



LOW DOSE NALTREXONE IN PREGNANCY

COMPARISON OF OUTCOMES BETWEEN USERS AND
NON-USERS DURING PREGNANCY

DR. PHIL BOYLE MICGP, MRCGP, CFCMC

WWW.NAPRO.IE

NALTREXONE IN PREGNANCY

- What is the story?.....
- Why would you want to use it?

NALTREXONE IN PREGNANCY

- Fertility Clinic
- Immediate goal is to improve health
 - Fatigue, PMS, Low mood, Anxiety, Difficulty sleeping
- Diet, LDN, Supplements – combined positive health effect

NALTREXONE IN PREGNANCY

- 2006 - Clinically miscarriages and premature delivery were more likely when we stopped LDN in pregnancy.
- Health gains from LDN were lost during pregnancy when we stopped medication and we had less favourable outcomes



NALTREXONE IN PREGNANCY

- Real concern about any medications in Pregnancy

THALIDOMIDE IN PREGNANCY

- Thalidomide
 - “Perfectly safe”
 - Relieves morning sickness
- 1957 Germany
- 1958 UK





DIETHYLSTILBESTROL (DES) IN PREGNANCY

- Diethylstilbestrol (DES) Synthetic oestrogen
 - 1940 to 1971
 - Given to pregnant women to try and reduce the risk of miscarriage
 - 1947 FDA Approved
 - Estimated 3 million women used it in USA

DIETHYLSTILBESTROL (DES) IN PREGNANCY

- 1971 – Proven to cause **clear cell carcinoma**, a rare vaginal tumor in girls and women who had been exposed to this drug *in utero*
- *24 years after FDA approval!*



DIETHYLSTILBESTROL (DES) IN PREGNANCY

First Generation

- **Breast Cancer risk increased**

Second Generation

- **Vaginal adenocarcinoma** x 40
- **Breast Cancer**
- **Abnormal repro organs**
 - **Infertility & miscarriage**



DIETHYLSTILBESTROL (DES) IN PREGNANCY

Third Generation

- Epigenetic changes in gene expression
- Trans generational effects



NALTREXONE IN PREGNANCY — WWW.MEDICINES.IE JAN 2016

- Animal studies do not suggest a teratogenic effect
- No experience of use during human pregnancy.

NALTREXONE IN PREGNANCY — WWW.MEDICINES.IE JAN 2016

- Animal studies do not suggest a teratogenic effect,
- No experience of use during human pregnancy.
- That is not entirely true.....



NALTREXONE IN PREGNANCY — WWW.MEDICINES.IE JAN 2016

- Animal studies do not suggest a teratogenic effect,
- No experience of use during human pregnancy.
- The drug should only be **used in pregnancy or lactation if considered essential by the physician.**



NALTREXONE IN PREGNANCY

- Clinically Dr. Hilgers, Omaha, NE, USA was using doses up to 100mg Naltrexone safely in pregnancy
- **Naltrexone in the treatment of opioid-dependent pregnant women:** [Jones HE¹](#), [Chisolm MS](#), [Jansson LM](#), [Terplan M](#). [Addiction](#). 2013 Feb;108(2):233-47

NALTREXONE IN PREGNANCY

- BUT – this is high dose naltrexone (HDN) which has a very different clinical effect to low dose naltrexone (LDN)
- HDN – blocks opioid activity
- LDN – promotes optimal opioid activity – clinically many benefits

NALTREXONE IN PREGNANCY — WWW.NAPRO.IE

- Clinically we observed more benefit with LDN in pregnancy
 - Auto-immune conditions
 - Recurrent miscarriage
 - Endometriosis
 - Polycystic Ovaries
 - Clinical endorphin deficiency — PMS, Fatigue, low mood, anxiety, brown bleed



NALTREXONE IN PREGNANCY — WWW.NAPRO.IE

- 50% of our patients take Low Dose Naltrexone (3 to 4.5mg nightly) often throughout pregnancy

NALTREXONE IN PREGNANCY — WWW.MEDICINES.IE

- Nothing published in literature
 - to support our practice
 - to encourage other doctors to do the same

LDN IN PREGNANCY – PATIENT SURVEY 2016

Questions

1. Is it safe to take LDN during pregnancy?
2. Are there additional benefits to mum or baby from taking LDN in pregnancy?
3. How long should you take LDN during pregnancy?

LDN IN PREGNANCY – PATIENT SURVEY 2016

Survey Design

<https://www.surveymonkey.com/r/LDNinPregnancy>

1. 39 questions in total
2. Anonymous – not possible to identify patients
3. Focus on safety and patient experience – positive or negative

LDN IN PREGNANCY – PATIENT SURVEY 2016

Survey Design - Deficiencies

1. Did not collect important data on
 1. Female age
 2. Duration of infertility
 3. Previous pregnancy history – miscarriage or prematurity
 4. Previous fertility treatment
2. Caution when interpreting data or drawing conclusions

Q1: DID YOU HAVE A SUCCESSFUL PREGNANCY WITH NAPRO FERTILITYCARE?

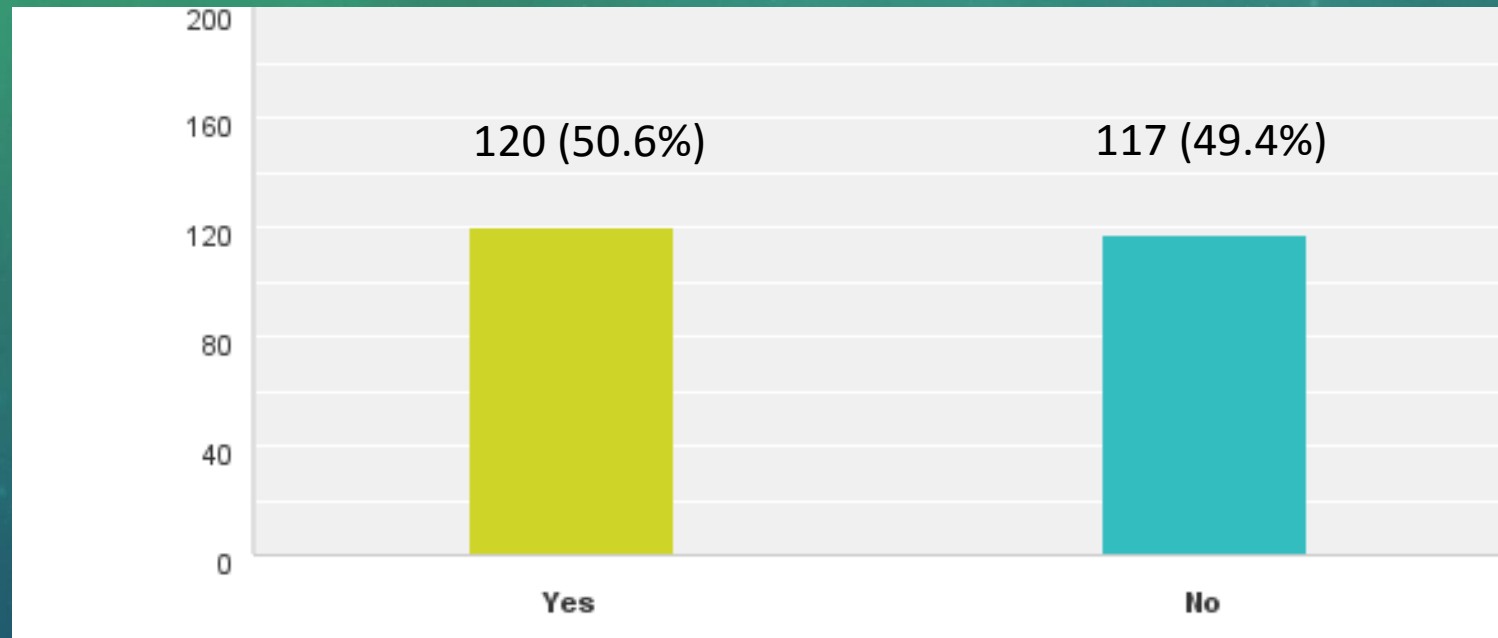
Response Rate

67% of full list

79.5% of opened e mails

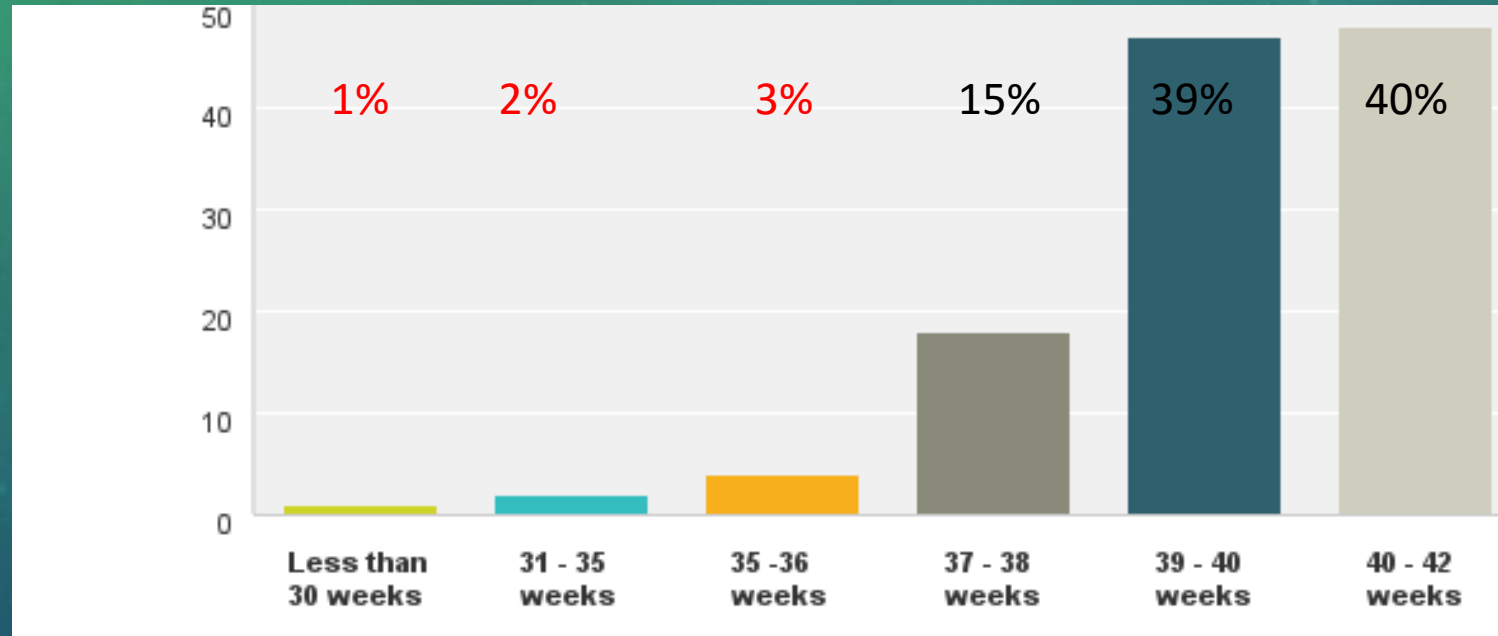
- 237 Successful pregnancies (11 miscarriages)
- **117 Did not use LDN** in Pregnancy (49.4%)
- **120 Used LDN** in Pregnancy (50.6%)

Q4: DID YOU TAKE LDN (LOW DOSE NALTREXONE) DURING PREGNANCY?



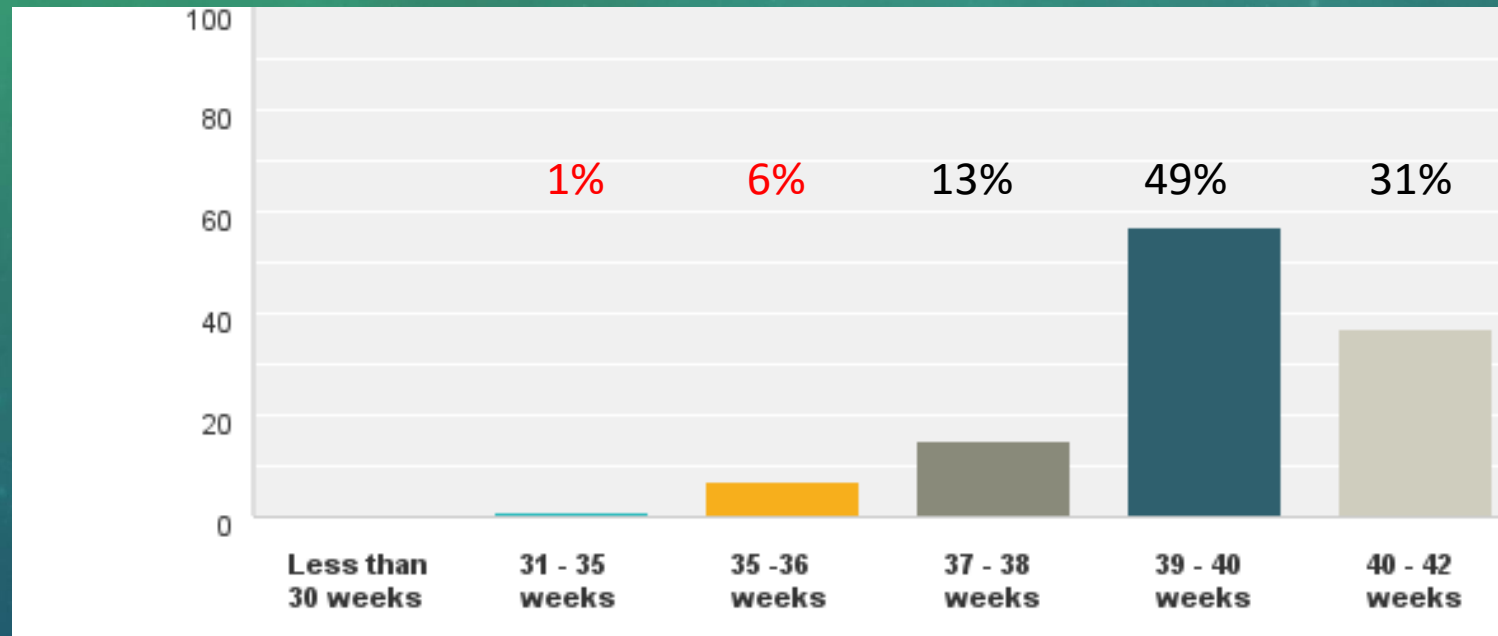
- Answered: 237 Skipped: 0

Q17: AT HOW MANY WEEKS WAS YOUR BABY BORN AT?



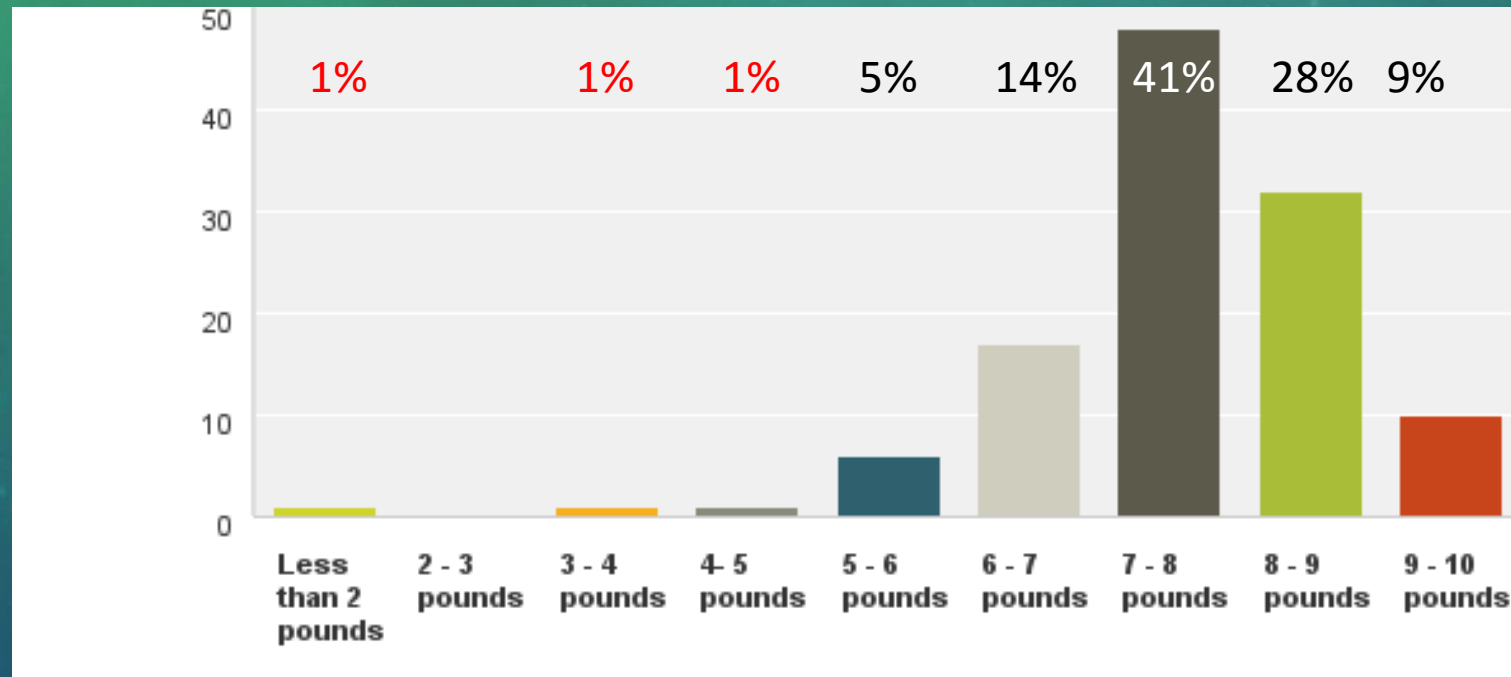
- Answered: 120 Used LDN

Q17: AT HOW MANY WEEKS WAS YOUR BABY BORN AT?



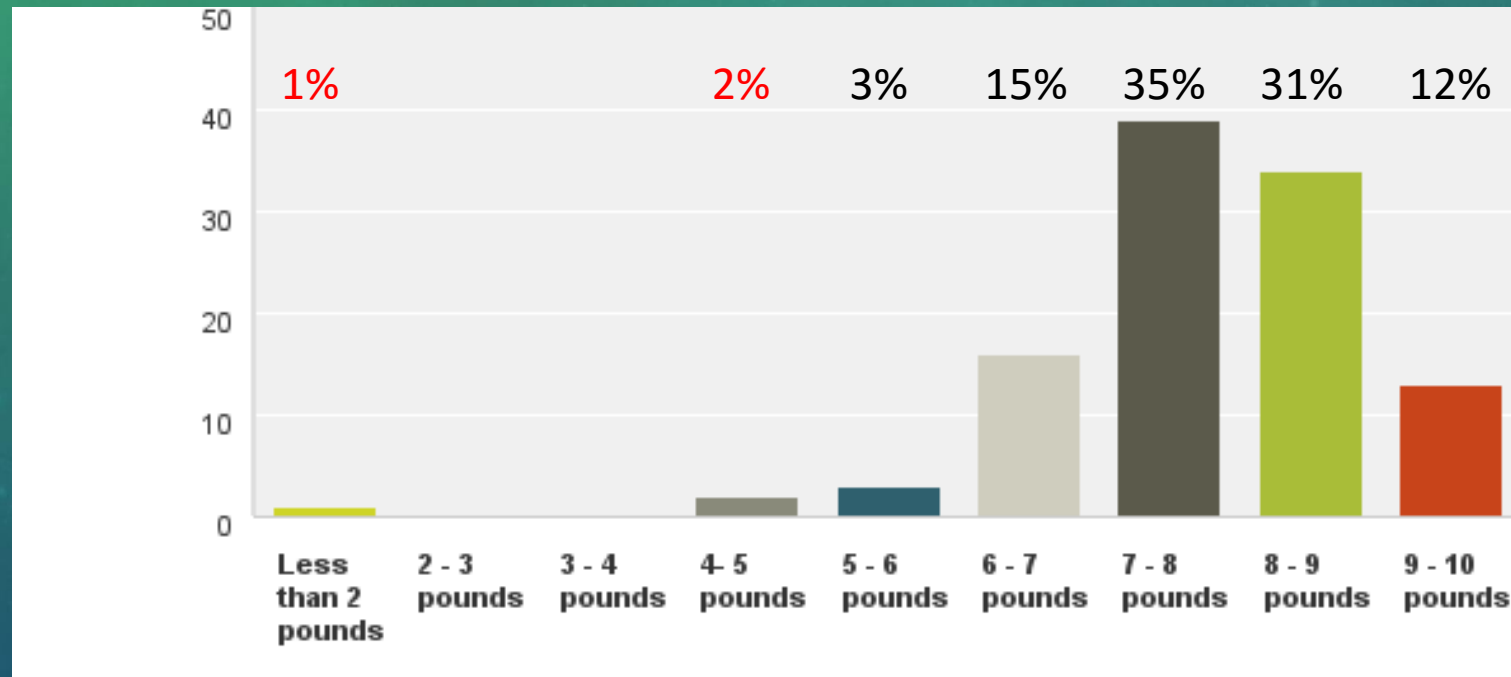
- Answered: 117 No LDN

Q19: WHAT WAS YOUR BABY'S BIRTH WEIGHT? (POUNDS AND OUNCES)



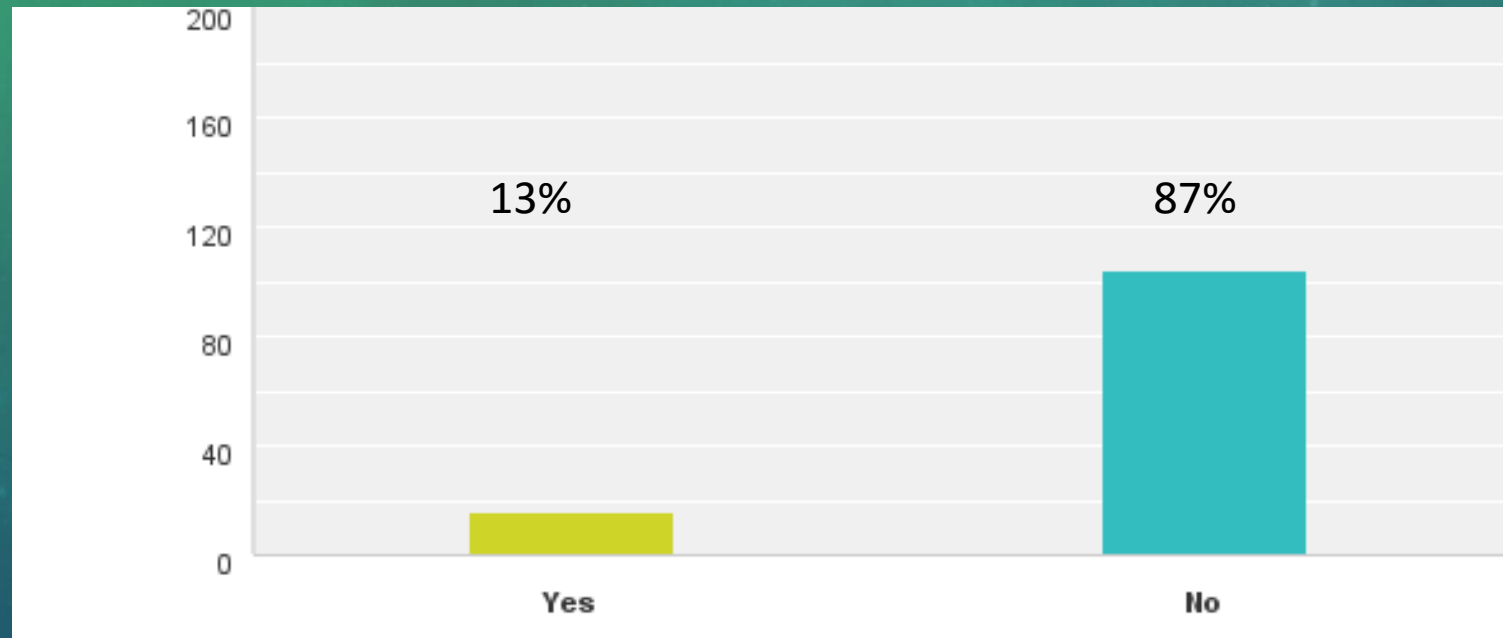
- Answered: 116 Skipped: 4 Used LDN

Q19: WHAT WAS YOUR BABY'S BIRTH WEIGHT? (POUNDS AND OUNCES)



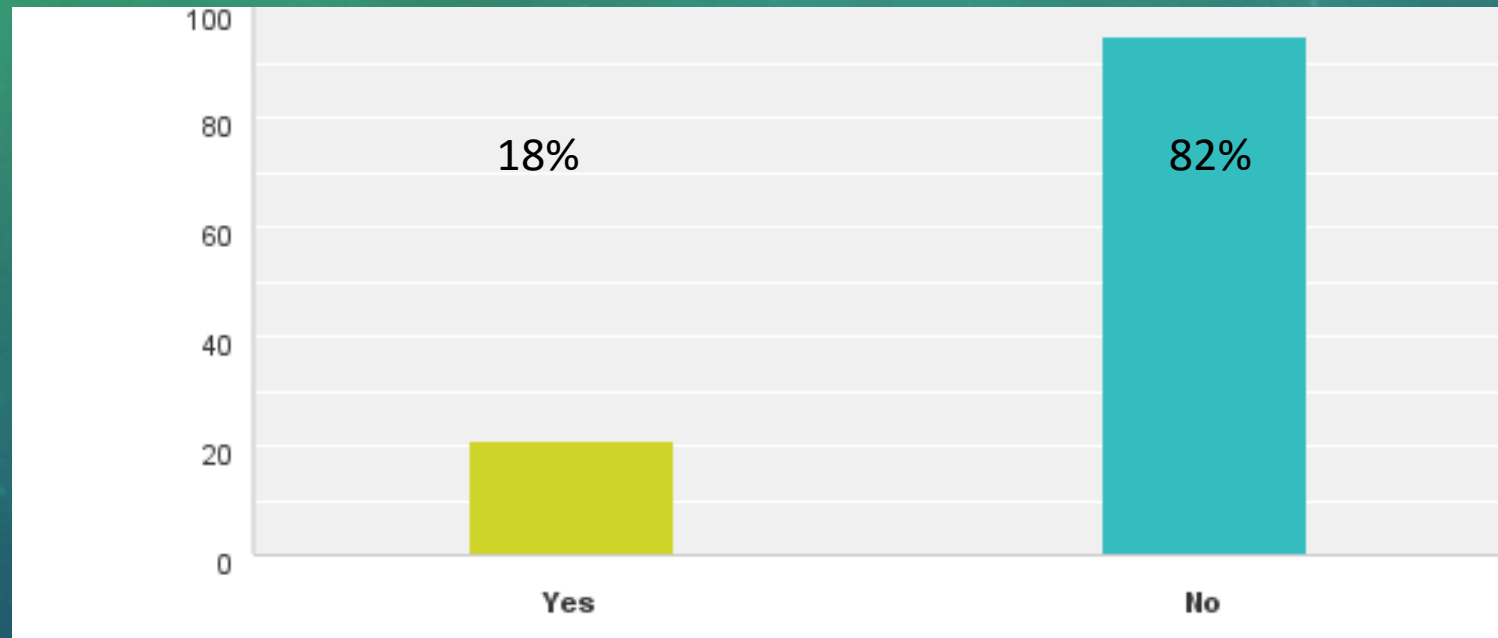
- Answered: 108 Skipped: 9 No LDN

Q21: WAS YOUR BABY IN SPECIAL CARE BABY UNIT?



