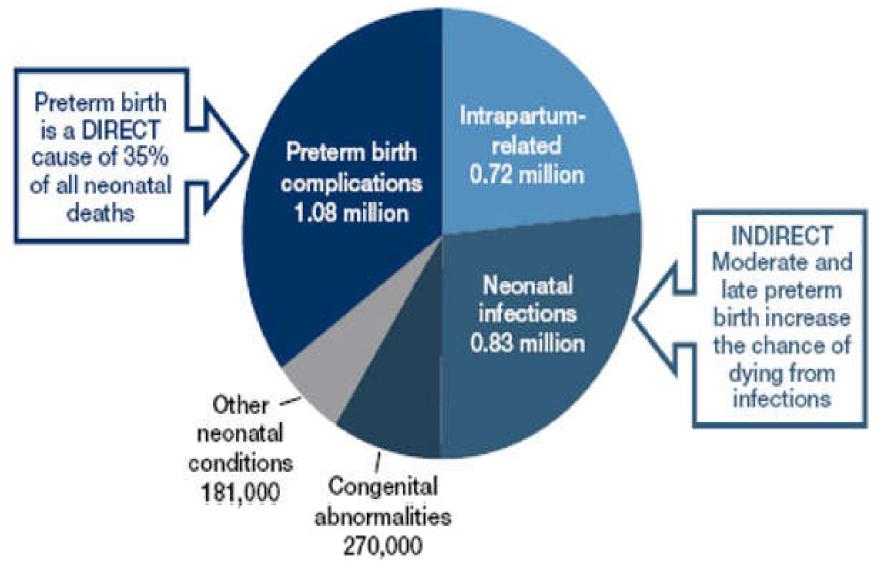
# ENTERAL NUTRION IN PRETERM NEONATES



Preterm birth is a risk factor for neonatal and postneonatal deaths At least 50% of all neonatal deaths are preterm

## ONG OUTCOME IN PRETERM

- Hospital re-admission
- Brain development
- Chronic diseases
- Behavioural and psychomotor problems
- **Respiratory function**



# Introdution

Proper nutrition is essential for Normal growth Immunity to infection Optimal neurologic and cognitive development Providing adequate nutrition to preterm infants is challenging because of several problems Immaturity of bowel function Inability to suck and swallow High risk of necrotizing enterocolitis (NEC) Illnesses that may interfere with adequate enteral feeding (e.g. RDS, PDA..)

# **Main questions**



- When to initiate enteral feeding
- Progession from minimal enteral feeding to nutritive feedings
- Bolus versus continuous feeding
- Choice of enteral formulation

# • When to initiate enteral feeding

• Progession from minimal enteral feeding to nutritive feedings

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# ry trophic feeding versus enteral fasting for very pre ry low birth weight infants (Review)

#### Morgan J, Bombell S, McG

rophic feeding defined as dilute or full strength feedings providing <= 25ml/kg/d for >= 5d (5 0 days)

- ropic feeding vs. no feeding (9 trials, N = 754): **NO SIGNIFICIANT DIFFERENCE** 
  - Days to full enteral feedings
  - The incidence of NEC
  - Mortality
  - Days of regain birth weight
  - Invasive infection
  - Days of phototherapy
  - Hospital stay

Tropic feeding vs. advancing feeding (one trial): infants given tropic feedings reqired more days of full enteral feeding and longer hospital stay. Tropic feeding were associated with a significiant reduction in NEC.

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# yed introduction of progressive enteral feeds to pre otising enterocolitis in very low birth weight infants Morgan J, Young L, McGuire V

The effect of delayed (more than 4 days after birth) versus earlie

ntroduction progressive enteral feeds (N = 1106): NO

### **SIGNIFICIANT DIFFERENCE**

- The incidence of NEC
- Mortality
- No intolerance
- The incidence of infection
- Hospital stav

rly or Delayed Enteral Feeding for Preterm owth-Restricted Infants: A Randomized Tria Alison Leaf et al

- Early (1 2 days) versus delayed (5 6 days) enteral feeding
- N = 404, 54 United Kingdom and Ireland hospitals)
  - Shorter duration of parental nutrition and high-dependency care
  - Lower incidence of cholestatic jaudice
  - Improved SD score for weight at discharge



