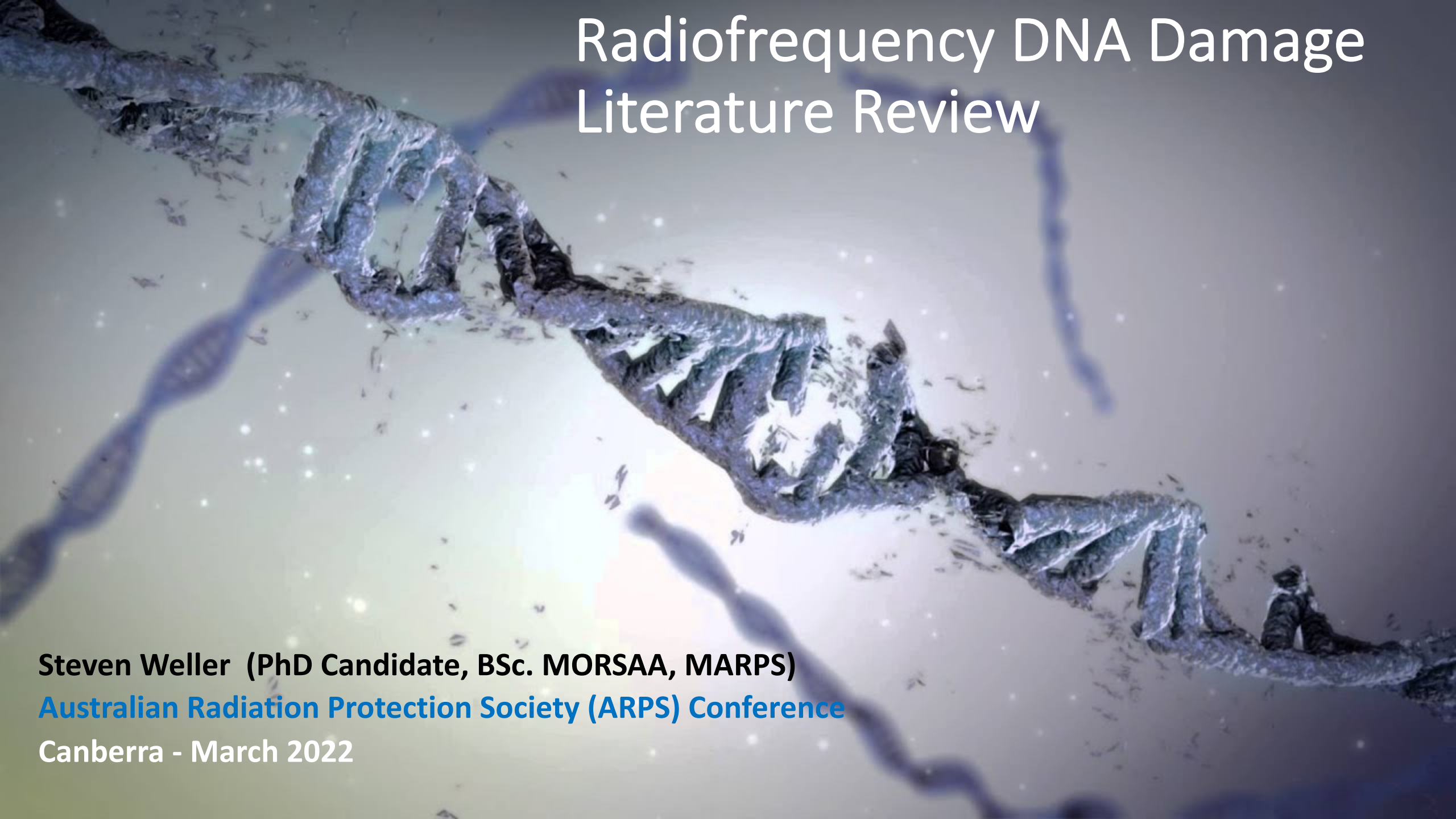
Radiofrequency DNA Damage Literature Review



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

Australian Radiation Protection Society (ARPS) Conference

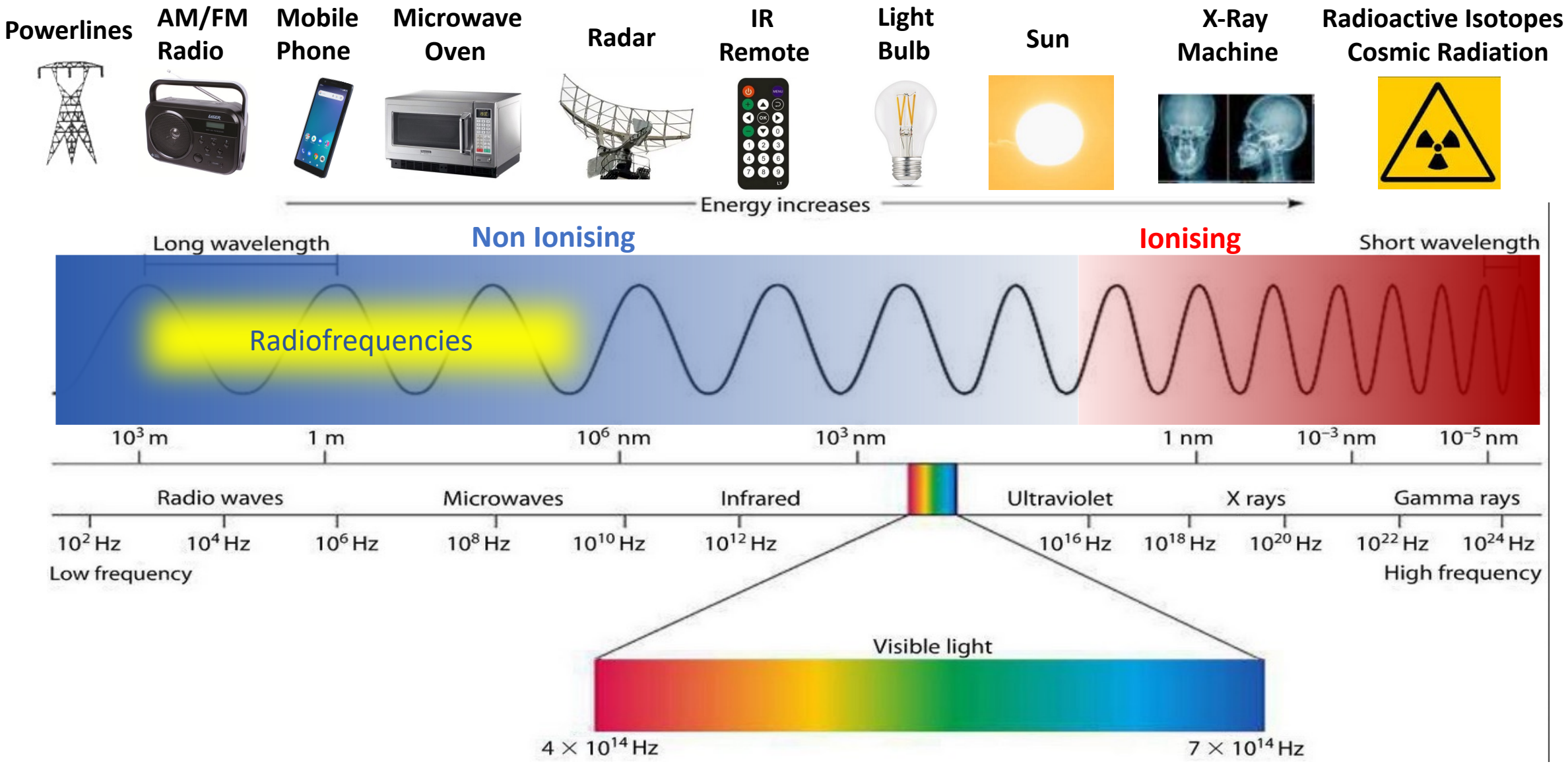
Canberra - March 2022

Introduction

About me

- PhD candidate investigating anthropogenic RF exposures and cancer
- An executive member of the Oceania Radiofrequency Scientific Advisory Association (ORSAA)
- Investigating the science on RF bioeffects for more than 10 years
- A major contributor to ORSAA RF bioeffect database
- Published a number of papers on this field

