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15th April 2018

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Department of Health and Human Services, Food and Drug Administration [Docket No. FDA-2018-N-1072]: International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; Cannabis Plant and Resin; Extracts and Tinctures of Cannabis; Delta-9-Tetrahydrocannabinol; Stereoisomers of Tetrahydrocannabinol; Cannabidiol; **Request for Comments** (FR Doc. 2018-07225).

Federal Register Submission

*Re: Re-Scheduling of Cannabinoids in USA
Pattern of Colorado Birth Defects 2000-2013*

As a researcher I am concerned about the public health impacts of the known genotoxic effects of cannabis at the population health level.

One of the more obvious places to look to pick up clues that this might be acting is in the Registers of Birth Defects. Unfortunately it appears that extracting quantitative data on birth defects is very difficult as very few make their data publicly available. I have written to Hawaii, Colorado, California, CDC Atlanta, Georgia and MACDP Atlanta, Georgia but as at the time of writing have not had meaningful responses.

Naturally your office is in a much better position to request data urgently from your counterparts in other branches of the American Government and I would strongly urge you to do so.

However a friend was able to send me a link to a registry in Colorado which is of some use and more than a little interest. The data is so concerning that I wished to bring it to your attention. The following notes are written as a commentary on the attached short slide series. Note that the data from the Colorado Registry is supplied only by a single abnormality one at a time, and only for a single year, one at a time. Hence actually downloading the data is very time consuming and more than a little laborious. The two URL's concerned to the Colorado Health Information Dataset are <http://www.chd.dphe.state.co.us/cohid/> and <http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsqli>. Colorado legalized cannabis for recreational use in 2012 and then again fully for recreational use in 2014. Hence the 2014 births defects data is of particular interest. I am told that this data was to be released four months ago, but at the time of writing it is not available.

The data series achieves particular significance in the light of a previously cited teratological literature linking cannabis to various major congenital malformations.

It should be noted that a major factor in interpreting these curves is the termination rate. Since therapeutic termination is a major management option chosen by many parents for the more severe defects, and widely recommended by many obstetricians, one cannot really form a comprehensive understanding of the applicable trends without knowledge of and due consideration to, the associated antenatal termination rate for the applicable defect.

Both for this reason, and because the data only goes to 2013 it is considered that this data is only reflecting the lower bound of the effects in question. That is to say that these estimates form a lower estimate of the putative cannabis -related teratogenic effect.

Slide Series

Slide 1 (S1) introduces a title slide for this slide series.

S2 shows the overall pattern of births in Colorado which is drawn on two scales for clarity. The equation given for the top line shows that whilst the birth rate in Colorado fluctuates somewhat over the study period there is an overall decline of 159 births per years over the study period, albeit the detailed pattern is somewhat irregular. It is important to bear this in mind in considering the following graphs showing numbers of defects and rates.

S3 shows Down's syndrome data from Western Australia. This slide makes it very clear that whilst the rate of Downs syndrome born as live births is declining somewhat, the termination rate for this anomaly has risen markedly, so that their sum shows a clear upward trend. This important graph clearly underscores the critical role played by the applicable termination data in interpreting the trend lines under consideration. One notes that the termination data for Colorado for the present defects is believed not to be available at the time of writing.

On the basis of this graph it may be that the effects described below are as much as one half to one third of their total level net of the effect of therapeutic termination – although the level of this is obviously highly defect specific.

S4 introduces a title slide for this section.

S5 shows a very important slide which graphs the numbers and rates for all major congenital anomalies. It shows a clear upward trend for both numbers and rates. The raw data is given in the table to the right hand side. The numbers show a 69% rise across this fourteen year period, whilst the rates show a 70% rise. This annualizes to approximately 4.93% annual rate of rise for numbers and a 5.01% annual rate of rise for rates. Maintained over a 14 year period this is a not insignificant increase in the health burden to both individuals and the health system which treats these significant inborn defects.

There is also a rich literature linking antenatal cannabis use with cardiovascular defects ¹⁻⁶, and a statement from the combined American Heart Association and American Academy of Pediatrics acknowledging that there is a causal link between cannabis and congenital heart disease ⁷.

S6 shows these rates as a percentage including the data on the graph.

The graphs in S7 show a significant rise in the rate of congenital heart disease. The equation on the upper graph shows an additional 40 cases per year (line slope). Both the numbers and rates of congenital heart disease are rising by about 4.5% annually, and about 61% over the whole period.

Ventricular Septal Defect (VSD) is also linked with cannabis use ^{1,6,7}. S8 shows that this is rising by about 6 cases annually, 35% overall, and about 2.5% annually.

S9 illustrates trends in the ostium secundum Artrial Septal Defect (ASD) which has previously been linked with cannabis exposure ^{6,7}. This is noted to be rising by about 46 cases annually; to have increased 260% over the whole period and to be rising at 18% annually. Indeed one also notes that the linear regression line accounts for 89% of the variance of the data. This implies that the rising trend is a strong and dominant factor in this trend line.

S10 shows data for microcephaly. One notes and average of 2 extra cases annually, a 96% rise over the 14 year period, and an annual rate of rise of 7%.

Chromosomal abnormalities have been reported as being associated with antenatal cannabis use. The data in S11 shows a increase of 3 cases per year, of 28% over the whole period and of 2% annually.

S12 introduces a summary slide for some of the selected stationary trends.

Many of the trends for congenital defects in Colorado are essentially stationary. Such data is shown for Cleft lip with or without cleft palette in S13, and for combined abdominal wall defects in S14. Several of the other defects which were inspected also appeared to be showing no real time dependent change or to occur at such low level that their trends are not stable. One notes in particular that gastroschisis, a defect which has been strongly linked with cannabis use in many studies ^{6,8-14} does not have data presented separately for it on the Colorado Health Information Dataset site at this time.

S15 presents a title slide for the cumulative and summative effect.

S16 shows a simple method, carry-forward projection for analyzing historcial trends. This is done first for births. The birth rate in the first 1-2 years (whichever is the lower) is simply carried forwards as if it had not changed in any of the subsequent years. The actual birth rate is listed in the second column. The difference appears in the fourth column and is the difference from the expected rate had the historical trends been simply continued along.

These various columns are then summed at their base as shown. One notes that an extra 33,311 births occurred than would have been expected, representing a 3.6% increase in births over this historical period, which annualizes to a 0.26% increase per year.

S17 shows the trend for all major congenital birth defects. This slide shows that whereas 67,620 would have been expected based on the historical trend, in fact 87,772 were observed, an excess of 20,152 cases or 29.8%.

S18 performs a similar calculation for all major cardiovascular defects and finds a 37% excess caseload.

S19 performs a similar function and finds a 17% excess for VSD.

S20 does the same function for ostium secundum ASD and finds a 98% excess caseload.

S21 shows a 30% excess for Microcephaly. The significance of this finding in a Zika virus era will I am sure not be lost on you.

S22 shows the data for the combined chromosomal anomalies and finds a 28% excess caseload.

S23 introduces a title slide for the final Summary section.

S24 shows the apparently very close correlation between all major congenital anomalies and cannabis use by various age groups in Colorado, as taken from the SAMHSA NSDUH survey at <https://www.samhsa.gov/data/population-data-nsduh/reports?tab=38>.

S25 Shows the key graph again with its data included.

S26 presents the output of the R statistical analytical software showing the correlation coefficient, $R=0.953852$ and $P = 0.00006594$.

S27 presents another correlation calculation this time with the young adult rate of cannabis use again from the NSDUH SAMHSA survey (Data given in S24). In this study $R=0.9254789$ and $P = 0.00003457$.

S28 shows similar data with the major anomaly rate compared to the cannabis use rate in all Colorado dwellers over the age of 12 years. $R=0.8825038$ and $P = 0.00002936$.

S29 again shows this key graph.

S30 shows a final slide which summarizes all of the above information in a single table. The first column lists the various rising defects which have been considered. The second column shows the numbers of actual cases observed over the study period. The third column shows the number which would have been expected had the baseline trend been simply projected forwards. The fourth column gives the observed excess of cases for these defects. The fifth column shows the percentage rise over the entire period. The first line shows the numbers of births which forms the baseline trend against which the other categories are compared. The numbers of births rose 3.6% in the period 2000-2013. The other anomalies are compared with the rise in births to calculate the final column as a multiplicand of the baseline increase in birth numbers.

As noted above, this factor is believed to be a lower bound baseline since it is expected that for many of these defects foetal wastage would have occurred either by natural spontaneous miscarriage or by induced therapeutic termination of pregnancy, as indicated in Slide 3.

Conclusion

Hence these data indicate a significant rise in the official numbers of major congenital anomalies in Colorado over the period when cannabis was gaining in popularity and into the very start of its medical legalization. Hence the figures are believed to be an underestimate of the cannabis related effect. They would almost certainly be substantially increased were data on therapeutic and other termination of pregnancy to become available. Hence these estimates included in the final table on S23 can only be seen as estimating the lower bound of the cannabis effect. Since the net effect shows an increase of 30% of all major defects, this can only be interpreted as a finding generating significant concern.

Matters of attributable risk effect arise in terms of interpreting how much of the increase might properly be attributed to cannabis itself and how much to various other extraneous and unknown confounding causes. Given that there is a published literature relating cannabis to all of these identified anomalies it seems likely that some significant fraction of the 20,152 excess cases can well be laid at the feet of cannabinoids. One notes also that these patients are exposed to mixed cannabinoids as occur in natural and cultured cannabis, including tetrahydrocannabinol, cannabidiol, cannabinol, cannabichromene, cannabiverin and many others so that all of them are potentially implicated on epidemiological grounds. Moreover many studies implicate multiple cannabinoids including cannabidiol in both genotoxic¹⁵⁻²⁴ and arteriopathic and / or arteritic²⁵⁻⁶⁵ pathways.

The above cited literature links both maternal and paternal cannabis exposure⁴ to teratological outcomes particularly congenital heart disease which is also the commonest of the major foetal malformations. The above citations also demonstrate significant multiple and complex interactions between cannabinoids and the cardiovascular system. Thus there are multiple potential mechanistic pathways from cannabis exposure to foetal pathology.

It was considered at the present time that it was important to bring these data to your attention as they are likely of significant public health import, particularly when amplified up to the national level. This is particularly so if, as is now a matter of record, cannabis use is becoming more common^{64,66}, if cannabis itself is becoming more concentrated as has also been amply documented⁶⁴ and if the major effect of therapeutic abortion is also included as seems only proper⁶⁷.

Please feel free to call on me if you would like further information concerning the research to which I have referred.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'S Reece', with a stylized flourish at the end.

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Australia.