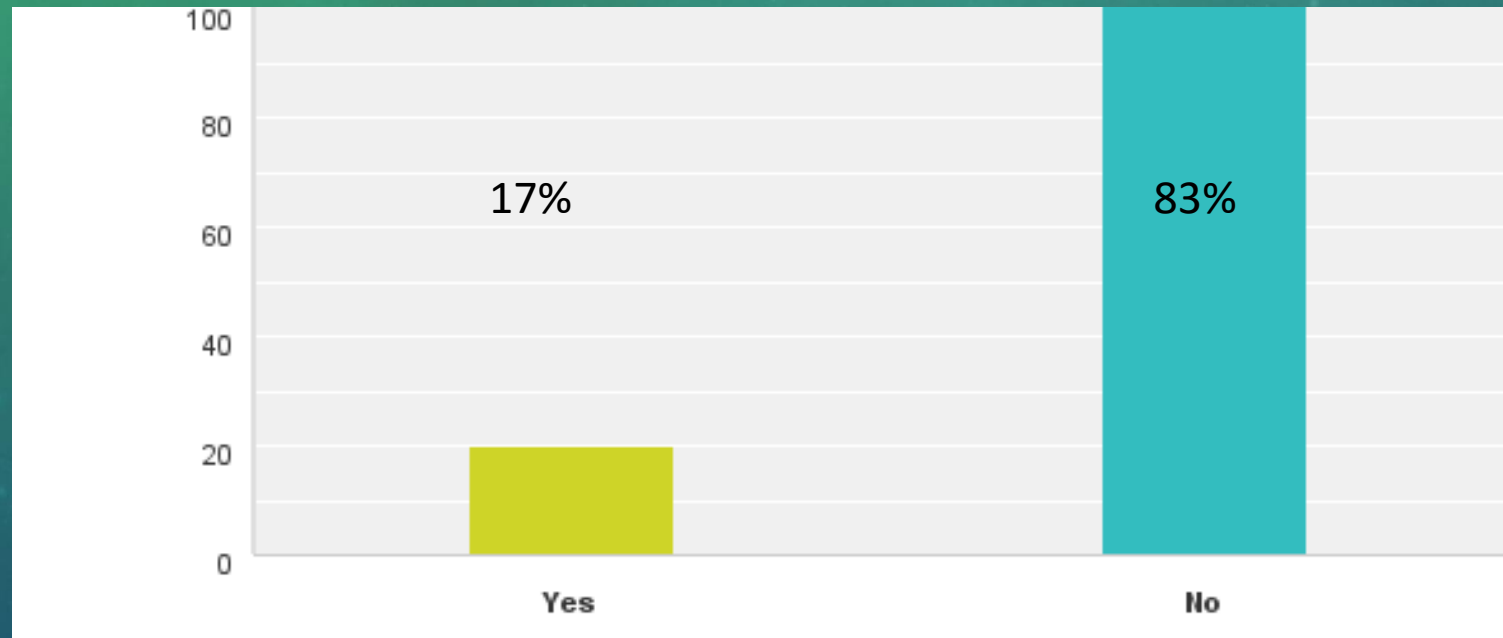
- Answered: 120 Used LDN

Q21: WAS YOUR BABY IN SPECIAL CARE BABY UNIT?



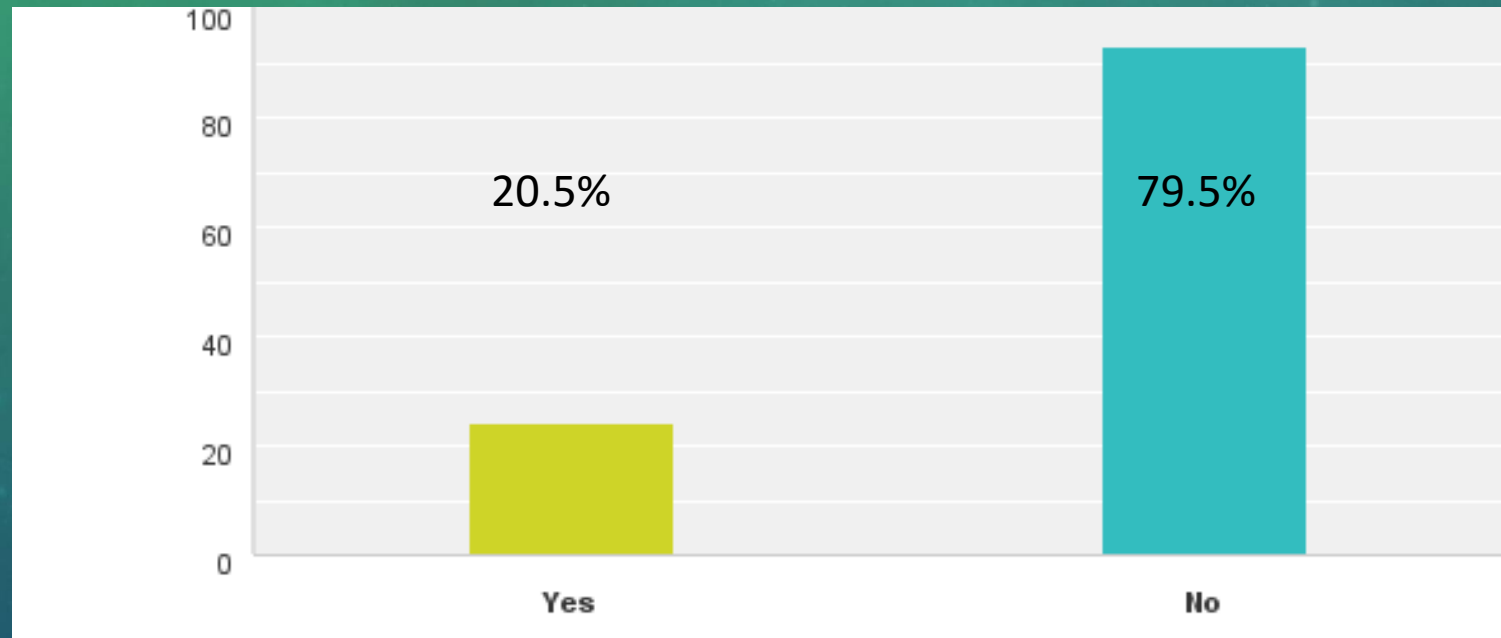
- Answered: 116 Skipped: 1 **No** LDN

Q23: DID YOU HAVE ANY COMPLICATIONS AFTER DELIVERY?



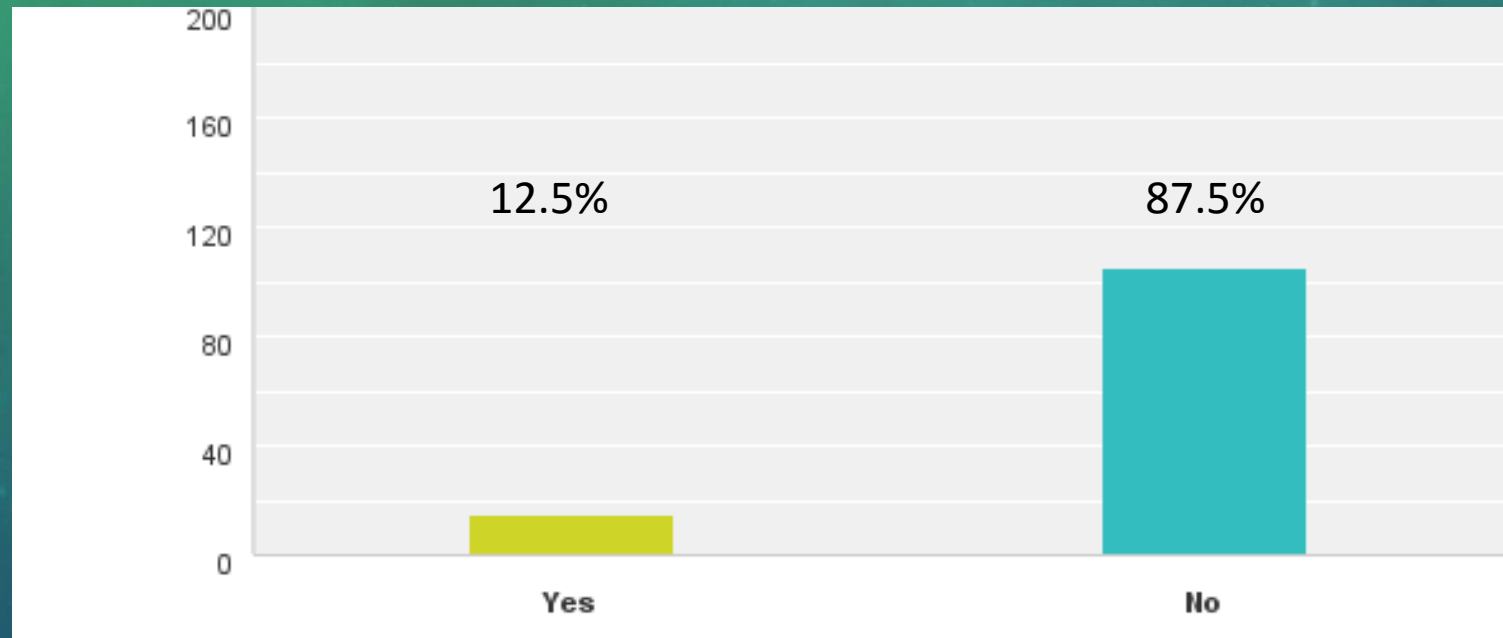
- Answered: 120 Used LDN

Q23: DID YOU HAVE ANY COMPLICATIONS AFTER DELIVERY?



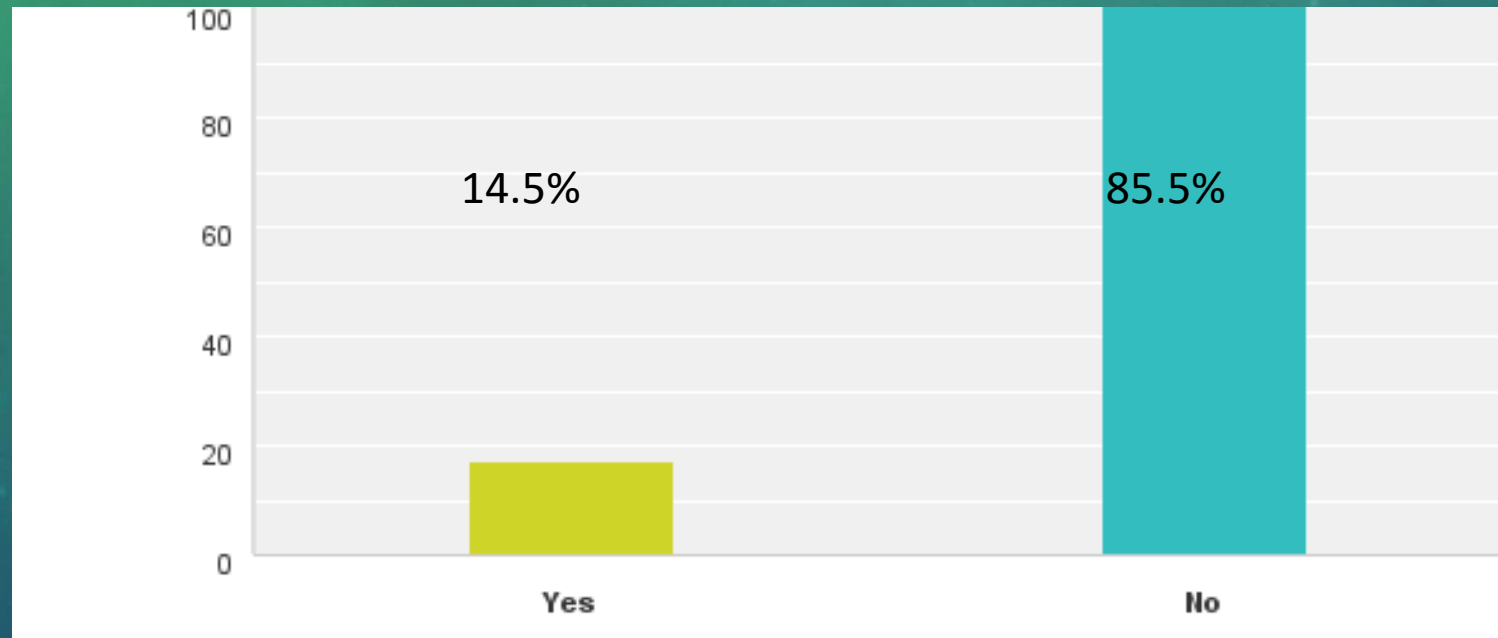
- Answered: 117 Skipped: 0 **No LDN**

Q25: DID YOUR BABY HAVE ANY COMPLICATIONS AFTER DELIVERY?



- Answered: 120 Used LDN

Q25: DID YOUR BABY HAVE ANY COMPLICATIONS AFTER DELIVERY?



- Answered: 117 Skipped: 0 **No LDN**

#	Responses	Date
1	Low sats(?) on day 2 In hindsight I think they may have been related to painkillers I was on at the time (Tylex)	12/14/2015 4:20 PM
2	When he was 2 days old he had a high temp and low glucose, we were both still in hospital,he was taken to the special care unit for 24hrs,put on iv antibiotics and fluids	12/12/2015 4:22 PM
3	Blocked salivary duct, 5 days of IV antibiotics	12/12/2015 4:01 PM
4	congenital anomaly Tongue tie	12/10/2015 8:18 PM
5	Comb s positive jaundice	12/9/2015 9:44 PM
6	Low blood sugars	12/8/2015 10:20 PM
7	No complications, had low blood sugar and green bile in vomit and was in SCU for 1 night after delivery	12/8/2015 4:52 PM
8	O2stats were below 90% so she had to stay in paed's for 18hrs approx because I had a general anaesthetic	12/8/2015 4:31 PM
9	congenital anomaly Had to spend 5 days in special care unit as sats 88% on birth. Needed O2 for slow closing valve (can't remember name ? PD something ??	12/7/2015 11:11 PM
10	Very difficult gut problems but we're fairly sure now that it was dairy related.	12/7/2015 4:45 PM
11	Torticollis	12/5/2015 4:27 PM
12	Low bloods sugars..difficult to feed	12/4/2015 3:39 PM
13	Reflux, GI issues	12/4/2015 11:16 AM
14	congenital anomaly My baby has a congenital defect on his lung called a CCAM (basically a cyst on his lung).Found at 20 week scan. But he is perfectly well and has no breathing problems. They'll just remove it when he's older.	12/4/2015 10:28 AM
15	Cord around neck, poor oxygen supply	12/4/2015 9:15 AM
16	Treated for breathing difficulty, was tube fed for a few days and had hip dysplasia - not diagnosed until 6 weeks	12/4/2015 12:50 AM
17	She was very jaundice and had to be placed in an incubator for 3 days .	12/3/2015 11:36 PM

- Answered: 120
- Used LDN

CONGENITAL CYSTIC ADENOMATOID MALFORMATION OF THE LUNG

Why does it occur?

This is a very rare abnormality only occurring in about 1 in 10,000 babies. We do not know why this happens. There is no evidence to suggest that it is caused by anything you have done or have not done during the pregnancy.

<http://www.uhs.nhs.uk/OurServices/Childhealth/Neonatalurgery/Conditionswetreat/CongenitalCysticAdenomatoidMalformationoftheLung.aspx>

CONGENITAL CYSTIC ADENOMATOID MALFORMATION OF THE LUNG

What are the long term effects and after care?

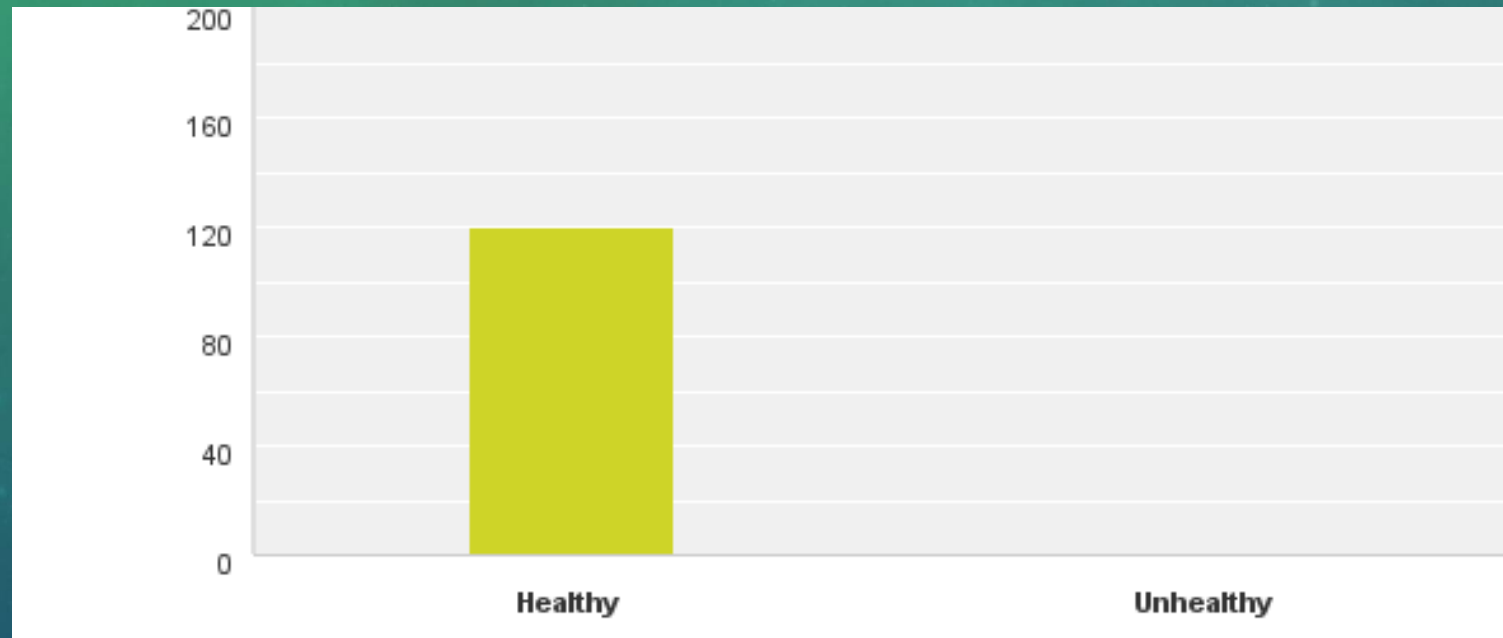
- In the long term,the vast majority of these babies will be normal and do not have any long term problems with their lungs at all.

