Calcium intake is not associated with kidney stone: Findings From the 2015 to 2018 National Health and Nutrition Examination Survey (NHANES)

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Abstract

Kidney stone is a common disease nowadays, whose main component is calcium oxalate. A large amount of people eagerly to supply calcium from the dietary food, however, they are still afraid of kidney stone. In addition, some patients with kidney stones are suggested to decrease the calcium intake but there are newly search which recommends to not cut down it. We wondered whether the kidney stones are associated with calcium intake in daily life. This study investigates the relation between calcium intake and kidney stone. We supposed that the calcium intake is linked to kidney stone. People, who participated in the NHANES, from 2015 to 2018, were included and they were screened by the constraints. Multi-variable logistic regression was used to assess the association between calcium intake and kidney stone, adjusting for other confounding factors. At the same time, to conduct stratification studies, we took calcium intake as a continuous variable and classification variables respectively. In the muti-variate analysis, calcium in food had no connection with kidney stone([odds ratio] 0.9999, [confidence interval] 0.9998-1.001 in model 3 which is fully adjusted. During the trend test, there was no prominent difference from calcium quality from Q1 to Q4 in those 3 models and the muti-variate analysis separated by confounding factors might affect the result according to the univariate analysis, we found there was no disparity. So, we conclude that having the history of kidney stone is no connection with calcium intake.

1. Introduction

Kidney stone is a common illness, whose estimated prevalence in USA was 11.0% (95% CI 10.1–12.0).[1] According to studies based on the NHANES, the prevalence in male is stable but the gender differences appear to be narrowing.[2] And it has high rate of recurrence and up to 50% chance of having a new kidney stone within ten years.[3] And the time of kidney stone recurrence is shorter than the time of new kidney stones formation.[4]Kidney stones are of great harm to the human body, hematuria, low back pain, and abdominal pain, which severely threaten the quality of the life.[5][6][7]More interestingly, the cost of curing kidney stones is much higher than the cost of prevention.[8][9] And according to recent studies, some countries in Europe or some association, like Italy, even the WHI OS(Women's Health Initiative Observational Study) focused on the impact of the nutritional factors on incident kidney stone formation[10], the composition of which is mainly calcium oxalate, which is the most common type.[11][12] It is easy to link the calcium intake to the kidney stone. Concerns about kidney stone are increasing year by year. Similarly, with booming development economic rapidly, people pay more attention to eating healthy and the nutrients values like calcium day by day. Not to mention it, the formation of kidney stones is inseparable from eating habits.

Previous researches highlighted the connection between calcium in dairy food and the kidney stone. A strong calcium intake in dietary food is suspected of increasing the risk of forming kidney stone. Therefore, patients having kidney stone are often suggested to decrease calcium intake[13]. However, in terms of the researches before, for those who had kidney stones, study found there is no need to cut the dietary calcium intake. Meanwhile, extreme restrictions on calcium intake increase the risk of having

kidney stones and some researchers found that kidney stones have little relationship with calcium intake in food. What's more, patients having calcium oxalate kidney stone are advised to take high calcium diet. [14][15]

Calcium is one of the most essential and common elements in our bodies and it maintains much of the bones and teeth.[16] Taking calcium supplements is a very common thing. This thought is almost carried out through the whole life. There are many ways to supply calcium, besides taking calcium tablets directly, but it's more to increase the calcium in the daily diet. During adolescence, parents add the milk, cheese, yogurt and many kinds of food full of calcium to prevent rickets [16][17]. While into middle and old age, they focus on calcium supplements more to reduce the risk of osteoporosis and other diseases caused by calcium loss. The latest studies also show that maintaining high calcium intake in young adults reduces the risk of obesity and cardiovascular disease.[18][19] The calcium is one of the Nutritional factors that play an important role in kidney stone formation.[20] Therefore, could it be that high calcium intake makes kidney stones more easily?

Thus, to dig out the connection between calcium intake and kidney stone, we use the data from National Center for Health Statistics (NHANES), ranging from 2015 to 2018. The target of study was to analyze the association between calcium intake in diet and the kidney stones.