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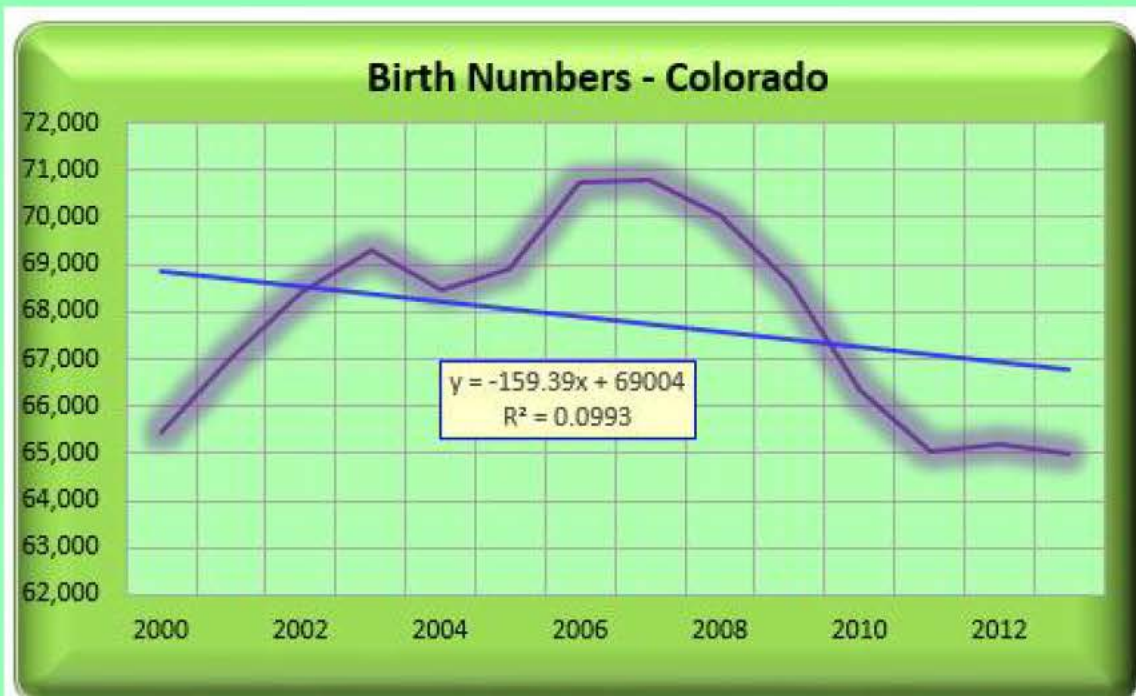
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Congenital Anomalies Colorado

2000-2013

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql>

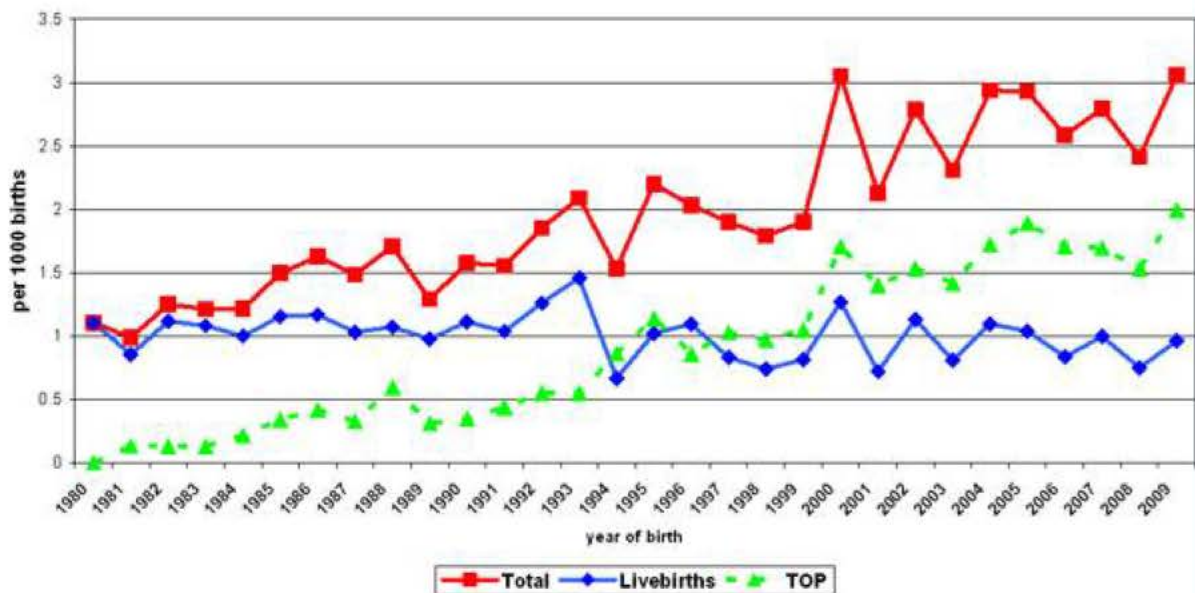
Births



Down's Syndrome in Western Australia

8. Down Syndrome: total, live births and terminations of pregnancy

Down syndrome: total, livebirths and terminations of pregnancy



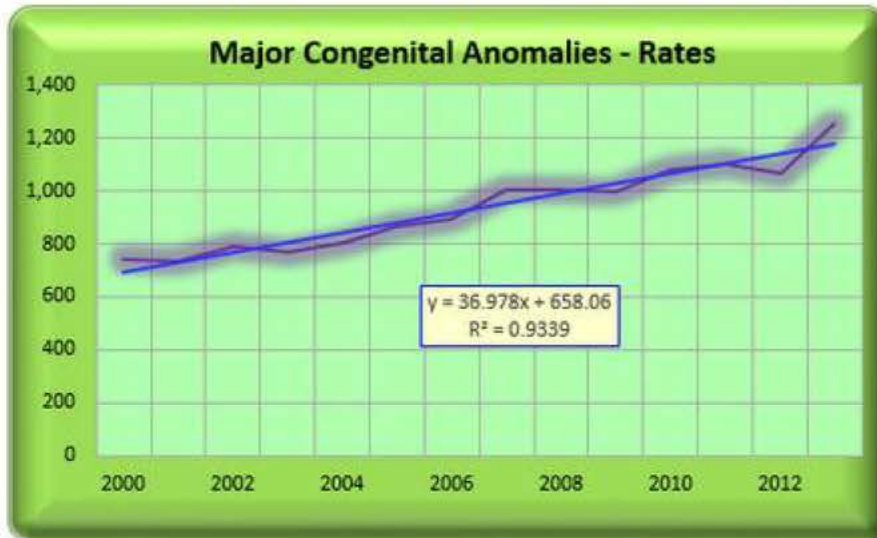
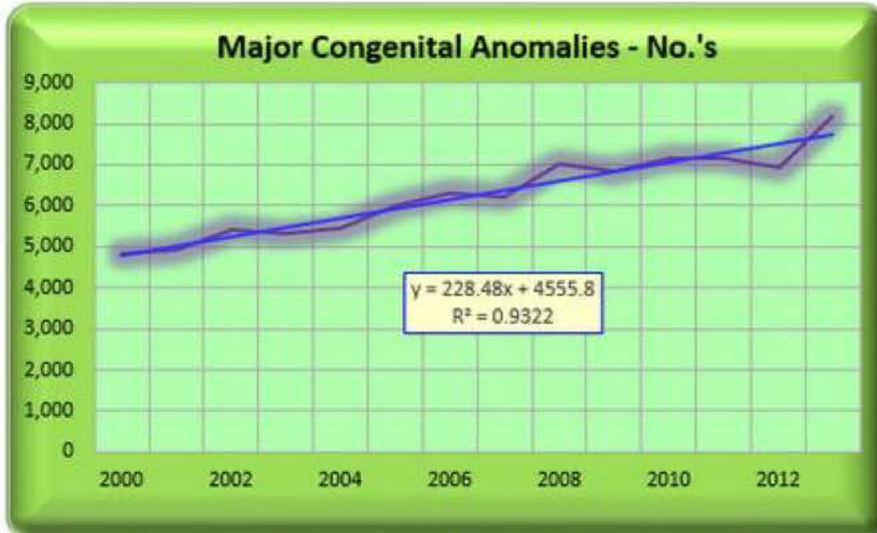
http://www.kemh.health.wa.gov.au/services/register_developmental_anomalies/monitoring_trends.htm

Rising Trends

Colorado 2000-2013

<http://www.chd.dphe.state.co.us/cohid/>
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Major Congenital Anomalies



Major Congenital Anomalies

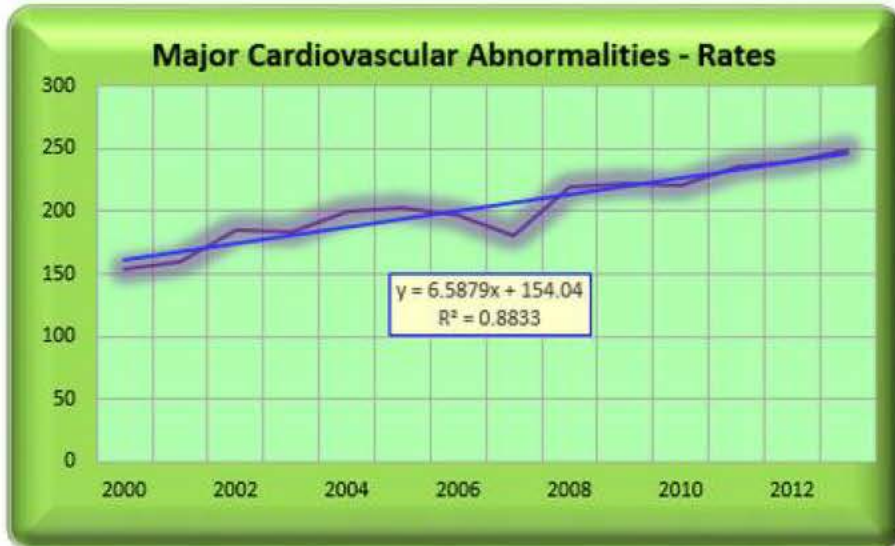
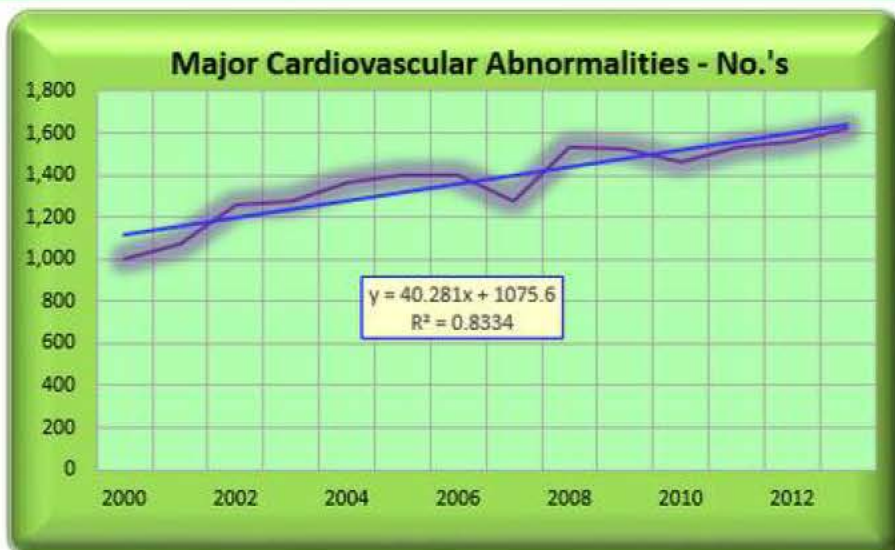
Rates/ 10,000 Live births
 (Excluding Terminations)

| Year | Majors | Majors Rate |
|-------------------|---------------|---------------|
| 2000 | 4830 | 738.2 |
| 2001 | 4942 | 737.5 |
| 2002 | 5406 | 790.1 |
| 2003 | 5311 | 766.3 |
| 2004 | 5482 | 800.6 |
| 2005 | 5978 | 867.4 |
| 2006 | 6325 | 894.2 |
| 2007 | 6213 | 1001.0 |
| 2008 | 7010 | 1001.0 |
| 2009 | 6826 | 995.0 |
| 2010 | 7171 | 1080.8 |
| 2011 | 7174 | 1102.8 |
| 2012 | 6939 | 1064.5 |
| 2013 | 8165 | 1256.1 |
| | | |
| Rise % | 69.04% | 70.16% |
| Annualized | 4.93% | 5.01% |

