



# Oral vitamin D, infants, toddlers, and autism in the United States: 1980 to 2010

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## Abstract

It has been suggested by some that increased consumption of vitamin D by infants and toddlers may decrease the risk of developing autism. To examine this hypothesis a model was constructed to estimate how much vitamin D was consumed on average by infants and toddlers in the United States at five year intervals between 1980 and 2010. In addition estimates of autism prevalence among children entering school in the United States from 1985 to 2012 were made using data from the California Department of Developmental Services and United States Department of Education. The model shows that oral vitamin D consumption among this population has increased by 94% between 1980 and 2005 and by about 112% between 1980 and 2010. Autism prevalence among the young also increased by approximately 2300% from 1985 to 2010. Thus vitamin D consumption increased significantly and autism prevalence increased even more over these time periods. Further analysis shows that the natural log of the autism prevalence is proportional to the average level of vitamin D consumption five years previously. In other words, the data suggest that the hypothesis is false.

**Keywords:** Epidemiology, supplementation, fortification, vitamins

## Introduction

Autism is a neurodevelopmental disorder that appears in the first three years of life and is characterized by communication impairments, social and behavioral deficits, and repetitive behaviors. Evidence suggests that both genetic and environmental factors are involved in its etiology [1]. Autism rates have increased substantially faster than population growth [1]. While some of this increase may be attributable to broader inclusion criteria and diagnosis of cases that previously would have remained unidentified, there appears to have been a substantial increase in the percentage of those affected by the underlying dysfunction of autism in recent decades. A number of researchers have examined various environmental factors as an explanation for this increase [1-3].

One environmental factor that has been considered is deficiency of vitamin D. Cannell has suggested that the increase in autism rates is due to greater avoidance of sun during the last few decades resulting in vitamin D deficiency. Cannell has also suggested that supplementation with vitamin D may reduce the symptoms of autism and supplementation among infants may serve as a way of preventing autism [4]. Mostafa and Al-Adhbi have observed that typically those with autism have

lower levels of 25-hydroxy vitamin D in the blood than controls and also have higher antibody levels to myelin associated glycoproteins. They have also hypothesized that these data are connected and that infant supplementation with vitamin D may serve as a way of preventing autism [5]. Patrick and Ames have observed that vitamin D plays a role in serotonin synthesis and homeostasis and have suggested that infant supplementation with vitamin D and tryptophan will decrease the incidence of autism [6]. In summary there appears to be a belief among many researchers that low vitamin D levels are involved in inducing autism and increased supplementation of vitamin D among infants and toddlers is a viable prophylactic.

As this author has highlighted in a separate paper infants and toddlers in the United States already receive significant amounts of oral vitamin D through fortification and supplementation and the levels of fortification and supplementation as well as feeding practices have changed over time [7]. Therefore it is reasonable to examine whether the level of vitamin D consumed by infants and toddlers in the United States affects the risk of autism based on data that may be gleaned from the historical record. In other words, based on the historical record is vitamin D an effective prophylactic? This is the subject of this paper.

## Materials and methods

In this paper historical autism rates will be regressed against the average level of vitamin D consumed by infants and toddlers in the United States as determined by a model from 1980 to 2010. Given that autism is generally diagnosed a number of years after birth and often years after the early signs of underlying dysfunction [8], if there is a relationship between oral vitamin D consumption and development of autism, changes in vitamin D consumption would only be expected to impact autism rates with a lag. Therefore the precise question examined is whether there is a relationship between the average level of vitamin D consumed by infants and toddlers and the level of autism rates five years later.

### Autism rates time series

High quality long term data series on autism rates are surprisingly difficult to find in the literature. Therefore in this study an attempt will be made to construct such a data series from two different sources. United States Department of Education (USDE) data as compiled by the National Center for Education Statistics on the number of those with an autism diagnosis in the public school system and the number of children entering kindergarten are available and seem to be reliable from the early 2000s [9-11]. The same can be said of California Department of Developmental Services (CDDS) data on autism cases in California and school enrollment data as reported by the California Department of Finance from the mid-1980s through the early 2000s [12,13]. As a larger data set is generally a better proxy for the overall population, this paper will compute autism rates by relying on USDE data from 2001 onward and will rely on CDDS data prior to this.

With respect to the USDE data, one can estimate how many individuals with autism entered the school system in a given year in the United States by taking the net increase in the population of those with autism in the education system and adding an estimate for the number who exited the system. If one then divides by the number of kindergarteners entering the system, one can come up with an estimated autism rate.

