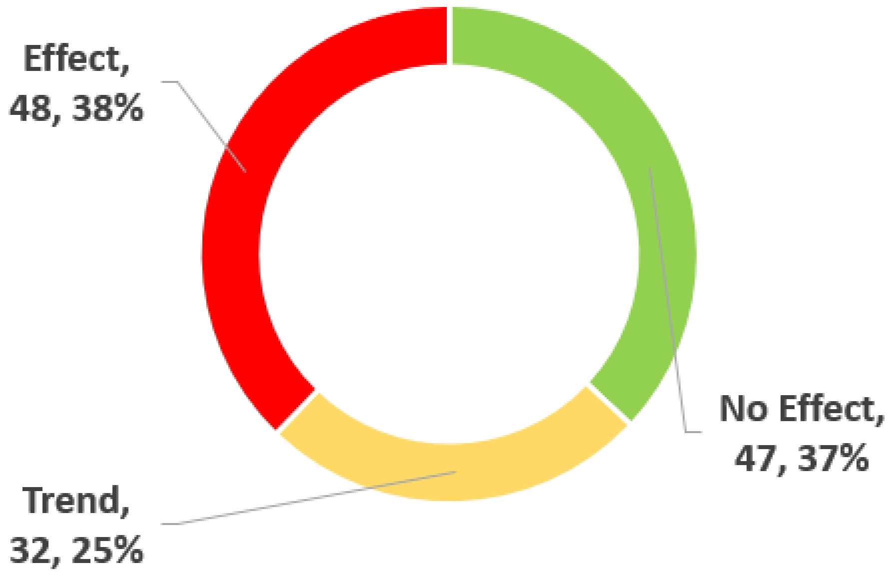
Specific focus on DNA breaks and fragmentation

