



## **Factors Affecting Uptake of Vitamin D in Gastro-Intestinal Tract**

**Abhishek Kumar <sup>a≡</sup>, Swati Garg <sup>a<sup>o</sup></sup>, Samarth Shukla <sup>b<sup>o</sup>#\*</sup>, Sourya Acharya <sup>c<sup>o</sup>#</sup>  
and Sunita Vagha <sup>b<sup>o</sup>#</sup>**

<sup>a</sup> *Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha, Maharashtra, India.*

<sup>b</sup> *Department of Pathology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha, Maharashtra, India.*

<sup>c</sup> *Department of Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha, Maharashtra, India.*

### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i60B34634

### **Open Peer Review History:**

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/79534>

**Review Article**

**Received 12 October 2021**

**Accepted 20 December 2021**

**Published 22 December 2021**

## **ABSTRACT**

Vitamin D deficiency affects about 50% of entire people. Vitamin D deficiency affects an estimated 100 million individuals worldwide, spanning all cultures and age groups. This catastrophic situation of vitamin D deficiency can mainly be attributed to lifestyle and the average impact that cuts down exposure to rays from the sun. It is required for the epithelium to produce vitamin D with the help of ultraviolet B (UVB). In comparison to fair-skinned people, dark-skinned people absorb a larger quantity of UVB in their epidermal melanin. Fairer folks require more solar exposition to get the same amount.

The increased cases of vitamin D deficiency is a significant prevalent ailment caused by vitamin D deficiency. It is a self-governing, deadly cause of widespread mortality worldwide. New research supports hypovitaminosis D as a cause of neoplastic, cardiac, orthopedic, immunological, NIDDM, and mental disorders. Vitamin D doses are usually compounded to a minimum of 1000 IU by physicians. According to a 2007 study, a high vitamin D intake decreases mortality risk. We've

<sup>≡</sup> MBBS Student;

<sup>o</sup> Dr.;

<sup>#</sup> Professor;

\*Corresponding author: E-mail: samarth21174@gmail.com;

focused on vitamin D research and abstracted the mechanisms that have been linked to vitamin D and its therapeutic implications.

Vitamin D is unique in that it may be produced from the epidermis in reaction to UV radiation. AFTER IRRADIATING THE ERGOSTEROL TO UV LIGHT, Vitamin D<sub>2</sub> is produced in sun-irradiated fungus. When UVB sunlight strikes the epidermis, vitamin D<sub>3</sub> is produced. It's the most "natural" recipe possible. Humans produce vitamin D<sub>2</sub>. Vitamin D<sub>3</sub> is produced mainly by oil-rich fish. Chylomicrons are generated when vitamin D is taken orally.

*Keywords: Vitamin D; absorption; GUT; micronutrients; physicochemical; fat-absorption; obesity.*

## 1. INTRODUCTION

### 1.1 Vitamin D Dietary Supplements

A chief basis of vitamin D for homo sapiens is produced due to irradiation of epidermis via UVB light. Vitamin D synthesized in the epidermis lasts double in the circulation relative to dietary vitamin D [1]. IF a grownup in a swimsuit is irradiated via UVB with the least amount of dose leads to the production of vitamin D similar to dietary intake of 10,000 and 25,000 IU [1]. A wide range of aspects lessens the epidermis capability of synthesizing vitamin D<sub>3</sub> [2]. It includes amplified skin coloration, aging, and the on-skin use of sunblock [2].

## 2. LEVELS IN THE GASTROINTESTINAL TRACT

The enteric destiny of vitamin D is supervised by aspects used in chief lipid [3]. It includes emulsification, dissolution in micelles, distribution over the still water layer, and entry into epithelial cell covering [3]. The enteric destiny of vitamin D is a complex mechanism with a physical, chemical, and enzymatic contribution [3]. Acid pH of enteric secretion can alter its availability in blood [4]. It's understood that no reliable data is present on the vulnerability of chief nutritional versions of vitamin D in enteric pH circumstances [4]. Additionally, a premise is present, which indicates that peptide-breaking tertiary proteins are aggressively used in vitamin D uptake due to the cutting property of vitamin D associating amino acid polymers in nutrition and helping in its secretion. also, in 1<sup>st</sup> part of the intestine, the digestive enzyme releases vitamin D via nutritional products [5].