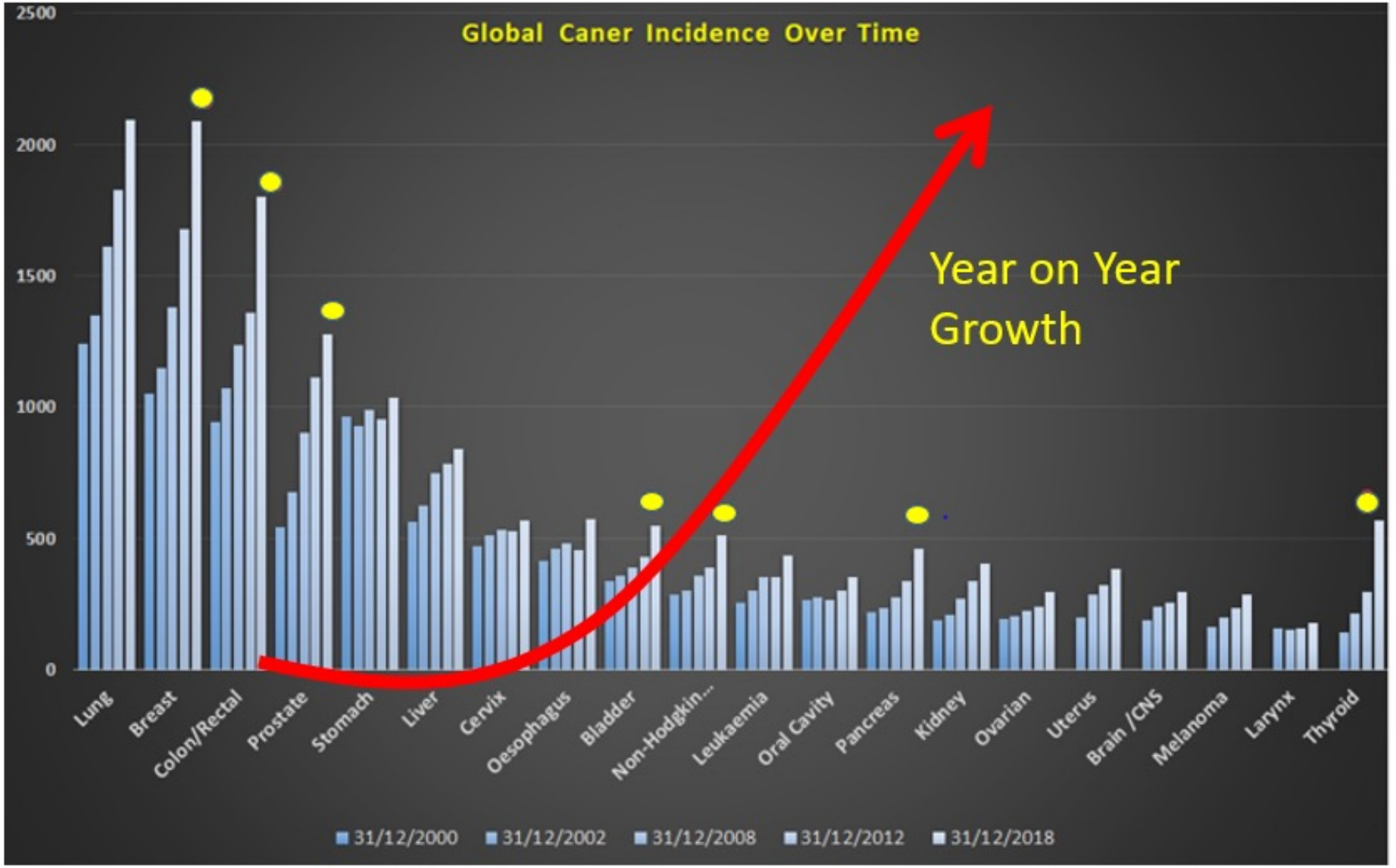
Electromagnetic Radiation Spectrum



Artist: Ade Stewart

Background

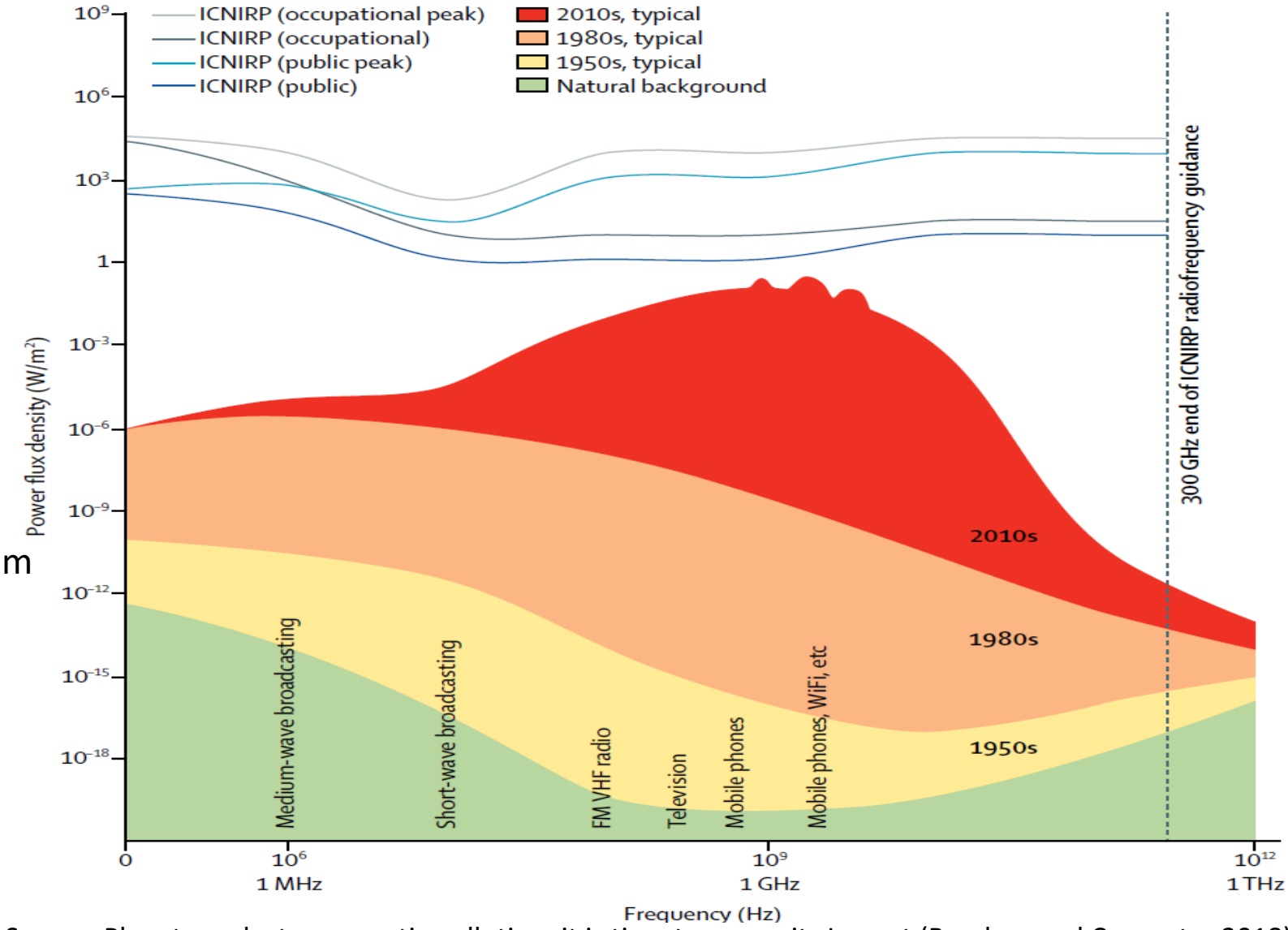
Rising incidence of cancer



- In 2014, a global cancer “tidal wave” was predicted by WHO
- Year on year growth in the incidence of the top 20 cancers globally
- Something in our environment and/or lifestyle is driving this increase
- A global phenomenon, not just limited to developed nations

Changing Radiofrequency (RF) Background Levels
Increasing Human Exposures

- Today mobile phone subscriptions exceed World's total population
- 5G is resulting in unprecedented densification of radio transmitters in our environment
- Current RF levels are 10^{18} (Quadrillion) times higher than natural background levels
- Children born today are exposed to RF from cradle to grave
- No option to "opt out"
- Earth lifeforms have not evolved under such novel exposure conditions



Source: Planetary electromagnetic pollution: it is time to assess its Impact (Bandara and Carpenter 2018)

IARC Perspective

- Classified all radiofrequencies as a Group 2B possible carcinogen (2011)
- Suggested evidence is credible but bias and confounding could not be ruled out
- Mechanism was not known
- IARC classification was controversial and has been 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

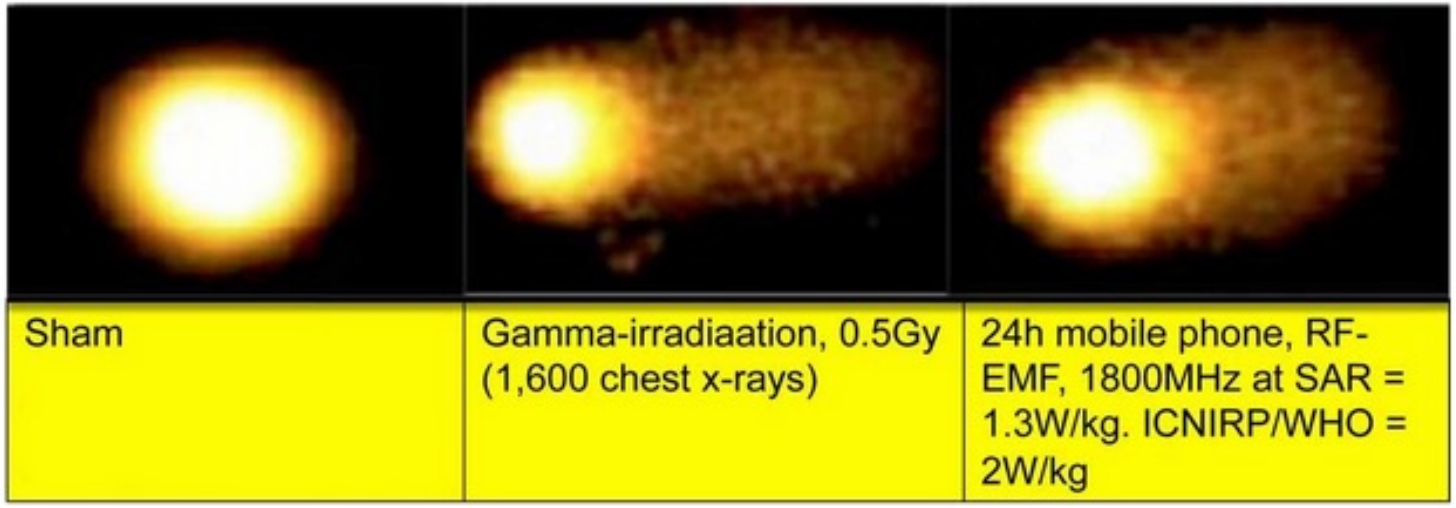
Rationale for RF genotoxicity review

- DNA damage is an important factor contributing to genetic mutations and recognised as a pathway in cancer development
- If RF is carcinogenic one would expect to see evidence of genotoxicity
- Possible mechanisms for genotoxicity would also need to be explored and qualified
- Existing literature base is quite substantial but results are inconsistent
- Past reviews have suffered from a number of 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 many cases

Types of DNA Damage

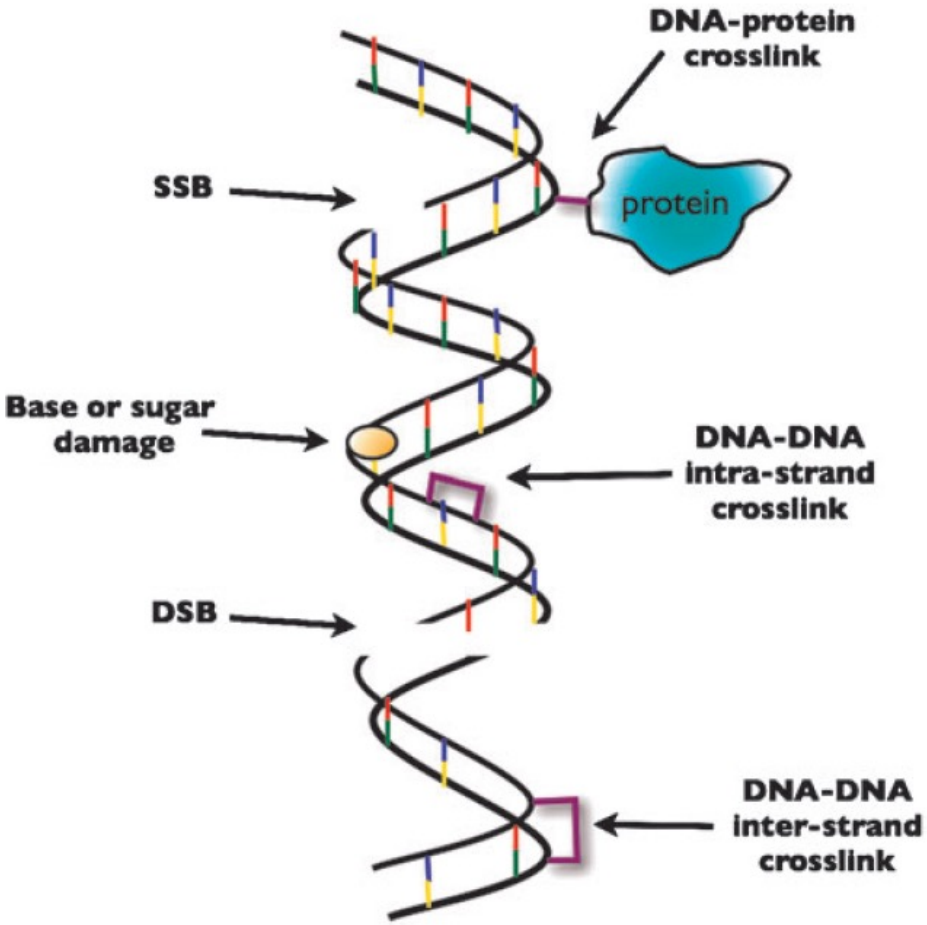
DNA Damage - Breaks and Fragmentation

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



Sham	Gamma-irradiaation, 0.5Gy (1,600 chest x-rays)	24h mobile phone, RF-EMF, 1800MHz at SAR = 1.3W/kg. ICNIRP/WHO = 2W/kg

EU Reflex study 2005

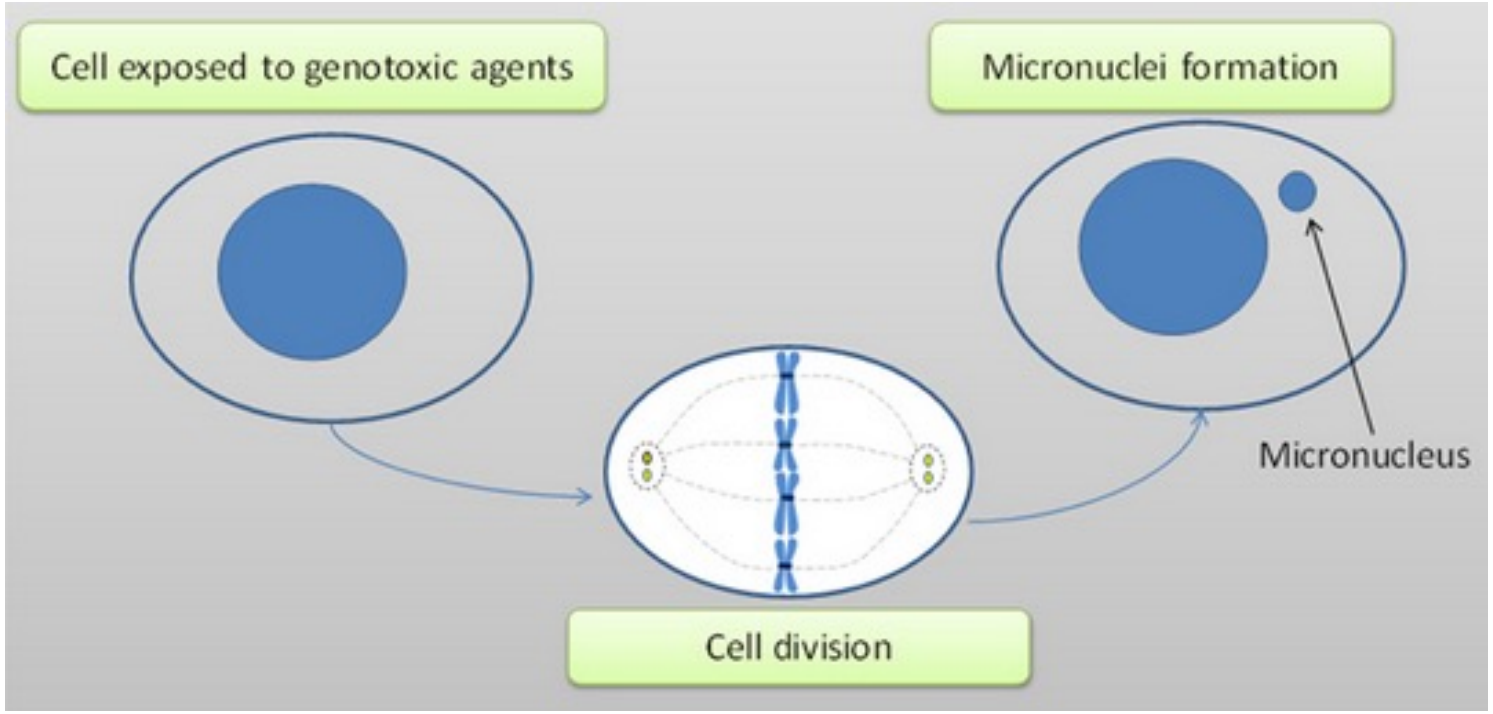


https://doi.org/10.1089/ars.2012.5151

DNA Damage – Micronuclei Induction

- Are extra-nuclear bodies containing whole or fragmented chromosomes
- Induced by defects in cell repair or accumulation of DNA damage or chromosomal aberrations