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# v advancement of enteral feed volumes to preve otising enterocolitis in very low birth weight inf view) Morgan J, Young L, McGuire W

- trials, N = 949, slow (15 24 ml/kg/day) versus rapid rate
- 40 ml/kg/day) advancement of feedings:
  - Incidence of NEC
  - Mortality
  - Feeds intolerance ( causing interruption of enteral feeding)
  - Incidence of invasive infection

idence of necrotising enterocolitis

| pup                       | Slow rate                          | Fast rate                 | Risk Ratio       | Weight  | Risk Ratio           |               |
|---------------------------|------------------------------------|---------------------------|------------------|---------|----------------------|---------------|
|                           | n/N                                | n/N                       | M-H,Fixed,95% CI |         | M-H,Fixed,95% CI     |               |
|                           |                                    |                           |                  |         |                      |               |
|                           | 13/98                              | 8/87                      |                  | 25.7 %  | 1.44 [ 0.63, 3.32 ]  |               |
|                           | 0/26                               | 2/27                      |                  | 7.4 %   | 0.21 [ 0.01, 4.12 ]  |               |
|                           | 2/74                               | 4/84                      |                  | 11.4 %  | 0.57 [ 0.11, 3.01 ]  |               |
| 2010                      | 1/50                               | 2/50                      |                  | 6.1 %   | 0.50 [ 0.05, 5.34 ]  |               |
|                           | 5/46                               | 4/46                      |                  | 12.1 %  | 1.25 [ 0.36, 4.36 ]  | NO SIGNIFICIA |
|                           | 1/51                               | 7/47                      | -                | 22.1 %  | 0.13 [ 0.02, 1.03 ]  | DIFFERENC     |
| 2014                      | 1/15                               | 2/15                      |                  | 6.1 %   | 0.50 [ 0.05, 4.94 ]  |               |
|                           | 9/52                               | 2/50                      |                  | 6.2 %   | 4.33 [ 0.98, 19.05 ] |               |
|                           | 2/65                               | 1/66                      |                  | 3.0 %   | 2.03 [ 0.19, 21.85 ] |               |
| 6 CI)                     | 477                                | 472                       | +                | 100.0 % | 1.02 [ 0.64, 1.62 ]  |               |
| low rate), 32             | (Fast rate)                        |                           |                  |         |                      |               |
| i <sup>2</sup> = 10.83, d | f = 8 (P = 0.21); I <sup>2</sup> = | =26%                      |                  |         |                      |               |
| ect: Z = 0.08             | (P = 0.93)                         |                           |                  |         |                      |               |
| nost infants w            | ere extremely prete                | rm or extremely low bir   | th weight        |         |                      |               |
|                           | 9/52                               | 2/50                      |                  | 21.9 %  | 4.33 [ 0.98, 19.05 ] |               |
|                           | 1/51                               | 7/47                      |                  | 78.1 %  | 0.13 [ 0.02, 1.03 ]  |               |
| 6 CI)                     | 103                                | 97                        | +                | 100.0 % | 1.05 [ 0.44, 2.51 ]  |               |
| low rate), 9              | (Fast rate)                        |                           |                  |         | $\square$            |               |
| i <sup>2</sup> = 7.42, df | $= 1 (P = 0.01); 1^2 = 0.01$       | 37%                       |                  |         |                      |               |
| ect: Z = 0.11             | (P = 0.91)                         |                           |                  |         |                      |               |
| nost infants w            | ere small for gestatio             | onal age or growth restri | cted             |         |                      |               |
|                           | 0/26                               | 2/27                      |                  | 55.1 %  | 0.21 [ 0.01, 4.12 ]  |               |
| 2014                      | 1/15                               | 2/15                      |                  | 44.9 %  | 0.50 [ 0.05, 4.94 ]  |               |
| 6 CI)                     | 41                                 | 42                        |                  | 100.0 % | 0.34 [ 0.06, 2.04 ]  |               |
| ow rate), 4 (F            | ast rate)                          |                           |                  |         |                      |               |

