THE UNIVERSITY OF WESTERN AUSTRALIA

Associate Professor Dr. Stuart Reece
MBBS (Hons.), FRCS(Ed.), FRCS(Glas.), FRACGP, MD(UNSW).
School of Psychiatry and Clinical Neurosciences

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.hsql . 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.

The University of Western Australia
Mooo, Perth WA 6009 Australia
T +61 7 3844-4000.
F +61 7 3844-4015
E stuart.reece@uwa.edu.au
E stuart.reece@bigpond.com

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 percetnage 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 gastroschsis, 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%. As shown in the equation shown in the graph above, this translates into an extra 228 cases annually.

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 chromsomal 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 congential anoamlies 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 analystical software showing the correlation coefficient, R=0.953852 and P = 0.00006594.

S27 presents abot correlaton calculatoin this time with the young adult rate of cannabis use again from the NSDUH SAMHSA surevy (Data given in S24). In this study R=0.9254789 and P = 0.00003457.

S28 shows similar data witht eh majro 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 signficant 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 been 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 genotoxic [15-24] and arteriopathic and / or arteritic [25-65] pathways.

The above cited literature links both maternal and paternal cannabis exposure [4] 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 documented [64] and if the major effect of therapeutic abortion is also included as seems only proper [67].

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

Yours sincerely,

Assoc. Prof. Dr. Stuart Reece.
University of Western Australia and
Edith Cowan University,
Perth,
Australia.

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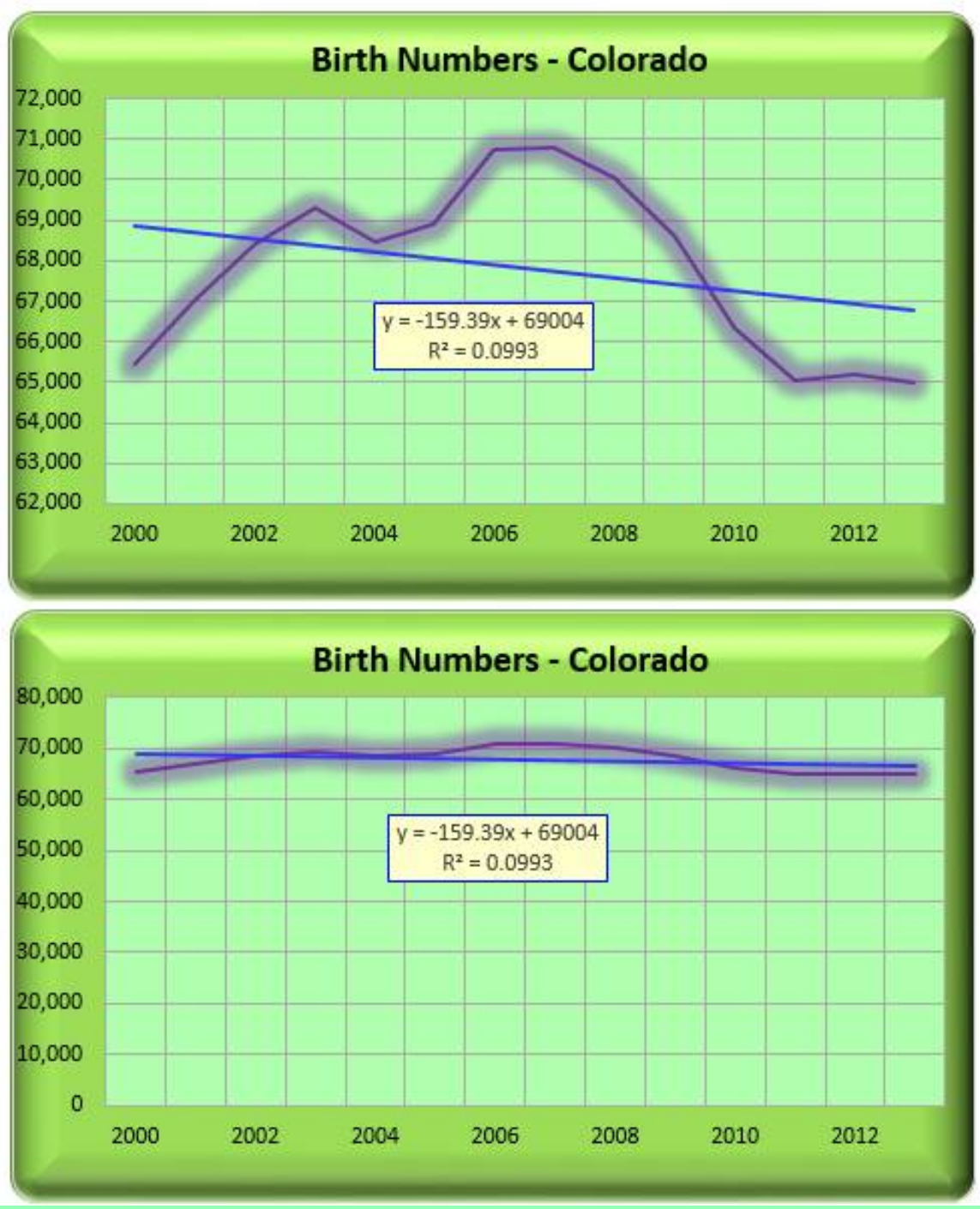
Congenital Anomalies Colorado