Findings by Experimental Type – DNA Breaks

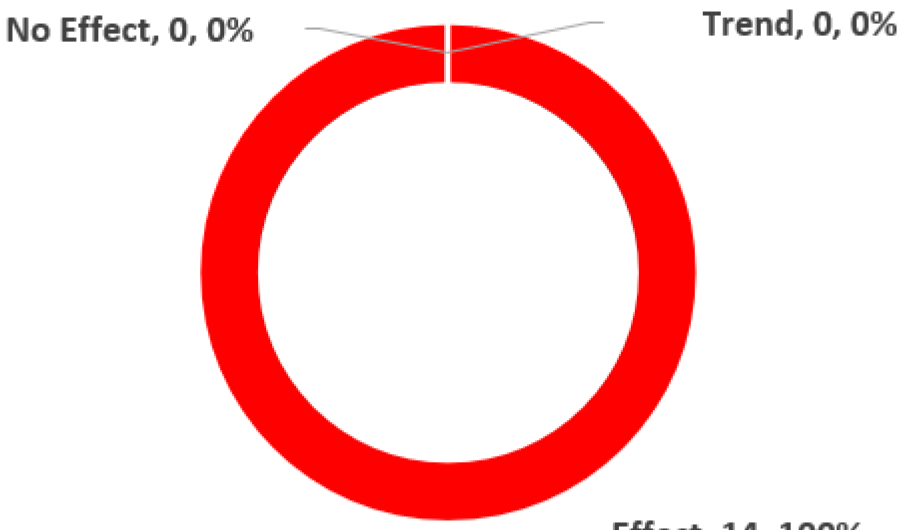
In vivo Studies - 68 Papers



In vitro Studies - 127 Papers

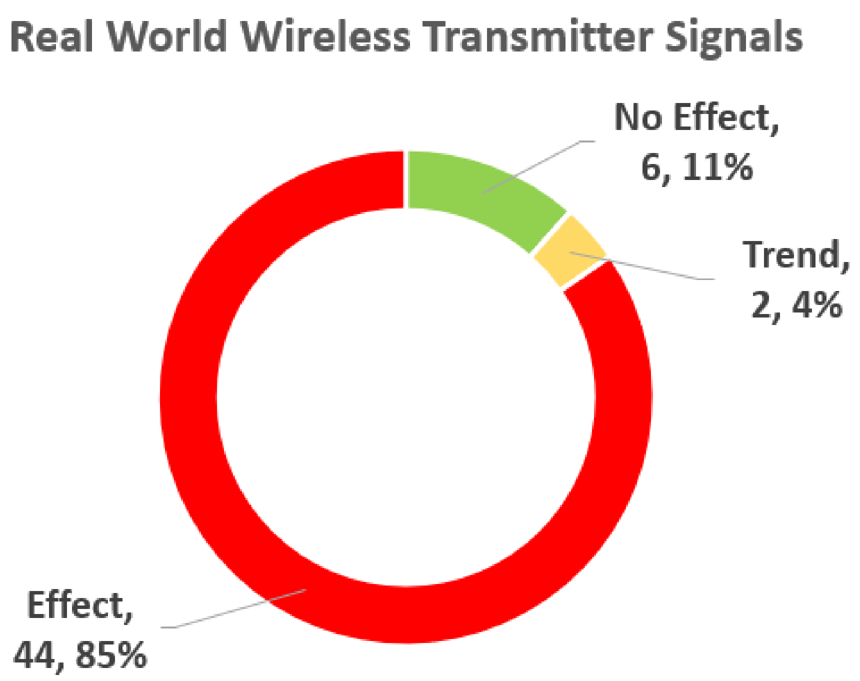


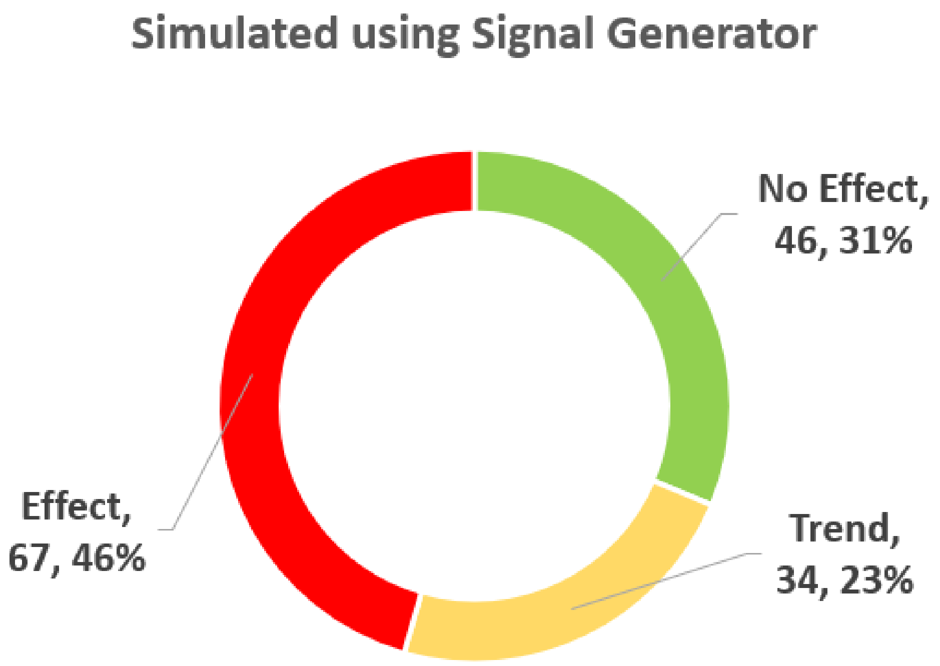
Epidemiological Studies - 14 Papers



A significant effect is recorded when p value < 0.05

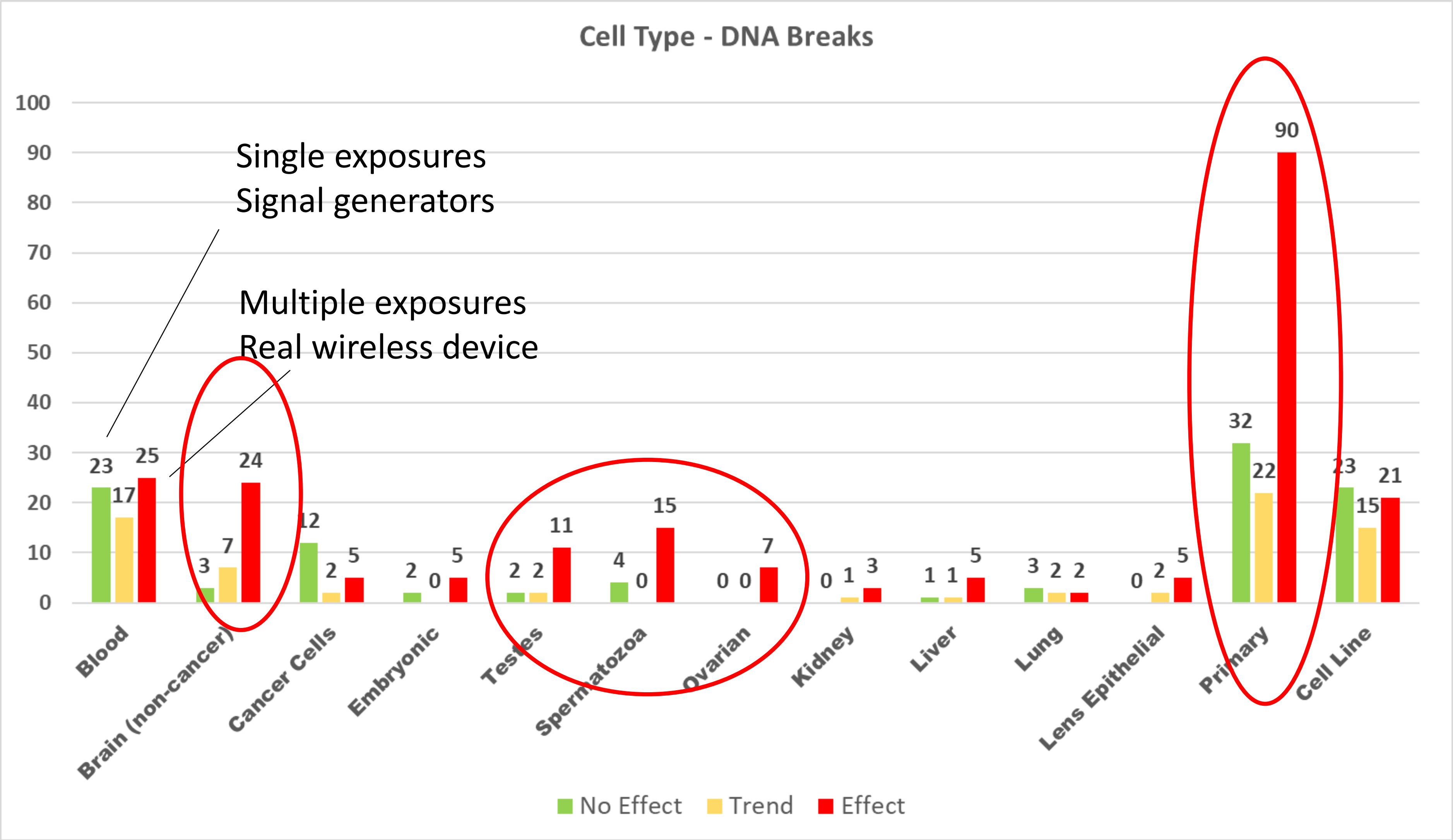
Real vs Simulated Signals





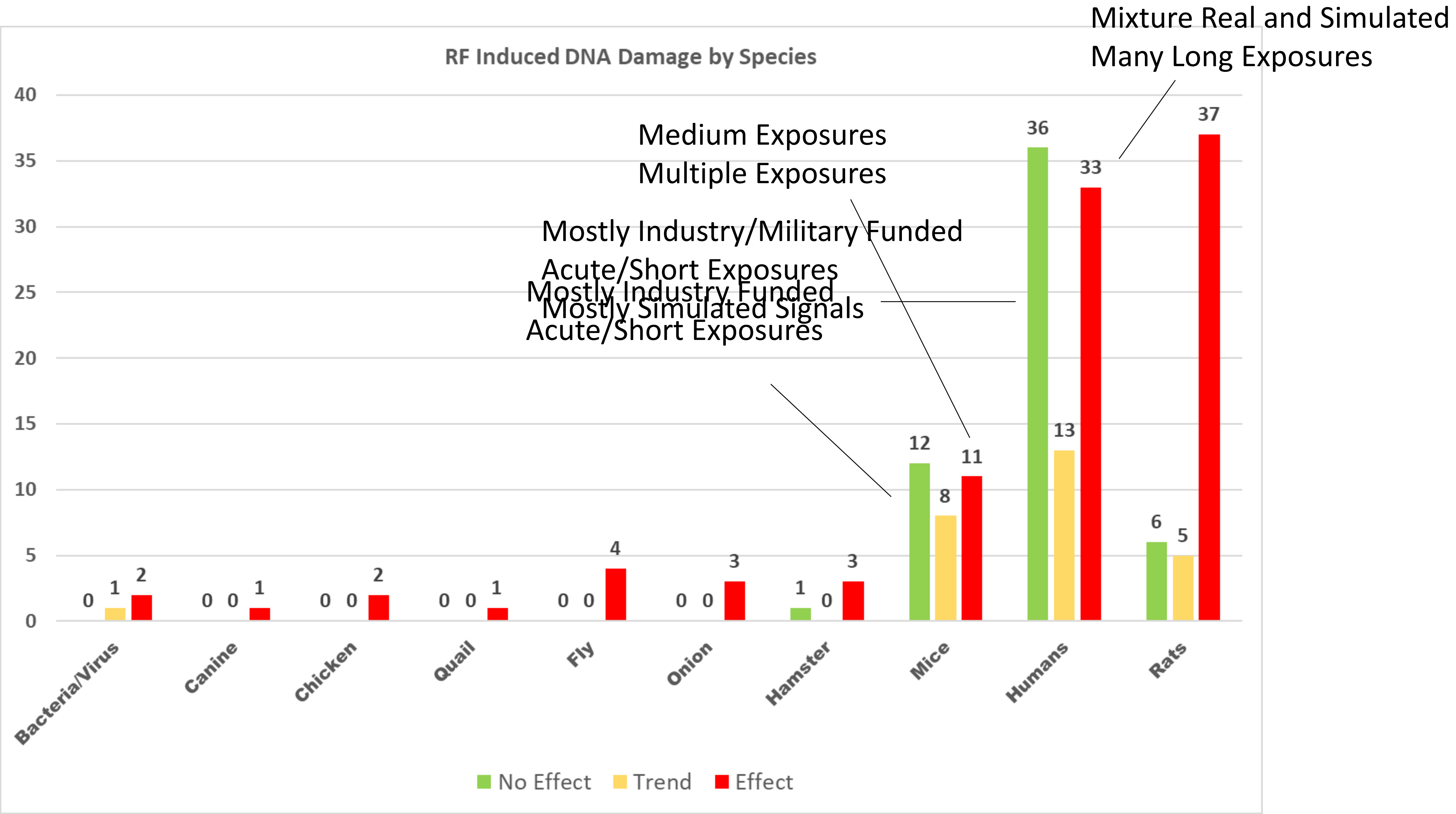
- Real world wireless transmitters show strong evidence for causing DNA damage
- The evidence for signal generators is less convincing