Major Congenital Anomalies as Percentage



Major Cardiovascular Anomalies

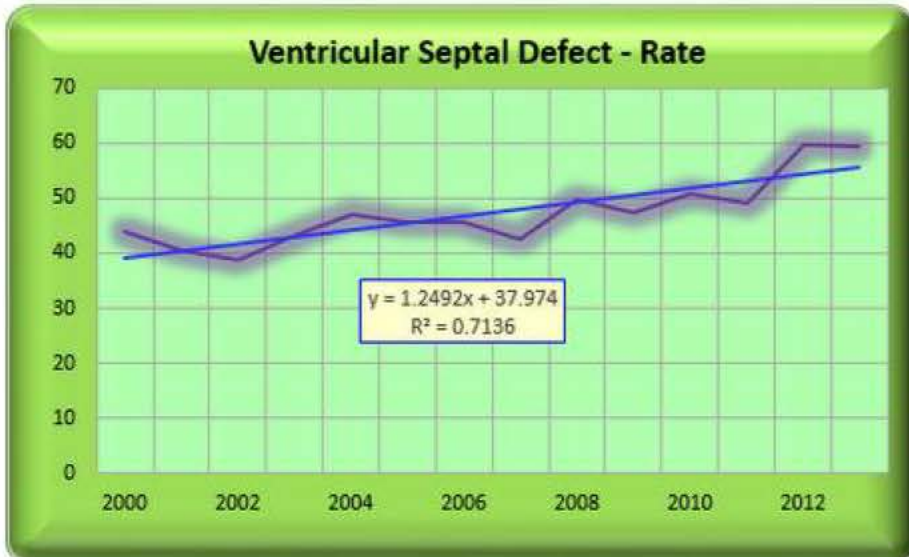
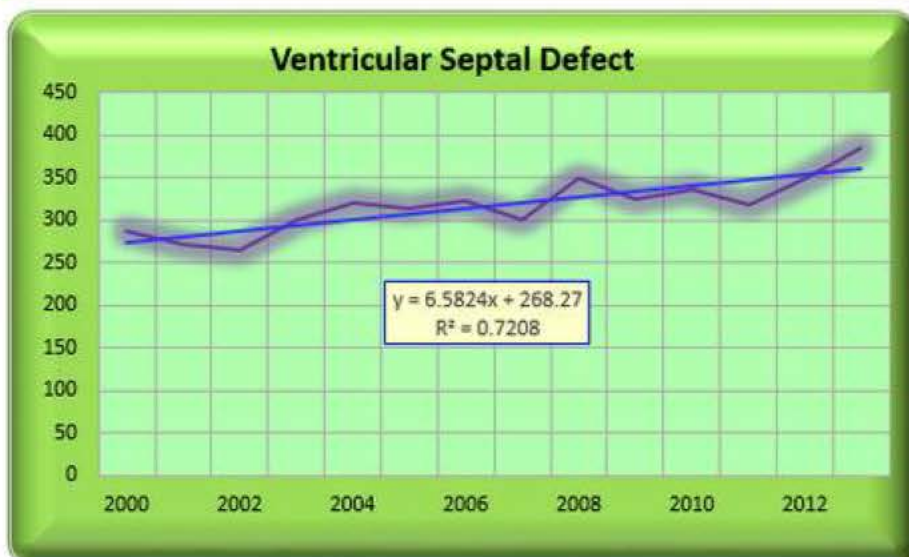


Major CVS Abnormalities

Rates/ 10,000 Live births
 (Excluding Terminations)

| Year | CVS | CVS Rate |
|------------|--------|----------|
| 2000 | 1002 | 153.1 |
| 2001 | 1071 | 159.8 |
| 2002 | 1263 | 184.6 |
| 2003 | 1273 | 183.7 |
| 2004 | 1368 | 199.8 |
| 2005 | 1398 | 202.8 |
| 2006 | 1397 | 197.5 |
| 2007 | 1274 | 179.9 |
| 2008 | 1530 | 218.5 |
| 2009 | 1528 | 222.7 |
| 2010 | 1464 | 220.7 |
| 2011 | 1536 | 236.1 |
| 2012 | 1562 | 239.6 |
| 2013 | 1622 | 249.5 |
| | | |
| Rise % | 61.88% | 62.97% |
| Annualized | 4.42% | 4.50% |

Ventricular Septal Defect

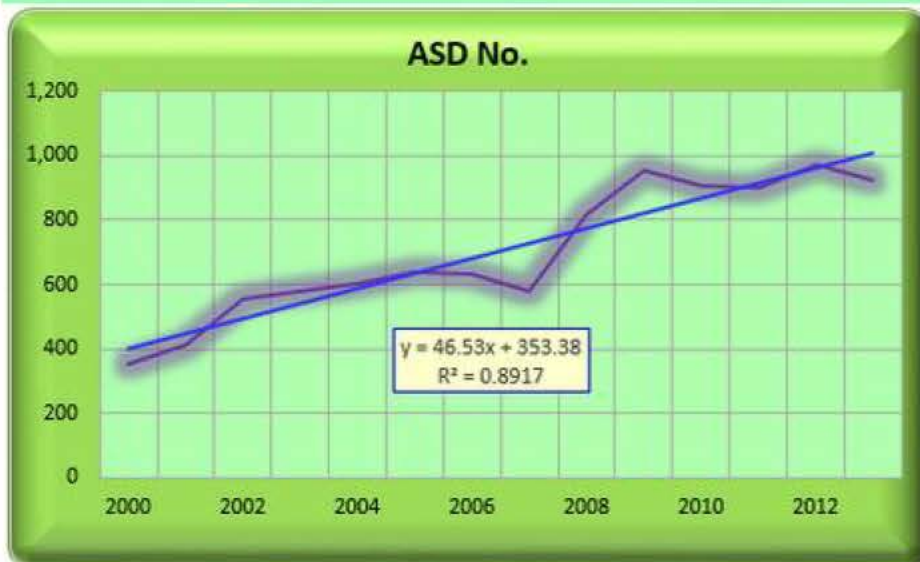


VSD

Rates/ 10,000 Live births
 (Excluding Terminations)

| Year | VSD | VSD Rate |
|-------------------|---------------|---------------|
| 2000 | 287 | 43.9 |
| 2001 | 271 | 40.4 |
| 2002 | 265 | 38.7 |
| 2003 | 300 | 43.3 |
| 2004 | 321 | 46.9 |
| 2005 | 315 | 45.7 |
| 2006 | 323 | 45.7 |
| 2007 | 300 | 42.4 |
| 2008 | 349 | 49.8 |
| 2009 | 324 | 47.2 |
| 2010 | 337 | 50.8 |
| 2011 | 319 | 49.0 |
| 2012 | 350 | 59.6 |
| 2013 | 386 | 59.4 |
| | | |
| Rise % | 34.49% | 35.31% |
| Annualized | 2.46% | 2.52% |

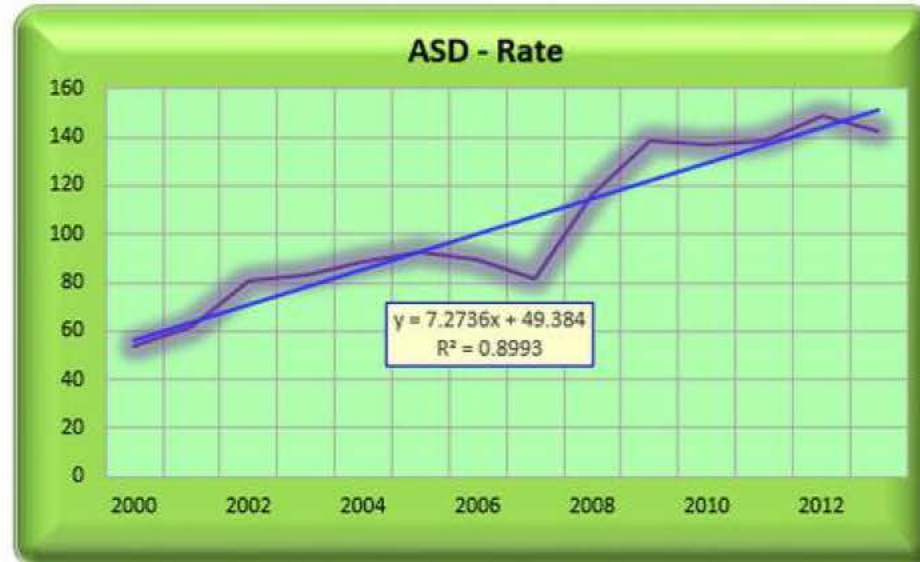
Atrial Septal Defects - Ostium Secundum



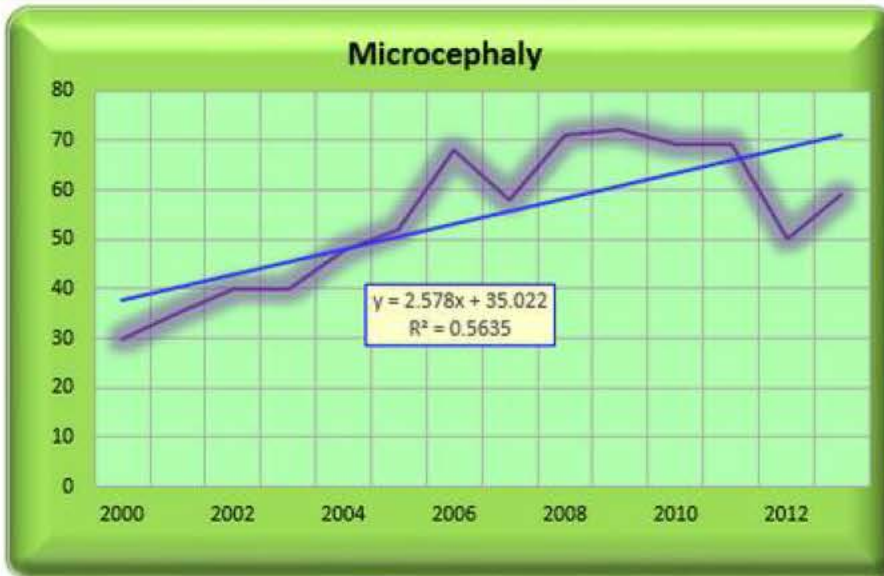
Ostium Secundum ASD's

Rates/ 10,000 Live births
 (Excluding Terminations)

| Year | ASD No. | ASD - Rate |
|-------------------|----------------|----------------|
| 2000 | 355 | 54.3 |
| 2001 | 415 | 61.9 |
| 2002 | 554 | 81 |
| 2003 | 579 | 83.5 |
| 2004 | 606 | 88.5 |
| 2005 | 637 | 92.4 |
| 2006 | 635 | 89.8 |
| 2007 | 579 | 81.8 |
| 2008 | 815 | 116.4 |
| 2009 | 951 | 138.6 |
| 2010 | 909 | 137 |
| 2011 | 903 | 138.8 |
| 2012 | 969 | 148.6 |
| 2013 | 926 | 142.5 |
| | | |
| Rise % | 260.85% | 262.43% |
| Annualized | 18.63% | 18.75% |



