HUS IN NEW ZEALAND –EPIDEMIOLOGY, CLINICAL ASPECTS AND OUTCOME DECEMBER 2015

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Where HUS can come from

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outline

- Headlines & outbreaks
- Epidemiology
- Clinical feature & treatment
- Results of NZ surveillance 1998-2014
- Demographics
  - Clinical features
  - Acute renal failure treatment
  - Outcomes at 12months post illness
- Long term outcomes

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German cucumber E.coli outbreak 'may last months'

The head of the German public health body tackling a deadly E.coli outbreak says it may be months before it stops.

Reinhard Burger, president of the Robert Koch Institute, told the BBC "we may never know" the infections' source.

He expressed sympathy for Spanish farmers affected by the false charge that their cucumbers were to blame.

More than 1,500 people have been infected by enterohaemorrhagic E.coli (EHEC), which can cause the deadly haemolytic-uraemic syndrome (HUS).

Seventeen people have died - 16 of them in Germany and one in Sweden.

Meanwhile, Russia has banned the import of fresh vegetables from European Union countries. A quarter of all

Spain says its farmers have lost millions of euros since being wrongly accused

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Bean sprouts to blame for E.coli outbreak

German-grown bean sprouts are the most likely cause of the deadly E.coli outbreak that has killed 22 people and made more than 2,000 ill across Europe, officials said last night.

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Case study

- PT, 22mo old from North Island -4 days of fever, loose bowel motions
- Bowel motions becoming blood stained by day 4 of symptoms
- Poor appetite

Past medical History – unremarkable

- On presentation to local hospital 28/09

lethargic, cool extremities, otherwise normal exam

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Progress

- Over next 48hrs, ongoing watery diarrhoea,
- Passing very little urine, stop passing urine 1100 on 1/10
- On call paediatric renal physician consulted at SCH – advice given to monitor kidney function, body chemistry with regular blood tests
  - Initial blood tests – Hb 97, platelets 32,000, Creatinine 174
- PICU contacted, transfer from local hospital arranged
- Transfer to Auckland uneventful
- Admitted to PICU – reduced LOC
- Acute peritoneal dialysis catheter inserted 2/10, and continuous dialysis started

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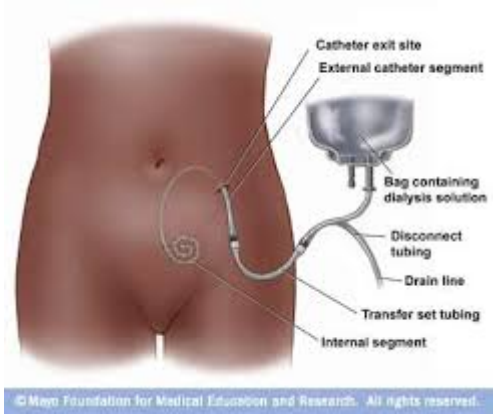
Progress



- Blood transfusions x 2
- Platelet transfusion x1
- Nasogastric tube feeding
- Returned to OR day 3 due to leaking from catheter exit site
- Received 12 days dialysis before sufficient recovery of kidney function to stop dialysis
- In hospital total – 18days

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Epidemiology

- Stx-E.coli colonise healthy cattle intestine, deer, goat, dogs, birds
- Found in manure, water troughs
- Humans infected from contamination of milk, water, meat, fruit, vegetables
- Recovery of organism is ~100% 0-2 days after diarrhoea onset, but only 33% 6 days after onset (J Infect Dis 1990)