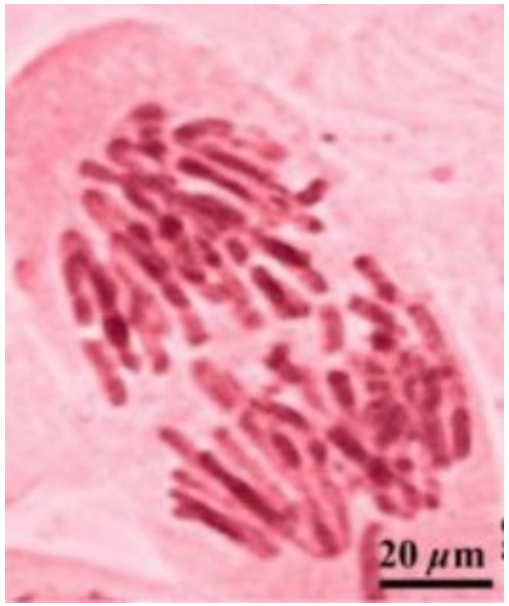
https://doi.org/10.4308/hjb.20.4.151



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

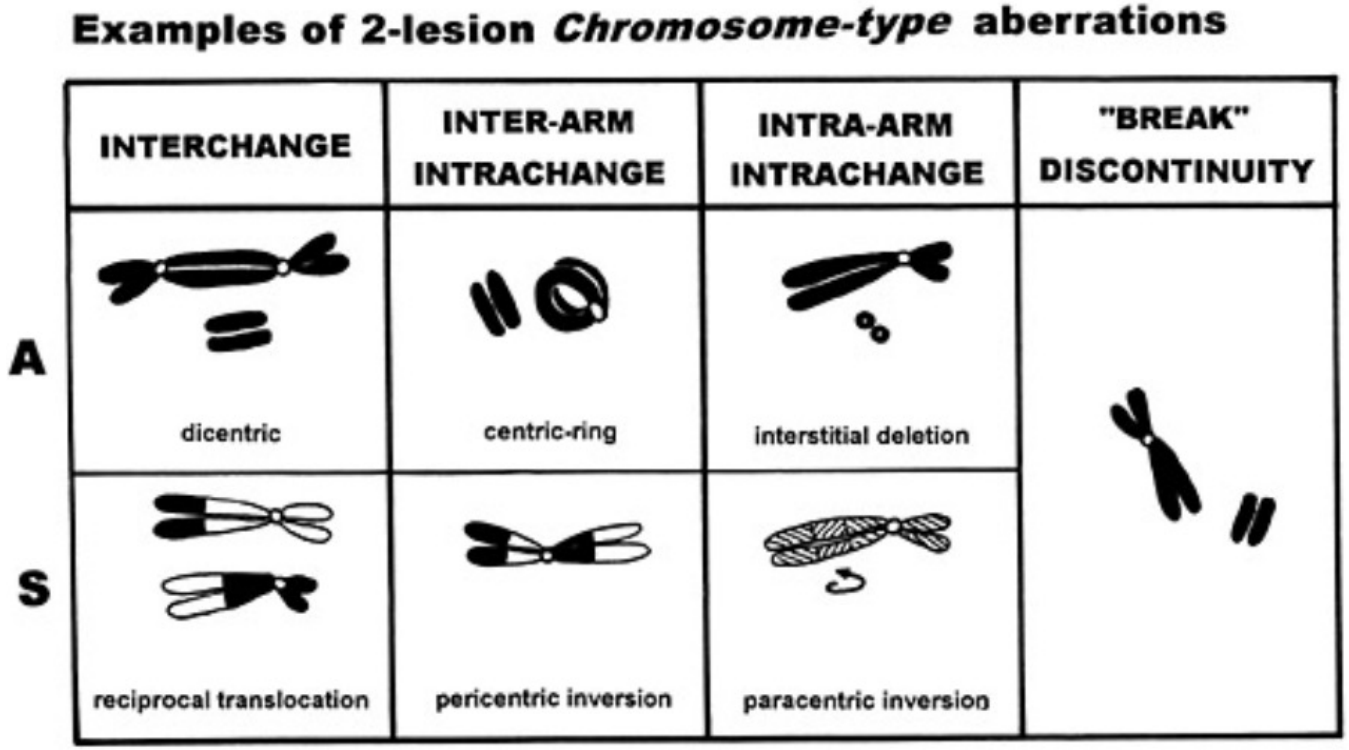
DNA Damage – Chromosome Aberrations

- Are changes in chromosome structure or number (aneuploidy)
- Structural changes occur as a result of chromosome breakage and abnormal reunion of broken chromosomes



Allium cepa (onion) exposed to 2100 MHz Radiofrequency fields – Chromosome Break

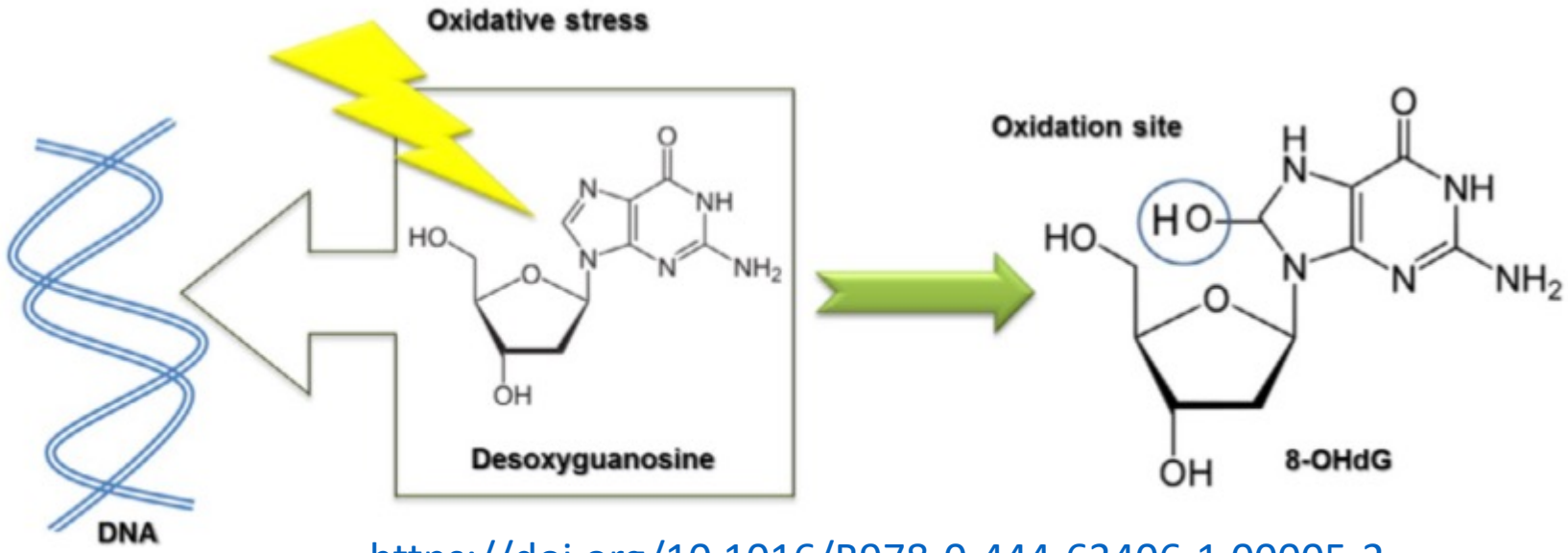
DOI: 10.1007/s00709-019-01386-y



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

DNA Damage – Base Damage

- DNA base damage can occur from exposure to reactive oxygen species
- Guanine has the lowest redox potential of the four DNA bases and is therefore the most easily oxidized



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

Approach

Radiofrequency DNA Damage Literature Review

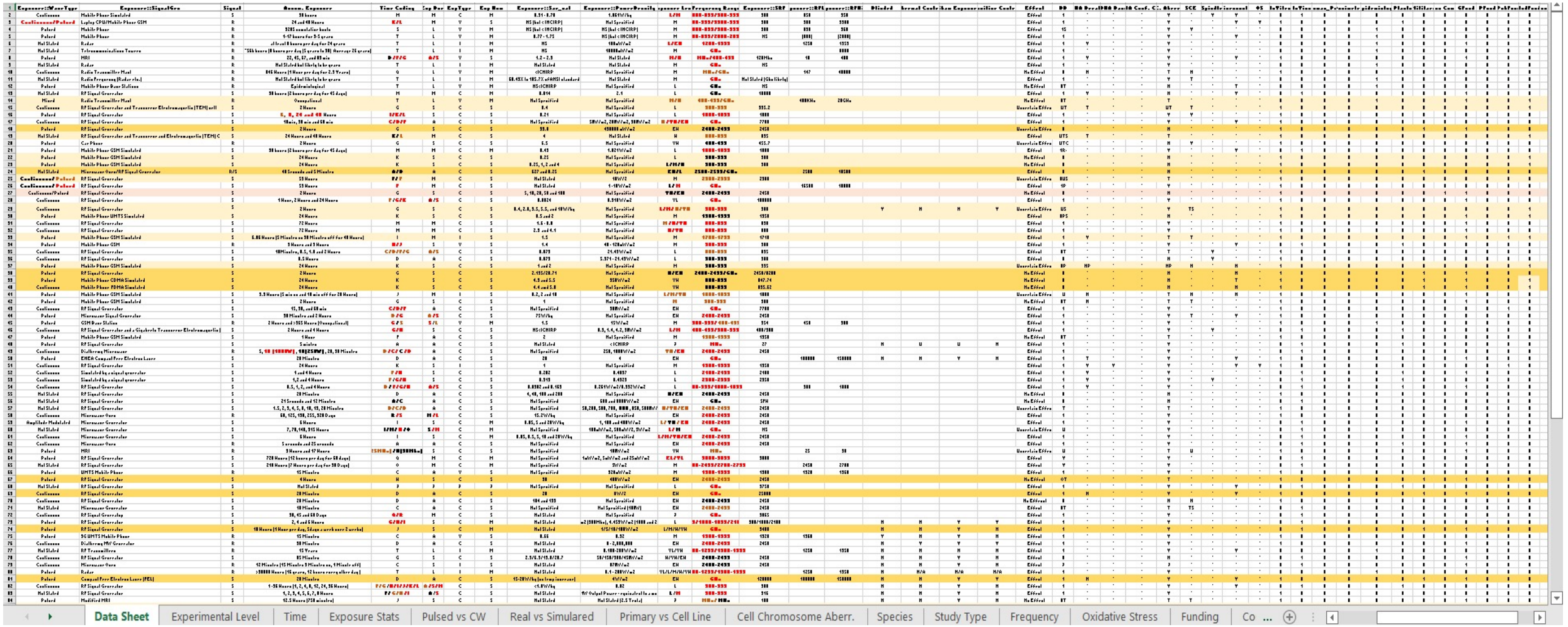
- Aim: To provide a preview of the results from a review of 370 scientific papers investigating Radiofrequency (RF) exposure & DNA Damage
- Method: Use specific keywords related to topic and search International research databases (Medline, EMF-Portal, ORSAA ODEB) + Lai 2021 reference list
- Included 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

