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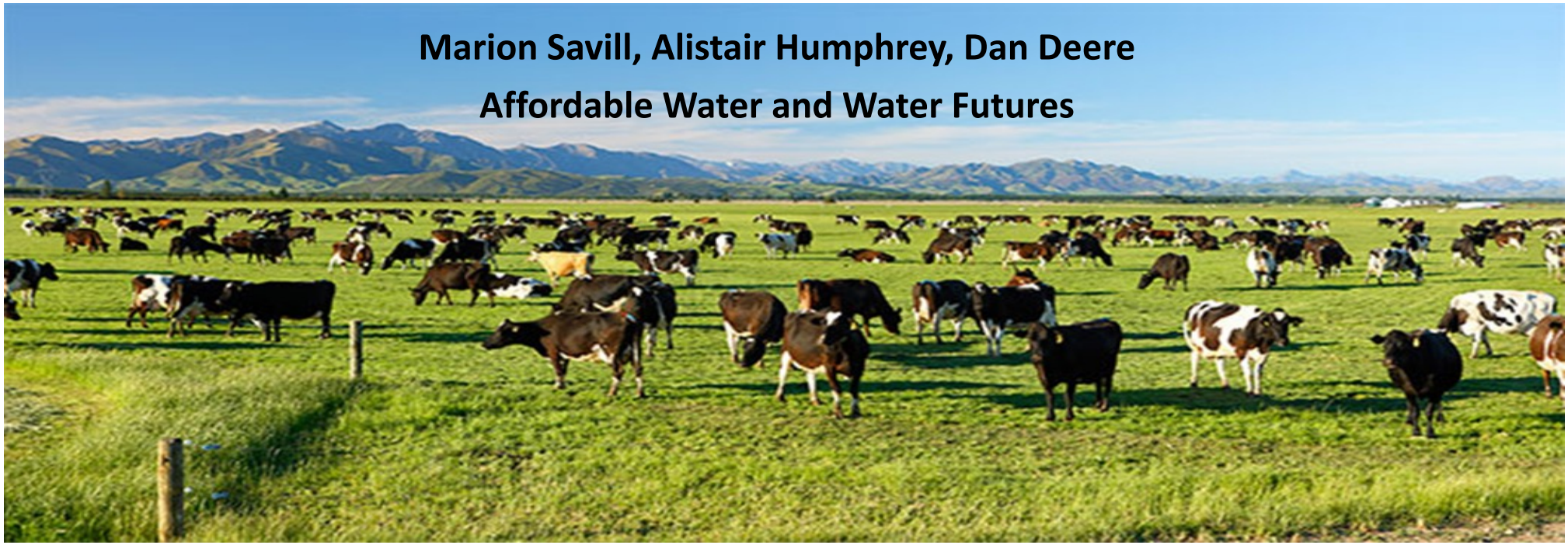
Colorectal Cancer and Nitrates: Implications for Health and the Economy

Marion Savill, Alistair Humphrey, Dan Deere

Affordable Water and Water Futures



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- The Current New Zealand (NZ) Maximum Acceptable Value (MAV) for nitrates: How and why?
- New evidence about nitrates and colorectal cancer (CRC)
- Increasing risk of nitrate contamination of groundwater
- How can the health risks of nitrates be mitigated?

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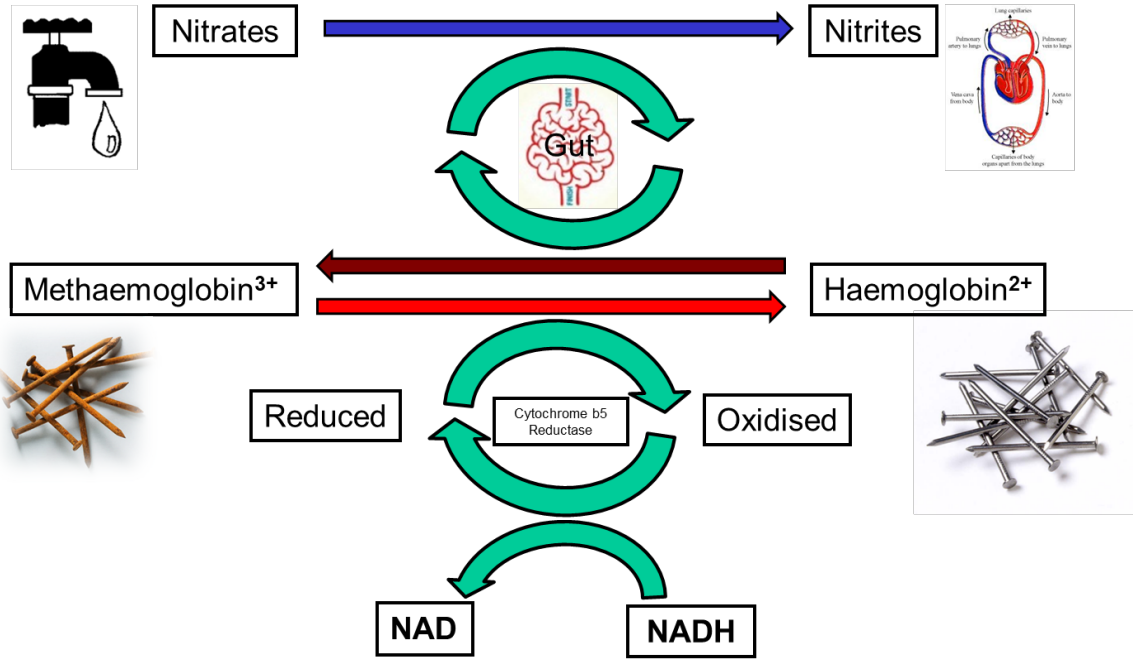
The physiology of Blue Baby syndrome (methaemaglobinaemia)



Current

MAV Nitrate

Based on acute risk of Blue Baby Syndrome

- **50 mg/L nitrate**
- **11.3 mg/L nitrate-N**

How was the MAV for nitrate derived?