2. Materials And Methods

Kidney stones have a certain recurrence rate, some studies found dietary control is effective.[21] To find out whether the calcium intake is associated with the kidney stone or not. We adopted the questionnaire data from the NHANES during the period from 2015 to 2018, including 19225 participants.[22] Information about the calcium intake and kidney stone was in the questionnaire, which was collected by the NHANES. Due to be lacking in exposure variable–calcium intake and outcome variable–answers to "Ever had a kidney stone?", we deleted 3414 data and 6073 data separately, 9487 in total. The simple flow chart(Figure 1) is below. To compare the calcium intake, individuals were divided into four groups based on calcium intake – 342.8 ± 113.6mg, 650.5 ± 80.8mg, 964.3 ± 105.0mg, 1670.8 ± 548.4mg. When we use the data on kidney stones, we use the answer "Yes" as having a kidney stone.[23] At the same time, different lifestyles and gender could affect kidney stones.[24][25]We had set up a number of confounding factors. Multivariable logistic regression was used to assess the association between calcium intake and kidney stone, adjusting for age, gender, alcohol use, race/ethnicity, level of education, diabetes[26], VD intake, BMI[26], marital status, family income and immigrant status.

In order to solve the lack and classification of the confounding factors, for the diabetes, we concluded the "Refused", "Missing" and "Don't know" into one group, and then distributed them into two groups in proportion; for alcohol, we did the same as diabetes; for family income, besides making $20,000 as the dividing boundary, the rest are divided in the same way; for marital status, we classified the spinsterhood into a scope as well as "Married" and "Living with a partner" , the "Missing" was put into the third set.

Besides, we converted continuous variable--age into categorical variable, whose dividing lines were 40 and 60. At last, we set “whether graduated from high school or not” as the boundary line, and the “Missing” was in another group.

To conduct stratification studies, we took calcium intake as a continuous variable and classification variables respectively. While we detected the possible relationship between outcome variable and confounding factors, to eliminate these distractions, we made single factor analysis. As for all the statistical analysis mentioned above, like multi-variable logistic regression, we finished them by feat of Empower Stats.3 and the mechanism of kidney stone formation was created by the BioRender.com.

3. Results

After screening(Fifure 1), 9,738 individuals from the NHANES database were surveyed, 1,024 of whom had a history of kidney stone. Table 1 shows the characteristic of individuals stratified by ever had kidney stone. The P-value between calcium intake and kidney stone was 0.681.

From the univariate analysis, there was no relation between these confounding factors and the history of kidney stone ([OR] 0.9999, [CI] 0.9998–1.0001; Table 2). Besides, in the muti-variate analysis, calcium in food had no connection with kidney stone. ([OR] 0.9999, [CI] 0.9998–1.0001 in model 1, [OR] 0.9999,95% [CI] 0.9998-1.000 in model 2, odds ratio [OR] 0.9999, [CI] 0.9998–1.001 in model 3). None was adjusted in model 1, diabetes, BMI, gender, age, race, statue and marriage were adjusted in model 2 and model 3 is fully adjusted. And those above factors are not related to the history of kidney stone.

4. Discussion

There are three stages of the calcium absorption: the absorption of the intestine, kidney and bone, which jointly maintain the balance of calcium ions in the body. The formation mechanism of kidney stone can be seen in Figure 2. The absorption of calcium ions in the small intestine can account for 90% of the total absorption[27], which is the most important part of calcium absorption. The other organs, the large intestine and colon, do not exceed 10% of the total absorption, besides, the calcium absorption needs energy that is mainly supplied by mitochondria. So the absorptive capacity is determined by the mitochondria integrity[27]. Then the calcium goes into the cells. It combines with oxalate to form calcium oxalate. The physicochemical process of CaOx kidney stone formation is mainly composed of four steps: crystalline nucleation, crystal growth, crystal accumulation, and crystal retention.