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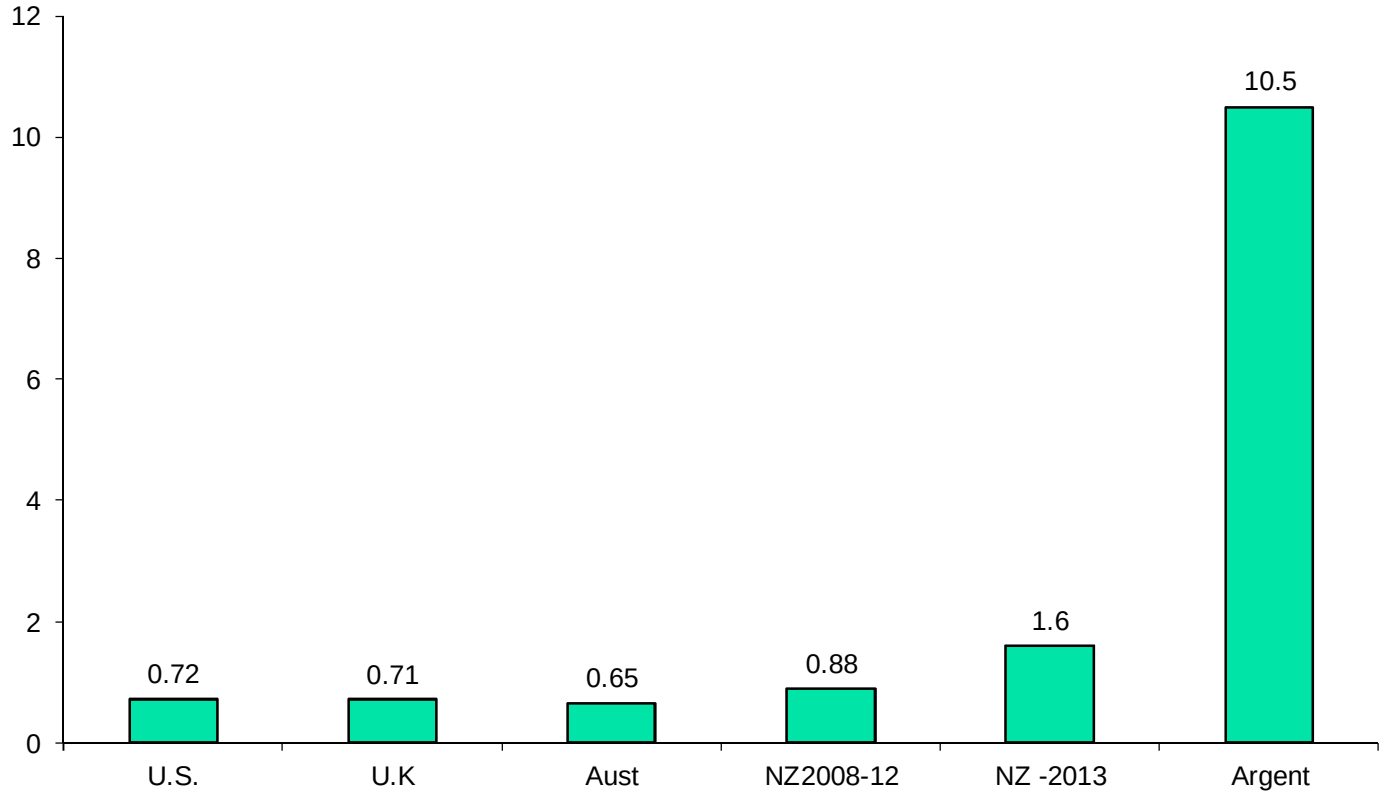
Comparative rates of HUS per 100,000 < age 15 across countries

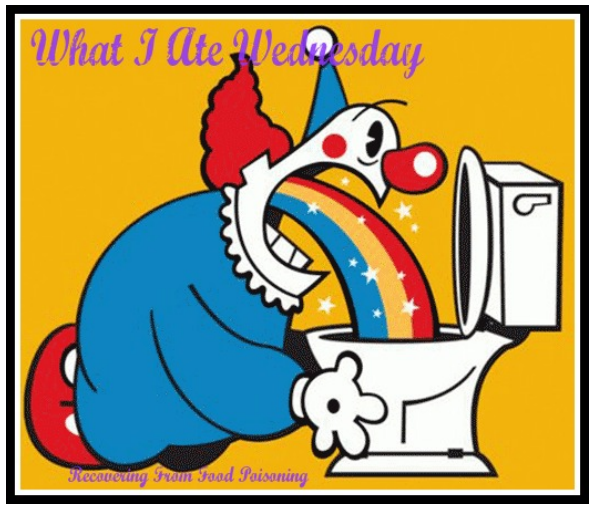


Emerg Inf Dis 2005,11:590-6
BMC Pub Health 2012;12:63
Int J Food Microbiol2004 96: 189–198,
NZPSU HUS surveillance

Rates in US and Australia vary state by state

Clinical presentation

- Average of 3-4 days between exposure and illness (up to 8d)
- Starts with crampy abdominal pain & diarrhoea
- Vomiting is common -30-60%
- Young children tend to excrete organism for more prolonged periods
- Increasing pallor, fever in 30%
- Diagnosis dependent on isolation of organism in stools and identification of Stx in tools or antibodies



Extra renal manifestations

- Haemorrhagic colitis – toxic megacolon – colon rupture
- Pancreatitis – exocrine and endocrine
- Hepatitis
- Haematological – anaemia, thrombocytopenia
- Neurologic – haemorrhage, stroke, coma seizures
- Myocardial ischemia

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Treatment D+HUS

- Supportive – careful fluid balance
  - Rbc transfusion
  - BP control
- Acute Dialysis
- Antibiotics – No established role
- Plasma exchange – No role
- FFP infusion – No role
- Eculizumab – No role

