

“Hypovolaemia” with generalized edema, what is wrong? Time for new guideline recommendations on fluid therapy for shock resuscitation?

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Abstract:

I read with great interest this recently published educational review article by Professors Fernando G. Zampieri, MD, PhD; Sean M. Bagshaw, MD, MSc; Matthew W. Semler, M D, MSc [1], identifying its limitations. I also read with great interest this recently published article by Professors Dull, R.O. and Hahn, R.G. [2]. The authors are commended on their reviews based on evidence from published reports that represent the current understanding of the condition and its scientific basis. The authors have faithfully and factually summarized the evidence based on published reports, including some of the commonly received errors and misconceptions on the scientific foundation [3] that identifying and correcting may help answer the vitally important question in the report's title [2]. I asked myself the very same question “What is wrong?” after attending the post-mortem examination of 3 patients who were killed by ARDS, complicating the TUR syndrome therapy back in 1981. It took me >40 years of hard, comprehensive, intensive, and profound scientific research to find the correct answer.

The authors acknowledge that Starling’s law represents the scientific foundation of the volume-pressure relationship of the vascular, capillary, and interstitial fluid compartments. It thus underlies and dictates the rules that govern fluid therapy in shock management. This is the subject on which the authors are among the top world authority. My research has demonstrated clearly and completely the substantial evidence that Starling’s law is wrong, and the correct replacement is the hydrodynamics of the porous orifice (G) tube [4,5]- that has been gathered in a new book [6]. This will revolutionize our understanding of the condition and related issues, particularly on the patho-etiology and management of ARDS. The hydrodynamics of the G tube in a surrounding chamber mimics the capillary-interstitial fluid (ISF) circulatory transfer (Figure 1).

Keywords: shock; fluid therapy; ards; starling’s law; edema; hypovolaemia; hypervolaemia; vascular pressure; and volume.

Introduction and text:

I read with great interest this recently published educational review article by Professors Fernando G. Zampieri, MD, PhD; Sean M. Bagshaw, MD, MSc; Matthew W. Semler, M D, MSc [1]. The review article is excellent and timely for it aimed at reviewing the evidence based on RCT and I thank them for their effort. However, it was a mistake to rely only on PubMed for their search which does not list all articles published in open-access journals. This has resulted in missing all the recent new substantial evidence on fluid therapy for shock, septic and others, and fluid resuscitation among which I reported >150 articles gathered later in 3 published books [6-8]. Off all my published articles only two were published in BJUI and Medical Hypothesis appear on PubMed search. The correct search engine to use is Google Scholar. A notable omission in the article is the scientific foundation of fluid therapy in septic and other types of shocks in acutely ill patients. There is no clear recommendation on how much fluid should be given to acutely ill patients with shock and when to stop to avoid the fluid creep that causes edema and ARDS in these patients as they did not mention Starling’s law on the causation of edema! That might be a good thing as it is now obsolete. Although I do understand and appreciate the seriousness of sepsis in destroying capillary-interstitial fluid circulation it is probably



not responsible for the edema formation of ARDS, hence sepsis may be as innocent as the Wolf in Josef's story. Sepsis is well covered and gets eradicated with the powerful antibiotics available today. Moreover, most acutely ill patients with massive, generalized edema and hypotension shock in ICU do not have evidence of sepsis. Furthermore, the condition may complicate fluid therapy for burns, trauma, acute pancreatitis, all known and newly recognized types of shock, and during prolonged major surgery. The fourth stage of fluid therapy that the authors called the "fluid removal stage" should be prevented or treated early- as mentioned later. Here is a brief summary or a mini-review of the new scientific foundation of fluid therapy for shock resuscitation and related issues.

I also read with great interest this recently published review article by Professors Dull, R.O. and Hahn, R.G. [5]. The authors are commended on this review based on evidence from published reports that represent the current understanding of the condition and its scientific basis for fluid therapy in the current clinical practice. The authors have faithfully and factually summarized the evidence based on published reports, including some of the commonly received errors and misconceptions on the scientific foundation [3] that identifying and correcting may help answer the vitally important question in the report's title [2]. I asked the very same question "What is wrong?" after attending the post-mortem examination of 3 patients who were killed by acute respiratory distress syndrome (ARDS), complicating the fluid therapy of the transurethral resection of the prostate (TUR) syndrome shock back in 1981. There was massive tissue edema with swollen vital organs and 3 litres of fluid in each peritoneal and pleural cavity. They were literally internally drowned by fluids infused for the resuscitation of shock. I asked the pathologist why he does not mention that in his report. His reply was: "Because it offends the treating physicians"! It took me >40 years of hard, dedicated, comprehensive, and intensive scientific research to find the correct answer. I knew then what was wrong, finished my physics experiments on the G tube by 1985, obtained my MD degree Thesis on understanding the TUR syndrome in 1988, and published my clinical prospective study in 1990 [9]. I reported the preliminary theory on capillary physiology in the Medical Hypothesis Journal in 2001 [4] but it took me >40 years to prove my new theory on the capillary-interstitial fluid circulatory transfer [10]. It is Galileo's story all over again!