By means of the data from the National Center for Health Statistics (NHANES), from 2015 to 2018, we initially conducted the multiple regression of the calcium intake and kidney stones. (Table 1) The P for trend in model 3 is 0.068.(Table 2) ([OR] 0.9999, [CI] 0.9998–1.001 in model 3.) Whether calcium intake was included as a continuous or classification variable, the final result was that calcium intake was not associated with kidney stones. We reckon that calcium supplementation in the diet is not related to

whether to have kidney stones at all. But in our view, some confounding factors might be connected with kidney stone.

Table 1
Characteristics of the participants

CALCIUM quartile(mg)		Q1	Q2	Q3	Q4	P-value
N		2434	2432	2436	2436	
Vitamin D (mg)		2.1 ± 4.8	3.2 ± 4.2	4.6 ± 4.7	7.7 ± 6.9	< 0.001
BMI (kg/m^2)		29.3 ± 7.9	29.5 ± 7.8	29.6 ± 7.8	29.5 ± 7.6	0.15
Kidney stone	Yes	267 (11.0%)	263 (10.8%)	246 (10.1%)	248 (10.2%)	0.681
Alcohol drinking	Yes	325 (13.4%)	317 (13.0%)	300 (12.3%)	388 (15.9%)	< 0.001
Diabetes	Yes	410 (16.8%)	404(16.6%)	373 (15.3%)	306 (12.6%)	< 0.001
Gender	Male	990 (40.7%)	1063 (43.7%)	1171 (48.1%)	1483 (60.9%)	< 0.001
Age	< 40	675 (27.7%)	714 (29.4%)	801 (32.9%)	925 (38.0%)	< 0.001
	40–60	816 (33.5%)	874 (35.9%)	841 (34.5%)	847 (34.8%)	
	> 60	943 (38.7%)	844 (34.7%)	794 (32.6%)	664 (27.3%)	
Race	Mexican American	290 (11.9%)	343 (14.1%)	409 (16.8%)	450 (18.5%)	< 0.001
	Other Hispanic	262 (10.8%)	291 (12.0%)	281 (11.5%)	264 (10.8%)	
	Non-Hispanic White	689 (28.3%)	783 (32.2%)	915 (37.6%)	1012 (41.5%)	
	Non-Hispanic Black	743 (30.5%)	566 (23.3%)	471 (19.3%)	405 (16.6%)	
	Other Race-Including Multi-Racial	450 (18.5%)	449 (18.5%)	360 (14.8%)	305 (12.5%)	
Statue	Citizen by birth or naturalization	2099(86.2%)	2070 (85.1%)	2074 (85.1%)	2067 (84.9%)	0.531
Education	Not graduate from high school	579 (23.8%)	513 (21.1%)	471 (19.3%)	470 (19.3%)	< 0.001
Marriage	Married or living with partner	1980 (81.3%)	1999 (82.2%)	2014 (82.7%)	1981 (81.3%)	0.536

CALCIUM quartile(mg)		Q1	Q2	Q3	Q4	P-value
Income ($)	≥ 20000	1746 (71.7%)	1847 (75.9%)	1907 (78.3%)	1920 (78.8%)	< 0.001
Numbers that do not add up to 100% are attributable to missing data						

Table 2
Association between calcium intake(mg) and the kidney stone.

		Model1 Odds ratio (95% CI)	Model2 Odds ratio (95% CI)	Model3 Odds ratio (95% CI)
Calcium(mg)		0.9999 (0.9998, 1.0001)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
Calcium quartile	**Q1**	Reference(1)	Reference(1)	Reference(1)
	Q2	0.9841(0.8217,1.1786)	0.9288(0.7726,1.1165)	0.9365(0.7784,1.1268)
	Q3	0.9117(0.7591,1.0949)	0.8286(0.6866,1.0001)	0.8449(0.6975,1.0235)
	Q4	0.9199(0.7663,1.1044)	0.8159(0.6739,0.9879)	0.8468(0.6883,1.0419)
P for trend		0.268	0.036	0.068