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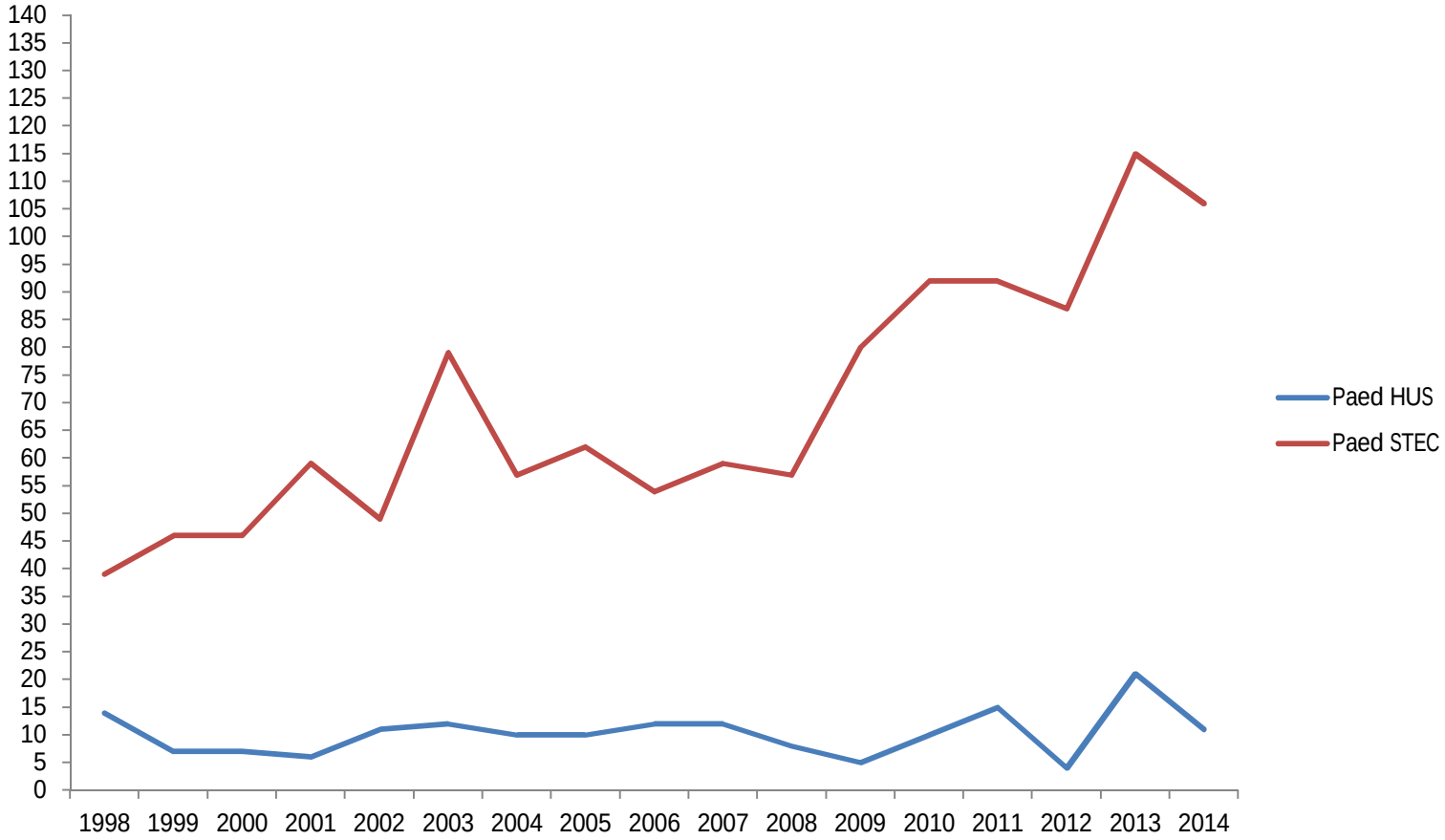
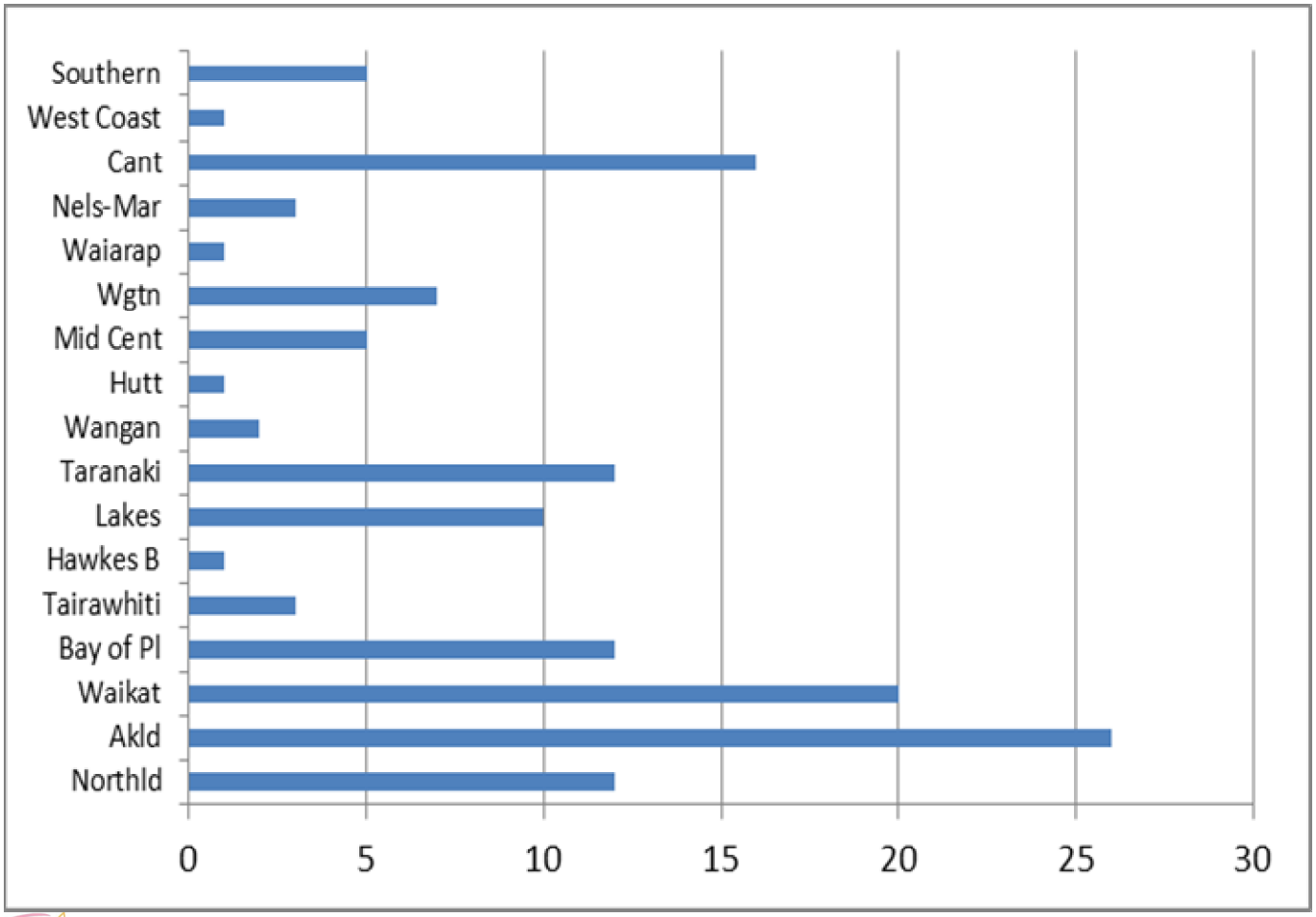
HUS and STEC isolation in children: 1998-2014