Cell Types – RF Induced DNA Breaks Assessment

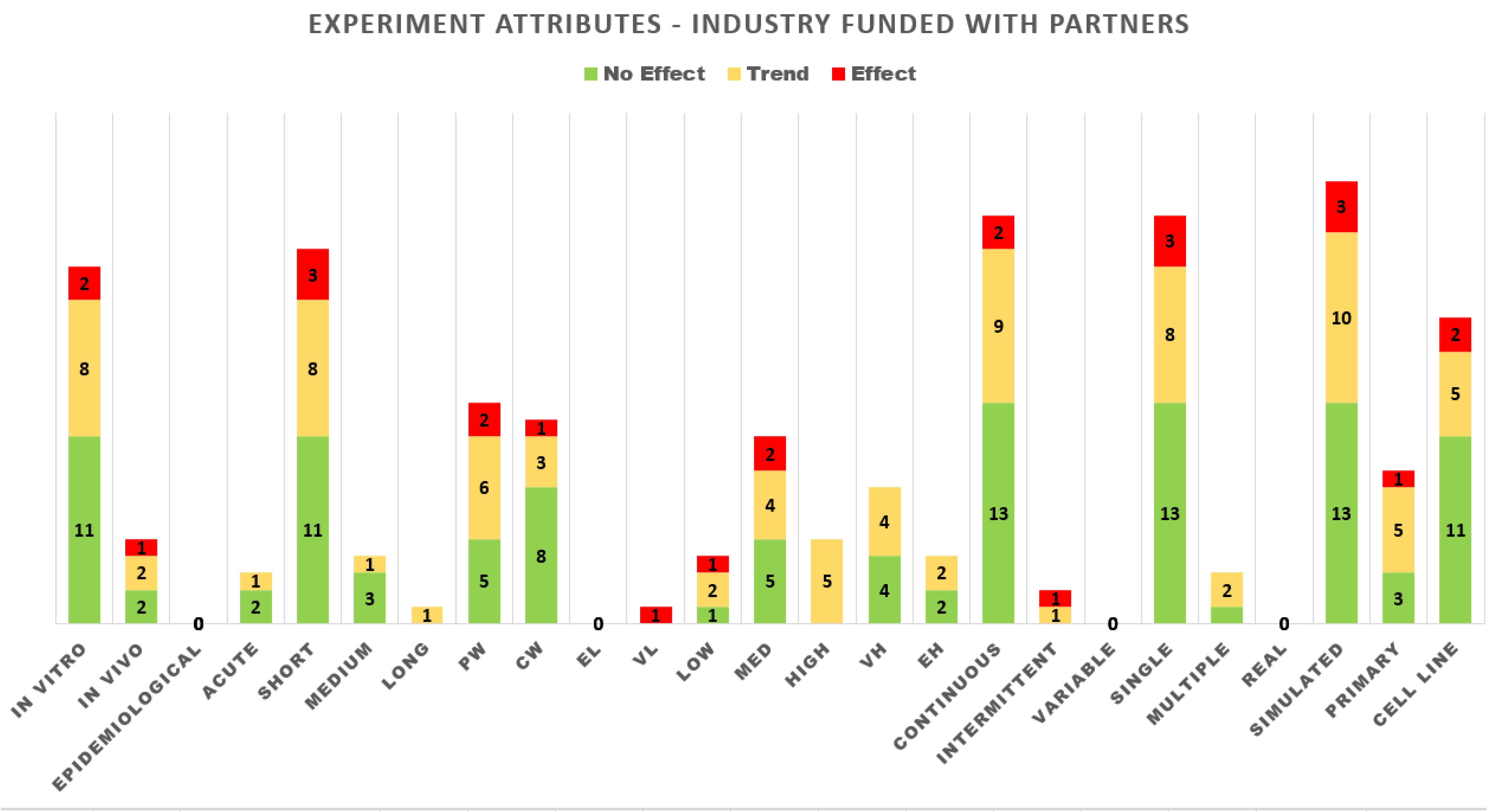


Results shown have not accounted for potential biases and methodological limitations – all DNA break papers used