Outcome variable: Kidney Stone

Exposure variable: Calcium

Model 1 adjusts for: None

Model 2 adjust for: Gender; Age; Race

Model 3 adjust for: Alcohol drinking; Diabetes; Vitamin D; BMI; Gender; Age; Race; Statue; Education; Marriage; Income

Table 3
Single-factor analysis

		Statistics	Kidney stone	P-value
Calcium(mg)		907.3311 ± 570.6161	0.9999(0.9998, Reference(1)001)	0.37
Diabetes	Yes	1493 (15.3317%)	Reference(1)	
	No	8245 (84.6683%)	0.4994 (0.4282, 0.5825)	**< 0.000001**
Alcohol drinking	**Yes**	1330 (13.6578%)	Reference(1)	
	No	6728 (69.0902%)	0.7883 (0.6594, 0.9425)	**0.009048**
	Missing	1680 (17.2520%)	0.6742 (0.5349, 0.8498)	**0.000842**
Vitamin D (mg)		4.3980 ± 5.6592	0.9944 (0.9825, 1.0065)	0.37
BMI		29.4828 ± 7.7761	1.0175 (1.0093, 1.0258)	**0.000027**
Gender	Male	4707 (48.3364%)	Reference(1)	
	Female	5031 (51.6636%)	0.7104 (0.6236, 0.8093)	**< 0.000001**
Age	< 40	3115 (31.9881%)	Reference(1)	
	40–60	3378 (34.6888%)	1.8906 (1.5777, 2.2656)	**< 0.000001**
	> 60	3245 (33.3231%)	2.4754 (2.0756, 2.9521)	**< 0.000001**
Race	Mexican American	1492 (15.3214%)	Reference(1)	0.02
	Other Hispanic	1098 (11.2754%)	1.3631 (1.0590, 1.7546)	
	Non-Hispanic White	3399 (34.9045%)	1.6700 (1.3672, 2.0398)	**< 0.000001**
	Non-Hispanic Black	2185 (22.4379%)	0.7186 (0.5640, 0.9156)	0.01
	Other Race-Including Multi-Racial	1564 (16.0608%)	0.7850 (0.6060, 1.0167)	0.07

		Statistics	Kidney stone	P-value
Statue	Citizen by birth or naturalization	8310 (85.3358%)	Reference(1)	
	Not a citizen of the US	1428 (14.6642%)	0.5382 (0.4306, 0.6726)	**< 0.000001**
Education	Not graduate from high school	2033 (20.8770%)	Reference(1)	
	Graduate from high school	7705 (79.1230%)	0.9539 (0.8148, 1.1168)	0.56
Marriage	Spinsterhood	1764 (18.1146%)	Reference(1)	
	Married or living with partner	7974 (81.8854%)	1.8845 (1.5388, 2.3079)	**< 0.000001**
Income	< 20000	1628 (16.7180%)	Reference(1)	
	> 20000	7420 (76.1963%)	0.9577 (0.8064, 1.1375)	0.63
	Missing	690 (7.0856%)	0.7709 (0.5672, 1.0479)	0.10

Patients with kidney stones were often accompanied with obesity and diabetes, so diabetes was also included in the confounding factors in our study. [28] For organ aging in the elderly, we focused on age as classified variables; income affects consumption level and dietary habits, even the treatment for the stone[29], so we also converted income into categorical variables; similarly, different races may have their own unique dietary habits, which is worth studying; and alcohol drinking, which can cause some damage to the kidney[30], we think it may also affect the kidney stones. Out of similar reasons, we also included vitamin D, marriage and gender, into the confounding factors. In Table 3, we can conclude that the kidney stone might be associated among the diabetes, age, alcohol drinking, vitamin D whose P value are below 0.05. While analyzing them, we performed another stratified analysis.