E coli 0157 first described in NZ 1993 – 11mo old with HUS

Distribution of D+ HUS by health region 1998-2013



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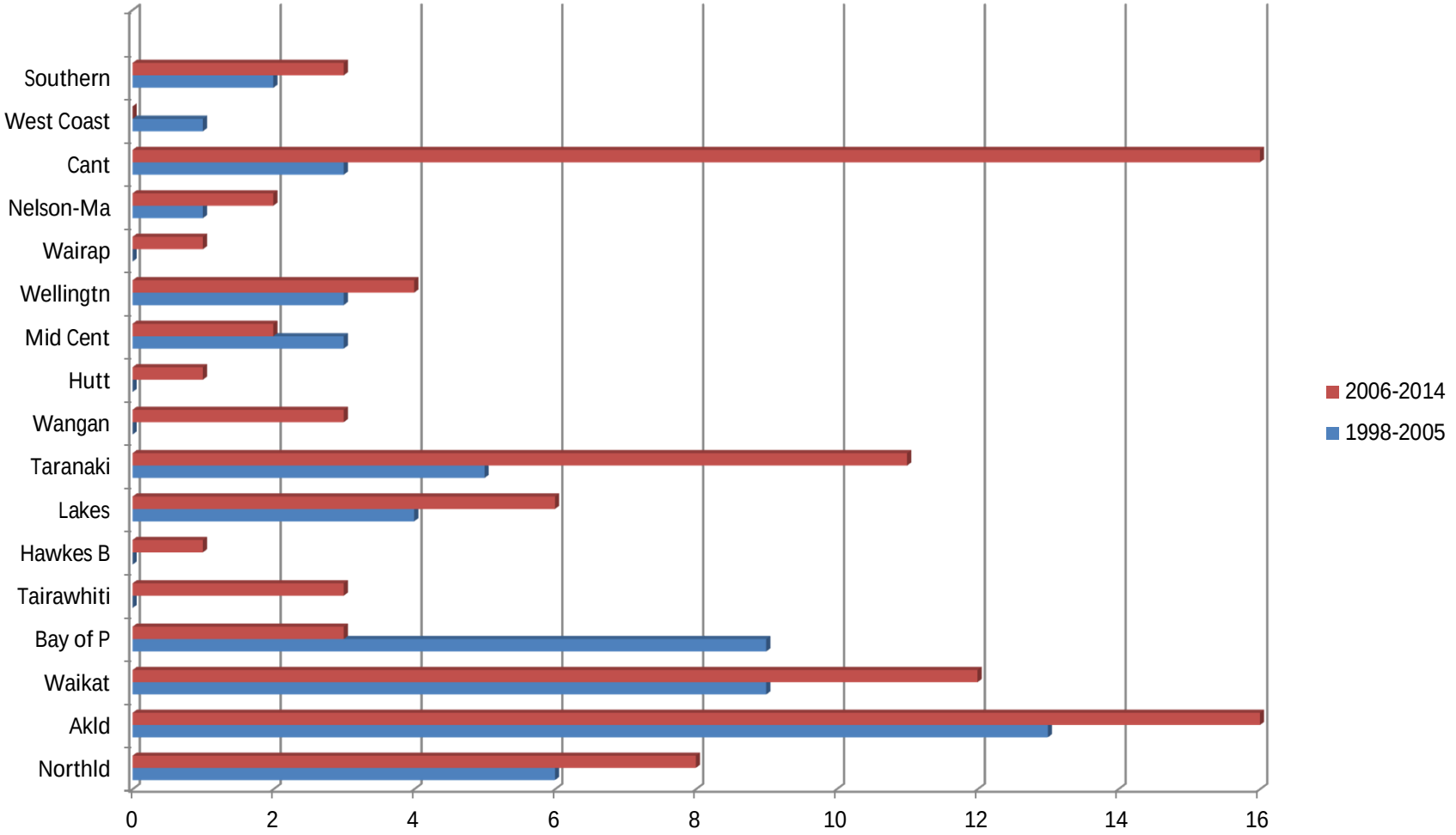
D+ Cases by Health region and era



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Demographics