The 10 mg/L Nitrate-N Maximum Contaminant Level (MCL) for nitrate in drinking water set in US (1960s) based on 214 human cases of methaemoglobinaemia

Based on no observed adverse effect level (NOAEL)

No margin of safety required as risks were considered well understood so **no safety factor was built in**.

World Health Organisation 50 mg/L nitrate

Drinking Water Standards for NZ MAV 50 mg/L nitrate, 11.3 mg/L nitrate-N

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How was the MAV for nitrate originally set?

No recorded cases of methaemoglobinaemia consuming drinking water with nitrate levels below the MAV

The US sees sporadic cases of methaemoglobinaemia in bottle-fed infants on private bores where the nitrate MAV has been exceeded

Levels of nitrate in groundwater in New Zealand are increasing, and are now exceeding the MAV

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June 16th 2006, Lyon France

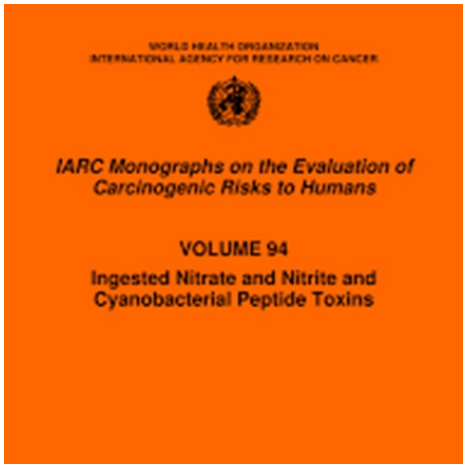
19 scientists from eight countries met at:

- International Agency for Research on Cancer (IARC)
- Assessed the carcinogenicity of ingested nitrate and nitrite

Conclusions:

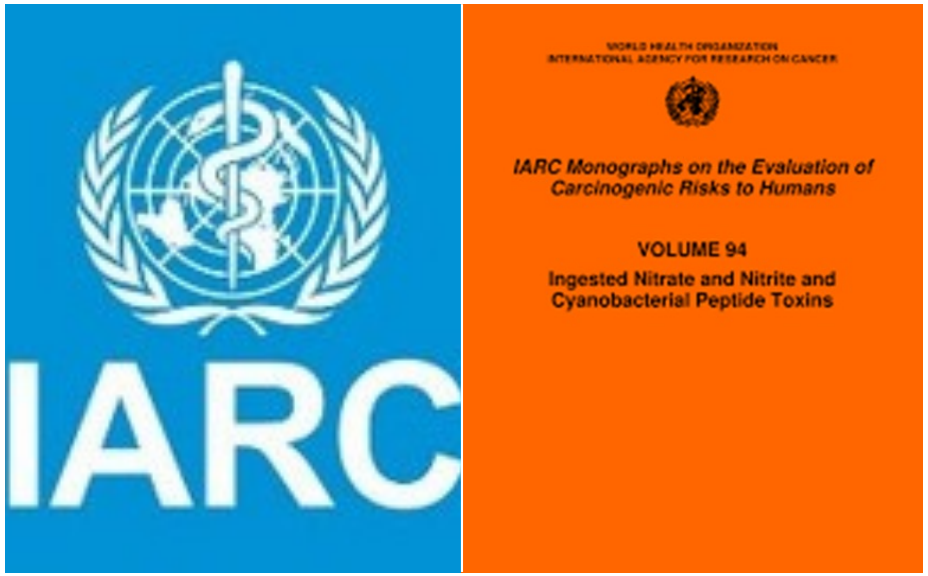
- “ingested nitrate or nitrite under conditions that result in endogenous nitrosation is probably carcinogenic to humans (group 2A)”
- Current work provides “inadequate evidence of carcinogenicity” for nitrate in food and nitrate or nitrite in drinking-water
- Protective effect of vitamin C, E and other antioxidants in food inhibit formation of cancer-causing N-nitroso compounds from nitrates.

IARC



Conclusions 2006:

- Nitrate in drinking-water could result in endogenous nitrosation because no vit C or other antioxidants in water
- Few studies available showing low exposure levels



Nitrates in drinking water and Colorectal Cancer (1) – Espejo-Herrera *et al* 2016

IJC
International Journal of Cancer

Colorectal cancer risk and nitrate exposure through drinking water and diet

Nadia Espejo-Herrera[1,2,3], Esther Gràcia-Lavedan[1,2,3], Elena Boldo[3,4,5], Nuria Aragonés[3,4,5], Beatriz Pérez-Gómez[3,4,5], Marina Pollán[3,4,5], Antonio J. Molina[6], Tania Fernández[6], Vicente Martín[3,6], Carlo La Vecchia[7], Cristina Bosetti[8], Alessandra Tavani[8], Jerry Polesel[9], Diego Serraino[9], Inés Gómez Acebo[3,10], Jone M. Altzibar[3,11,12], Eva Ardanaz[3,13], Rosana Burgui[3,13], Federica Pisa[14], Guillermo Fernández-Tardón[3,15], Adonina Tardón[3,15], Rosana Peiró[3,16], Carmen Navarro[3,17,18], Gemma Castaño-Vinyals[1,2,3,19], Victor Moreno[3,20,21], Elena Righi[22], Gabriella Aggazzotti[22], Xavier Basagaña[1,2,3,19], Mark Nieuwenhuijsen[1,2,3,19], Manolis Kogevinas[1,2,3,19] and Cristina M. Villanueva[1,2,3,19]

Espejo-Herrera *et al* conclusions 2016:

- Water nitrate ingestion from public supplies, bottled water, private wells and springs over the adult lifetime was estimated using pooled case-control studies (**1,869 cases and 3,530 controls**)

- Risk of colorectal cancer was increased among those **with >2.3 mg/day NO3-N** (vs. <1.1 mg/day).