#### lortality

| roup                | Slow rate  | Fast rate             | Risk Ratio       | Weight  | Risk Ratio            |                    |
|---------------------|--|-----------------------|------------------|---------|-----------------------|--------------------|
|                     | n/N  | n/N                   | M-H,Fixed,95% Cl |         | M-H,Fixed,95% Cl      |                    |
|                     |  |                       |                  |         |                       |                    |
|                     | 2/98   | 3/87                  | • • •            | 4.4 %   | 0.59 [ 0.10, 3.46 ]   |                    |
|                     | 12/26  | 7/27                  |                  | 9.6 %   | 1.78 [ 0.83, 3.81 ]   |                    |
| 2010                | 6/50   | 4/50                  |                  | 5.6 %   | 1.50 [ 0.45, 4.99 ]   |                    |
|                     | 4/46   | 3/46                  |                  | 4.2 %   | 1.33 [ 0.32, 5.63 ]   |                    |
|                     | 16/52  | 14/50                 | -                | 20.0 %  | 1.10 [ 0.60, 2.01 ]   |                    |
|                     | 13/51  | 19/47                 |                  | 27.7 %  | 0.63 [ 0.35, 1.13 ]   |                    |
| y 2014              | 3/15   | 0/15                  |                  | 0.7 %   | 7.00 [ 0.39, 124.83 ] |                    |
|                     | 28/65  | 20/66                 |                  | 27.8 %  | 1.42 [ 0.90, 2.25 ]   |                    |
| % CI)               | 403  | 388                   | +                | 100.0 % | 1.18 [ 0.90, 1.53 ]   |                    |
| Slow rate), 70      | (Fast rate)  |                       |                  |         |                       |                    |
| hi² = 8.46, df =    | = 7 (P = 0.29);   <sup>2</sup> =   | 7%                    |                  |         |                       |                    |
| fect: Z = 1.19      | (P = 0.23)   |                       |                  |         |                       |                    |
| most infants we     | and the second | m or extremely low b  | birth weight     |         |                       |                    |
|                     | 16/52  | 14/50                 |                  | 41.9 %  | 1.10 [ 0.60, 2.01 ]   | Faster rates of fe |
|                     | 13/51  | 19/47                 |                  | 58.1 %  | 0.63 [ 0.35, 1.13 ]   | advancement:       |
| % CI)               | 103  | 97                    | -                | 100.0 % | 0.83 [ 0.55, 1.25 ]   |                    |
| Slow rate), 33      | (Fast rate)  |                       |                  |         |                       | decrease mortality |
| $hi^2 = 1.68, df =$ | = 1 (P = 0.19); l <sup>2</sup> = 4   | 11%                   |                  |         |                       | ELBW               |
| fect: Z = 0.90      | (P = 0.37)   |                       |                  |         |                       | ELDVV              |
| most infants we     | ere small for gestatic   | nal age or growth res | tricted          |         |                       | 7                  |
|                     | 12/26  | 7/27                  |                  | 93.2 %  | 1.78 [ 0.83, 3.81 ]   |                    |
| y 2014              | 3/15   | 0/15                  |                  | 6.8 %   | 7.00 [ 0.39, 124.83 ] |                    |
| % CI)               | 41   | 42                    |                  | 100.0 % | 2.13 [ 1.02, 4.47 ]   |                    |
| Slow rate), 7 (I    | Fast rate)   |                       |                  |         |                       |                    |
| hi² = 0.87, df =    | = 1 (P = 0.35); l <sup>2</sup> =0  | ).0%                  |                  |         |                       |                    |

advancement of enteral feed volumes to prevent necrotising enterocolitis in very low birth weight infants

I Slow versus faster rates of feed advancement

eeds intolerance (causing interruption of enteral feeding)