While this method is crude, it has advantages over other methods which attempt to obtain more precision by using birth year cohorts. To obtain satisfactory statistics by birth year cohorts one must wait for diagnosis of all people in a given birth-year to be complete. As autism is often diagnosed late this means there is no reliable recent data in time series based on birth year cohorts. In addition pure birth year cohorts often lack data on year of diagnosis which is important when doing regressions against environmental factors. For example the CDC has a data series that has estimated autism rates among 8-year olds from 2000 to 2010. As of summer 2014, the last reported date in the data series is for the year 2010 and applies to those who were born in 2002 [14]. The short time frame, lack of recent data, and lack of data on year of diagnosis makes this series of little use in regressing against an environmental factor.

An analogous approach will be used with the CDDS data which will determine rates prior to 2001. Based on the number of new cases of autism in a given year one can obtain a rate among those entering the system by taking the number of new cases served by CDDS and dividing by the number of kindergartners served by the California Department of Education in that year. As the CDDS series lacks data for the 1985-1986 school year a rate will be approximated by using the 1986-1987 rate.

### Vitamin D consumption time series

Evidence suggests that autism is usually induced early in life [15,16]. Therefore, if vitamin D is an effective prophylactic, it is the level consumed early in life that would be critical to outcome. So a model will be made to compute the average level of vitamin D consumed during the first thirty months of life. The first thirty months will be divided into four time periods: 0-6 months, 6 months to the transition to cows' milk, transition to cows' milk to 24 months, and 24 months to 30 months. Estimates of how much vitamin D is consumed by breast-fed infants and formula-fed infants will be made for the first two periods. Estimates for the latter periods will apply to infants in general. Variables such as vitamin D content of infant formula, human milk, whole cows' milk, 2% cows' milk, vitamins, and other vitamin D fortified foods and changes in consumption patterns of these same beverages and foods will be critical to this analysis. Estimates will be made for the value of each variable at 5 year intervals between 1980 and 2010. For a given variable in some years there is solid data in the literature but in other years there is no data available in the literature and an educated guess will be used to guide the analysis. Where educated guesses are made, they will appear in italics. Using this data an Excel model will estimate vitamin consumption in IU per day for every five-year interval. **Table 1** provides the variables and numeric estimates used as inputs to the model for estimating vitamin D consumption. Details on individual variables and the sources of assumptions appear below:

1) **% of babies ever breast-fed, % of babies breast-fed at 6 months, % of babies breast-fed at 12 months.**

Data from 2000, 2005, and 2010 are from interviews conducted by the CDC [17]. Data for the first two variables from 1990 (really 1989) and 1995 come from Ross Medical surveys as reported by Ryan [18]. She also provides a figure for those who initiated breastfeeding from 1984, which is used for the 1985 estimate [18]. Data for the % of babies breast-fed from 1980 also comes from a Ross Medical Survey as reported by Martinez, et al. [19]. Other points are estimated by assuming that the values are proportional to years nearby.

2) **% of breast-fed babies given D drops.** A study by Taylor et al., from 2009 estimated that 16% of breast-fed babies received vitamin D drops [20]. This level will be used for the 2010 estimate in the model. The 2005 estimate is

**Table 1. Inputs to Vitamin D consumption model.**

Measure	Units	Year						
		1980	1985	1990	1995	2000	2005	2010
% of babies who are ever breast-fed	%	55%	60%	53%	60%	71%	74%	77%
% of babies who are breast-fed at 6 mos	%	19%	20%	18%	22%	34%	43%	49%
% of babies who are breast-fed at 12 mos	%	9%	10%	8%	10%	16%	22%	27%
% of breast-fed babies given D drops	%	0%	0%	0%	0%	0%	11%	16%
Age starting D drops	months	--	--	--	--	2	2	0
Age in months of typical transition to milk	months	8	9	10	11	12	12	12
Human milk consumption by breast-fed	ml	600	600	600	600	600	600	600
Formula consumption by formula-fed	ml	600	600	600	600	600	600	600
Milk consumption by toddlers	ml	500	500	500	500	500	500	500
Vitamin D per liter in human milk	IU	45	45	45	45	45	45	45
Vitamin D per liter in formula	IU	400	586	772	713	654	595	536
Vitamin D per liter in whole milk	IU	200	200	200	320	439	483	526
Vitamin D per liter in 2% milk	IU	271	271	271	331	391	446	500
Vitamin D per vitamin D drop	IU	400	400	400	400	400	400	400
Vitamin D in kids multivitamins	IU	400	400	400	400	400	400	400
Vitamin D from diet without fortification	IU	18	18	18	18	18	18	18
% of toddlers receiving vitamins	%	11%	11%	18%	26%	33%	39%	45%
Vitamin D from other fortified foods	IU	21	21	21	21	31	51	71

assumed to be two-thirds of the 2010 estimate as the American Academy of Pediatrics recommendation from 2008 and associated publicity may be assumed to have raised the rate [21]. Data for prior years is assumed to 0% as the American Academy of Pediatrics only began recommending vitamin D drops in 2003 [22].