<http://www.uhs.nhs.uk/OurServices/Childhealth/Neonatalurgery/Conditionswetreat/CongenitalCysticAdenomatoidMalformationoftheLung.aspx>

#	Responses	Date
1	2 episodes of choking on mucus (as is common following a c.section) so he was in the special care unit overnight	12/21/2015 10:35 PM
2	Jaundice	12/14/2015 9:50 AM
3	Cord wrapped around baby so was brought out of delivery room for while to be checked over	12/13/2015 10:59 PM
4	Apgar score low Low o2	12/13/2015 2:41 PM
5	Torticollis. Sterno mastoid muscle (neck) damaged at delivery - ventouse - kiwi vacuum used.	12/11/2015 3:42 PM
6	Eye infection which she picked up from mother during birth	12/8/2015 2:48 PM
7	Baby was in shock when delivered and did not cry	12/7/2015 11:49 PM
8	Was a little shocked by quick entry into the world but no intervention was required in the end	12/7/2015 11:41 PM
9	congenital anomaly Congenital hypothyroidism	12/7/2015 3:18 PM
10	Put on iv antibiotics due to mother's high temp	12/7/2015 2:38 PM
11	Treated for meningitis due to me having gbs	12/7/2015 2:28 PM
12	Breathing Low muscle tone Reflux	12/7/2015 12:58 PM
13	NA	12/7/2015 11:34 AM
14	I had high temperature prior to and during delivery so baby was on antibodies after birth for few days	12/5/2015 10:13 PM
15	congenital anomaly Seizures when he was 3 days old, peaking at one week old when he was admitted to hospital. Now 15mts and one medications no seizures since he was a week old	12/4/2015 3:26 PM
16	low blood sugars	12/4/2015 1:48 PM
17	Baby had mucus and was suctioned immediately after delivery. I was given baby 15 minutes after delivery. All was well then.	12/4/2015 10:54 AM
18	Couldn't regulate body temperature	12/4/2015 9:53 AM
19	But was put on antibiotics in case the infection had spread to her but tests later showed it had not	12/4/2015 7:56 AM

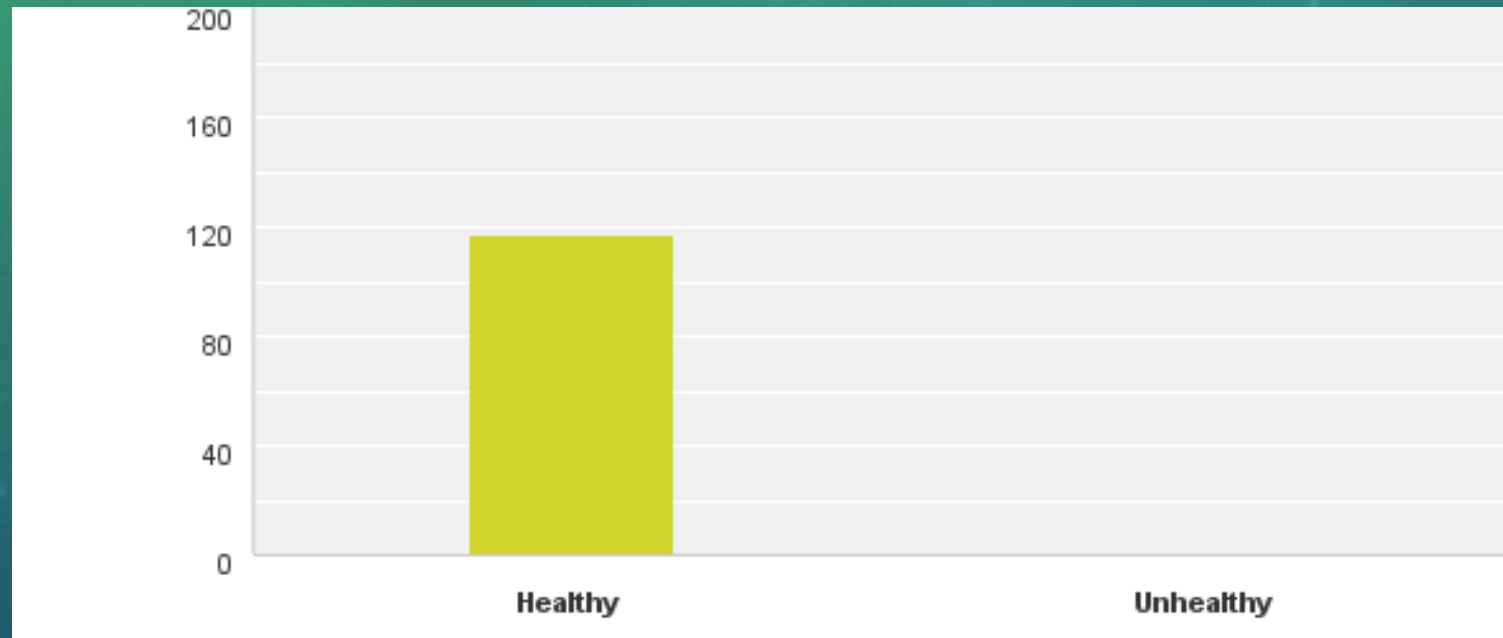
- Answered: 117
- No LDN

Q27: OVERALL WOULD YOU SAY YOUR CHILD IS?



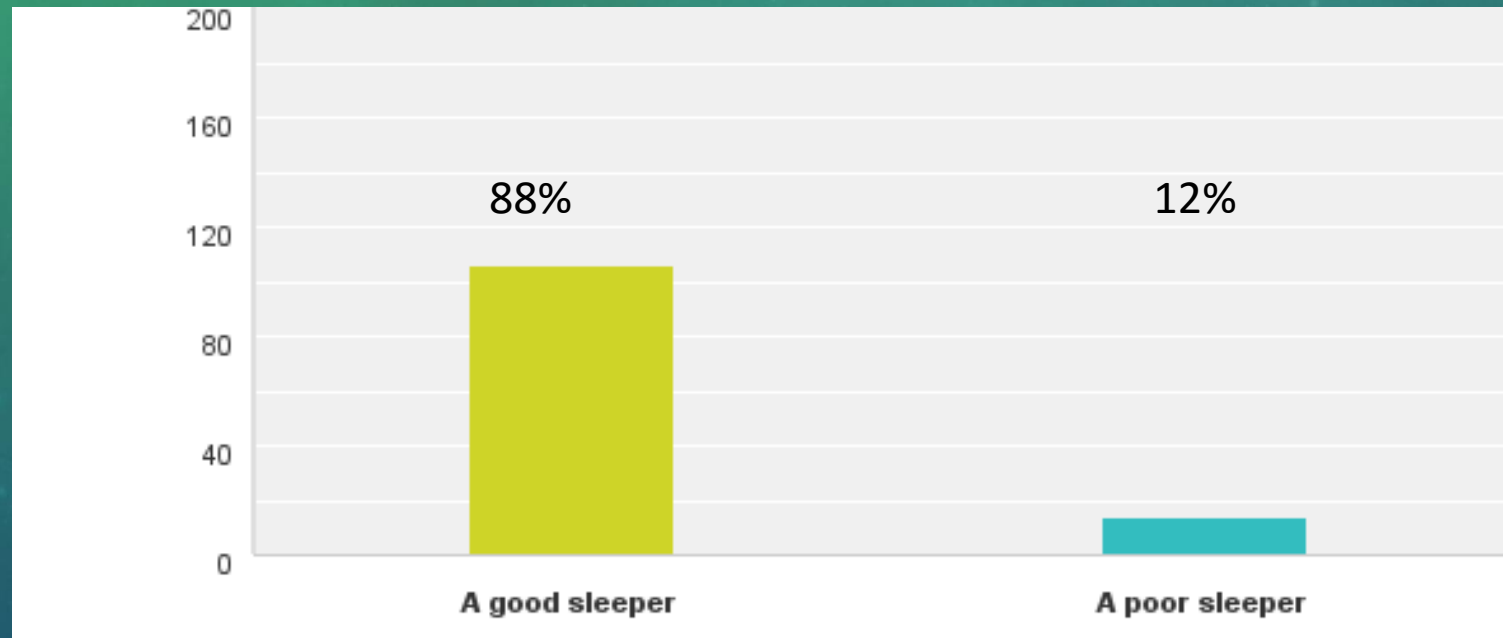
- Answered: 120 Used LDN

Q27: OVERALL WOULD YOU SAY YOUR CHILD IS?



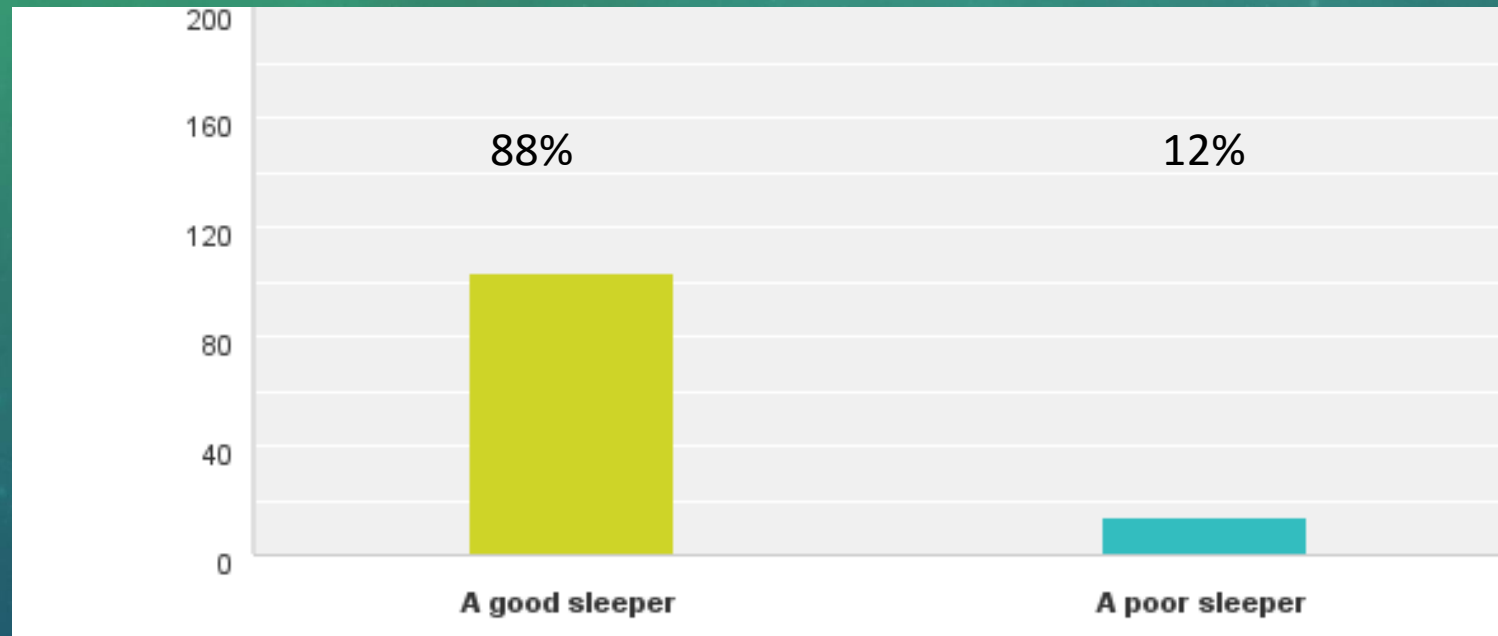
- Answered: 117 Skipped: 0 **No LDN**

Q28: OVERALL WOULD YOU SAY YOUR CHILD IS



- Answered: 120 Used LDN

Q28: OVERALL WOULD YOU SAY YOUR CHILD IS



- Answered: 117 Skipped: 0 **No LDN**

Q29: OVERALL WOULD YOU SAY YOUR CHILD IS



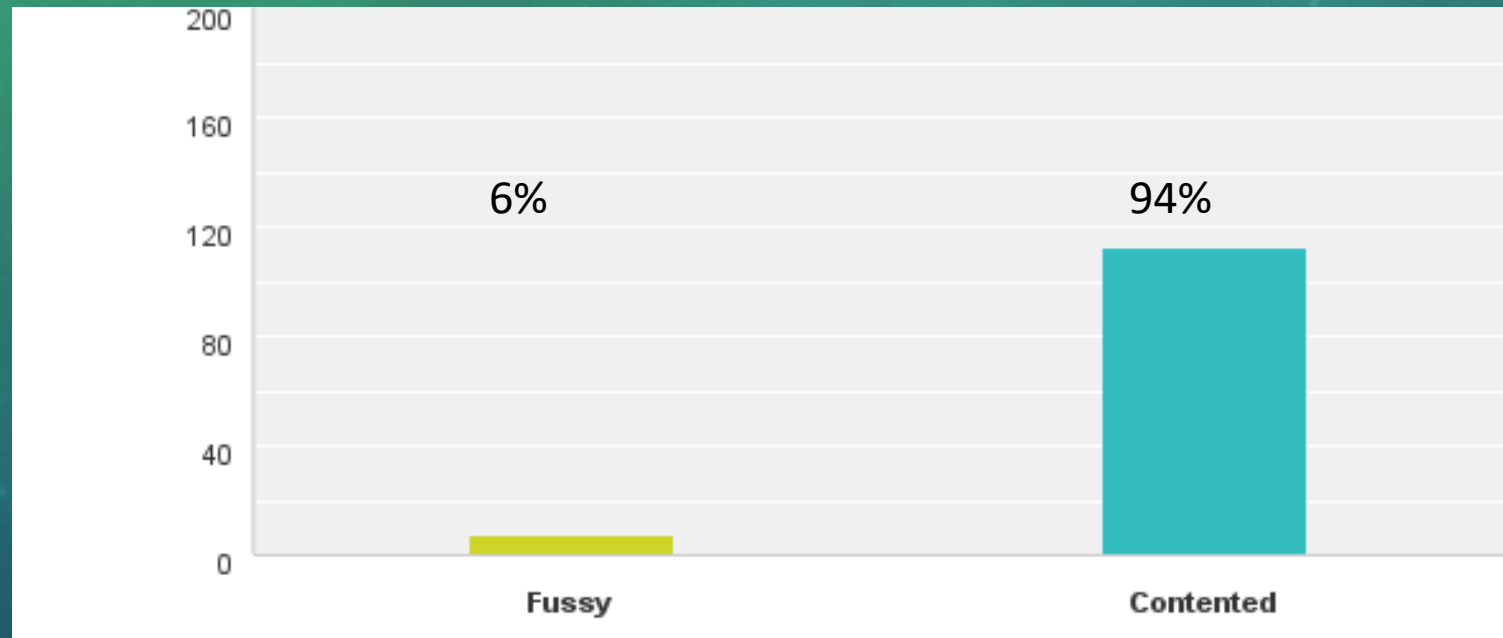
- Answered: 120 Used LDN

Q29: OVERALL WOULD YOU SAY YOUR CHILD IS



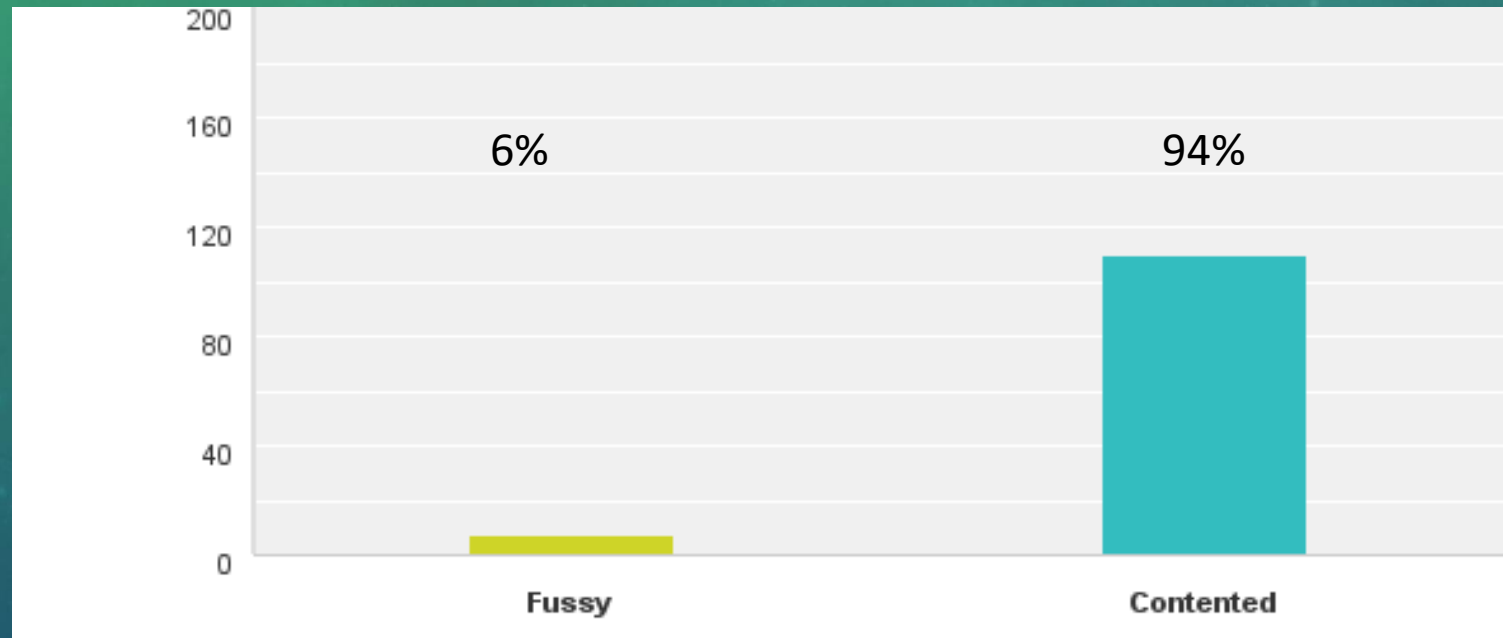
- Answered: 114 Skipped: 3 No LDN

Q30: WOULD YOU DESCRIBE YOUR CHILD AS



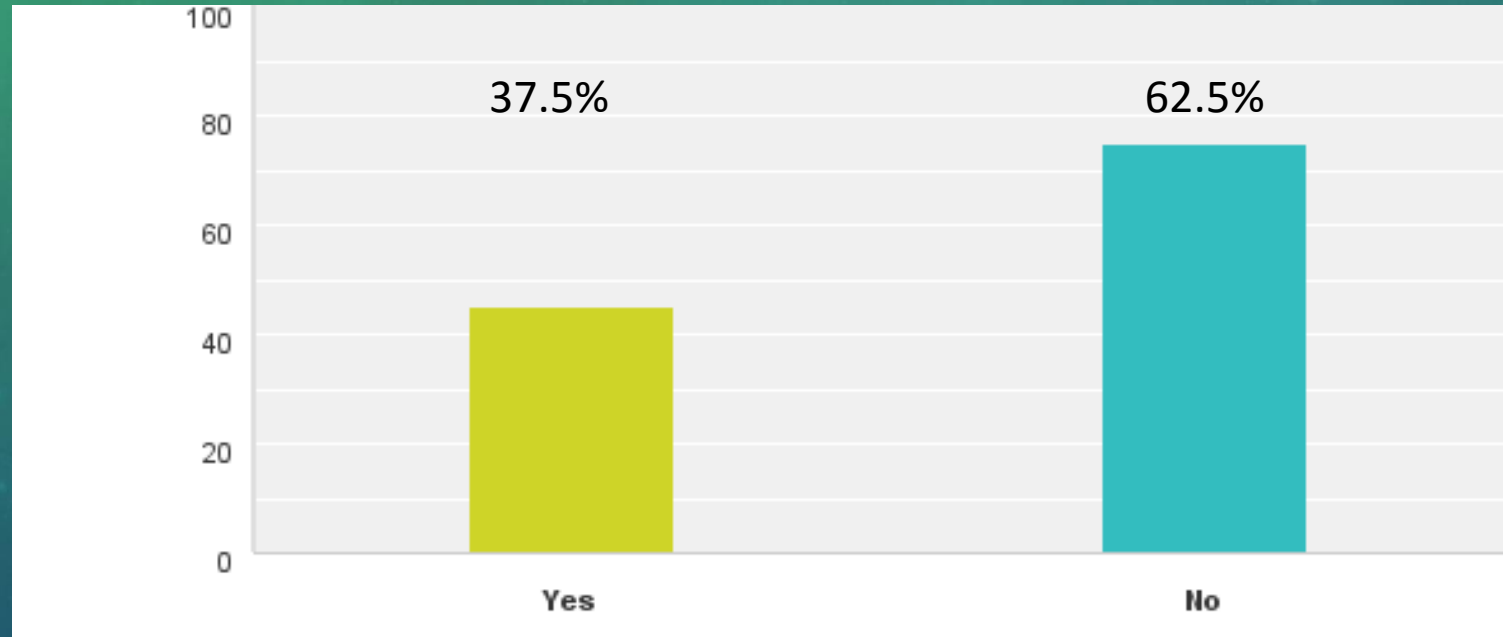
- Answered: 120 Used LDN

Q30: WOULD YOU DESCRIBE YOUR CHILD AS



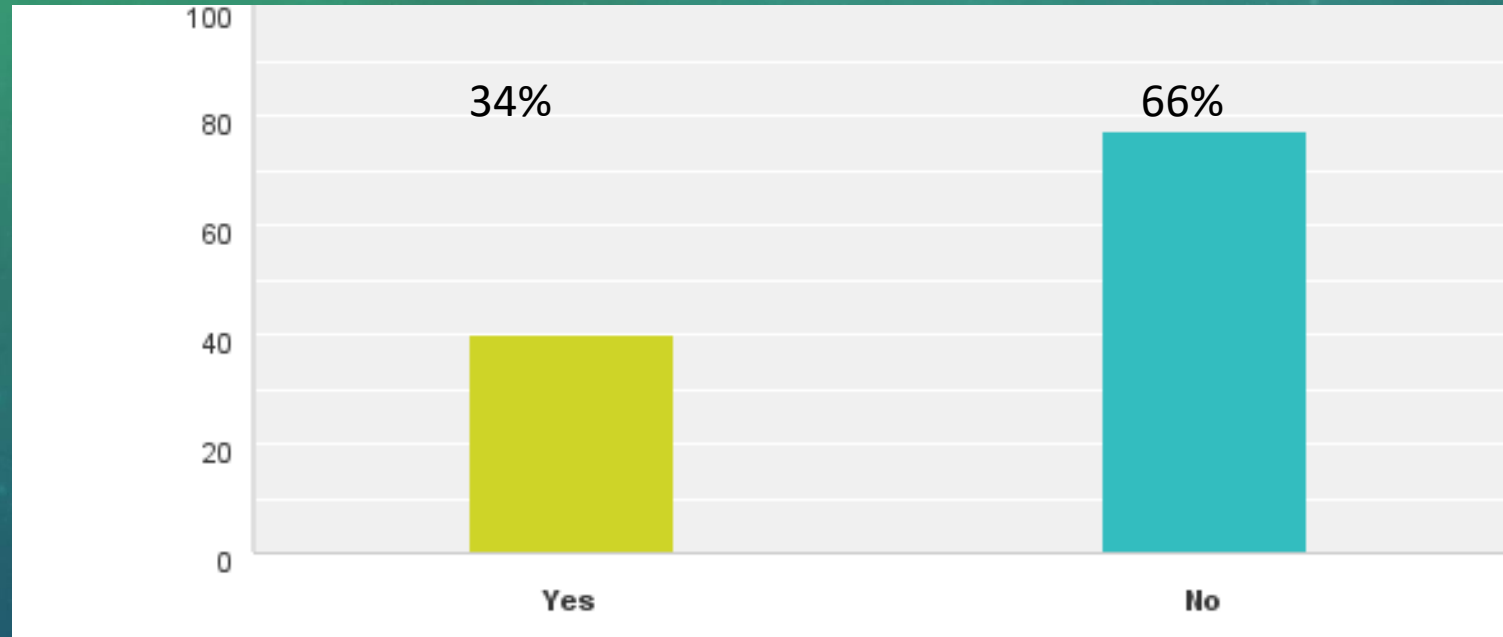
- Answered: 117 Skipped: 0 **No LDN**

Q31: HAS YOUR CHILD NEEDED ANTIBIOTICS FOR A CHEST INFECTION?



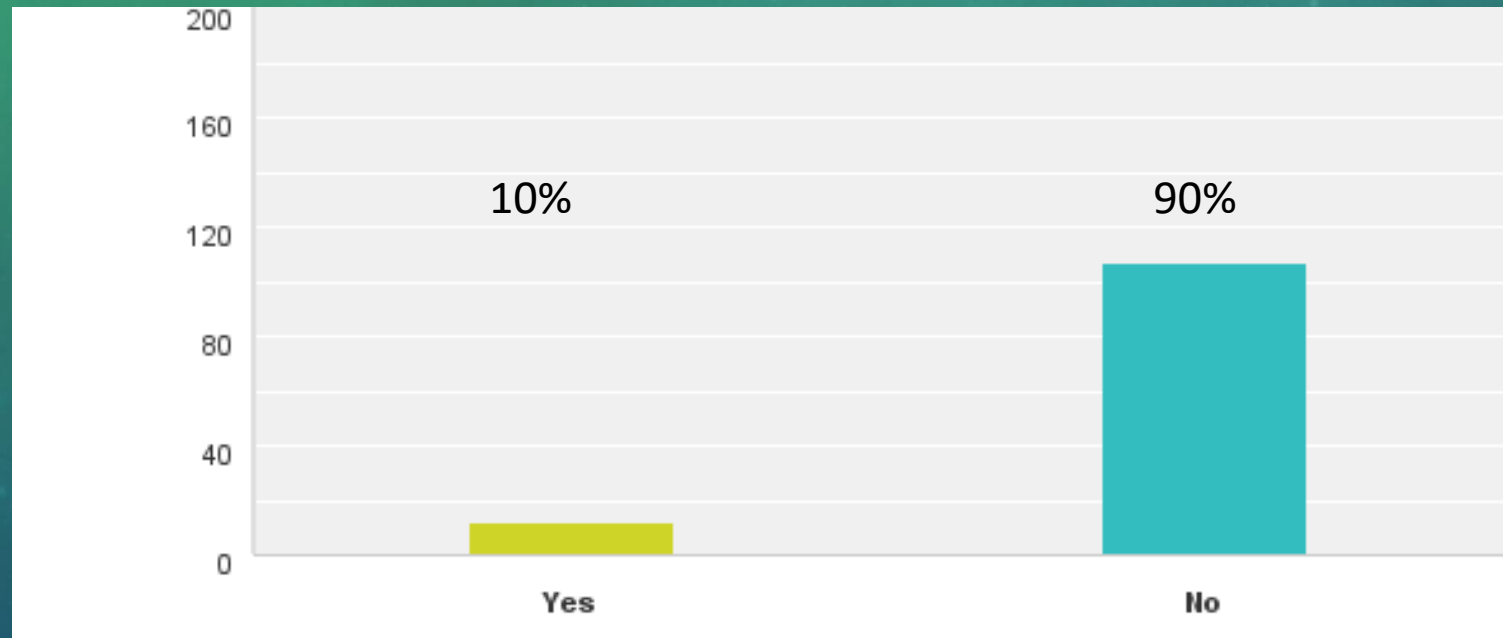
- Answered: 120 Used LDN

Q31: HAS YOUR CHILD NEEDED ANTIBIOTICS FOR A CHEST INFECTION?