The results showed that in the multiple regression equation, these factors would affect the relationship between calcium intake and kidney stones, but after conducting stratified studies, we found that they did not affect the outcome of developing kidney stones, so we believed that these factors did not affect the relation between calcium intake and kidney stone. Ultimately, these were found as factors largely unrelated to the formation of kidney stone, either. (Table 4)

Table 4
The stratification analysis between kidney stone and calcium intake

		Model1 Odds ratio (95% CI)	Model2 Odds ratio (95% CI)	Model3 Odds ratio (95% CI)
Separated by Age	< 40	1.0000 (0.9998, 1.0003)	1.0000 (0.9998, 1.0003)	1.0001 (0.9998, 1.0003)
	40–60	1.0000 (0.9998, 1.0002)	0.9999 (0.9997, 1.0001)	0.9999 (0.9997, 1.0002)
	> 60	1.0000 (0.9998, 1.0002)	0.9998 (0.9996, 1.0000)	0.9998 (0.9996, 1.0001)
	Total	1.0000 (0.9999, 1.0001)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
Separated by Gender	Male	0.9999 (0.9998, 1.0001)	1.0000 (0.9998, 1.0001)	1.0000 (0.9999, 1.0002)
	Female	0.9998 (0.9996, 1.0000)	0.9997 (0.9995, 1.0000)	0.9997 (0.9995, 1.0000)
	Total	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
Separated by Race	Mexican American	0.9998 (0.9995, 1.0001)	0.9999 (0.9996, 1.0002)	0.9999 (0.9996, 1.0003)
	Other Hispanic	0.9996 (0.9992, 1.0000)	0.9996 (0.9992, 1.0000)	0.9997 (0.9992, 1.0001)
	Non-Hispanic White	0.9999 (0.9998, 1.0001)	0.9999 (0.9998, 1.0001)	1.0000 (0.9998, 1.0002)
	Non-Hispanic Black	1.0000 (0.9997, 1.0003)	1.0000 (0.9996, 1.0003)	1.0000 (0.9997, 1.0004)
	Other Race-Including Multi-Racial	0.9998 (0.9994, 1.0002)	0.9999 (0.9994, 1.0003)	0.9998 (0.9994, 1.0003)
	Total	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
Separated by Diabetes	Yes	1.000(0.9997, 1.0002)	0.9998 (0.9996, 1.0001)	0.9998 (0.9995, 1.0001)
	No	1.0000 (0.9999, 1.0001)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
	Total	1.0000 (0.9999, 1.0001)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
Separated by Statue	Citizen by birth or naturalization	1.0000 (0.9998, 1.0001)	0.9999 (0.9997, 1.0000)	0.9999 (0.9998, 1.0001)

		Model1 Odds ratio (95% CI)	Model2 Odds ratio (95% CI)	Model3 Odds ratio (95% CI)
	Not a citizen of the US	0.9999 (0.9995, 1.0002)	0.9999 (0.9995, 1.0003)	0.9999 (0.9994, 1.0003)
	Total	1.0000 (0.9998, 1.0001)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
Separated by Marriage	Spinsterhood	0.9999 (0.9996, 1.0002)	0.9999 (0.9995, 1.0002)	0.9998 (0.9994, 1.0002)
	Married or living with partner	1.0000 (0.9998, 1.0001)	0.9999 (0.9997, 1.0000)	0.9999 (0.9998, 1.0001)
	Total	1.0000 (0.9998, 1.0001)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
Separated by BMI	22.0800 ± 4.4909	0.9999 (0.9997, 1.0001)	0.9998 (0.9996, 1.0000)	0.9998 (0.9995, 1.0001)
	28.5889 ± 1.5748	1.0000 (0.9998, 1.0002)	1.0000 (0.9998, 1.0002)	1.0000 (0.9998, 1.0003)
	37.7253 ± 5.9583	0.9999 (0.9997, 1.0001)	0.9998 (0.9996, 1.0000)	0.9999 (0.9996, 1.0001)
	Total	0.9999 (0.9998, 1.0001)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)
Separated by Alcohol Drinking	Yes	0.9997 (0.9994, 1.0000)	0.9996 (0.9993, 0.9999)	0.9996 (0.9992, 0.9999)
	No	1.0000 (0.9998, 1.0001)	0.9999 (0.9998, 1.0001)	1.0000 (0.9998, 1.0001)
	Missing	1.0001 (0.9997, 1.0004)	1.0001 (0.9997, 1.0004)	1.0001 (0.9998, 1.0005)
	Total	0.9999 (0.9998, 1.0001)	0.9999 (0.9998, 1.0000)	0.9999 (0.9998, 1.0001)