- 3) **Age starting vitamin D drops.** For babies who are given vitamin D drops this is the age at which they are first given. The model will assume that babies who are given vitamin D drops will receive them according to the American Academy of Pediatrics recommended schedule. In 2003 the recommendation was to start at 2 months [22]. In 2008 the recommendation was to start at birth [21].
- 4) **Age of typical transition to milk.** This is the average age at which infants transition from infant formula to cows' milk or in some cases from human milk to cows' milk. Fomon et al., has highlighted that this age has increased over time based on data from various surveys [23]. Using data Fomon has aggregated, the model will assume 8 months in 1980, 10 months in 1990, and 12 months in 2000 [23].
- 5) **Human milk consumption by breast-fed.** How much human milk in milliliters does an infant that is not fed formula consume in a day? Picciano et al., has determined that this is about 600 ml per day [24].
- 6) **Formula consumption by formula-fed.** How much

formula in milliliters does an infant that is not fed human milk consume in a day? Bonuck, et al., found in a sample of 12 month olds from low-income families that they consumed about 700 ml per day [25]. As this sample consisted of 12 month olds who transitioned late and most consumption of formula would be done by younger and smaller babies who consume marginally fewer calories, the model will assume an average of 600 ml per day.

- 7) **Milk consumption by toddlers.** Lampe and Velez found that milk consumption among a sample of 18-month olds was about 500 ml per day but there were some which consumed much more [26]. The model will assume 500 ml per day.
- 8) **Vitamin D per liter in human milk.** Reeve et al., estimated that there is 33 IU per liter of vitamin D3 in human milk and in total about 40 to 50 IU per liter of various forms [27]. So the model will assume 45 IU.
- 9) **Vitamin D per liter of infant formula.** The model will be based on the vitamin D per liter of regular iron-fortified cows' milk based infant formula as it is more commonly used than specialized formulas especially prior to the mid-1990s [28]. The Infant Formula Act was passed in 1980 motivated by some cases of brain damage among infants from inadequate salt levels in a single brand of infant formula [29]. Implementation was gradual but it mandated minimum levels of various nutrients

including vitamin D. The level it mandated was at least 40 IU per 100 calories [30]. As infant formulas typically contain about 700 calories per liter, this level is about 280 IU per liter [31]. It also established penalties for not achieving minimums and a culture of over-fortification relative to human milk [32]. Holick, et al., found when they analyzed infant formulas in 1991 that they were all significantly over-fortified relative to the label [33]. Pehrsson et al., found when they analyzed vitamin D in infant formulas around 2008 that infant formulas were still significantly over-fortified relative to the label but at lower levels than when Holick had tested [34]. The vitamin D per liter of infant formula in 1990 is assumed to be 772 IU per liter which is the average of the two types of regular 6-12 month brand N powder from Holick's analysis. The vitamin D per liter in 2010 is assumed to be 536 IU per liter based on Pehrsson's findings. The vitamin D level in 1980 is assumed to be 400 IU per liter which is above the minimum level in the Infant Formula Act but below that which Holick found in 1991 after the Act was fully implemented.