- Red meat (and high nitrate) increased risk for CRC, High Vit E (and low nitrate) decreased risk of CRC

Nitrates in drinking water and CRC (2)
Schullehner *et al* 2018

- Population-based health register, linked with longitudinal drinking water quality data
- Individual nitrate exposure was calculated for 2.7 million adults (1978 and 2010)
- 9,844 incident CRC cases identified during 23 million person-years at risk
- Dietary confounders not examined but if anything thought to suffer a positive effect

IJC
International Journal of Cancer

Nitrate in drinking water and colorectal cancer risk: A nationwide population-based cohort study

Jörg Schullehner [1,2,3,4], Birgitte Hansen[2], Malene Thygesen[3,4], Carsten B. Pedersen[3,4] and Torben Sigsgaard[1]

[1]Department of Public Health, Aarhus University, Aarhus, Denmark

Schullehner *et al* conclusions 2018:

- "Statistically significant increased risks at drinking water levels above 3.87 mg/L Nitrate"
  - well below the current drinking water standard of 50 mg/L nitrate
- Carcinogenic water nitrate concentrations are [well] below the current drinking water standard."
- 0.87 mg/L MAV for nitrate-N

- *Int. J. Cancer: 143, 73–79 (2018) © 2018 UICC*

Nitrates in drinking water and CRC (3)
Jayne Richards *et al* 2021

Contents lists available at ScienceDirect

Environmental Research

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

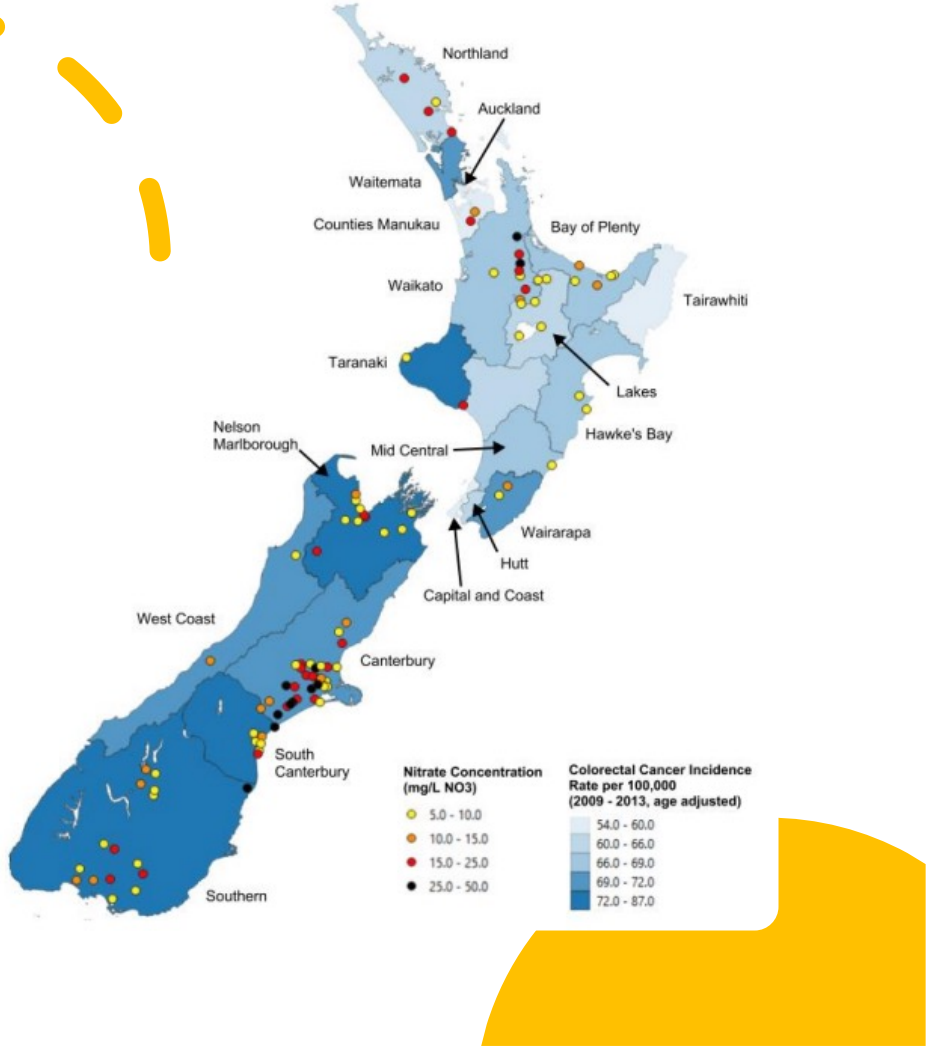
Nitrate contamination in drinking water and colorectal cancer: Exposure assessment and estimated health burden in New Zealand

Jayne Richards [a], Tim Chambers [b,*], Simon Hales [b], Mike Joy [c], Tanja Radu [a], Alistair Woodward [d], Alistair Humphrey [e], Edward Randal [b], Michael G. Baker [b]

[a] *School of Architecture, Building and Civil Engineering, Loughborough University, Epinal Way, Loughborough, LE11 3TU, UK*