- 150 children with diarrhoeal HUS reported (31.12.14)
- Females – 84 (56%)
- Mean age of group – 3.8yrs (3.3 -4.4 CI)
- Median age – 3yrs
- Age range – 0.3 – 14yrs

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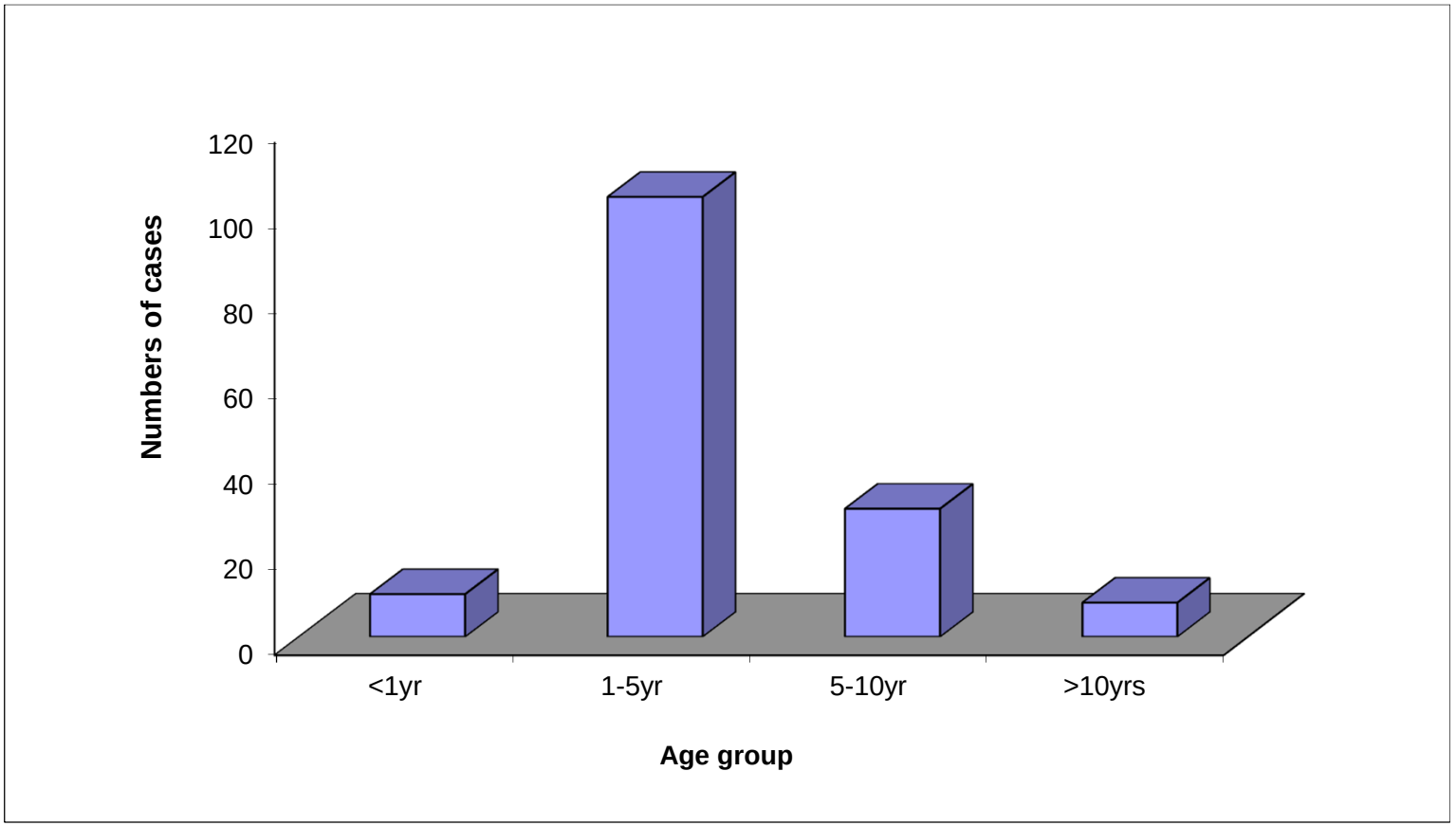
Age distribution of D+ patients (n=150)