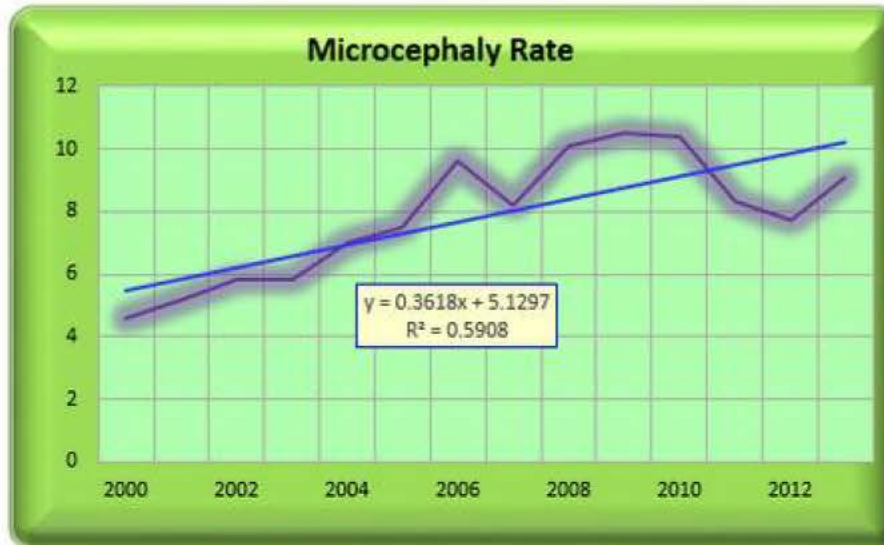
Microcephaly



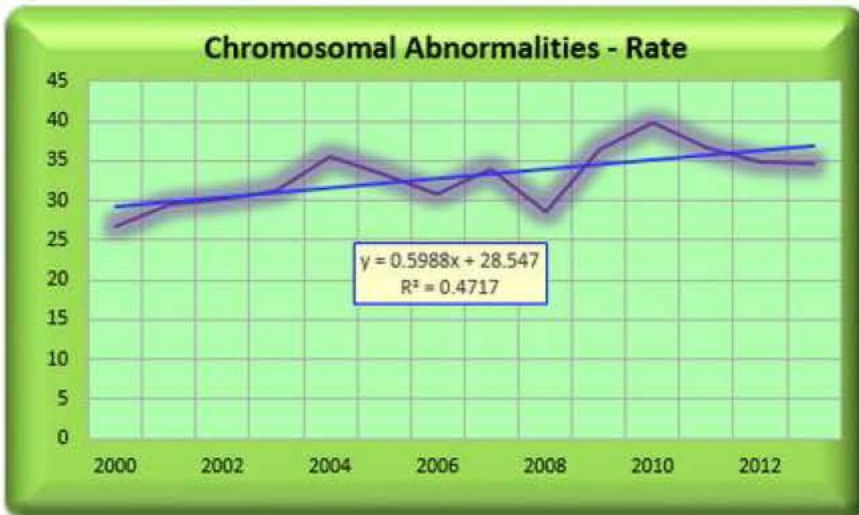
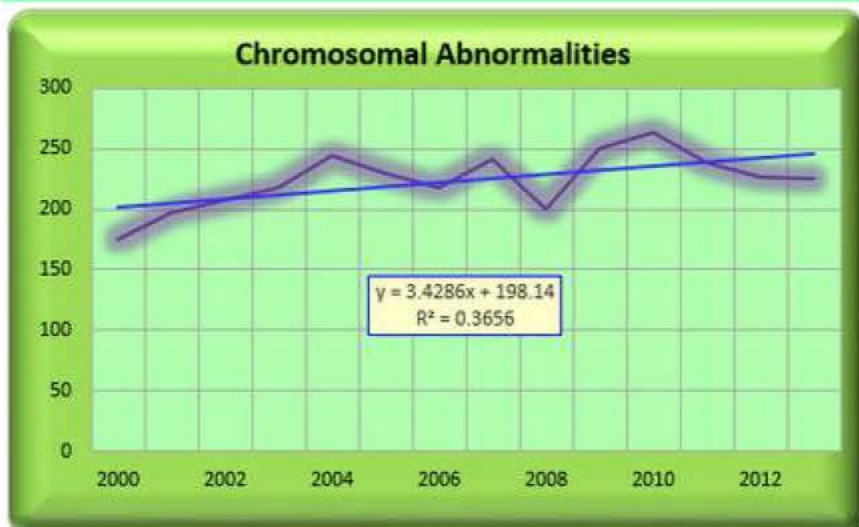
Microcephaly

Rates/ 10,000 Live births
 (Excluding Terminations)

| Year | Microcephaly No. | Microcephaly Rate |
|------------|------------------|-------------------|
| 2000 | 30 | 4.6 |
| 2001 | 35 | 5.2 |
| 2002 | 40 | 5.8 |
| 2003 | 40 | 5.8 |
| 2004 | 48 | 7 |
| 2005 | 52 | 7.5 |
| 2006 | 68 | 9.6 |
| 2007 | 58 | 8.2 |
| 2008 | 71 | 10.1 |
| 2009 | 72 | 10.5 |
| 2010 | 69 | 10.4 |
| 2011 | 69 | 8.3 |
| 2012 | 50 | 7.7 |
| 2013 | 59 | 9.1 |
| Rise % | 96.67% | 97.83% |
| Annualized | 6.90% | 6.99% |



Chromosomal Anomalies



Chromosomal Abnormalities

Rates/ 10,000 Live births
 (Excluding Terminations)

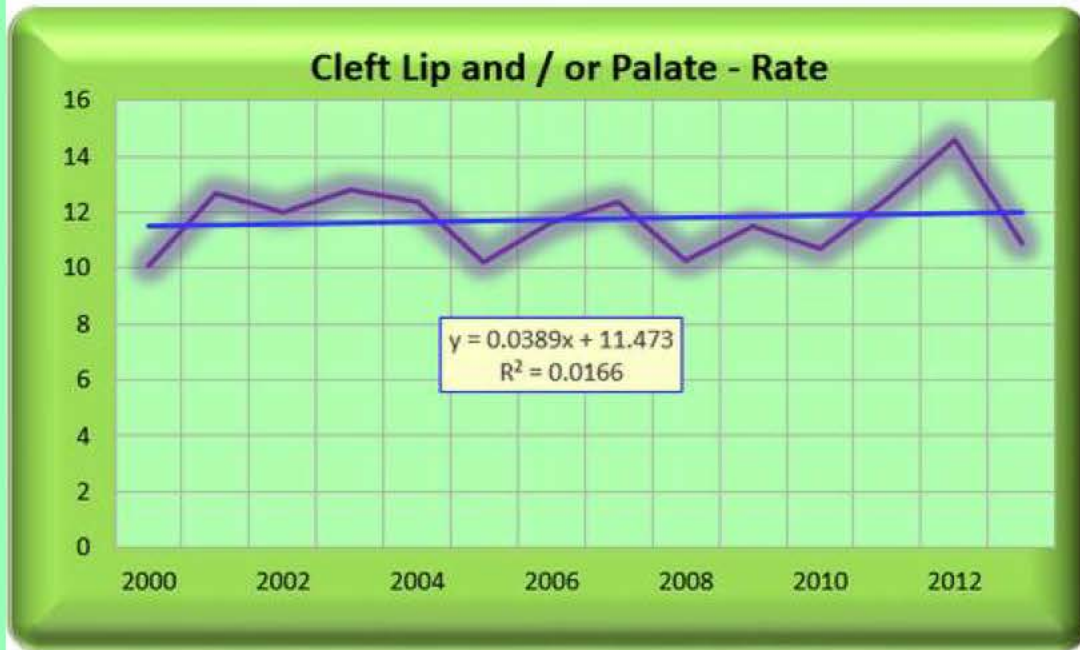
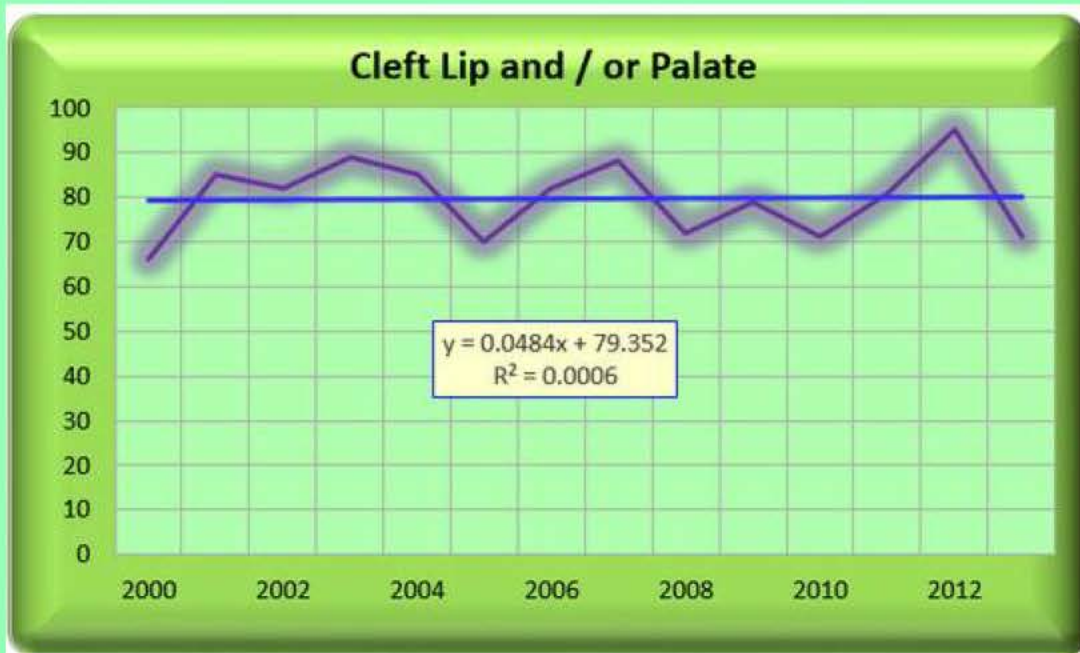
| Year | Chromosomal Abnormalities Number | Chromosomal Abnormalities Rate |
|------------|----------------------------------|--------------------------------|
| 2000 | 175 | 26.7 |
| 2001 | 197 | 29.4 |
| 2002 | 207 | 30.3 |
| 2003 | 217 | 31.3 |
| 2004 | 244 | 35.6 |
| 2005 | 230 | 33.4 |
| 2006 | 218 | 30.8 |
| 2007 | 241 | 34.0 |
| 2008 | 200 | 28.6 |
| 2009 | 250 | 36.4 |
| 2010 | 264 | 39.8 |
| 2011 | 239 | 36.7 |
| 2012 | 227 | 34.8 |
| 2013 | 225 | 34.6 |
| | | |
| Rise % | 28.57% | 29.41% |
| Annualized | 2.04% | 2.10% |