Richards *et al* - Conclusions 2021

- Most New Zealanders are not exposed to nitrates in drinking water
- About 14% are exposed to >1mg/L NO_3-N
- 3% of all CRC in NZ is attributable to nitrates in drinking water
- Highest levels of CRC correlate to highest levels of nitrates (which correlate to highest levels of cattle)



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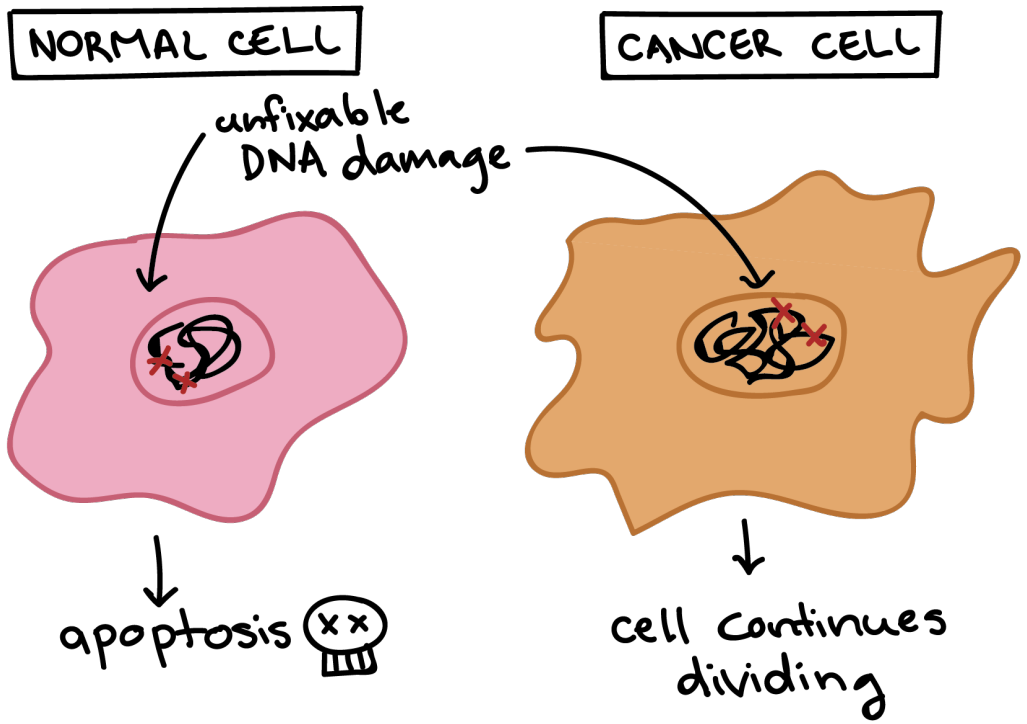
No MAV for Chronic Effects

Ingested Nitrate Probably Carcinogenic to humans



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Studies on Colorectal Cancer

CURRENT MAV 11.3mg/L Drinking Water

Author	Country	Lowest NO3-N mg/L	Inc Risk %
Espejo-H et al 2016	Spain/Italy	2.3	49
Schullehnmer et al 2018	Denmark	0.87	11
		2.1	15
Jones 2019	US Iowa	0.81	32
Richards et al 2021	NZ	>0.49	
2021	Mexico	>4.7	Not CRC

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Parliamentary Commissioner for the Environment
Water quality in New Zealand (2013):
Land use change and nutrient pollution

Declining water quality is attributed to dairy farming:

1. Intensification:
   More cows per hectare

2. **Expansion:**
   More hectares for cows

Dr. Jan Wright – Parliamentary Commissioner for the Environment

http://www.parliament.nz/en-nz/parl-support/research-papers/00PLEcoC51261/freshwater-quality-in-new-zealand

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Freshwater quality in New Zealand

Freshwater quality in our lakes and rivers is a subject of high public concern and vigorous debate. There are three main water pollutants of greatest concern in New Zealand. These are pathogens, sediment, and nutrients (Parliamentary Commissioner for the Environment). Pathogens are invisible microbes that cause disease. Typical sources are raw and partially treated sewage entering lakes and rivers (usually at specific points); another source is the diffuse entry of faecal coliforms from farm animal excrement leaching into waterways. Soil erosion, particularly along river banks, causes sediment. Phosphorus and nitrogen, primarily from animal urine and fertilisers, are the main sources of nutrient pollution.

In 1991 the "sustainable management" of fresh water was assigned to the regional councils under the Resource Management Act 1991. End-of-pipe (or point) sources of water pollution, which require resource consents, became increasingly controlled and much has been invested in upgrading wastewater treatment. Today diffuse sources of water pollutants, principally from land-use practices, are a much greater challenge.

The biggest source of nitrogen in New Zealand's waterways is urine from farm animals

common forms of nitrogen—nitrate and ammonia— are highly soluble in water and easily leach into waterways. In contrast phosphorous in the form of phosphate usually clings to soil particles. The main way in which phosphorus gets into water is when soil is washed into lakes and rivers and becomes sediment.