Bacteriology & origin of infection causing D+HUS

- After 2009 additional information sought
  - Visit to farm within 2 weeks of illness
  - Residence on a farm
- 20/45 cases from farms/lifestyle blocks with animals/visited farm within 2 weeks
  - 3 cases implicated raw milk
- E coli 0157 isolation -54%
- Non E coli – Aeromonas, Campylobacter,

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Clinical features of D+HUS (n=150)

Clinical feature	n (%)
Vomiting	111 (80)
Bloody diarrhoea	97 (65)
Jaundice	20 (13)
Anaemia (at presentation)	145 (96)
Anuria	75 (50)
Seizures	14 (9)
Hypertension during illness	54 (37)

- Duration of symptoms before Diagnosis
  - Mean (days) – 6.5 (CI 5.9-7.2)
  - Median - 6
  - Range 1-25days

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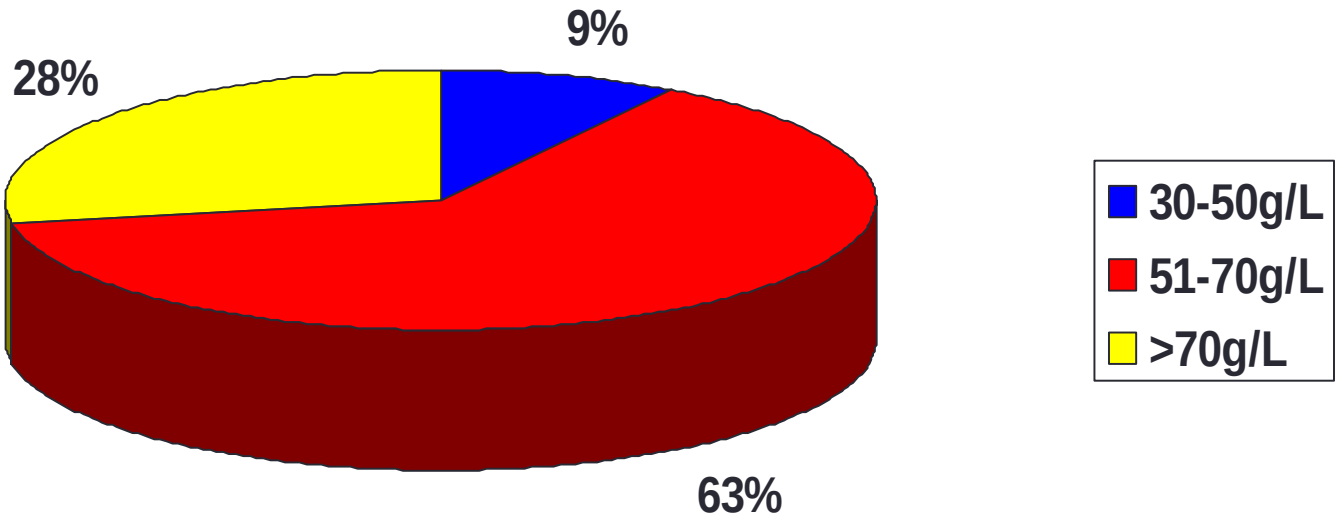
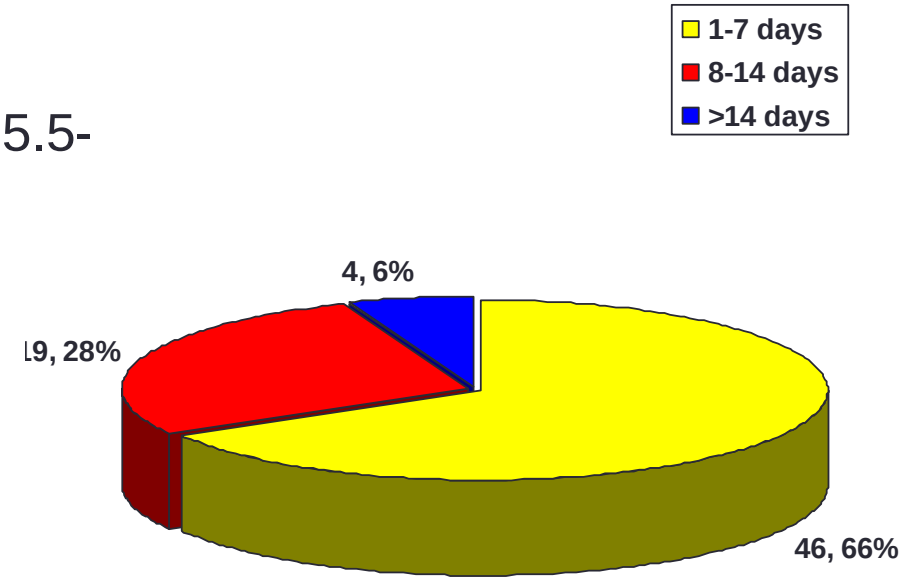
Severity of anaemia during illness