## SIGNIFICIANT DIFFERENCE

| N n/N<br>6 14/27<br>0 8/50<br>6 11/46<br>1 19/47<br>2 19/50 | M-H,Fb    | ked,95% Cl                                | 15.5 %<br>9.0 %<br>12.4 %<br>22.3 %<br>21.8 %               | M-H,Fixed,95% Cl<br>1.26 [ 0.80, 1.99 ]<br>1.50 [ 0.67, 3.35 ]<br>1.18 [ 0.59, 2.36 ]<br>0.97 [ 0.60, 1.58 ] |
|---|-----------|---|---|--|
| 0 8/50<br>6 11/46<br>1 19/47<br>2 19/50                     |           |   | 9.0 %<br>12.4 %<br>22.3 %                                   | 1.50 [ 0.67, 3.35 ]<br>1.18 [ 0.59, 2.36 ]<br>0.97 [ 0.60, 1.58 ]  |
| 6 11/46<br>1 19/47<br>2 19/50                               |           |   | 12.4 %<br>22.3 %  | 1.18 [ 0.59, 2.36 ]<br>0.97 [ 0.60, 1.58 ]   |
| 1 19/47<br>2 19/50  |           |   | 22.3 %  | 0.97 [ 0.60, 1.58 ]  |
| 2 19/50   |           |   |   |  |
|   |           |   | 21.8%   | 121 50 77 102 5  |
|   |           |   | 2110 70   | 1.21 [ 0.77, 1.92 ]  |
| 5 5/15  | •         | •   | 5.6 %   | 0.80 [ 0.27, 2.41 ]  |
| 5 12/66   | 3 <u></u> | • •                                       | 13.4 %  | 1.44 [ 0.75, 2.77 ]  |
| 5 301   |           | -   | 100.0 %   | 1.20 [ 0.95, 1.50 ]  |
|   |           |   |   | $\square$  |
| 3); l <sup>2</sup> =0.0%                                    |           |   |   |  |
|   |           |   |   |  |
| e   |           |   |   |  |
|   | 16        |   |   |  |
| -   |           | <b>5 301</b><br>93); I <sup>2</sup> =0.0% | 5 301<br>93); 1 <sup>2</sup> =0.0%<br>le<br>0.5 0.7 1 1.5 2 | 5 301<br>93); 1 <sup>2</sup> =0.0%<br>le<br>0.5 0.7 1 1.5 2  |

### **NO INTOLERANCE**

advancement of enteral feed volumes to prevent necrotising enterocolitis in very low birth weight infants

Slow versus faster rates of feed advancement

cidence of invasive infection



| roup             | Slow rate                 | Fast rate | Risk Ratio  | Weight  | Risk Ratio          |
|------------------|---------------------------|-----------|---|---------|---------------------|
| 129              | n/N                       | n/N       | M-H,Fixed,95% Cl  | 2510    | M-H,Fixed,95% Cl    |
|                  | 10/46                     | 6/46      |   | 14.2 %  | 1.67 [ 0.66, 4.21 ] |
| y 2010           | 5/50                      | 4/50      |   | 9.5 %   | 1.25 [ 0.36, 4.38 ] |
|                  | 24/65                     | 17/66     |   | 39.9 %  | 1.43 [ 0.85, 2.41 ] |
| iy 2014          | 4/15                      | 2/15      |   | 4.7 %   | 2.00 [ 0.43, 9.32 ] |
|                  | 9/51                      | 9/47      |   | 22.1 %  | 0.92 [ 0.40, 2.12 ] |
|                  | 10/52                     | 4/50      | - • - ·   | 9.6 %   | 2.40 [ 0.81, 7.17 ] |
| CI)              | 279                       | 274       | •   | 100.0 % | 1.46 [ 1.03, 2.06 ] |
| (Slow rate), 4   | 2 (Fast rate)             |           |   |         |                     |
| $hi^2 = 2.27, c$ | $f = 5 (P = 0.81); 1^2 =$ | 0.0%      |   |         |                     |
| ffect: Z = 2.1   | 2 (P = 0.034)             |           |   |         |                     |
| o differences:   | Not applicable            |           |   |         |                     |
|                  |                           |           |   |         |                     |
|                  |                           |           | 0.1 0.2 0.5 1 2 5 10<br>Favours slow rate Favours fast rate |         |                     |

#### 

## Bolus or continuous tube feeding

# ntermittent bolus milk for premature infant less han 1500gram, 2008 Cochrane collaboration

- 7 trials, N= 511, found no differences in time to achieve full enteral.
- No significiant difference in somatic growth and incidence of NEC

### Authors' conclusions:

Small sample sizes, methodologic limitations, inconsistencies in controlling variables that may affect outcomes, and conflicting esults of the studies to date make it difficult to make universal ecommendations regarding the best tube feeding method for premature infants less than 1500 grams. The clinical benefits and isks of continuous versus intermittent nasogastric tubemilk eeding cannot be reliably discerned from the limited information available from randomised trials to date.