Species - RF Induced DNA Breaks Assessment



Funding Source Matters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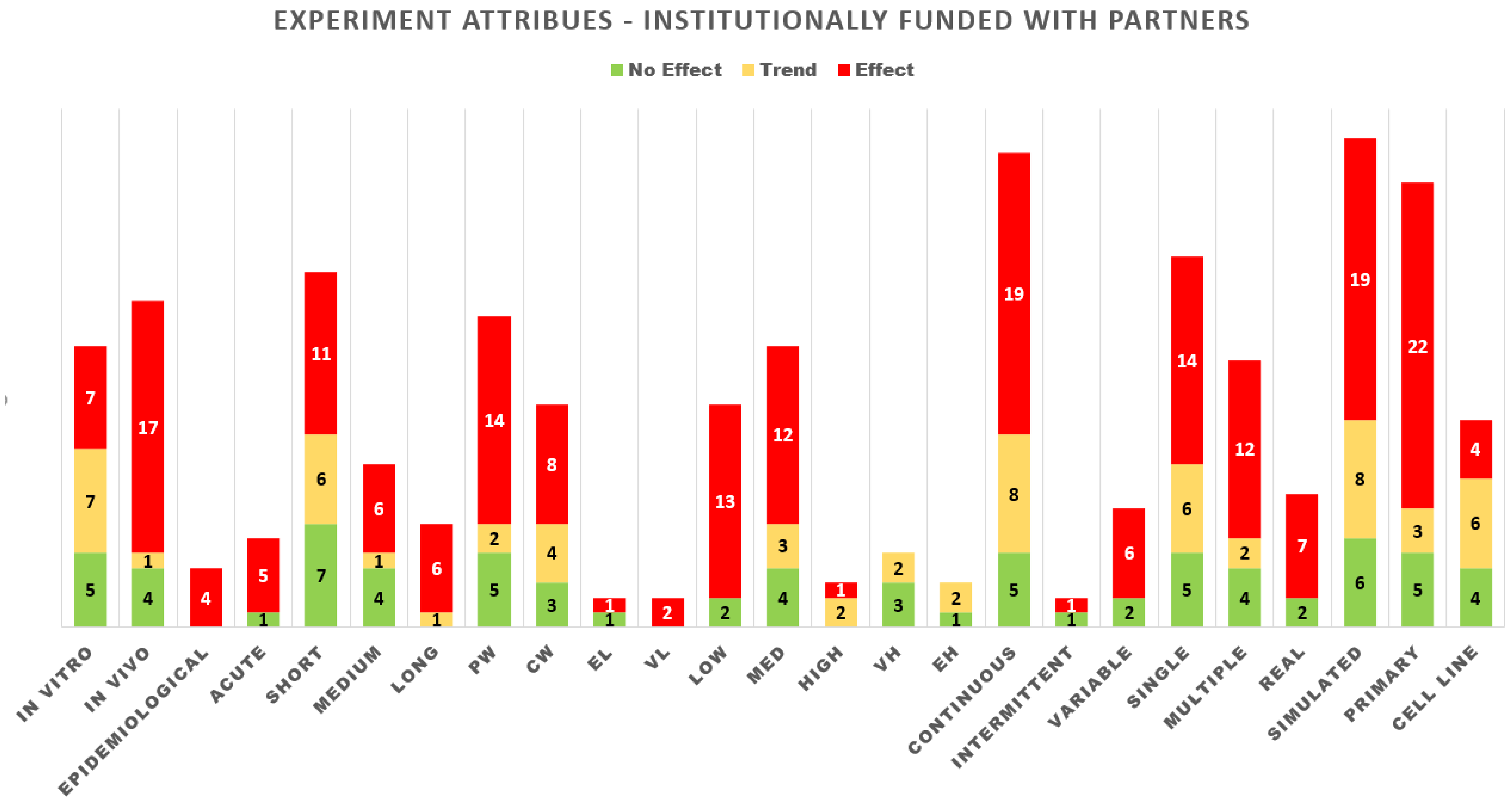
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