2000-2013

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

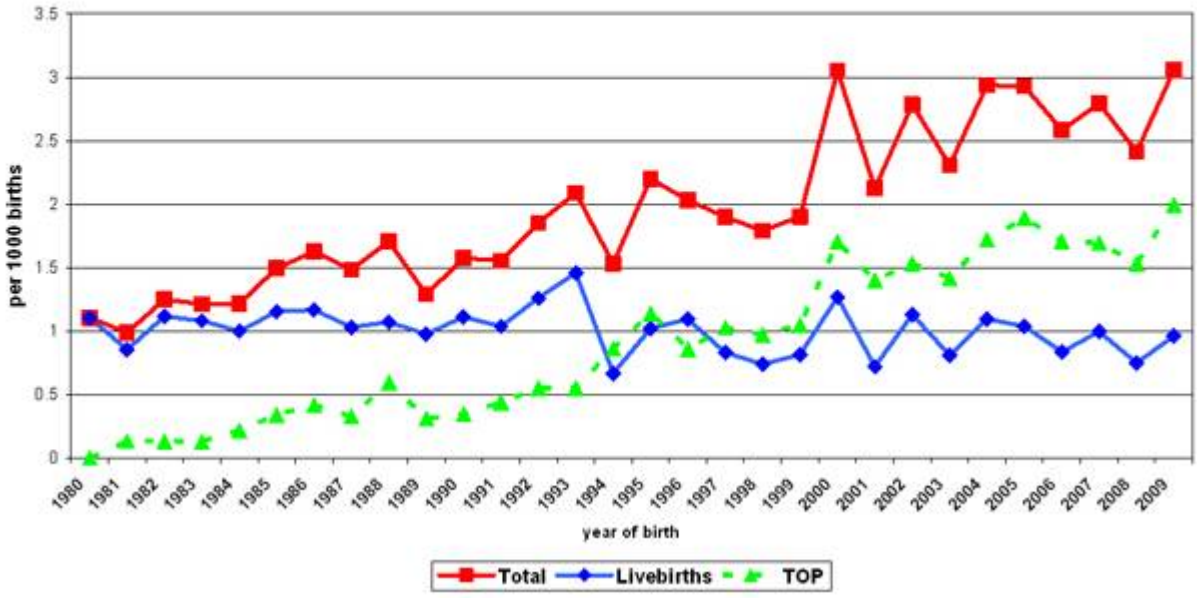
Births



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

Down's Syndrome in Western Australia

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



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

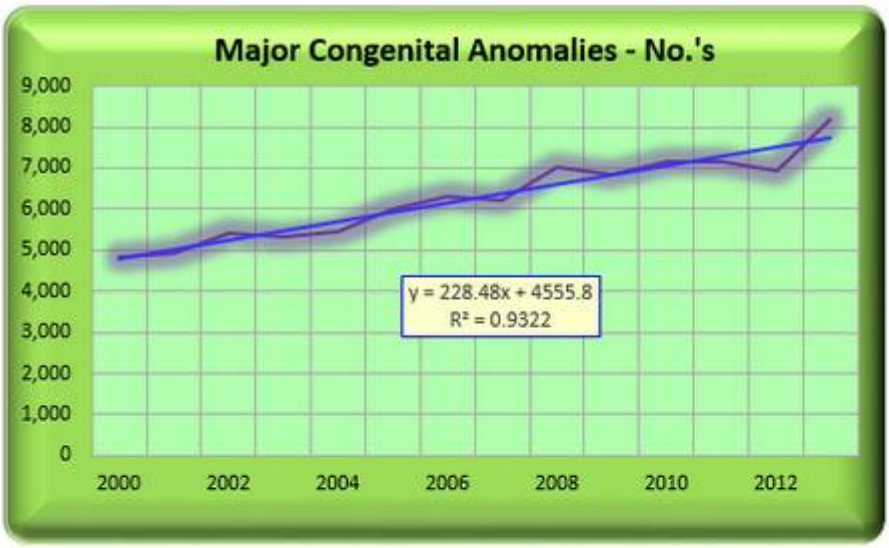
Rising Trends

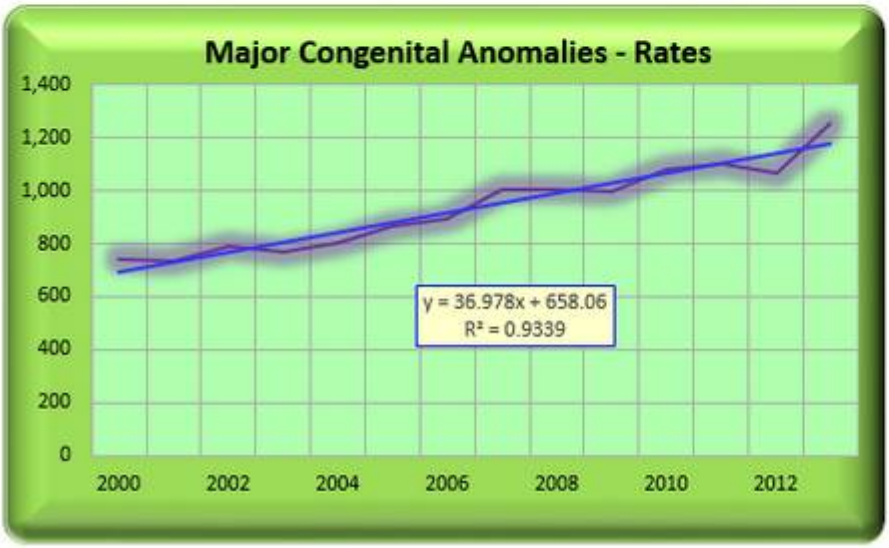
Colorado

2000-2013

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

Major Congenital Anomalies





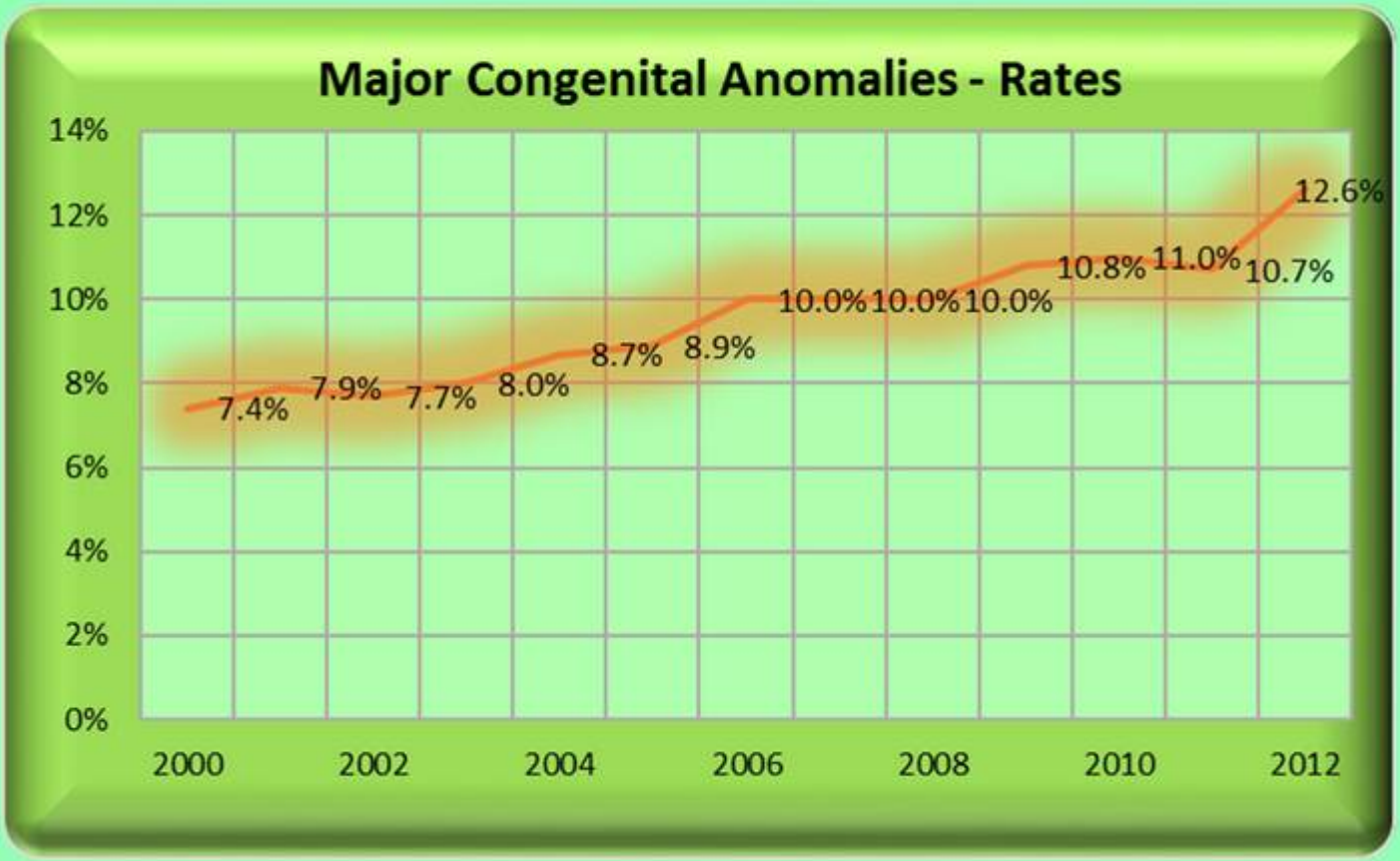
Major Congenital Anomalies

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%

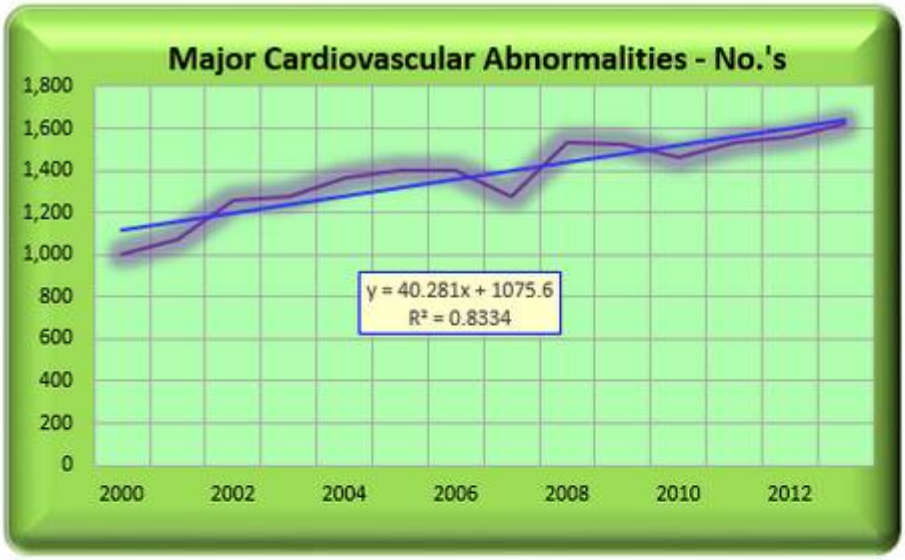
http://www.chd.dphe.state.co.us/cohid/
http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql

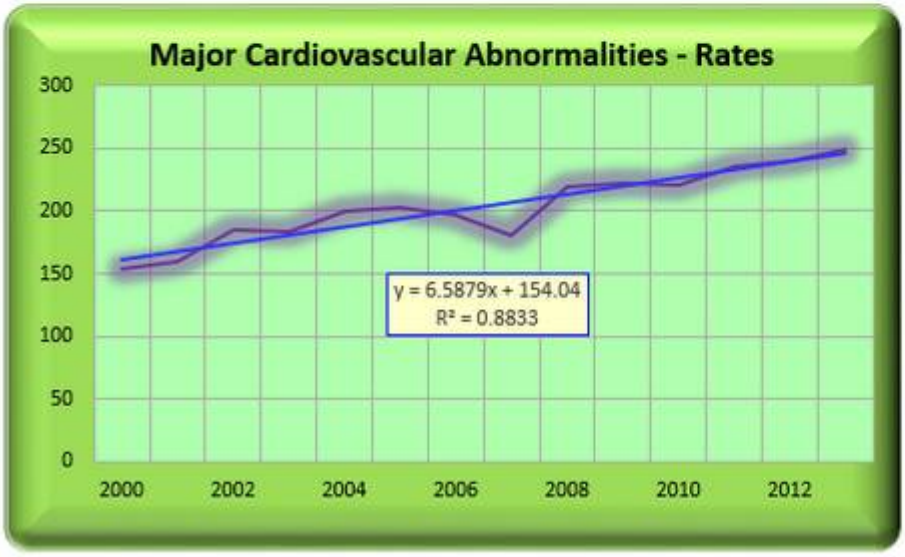
Major Congenital Anomalies as Percentage