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# oiotics for prevention of necrotizing enterocolit erm infants (Review)

Compare probiotics versus placebo: 24 trials

- Reduced the incidence of severe NEC(stage II III): RR 0,43 (95% CI 0.33 0.56, 20 trials, N = 5529)
- Reduced mortality: RR 0.65 (95% CI 0.52 0.81, 17 trials, N = 5112)
- Nosocomial sepsis : no difference RR 0.91 (95% CI 0.80 1.03, 19 trials, N = 5338)
- Lactobacillus alone or in combination with Bifidobacterium: effective

## ENTERAL FEEDING JpToDate (2016)

The final goal: 160 ml/kg/days( PN stop when enteral feeds 00ml/kg/day)

1000g:

- Day 1 3: 15 ml/kg/day
- Day 4: increase 15 ml/kg/day

001 - 1500g:

- Day 1 2: 20 ml/kg/day
- Day 3: increase 20 ml/kg/day

501 - 1800g:

- Day 1: 25 ml/kg/day
- Increase 25 ml/kg/day

## ENTERAL FEEDING John Hunter Children's Hospital (2013)

| BW            | Initial feeding<br>(ml/kg/day) | Increasing<br>(ml/kg per 12<br>hours) |
|---------------|--------------------------------|---------------------------------------|
| < 1000 g      | 10                             | 10                                    |
| 1001 - 1250 g | 10 - 20                        | 10                                    |
| 1251 - 1500 g | 20 - 30                        | 10 - 15                               |
| 1501 - 1800 g | 30                             | 15                                    |
| 1901 2500 a   | 20 40                          | 15 20                                 |

#### ichnes for recumg very how birth weight in

on of Neonatology, Department of Pediatrics, McMaster University Children's H

- Time to full feeding (150 180 ml/kg/day)
  - < 1kg: 2 weeks
  - ≥1kg: 1 week
- nitial and increasing feeding
  - < 1kg: 15 20 ml/kg and increase 15 20 ml/kg/day</li>
  - ≥ 1kg: 30 ml/kg and increase 30 ml/kg/day
- The frequency of feeding:
  - < 1250g: every 2 hours</li>
  - $\geq$  1250g: every 3 hours

## **ASSESSMENT OF FEED TOLERANCE**

- Nause, vomiting
- Abdomen : distension, pain, visible bowel loops
- Gastric residuals: GRV, green, yellow, brown
- Stool: diarrhea, bloody
- Symptoms : apnea, bradycardia, temperature instability

# eeding preterm or low birth weight infants 2008 Cochrane Collaboration

- There are no data from randomised trials of formula milk versus maternal breast milk for feeding preterm or low birth weight infants.
- Maternal breast milk remains choice of enteral nutrition because observational studies, and meta-analyses of trials comparing feeding with formula milk versus donor breast milk, suggest that feeding with breast milk has major nonnutrient advantages for preterm or low birth weight infants.

# oreterm infants: systematic review and metaanalysis. Cochrane collaboration 2006

#### 7 trials, N 471

- Lower risk of NEC in infants receiving donor breast milk (RR 0.1, 95% CI 0.06-0.76)
- Donor breast milk: slower growth in the early postnatal period, but its long-term effect is unclear

## Multi-nutrition fortification of breast milk for preterm infants, Cochrane 2016

#### 14 trials, N 1071

Increase growth rates preterm infants during their initial hospital admission (low-quality evidence)

# **Breastfeeding**

#### luman milk:

- Reduce rates of sepsis, NEC
- Fewer hospital readmissions
- Vitamins or minerals: vit A, vit D, Vit K, iron, zinc, calcium and phosphorus

**HMF** product

# CONCLUSION

- Early initiation of enteral nutrtion
- Advancement of feeds depend on gestational age and
- birth weight
- Use of approriate enteral products
- Monitoring of growth and nutrition