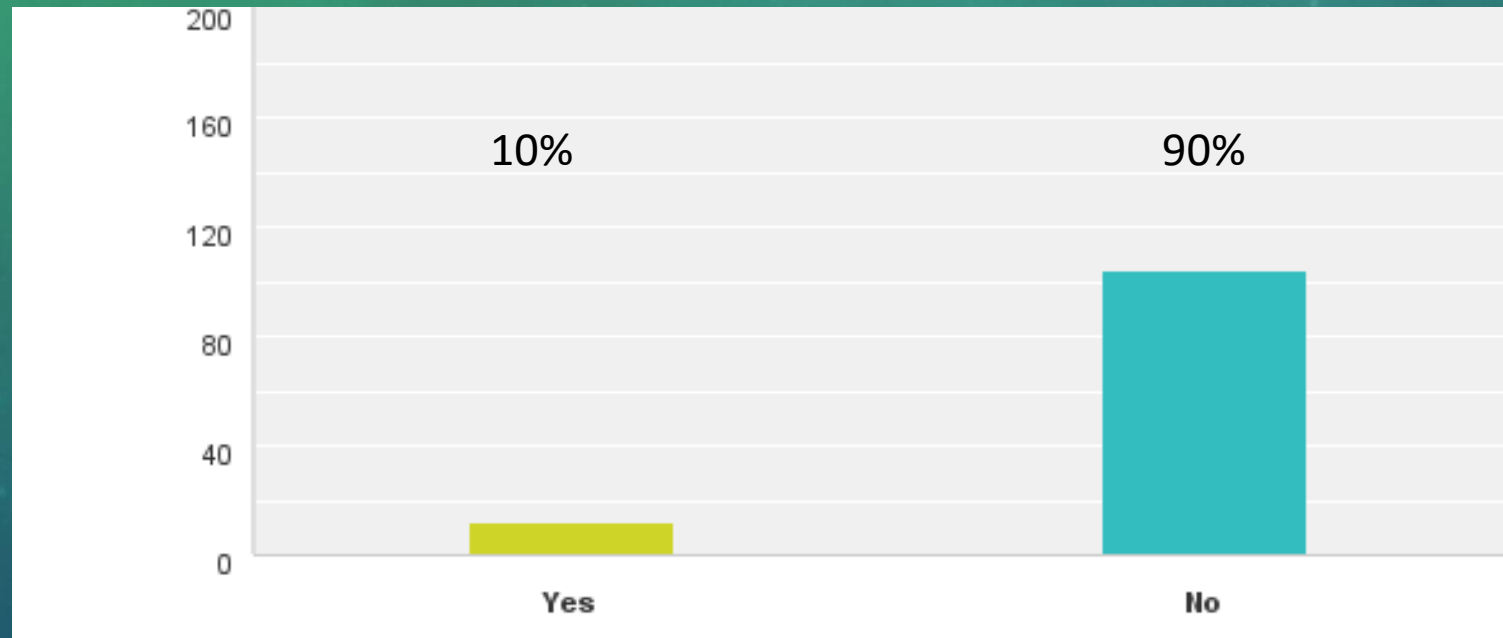
- Answered: 117 Skipped: 0 **No** LDN

Q33: DOES YOUR CHILD HAVE ALLERGIES?



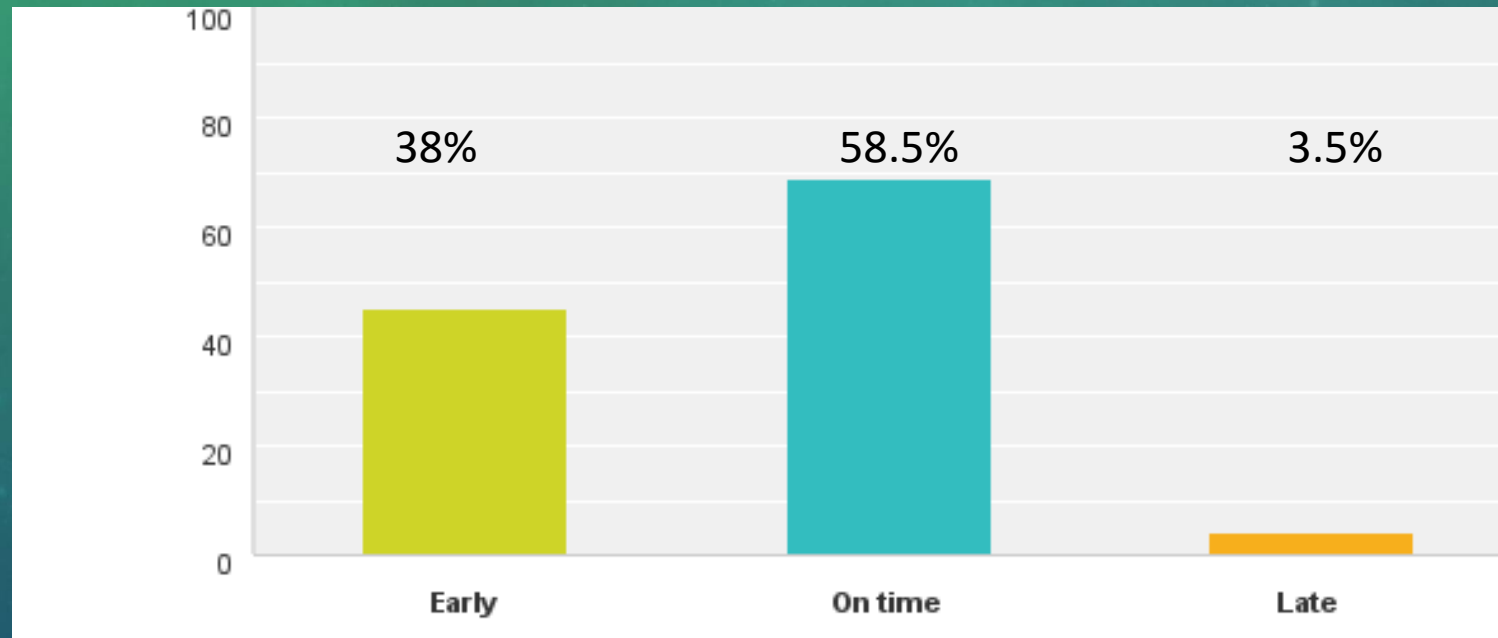
- Answered: 119 Skipped: 1 Used LDN

Q33: DOES YOUR CHILD HAVE ALLERGIES?



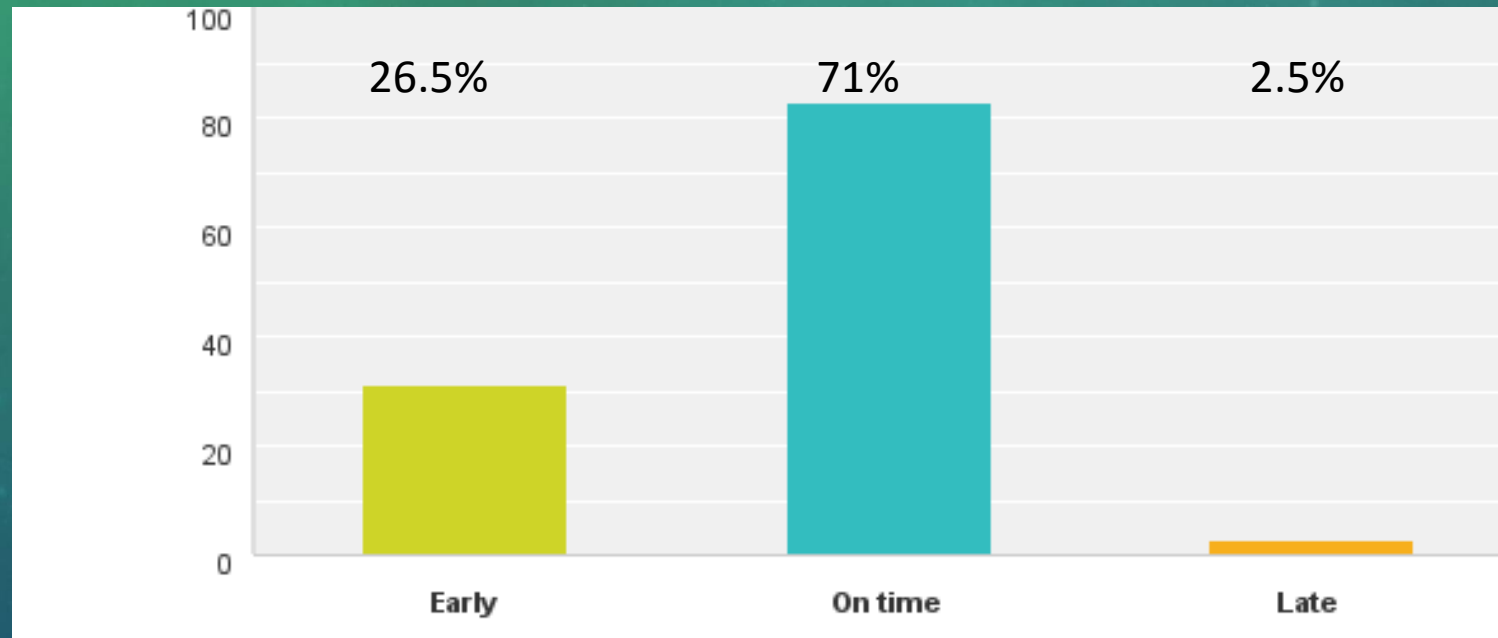
- Answered: 116 Skipped: 1 **No LDN**

Q35: OVERALL, HAS YOUR CHILD REACHED THEIR DEVELOPMENTAL MILESTONES



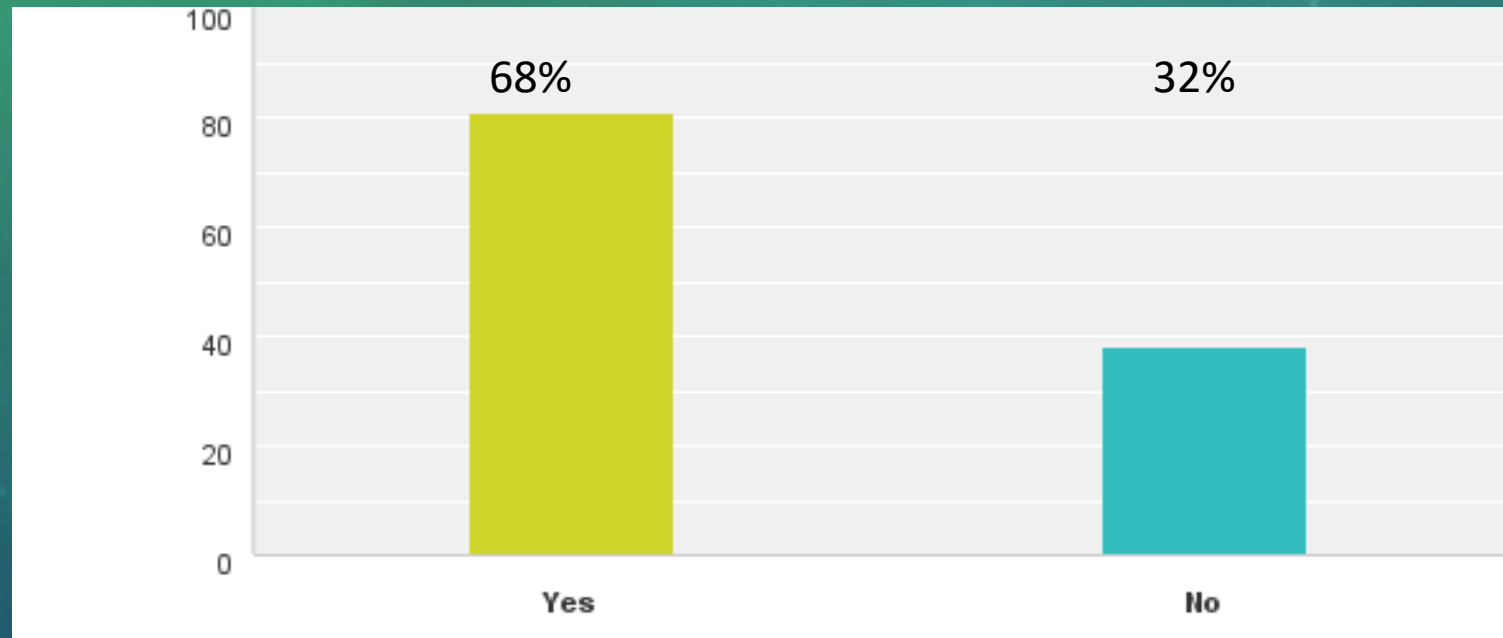
- Answered: 118 Skipped: 2 Used LDN

Q35: OVERALL, HAS YOUR CHILD REACHED THEIR DEVELOPMENTAL MILESTONES



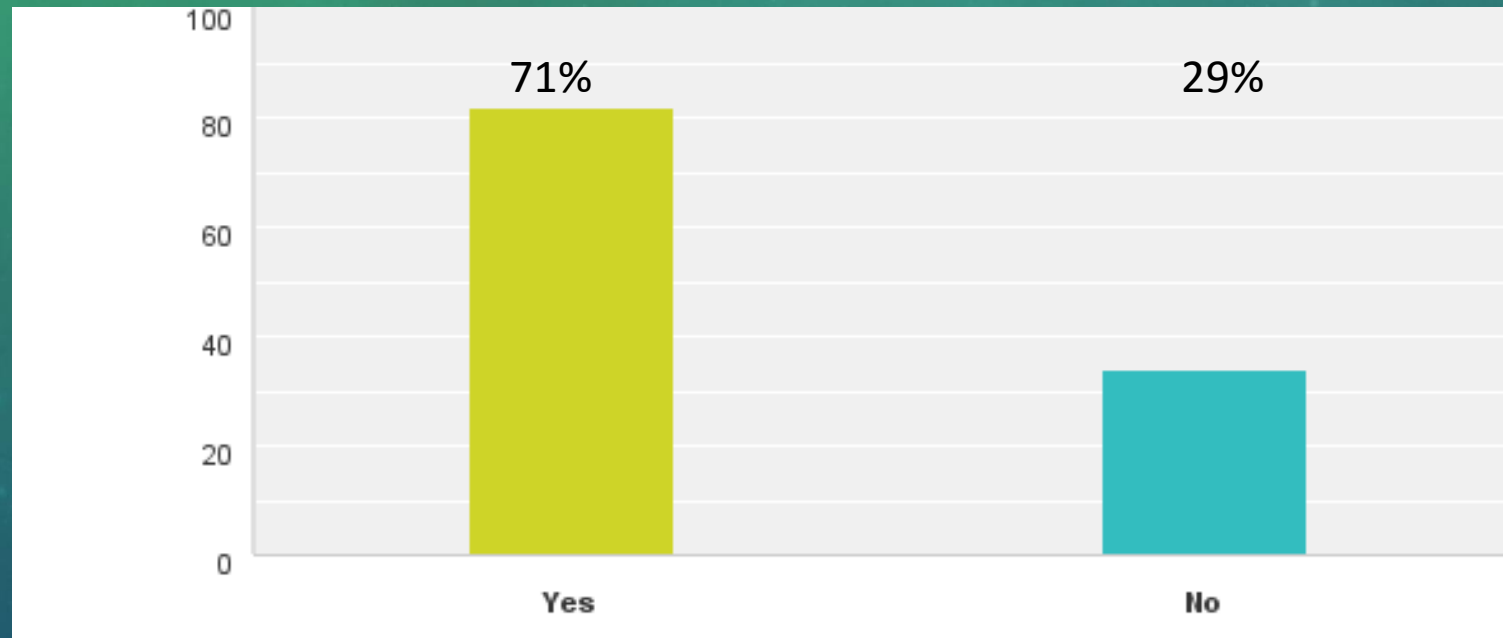
- Answered: 117 Skipped: 0 No LDN

Q37: WAS YOUR CHILD BREAST-FED?



- Answered: 119 Skipped: 1 Used LDN

Q37: WAS YOUR CHILD BREAST-FED?

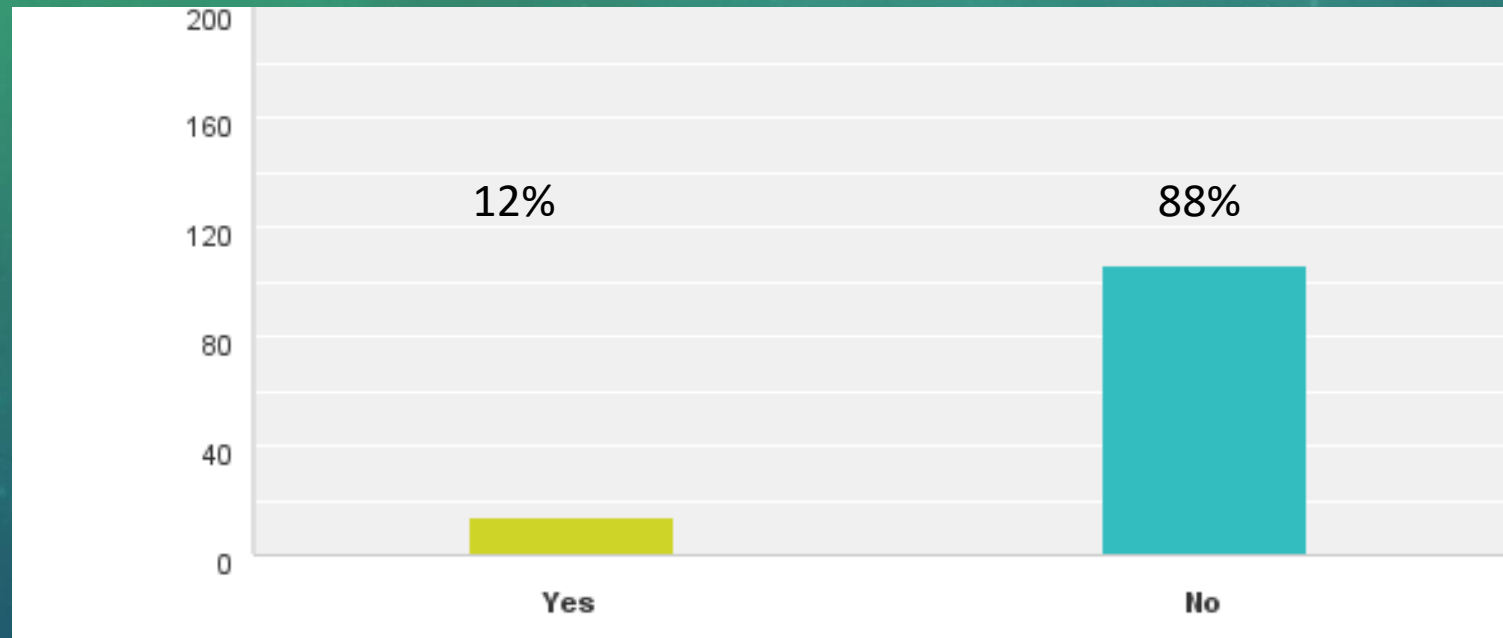


- Answered: 116 Skipped: 1 **No** LDN

WHAT WAS LDN LIKE FOR THOSE WHO USED IT?

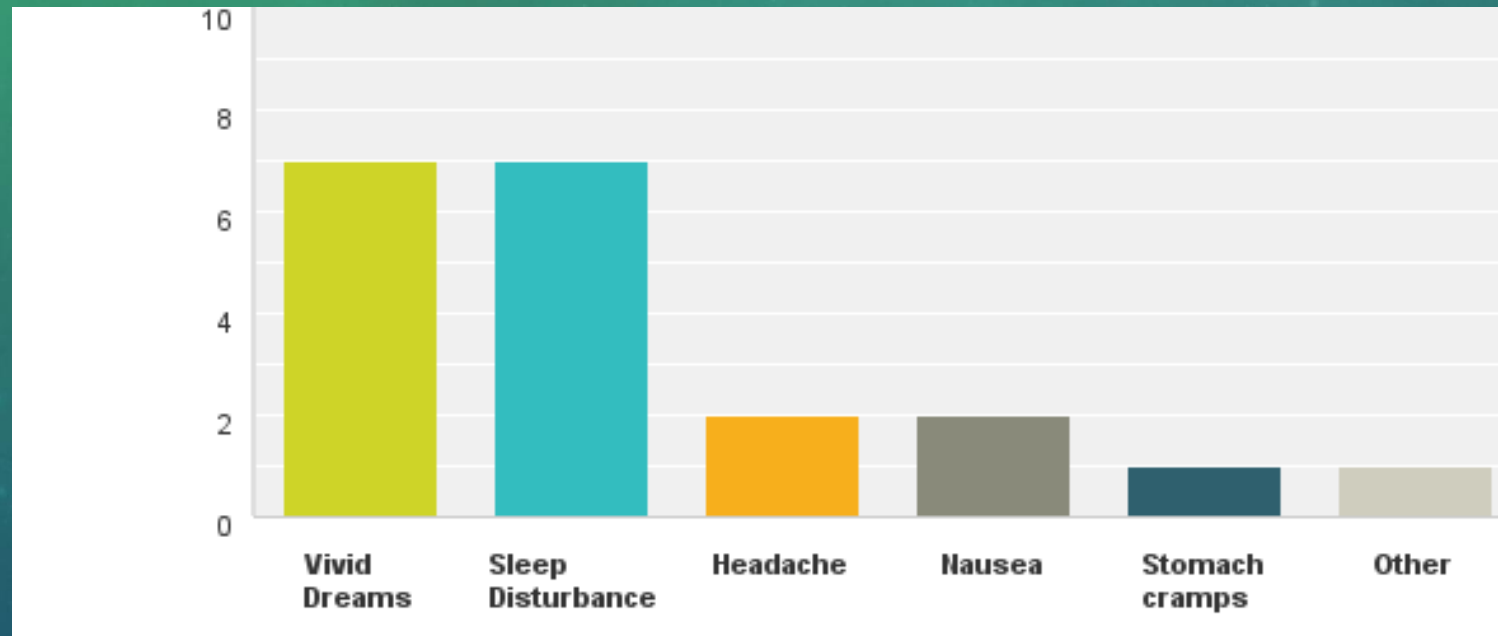
- 120 Used LDN in Pregnancy (50.6%)
- Most women started LDN before conception

Q8: DID YOU NOTICE ANY SIDE EFFECTS (BEYOND THE FIRST TWO WEEKS) TO TREATMENT WITH LDN ?