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

Major Cardiovascular Anomalies





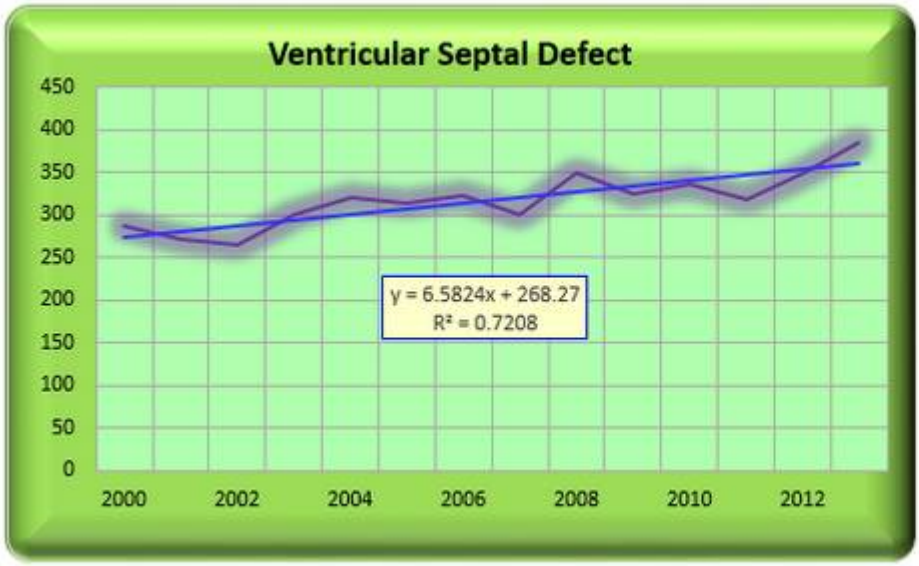
Major CVS Abnormalities

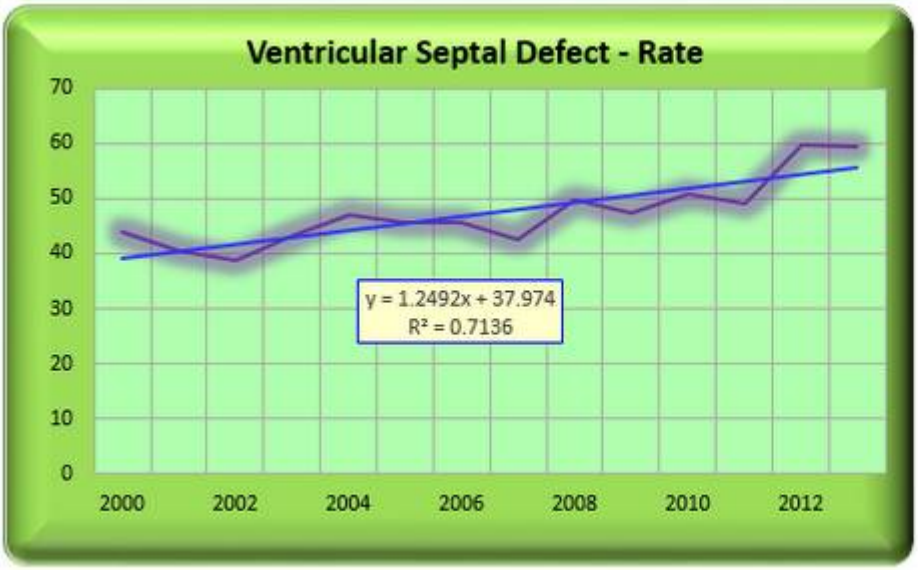
Rates/ 10,000 Live births
(Excluding Terminations)

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%

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

Ventricular Septal Defect





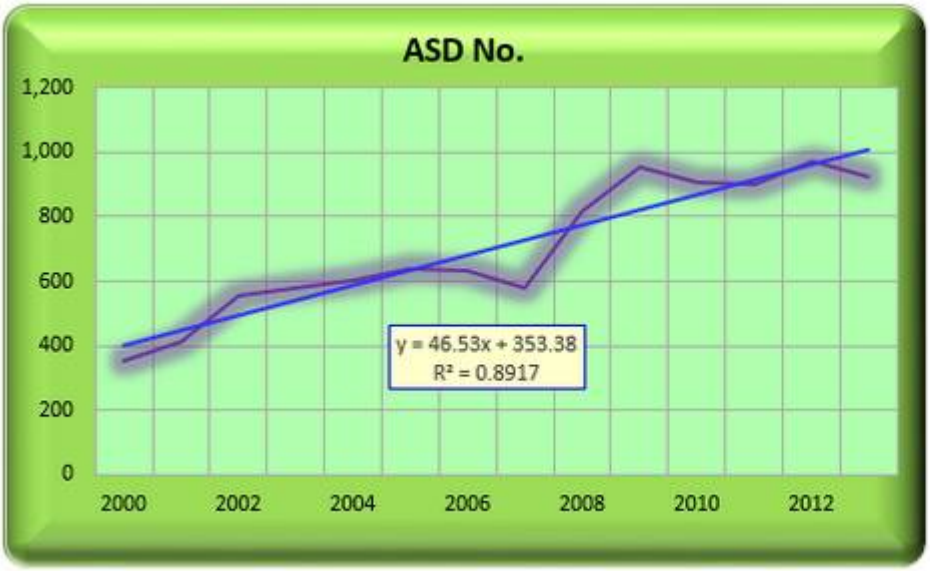
VSD

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%

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

Atrial Septal Defects - Ostium Secundum



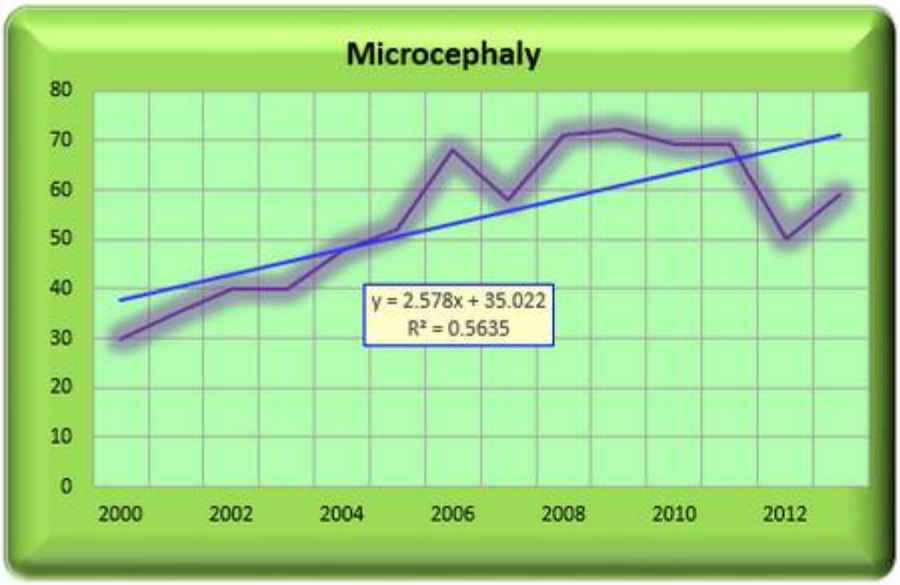
Ostium Secundum ASD's

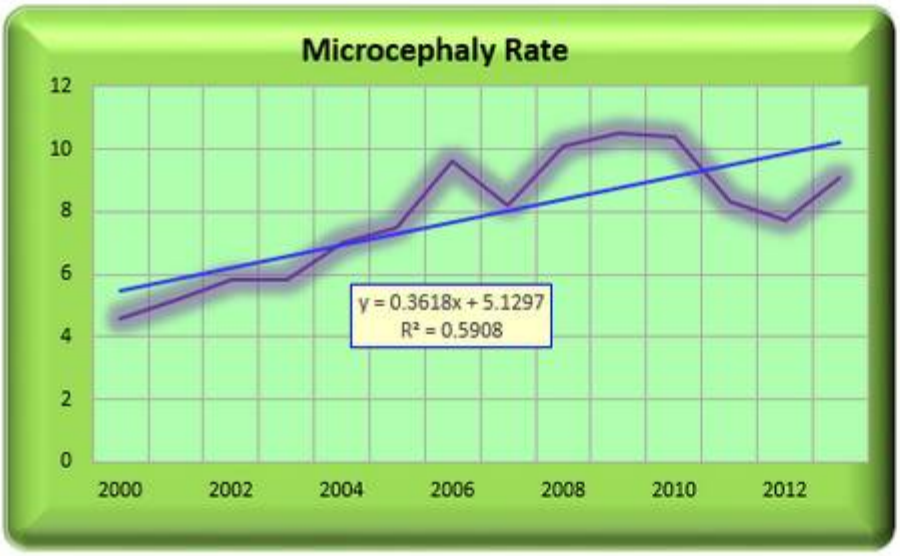
Rates/ 10,000 Live births
(Excluding Terminations)