Kidney function

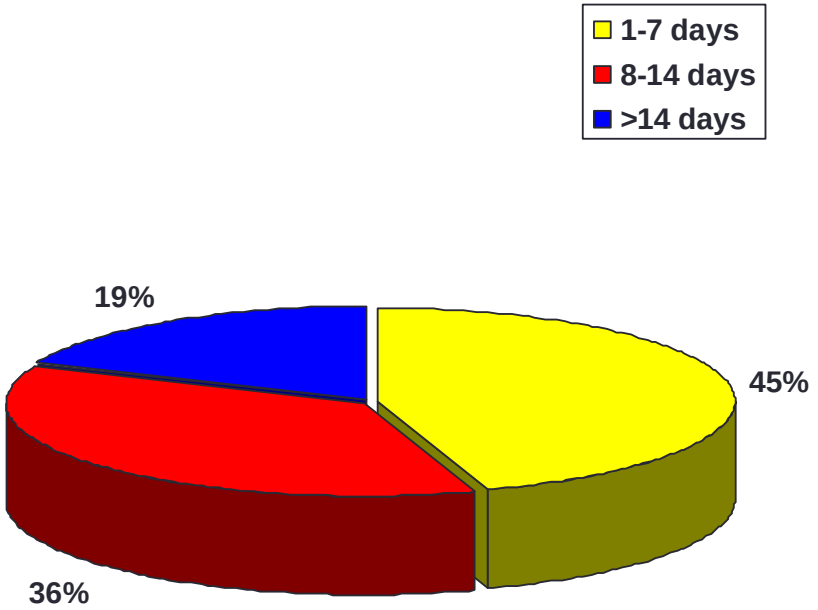
72/138 (52%)patients stopped passing urine

- Mean duration 6.6 (CI 5.5-7.7)
- Median 6 days
- Range 1-28



Acute dialysis

- 102 (74%) needed dialysis (mostly peritoneal dialysis)
- Dialysis duration
  - Mean 10.2 (CI 8.9.6-11.4)
  - Median 9 days
  - Range 2-38 days



Extra renal complications of initial illness in D+HUS

• Seizures	15
• Transient DM	1
• Cardiomyopathy	1
• Severe haemorrhagic colitis	3
• Intracranial haem	2
• Pancreatitis	1
• Death	2

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Follow up at 12 months

Abnormal urine sediment

- significant proteinuria defined ≥1+ or urine protein to creatinine ratio of >20mg/mmol
- Haematuria ≥ 1+ blood on urinalysis

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Results of D+HUS follow up

- 32/91 abnormal UA at mean of 12 months after initial illness
  - 8 nephrotic proteinuria or reduced GFR
- 2 isolated HTN
- renal biopsies in 2 with decreased GFR showed secondary FSGS

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What happens in the long term?