Stationary Time Trends

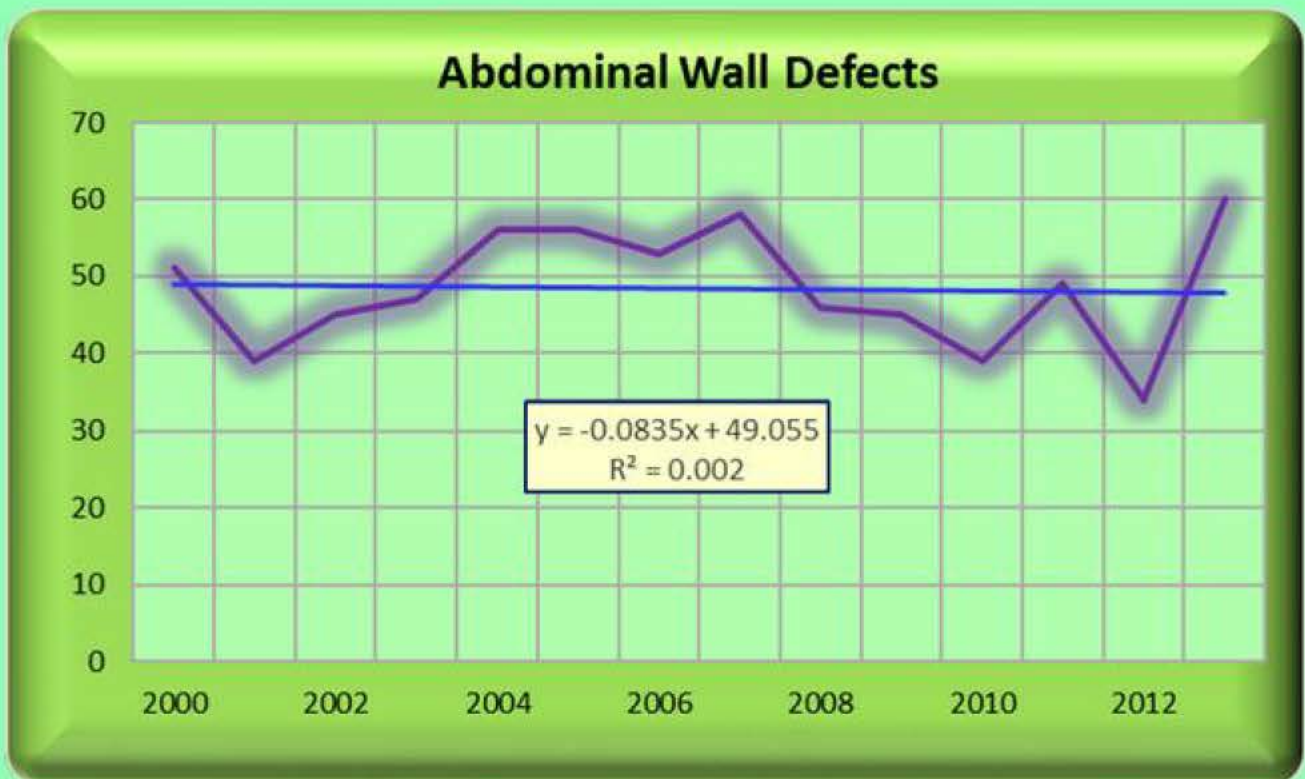
*Colorado
2000-2013*

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql>

Cleft Lip +/- Palate



Abdominal Wall Defects

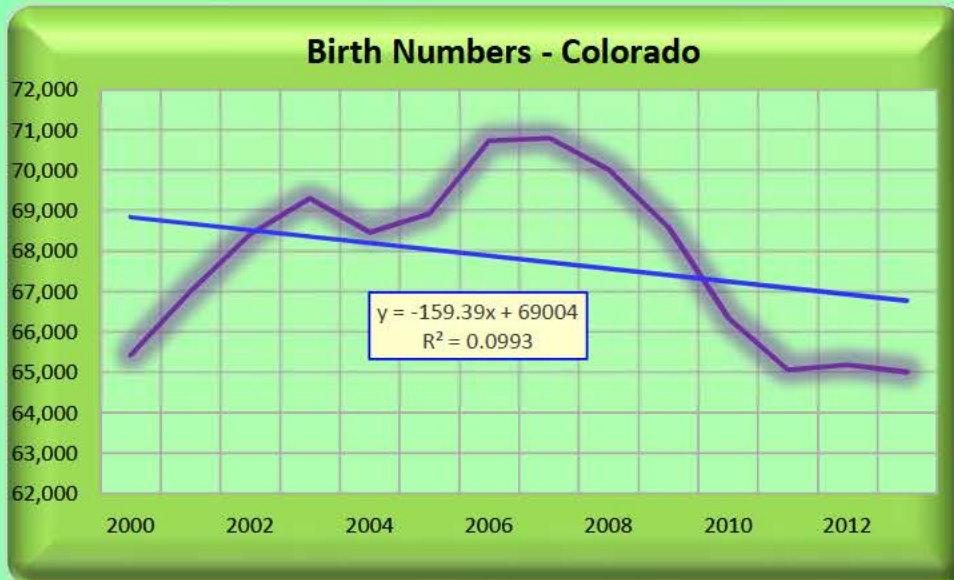


Cumulative Effects

Colorado *2000-2013*

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hspl>

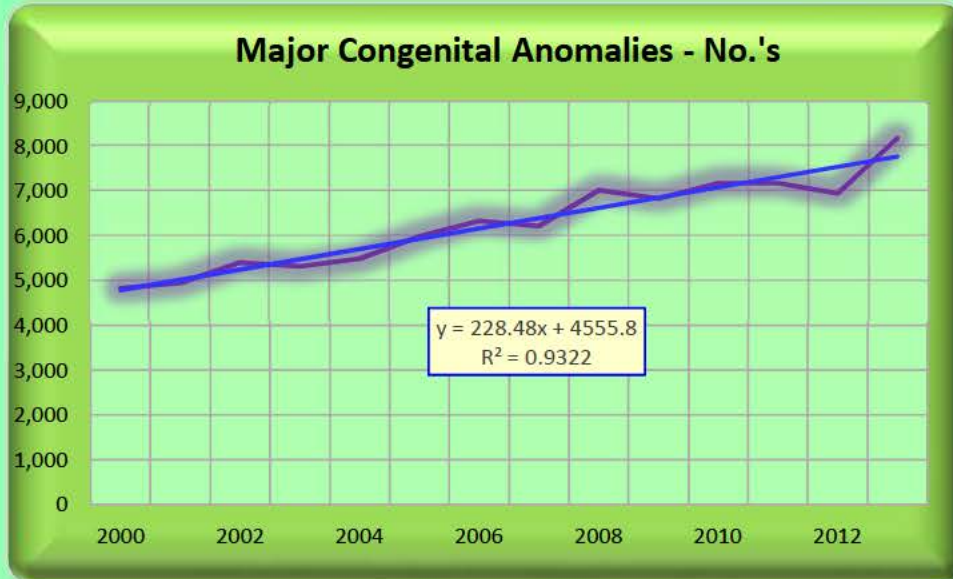
Cumulative Effects - Births



| Year | Births | Projected | Difference |
|-------------------|---------------|---------------|--------------|
| 2000 | 65429 | 65429 | 0 |
| 2001 | 67006 | 65429 | 1577 |
| 2002 | 68420 | 65429 | 2991 |
| 2003 | 69304 | 65429 | 3875 |
| 2004 | 68475 | 65429 | 3046 |
| 2005 | 68922 | 65429 | 3493 |
| 2006 | 70737 | 65429 | 5308 |
| 2007 | 70804 | 65429 | 5375 |
| 2008 | 70028 | 65429 | 4599 |
| 2009 | 68602 | 65429 | 3173 |
| 2010 | 66346 | 65429 | 917 |
| 2011 | 65052 | 65429 | -377 |
| 2012 | 65188 | 65429 | -241 |
| 2013 | 65004 | 65429 | -425 |
| | | | |
| Cumulative | 949317 | 916006 | 33311 |
| % Change | | | 3.6% |
| Annualized | | | 0.26% |