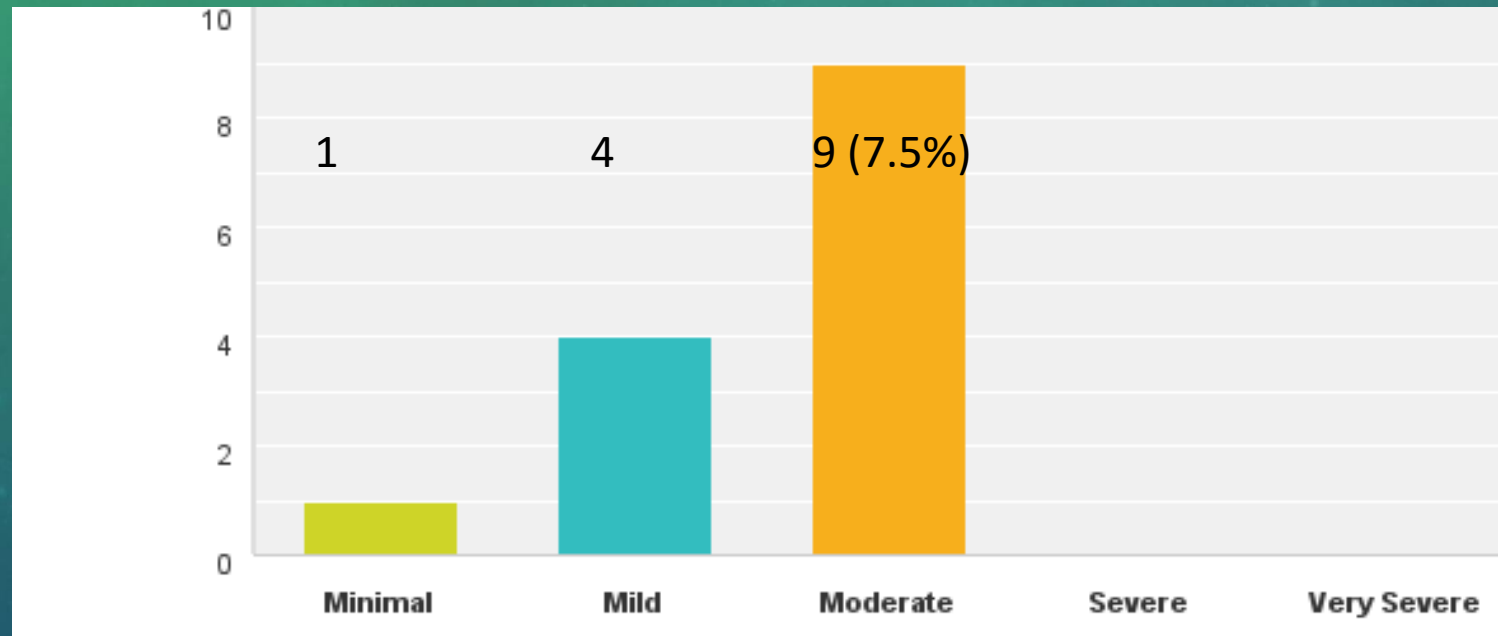
- Answered: 120 Skipped: 0

Q9: IF YOU HAD SIDE EFFECTS TO LDN (BEYOND THE FIRST TWO WEEKS) WHAT WERE THEY?



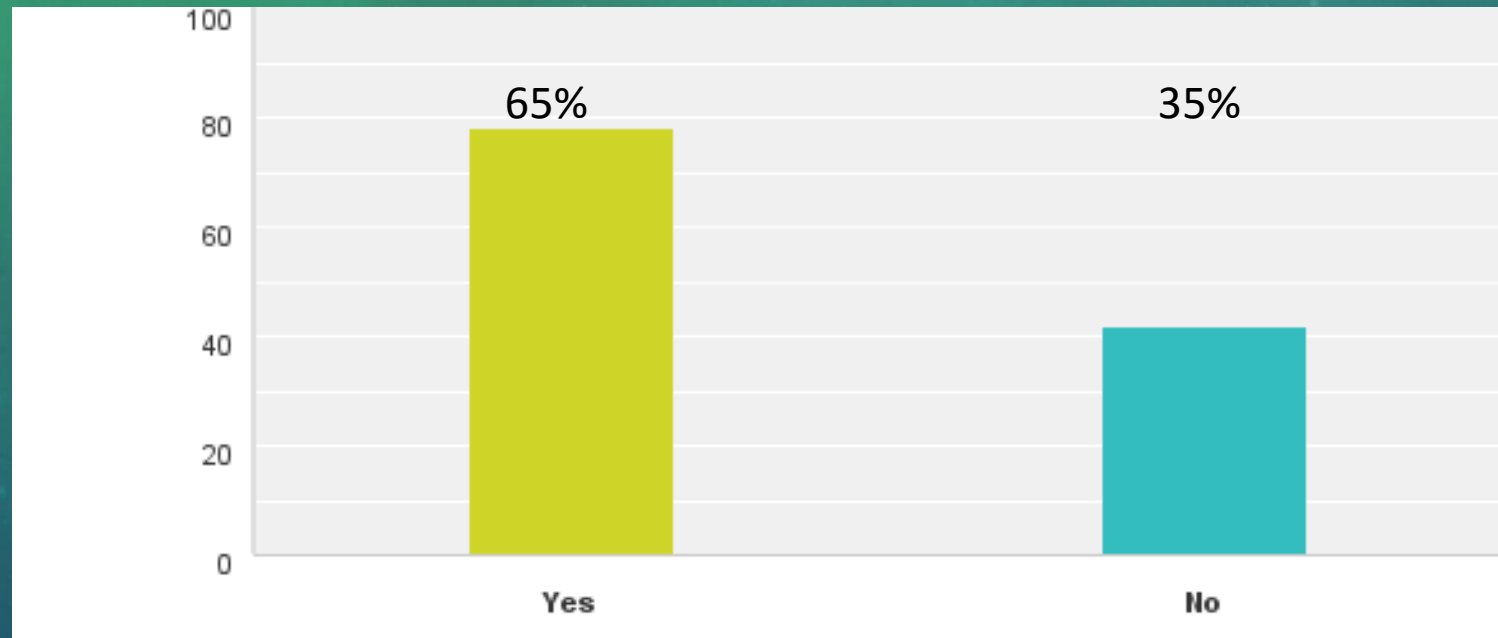
- Answered: 14 Skipped: 106 Used LDN

Q10: HOW SEVERE WERE THESE SIDE EFFECTS?



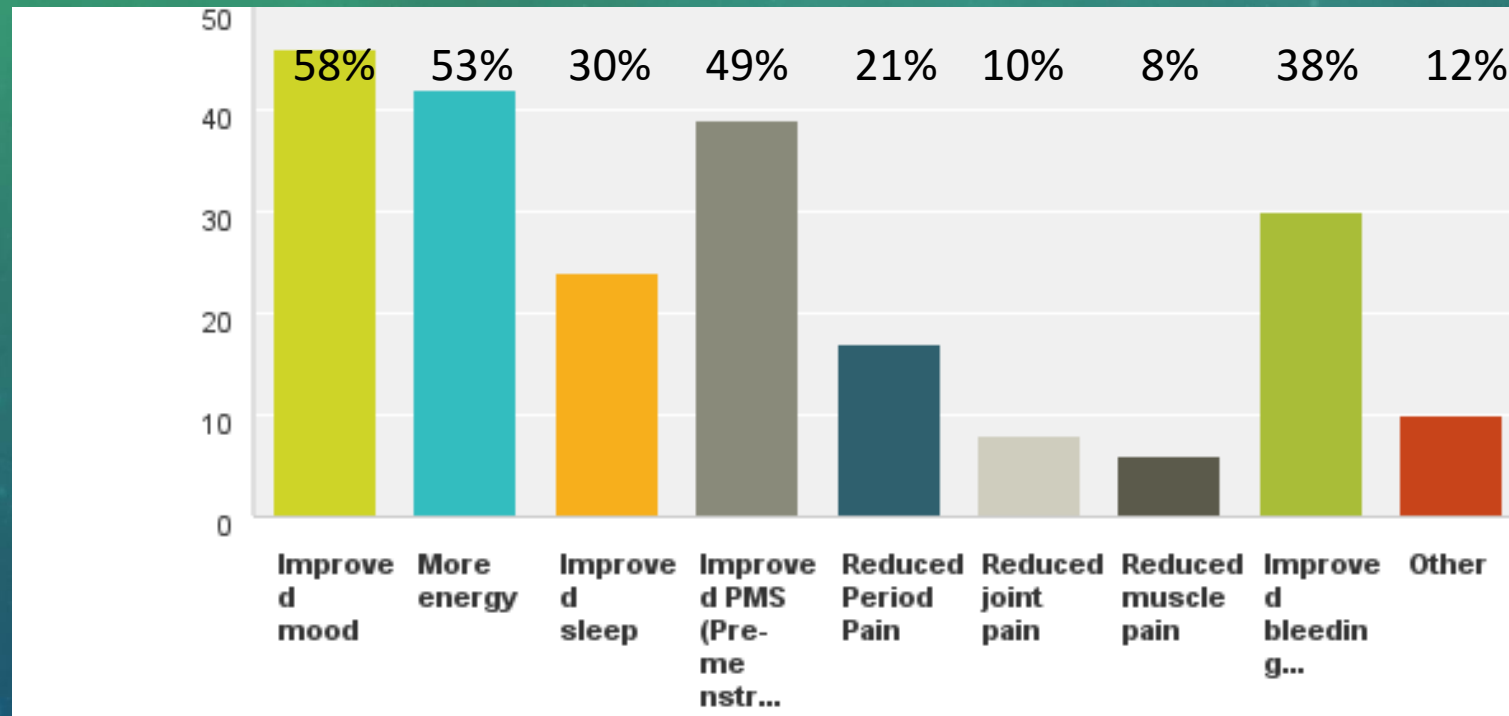
- Answered: 14 Skipped: 106

Q11: DID YOU NOTICE ANY BENEFITS TO TREATMENT WITH LDN?



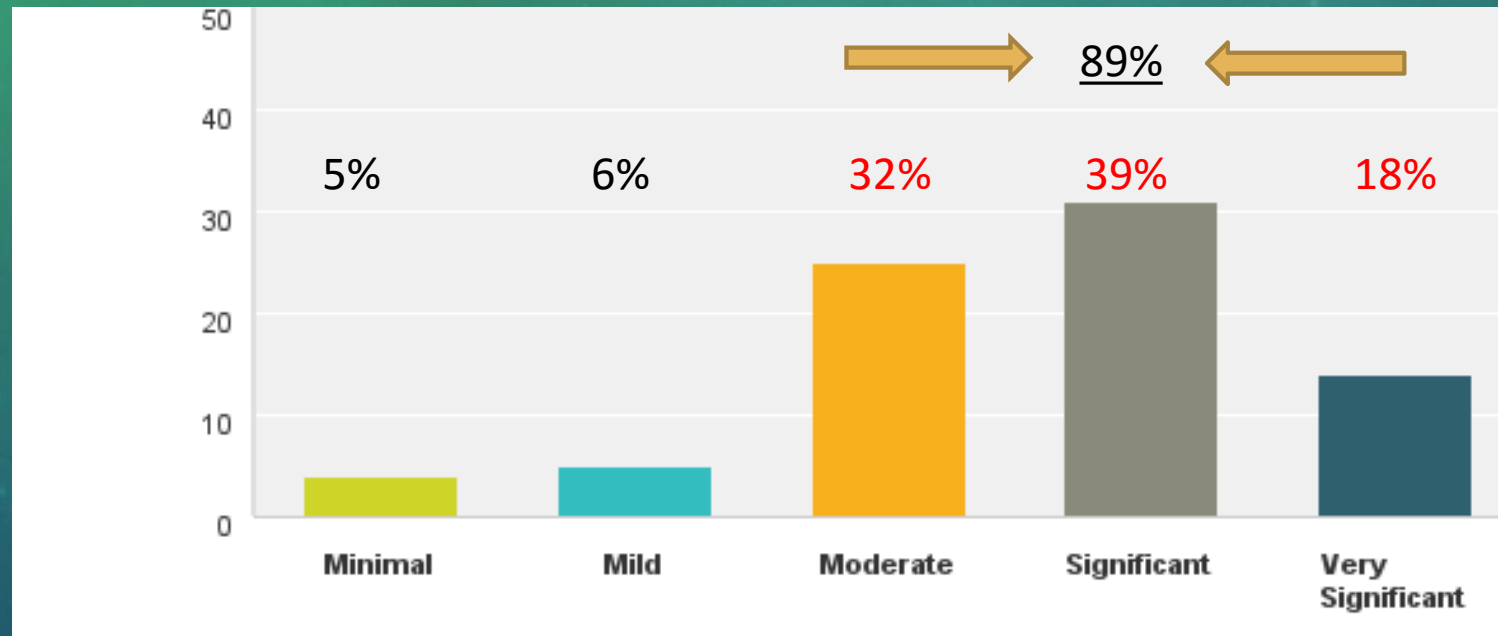
- Answered: 120 Skipped: 0 Used LDN

Q12: IF YOU NOTICED A BENEFIT TO LDN TREATMENT, WHAT WAS THAT BENEFIT?



- Answered: 79 Skipped: 41

Q13: HOW SIGNIFICANT WAS THAT BENEFIT?



- Answered: 79 Skipped: 41 Used LDN

Q1: DID YOU HAVE A SUCCESSFUL PREGNANCY WITH NAPRO FERTILITYCARE?

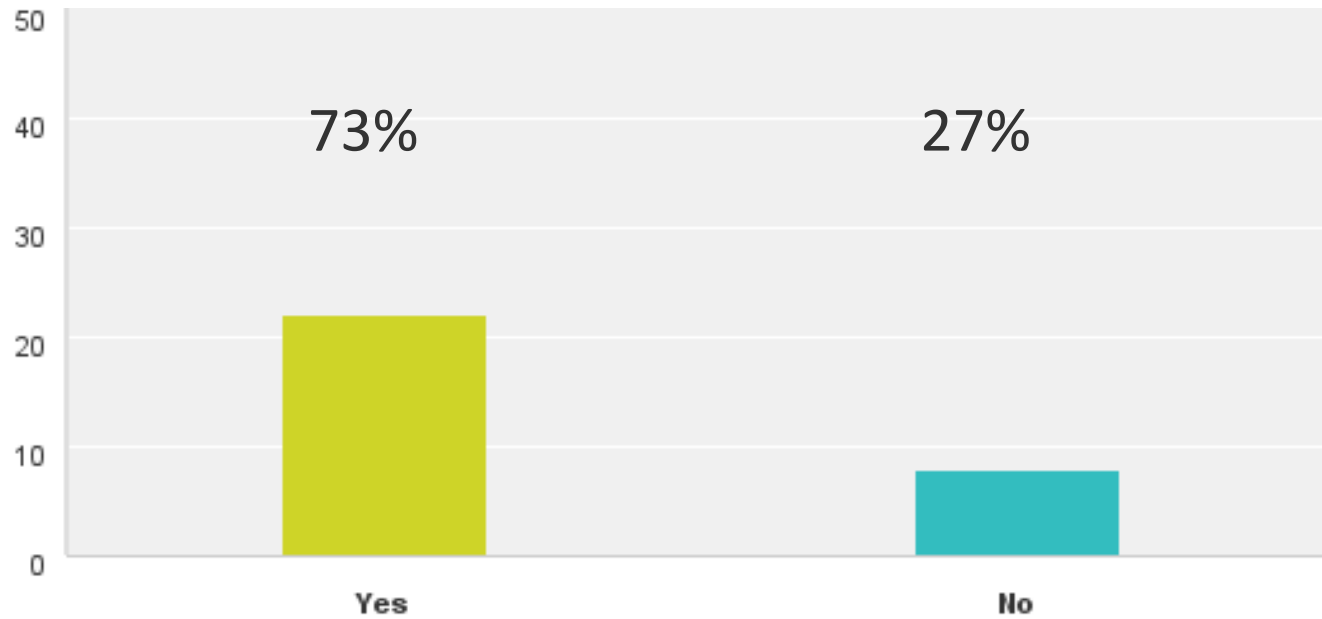
- 120 Used LDN in Pregnancy (50.6%)
 - 30 did not take LDN during pregnancy
 - 30 LDN only until 25 weeks
 - 47 LDN beyond 26 weeks
 - 13 Unconfirmed duration LDN use

.....HOW DID THEY DO?.....



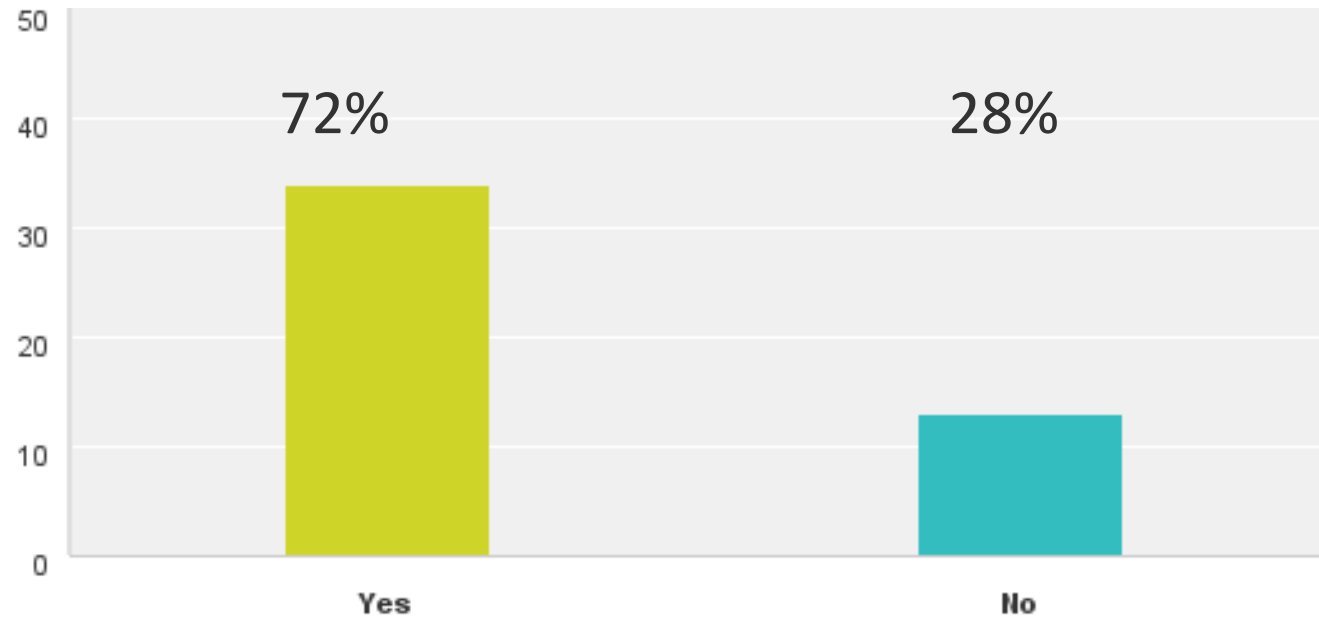
Q11: Did you notice any benefits to treatment with LDN?

Answered: 30 <25weeks



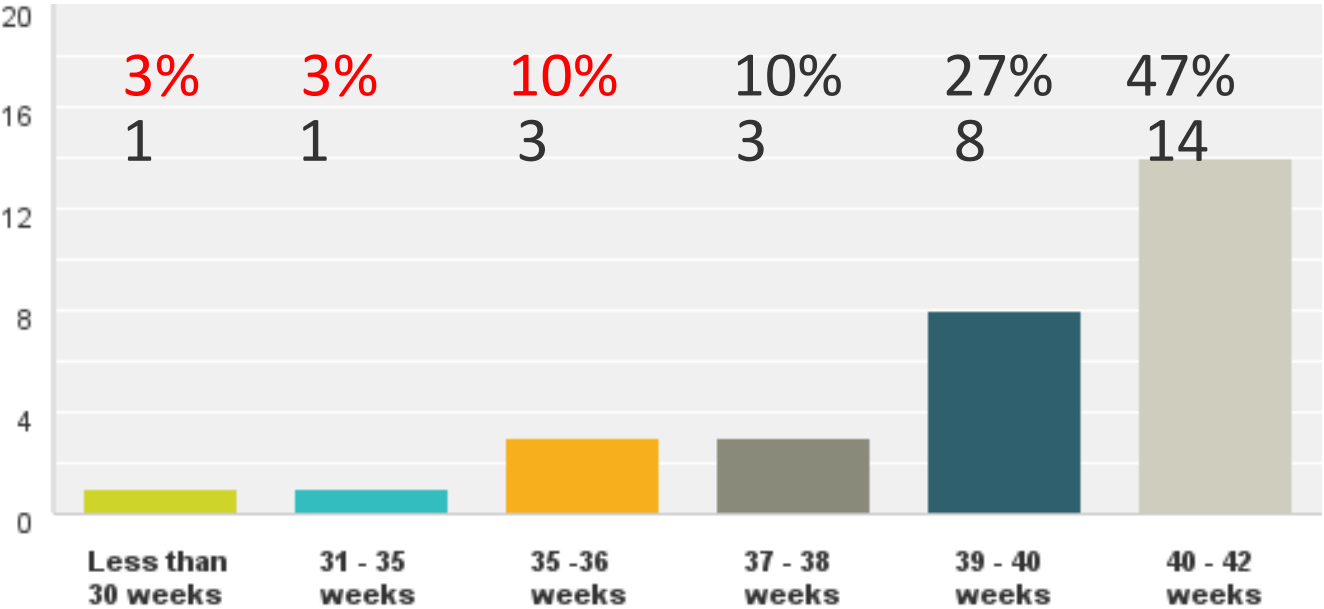
Q11: Did you notice any benefits to treatment with LDN?

Answered: 47 [26 weeks+](#)



Q17: At how many weeks was your baby born at?

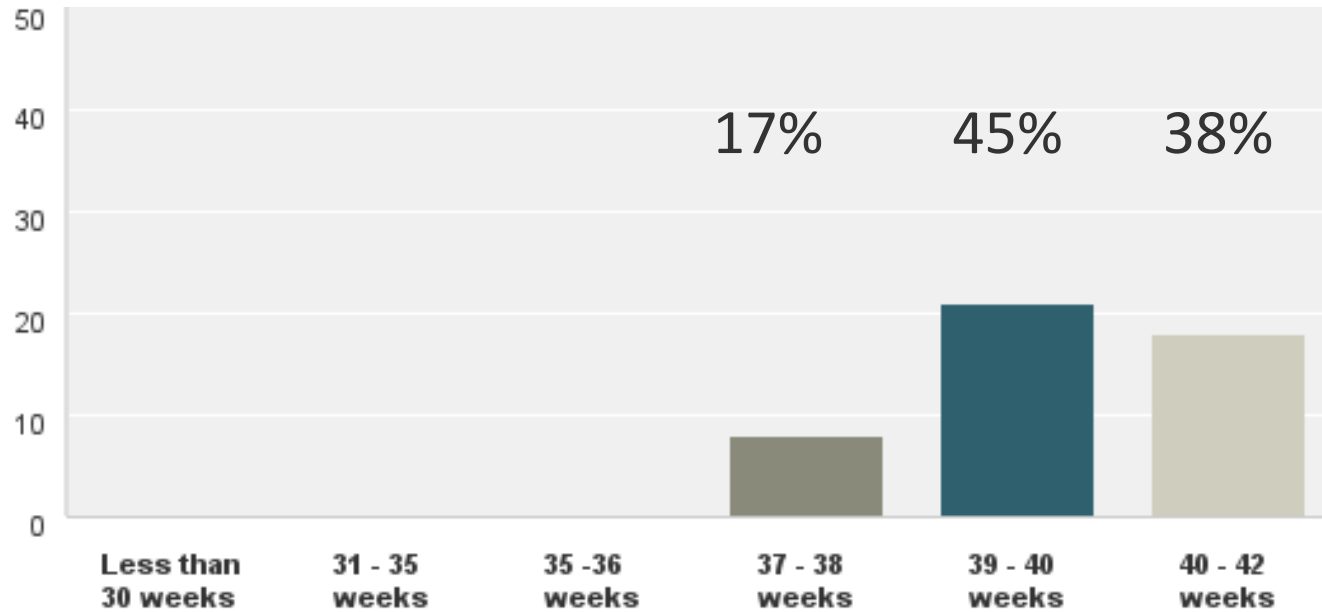
Answered: 30 <25weeks



P value =

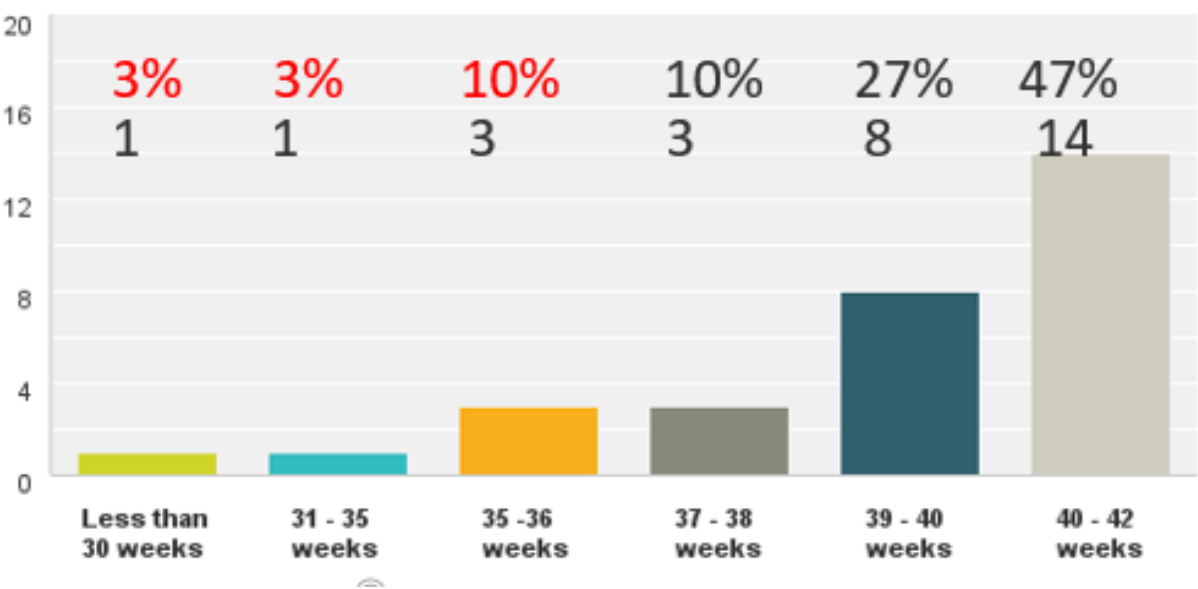
Q17: At how many weeks was your baby born at?