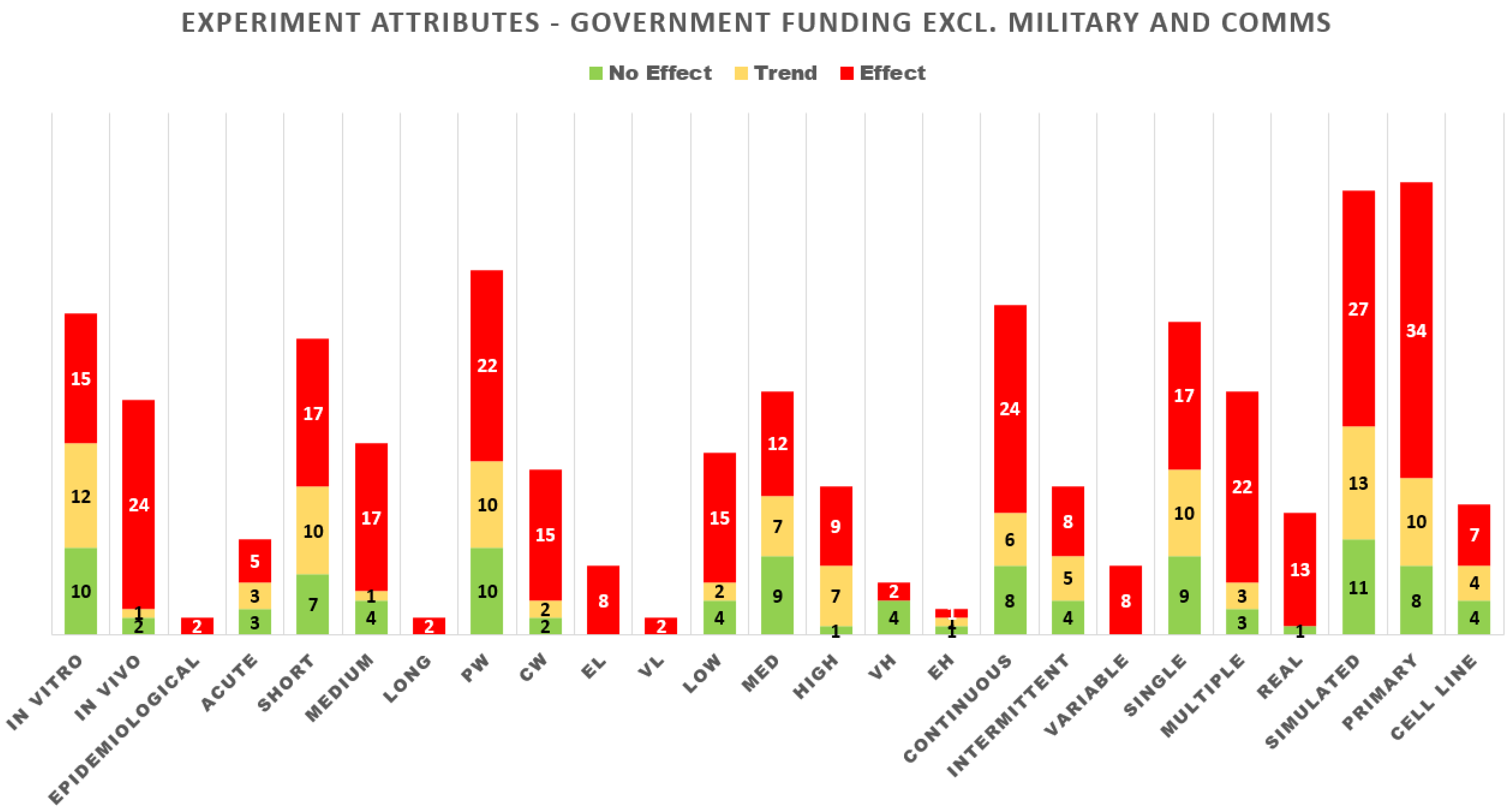
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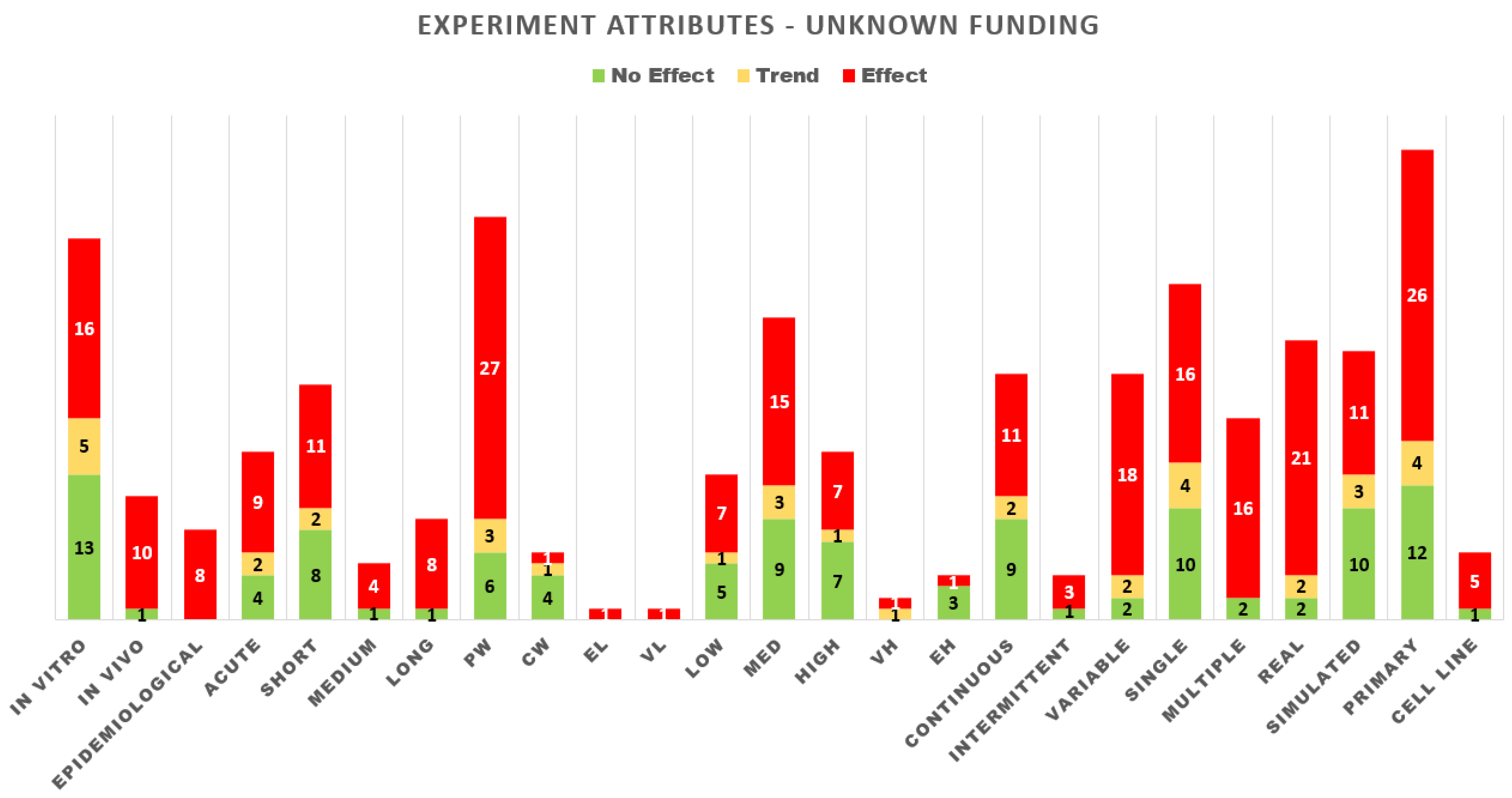
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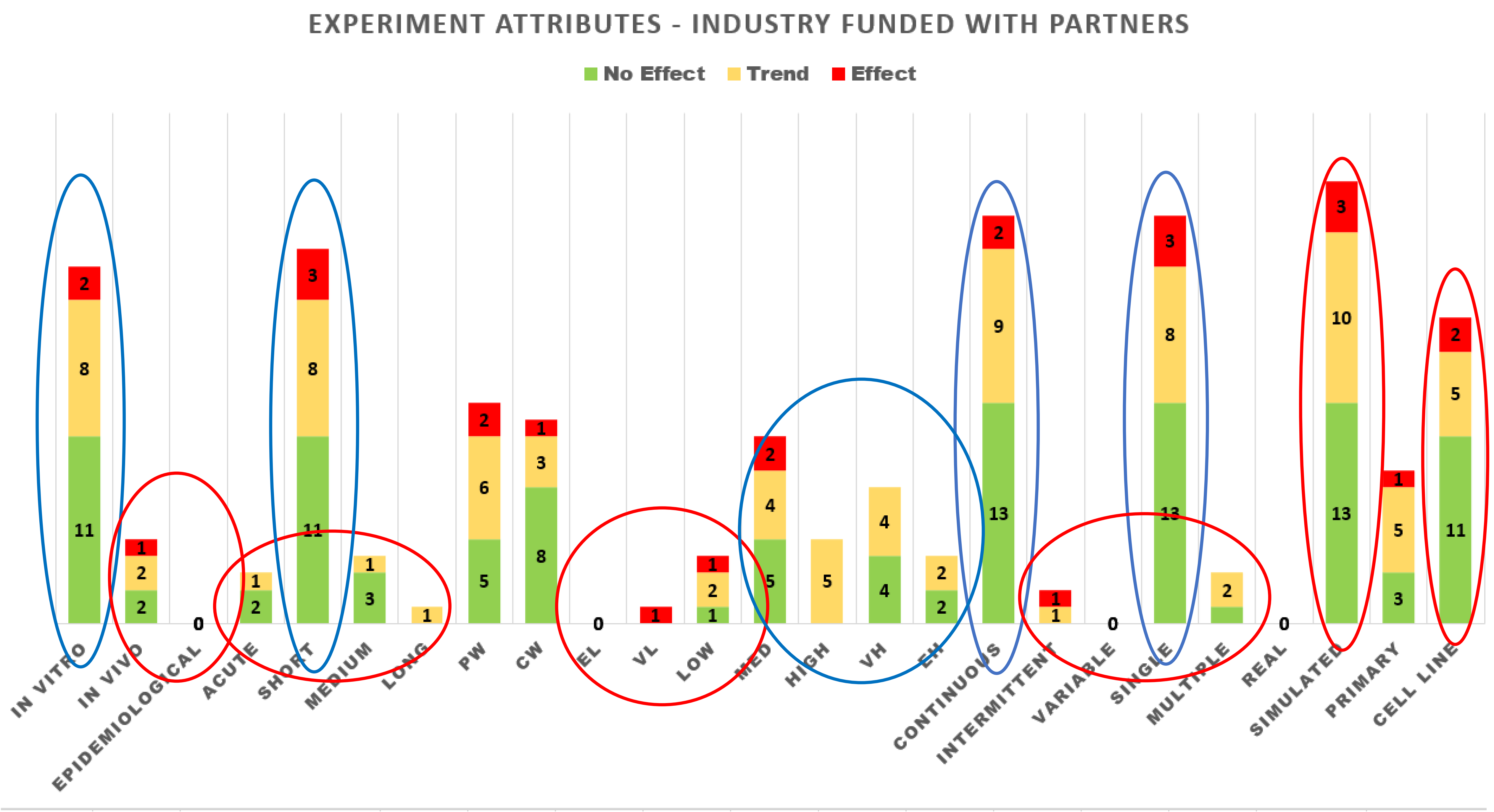