Back to our calcium intake with kidney stones study, it is the same as some studies where kidney stones were not associated with this intake. We all concluded that dietary calcium supplementation was not associated with developing kidney stone. And high intake of dietary calcium or supplemental calcium (500 mg/d) could lower the possibility of kidney stones formation.[31][32] Moreover, calcium intake should not be limited in patients with kidney stones.[14][15] However, some observational studies found that decreasing the calcium intake can lower the risk of first stone. [32][33] But in the long run, we believe that the control of kidney stones by reducing calcium intake is dispensable, given the complex formation[34] causes that calcium intake may have no effect on this. For example, the microbiome play a role.[35] It not only relies on the calcium intake and oxalate, some confounding factors, like vitamin D which can promote the absorption of the calcium from intestinal tract.[36] They may have indirect effects on kidney stones. And in contrast, we believe that drinking enough water is more effective and easier to attain,

which can help to promote the excretion of urinary oxalate.[37] Some studies also found that controlling the salt and protein intake is more effective.[38]

Reflecting on our results may be due to insufficient accurate accuracy in the following aspects: We did not classify the types of kidney stones, and a proportion of kidney stones may not be calcium oxalate, unrelated to our study. Moreover, oxalate, one of the forming components of calcium oxalate kidney stones[39], which we did not include in confounding factors. Besides, we did not take the calcium supplement into the consideration and did not classify the kind of the diabetes. There are also some kidney diseases, which probably influence the kidney stone[40][41][42], which we did not study. Furthermore, the calcium absorption is related to some bacteria in the gut[43] and some common drinks, tea and coffee.[44] Therefore, we hope that we can further analyze those factors and exclude the effects of other types of kidney stones on the study in future. Although there are some parts of our study not considered, overall, it still has some advantages. Our study focused on calcium intake in daily life, rather than conducting group experiments from the perspective of calcium supplements, which is more reference and closer to people's daily life. This saves both financial and material resources, and it is convenient and efficient especially during the epidemic. In addition, we have enough and huge database which make our study more objective and general.

Finally, based on our study data, we speculated that dietary calcium supplementation would not increase the risk of developing kidney stones. And the calcium is not the only factor to affect kidney stone formation, many confounding factors which act together may produce very different results. So, the correct prevention method of kidney stones, should have a rational balanced diet and live in a healthy life.[45][46][47] It is neither high calcium intake nor low calcium intake in the long term. You and I work hand in hand to build a healthy world together!

Declarations

Ethics approval and consent to participate

Approval of this study was obtained from the ethics review board of the National Center for Health Statistics. All participants gave written informed consent. The experimental protocol was established according to the ethical guidelines of the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

Data supporting reported results can be found in NHANES.

Competing interests

Not applicable.

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Authors' contributions

Conceptualization, L.W., X.W., X.Z., L.M. and J.H.; methodology, L.W., X.W., X.Z., L.M. and J.H.; software, L.W., X.W., X.Z., L.M. and J.H.; validation, L.W., X.W., X.Z., L.M. and J.H.; formal analysis, L.W., X.W., X.Z., L.M. and J.H.; investigation, L.W., X.W., X.Z., L.M. and J.H.; resources, L.W., X.W., X.Z., L.M. and J.H.; data curation, L.W., X.W., X.Z., L.M. and J.H.; writing—original draft preparation, L.W., X.W., X.Z., L.M. and J.H.; writing—review and editing, L.W., X.W., X.Z., L.M. and J.H.; visualization, L.W., X.W., X.Z., L.M. and J.H.; supervision, L.W., X.W., X.Z., L.M. and J.H.; project administration, L.W., X.W., X.Z., L.M. and J.H.; funding acquisition, L.W., X.W., X.Z., L.M. and J.H. All authors have read and agreed to the published version of the manuscript.

