Dairy Food Consumption and Risk of Incident Type 2 Diabetes : A Systematic Review and Meta-Analysis

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TYPE 2 DIABETES



<u>Manuscript Title:</u> Association of dairy products with type 2 diabetes: A global systematic review and meta-analysis

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What are Dairy Products?

"Raw and processed or manufactured

milk and milk-derived products. These are

usually from cows (bovine) but are also

from goats, sheep, reindeer, and water

buffalo."

- PubMed MeSH Term Definition





The History of it's Consumption

NEWS AFRICA

Humans were drinking milk before they could digest it

Study of ancient Africans suggests dairy consumption predated evolution of lactase persistence genes

27 JAN 2021 · BY ANDREW CURRY

Set against the 300,000-year history of our species, drinking milk is quite a new habit. Before about 10,000 years ago or so, hardly anybody drank milk, and then only on rare occasions. The first people to drink milk regularly were early farmers and pastoralists in western Europe – some of the first humans to live with domesticated animals, including cows.





The Dairy Industry

- ➢ Globally 81% of milk produced is from cows
- India is the largest producer of milk accounting 1/4th of world production
- > Dairy sector contributes 4.2% of India's GDP
- India exports dairy foods worth Rs 3000 crores
- > Dairy the primary source of income for 7 crore Rural families
- India is the largest consumer of milk
- Asia pacific region is expected to dominate the Global dairy market (46%)



Poultry and Egg (g)

Vegetables (g)



The relationship between dairy and new onset type 2 diabetes remains inconclusive despite several prospective cohort studies. Studies proposing and opposing the consumption exist- therefore there is an pressing need for a global SR and MA

PRIMARY OUTCOME

To examine the available literature from prospective studies on the association between dairy and incident T2D in Asian and Western populations.



Specific to this study dairy products chosen were all naturally occurring without the addition of concentrated sugar (e.g., ice cream), flavourings (e.g., flavoured yoghurt) or concentrated fat – (e.g.,butter) to report translatable results even in the absence of a dose response analysis.



INCLUSION CRITERIA

- Dairy intake as the main exposure
- Prospective cohort studies
- T2D as an outcome,
- Studies on adults aged 18 years and above,
- Published in English language



METHODOLOGY- Search Strategy

MeSH terms:

(("buttermilk"[MeSH Terms] OR "buttermilk"[Title/Abstract] OR "cheese"[MeSH Terms] OR "cheese*"[Title/Abstract] OR "cultured milk products"[MeSH Terms] OR "dairy"[Title/Abstract] OR "dairy product"[Title/Abstract] OR "dairy products"[MeSH Terms] OR "dairy products"[Title/Abstract] OR "milk"[MeSH Terms] OR "milk*"[Title/Abstract] OR "yoghurt*"[Title/Abstract] OR "yogurt"[MeSH Terms] OR "yogurt*"[Title/Abstract])) AND (("diabetes mellitus"[MeSH Terms] OR "diabetes mellitus"[Title/Abstract] OR "diabetes mellitus, type 2"[MeSH Terms] OR "diabetes mellitus type 2"[Title/Abstract] OR "type 2 diabetes*"[Title/Abstract])) **NOT** (("butter"[MeSH Terms] OR "butter"[Title/Abstract] OR "dairy cream"[Title/Abstract] OR "ice cream"[MeSH Terms OR "ice cream*"[Title/Abstract] OR "milk cream"[Title/Abstract] OR "whipping cream"[Title/Abstract] OR "goat milk"[Title/Abstract] OR "yak milk"[Title/Abstract] OR "breast milk"[Title/Abstract] OR "human milk"[Title/Abstract] OR "sheep milk"[Title/Abstract] OR "camel milk"[Title/Abstract] OR "horse milk"[Title/Abstract] OR "mare milk"[Title/Abstract] OR "donkey milk"[Title/Abstract] OR "cross sectional*"[Title/Abstract] OR review*[Title/Abstract] OR soy[Title/Abstract] OR "soya milk*"[Title/Abstract] OR "oat milk" [Title/Abstract] OR "almond milk" [Title/Abstract] OR "coconut milk" [Title/Abstract] OR "cashew milk" [Title/Abstract] OR "rice milk" [Title/Abstract] OR "pea milk" [Title/Abstract] OR "plant milk" [Title/Abstract]))