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%

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

Microcephaly





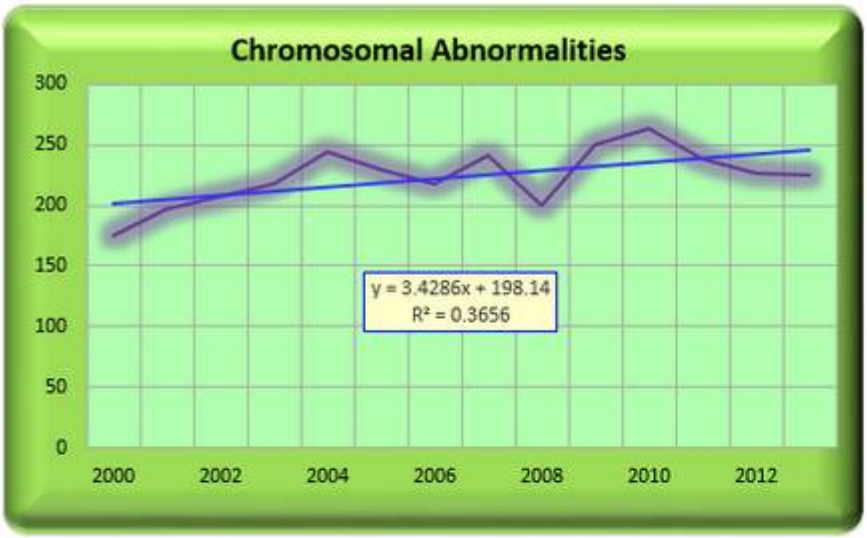
Microcephaly

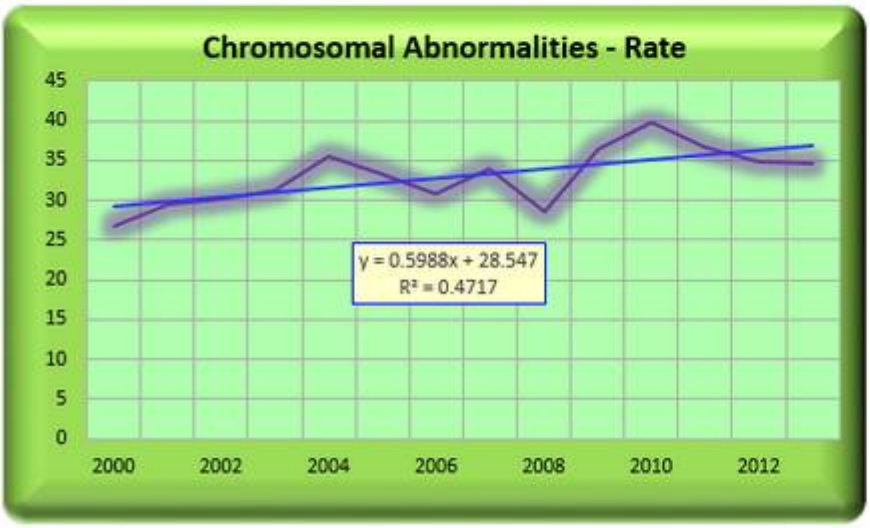
Rates/ 10,000 Live births
(Excluding Terminations)

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%

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

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%

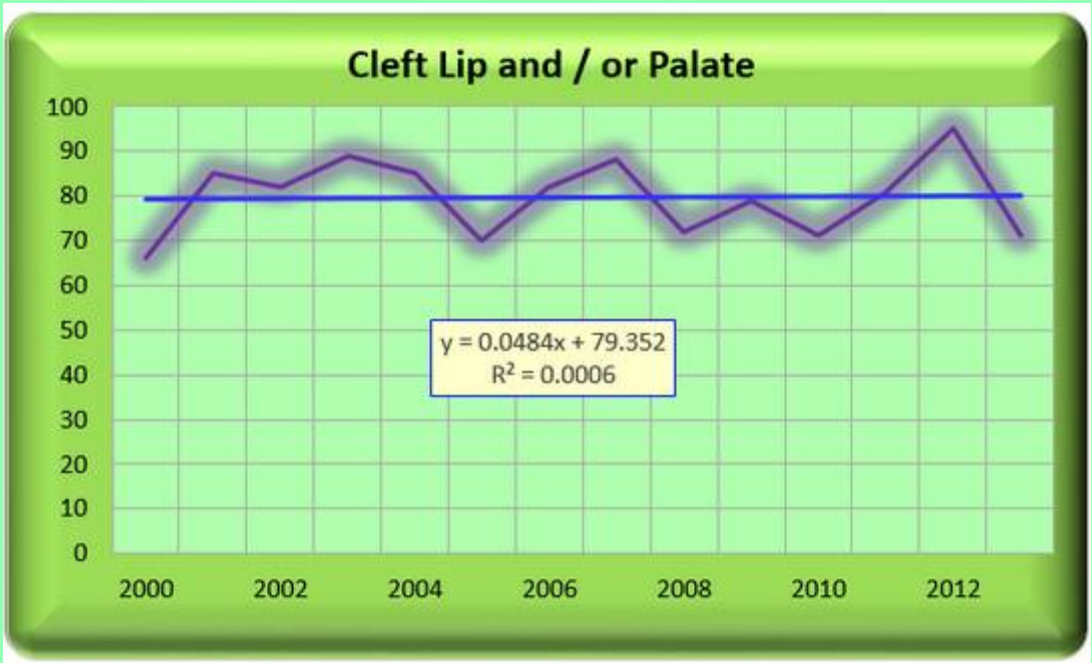
http://www.chd.dphe.state.co.us/cohid/
http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql

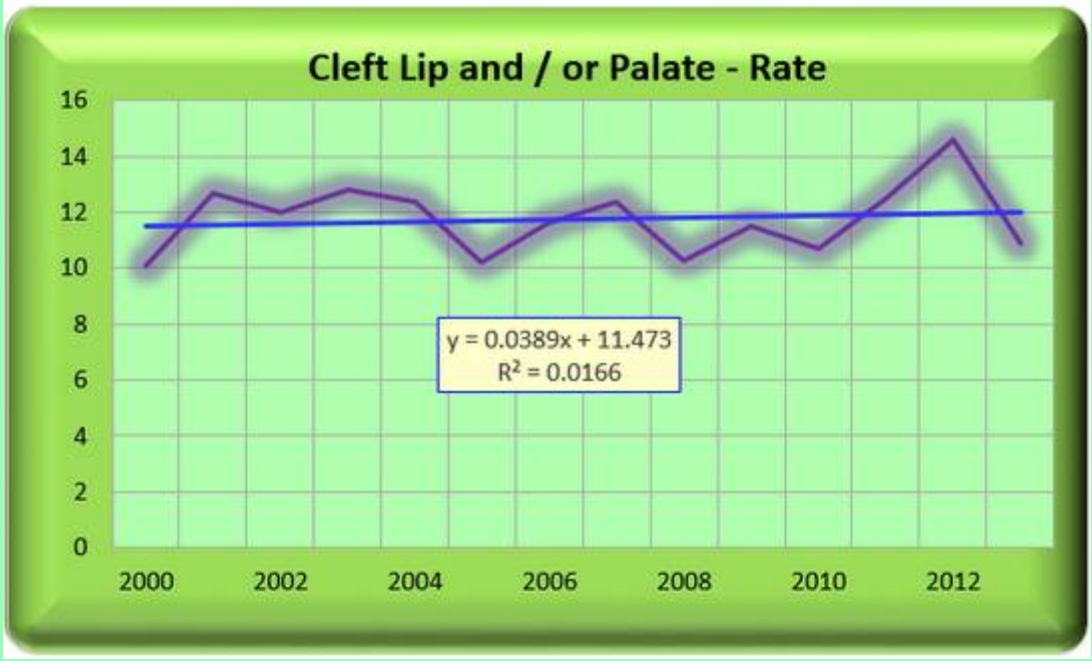
Stationary Time Trends

Colorado 2000-2013

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

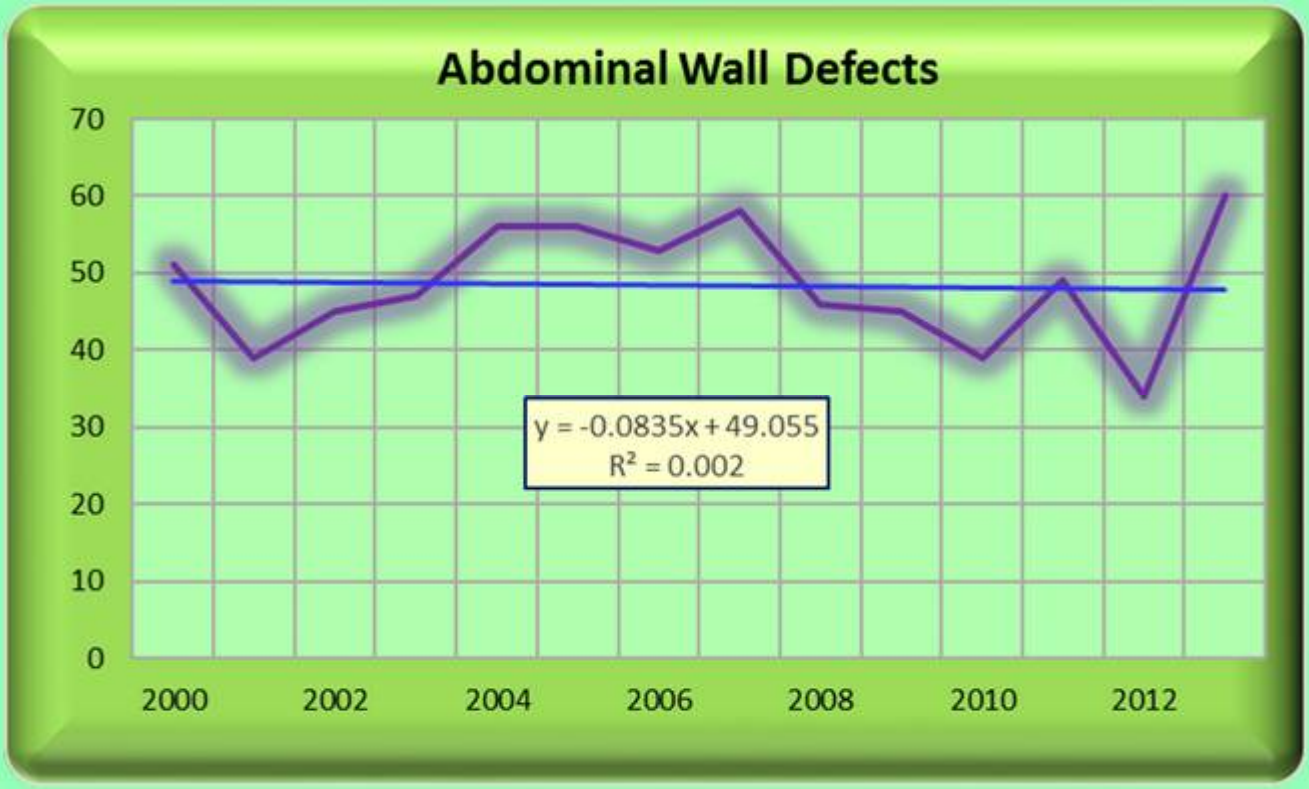
Cleft Lip +/- Palate





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

Abdominal Wall Defects



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

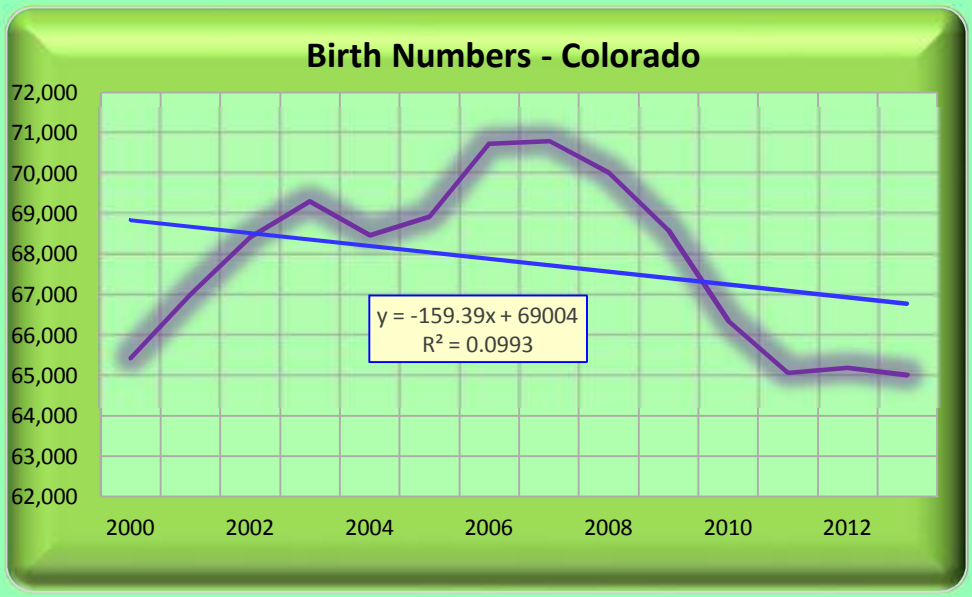
Cumulative Effects

Colorado

2000-2013

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

Cumulative Effects - Births

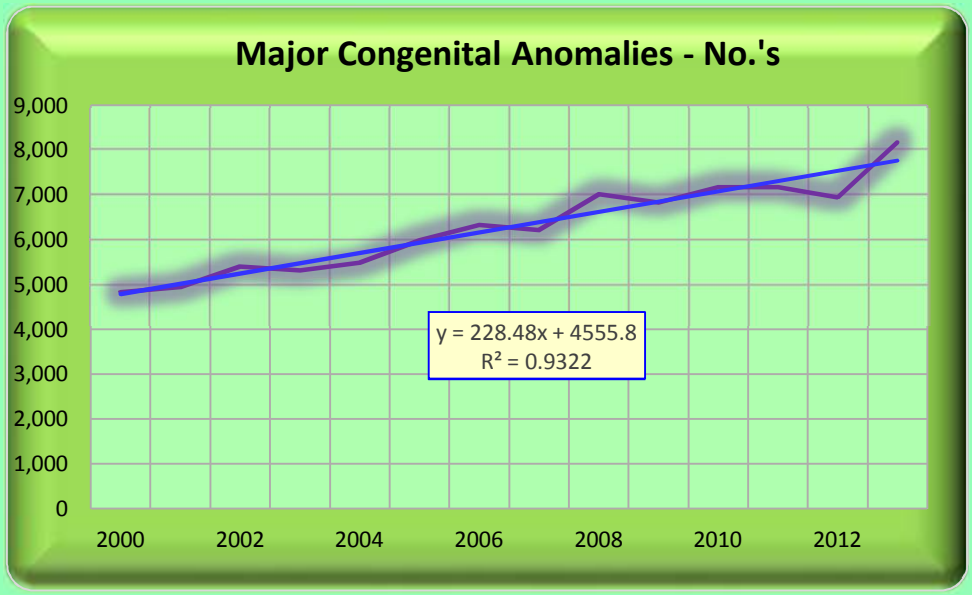


Year	Births	Projected	Difference
2000	65429	65429	0
2001	67006	65429	1577
2002	68420	65429	2991
2003	69304	65429	3875
2004	68475	65429	3046
2005	68922	65429	3493
2006	70737	65429	5308
2007	70804	65429	5375
2008	70028	65429	4599
2009	68602	65429	3173
2010	66346	65429	917
2011	65052	65429	-377
2012	65188	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.hsql