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hspl>

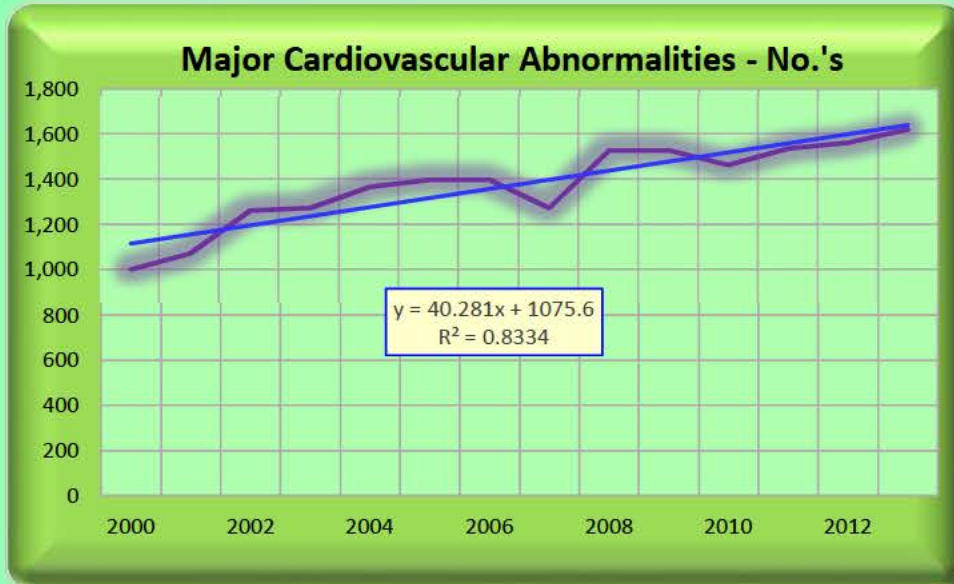
Cumulative Effects - All Major Defects



| Year | Majors | Projection | Difference |
|-------------------|--------------|--------------|--------------|
| 2000 | 4830 | 4830 | 0 |
| 2001 | 4942 | 4830 | 112 |
| 2002 | 5406 | 4830 | 576 |
| 2003 | 5311 | 4830 | 481 |
| 2004 | 5482 | 4830 | 652 |
| 2005 | 5978 | 4830 | 1148 |
| 2006 | 6325 | 4830 | 1495 |
| 2007 | 6213 | 4830 | 1383 |
| 2008 | 7010 | 4830 | 2180 |
| 2009 | 6826 | 4830 | 1996 |
| 2010 | 7171 | 4830 | 2341 |
| 2011 | 7174 | 4830 | 2344 |
| 2012 | 6939 | 4830 | 2109 |
| 2013 | 8165 | 4830 | 3335 |
| | | | |
| Cumulative | 87772 | 67620 | 20152 |
| % Change | | | 29.8% |

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsqli>

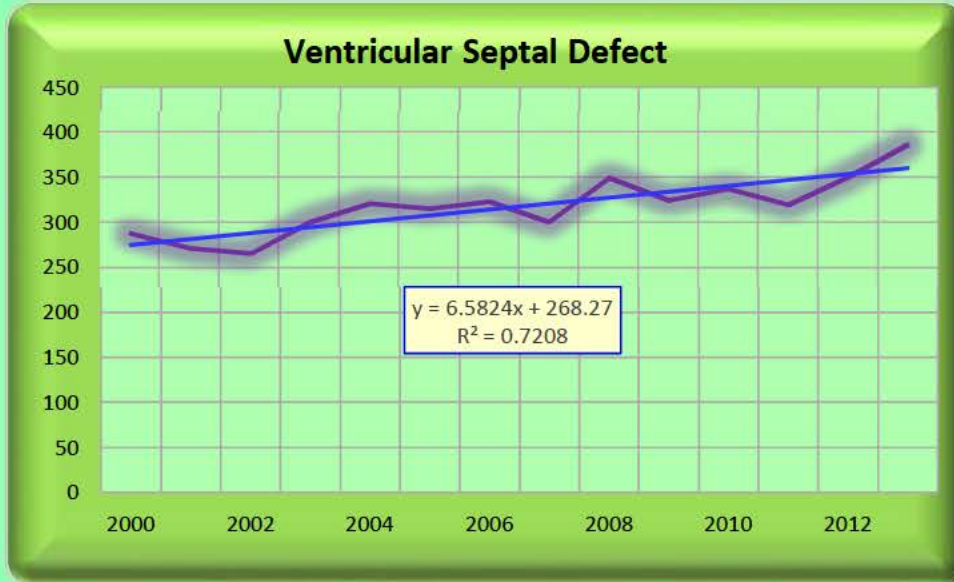
Cumulative Effects - All CVS Anomalies



| Year | CVS | Projected | Difference |
|-------------------|--------------|--------------|--------------|
| 2000 | 1002 | 1002 | 0 |
| 2001 | 1071 | 1002 | 69 |
| 2002 | 1263 | 1002 | 261 |
| 2003 | 1273 | 1002 | 271 |
| 2004 | 1368 | 1002 | 366 |
| 2005 | 1398 | 1002 | 396 |
| 2006 | 1397 | 1002 | 395 |
| 2007 | 1274 | 1002 | 272 |
| 2008 | 1530 | 1002 | 528 |
| 2009 | 1528 | 1002 | 526 |
| 2010 | 1464 | 1002 | 462 |
| 2011 | 1536 | 1002 | 534 |
| 2012 | 1562 | 1002 | 560 |
| 2013 | 1622 | 1002 | 620 |
| | | | |
| Cumulative | 19288 | 14028 | 5260 |
| % Change | | | 37.5% |

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsqli>

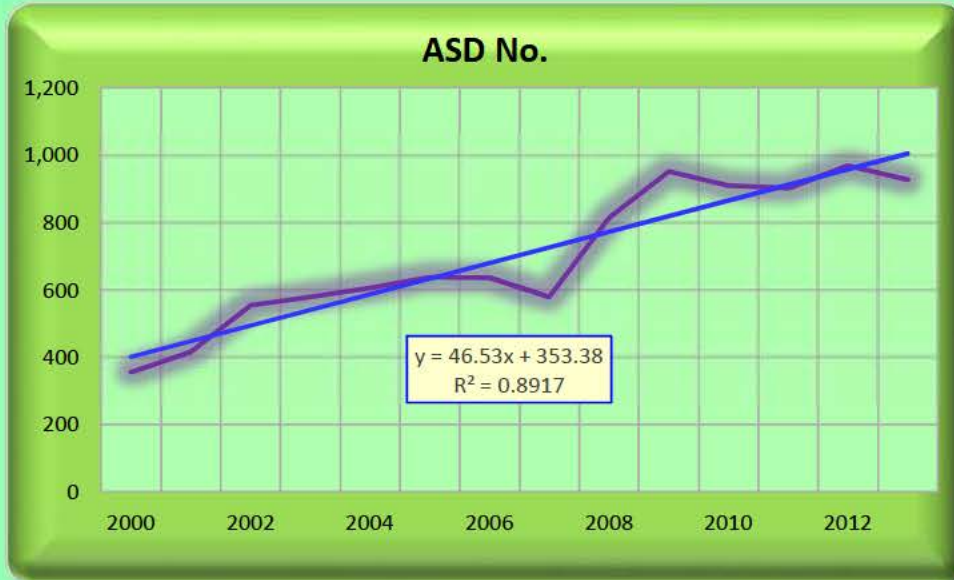
Cumulative Effects - VSD



| Year | VSD | Projected | Difference |
|-------------------|-------------|-------------|--------------|
| 2000 | 287 | 271 | 16 |
| 2001 | 271 | 271 | 0 |
| 2002 | 265 | 271 | -6 |
| 2003 | 300 | 271 | 29 |
| 2004 | 321 | 271 | 50 |
| 2005 | 315 | 271 | 44 |
| 2006 | 323 | 271 | 52 |
| 2007 | 300 | 271 | 29 |
| 2008 | 349 | 271 | 78 |
| 2009 | 324 | 271 | 53 |
| 2010 | 337 | 271 | 66 |
| 2011 | 319 | 271 | 48 |
| 2012 | 350 | 271 | 79 |
| 2013 | 386 | 271 | 115 |
| | | | |
| Cumulative | 4447 | 3794 | 653 |
| % Change | | | 17.2% |

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql>

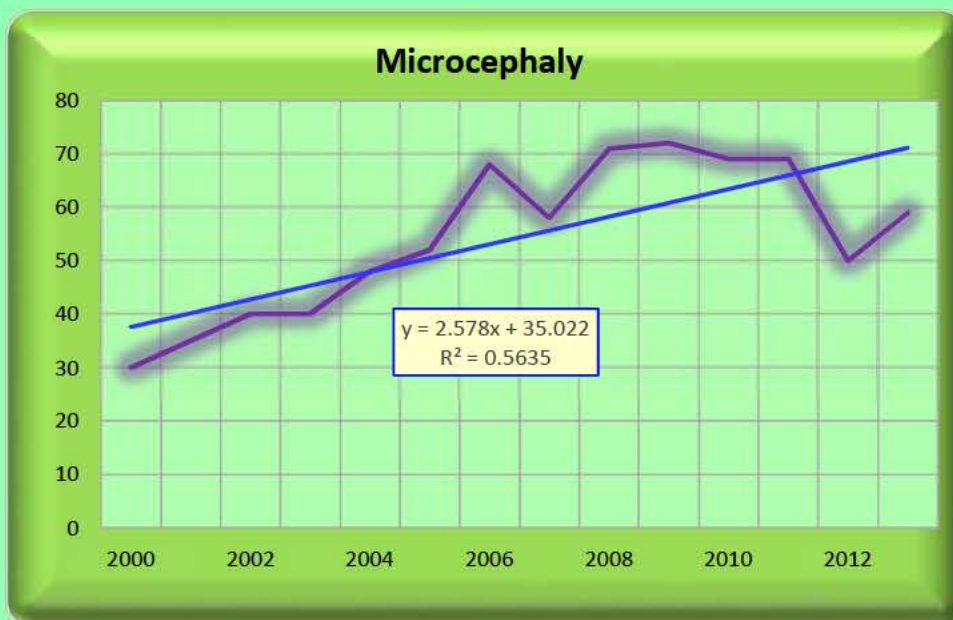
Cumulative Effects - ASD - Secundum



| Year | ASD No. | Projection | Difference |
|-------------------|-------------|-------------|--------------|
| 2000 | 355 | 355 | 0 |
| 2001 | 415 | 355 | 60 |
| 2002 | 554 | 355 | 199 |
| 2003 | 579 | 355 | 224 |
| 2004 | 606 | 355 | 251 |
| 2005 | 637 | 355 | 282 |
| 2006 | 635 | 355 | 280 |
| 2007 | 579 | 355 | 224 |
| 2008 | 815 | 355 | 460 |
| 2009 | 951 | 355 | 596 |
| 2010 | 909 | 355 | 554 |
| 2011 | 903 | 355 | 548 |
| 2012 | 969 | 355 | 614 |
| 2013 | 926 | 355 | 571 |
| | | | |
| Cumulative | 9833 | 4970 | 4863 |
| % Change | | | 97.8% |