## 3. VITAMIN D ABSORPTION MECHANISM

The intake process of non-hydroxylated forms is believed to be facilitated via unsaturable non-ATP-based passage in the cell [4-5]. Current

research on homo sapiens enteric cell line CaCO<sub>2</sub> and HEK transfected cells reveals the connection of enteric cells covering peptidyl polymers intaking the no hydroxylated version on the edge of intestinal cells. intake of cholesterol and other lipid-loving compounds is mediated via SR-BI, CD 36, and NPC1L1 [4-5].

Considering the long term interventional and follow-up protocols, also taking into account the discomfort, one's routine gets hampered as basic chores are also challenging to perform, and this leads to an emotional setback for the affected individual and also an added responsibility for their relatives and friends which eventually becomes burdening [5]. There is no leisure left in that family's life as the patient cannot perform their duties, and the family members have to take care of the patient, the patient's duties, and their routine [6]. In addition, social relationships are affected as all the parties cannot cope emotionally [6].

The inferences of these proteins indicate a swing in intake via facilitated. It relies on the density of vitamin D. protein facilitated carriage at less density and non-energy dependent passage across increased densities [7]. Also, varying vitamin D absorption in various parts of the intestine signifies the occurrence of some different transporter mainly voiced in the 2<sup>nd</sup> part of the intestine [7]. So, the uptake effectiveness of hydroxylated vitamin D versions is much more than the no hydroxylated forms. No cases of dealing with the cellular intake of hydroxylated species of vitamin D have ever been seen [8].

## 4. VITAMIN D DEFICIENCY IN THE DIET

It's thought that unaided vitamin D, created in the epidermis, would serve to encounter the day-to-day vitamin D prerequisite. Solid research shows solar irradiation fails to meet the recommended dietary allowance of .vitamin D may be caused in response to varying solar contact reliant on

weather factors, dress, epidermal color, time of life, thinness, and location on the globe time of year, also day [7-8]. It necessitates meet recommended vitamin D dietary requirements. One of the essential nutrition-based vitamin D contains vitamin D<sub>2</sub> and D<sub>3</sub> [6-8]. It is also obtained via pharmaceutical multivitamins, enriched foods, or foods via floral and faunal occurrence [8]. Nutritional intake and skin in vivo formation are believed to be the intake method of vitamin D that must be extensively managed to prevent an excess of vitamin D in the body [9]. Due to the Insufficient ground report, it's painstaking to evaluate vitamin D daily consumption precisely as the diet intake design differs through community financial position [9]. Research is done to venture into the day-to-day consumption of vitamin D through diet unaided and coalescing additions and diet [5-9].

## 5. FIBERS IN THE DIET

Dietary fibers are presumed an essential performer in determining the destiny in the enteric system [9]. It impacts the availability of vitamin D in blood by given mechanism:

- Hampers the micelle creation
- impacts the discharge of lipid loving substances out of the fat drop
- Upsurges the viscosity of chyme resulting in dissemination of lipid-loving dietary substance holding micelles to the cell of the enteric wall.

More than recommended fiber consumption was believed to cause decreased availability of vitamin D in the body [10]. Also, more significant rickets and osteomalacia are seen in Asian migrant people [10]. "This presumption was backed by research on the comparative vanishing of D<sub>3</sub> in fit volunteers served high fiber diet (20 g/day) or usual dietary intake [11]. It showed, average via usual dietary intake people was increased (27.5 ± 2.1 days) relative to that of increased fiber intake people (19.2 ± 1.7 days)" [11]. Increased removal of 3H-25(OH)D<sub>3</sub> in increased fiber intake people might be a result of meddling of the fiber products in blood, i.e., an association of 3H-25(OH)D<sub>3</sub> to dietary fiber [11].

The availability of insufficient data on vitamin D uptake about diet included fibers, so making an opinion on vitamin D uptake will be a novice. In addition, several devoted retypes of research are needed to appreciate the outcome of fibers on vitamin D's availability in the body [11].

## 6. LEVELS IN THE HOST

The overall vitamin D profile of a person depends on dietary and self-derived vitamin D [12]. Relation between personally taken and self-derived formation of vitamin -D is hard to prove [11-12]. It results from the fat-loving nature of vitamin D, which acts as a reservoir in fatty tissue and its regulated release. Increased consumption accompanied by increased daytime synthesis may cause a severe increase in concentration [10-12]. So, it is believed that increased intake via diet and more irradiation via UVB may increase body levels [10-12]. It leads to a decrease in dietary uptake and formation in the skin, but no studies indicate this correlation. It is due to difficulty correlating due to varying amounts of UV radiation [12].