*Covered in detail in this presentation

Assumptions

- All papers reviewed contain legitimate findings (no false data)
- Researchers have not withheld data and all experimental findings are published
- Recorded measurements are accurate
- Funding sources are fully disclosed (when declared)

Data Capture – Multiple Dimensions



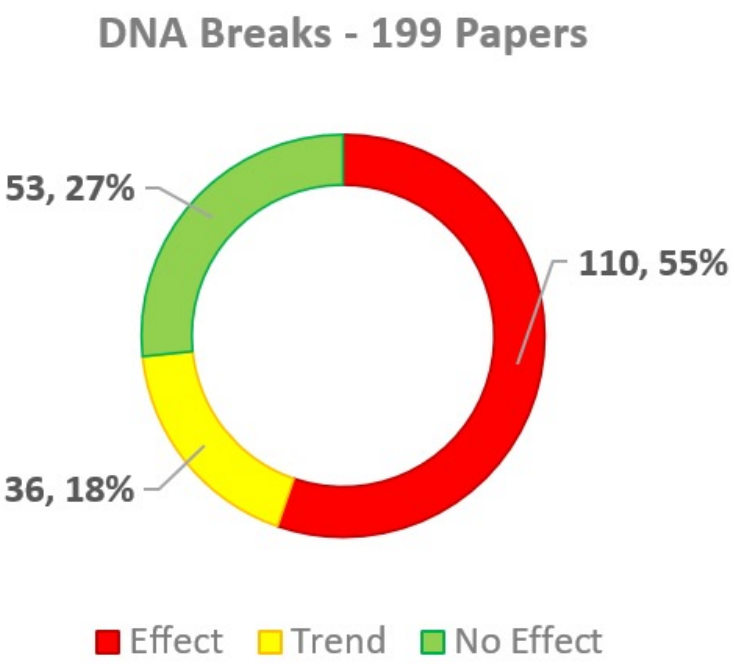
4 Workbooks (DNA Breaks, Chromosome Aberrations, Micronuclei, DNA Base Damage)

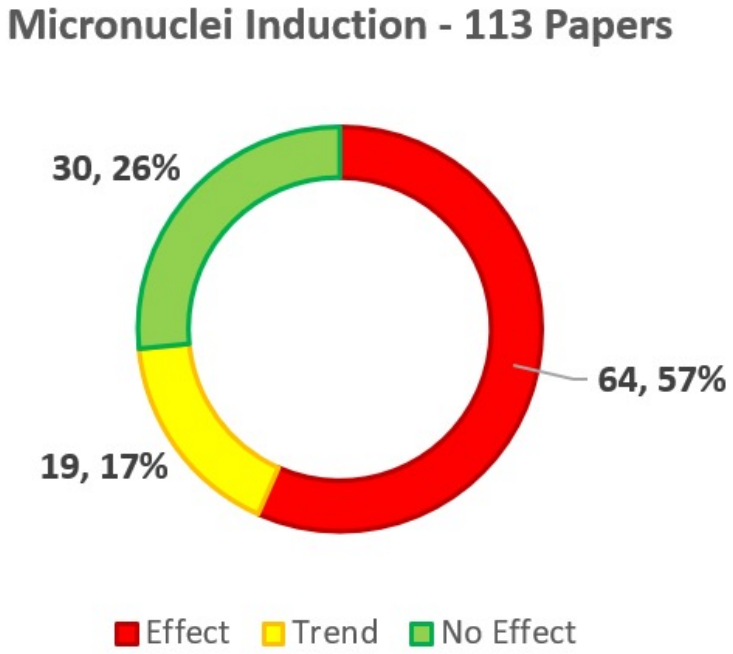
58 Columns in main Data Sheet (Study variables including experimental data, funding source, journal and quality attributes)

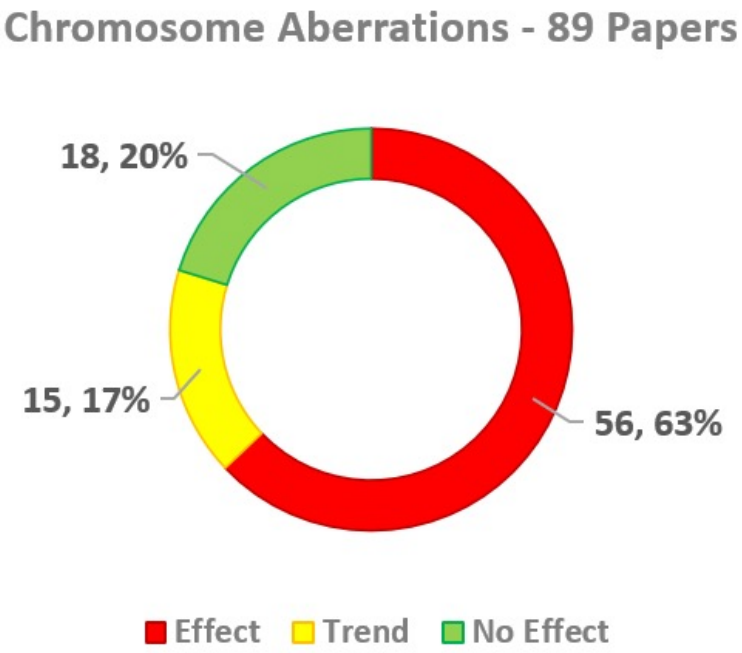
15 Tabs investigating various experimental variable interactions (exposure time, intensity, signal modulation, source etc.)

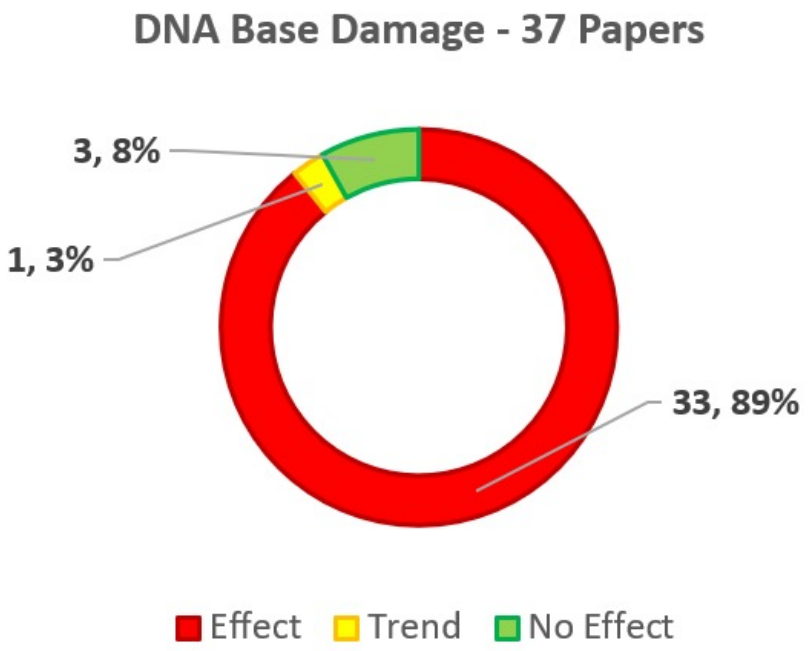
Overall Summary Findings

Balance of Evidence – Paper Level









A significant effect is recorded when p value < 0.05

Exposure duration - A factor for DNA damage

	DNA Breaks		Micronuclei Induction		Chromosome Aberrations		DNA Base Damage	
	# Papers		#Papers		# Papers		#Papers	
Exposure Time	Effect	%	Effect	%	Effect	%	Effect	%
<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

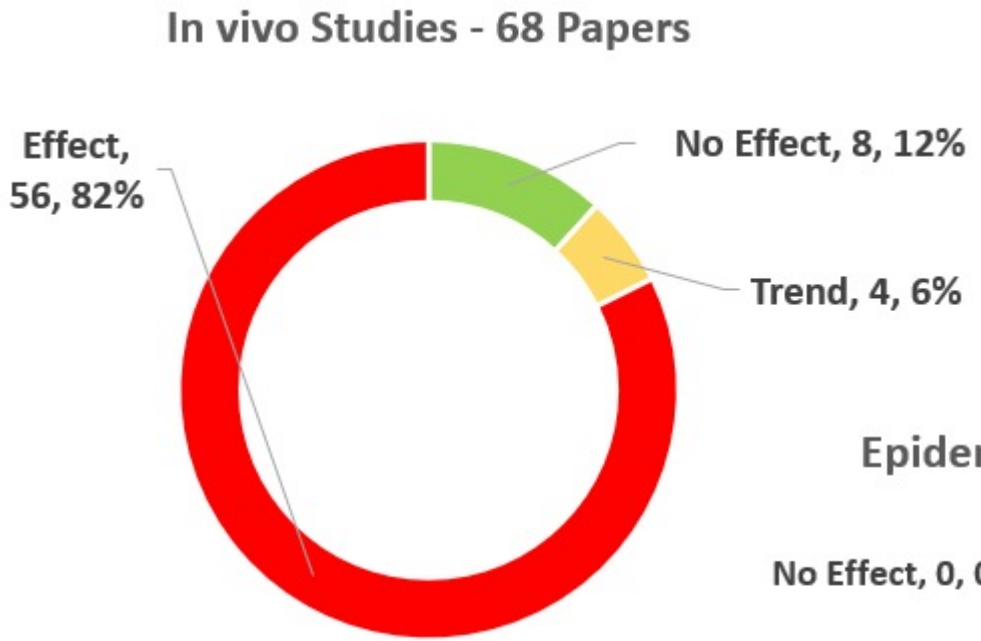
Key

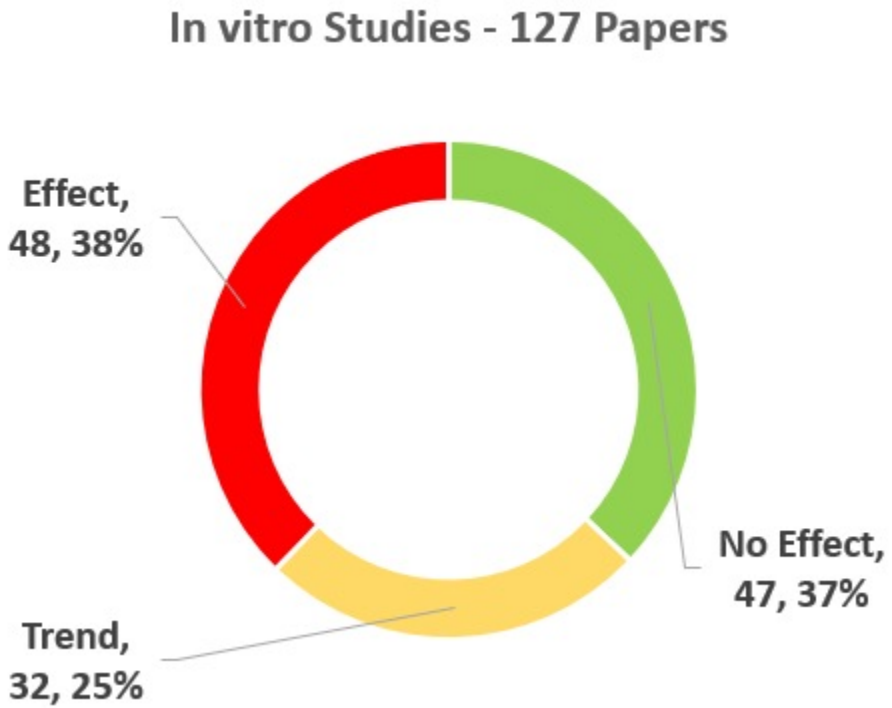
- No papers
- 70% > Effect
- 55 - 69% Effect
- 45 - 54% Effect
- 30 - 44% Effect
- < 29 % Effect