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Freshwater quality in New Zealand [PDF 179k]

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Parliamentary Library
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Parliament Buildings
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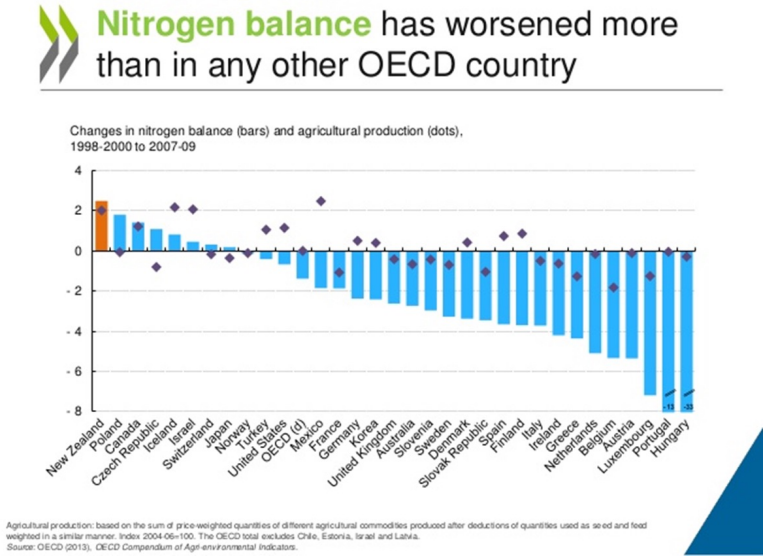
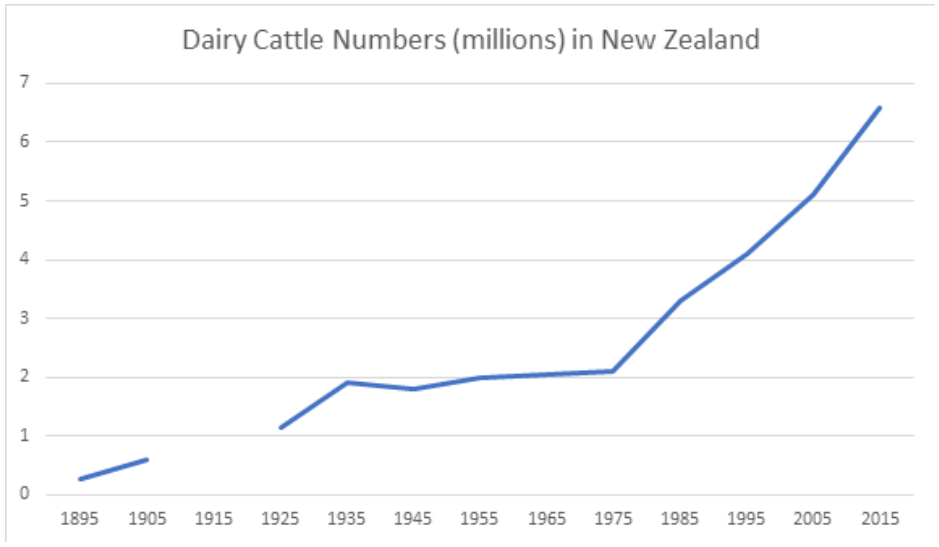
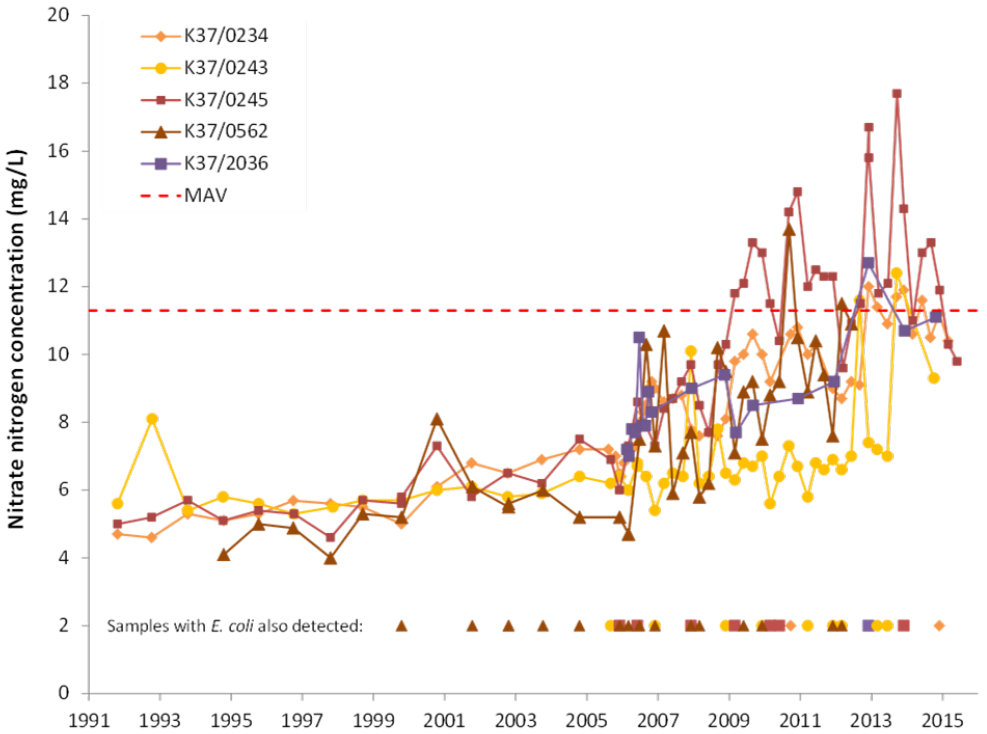
More farming = More fertiliser = More nitrates in groundwater