EXPERIMENT ATTRIBUTES - INDUSTRY FUNDED WITH PARTNERS
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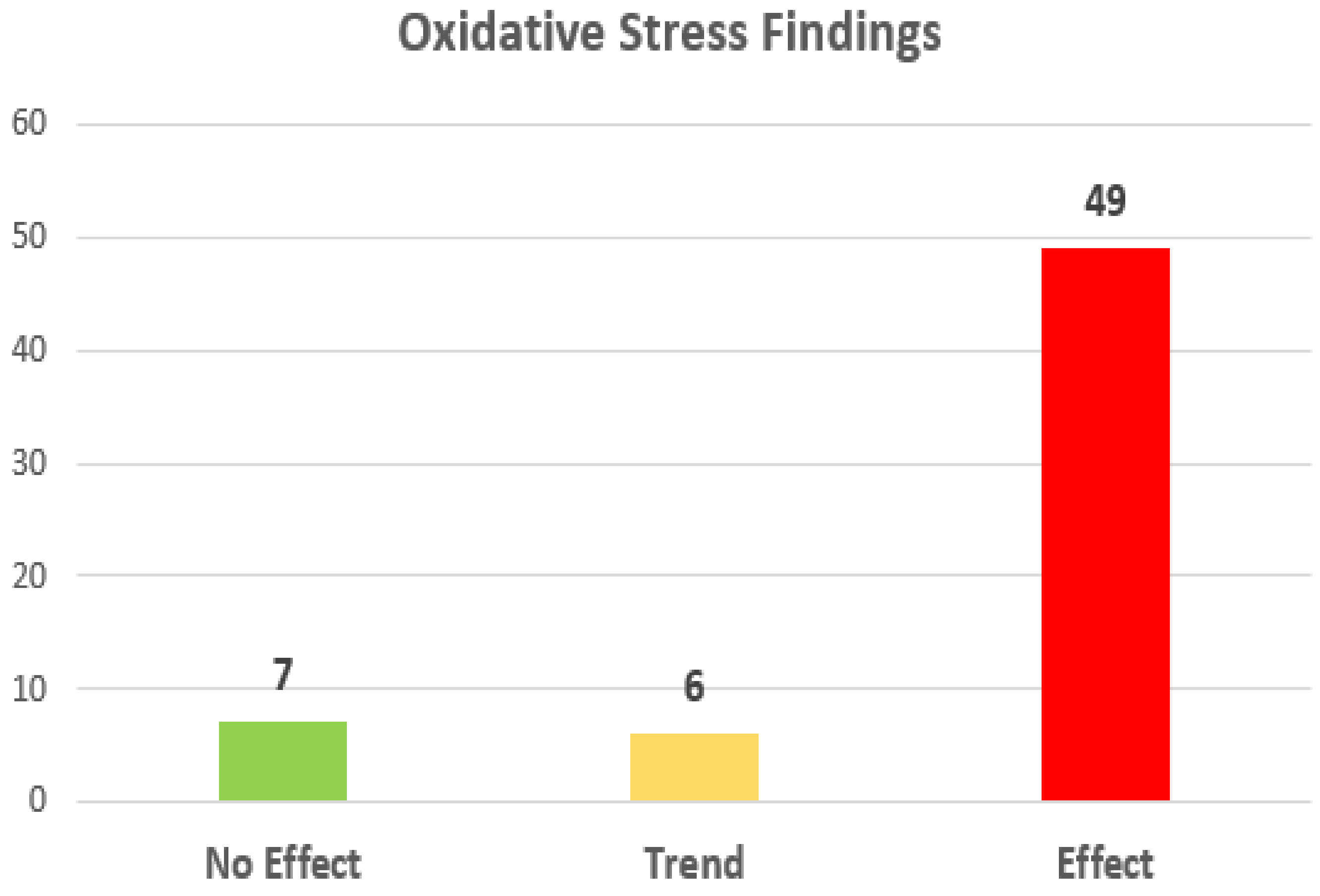
DNA Damage – Mechanism?