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql>

Cumulative Effects - Microcephaly

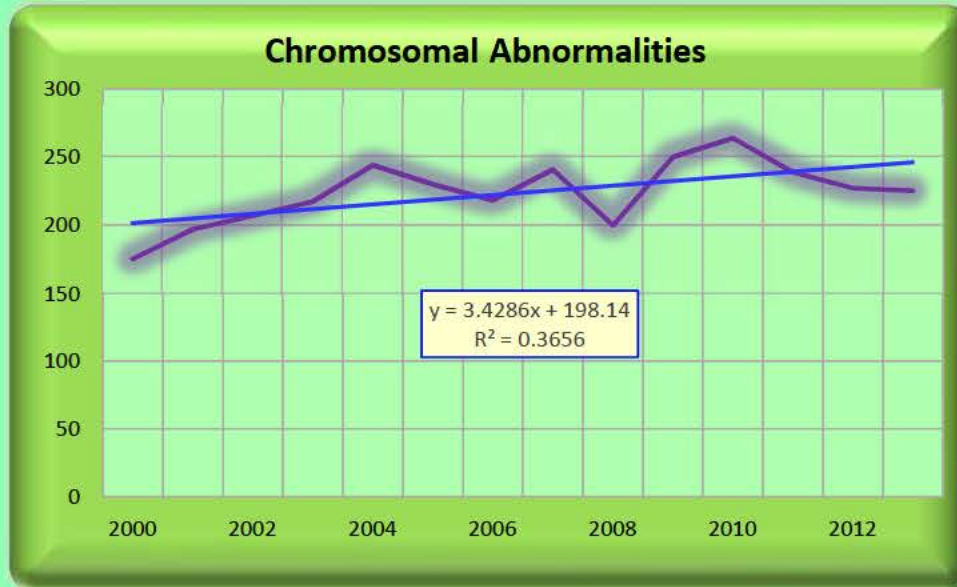


| Year | Majors | Projection | Difference |
|-------------------|--------------|--------------|--------------|
| 2000 | 4830 | 4830 | 0 |
| 2001 | 4942 | 4830 | 112 |
| 2002 | 5406 | 4830 | 576 |
| 2003 | 5311 | 4830 | 481 |
| 2004 | 5482 | 4830 | 652 |
| 2005 | 5978 | 4830 | 1148 |
| 2006 | 6325 | 4830 | 1495 |
| 2007 | 6213 | 4830 | 1383 |
| 2008 | 7010 | 4830 | 2180 |
| 2009 | 6826 | 4830 | 1996 |
| 2010 | 7171 | 4830 | 2341 |
| 2011 | 7174 | 4830 | 2344 |
| 2012 | 6939 | 4830 | 2109 |
| 2013 | 8165 | 4830 | 3335 |
| | | | |
| Cumulative | 87772 | 67620 | 20152 |
| % Change | | | 29.8% |

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql>

Cumulative Effects

- Chromosomal Abnormalities



| Year | Chromosomal Abnormalities Number | Projection | Difference |
|-------------------|----------------------------------|-------------|--------------|
| 2000 | 175 | 175 | 0 |
| 2001 | 197 | 175 | 22 |
| 2002 | 207 | 175 | 32 |
| 2003 | 217 | 175 | 42 |
| 2004 | 244 | 175 | 69 |
| 2005 | 230 | 175 | 55 |
| 2006 | 218 | 175 | 43 |
| 2007 | 241 | 175 | 66 |
| 2008 | 200 | 175 | 25 |
| 2009 | 250 | 175 | 75 |
| 2010 | 264 | 175 | 89 |
| 2011 | 239 | 175 | 64 |
| 2012 | 227 | 175 | 52 |
| 2013 | 225 | 175 | 50 |
| | | | |
| Cumulative | 3134 | 2450 | 684 |
| % Change | | | 27.9% |

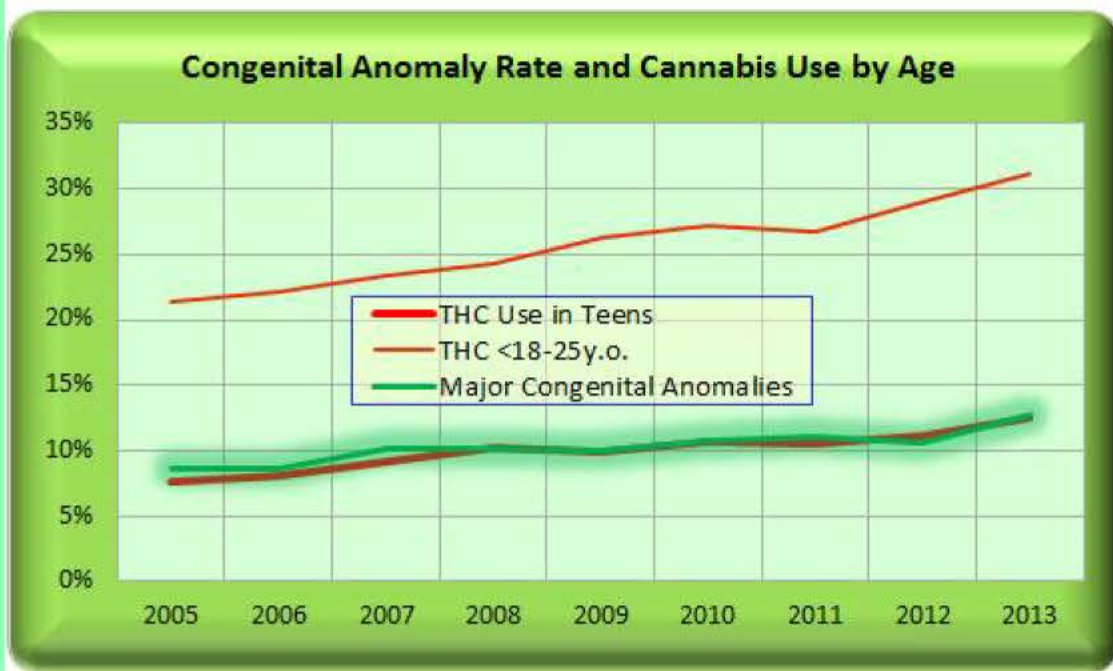
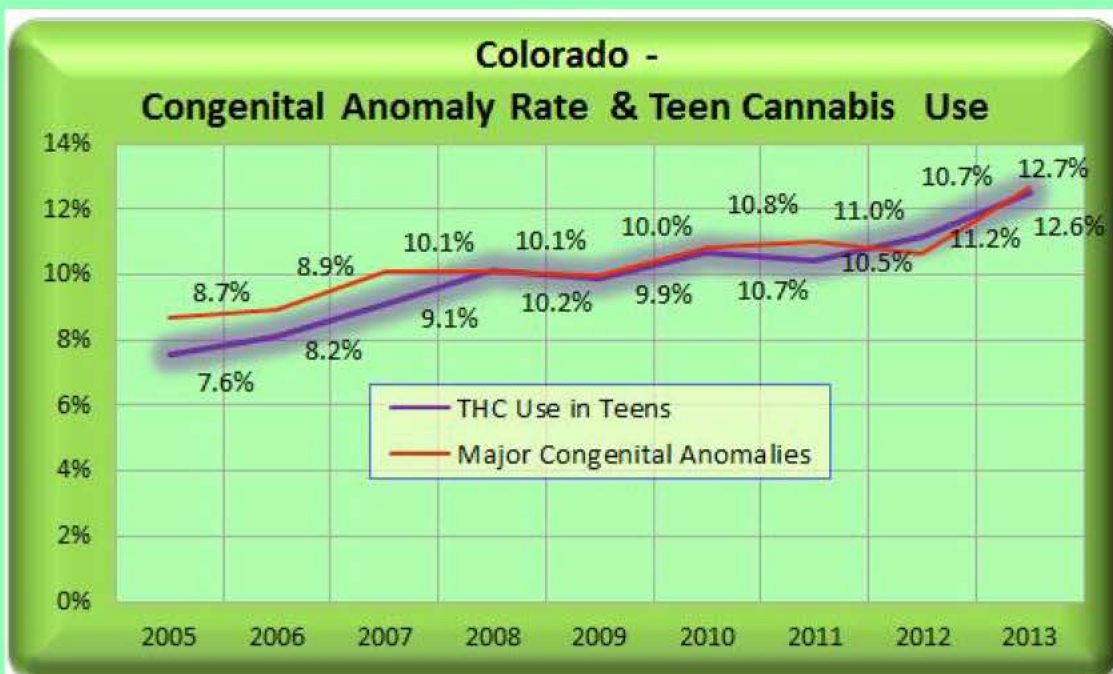
<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsqli>

Overall Cumulative Summary

Colorado 2000-2013

<http://www.chd.dphe.state.co.us/cohid/>
<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql>

Close Correlation between Cannabis Consumption and Congenital Anomalies Rates

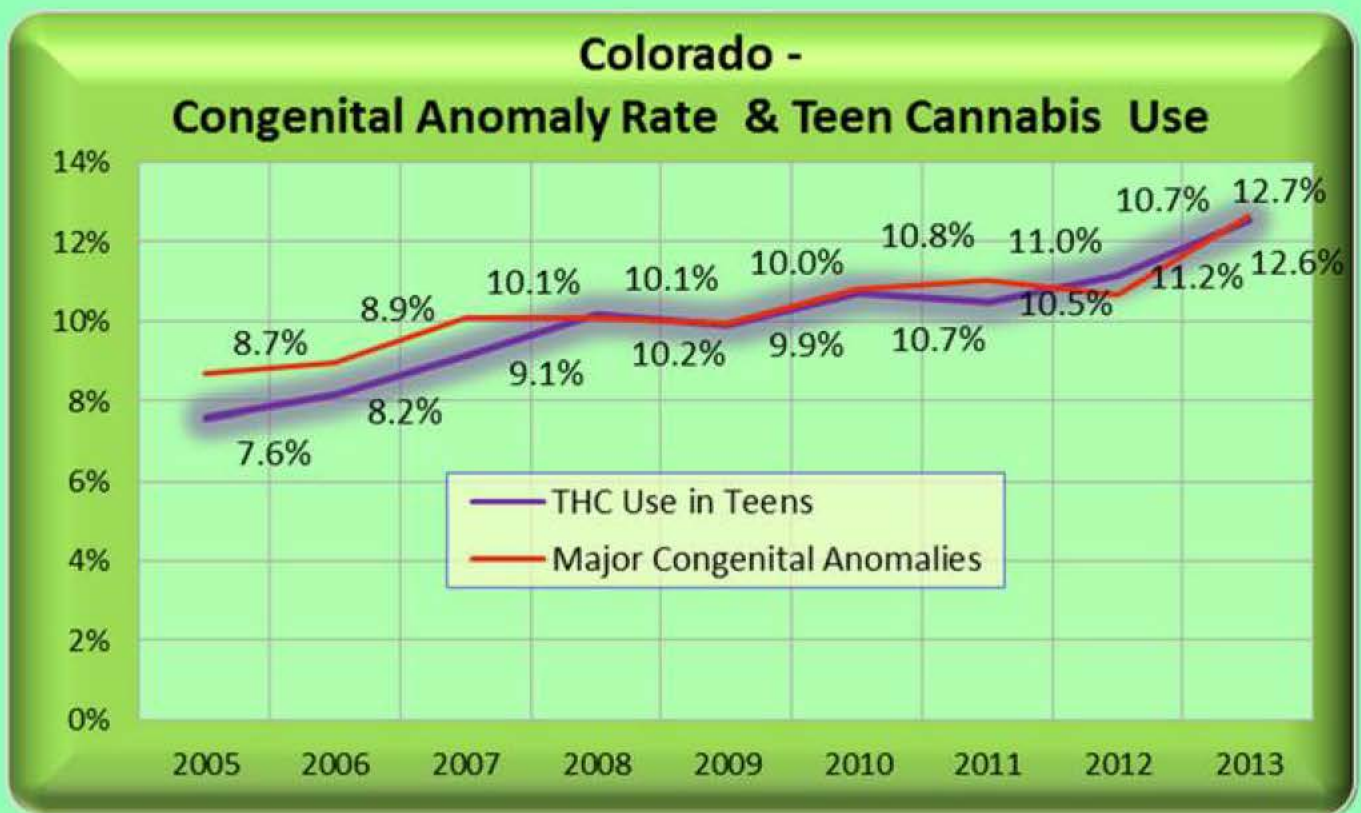


<http://www.chd.dphe.state.co.us/cohid/>

<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql>

<https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.pdf>

Close Correlation between Cannabis Consumption and Congenital Anomalies Rates



<http://www.chd.dphe.state.co.us/cohid/>

<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql>

<https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.pdf>

Correlation == 0.9539
P == 0.00006594

```
> cor.test (a,x, alternative="two.sided",  
+          method="pearson", exact=TRUE, conf.level = 0.95)  
  
Pearson's product-moment correlation  
  
data: a and x  
t = 8.4142, df = 7, p-value = 6.594e-05  
alternative hypothesis: true correlation is not equal to 0  
95 percent confidence interval:  
 0.7908924 0.9905319  
sample estimates:  
      cor  
0.953952
```