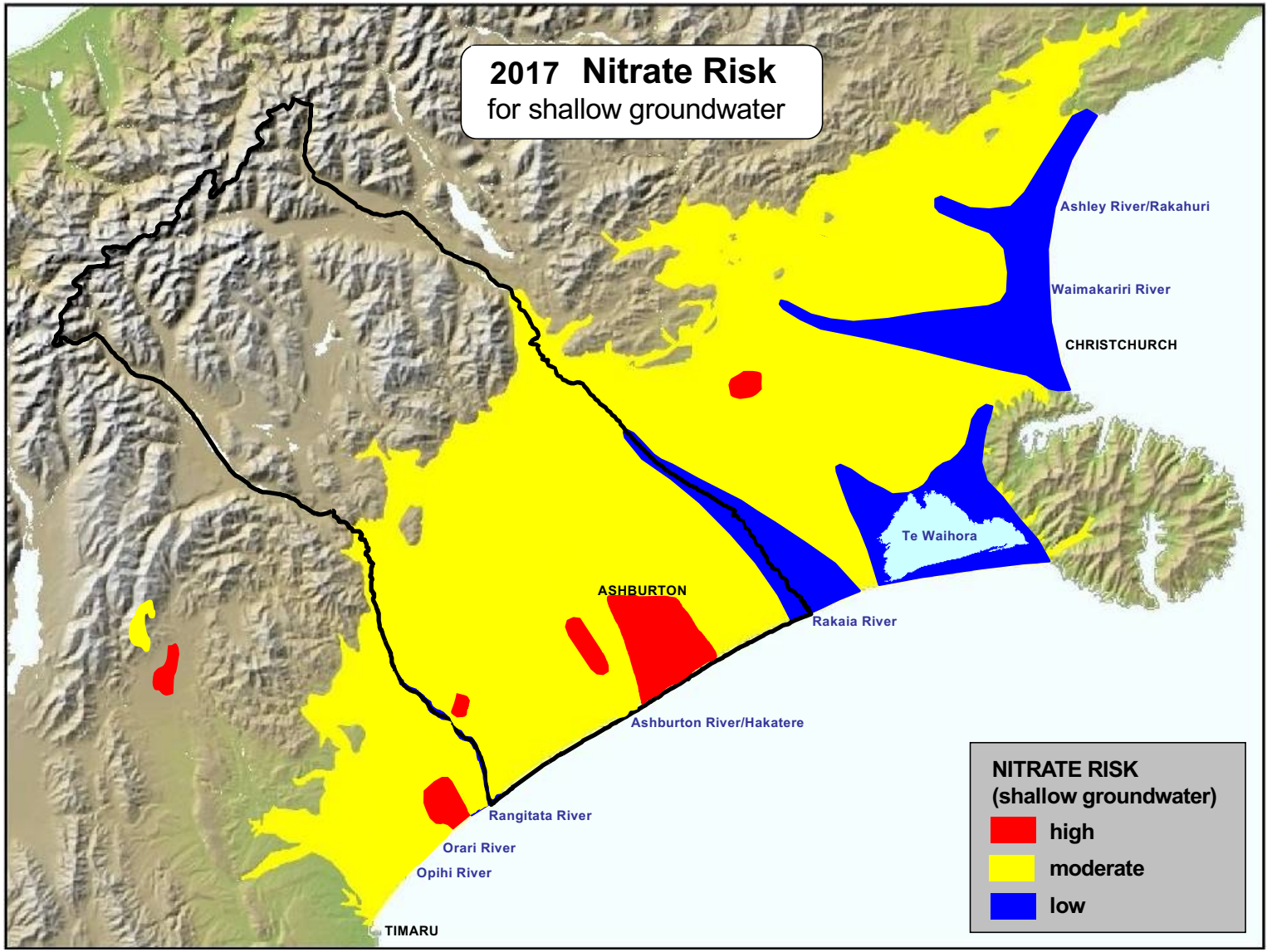




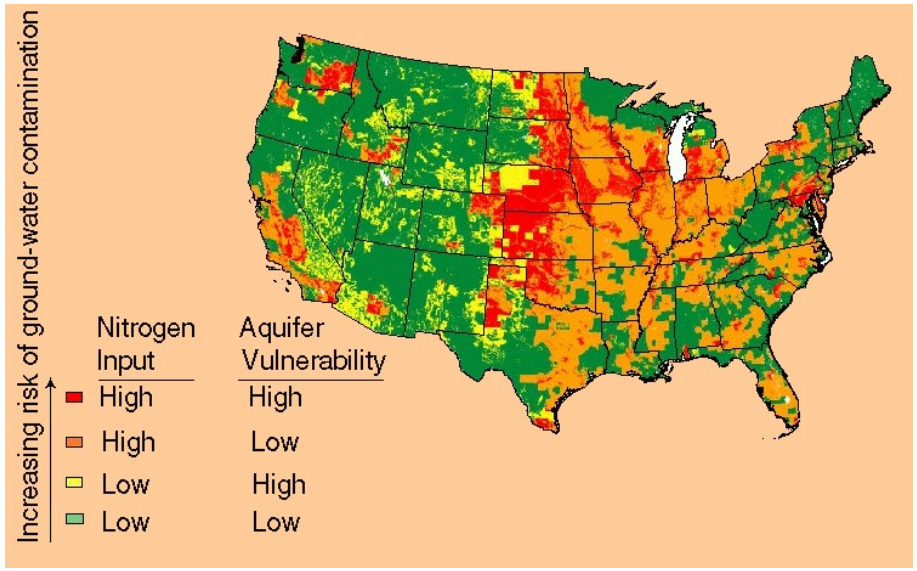
Local increases in groundwater nitrates

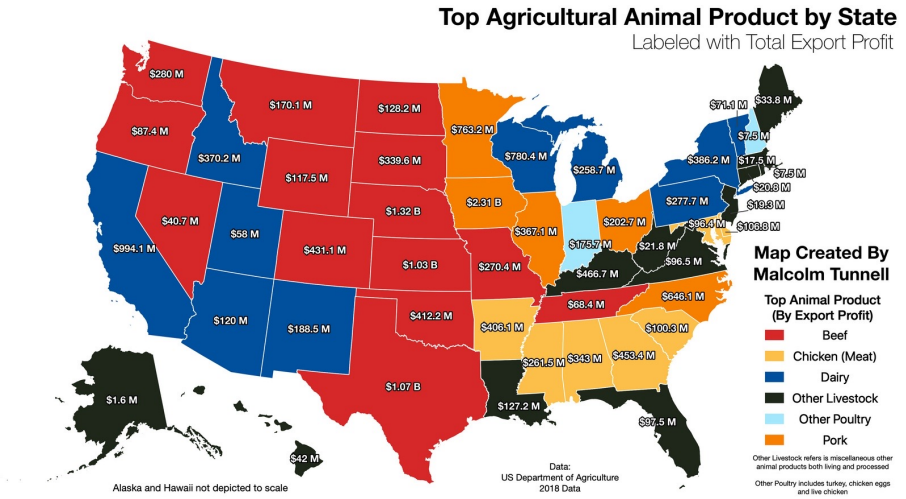
Ealing Hinds area –South Canterbury, New Zealand