Answered: 47 [26 weeks+](#)

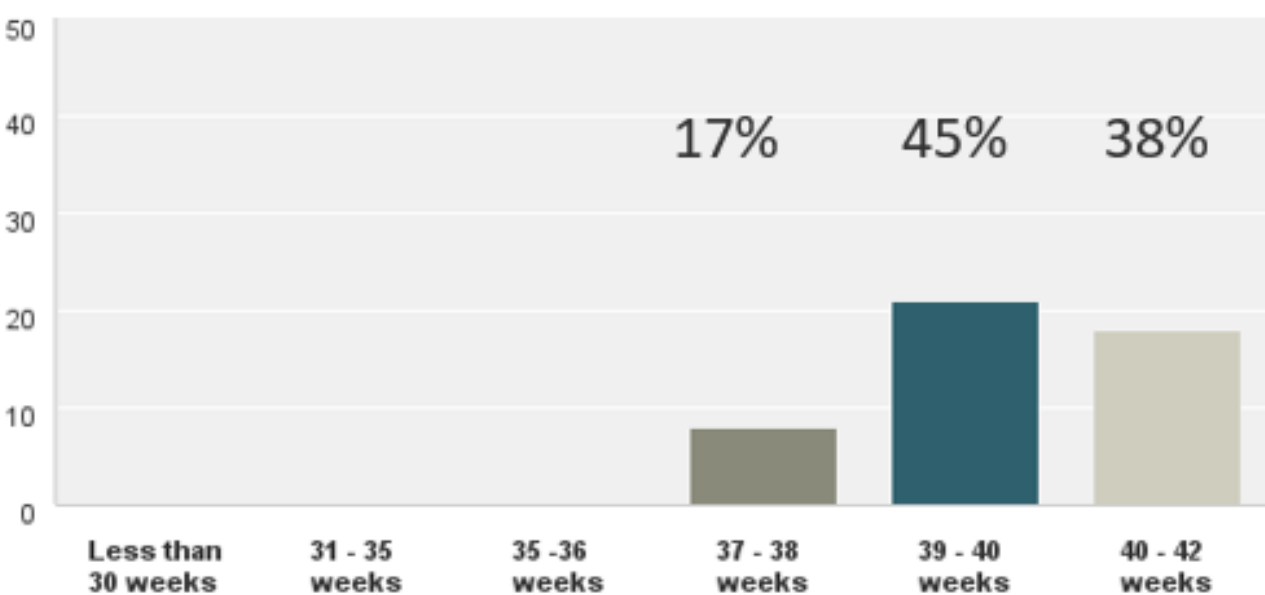


Q17: At how many weeks was your baby born at?

Answered: 30 <25weeks



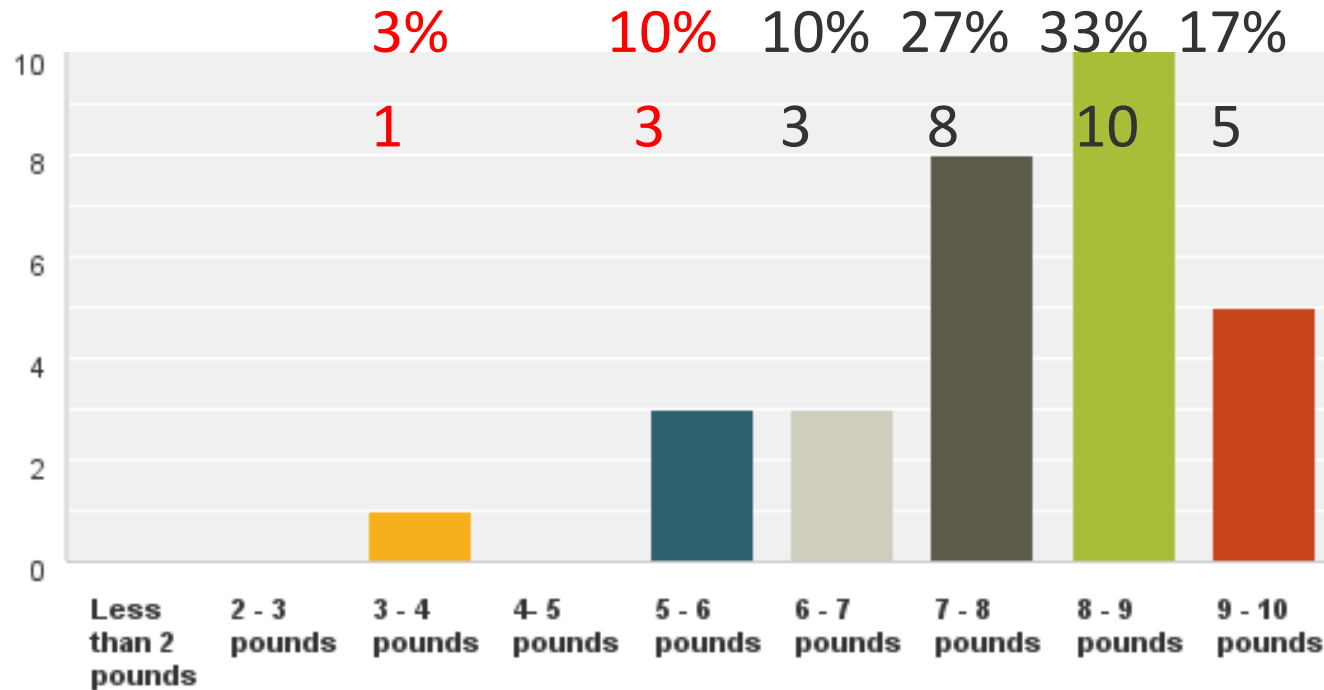
Answered: 47 26 weeks+



P value =

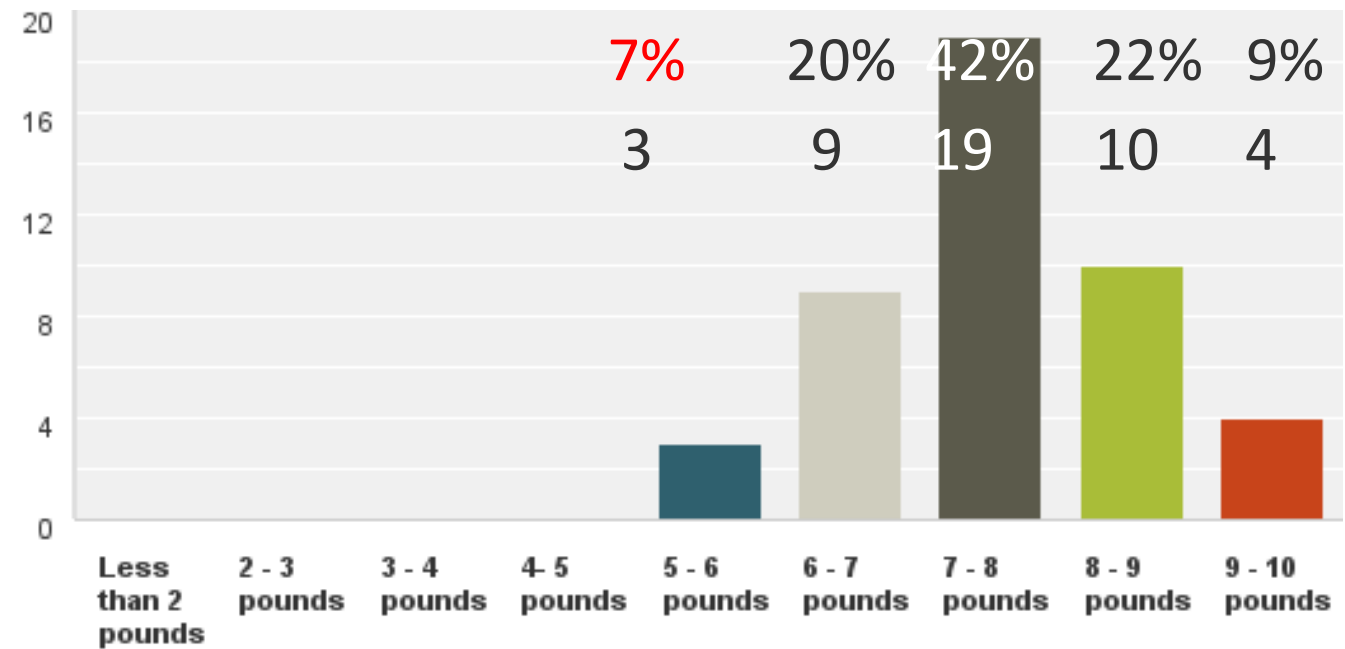
Q19: What was your baby's birth weight? (pounds and ounces)

Answered: 30 <25weeks



Q19: What was your baby's birth weight? (pounds and ounces)

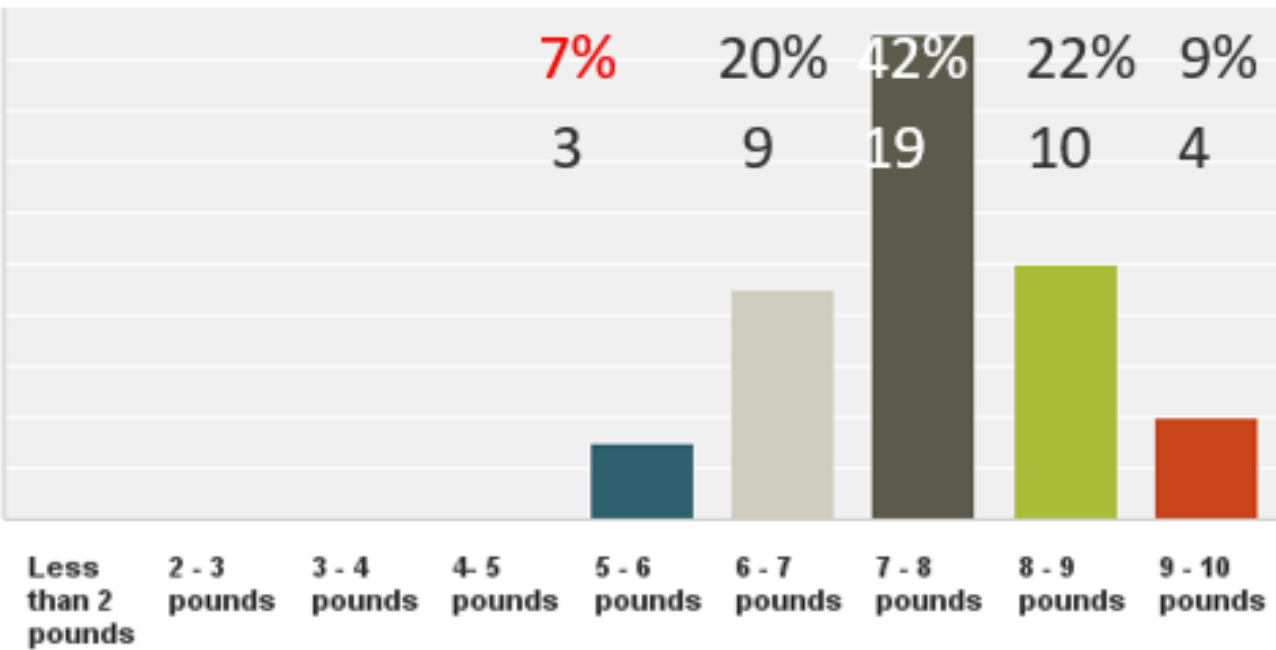
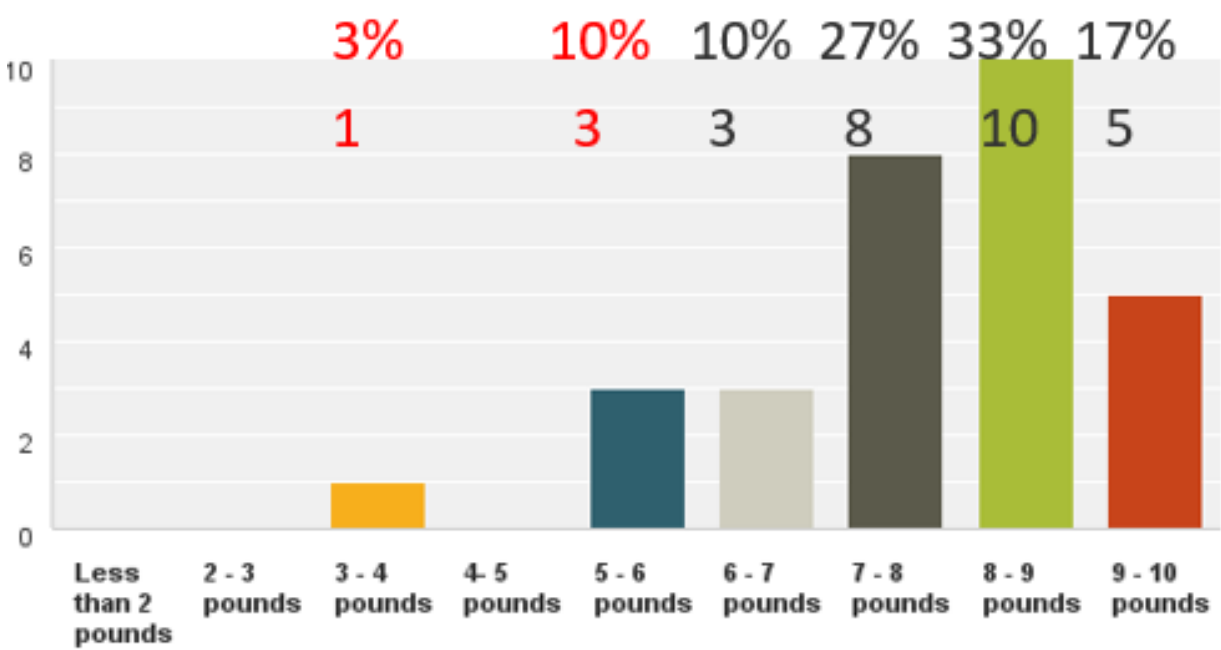
Answered: 45 Skipped: 2 [26 weeks+](#)



Q19: What was your baby's birth weight? (pounds and ounces)

Answered: 30 <25weeks

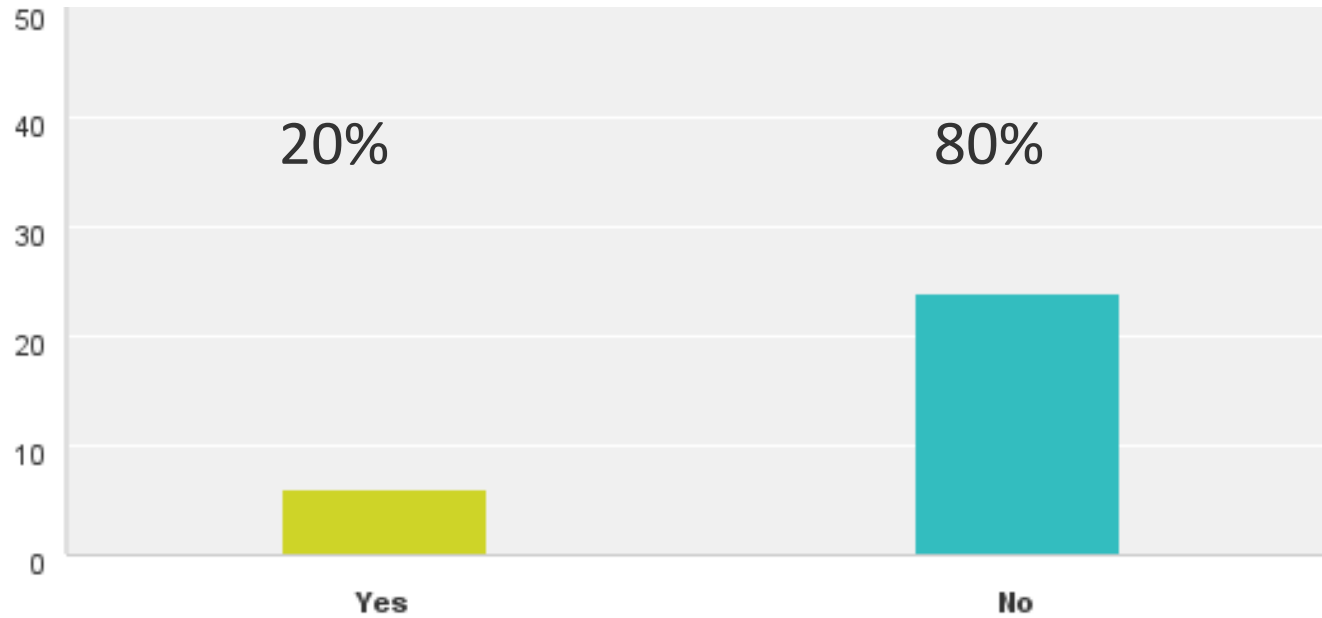
Answered: 45 Skipped: 2 26 weeks+



P value =

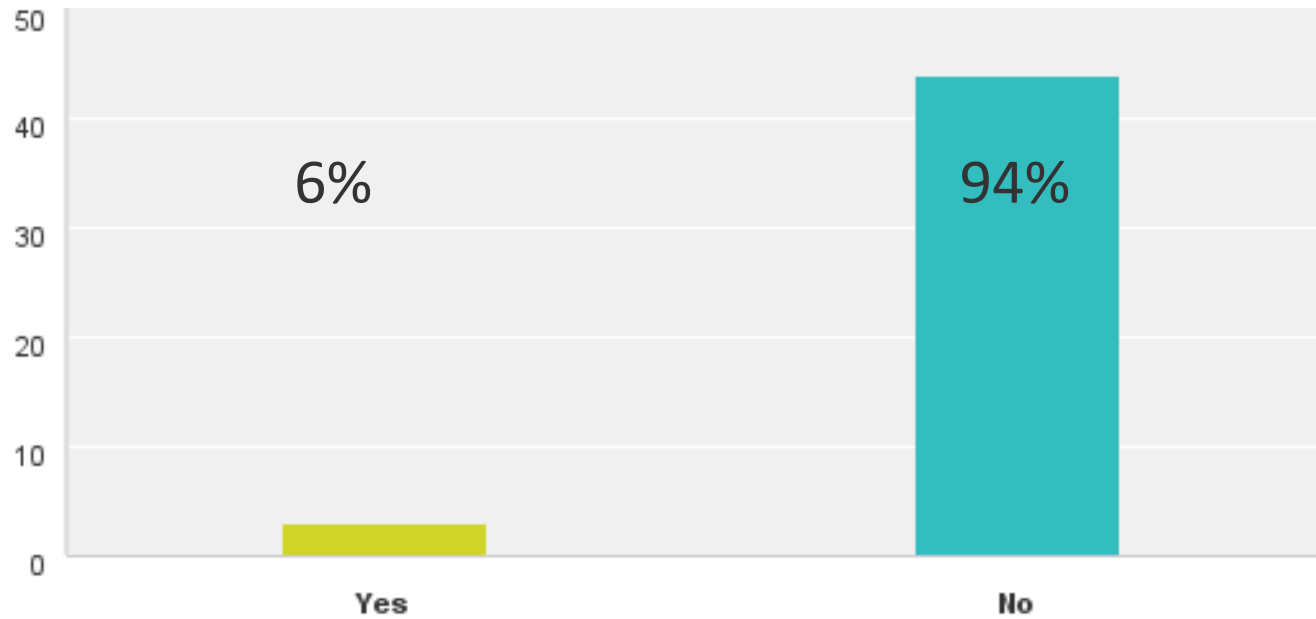
Q21: Was your baby in Special care baby unit?

Answered: 30 <25weeks



Q21: Was your baby in Special care baby unit?

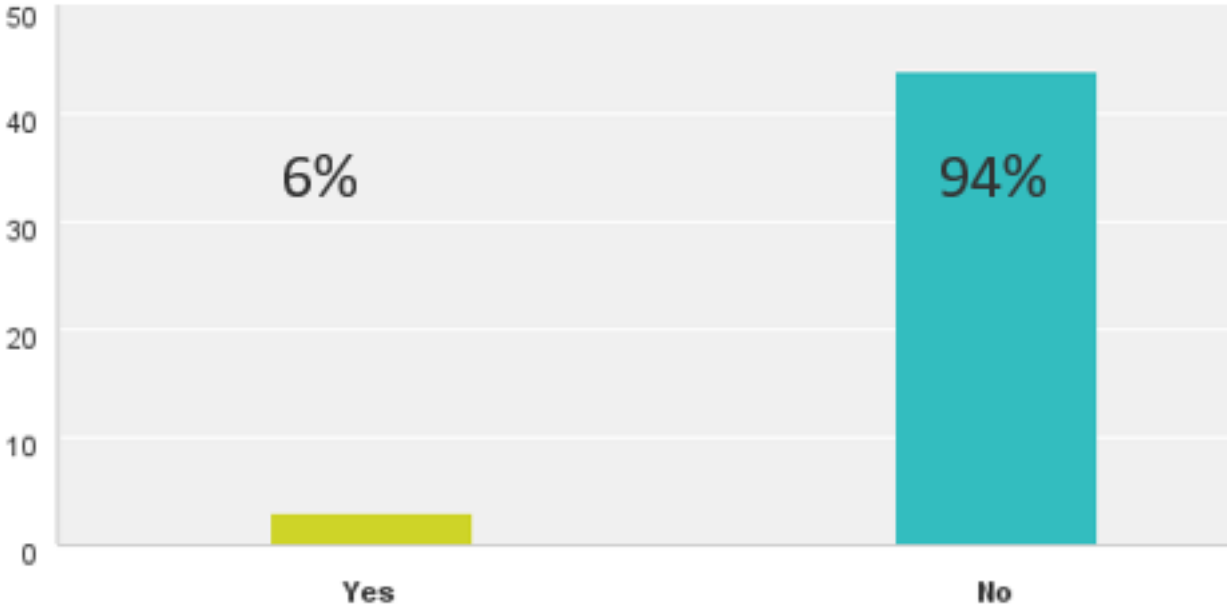
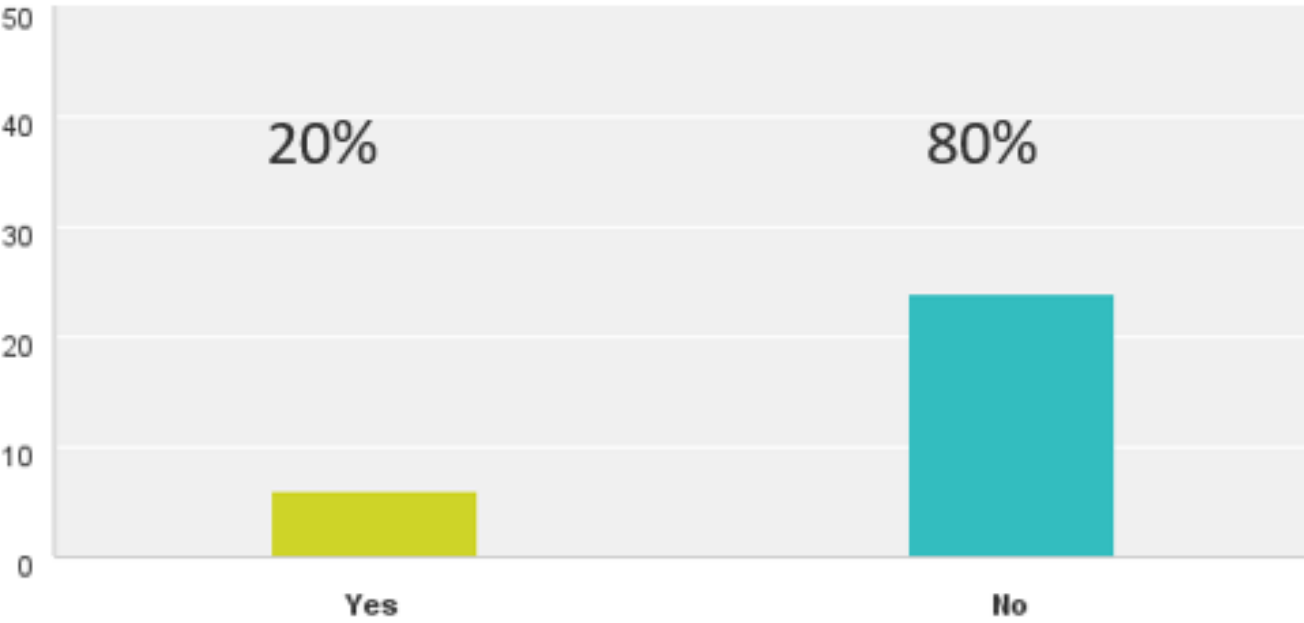
Answered: 47 [26 weeks+](#)



Q21: Was your baby in Special care baby unit?