Free Radicals – Oxidative Stress

- Of the 199 papers looking at DNA strand breaks, 62 papers also looked at free radical production



- Free radicals can:
  - Break chemical bonds
  - Cause single strand breaks
  - Cause double strand breaks
  - Cause DNA Base damage

- 89% of papers (216 of 242) investigating RF and OS find it (Bandara *et al.* 2018)

Result Summary

Summary Findings

- DNA damage is associated with field intensity and exposure duration
  - Non linear intensity response (Lower intensities vs Higher intensities)
    - Non thermal effects are obvious
    - Higher number of papers report damage at lower intensities
  - Non thermal action via oxidation/free radical damage, conformation changes (DNA/Proteins) and possibly repair Inhibition?
  - Dose response tendency noted – longer the exposure higher chance of DNA damage
  - DNA damage caused by RF is comparatively lower than other known genotoxic agents (ionising radiation, chemicals etc.)

Exposure to RF is occurring 24x7, unlike other agents which are typically sporadic

Closing Statements

Controversial findings and issues

- Results show a real risk for genotoxicity, particularly long exposures
- Case for carcinogenicity is made stronger
- All species are at risk as we blanket the earth with RF
- ARPANSA and ICNIRP do not consider these risks because they
  - Require consistency in results
  - and confirmed evidence of harm (proof)
- No pre-market health testing when rolling out new wireless technology
- Safety is assumed if operating within public limits
- Precaution is absent, ARPANSA explicitly removed precautionary principle from latest RF Standard (RPS S-1), was present in RPS 3 (previous version)
- Sensitive populations do exist and are not considered

Recommendations

- A precautionary approach is required
- RF Standards are inadequate and need larger safety margins
- Future experiments should consider
  - Longer and multiple exposures
  - Use real life devices and signals that include data transmission
  - Perform assays at different time intervals
  - Use primary cells
  - Investigate mechanisms by also measuring
    - Free radical production/damage
    - Gene expression (anti oxidant enzymes, DNA repair proteins)