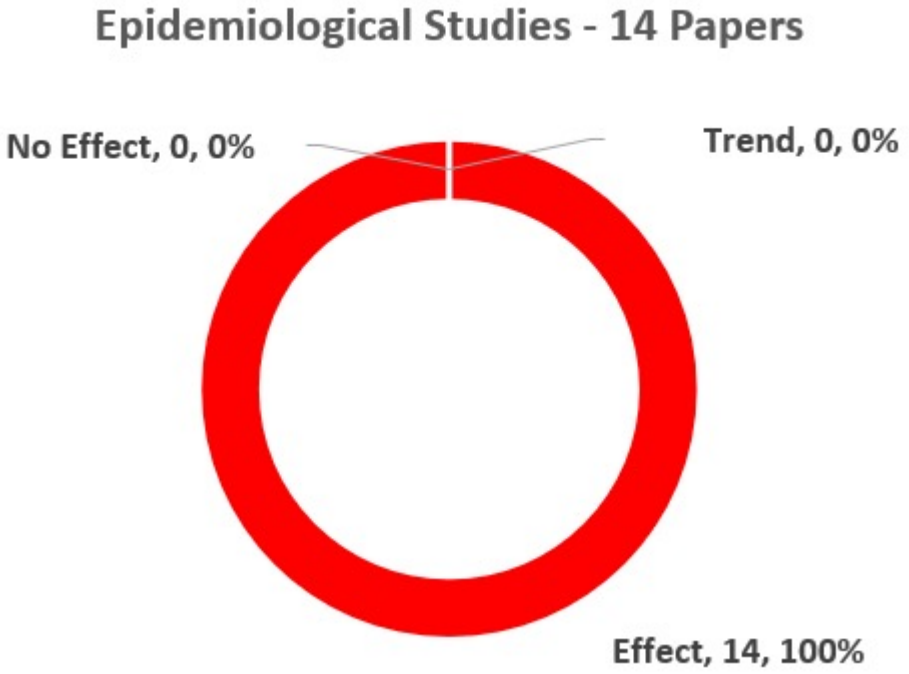
Findings

Specific focus on DNA breaks and fragmentation

Findings by Experimental Type – DNA Breaks

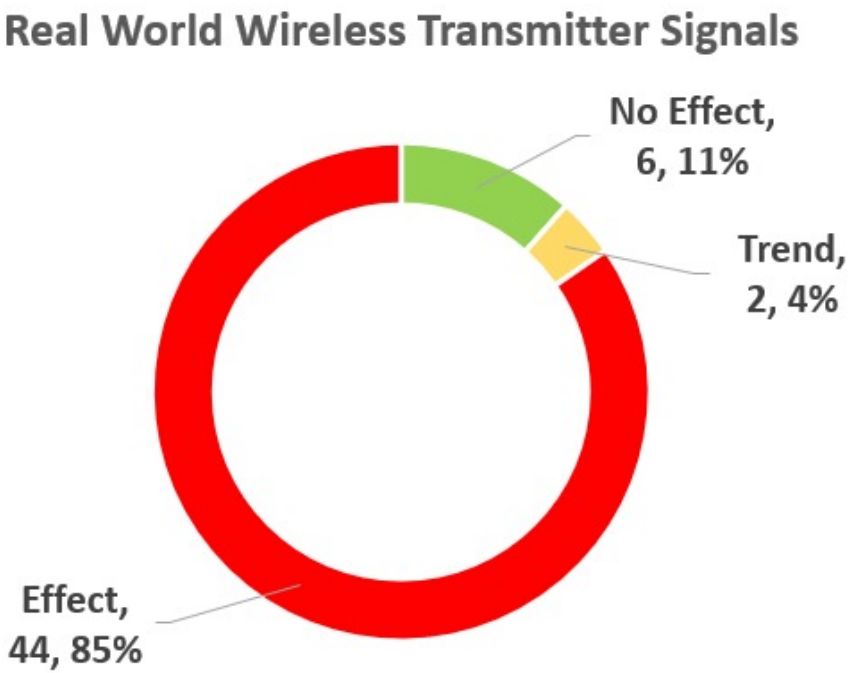


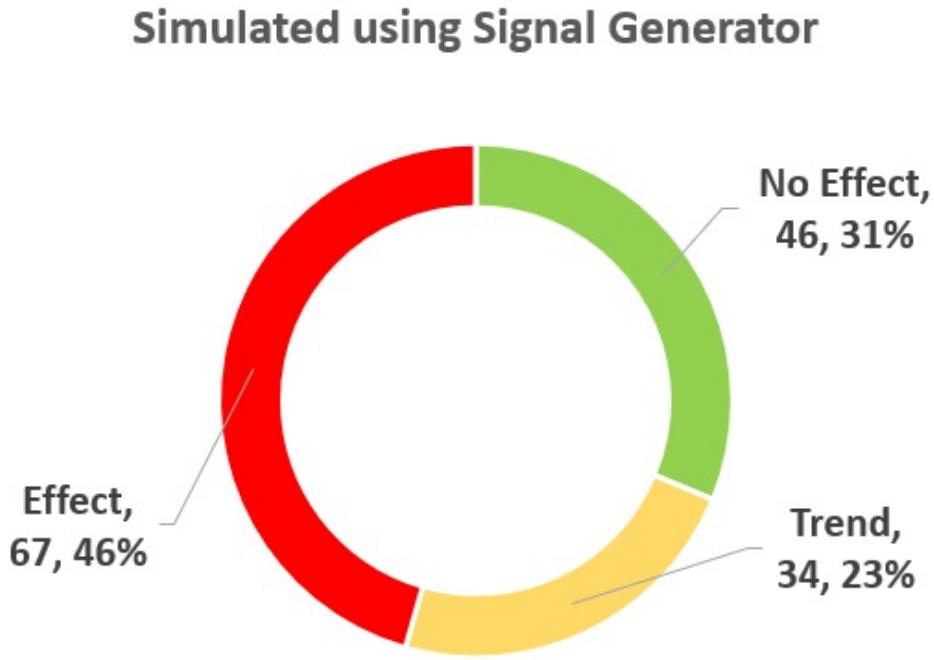




A significant effect is recorded when p value < 0.05

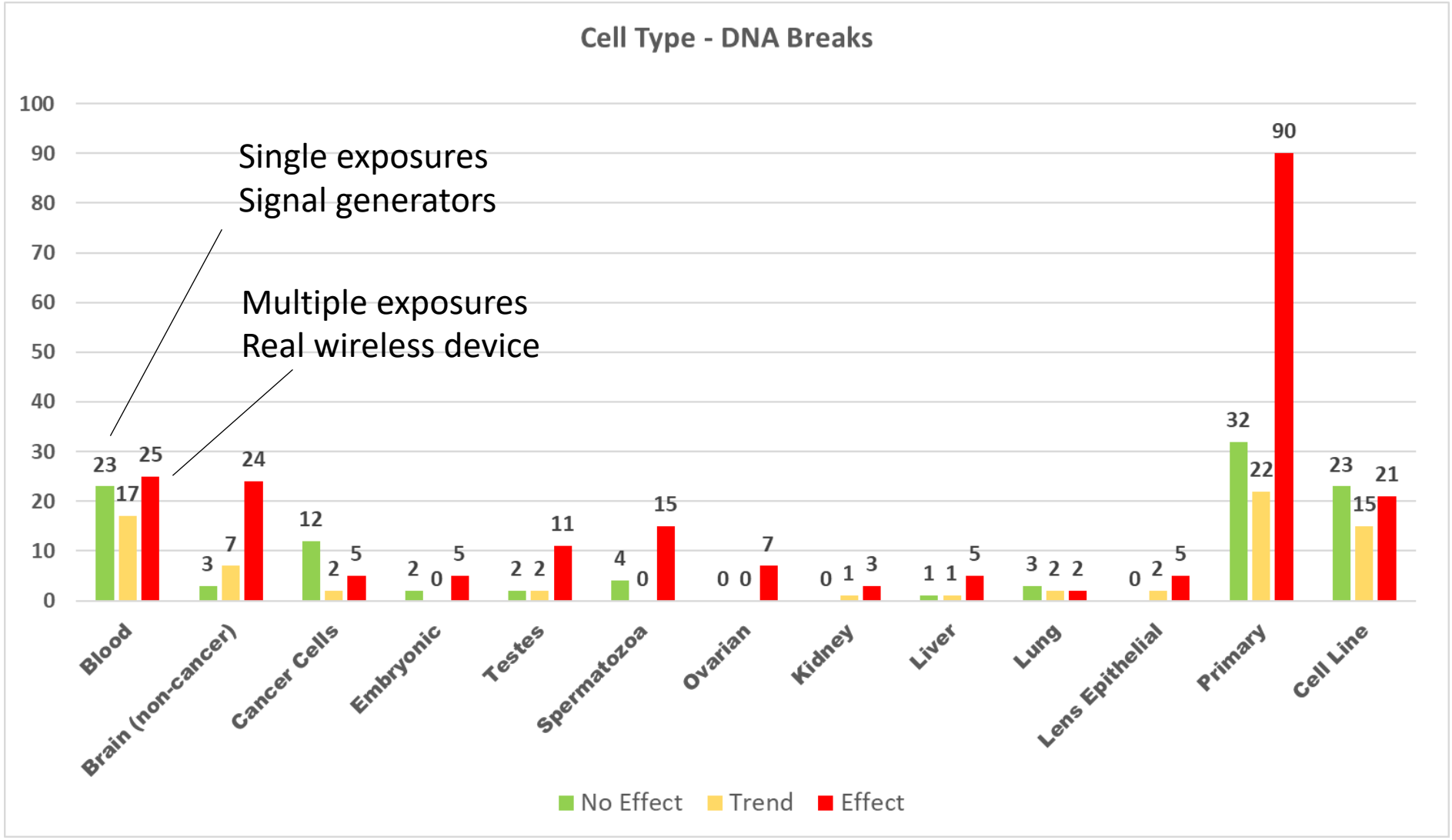
Real vs Simulated Signals





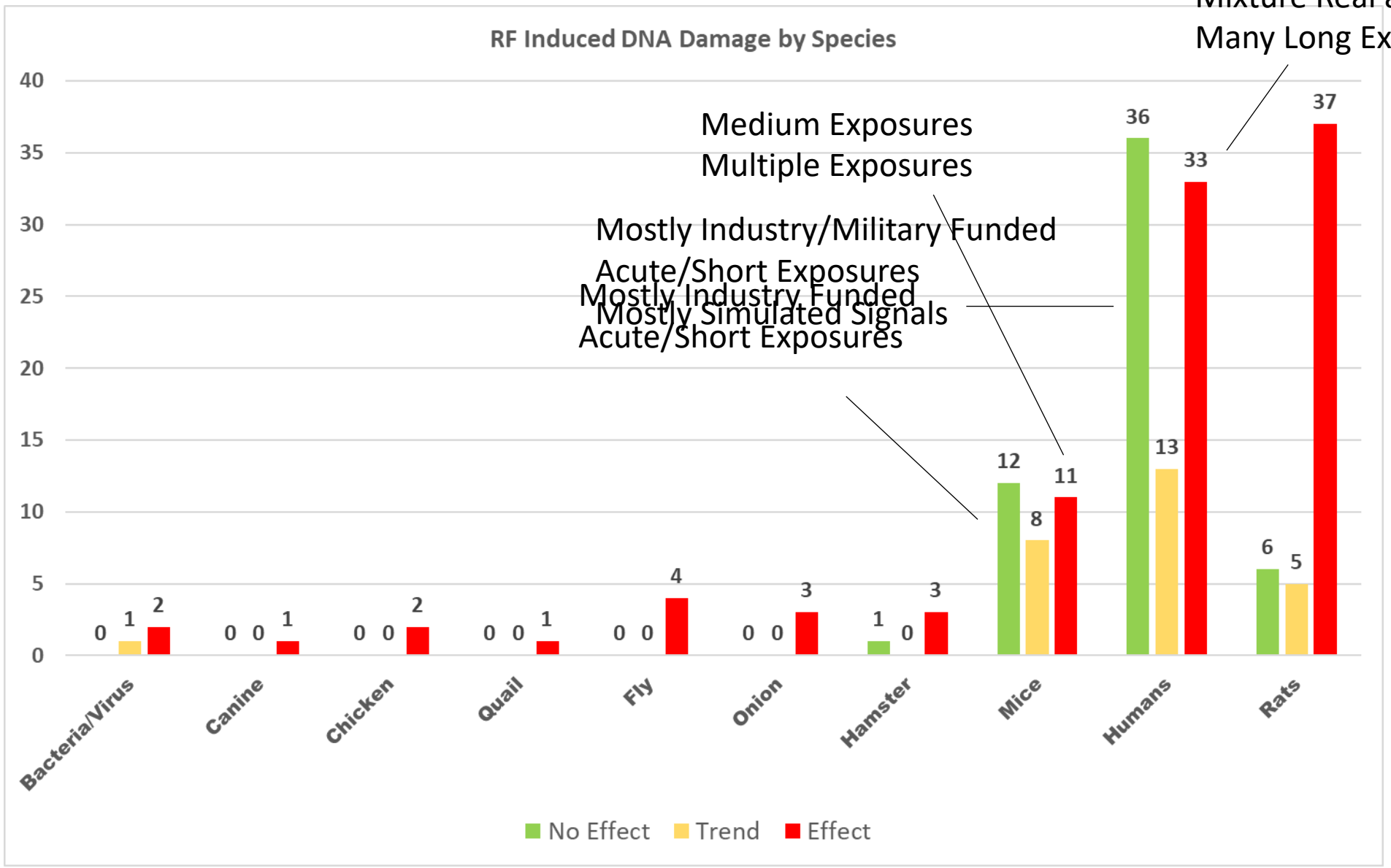
- Real world wireless transmitters show strong evidence for causing DNA damage
- The evidence for signal generators is less convincing and maybe due to:
  - Not all attributes found in real life signals are being simulated
  - Not all frequencies or modulations are reproduced
  - Variability in signal intensity missing
  - Often use a carrier wave with no data transmission