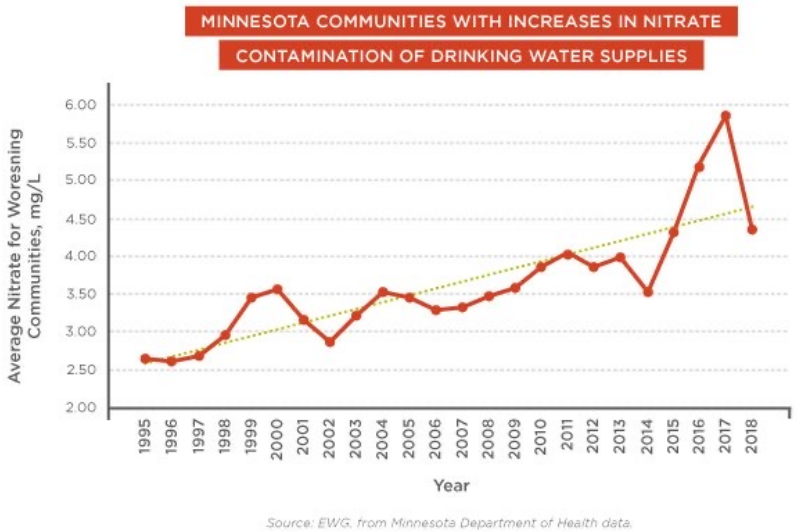


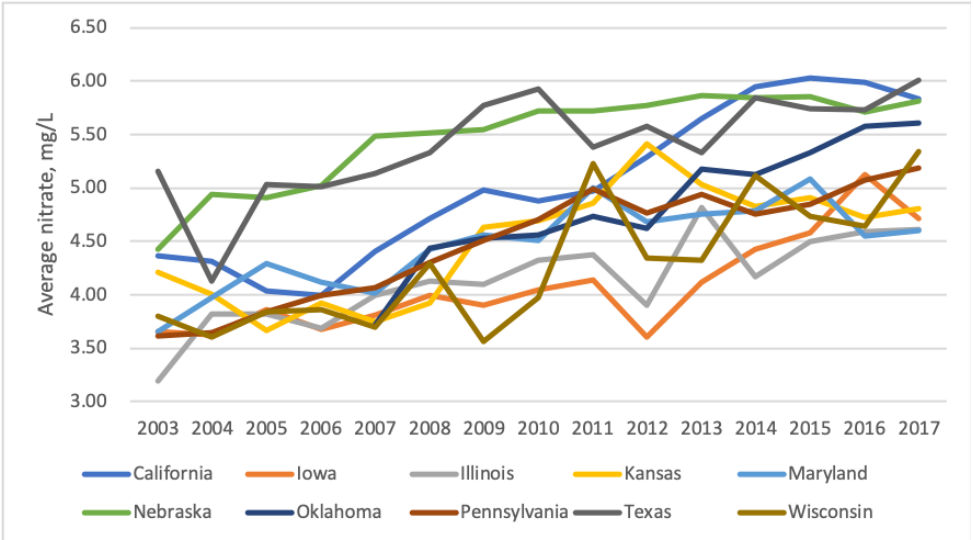

2017 Nitrate Risk
for shallow groundwater
Ashley River/Rakahuri
Waimakariri River
CHRISTCHURCH
Te Waihora
ASHBURTON
Rakaia River
Ashburton River/Hakatere
Rangitata River
Orari River
Opihi River
TIMARU
NITRATE RISK
(shallow groundwater)
high
moderate
low

US Farming and Nitrate levels






MINNESOTA COMMUNITIES WITH INCREASES IN NITRATE
CONTAMINATION OF DRINKING WATER SUPPLIES
Average Nitrate for Woresning Communities, mg/L
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018
Year
Source: EWG, from Minnesota Department of Health data.


Average nitrate, mg/L
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017
California
Iowa
Illinois
Kansas
Maryland
Nebraska
Oklahoma
Pennsylvania
Texas
Wisconsin

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Global distribution of problem

To Date

-Denmark
-USA
-Spain/Italy
-NZ
-Mexico with different cancer issues

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The cost of drinking water induced CRC

Environmental Research 176 (2019) 108442

Contents lists available at ScienceDirect

Environmental Research

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

Exposure-based assessment and economic valuation of adverse birth outcomes and cancer risk due to nitrate in United States drinking water.