## 7. INVOLVEMENT OF MICRONUTRIENTS

Vitamin E and K have a similar mechanism for absorption as vitamin D, which may cause competitive inhibition in the gut. It was proved after research on the CaCO<sub>2</sub> cell line [13]. It approves involvement of vitamin E in hampering vitamin D uptake (decreased by 15% on intermediate and 17% at high conc. of vitamin E) uptake in the GUT [13]. It was proved via an in vitro research on CaCO<sub>2</sub> enteric cell in which it was related to being a probable contender to hampering vitamin D<sub>3</sub> uptake by 16–36% [12-13].

Relative abundance was seen to be similar uptake. Additionally, it also distinguishes diet in taken D<sub>3</sub> and self-produced D<sub>3</sub> in its use, i.e.[12] hindering the use of diet in taken vitamin D<sub>3</sub>, but not to self-derived vitamin D<sub>3</sub>. In recent times, a study showed that increased presence of vitamin A decreases its uptake in body 30% [14]. However, vitamin A way of hampering the vitamin D uptake is still not found [14].

## 8. VITAMIN D ABSORPTION ENHANCERS AND INHIBITORS

Scholarly articles regarding varied mediators can initiate or diminish vitamin D uptake via the intestine. Such mediators may be available in dietary products or can be supplemented to facilitate greater uptake of vitamin D. context from such literary articles [15].

## 9. FAT-ABSORPTION INHIBITORS

An individual struggling with obesity takes various obesity-reducing pills and fat alternates

to decrease the fat amount. Pills and fat alternate decrease the uptake of triglycerides [12]. Vitamin D trails the same league of triglyceride in the GUT. It is believed that fat reduction can hinder vitamin D availability in the body, causing a decrease in its uptake [13]. "The uptake of vitamin D is hindered if vitamin D was given with a fat alternative to 102 fit men and women. also, the cholesterol derived via plant source which is taken to decrease cholesterol uptake affects availability of vitamin D in the body" [13-15]. It was established by numerous researches. Reduction in vitamin D conc. in serum and the liver was found in rats after they were administered stanol ester for 3 months [13-15]. It was done for numerous phytosterols in rat and in vitro and inferred that phytocholesterols are a reason for decreased micelles production and passage in enteric cells, causing availability decrease in the body. Newer reports on patients don't recommend this theory by opposing the outcome of phytosterol on availability vitamin D in body. Such inferences are generally disproved as assessment was done on the basis of the serum level of 25(OH)D [13-15]. It might be changed by endogenous vitamin D production, which relies on the various elements, i.e. [14] "UVB irradiation and weather. Additionally, it was once more backed by findings of two clinical trials where serum level of 25(OH)D was monitored in diverse people" [15]. They were given plant sterol ester improved meal. The fat decreasing mediators decrease fat uptake hampering uptake of vitamin D. the precise quantity of lipid desired for maximum uptake of vitamin D is not adjusted. The patients are burning with anxiety and questions for the oncologists [15]. If a psycho-oncologist can take care of this professionally, both the patients and the treating clinician will be at ease with each other, and there will be a better understanding from both parties [15]. The patients and families, amidst the chaos, can have someone to counsel them [15]. Even if the patient succumbs, the psycho-oncologist must counsel the family members as their spectrum is not limited to one individual [15]. Even the family trusts the psycho-oncologists more as they have a one-on-one interaction for a long time [15].

## 10. VITAMIN D ENHANCERS

D vitamin D transport in dedicated preparation improves the vitamin D availability in the body's enteric canal [16,17]. It can cause increased availability of micro/nano covered vitamin D compared to its enriched dietary products.

Presence of Inadequate works on these factors causes the inability to a conclusion about the effects of such forms of vitamin D on its availability in the body [17].

## 11. GIT SECRETION PHYSIOCHEMICAL INTERACTION

Uptake of vitamin D via gut wall is thought to be highest inside a bracket of salt ionic concentration and pH past which its absorption might be hindered. This supposition was found in numerous researches [16]. Absorption of vitamin D<sub>3</sub> was found to be hindered with varying salt conc. Within normal [15]. The Gradual decrease in vitamin D<sub>3</sub> uptake was found as the sodium taurocholate salt levels were changed beyond the five mM (10 or 15 mM) [15].