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Figures

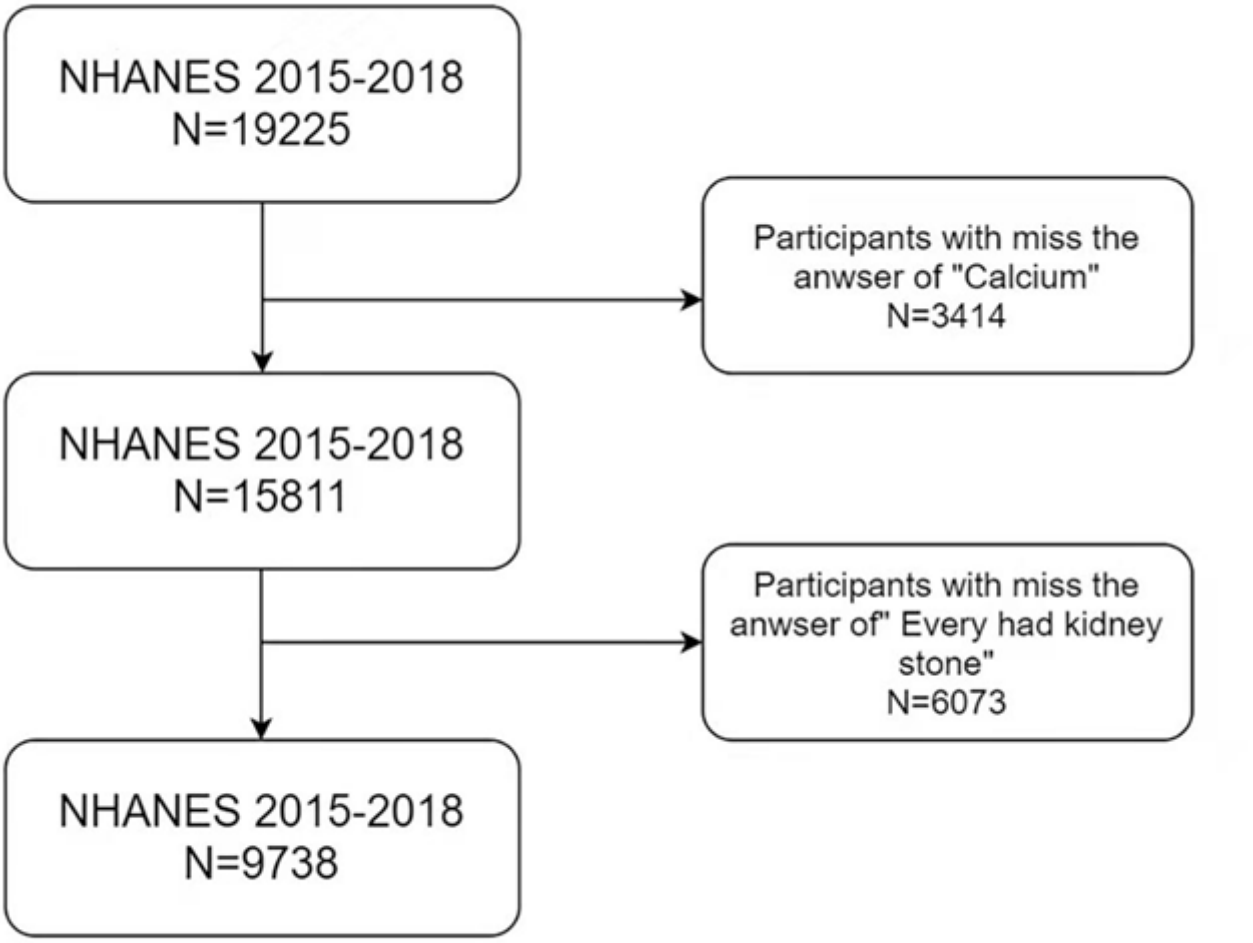

Figure 1