- Predictors of poor outcome
- clinical
  - Duration of dialysis
  - Severe brain involvement
  - Severe Gastro-intestinal disease
- Lab
  - Persistent proteinuria after the first year
  - Neutrophil count

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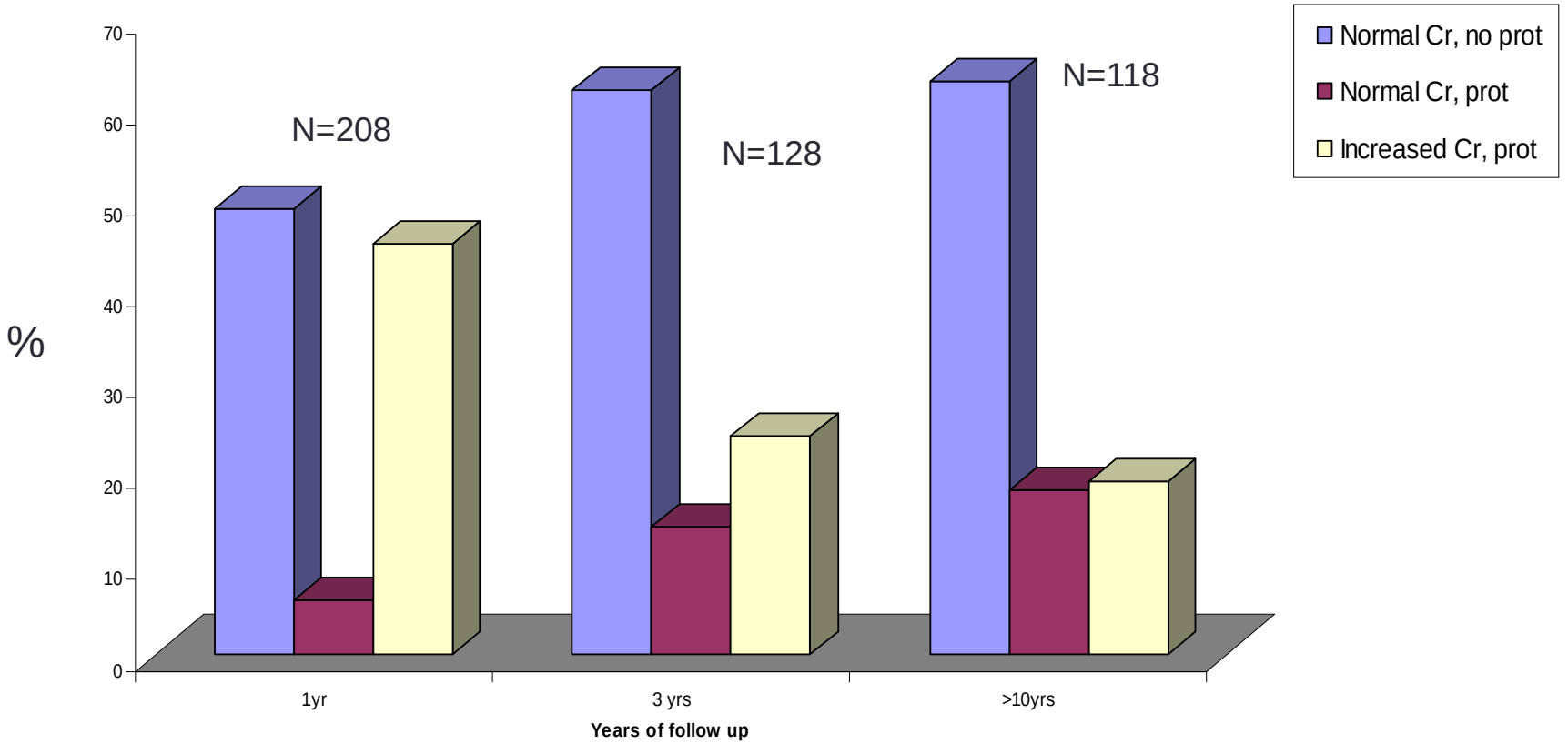
Renal status 1-10yrs after HUS



Kidney Int 1997 -Repetto

Long term prognosis –Walkerton outbreak

- Large outbreak of E coli related diarrhoea following water contamination after flooding 2000 SW Ontario
- 564 children developed gastroenteritis
- 24 developed HUS,
  - 19 followed 5 years later
  - None had significantly reduced renal function, hypertensive
  - 20% had micro-albuminuria vs 3% in controls

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Outcome of those severe enough to have dialysis

- 130 patients, mean follow up 12.2yrs, (5-30)
  - 83(63.9%) completely recovered
  - 27(20.8%) microalbuminuria
  - 15(11.5%) overt proteinuria –mean time to detection-103months
  - 5(3.8%) chronic renal failure

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Pediatr Nephrol 2007;22:1343-47

Prevention

- Public health and food hygiene education
  - Early diagnosis
  - Food preparation
  - Food storage
  - Adequate cooking

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Conclusions

- HUS is the single most common cause of acute kidney failure in NZ children needing acute dialysis
- E coli 0157 is the most common organism
- Seasonal pattern similar to Northern Hemisphere
- Cases are sporadic
- Most cases occur in the North Is, but more recently, cases have been appearing in the South Is as well most occurring in the 2nd era of the study

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