Cell Types – RF Induced DNA Breaks Assessment



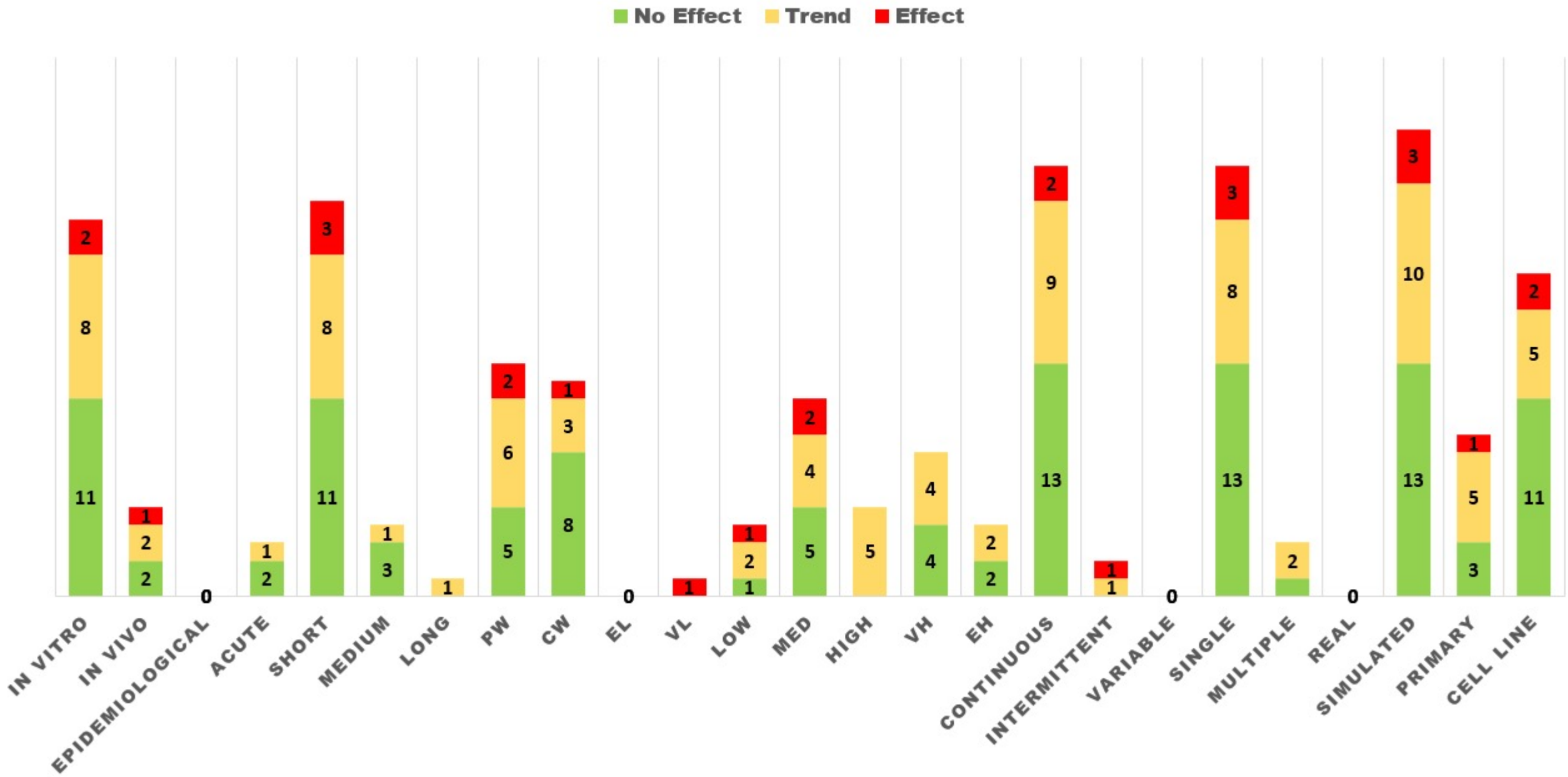
Results shown have not accounted for potential biases and methodological limitations – all DNA break papers used