## 12. FACTORS AFFECTING THE HOST

Articles reflect the participation of numerous host-related aspects that might be related factors in determining its availability in the body. numerous researches leading to enhanced suggested dietary recommendation due to aspects (age and disease obesity) [18].

## 13. HOST'S AGE

Biological changes in body functioning are observed with advancing age. It's presumed that the age-encouraged physical deviations might affect vitamin D availability in the body [19]. Age-related discrepancies in lipoprotein breakdown were supposed to decrease uptake and post food intake carriage of vitamin D [19]. Numerous researches have led to the finding that indicates decreased vitamin D grade in aged persons compared to younger progenies [19]. Initial research was done with 20 aged females; they presented with decreased levels of [3H]cholecalciferol compared to young females [19]. It suggested that Gut of aged females was competent compared to their younger progenies [20]. Similar results were not replicated in mice [20]. Convincing reports concerning variations in serum 25OHD levels in aged compared to younger people might be because of low self-produced vitamin D epidermis, lesser solar irradiation, and its less amount in food intake [20].

## 14. OBESITY

it's usually destructively associated with a lack of vitamin D [21]. It was backed by Liel et al.'s

(1988) research and. They found better uptake and increased removal of vitamin D by overweight patients compared to regular. Contrariwise vitamin D's storage in fatty tissue doesn't cause its release during requirement , causing its increased availability of vitamin D [21] in a research conducted on aged subjects concluded that on supplementing [21]. Decreased concentration in overweight people might be a result of Dec. conc. Of vitamin in their big fatty build. The findings here are that vitamin D accumulated in fatty structures isn't released quickly [21]. Overweight people might need a greater dosage to establish a serum 25OHD concentration similar to proper weight. Increased serum 25(OH)D concentration in a period of fat loss in overweight people proves this speculation [21].

## 15. DISEASES AND SURGERIES INVOLVING THE DIGESTIVE TUBE

According to many research and investigations, Vitamin D is readily absorbed if ingested with fat-containing meals. First, researches revealed that those with a clogged GI tract had much lower vitamin D uptake [3-6]. Roux-en-Y gastric bypass surgery resulted in a 30% decrease in blood vitamin D3 levels compared to previously [3-6,7]. Moreover, people with cystic fibrosis were found to have worse vitamin D intake efficiency than their healthy counterparts [7]. "Vitamin D is also believed to have a favorable effect on the intestine and CD8+ cells, which might also help to maintain the stability of the Gut mucosal lining by modulating intercellular connections, reducing mucosal leakage, and raising CD8+ cell numbers Furthermore, certain clinical investigations have shown that vitamin D has a role in cancer prevention, particularly Gi cancer, by modifying tumorigenic indicators, VDR polymorphism, and other VDR regulations [22]. However, these findings support the role of vitamin D in prevention of illness; there is a lack of information absorption in the gastrointestinal tract is affected by these conditions" [7] medical stage, treatment protocols as mentioned above, and the patient's prognosis in coordination with the medical oncologist [3-5]. If the patient has a poor prognostic outcome, the psycho-oncologist should be ready with cognitive therapy for the patient in such situations [3-5]. The patient's past and current medical illness course are noted. Risk factors for cancer, including environmental, genetic, and behavioral, are looked for, and the current medications are studied to determine if the

behavioral changes result from the adverse reactions [8-15].

### 15.1 Variations in Genetics

Vitamin D intake is controlled by a fat-digesting enzyme, bile secretion, and a vitamin D converting liver enzyme [11]. Modifying the gene sequence can affect the production and function of these proteins, resulting in a partial or complete loss in performance [12]. Moreover, changes in the genetic sequence of neighboring genes may disrupt transcription factor engagement, resulting in the lack of these protein transporters. There is currently no data in the literature that addresses this topic [12]. In the same way, genetic variations in fat-digesting enzyme and vitamin D protein complex might alter vitamin D uptake. Entities like support groups and psychotherapy are familiar for cancer patients in developed countries [16-22]. With this review, the authors wish to emphasize making psychological care obligatory for cancer patients, in the form of regular counseling, support groups, inclusion on psycho-oncological consultation in the treatment protocols, feedback of the psycho-oncologists to the treating clinician [23-31].