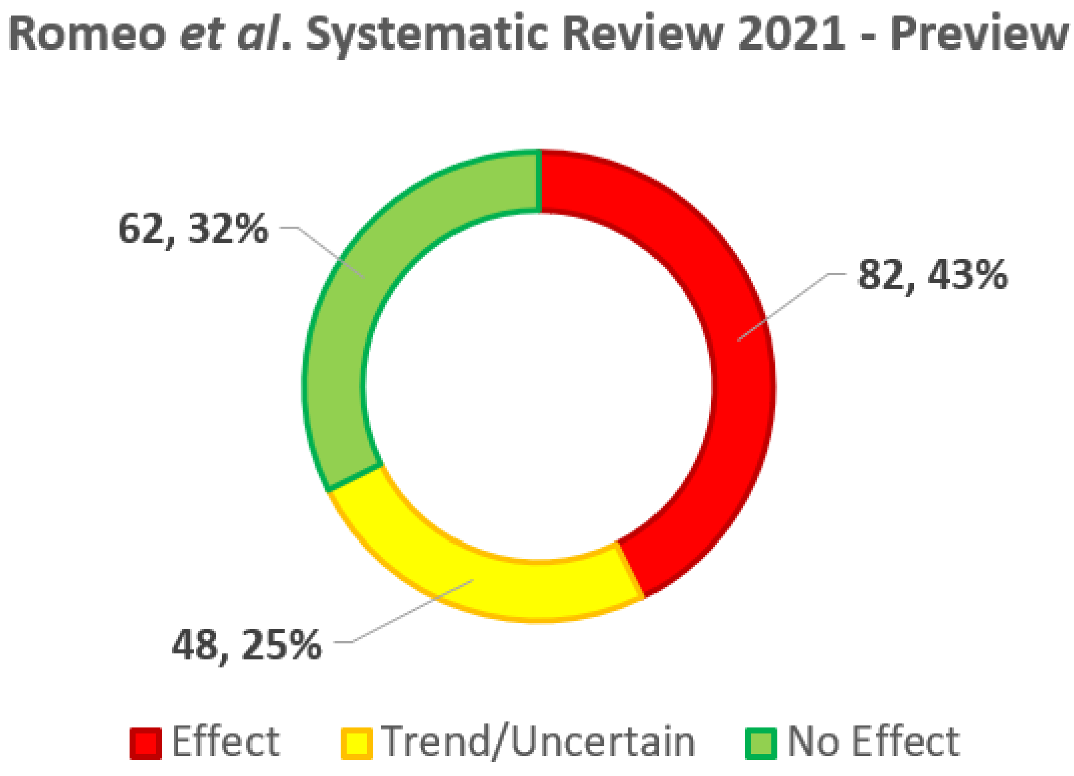
Thank You

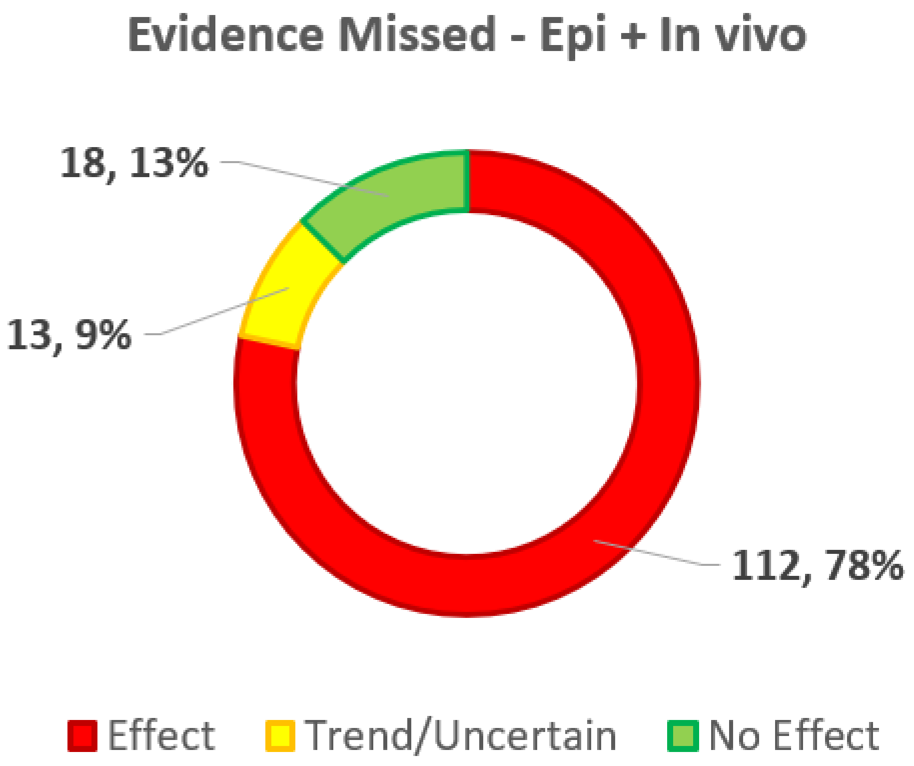
Future Publication
Other's Work – A Prediction

Genotoxicity of radiofrequency electromagnetic fields: Protocol for a systematic review of in vitro studies (2021)

Stefania Romeo, Olga Zeni , Anna Sannino, Susanna Lagorio, Mauro Biffoni, Maria Rosaria Scarfì

Eligibility criteria (taken from abstract): We will include experimental in vitro studies addressing the relationship between controlled exposures to RF-EMF and genotoxicity in mammalian cells only. (English papers only)





Late Lessons from early warnings

ON BEING WRONG: Environmental and health sciences and their main directions of error.

Scientific studies	Some methodological features	Main[a] directions of error-increases chances of detecting a:
Experimental Studies (Animal Laboratory)	• High doses	• False *positive* (negative for low dose effects)
	• Short (in biological terms) range of doses	• False negative
	• Low genetic variability	• False negative
	• Few exposures to mixtures	• False negative
	• Few Foetal-lifetime exposures	• False negative
	• High fertility strains	• False negative (developmental/reproductive endpoints)
Observational Studies (Wildlife & Humans)	• Confounders	• *False positive* (negative with multi-causality?)
	• Recall bias	• *False positive*
	Inappropriate controls	• *False positive*/negative
	• Non-differential exposure misclassification	• False negative
	• Inadequate follow-up	• False negative
	• Lost cases	• False negative
	• Simple models that do not reflect complexity	• False negative
Both Experimental and observational studies	• Publication bias towards positives	• *False positive*
	• Scientific cultural pressure to avoid false positives	• False negative
	• Low statistical power (e.g. From small studies)	• False negative
	• Use of 5% probability level to minimise chances of false positives	• False negative
	• Much scrutiny of positive studies cf. negative studies	• False negative

[a] Some features can go either way (e.g. inappropriate controls) but most of the features mainly err in the direction shown in the table.

Source: doi:10.1016/j.pathophys.2009.01.004