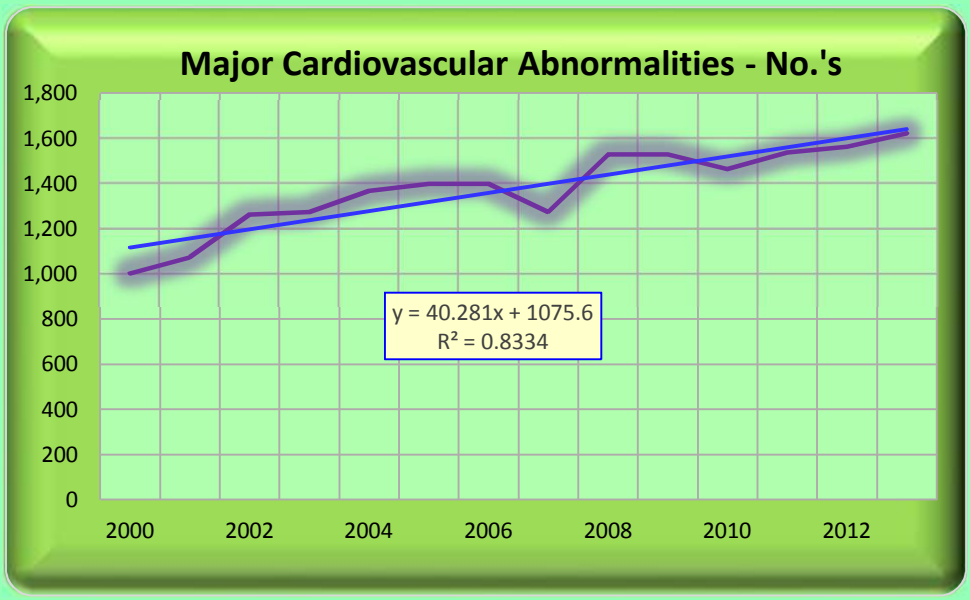
Cumulative Effects - All Major Defects



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.hsql

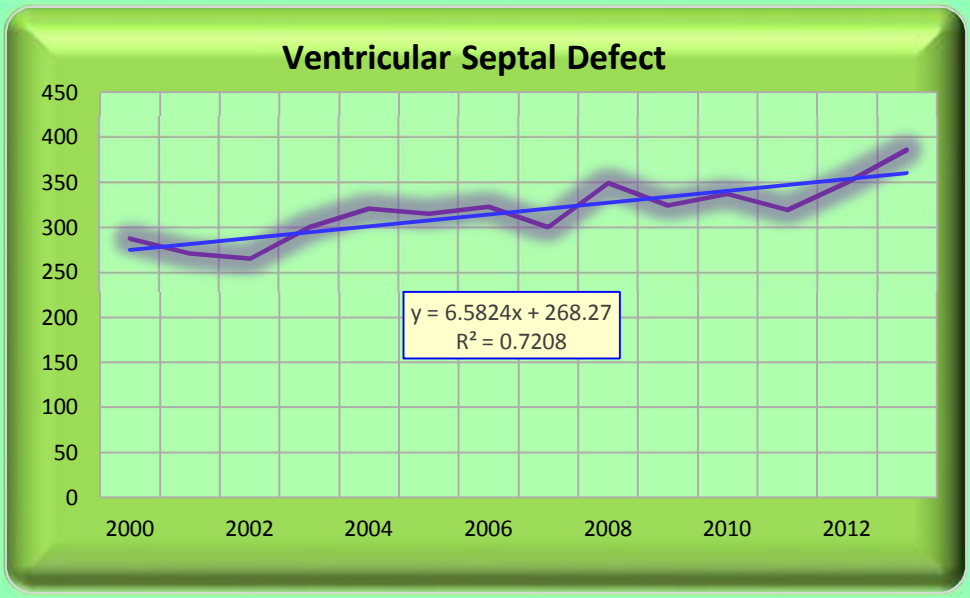
Cumulative Effects - All CVS Anomalies



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.hsql

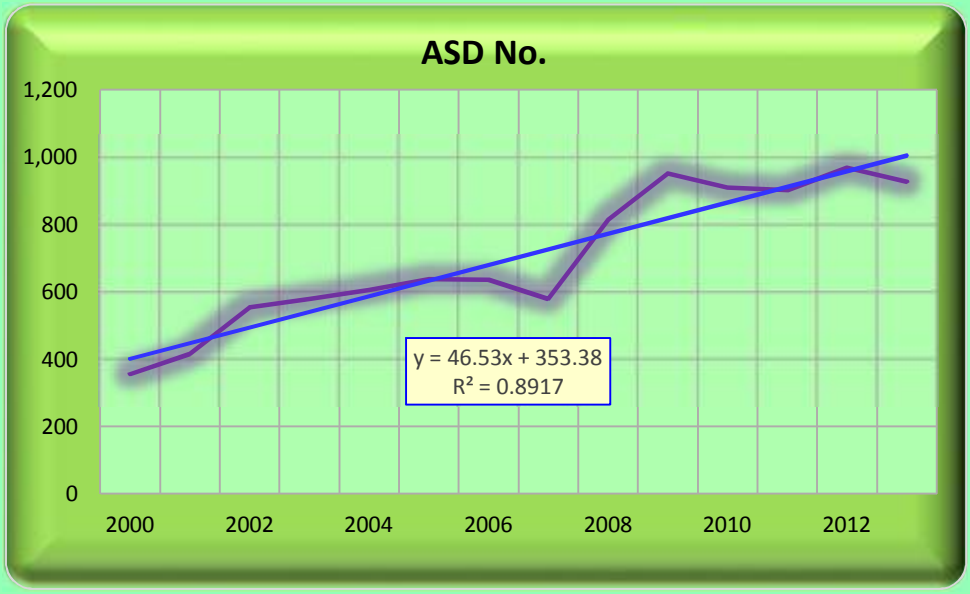
Cumulative Effects - VSD



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

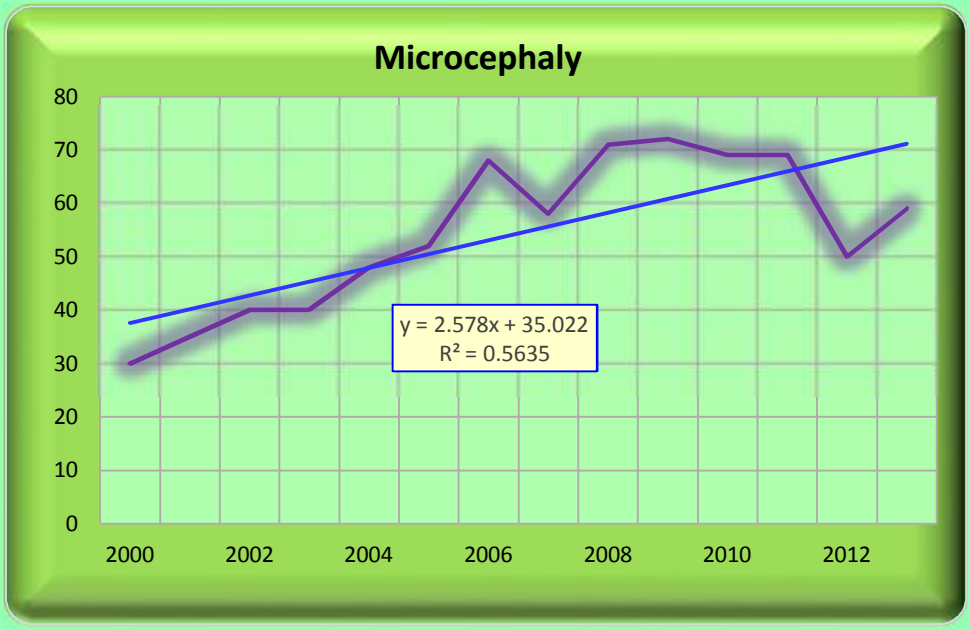
Cumulative Effects - ASD - Secundum



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

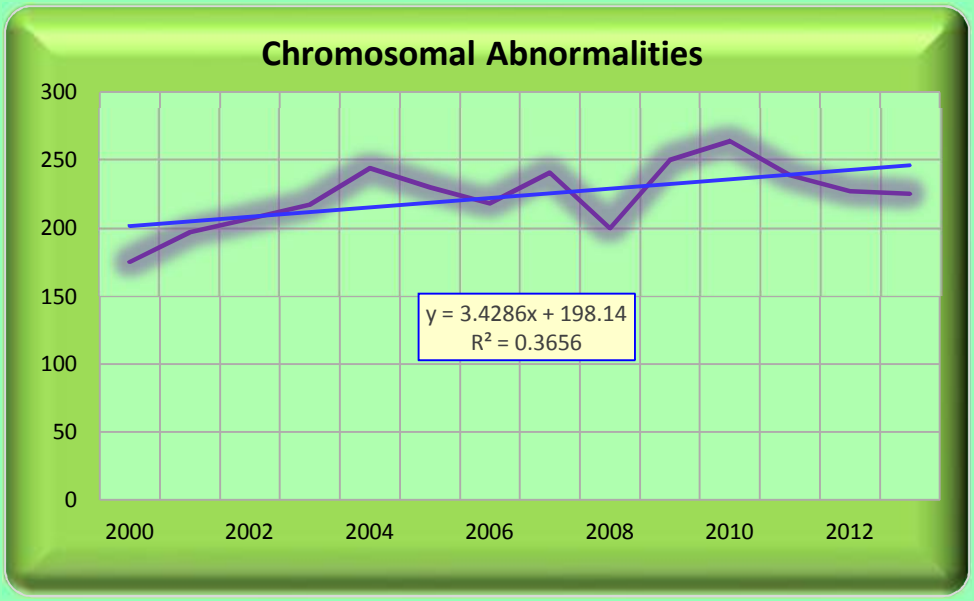
Cumulative Effects - Microcephaly



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%**

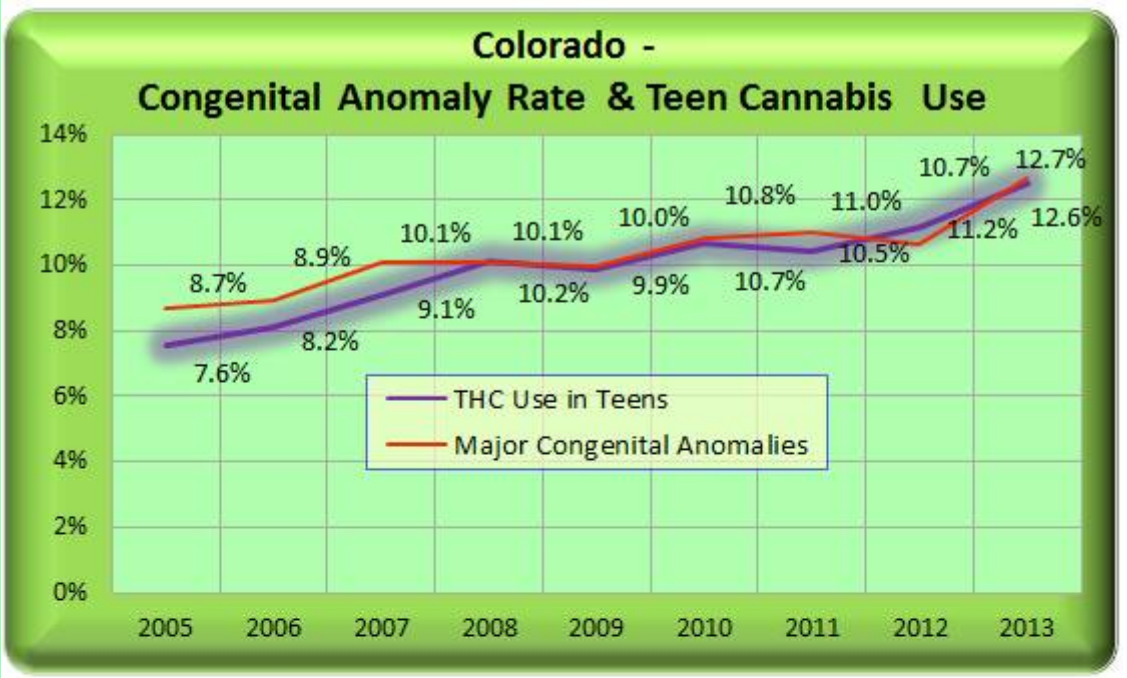
http://www.chd.dphe.state.co.us/cohid/
http://www.cohid.dphe.state.co.us/scripts/htmsql.exe/CrcsnPub.hsql