## 16. CONCLUSION

Many food items are accessible; each meal product's matrix varies due to differences in nutritional value, lipid content, dietary fibers, and other factors. These factors make estimating vitamin D absorption in a specific diet challenging. The method of vitamin D uptake is not well understood in the current research. Even though some factors governing vitamin D fate in the GI tract have been well documented, but others, such as genetic differences and dietary fibre. More specialized studies using labeled vitamin D are necessary for understanding absorption, targeting research directions potential. Biological changes in body functioning are observed with advancing age. It's presumed that the age encouraged physical deviations might affect vitamin D availability in body. Age related discrepancies in lipoprotein breakdown was supposed for decrease of uptake and post food intake carriage of vitamin D. Numerous researches have led to the finding which indicate towards decreased vitamin D grade in aged persons compared to younger progenies. Initial research was done with 20 aged females, they presented with decreased levels of [3H] cholecalciferol compared to of young female. It

suggested that Gut of aged females was competent as compared to their younger progenies. Similar results were not replicated in mice . Convincing reports concerning variations in serum 25OHD levels in aged compared younger people might be because of low self-produced vitamin D epidermis, lesser solar irradiation and its less amount in food intake.

## CONSENT AND ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

- Holick MF. Vitamin D deficiency. *N Engl J Med.* 2007;357:266–81.
- Gordon CM, DePeter KC, Feldman HA, Grace E, Emans SJ. Prevalence of vitamin D deficiency among healthy adolescents. *Arch Pediatr Adolesc Med.* 2004;158:531–7.
- Lips P, Hosking D, Lippuner K, Norquist JM, Wehren L, Maalouf G, et al. The prevalence of vitamin D inadequacy amongst women with osteoporosis: An international epidemiological investigation. *J Intern Med.* 2006;260:245–54.
- Rostand SG. Ultraviolet light may contribute to geographic and racial blood pressure differences. *Hypertension.* 1997;30:150–6.
- Melamed ML, Michos ED, Post W, Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. *Arch Intern Med.* 2008;168:1629–37.
- Harvard School of Public Health Nutrition Source. Vitamin D and health. [Last accessed on 2010 Aug 30].
- Autier P, Gandini S. Vitamin D supplementation and total mortality: A meta-analysis of randomized controlled trials. *Arch Intern Med.* 2007;167:1730–7.
- Standing Committee on the Scientific Evaluation of Dietary Reference Intakes Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Chapter 7. Vitamin D. [Last accessed on 2010 Aug 02].
- NIH Office of Dietary Supplements. Dietary supplement fact sheet: Vitamin D. [Last accessed on 2010 Aug 04].
- Nair S. Symptoms of low vitamin D levels. [Last accessed on 2010 Sep 02].
- MedlinePlus. 25-hydroxy vitamin D test. [Last accessed on 2010 Aug 04].
- Moyad MA. Vitamin D: A rapid review: Side effects and toxicity. [Last accessed on 2010 Sep 02].
- Lappe JM, Travers-Gustafson D, Davies KM, Recker RR, Heaney RP. Vitamin D and calcium supplementation reduces cancer risk: Results of a randomized trial. *Am J Clin Nutr.* 2007;85:1586–91.
- Chlebowski RT, Johnson KC, Kooperberg C, Pettinger M, Wactawski-Wende J, Rohan T, et al. *J Natl Cancer Inst.* 2008;100:1581–91.
- Stolzenberg-Solomon RZ, Vieth R, Azad A, Pietinen P, Taylor PR, Virtamo J, et al. A prospective nested case-control study of vitamin D status and pancreatic cancer risk in male smokers. *Cancer Res.* 2006;66:10213–9.
- Stolzenberg-Solomon RZ, Hayes RB, Horst RL, Anderson KE, Hollis BW, Silverman DT. Serum vitamin D and risk of pancreatic cancer in the Prostate, Lung, Colorectal, and Ovarian Screening Trial. *Cancer Res.* 2009;69:1439–47.
- Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. *Circulation.* 2008;117:503–11.
- Hollis BW. Circulating 25-hydroxy-vitamin D levels indicative of vitamin D sufficiency: Implications for establishing a new effective dietary intake recommendation for vitamin D. *J Nutr.* 2005;135:317–22.
- Holick MF, Chen TC. Vitamin D deficiency: A worldwide problem with health consequences. *Am J Clin Nutr.* 2008;87:1080S–6S.
- Matsuoka LY, Ide L, Wortsman J, MacLaughlin JA, Holick MF. Sunscreens suppress cutaneous vitamin D3 synthesis. *J Clin Endocrinol Metab.* 1987;64:1165–8.
- Clemens TL, Henderson SL, Adams JS, Holick MF. Increased skin pigment reduces the capacity of skin to synthesise vitamin D3. *Lancet.* 1982;1:74–6.
- Patil DJ. “Clinical implications of vitamin D in oral diseases- A Review”. *Journal of Pharmaceutical Research International.* 2021;33(30A):103-110.
- Sahu, Preeti Rajendra, Kishor Madhukar Hiwale, Sunita Jayant Vagha, and Samarth