Young Adult Correlation == 0.9258
P == 0.0003457

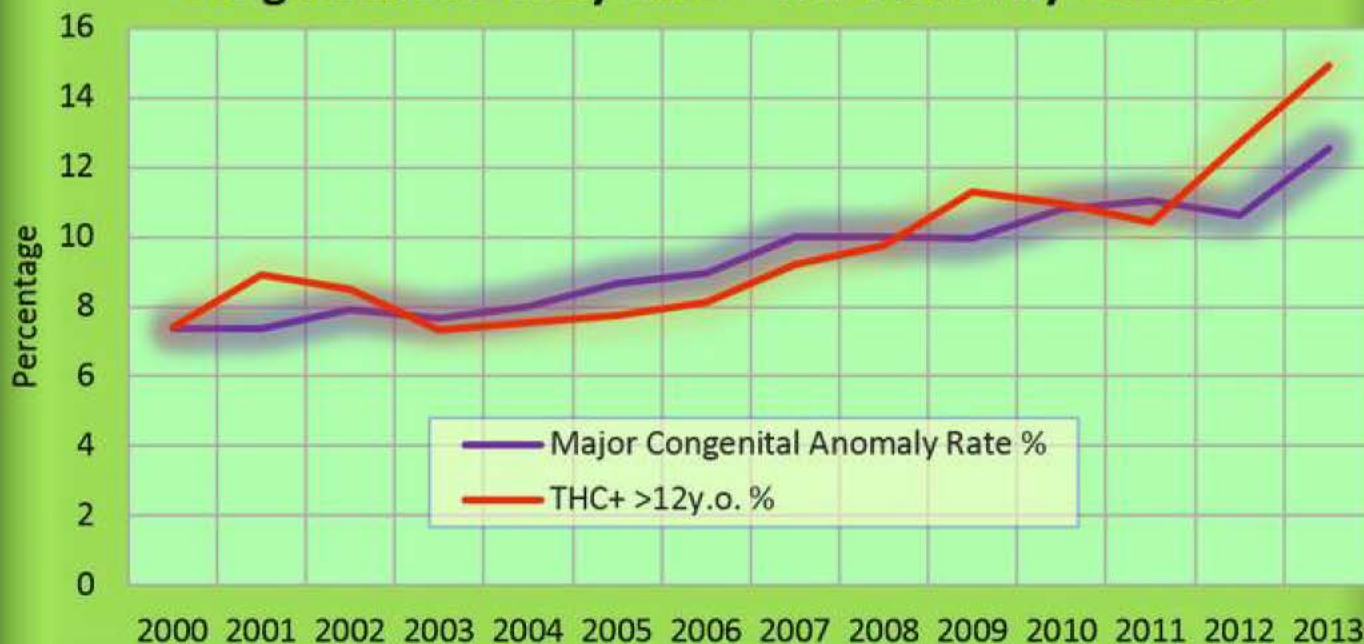
```
> CTD
  Year THCTeens THC18.25 MeanUse Majors
1 2005  0.0760   0.2143  0.1452 0.0867
2 2006  0.0815   0.2221  0.1518 0.0894
3 2007  0.0913   0.2344  0.1629 0.1001
4 2008  0.1017   0.2428  0.1723 0.1001
5 2009  0.0991   0.2635  0.1813 0.0995
6 2010  0.1072   0.2726  0.1899 0.1081
7 2011  0.1047   0.2681  0.1864 0.1103
8 2012  0.1116   0.2905  0.2011 0.1065
9 2013  0.1256   0.3124  0.2190 0.1265
>
> x <- CTD$THCTeens
> y <- CTD$THC18.25
> z <- CTD$MEanUse
> a <- CTD$Majors
>
> cor.test (a,y, alternative="two.sided",
+          method="pearson", exact=TRUE, conf.level = 0.95)

      Pearson's product-moment correlation

data:  a and y
t = 6.4639, df = 7, p-value = 0.0003457
alternative hypothesis: true correlation is not equal to 0
95 percent confidence interval:
 0.6781881 0.9844974
sample estimates:
      cor
0.9254759
```

Close Correlation between Cannabis Consumption and Congenital Anomalies Rates

**Colorado Percentages -
Congenital Anomaly Rate ~ THC Positivity >12Years**



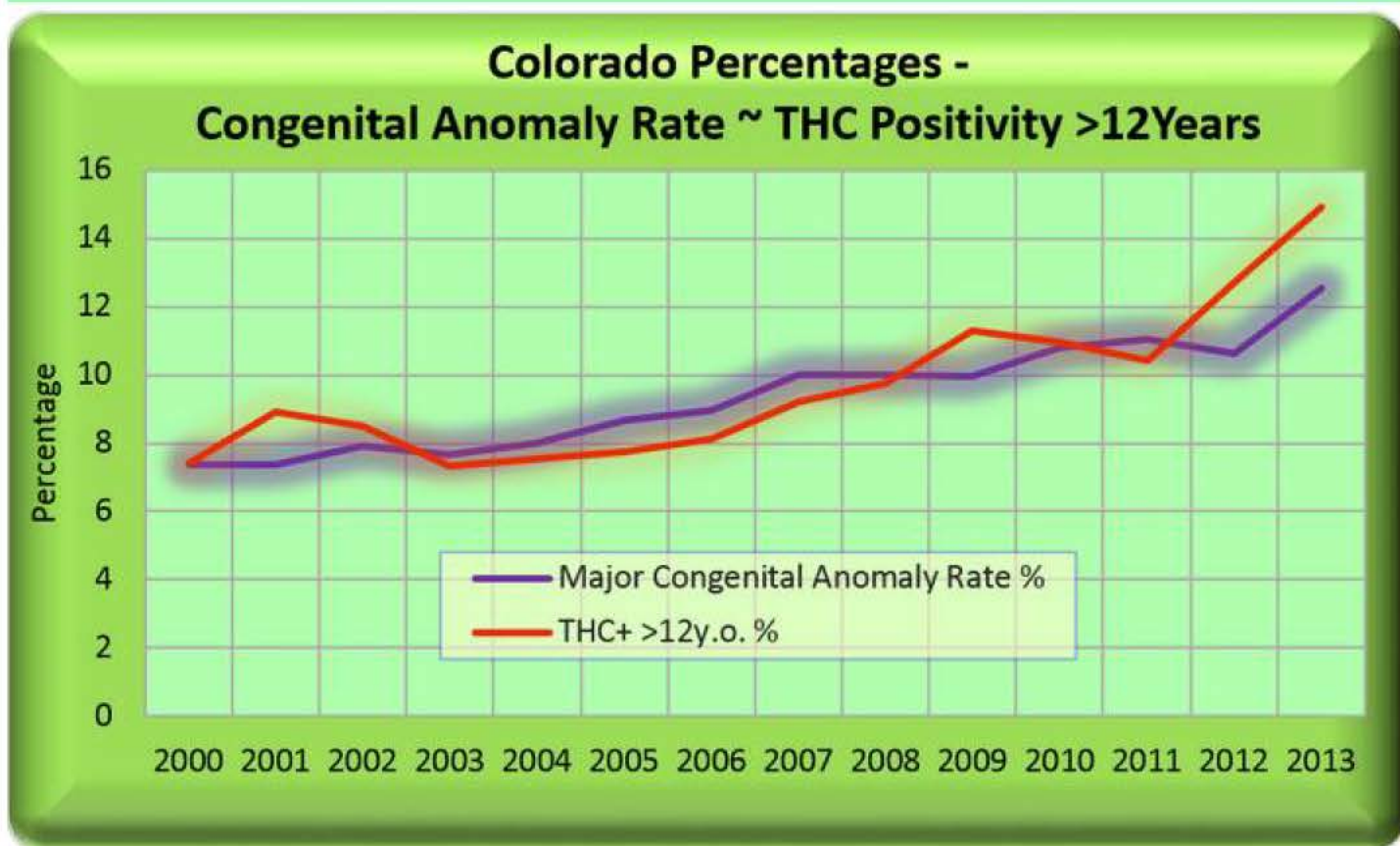
```
> cor.test (x,y, alternative="two.sided",  
+          method="pearson", exact=TRUE, conf.level = 0.95)  
  
Pearson's product-moment correlation  
  
data: x and y  
t = 6.5002, df = 12, p-value = 2.936e-05  
alternative hypothesis: true correlation is not equal to 0  
95 percent confidence interval:  
 0.6618084 0.9624345  
sample estimates:  
      cor  
0.8825038
```

<http://www.chd.dphe.state.co.us/cohid/>

<http://www.cohid.dphe.state.co.us/scripts/htmlsql.exe/CrcsnPub.hsrl>

<https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.pdf>

Colorado Percentages - Congenital Anomalies Rates & Cannabis Consumption Rates >12 Years



www.samhsa.gov

<http://www.chd.dphe.state.co.us/cohid/>

<http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hspl>

<https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/NSDUH-FFR1-2016.pdf>

Cumulative Overall Effects

| Anomaly | Cumulative Total 2000-2013 | Projected Total from Baseline | Excess Above Baseline | % Change 2000-2013 | Increase Relative to Births |
|---------------------------------|----------------------------|-------------------------------|-----------------------|--------------------|-----------------------------|
| Births | 949,317 | 916,006 | 33,311 | 3.6% | 1.00 |
| Major Congenital Defects | 87,772 | 67,620 | 20,152 | 29.8% | 8.20 |
| Major CVS | 19,288 | 14,028 | 5,260 | 37.5% | 10.31 |
| VSD | 4,447 | 3,794 | 653 | 17.2% | 4.73 |
| ASD-Secundum | 9,833 | 4,970 | 4,863 | 97.8% | 26.91 |
| Microcephaly | 761 | 420 | 341 | 81.2% | 22.33 |
| Chromosomal | 3,134 | 2,450 | 684 | 27.9% | 7.68 |