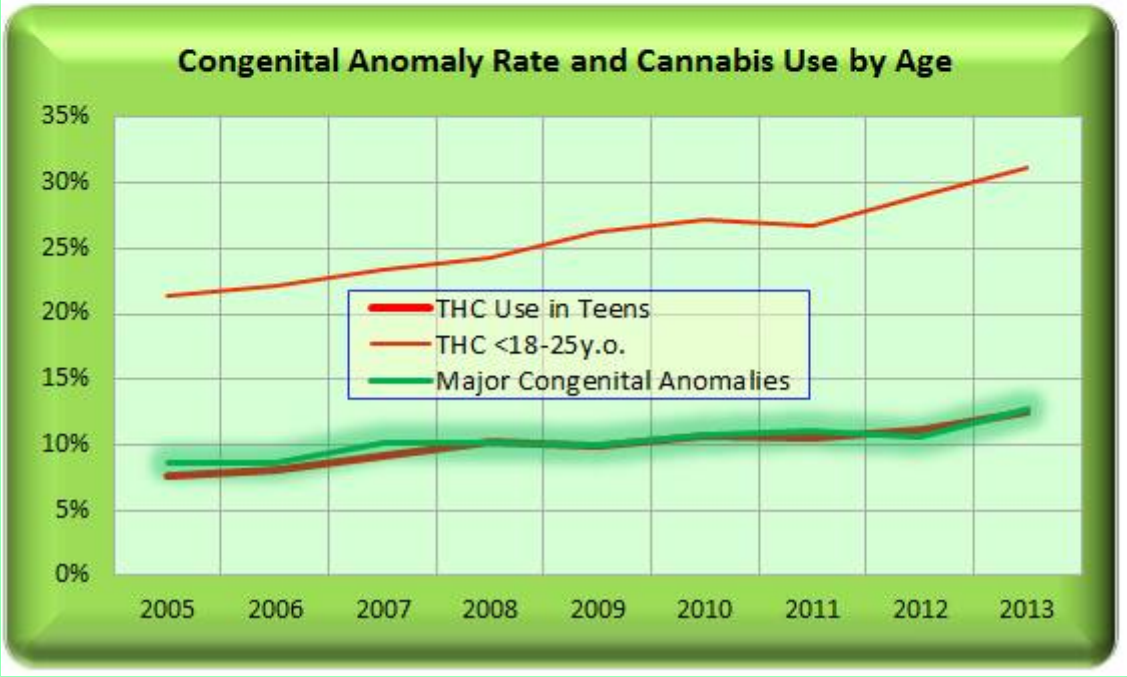
Overall Cumulative Summary

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



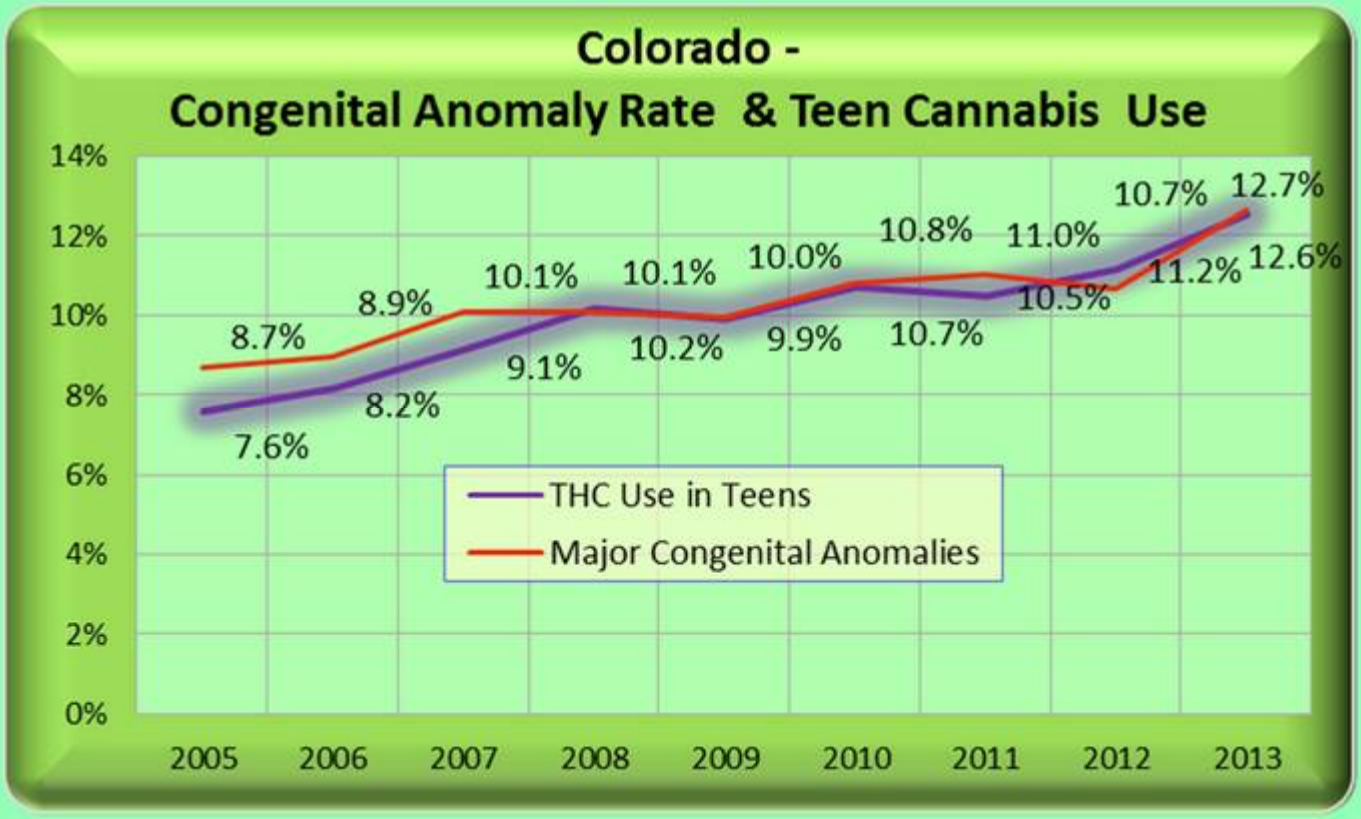


http://www.chd.dphe.state.co.us/cohid/

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
```

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

Young Adult Correlation == 0.9258
P == 0.0003457

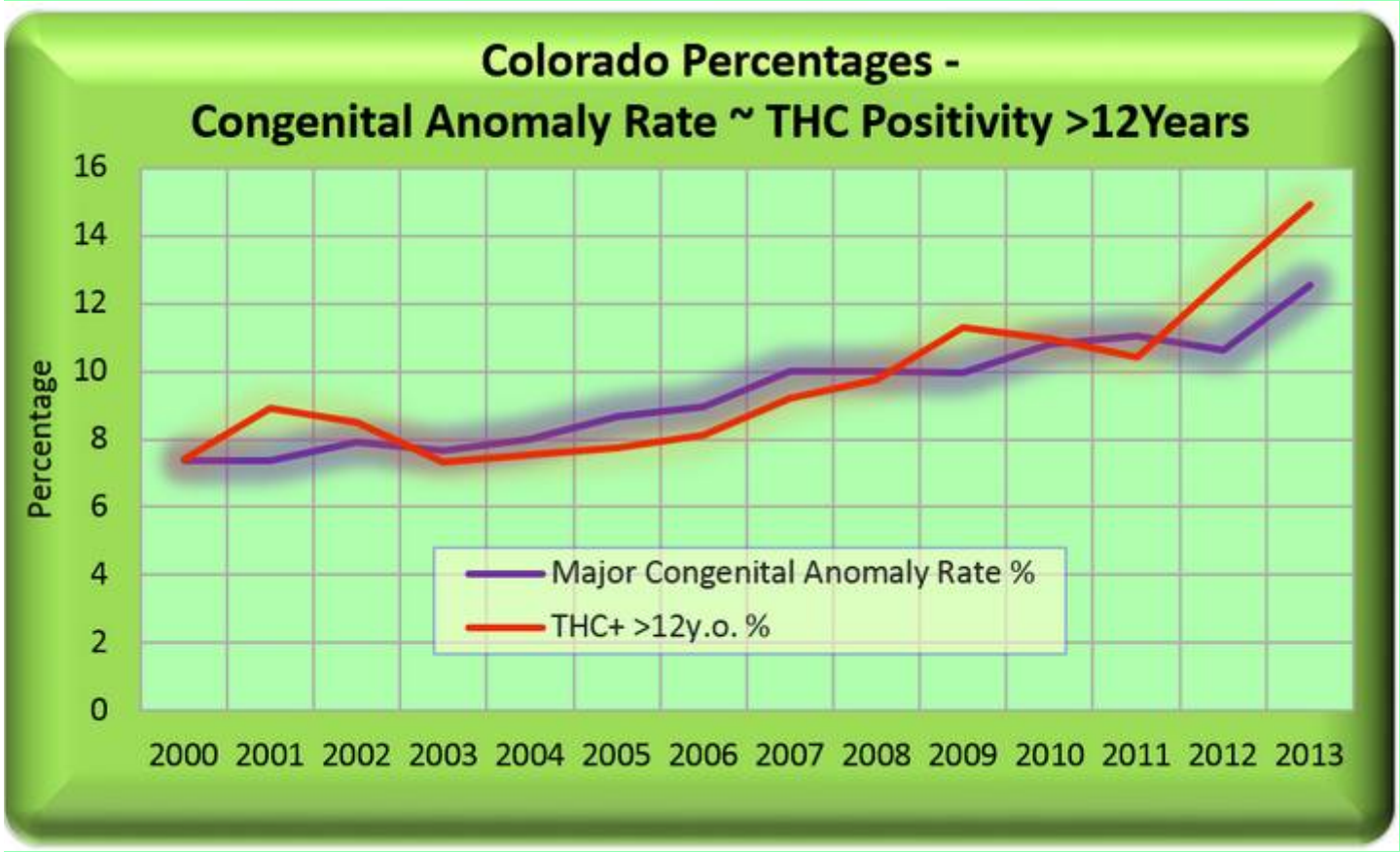
```
> CTD
  Year THCTeens THC18.25 MeanUse Majors
1 2005   0.0760   0.2143  0.1452 0.0867
2 2006   0.0815   0.2221  0.1518 0.0894
3 2007   0.0913   0.2344  0.1629 0.1001
4 2008   0.1017   0.2428  0.1723 0.1001
5 2009   0.0991   0.2635  0.1813 0.0995