Answered: 30 <25weeks

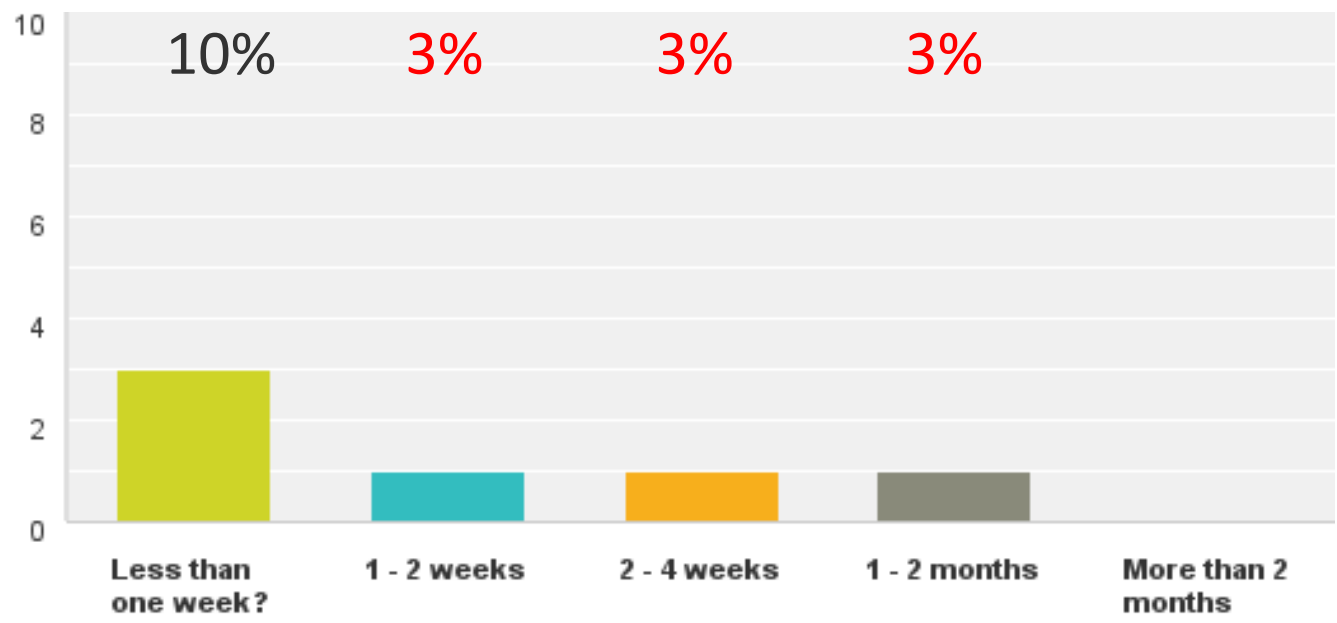
Answered: 47 26 weeks+



P value =

Q22: If your baby was in the Special Care Baby, unit how long were they there for?

Answered: 6 Skipped: 24 <25weeks



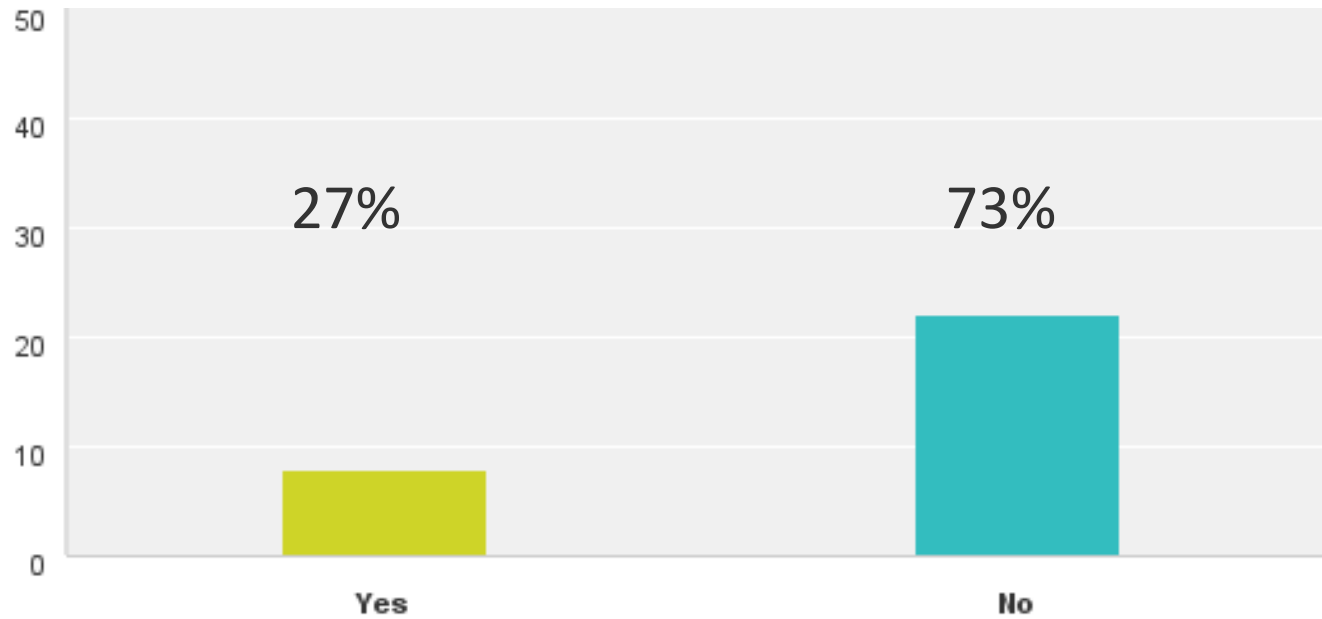
Q22: If your baby was in the Special Care Baby, unit how long were they there for?

Answered: 3 Skipped: 44 26 weeks+



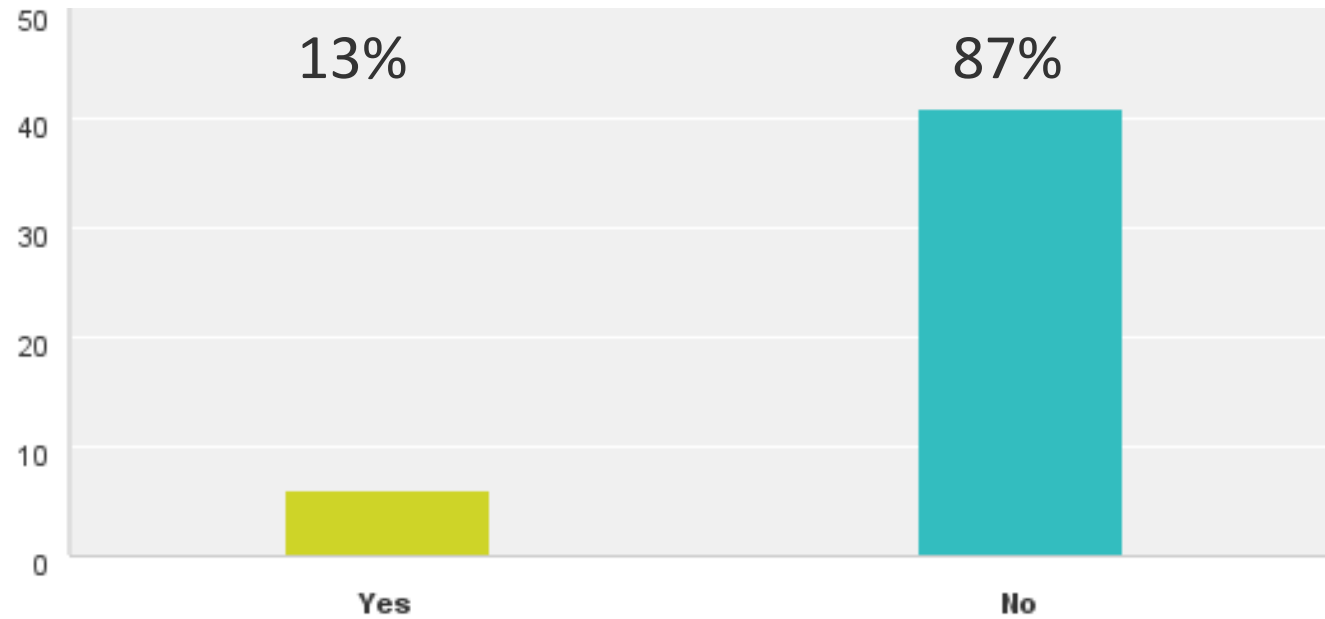
Q23: Did YOU have any complications after delivery?

Answered: 30 <25weeks



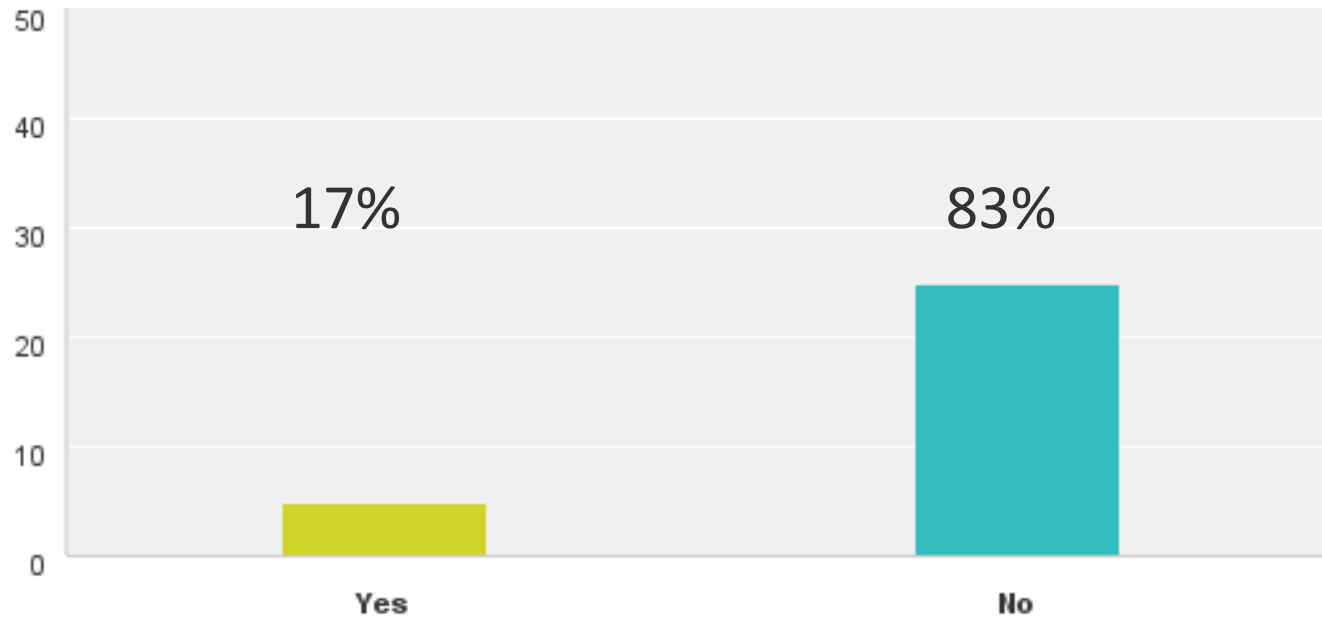
Q23: Did YOU have any complications after delivery?

Answered: 47 [26 weeks+](#)



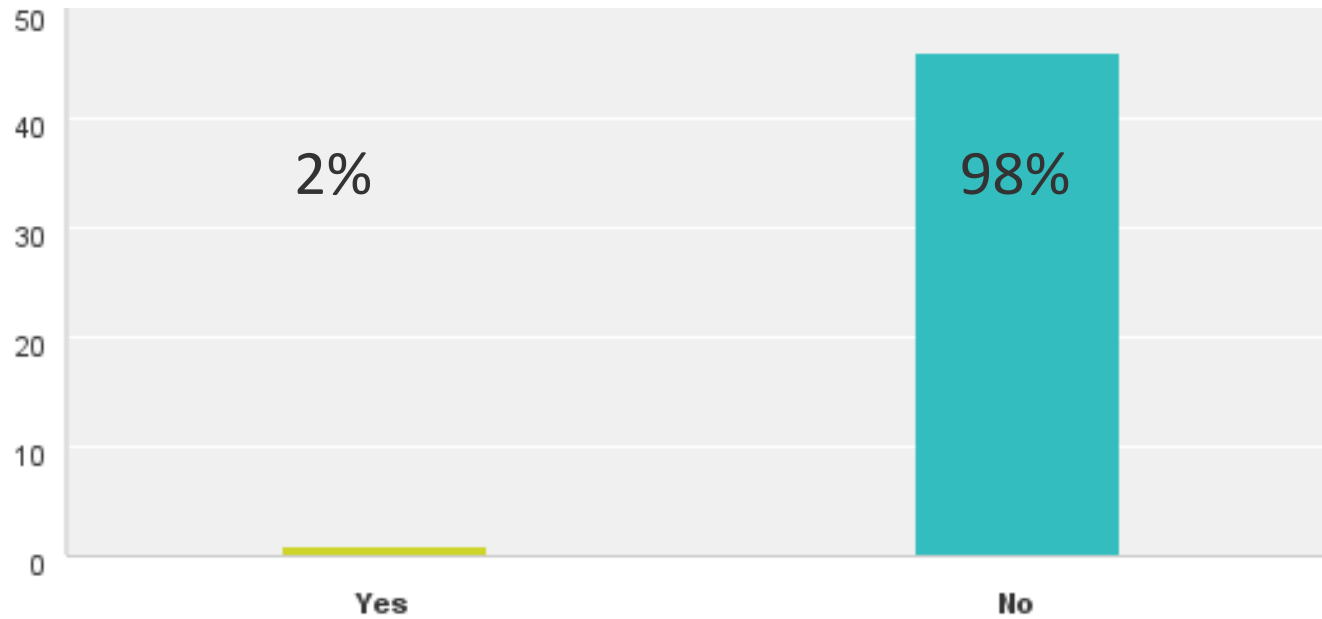
Q25: Did your baby have any complications after delivery?

Answered: 30 <25weeks



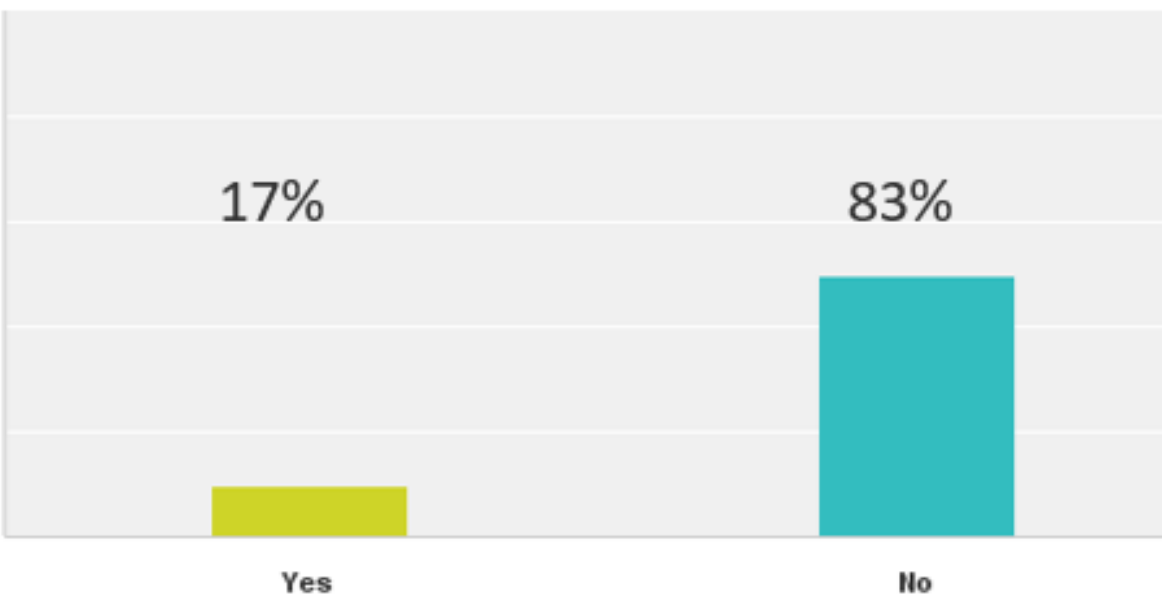
Q25: Did your baby have any complications after delivery?

Answered: 47 26 weeks+

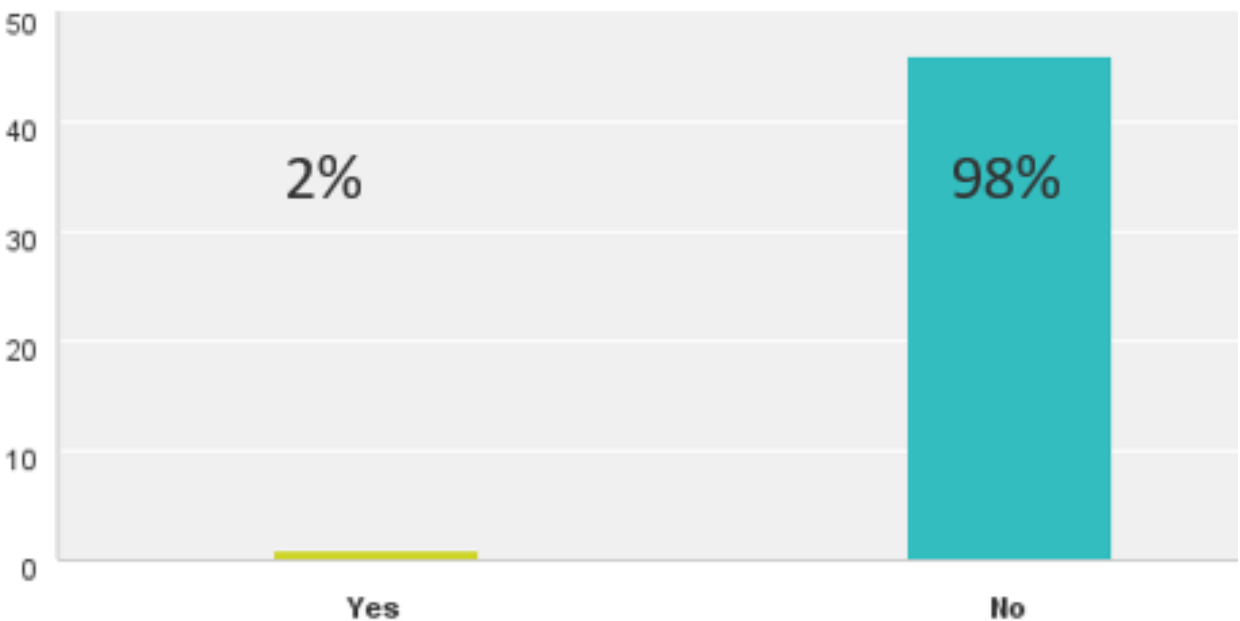


Q25: Did your baby have any complications after delivery?

Answered: 30 <25weeks



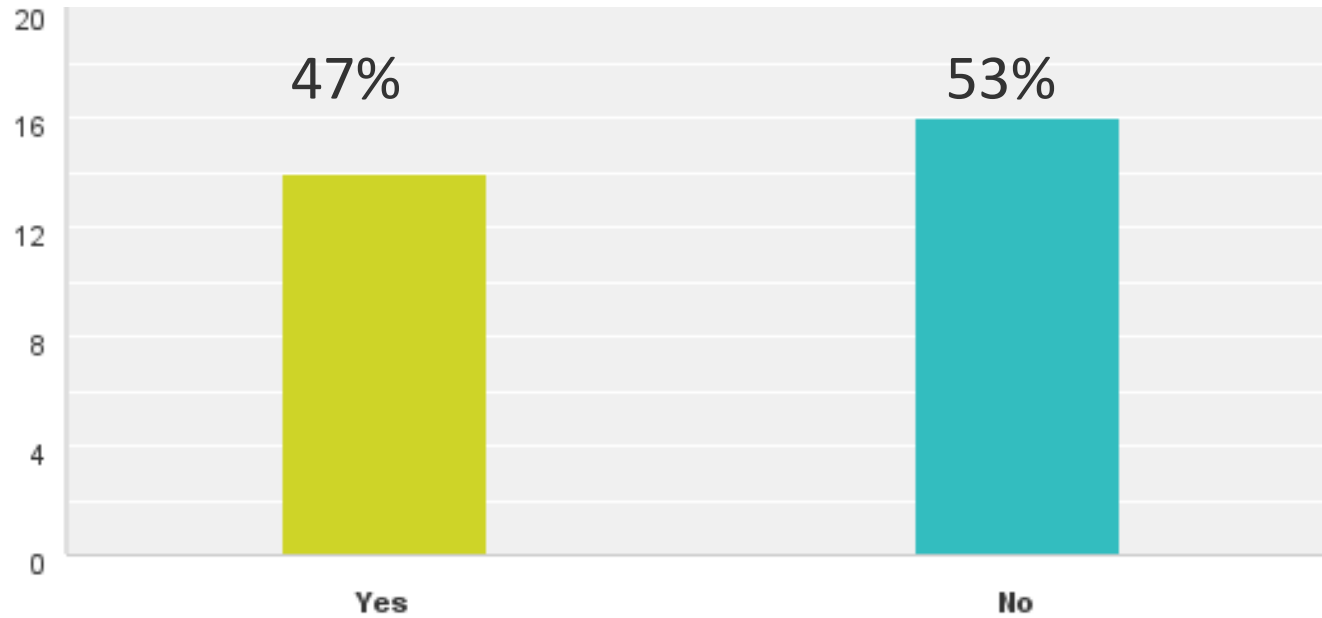
Answered: 47 26 weeks+



P value =

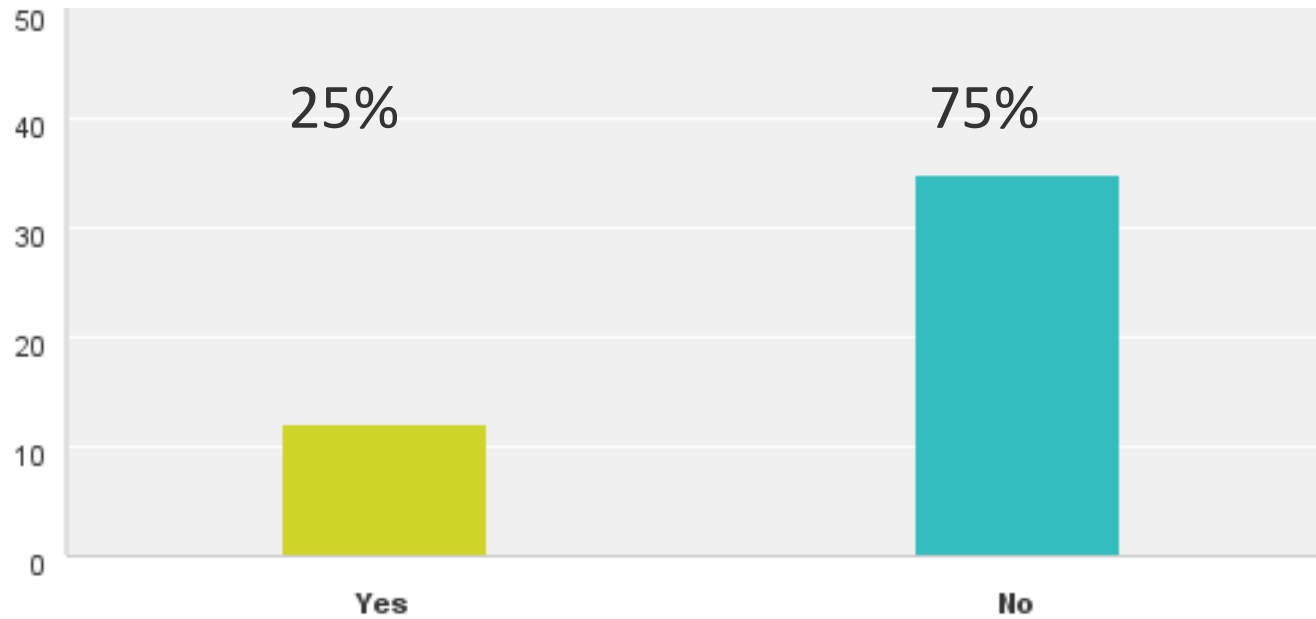
Q31: Has your child needed antibiotics for a chest infection?