- 10) **Vitamin D per liter of whole milk.** Most toddlers through 24-months of age consume whole milk although there is a substantial minority that consume 2% or reduced fat milks for some of this time period [35]. So the model will assume any milk consumed through 24-months of age is whole milk. Holick, et al., found that whole milk averaged 200 IU per liter when tested in 1991 [33]. So vitamin D per liter of whole milk in the model is assumed to be 200 IU per liter for 1990 and before. Holick's findings resulted in new regulations to increase fortification of milk with no change in the label [36]. Later Murphy et al., analyzed vitamin D in milk samples in New York between 1997 and 2000. Murphy et al., did not report an average level of vitamin D in whole milk but instead stratified the samples into buckets by the level of vitamin D in each sample [37]. Making some simple assumptions one can deduce that Murphy's whole milk samples had an average vitamin D level near 414 IU per quart which is 439 IU per liter which is what the model will assume for the year 2000. Patterson, et al., reported that samples of whole milk in 2007 were found to have an average of 526 IU per liter [38]. So for 2010 the model will use this figure.
- 11) **Vitamin D per liter of 2% milk.** Most toddlers switch to 2% milk by 24-months of age [39]. The model will assume that all milk consumed after 24-months of age is 2% milk. While some do in reality consume whole milk after 24-months offsetting this are toddlers who consume 2% milk before 24-months of age. Averaging the samples that Holick et al., examined in 1991, it appears that 2% milk averaged 271 IU of vitamin D per liter in 1991 [33]. Doing some calculations based on Murphy et al., samples from 1997 to 2000, it appears that the average level

of vitamin D in 2% milk at the time was 391 IU per liter [37]. Patterson's samples of 2% milk from 2007 averaged 500 IU per liter [38]. So the model will assume 2% milk had 271 IU per liter in 1990, 391 IU per liter in 2000, and 500 IU per liter in 2010.

- 12) **Vitamin D per dose of vitamin D drops.** Mouser and Sacks mention in passing in a paper from 1999 that the typical dose of vitamin D drops is 400 IU [40]. Wagner et al., in 2008 while recommending supplementation at 400 IU per day for infants also observed that vitamin D drops were available in the 400 IU dose [21]. So the model will assume this is the standard dose.
- 13) **Vitamin D on label in kids multivitamins.** Flintstones Kids, the most popular children's multivitamin, contained 400 IU by the label prior to 1985 and through the 1990s [41,42]. In 2012, which is outside the time period of this study, the level of vitamin D in Flintstones was raised to 600 IU [43]. The model will assume 400 IU as the dose through time although some children's multivitamins have lower doses and it seems probable to this author that the average dose in children's multivitamins increased modestly over the time period of this study.
- 14) **Vitamin D from diet excluding fortified products.** Toddlers obtain some vitamin D through foods that are not fortified. Moore et al., found that those from 1 to 8 years old obtained about 32 IU of vitamin D from unfortified sources in the year 2000 [44]. The Institute of Medicine found that 1 to 2 year olds consumed about 1019 calories a day and those 3 to 8 years old consumed 1692 calories per day [45]. Moore et al., also found that those 1 to 8 years old consumed about 380 ml of milk per day on average [44]. Toddlers who are 18-months old consume on average about 500 ml from an earlier section. Whole milk is 629 calories per liter [46]. If one makes the assumption that vitamin D from unfortified foods of a toddler is comparable to 1 to 8 year olds but in smaller portions due to smaller caloric consumption of food excluding milk, one can calculate that toddlers would on average obtain about 18 IU per day from natural sources. This is what will be assumed by the model.
- 15) **% of toddlers receiving vitamins.** Based on surveys between 2007 and 2010, Bailey et al., found that 45% of those 2 to 5 years of age were taking a dietary supplement [47]. Based on surveys between 1999 and 2002 Picciano et al., reported that 33% of those age 1 to 4 years old were on some form of supplement including vitamin D [48]. Sharpe and Smith reported in a 1985 study of AFDC children in rural Mississippi that 11% were on a multivitamin and the brands consumed were those that were widely advertised on television [49]. One might suppose that multivitamin use would be higher among the more affluent but

one might also suppose that those who are poor and less well educated are more susceptible to marketing. The model will assume 45% for 2010, 33% for 2000, and 11% for 1985.

16) **Vitamin D from other fortified foods.** Moore et al., found that as of 2000 on average 1 to 8 year olds consumed about 56 IU per day from fortified foods excluding milk [44]. So examining caloric intakes and excluding milk as was done for a prior variable, one can estimate that toddlers would have consumed about 31 IU per day from fortified foods excluding milk. Thus the model will assume 31 IU per day for this parameter for 2000. As of 2003 most ready-to-eat cereals that were fortified with vitamin D had 40 IU per serving based on the label [50]. By 2011 the level of fortification in many fortified cereals had been raised to substantially higher levels. For example many Kellogg's cereals had 90 IU per serving [51]. In 2003 fortified orange juice was a novelty, but by 2010 it was a staple [52,53]. Prior to 2005 several brands began adding vitamin D to yogurt at a level of 60 to 80 IU per serving [44]. These data suggest that there was a large increase in fortification levels between 2000 and 2010. So the model will assume 31 IU for 2000, 51 IU for 2005, and 71 IU for 2010. It will also assume 21 IU for 1995 and before.