6 2010   0.1072   0.2726  0.1899 0.1081
7 2011   0.1047   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
```

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



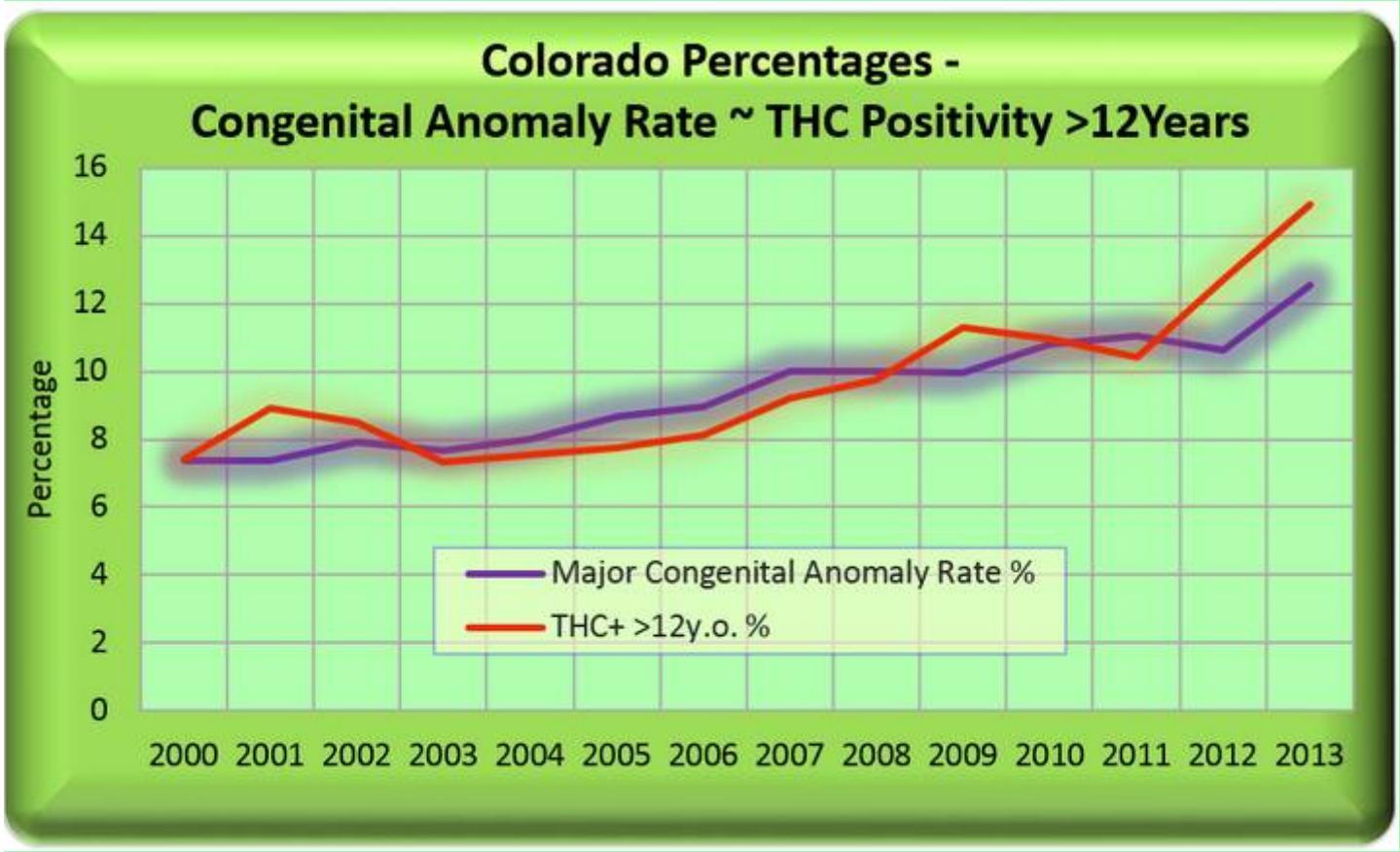

```
> cor.test (x,y, alternative="two.sided",
+           method="pearson", exact=TRUE, conf.level = 0.95)

        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/htmsql.exe/CrcsnPub.hsql

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/
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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

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