Alexis Temkin[a,*], Sydney Evans[a], Tatiana Manidis[b], Chris Campbell[a], Olga V. Naidenko[a]

[a] Environmental Working Group, 1436 U Street NW Suite 100, Washington, DC, 20009, USA
[b] Duke University, Nicholas School of the Environment, 9 Circuit Dr, Durham, NC, 27710, USA

Temkin *et al* conclusions 2019

- 1-8% of CRC is caused by nitrates in drinking water in the US
- 1,233 – 10,379 cases per year (up to 24% on private supplies)
- Costing $0.74 billion to $6.2 billion (1/3 of which are medical costs)
- **Lowering the MAV for nitrate could have economic benefits if we can find a cheaper way to remove**

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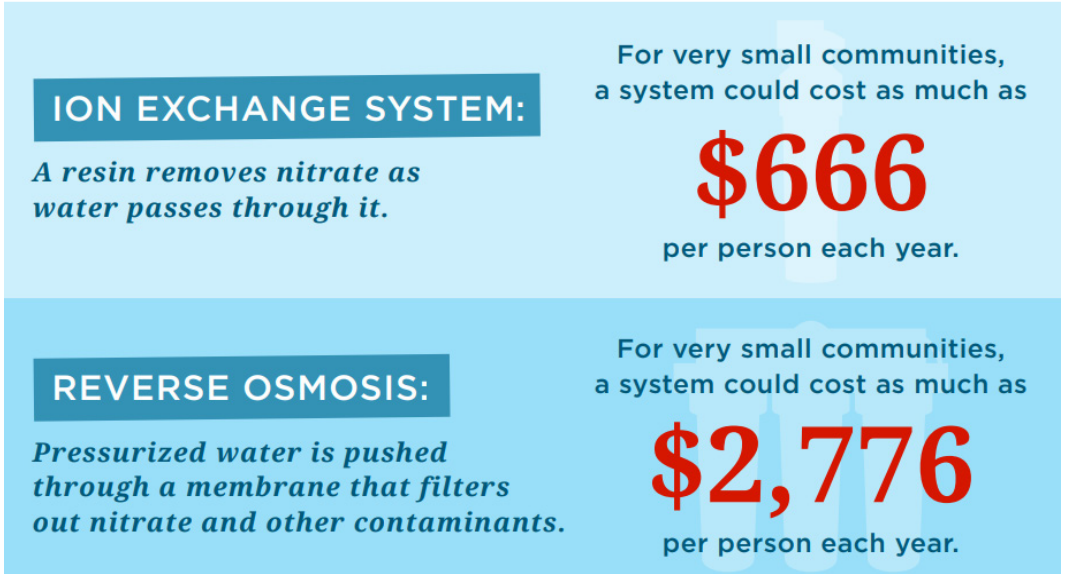
The cost of removing nitrates

There are two common ways to treat water contaminated with nitrate. Both are costly—especially for small communities with a small tax base and, often, a low average income.



- Ion exchange only removes 80% of nitrates
- Disposal of by product (nitrate) is still a problem
- Ion exchange removal cost $198 B USA
- RO removal cost $924 B USA

Broader benefits of affordable treatment

- Nitrogen fixation in regional Australia:
  - Up to tens of mg/L nitrate due to mulga
  - Up to hundreds of mg/L nitrate due to termites

Conclusions

1. Nitrates in drinking water worldwide are increasing due to increasing intensified farming and concomitant use of fertilisers
2. Evidence is accumulating that drinking water in nitrates causes colorectal cancer (CRC) at low levels (well below MAV)
3. The cost of colorectal cancer is high
4. More sophisticated farming practices are needed to prevent nitrate contamination
5. More research (especially data linkage between drinking water and cancer registries) is essential to review the MAV for nitrates in drinking water
6. Need cheaper methods to remove nitrates from water for both anthropogenically polluted groundwaters and areas with naturally elevated nitrate

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End

Contact Details

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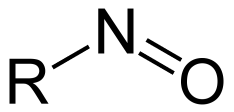
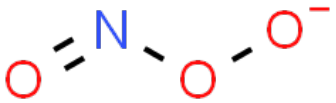
Hazards

Can form N-nitroso compounds (potential carcinogens):

general nitroso compound 

eg **ONOO**$^{-}$ peroxynitrite 

All can generate oxidative stress which can damage

DNA
Proteins
lipids
cell tissues
compromise function of organs eg liver

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Drinking water nitrate limit 11 times higher than it should be – NZ health expert

11.3mg/L to 1mg/L.

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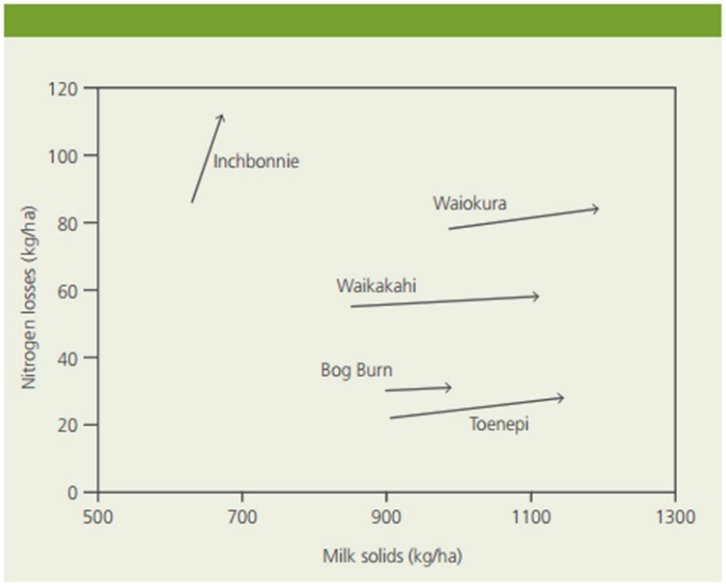
Is removal the only answer?



Data source: Monaghan and De Klein, 2014

Figure 4.1. 'Standard' mitigation techniques on dairy farms struggle to keep nitrogen losses from rising as productivity rises.

- Best practice farming mitigation techniques fail to reduce nitrate increase in groundwater
- Fertiliser use is driven strongly by powerful industry ($174 billion per annum)