## Results

A time series of autism rates per 10,000 in the United States was made as described in the methodology section using USDE data and CDDS data spliced together (Table 2). The results show from 1985 to 2005 that raw autism rates increased by about 1550%. In addition from 1985 to 2010 rates increased by about 2300%.

Estimates of average vitamin D consumption up to 30-months of age were made at five year intervals starting from 1980 using a model as described previously. Results for various subgroups and the aggregated average appear in Table 3. The results show that vitamin D consumption among infants and toddlers increased from approximately 188 IU per day in 1980 to approximately 365 IU per day in 2005 and 399 IU per day in 2010. In other words, vitamin D consumption increased by about 94% between 1980 and 2005 and increased by about 112% between 1980 and 2010.

Autism rates per 10,000, the square root of the autism rates per 10,000, and the natural logarithm of the autism rates per 10,000 were each individually regressed against the estimates of vitamin D consumption 5 years earlier. The data show that the autism rate is correlated to the consumption of vitamin D five years previously. The R squared based on a linear regression is 0.884 and standard error 21.1; the R squared for the square root regression is 0.965 with standard error 0.80; and the R squared for the natural log regression is 0.994 with standard error 0.113. It appears that the natural log regression

Table 2. Estimated autism rate.

Year of enrollment	Autism rate
1985-86	0.060%
1986-87	0.060%
1987-88	0.074%
1988-89	0.089%
1989-90	0.099%
1990-91	0.111%
1991-92	0.113%
1992-93	0.113%
1993-94	0.171%
1994-95	0.220%
1995-96	0.233%
1996-97	0.312%
1997-98	0.369%
1998-99	0.435%
1999-00	0.478%
2000-01	0.578%
2001-02	0.696%
2002-03	0.763%
2003-04	0.847%
2004-05	0.916%
2005-06	0.986%
2006-07	1.148%
2007-08	1.264%
2009-10	1.333%
2010-11	1.452%
2011-12	1.446%
2012-13	1.461%

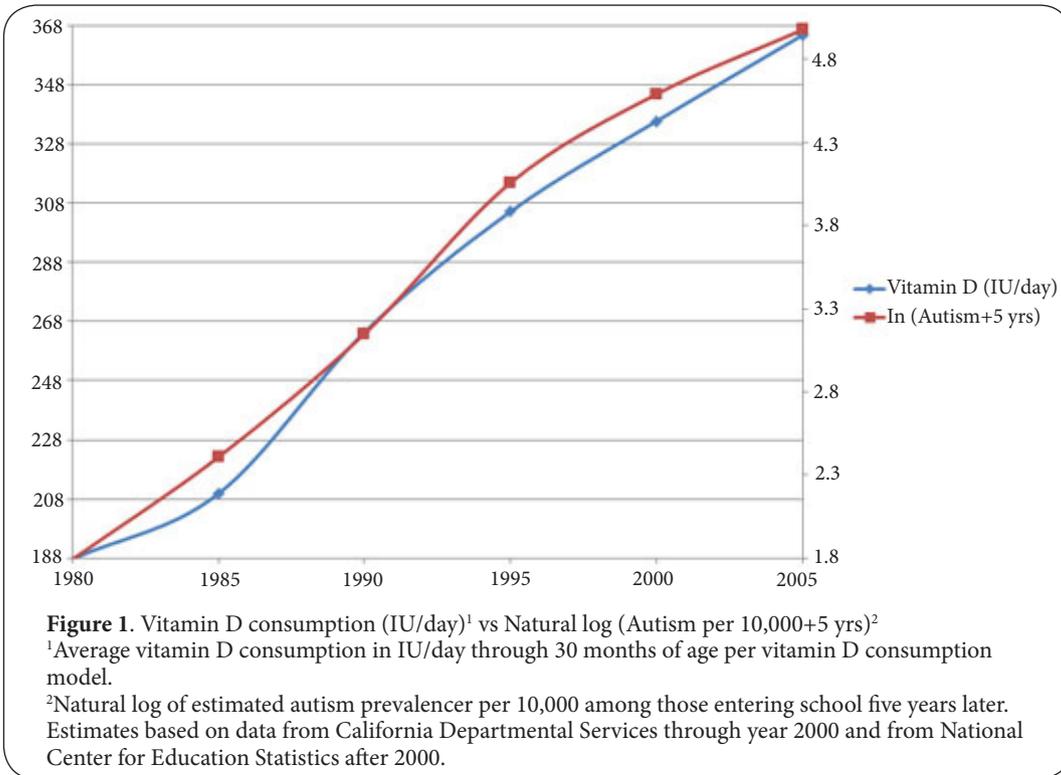
provides the best fit. The t-statistic for the intercept and slope are -7.2 and 25.0. The p-values are 0.0020 and 0.000015 respectively. This suggests that based on the historical data, the consumption of vitamin D is a good predictor of the autism rate five years later and the relationship is that the natural log of the autism rate is proportional to the average level of vitamin D consumed five years previously (Figure 1). Thus, the data suggest that the hypothesis that consumption of oral vitamin D is a prophylactic for autism is false. Instead the data support the opposite hypothesis that consumption of oral vitamin D may be a risk factor in inducing autism. The model and accompanying data is available as an Excel file (Supplementary Data).