Filters applied: Humans, English, Female, Male, Adult: 18+ years, from 2000/1/1 - 2021/12/24

*These MeSH Terms and Boolean were used for PubMed and the same was modified for other databases



NEWCASTLE-OTTAWAQuality Assessment Form

Newcastle-Ottawa Quality Assessment Form for Cohort Studies

Note: A study can be given a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Selection

- 1) Representativeness of the exposed cohort
 - a) Truly representative (one star)
 - b) Somewhat representative (one star)
 - c) Selected group
 - d) No description of the derivation of the cohort
- 2) Selection of the non-exposed cohort
 - a) Drawn from the same community as the exposed cohort (one star)
 - b) Drawn from a different source
 - c) No description of the derivation of the non exposed cohort
- 3) Ascertainment of exposure
 - a) Secure record (e.g., surgical record) (one star)
 - b) Structured interview (one star)
 - c) Written self report
 - d) No description
 - e) Other
- Demonstration that outcome of interest was not present at start of study
 - a) Yes (one star)
 - b) No

Comparability

- 1) Comparability of cohorts on the basis of the design or analysis controlled for confounders
 - a) The study controls for age, sex and marital status (one star)
 - b) Study controls for other factors (list) b) Study controls for other factors (list) ______ (one star)
 c) Cohorts are not comparable on the basis of the design or analysis controlled for confounders (one star)

Outcome

- 1) Assessment of outcome
 - a) Independent blind assessment (one star)
 - b) Record linkage (one star)
 - c) Self report
 - d) No description
 - e) Other
- Was follow-up long enough for outcomes to occur 2)
 - a) Yes (one star)
 - b) No

Indicate the median duration of follow-up and a brief rationale for the assessment above:

- 3) Adequacy of follow-up of cohorts
 - a) Complete follow up- all subject accounted for (one star)
 - b) Subjects lost to follow up unlikely to introduce bias- number lost less than or equal to 20% or description of those lost suggested no different from those followed. (one star)
 - c) Follow up rate less than 80% and no description of those lost
 - d) No statement

Thresholds for converting the Newcastle-Ottawa scales to AHRO standards (good, fair, and poor):

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain



METHODOLOGY- PRISMA CHART





METHODOLOGY- STATISTICAL ANALYSIS

Measures of Association:

Relative risk (RR) or Hazard Ratios (HR) in cohort studies and the **random effects model was used.**

Heterogeneity:

Measured using the *I*² **index**. Percentages of around 25% (I² = 25), 50% (I² = 50), and 75% (I² = 75) would suggest low, medium, and high heterogeneity, respectively. Desirable is towards '0' or as low as possible heterogeneity index

Publication Bias:

Judged by using the **Egger's test – a** visual inspection of the funnel plot



THE VISUAL INSPECTION OF THE FUNNEL PLOT



	Study Details
Data extracted from:	27
Participants :	1,771,026
Incident T2D :	71910
Years of follow up:	3.5 - 30

There were 6 studies from the United States of America, 14 from Europe, 1 from Australia, 5 from Asia (CHINA, JAPAN, KOREA, INDIA, MALAYSIA) and 1 study with global data.



RESULTS FROM THE SYSTEMATIC REVIEW-(TOTAL and other forms of DAIRY)

		No. of studies	No. of studies with	No. of studies with
	Total Number	with Positive	Negative	Neutral
Dairy Products	of Studies	Finding	Finding	Finding
Total Dairy	5 + 2 ^{o†}	2	0	5
Total Dairy- Western Population	2	0	0	2
Total Dairy- Asian Population	2	2	0	2
High Fat Dairy	14 + 3* + 2 ^{\$}	0	1	18
Low Fat Dairy	16 + 4 [*] + 4 ^{\$}	2	3	19
Total Milk	14 + 2 ^{o†}	0	1	15
Total Milk- Western Population	11	0	1	10
Total Milk- Asian Population	3 + 2 ^{o†}	0	0	5
High Fat milk	5 + 1 [*] + 2 ^{\$}	0	1	7
Low fat Milk	8 + 4 \$	3	2	7