Species - RF Induced DNA Breaks Assessment

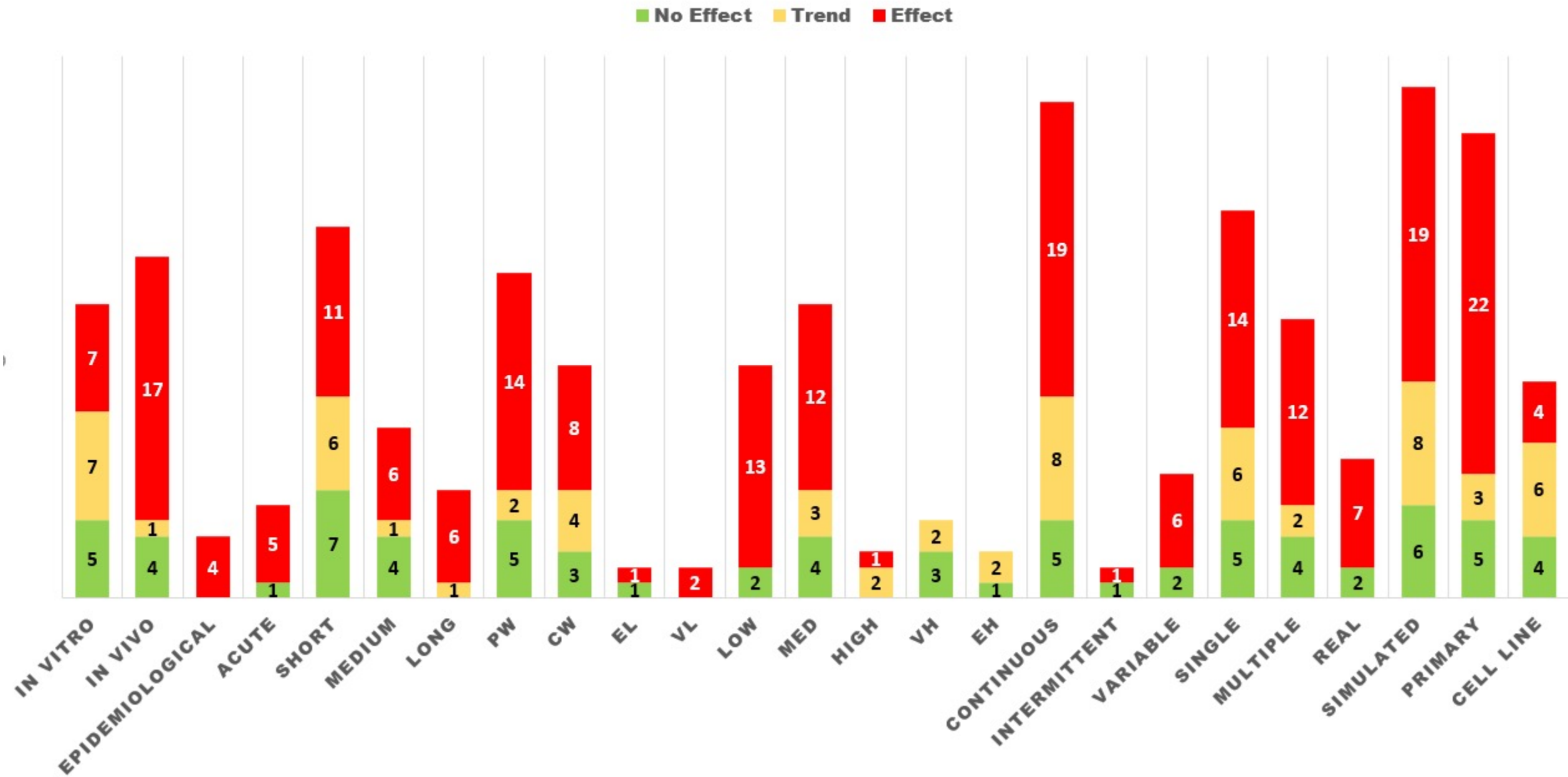


Funding Source Matters

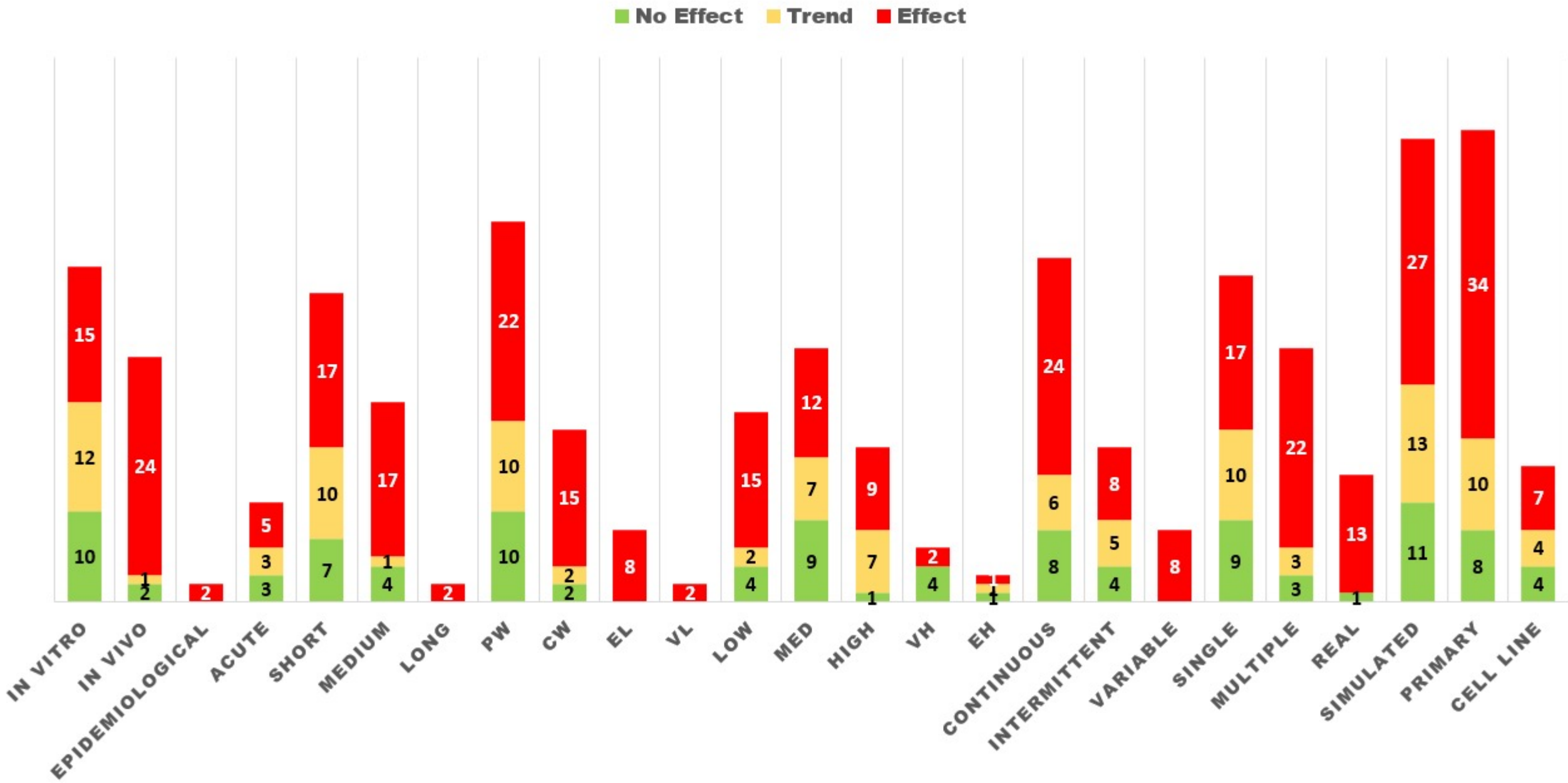
EXPERIMENT ATTRIBUTES - INDUSTRY FUNDED WITH PARTNERS



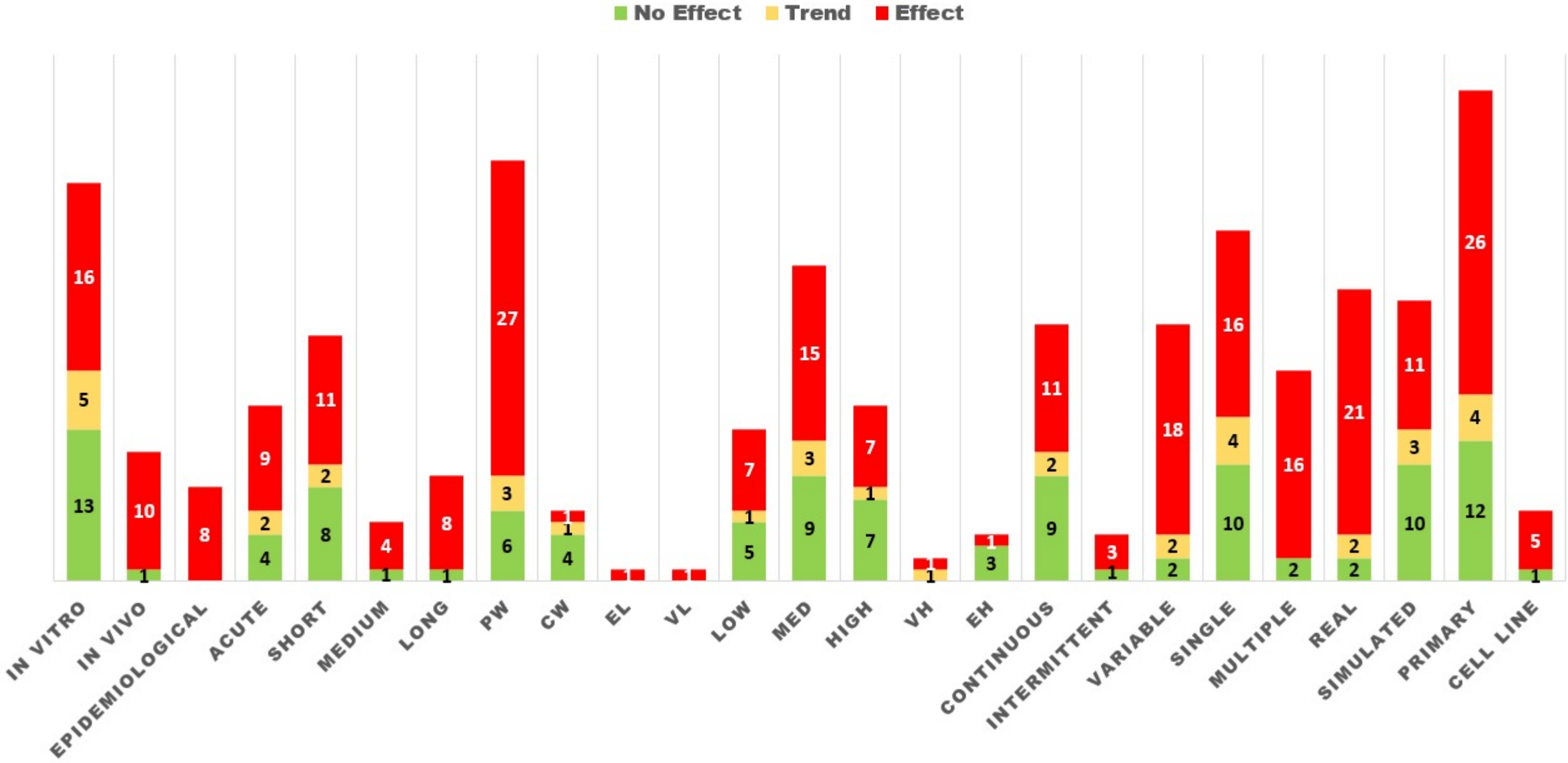
EXPERIMENT ATTRIBUES - INSTITUTIONALLY FUNDED WITH PARTNERS

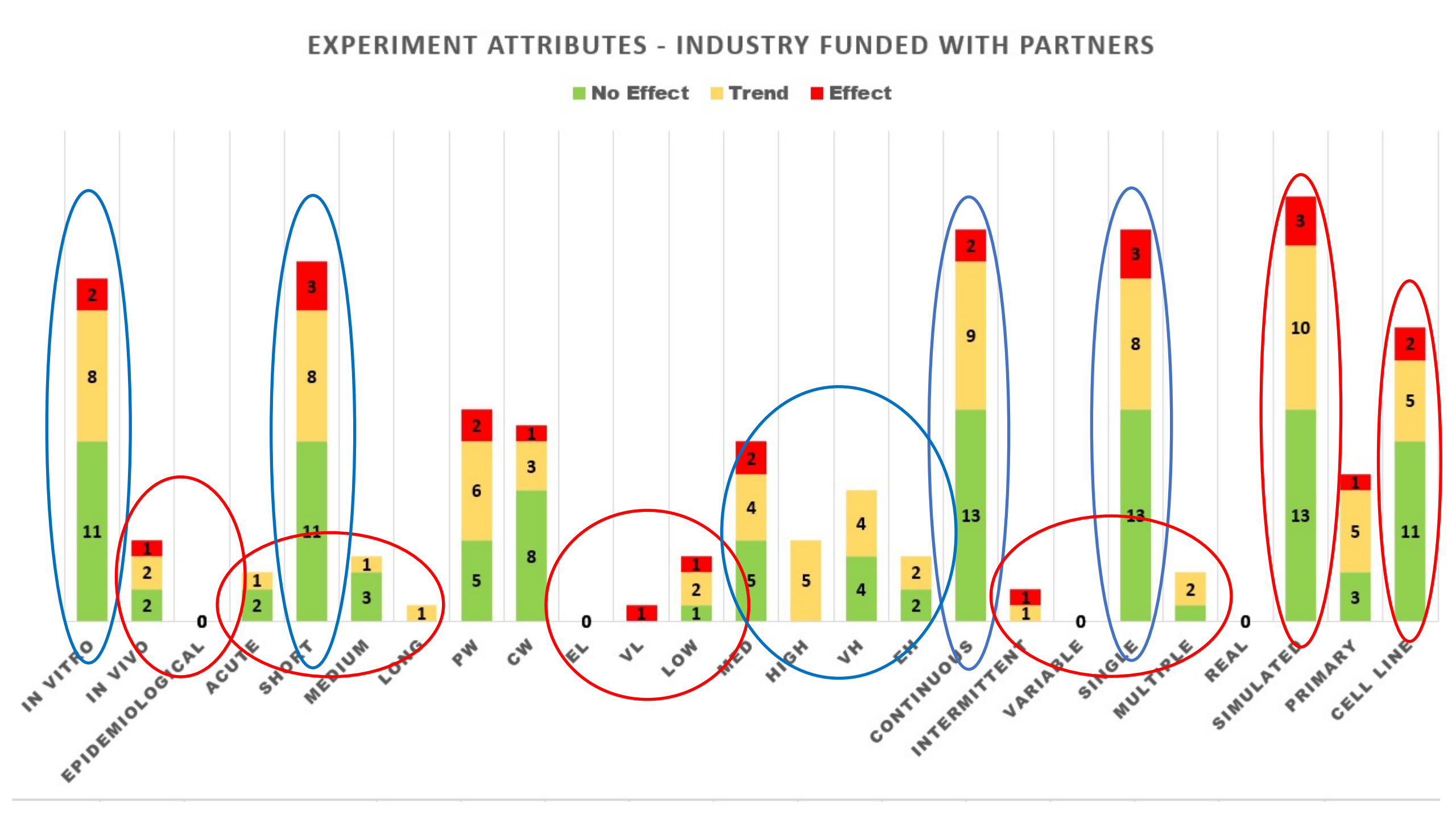


EXPERIMENT ATTRIBUTES - GOVERNMENT FUNDING EXCL. MILITARY AND COMMS



EXPERIMENT ATTRIBUTES - UNKNOWN FUNDING




EXPERIMENT ATTRIBUTES - INDUSTRY FUNDED WITH PARTNERS
No Effect
Trend
Effect
IN VITRO
IN VIVO
EPIDEMIOLOGICAL
ACUTE
SHORT
MEDIUM
LONG
PW
CW
EL
VL
LOW
MED
HIGH
VH
EH
CONTINUOUS
INTERMITTENT
VARIABLE
SINGLE
MULTIPLE
REAL
SIMULATED
PRIMARY
CELL LINE

Result Summary

Result Summary

- Epidemiological and in vivo studies provide convincing evidence RF exposure damages DNA
  - Exposure durations are typically longer
  - Often exposure is to real RF devices
  - Signal intensity – variable
  - Includes transmission of data
- In vitro studies are not so convincing
  - Short exposure times
  - Predominantly single exposures [85%] rather than multiple exposures [15%]
  - Often using RF signal generators [83%] rather than real world wireless devices [17%]
  - Tendency to use cell lines [57%] over primary cells [43%], including cancers [25% of Cell Line studies] which can be more resilient to damage

Result Summary

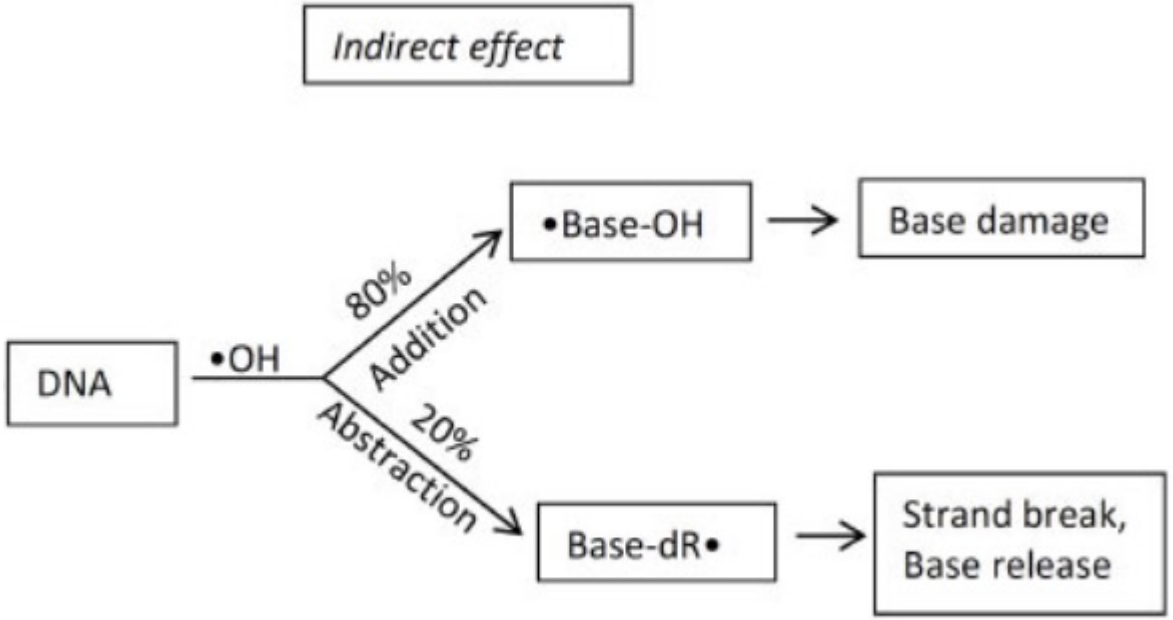
- DNA damage related to field intensity (windows) and exposure duration
  - Non linear intensity response (Lower intensities vs Higher intensities)
    - Non thermal effects are obvious
    - Higher number of reported damage at lower intensities
  - Non thermal action via oxidation/free radical damage, conformation changes (DNA/Proteins), repair Inhibition?
  - Dose response tendency noted – longer the exposure higher chance of DNA damage
  - Some studies suggest there are heterogenous populations with varying sensitivity to EM fields (pooling of data will hide those who are sensitive)
  - DNA damage caused by RF is comparatively lower than other known genotoxic agents