## Discussion

Some may question data or assumptions underlying the autism rate estimates or the vitamin D consumption model.

**Table 3. Output from Vitamin D consumption model.**

Measure	Units	Year						
		1980	1985	1990	1995	2000	2005	2010
Vitamin D to 6 mos by breast-fed	IU	27	27	27	27	27	55	91
Vitamin D to 6 mos by formula-fed	IU	240	352	463	428	392	357	322
Average vitamin D to 6 months	IU	162	221	308	263	201	181	177
Vitamin D to transition by breast-fed	IU	27	27	27	27	27	70	91
Vitamin D to transition by formula-fed	IU	240	352	463	428	392	357	322
Average vitamin D to transition	IU	211	303	405	363	301	264	234
Vitamin D from transition to 24 mos	IU	183	183	212	301	401	466	532
Vitamin D from 24 months to 30 mos	IU	219	219	248	307	377	448	519
Average vitamin D to 24 mos	IU	180	208	269	305	326	344	369
Average vitamin D to 30 mos	IU	188	210	264	305	336	365	399



On autism rates some authors have noted that the increase in rates of autism have been over-estimated or may in fact not represent a true increase due to broader inclusion criteria and cases that have previously been missed [54]. However, Hertz-Picciotto et al., and Grether et al., found that the increasing rates of autism cannot be completely explained by such factors [55,56]. So even if some off setting factors associated with greater recognition were modeled, it would not change the fundamental result that there has been an increase in autism between 1985 and 2010.

On the vitamin D model one might note that different and

justifiable estimates of vitamin D consumption could be obtained by varying some of the assumptions in the model. This is true. However, due to the wealth of data in the literature that indicate that there has been a true increase in fortification and supplementation among the young over this time period, it seems that any defensible model based on real data and realistic assumptions would find that there has been a substantial increase in consumption of vitamin D among this population.

One might acknowledge the increase in vitamin D consumption and still question its materiality. In fact supplementing

with 400 IU per day in elderly adult human subjects has been found to result in significant increases in blood levels of 25-hydroxy vitamin D and result in biochemical effects such as decreasing bone loss [57,58]. Infants and toddlers are much smaller by weight than adults and consume fewer calories. Therefore it seems reasonable to suppose that an average increase in vitamin D consumption of 177 IU per day among infants and toddlers as seen during the 25 years between 1980 and 2005 would have significant effects on biochemistry. This is especially true as the levels of consumption in 1980 were already high relative to levels available in human milk [27].

## Conclusions

The model grounded in historical data shows that there has been a substantial increase in consumption of vitamin D by infants and toddlers in the United States between 1980 and 2005. Specifically, infants and toddlers through 30 months of age consumed on average about 188 IU of vitamin D per day in 1980 and about 365 IU of vitamin D in 2005. This represents a 94% increase in consumption of vitamin D in this population. The model also found that on average 399 IU of vitamin D per day was consumed by this population in 2010 which represents a 112% increase in vitamin D consumption from 1980.

Regressing various functions of autism rates against the level of vitamin D consumption shows that based on the historical data, the natural logarithm of autism rates is proportional to the level of vitamin D consumption five years previously. The R squared is 0.994; the Standard Error is 0.11; the t-statistic for the intercept and slope are -7.2 and 25.0 and the p-values are 0.0020 and 0.000015 respectively. So based on historical data increasing the level of vitamin D supplementation among infants and toddlers will not decrease the rate of autism.

## Additional files

[Supplementary Data](#)

## Competing interests

The author declares that he has no competing interests.

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