Q[†] – Men & Women; *- Studies Reported different types of Dairy Products; \$ - Studies Reported sub-studies



RESULTS FROM THE SYSTEMATIC REVIEW- FERMENTED DAIRY PRODUCT

				No. of
		No. of studies	No. of studies	studies with
	Total Number of	with Positive	with Negative	Neutral
Fermented Dairy Products	Studies	Finding	Finding	Finding
Fermented dairy	10 + 4*	2	0	12
Yogurt	16 + 2 ^{o†} + 4 ^{\$}	7	0	15
Yogurt- Western Population	13 + 4 ^{\$}	5	0	12
Yogurt- Asian Population	3 + 2 ^{o†}	2	0	3
Cheese	$19 + 1^{o+} + 4^* + 2^{$}$	1	0	25
Cheese- Western Population	$17 + 4^* + 2^{\$}$	1	0	22
Cheese- Asian Population	2 + 1 ^{o†}	0	0	3

Q[†] – Men & Women; *- Studies Reported different types of Fermented Dairy Products; \$ - Studies Reported sub-studies



the random effect model.

RESULTS FROM THE META-ANALYSIS - TOTAL DAIRY AND OTHER FORMS OF DAIRY PRODUCTS EXCLUDING FERMENTED DAIRY PRODUCTS

Dairy products	Total Number of Studies	Relative Risk	RR	95%-CI	P	I ²	
Total Dairy Total Dairy-Western Population Total Dairy-Asian Population Total Dairy-Asian Population Total Dairy Ow Fat Dairy Total Milk Total Milk-Western Population Total Milk-Asian Population Total Milk-Asian Population Total Milk-Asian Population Total Milk-Asian Population Total Milk	5 2 14 16 14 11 3 5 8		-0.14 -0.13 -0.19 -0.02 0.01 0.01 -0.00 0.02 -0.00 -0.00	[-0.23; -0.05] [-0.38; 0.12] [-0.35; -0.03] [-0.06; 0.02] [-0.04; 0.06] [-0.05; 0.07] [-0.09; 0.08] [-0.07; 0.11] [-0.07; 0.07] [-0.08; 0.07]	< 0.01 0.32 0.02 0.38 0.70 0.74 0.94 0.68 0.98 0.90	30 % 50 % 33 % 47 % 47 % 8 % 23 % 0 % 49 % 68 %	
Note: All of these as represented	by	-0.3-0.2-0.1 0 0.1 0 Protective	.2 0.3 isk	The I ² is 25%, 75% may repre high heteroger	50%, and esent low, neity, resp	medium ectively.	, and



RESULTS FROM THE META ANALYSIS- TOTAL FERMENTED DAIRY

of Studies

10

16

13

3

19

17

2

Dairy products

Fermented Dairy ***** Yogurt 🗰 Yogurt - Western Population * Yogurt - Asian Population * Cheese Cheese- Western Population **Cheese- Asian Population**

Note: All of these as represented by the random effect model.



The I² is 25%, 50%, and 75% may represent low, medium, and high heterogeneity, respectively.

1²

31 %

31 %

30 %

12 %

22 %

29 %

0 %

Ρ

0.03

0.19

0.19

0.67



STRENGTHS

- Several studies conducted in different geographies were included
- Studies with long duration of follow-ups are included
- A novel initiative- to test the robustness of the results in Asian and Western ethnicities



LIMITATIONS

- Like other meta-analyses, we did not include butter and dairy products with added sugar or flavouring agents
- Some studies could not be done in Asians due to insufficient sample size
- Could not evaluate the effect of Indian Curds as no study on this has been published.
- A dose-response relationship between dairy and incidence of T2D could not be established



Conclusions



Robust inverse associations found between intakes of total dairy, fermented dairy, and plain yogurt with the incident T2D.