- Shukla. Spectrum of lesions on upper gastrointestinal endoscopy and its correlation with histopathological evaluation. *Journal of Evolution of Medical and Dental Sciences-JEMDS*. 2020;9(32): 2301–6.  
Available: <https://doi.org/10.14260/jemds/2020/498>.
24. Kirnake, Vijendra, Anil Arora, Praveen Sharma, Mohan Goyal, Romesh Chawlani, Jay Toshniwal, and Ashish Kumar. Non-invasive aspartate aminotransferase to platelet ratio index correlates well with invasive hepatic venous pressure gradient in cirrhosis. *Indian Journal of Gastroenterology*. 2018;37(4):335–41.  
Available: <https://doi.org/10.1007/s12664-018-0879-0>.
25. Sahu PR, Hiwale KM, Vagha SJ. Study of Various Gastrointestinal Tract Lesions by Endoscopic Biopsies in a Tertiary Care Centre of Rural District of Maharashtra. *Journal of Evolution of Medical and Dental Sciences-JEMDS*. 2021;10(16):1135–9.
26. Abbafati Cristiana, Kaja M. Abbas, Mohammad Abbasi, Mitra Abbasifard, Mohsen Abbasi-Kangevari, Hedayat Abbastabar, Foad Abd-Allah, et al. Five insights from the global burden of disease study 2019. *LANCET*. 2020;396(10258): 1135–59.
27. Abbafati Cristiana, Kaja M. Abbas, Mohammad Abbasi, Mitra Abbasifard, Mohsen Abbasi-Kangevari, Hedayat Abbastabar, Foad Abd-Allah, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: A systematic analysis for the global burden of disease study 2019. *LANCET*. 2020; 396(10258):1204–22.
28. James Spencer L, Chris D Castle, Zachary Dingels V, Jack T. Fox, Erin B. Hamilton, Zichen Liu, Nicholas L. S. Roberts, et al. Estimating global injuries morbidity and mortality: Methods and data used in the global burden of disease 2017 study. *Injury Prevention*. 2020;26(SUPP\_1):125–53.  
Available: <https://doi.org/10.1136/injuryprev-2019-043531>.
29. James Spencer L, Chris D. Castle, Zachary Dingels V, Jack T. Fox, Erin B. Hamilton, Zichen Liu, Nicholas L. S. Roberts, et al. Global injury morbidity and mortality from 1990 to 2017: Results from the Global Burden of Disease Study 2017. *Injury Prevention*. 2020;26(SUPP\_1):96–114.  
Available: <https://doi.org/10.1136/injuryprev-2019-043494>.
30. James Spencer L, Chris D. Castle, Zachary Dingels V, Jack T. Fox, Erin B. Hamilton, Zichen Liu, Nicholas L. S. Roberts, et al. Estimating global injuries morbidity and mortality: Methods and data used in the global burden of disease 2017 study. *Injury Prevention*. 2020; 26(SUPP\_1):125–53.  
Available: <https://doi.org/10.1136/injuryprev-2019-043531>.
31. James Spencer L, Chris D. Castle, Zachary Dingels V, Jack T. Fox, Erin B. Hamilton, Zichen Liu, Nicholas L. S. Roberts, et al. Global injury morbidity and mortality from 1990 to 2017: Results from the global burden of disease study 2017. *Injury Prevention*. 2020;26(SUPP\_1):96–114.  
Available: <https://doi.org/10.1136/injuryprev-2019-043494>.

© 2021 Kumar et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*

*The peer review history for this paper can be accessed here:*  
<https://www.sdiarticle5.com/review-history/79534>