Exposure to RF is occurring 24x7, while typically sporadic for other agents

DNA Damage Mechanism
Discussion

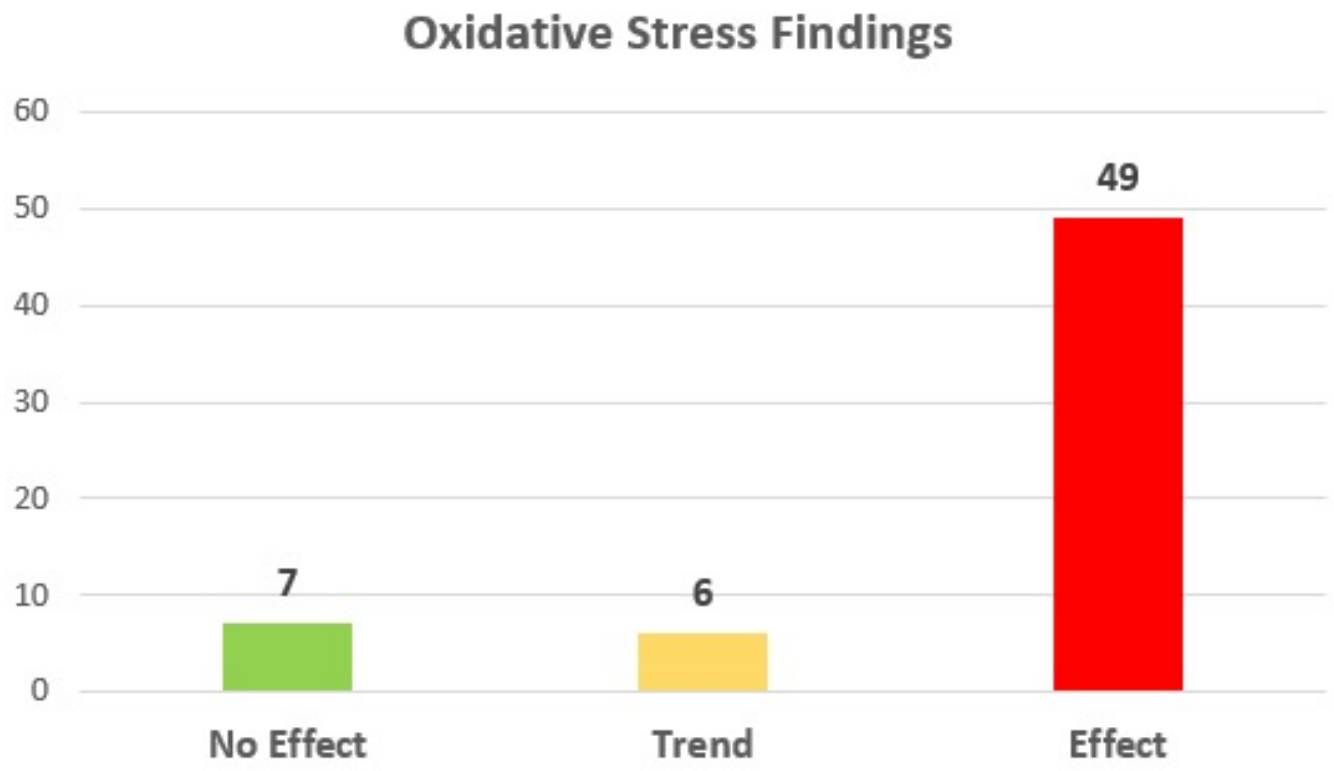
Possible Mechanism for DNA Damage

- Most probable mechanism for RF induced DNA Damage is via free radical production



Free Radicals – Oxidative Stress

- The weight of evidence suggest RF exposures are linked to free radical production and oxidative (OS) 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)



Current view of WHO, ICNIRP and ARPANSA

- “Non-ionizing radiation is a general term for that part of the electromagnetic spectrum which has photon energies too weak to break chemical bonds”

Not completely relevant as UV (A/B) radiation is also non-ionising, damages DNA and is a recognised Group 1 carcinogen. Both RF and UV generate free radicals. Free radicals are proven to damage DNA.

- “Despite considerable research efforts, no mechanism relevant for carcinogenesis of radiofrequency electromagnetic fields has been consistently identified to date.”

This is incorrect – Free radical production provides a plausible mechanism with 89% of papers[1] showing RF exposures create free radicals, which can damage DNA. Accumulated DNA damage is a recognised pathway for carcinogenisis

- “Most of the epidemiological research does not indicate carcinogenicity of radiofrequency electromagnetic fields.”

This statement is factually challenged by epidemiological evidence for brain tumours which shows an association[2] and was the principle reason for the IARC to classify RF as a Group 2B carcinogen in May 2011. Animal evidence was seen to be limited at the time, however, clear evidence has since been found[3,4] reinforcing the need to revisit the original IARC classification

Source of quotes: World Cancer Report Cancer Research for cancer prevention (2020)

1. Bandara *et.al.* 2018
2. IARC Monograph 2013
3. NTP Study 2018
4. Ramazzini Institute lifetime study 2018

Comparison: UV vs RF

Common biological effects shared by UV and RF

- Ultra Violet (UV) radiation is non ionising
- UV is a Group 1 carcinogen and is genotoxic
- UV A exposure generates free radicals and creates an oxidative stress state
- Free Radicals can damage DNA - > single and double strand breaks, DNA Base damage
- UV has been shown to modulate the immune system
- UV effects permeability of cell membrane

- Radiofrequency (RF) radiation is non-ionising
- RF is classified as a Group 2B carcinogen
- RF exposures generates free radicals and creates an oxidative stress state
- Free Radicals can damage DNA - > single and double strand breaks, DNA Base damage
- RF has been shown to modulate the immune system (bi-phasic)
- RF effects permeability of cell membrane

What we have today is inconsistent handling of evidence and recognition of genotoxic potential.
A possible explanation: One EMF source generates significant revenues, the other does not

Other important facts for UV and RF

- UV penetration of skin is based on wavelength and optical properties of skin
- Penetrates µm (20-240) of skin

- Majority of UV exposure comes from Sun
- Clothing, sun cream, hats and tinted glass can protect from UV exposure
- UV exposure can be completely avoided at night when sleeping -> a chance for the body to heal

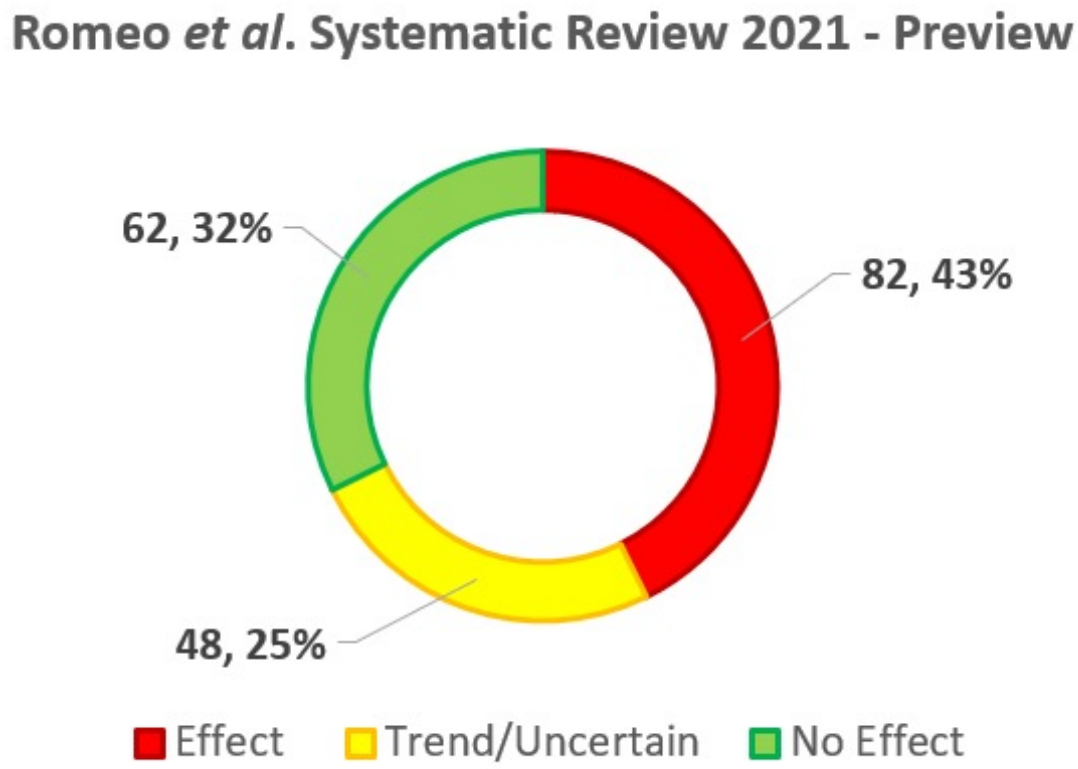
- RF penetration is also based on wavelength, longer wave lengths penetrating deeper into body
- Current microwave technology -> All organs are vulnerable (reachable)
- mmWave (advanced 5G) technology -> penetrates mm of skin
- Most RF exposure is from manmade sources
- RF can penetrate clothing, bricks, wood, plaster etc.
- RF exposures generally cannot be avoided and are occurring 24x7

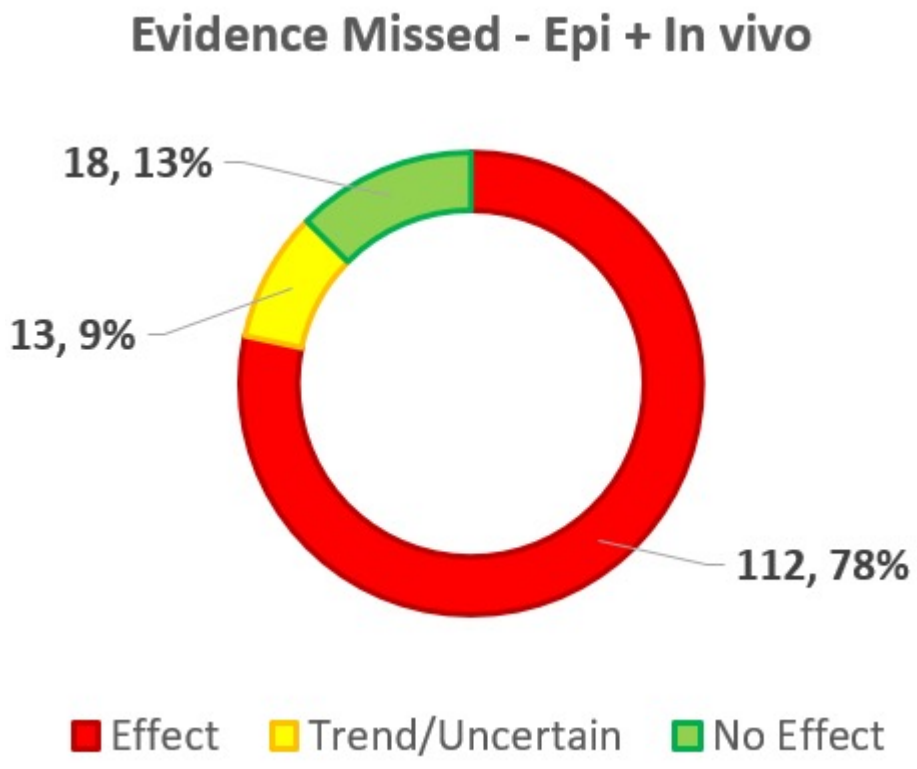
Future Publication
Other's Work – A Prediction

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)





Closing Statements

Controversial findings and issues

- Results demonstrate a real risk for genotoxicity, particularly chronic long term exposures
- Because we are blanketing the earth with RF, all species are at risk
- Balance of probability also supports a case for carcinogenicity
- ARPANSA and ICNIRP do not consider these risks, they look for confirmed evidence of harm
- New wireless technology is being rolled out without pre-market health testing
- Safety is assumed if operating within public limits
- Precaution is absent, with ARPANSA explicitly removing precautionary principle that was present in RPS 3 from the latest RF Standard (RPS S-1)

Future Research Recommendations

- Experiments should be conducted that approximate typical real life exposures
- Use exposure regimes > 48 hours in accumulated duration
- Real wireless devices should be used
- Include assays for both DNA damage and free radical production
- Assays should be taken at different intervals to measure changes over time
- PCR tests to verify gene expression changes (DNA repair genes, OS genes)
- Multiple exposures rather than a single continuous exposure
- Controlled experiments should contrast constant exposure intensity with variable intensities over the same time period

Thank You

Historical Perspective - Past Reviews & Findings

- Vijayalaxmi et al. (2004) – Review found 58% of papers did not find increased damage, 23% found damage and 19% were inconclusive
- Vijayalaxmi et al. (2008) – Review & meta analysis of 63 papers (1990-2005) suggested publication bias was associated with “effect” papers
  - Noted DNA damage was found but “within the spontaneous levels reported in the historical database”
- Rudiger (2009) – Narrative review of 101 publications and found 49 reported damage and 42 did not.
- Vijayalaxmi et al. (2012) – Review & meta analysis of 88 papers (1990-2011) suggested publication bias was associated with “effect” papers
- Lai 2021 – Narrative review of 361 papers (bundled genetic changes and damage together) with 66% showing effects and 34% not finding anything