Milk (high-fat and low-fat) and cheese were not associated with incident T2D



FUTURE DIRECTIONS

A dose – response meta analysis is required to further strengthen the present findings of the study.

- More studies pertaining to geography specific fermented dairy products are required. E.g. The effects of Curd vs Yoghurt
- Studies evaluating the mechanistic effects of the associations between dairy and diabetes(Robust empirical evidence).
- Studies distinguishing the effects of vegan and lactovegetarian diets in relation to risk factors of non- communicable diseases will provide robust evidences in the field of dairy

"The complexity of the emerging mechanistic pathways and responses is remarkable".Mozaffarian, D



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The Dairy Industry in India

81% of the milk produced globally is from various species of cows, 15% from buffalos and 4% goat, sheep and camel.

In 2019 globally 852 million tons of milk was produced and 190 million tons were consumed The dairy and animal husbandry sector contributes around 4.2% of India's GDP. It is a primary source of income for about 7 crore rural families.

The Asia Pacific region is expected to dominate the global dairy products market (45.7%). India is the largest producer
 of milk accounting for 22% of I
 the world's production

India's Export of Dairy products was 108,711.27 MT to the world for the worth Rs. 2,928.79 Crores

India is the largest consumer of milk accounting for ~83 million ton consumption



Nutritive Value of Dairy Products Cont... <u>FATS AND FATTY ACIDS:</u>

- The fatty acids in milk fat are approximately **65% saturated**, **29% monounsaturated**, **and 6% polyunsaturated**.
- Essential fatty acid present as Conjugated linoleic acid is best known for maintain lean body mass while promoting the loss of body fat.
- Dairy has a greater proportion of short-chain and medium-chain saturated fatty acids.
- The odd-chain saturated fats pentadecanoic acid (15:0) and heptadecanoic acid (17:0), trans-palmitoleate (t-16:1n-7) have been specifically found to be protective against incident diabetes



Nutritive Value of Dairy Products

CARBOHYDRATES

• Milk is approximately **4.9% carbohydrate in the form of lactose**.

PROTEINS

- Milk proteins contain all **9 essential amino acids** required by humans.
- Casein and whey protein are the major proteins of milk
- Whey protein is also a rich source of amino acids, and these can directly stimulate beta cells to secrete insulin, which contributes to the reduction in postprandial glycaemia.

Risk For Newly Diagnosed Type 2 Diabetes According To Quartiles Of Food Intake (n= 1843)



Mohan V et al., British Journal of Nutrition (2009)

The 27 studies selected for data extraction and analysis had a total of 1,771,026 participants, which included 71,910 cases of incident T2D. The mean age of the participants was 53.7 years and the duration of follow-up varied from 3.5 – 30 years. There were 6 studies from the United States of America, 14 from Europe, 1 from Australia, 5 from Asia, and 1 study with global data.



Dairy products	Relative Risk	RR	95%-CI	Ρ	I ²
Total Dairy 🏚	■ ┊	-0.14	[-0.23; -0.05]	< 0.01	30 %
Total Dairy-Western population	-	-0.13	[-0.38, 0.12]	0.32	50 %
Total Dairy-Asian population 🏚		-0.19	[-0.35; -0.03]	0.02	33 %
Highfat dairy		-0.02	[-0.06; 0.02]	0.38	47 %
Lowfat dairy		0.01	[-0.04; 0.06]	0.70	47 %
Total milk		0.01	[-0.05; 0.07]	0.74	8 %
Total Milk-Western population	— # —	-0.00	[-0.09; 0.08]	0.94	23 %
Total Milk-Asian population		0.02	[-0.07; 0.11]	0.68	0 %
Highfat milk		-0.00	[-0.07; 0.07]	0.98	49 %
Lowfat milk		-0.00	[-0.08; 0.07]	0.90	68 %
		The	l ² is 25%, 50%,	and	dium and
	-0.3-0.2-0.1 0 0.1 0.2 0.3	hiah	heterogeneity	respectiv	velv
	Protective Risk	ingii	notorogeneity,		vory.



RESULTS FROM THE META ANALYSIS- TOTAL FERMENTED DAIRY