A flow chart for the screening

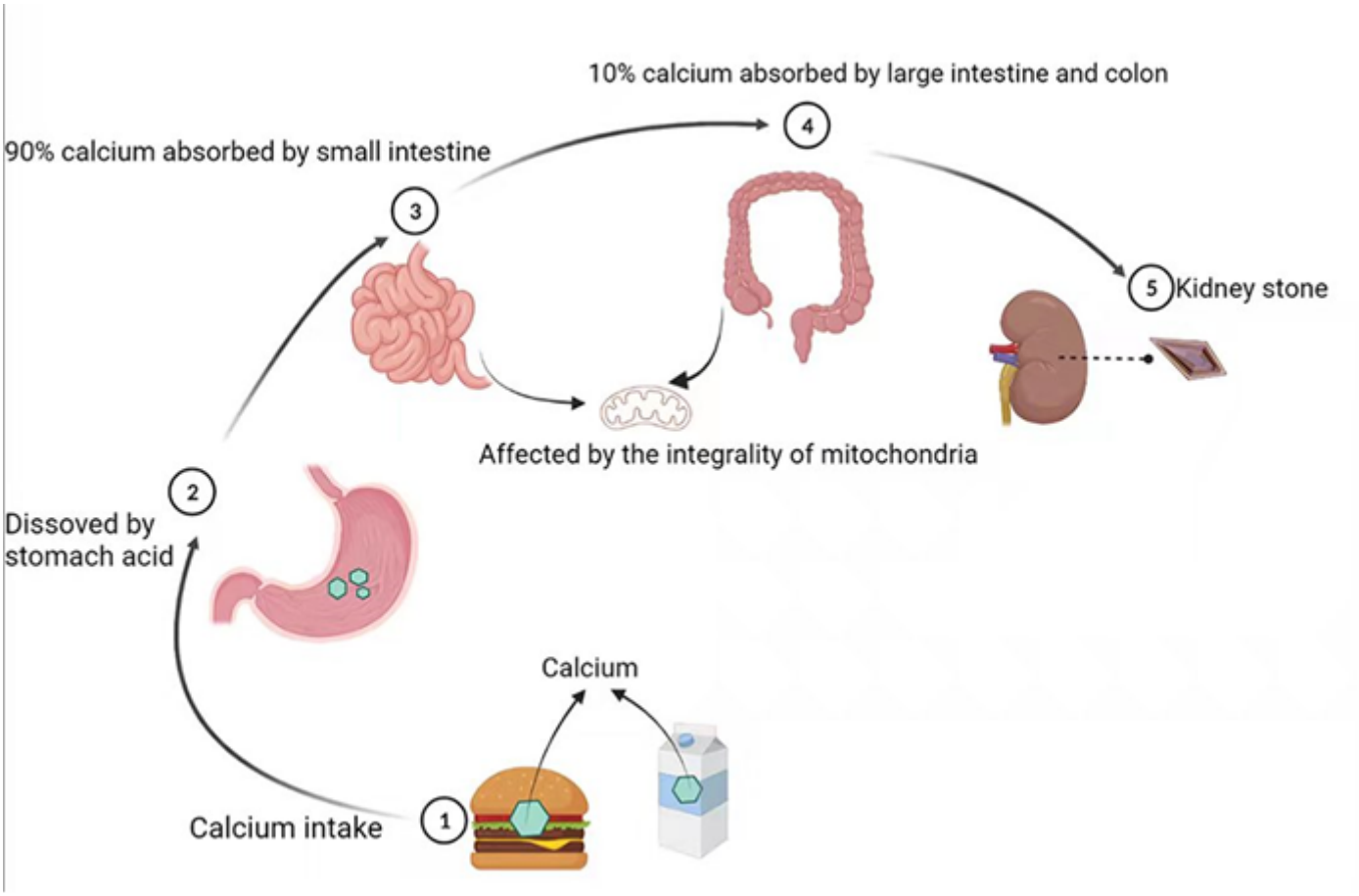

Figure 2

The formation mechanism of kidney stone