Answered: 30 <25weeks



Q31: Has your child needed antibiotics for a chest infection?

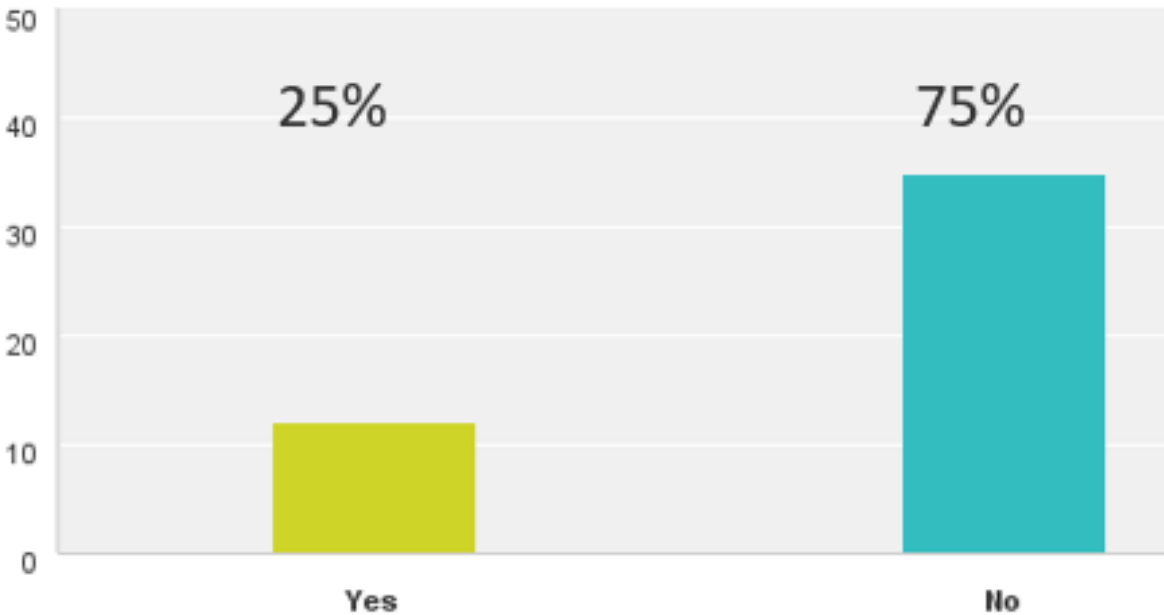
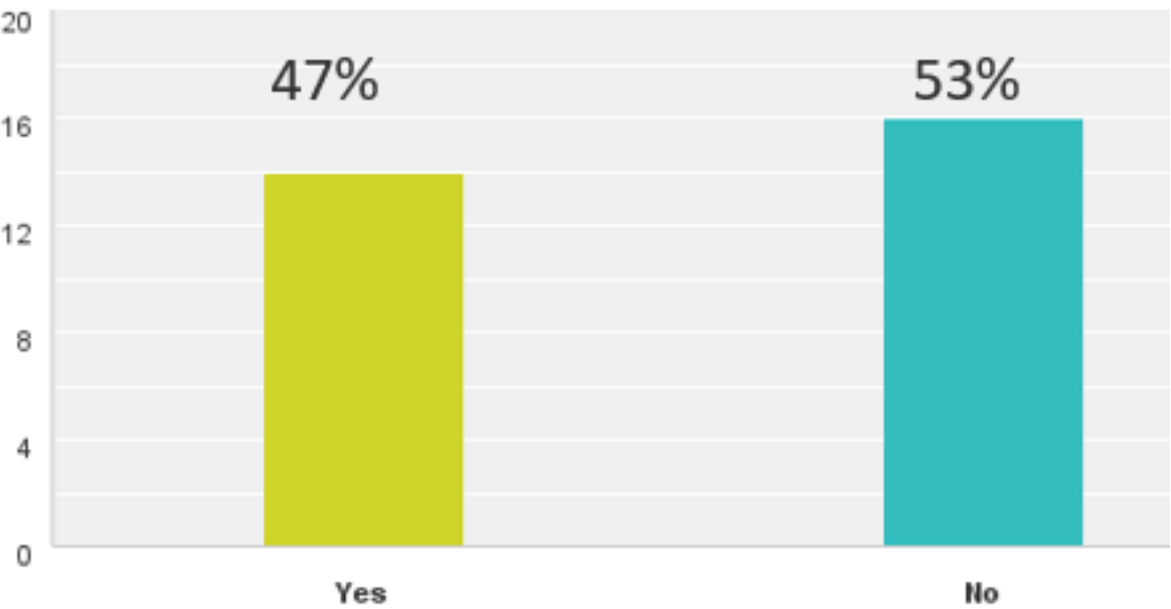
Answered: 47 [26 weeks+](#)



Q31: Has your child needed antibiotics for a chest infection?

Answered: 30 <25weeks

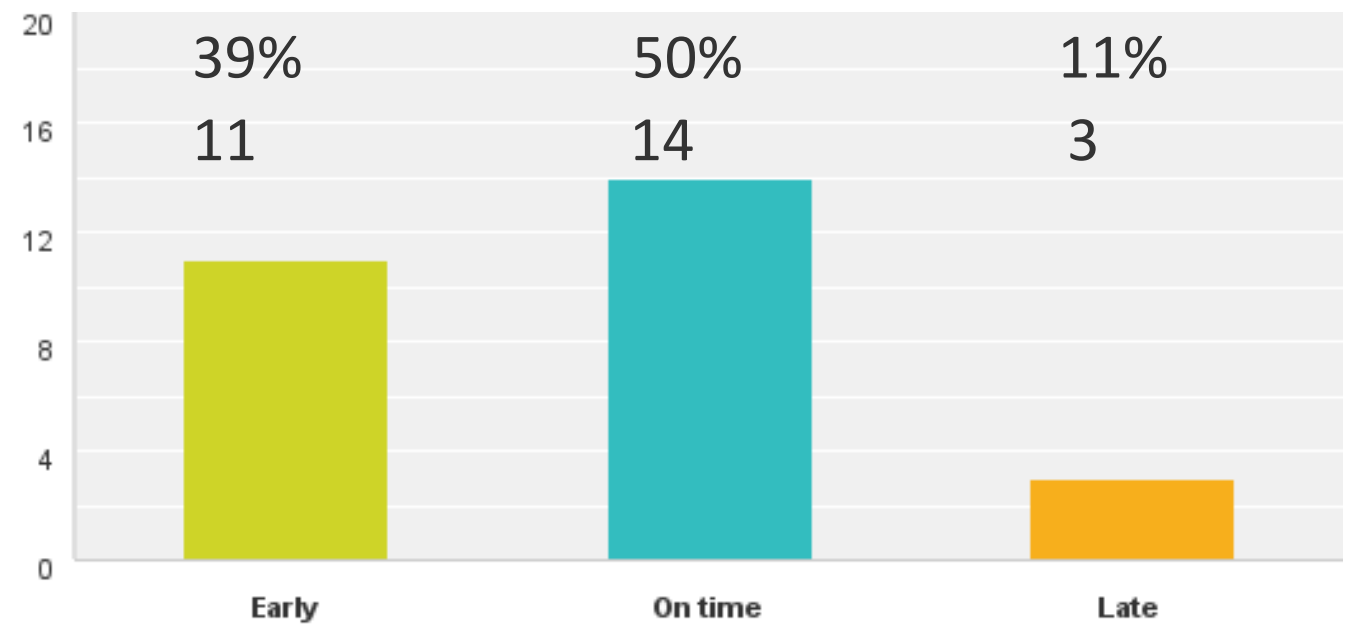
Answered: 47 26 weeks+



P value =

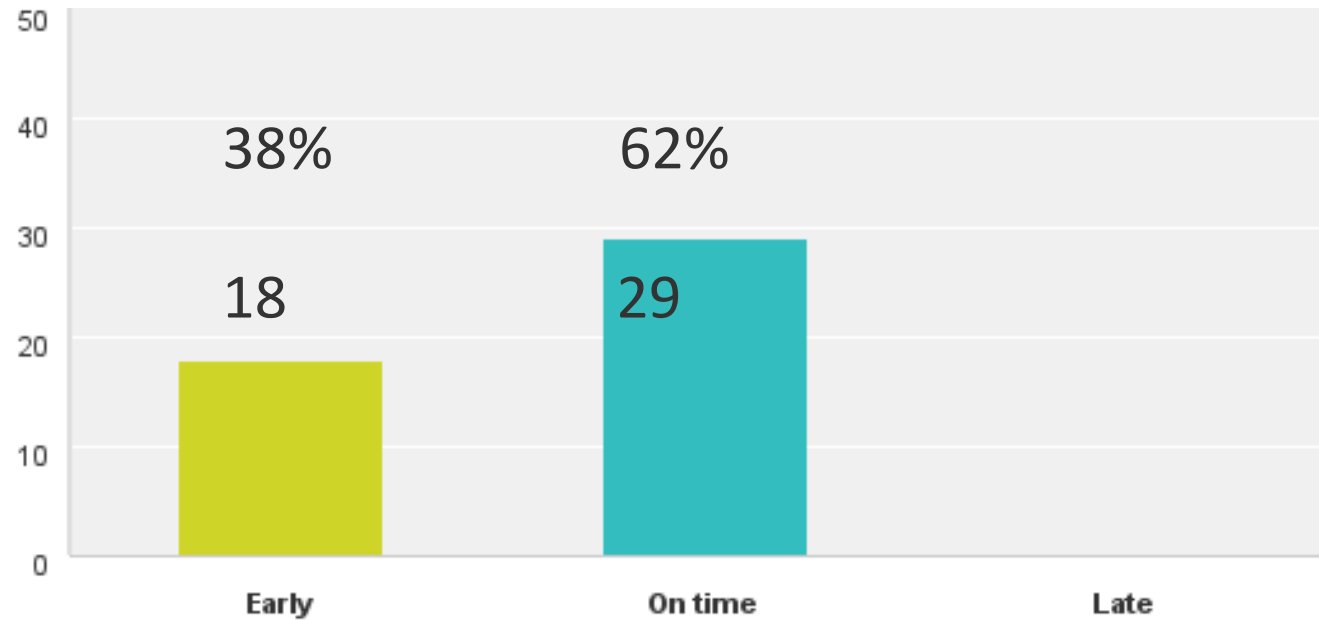
Q35: Overall, has your child reached their developmental milestones

Answered: 28 Skipped: 2 <25weeks



Q35: Overall, has your child reached their developmental milestones

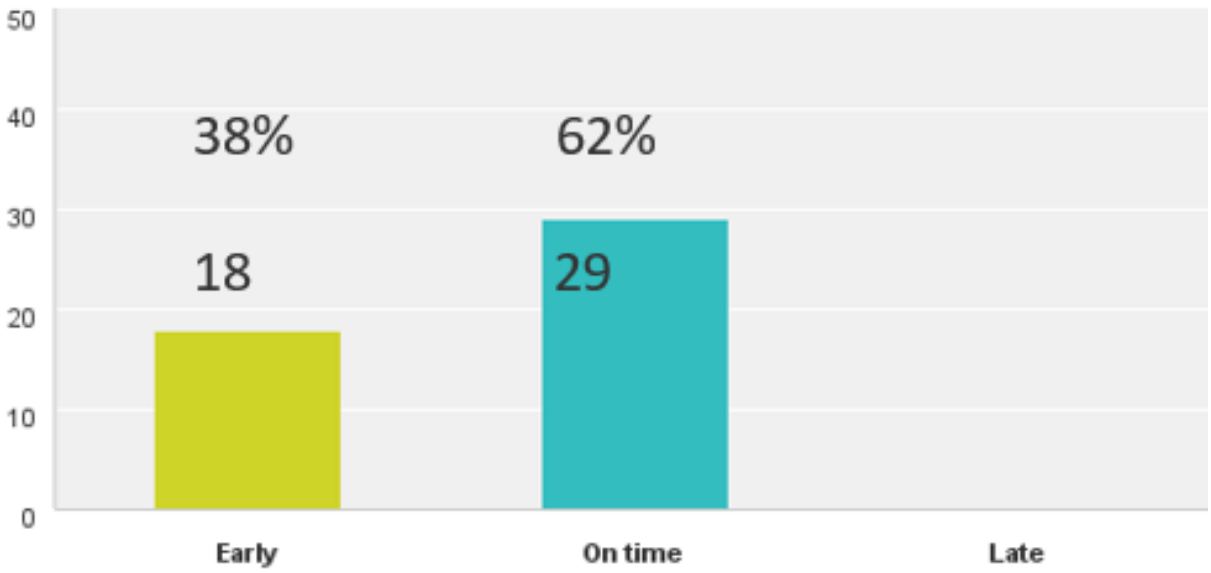
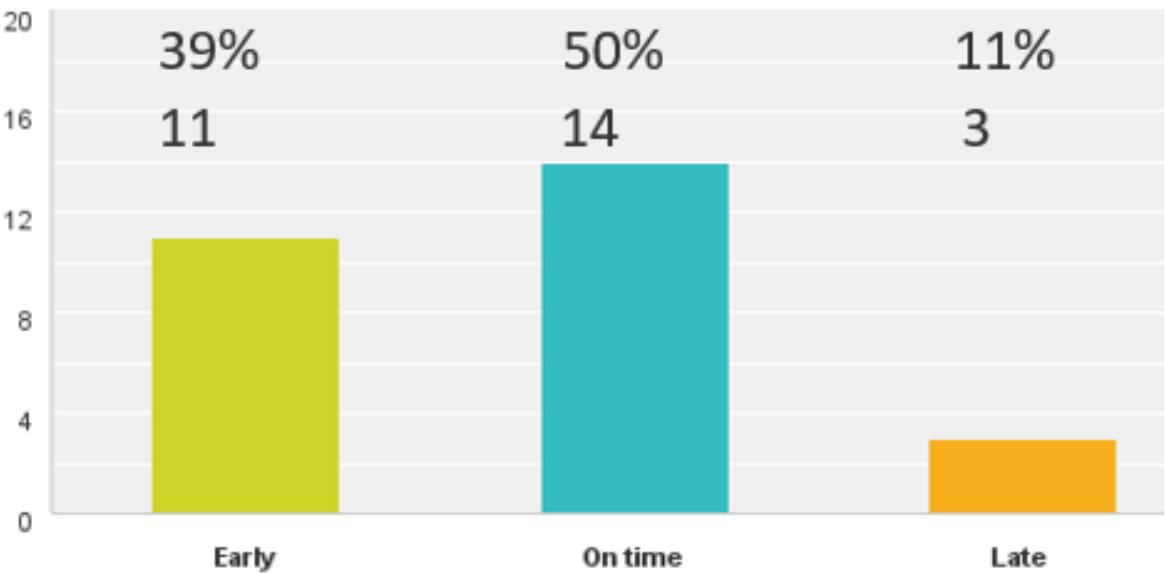
Answered: 47 [26 weeks+](#)



Q35: Overall, has your child reached their developmental milestones

Answered: 28 Skipped: 2 <25weeks

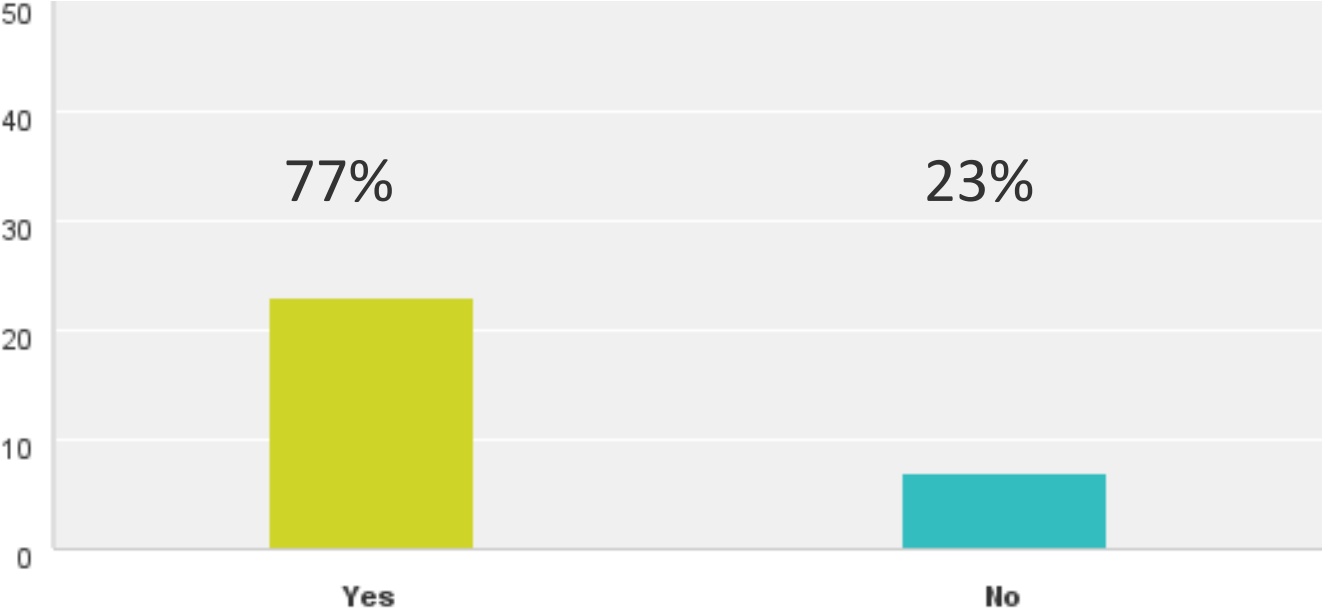
Answered: 47 26 weeks+



P value =

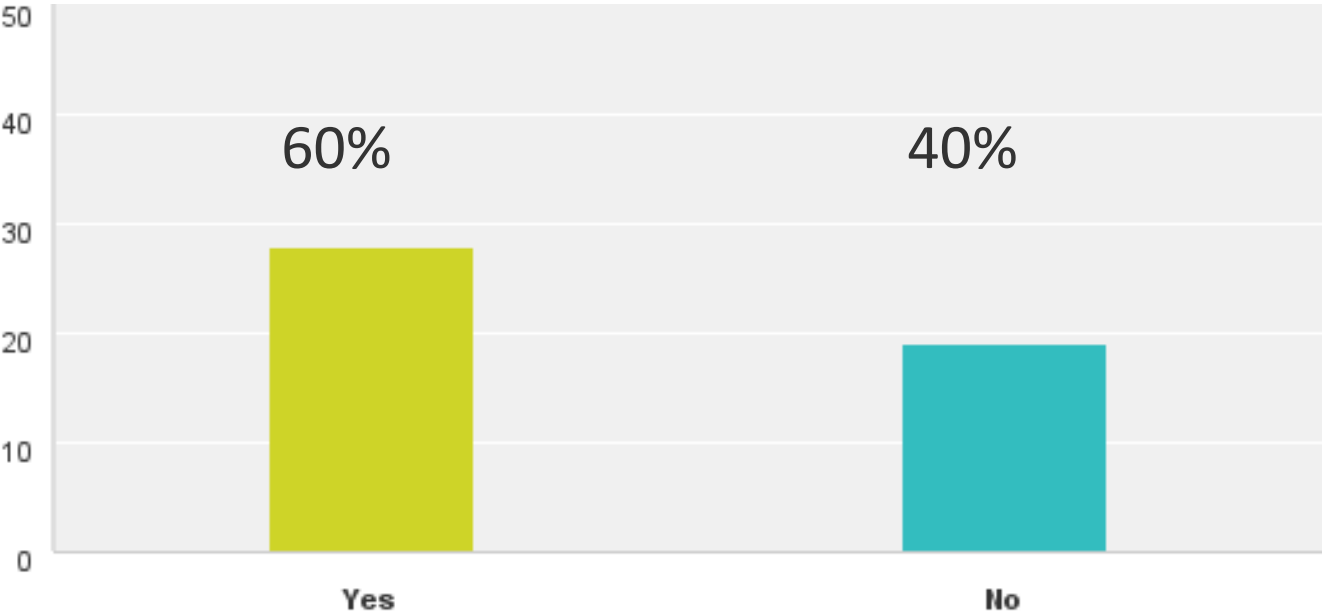
Q37: Was your child breast-fed?

Answered: 30 <25weeks



Q37: Was your child breast-fed?

Answered: 47 26 weeks+



LDN IN PREGNANCY – PATIENT SURVEY 2016

Questions

1. Is it safe to take LDN during pregnancy?
2. Are there additional benefits to mum or baby from taking LDN in pregnancy?
3. How long should you take LDN during pregnancy?

LDN IN PREGNANCY – PATIENT SURVEY 2016

Questions

1. Is it safe to take LDN during pregnancy? YES
2. Are there additional benefits to mum or baby from taking LDN in pregnancy?
3. How long should you take LDN during pregnancy?

LDN IN PREGNANCY – PATIENT SURVEY 2016

Questions

1. Is it safe to take LDN during pregnancy? YES
2. Are there additional benefits to mum or baby from taking LDN in pregnancy? Yes – for mum and baby
3. How long should you take LDN during pregnancy?

LDN IN PREGNANCY – PATIENT SURVEY 2016

Questions

1. Is it safe to take LDN during pregnancy? YES
2. Are there additional benefits to mum or baby from taking LDN in pregnancy? Probably yes– for mum and baby
3. How long should you take LDN during pregnancy? 37wks

BUTIF I CAN
DREAM...!



WE HAVE THE POTENTIAL.....

WE HAVE THE POTENTIAL.....

- To improve the health of future generations.....

Epigenesis on endometriosis



Dr. Alejandro Leal

Environment



Methylation pattern



Pattern inherited

Hormonal response
changes

Immunological
response changes

Effects of environment in inheritance



Source: <http://www.specialneedsdigest.com/2013/08/epigenetics-how-early-life-environment.html>

Large Study Links Autism to Autoimmune Disease in Mothers

About one in ten women who have a child with autism have immune molecules in their bloodstream that react with proteins in the brain, according to a study published 20 August in Molecular Psychiatry (1).

“It’s a very large sample size with 2,700 mothers of children with Autism,”

Mothers of an ASD child were four times more likely to harbour anti-brain antibodies than unselected women of child-bearing age (10.5 vs 2.6%).

This study provides robust evidence that brain-reactive antibodies are increased in mothers of an ASD child and may be associated with autoimmunity.

<http://www.ncbi.nlm.nih.gov/pubmed/23958959>

THANK YOU