The authors acknowledge that Starling's law represents the scientific foundation of the volume-pressure relationship of the vascular, capillary, and interstitial fluid compartments. It thus underlies and dictates the rules that govern fluid therapy in shock management. This is the subject on which the authors are among the top world authority. My research has demonstrated clearly and completely the substantial evidence that Starling's law is wrong, and the correct replacement is the hydrodynamics of the porous orifice (G) tube [4,5]. The reported articles have been gathered in a completely new book [6]. This will revolutionize our understanding of the condition and related issues, particularly on the path-etiology and management of ARDS. The hydrodynamics of the G tube in a surrounding chamber mimics the capillary-interstitial fluid (ISF) circulatory transfer (Figure 1).

"Hypovolaemia and peripheral edema" [2] refer to the condition that affects acutely ill surgical patients presenting with any shock

then suffer clinically with ARDS induced by excessive fluid therapy in whom there is massive volumetric overload with hypotensive shock (Hypovolaemia?) and massive fluid creep on the interstitial fluid space and vital organs causing generalized edema [11]. It complicates fluid therapy for shock resuscitation of burns, sepsis, haemorrhage, trauma, and acute pancreatitis, and during prolonged major surgery [12]. It initially presents and seamlessly occurs as volume kinetic or volumetric overload shock (VOS) [13], among new 13 scientific discoveries in physics, physiology, and medicine [14]. It has high morbidity and mortality and affects thousands of patients every year all over the world. Although there is hypotensive shock here, it is probably incorrect to assume "hypovolaemia" exists. In other words, and contrary to what is generally believed, hypotension is not synonymous with hypovolaemia. Frank-Starling's law for the heart works with a physiological volumetric overload of <2 litres only, but with pathological VO it works paradoxically. It is a simple physics: if the cardiovascular system is overfilled to above its maximum capacity, the surplus fluid will simply spill into the ISF space!

Starling's law has proved wrong on both of its hydrostatic and oncotic pressure forces [4,5] However, it continues to dictate the current faulty rules on fluid therapy in the management of shock. It thus misleads physicians into giving too much fluid during shock resuscitation [15]. More than 21 reasons were reported to show that Starling's law is wrong [16]. The correct replacement is the hydrodynamic of the porous orifice (G) tube (Figure 1) that was built on the capillary ultrastructure anatomy of the precapillary sphincter [17] and a porous wall [18] that allows the passage of plasma proteins thus nullifying the oncotic pressure in Vivo. It follows that the extended Starling Principle is wrong, and a misnomer, and all the equations are also wrong [19]. Commonly received but erroneous concepts and laws represent fraud in modern science [20].

The clinical significance is that Starling's law dictates the faulty rules on fluid therapy causing many errors and misconceptions that mislead physicians into giving too much fluid infusions of colloids and crystalloids for the resuscitation of shock [15] which both cause edema of ISF space and vital organs as well as "hypervolemia" with hypotension [13]. This shock is mistaken for septic shock or any known shock and is wrongly treated with further huge volume expansion, occurring with both liberal and conservative approaches of fluid therapy. This has been newly recognized as volume kinetic or volumetric overload shocks (VOS) [13]. Figures 2 and 3 show the volumetric overload and Table 1 shows its statistical significance ($p=0.0007$) in the path-etiology of the TUR syndrome and ARDS.

Volumetric overload (VO) inducing VOS is of 2 types: VOS 1 is induced by sodium-free fluids such as 1.5% Glycine, 5% Glucose, 3% Mannitol, and Sorbitol fluids that cause the TUR syndrome [9] which has a lifesaving therapy now [21]. It is predicted to reincarnate into ARDS after the shift to saline use as irrigant in endoscopic surgery [22]. VOS 2 is induced by sodium-based fluids of crystalloids and plasma proteins and causes ARDS and acute kidney injury (AKI) as part of the multiple organ dysfunction syndrome (MODS) with high morbidity and mortality [23]. VOS 2 may complicate VOS 1 or occur de novo. Volumetric overload shock induced by persistence to elevate CVP to a high level of 20-22 mmHg during shock resuscitation [24] is also based on the



faulty Starling's law and induces ARDS [23] that was originally reported by Ashbaugh et al in 1967 in which the dead patients had 12-14 Litres of fluid creep retained in their bodies [25]. In recent huge prospective multicentre clinical trial studies, fluid retention is 7-10 L in surviving ARDS patients [26].

I trust the respected authors, and invite the world authorities, to kindly fulfill their authority and responsibility by writing an update on the subject that summarises the results of my recently reported research for the awareness of the doctors' readers and the undoubted benefit of their patients. Fortunately, the treatment is currently available which is hypertonic sodium therapy (HST) of 5% NaCl and 8.4% NaCO₃ that simply saves lives [27]. This HST should be given as early and as quickly as possible while refraining from giving isotonic fluids of crystalloids and colloids when the retained fluid creep is 2-3 L or KG in weight. The HST induces massive diuresis when diuretics have failed. I also believe it is the right time to write new guidelines and recommendations on the use of fluid therapy for shock resuscitation [6].

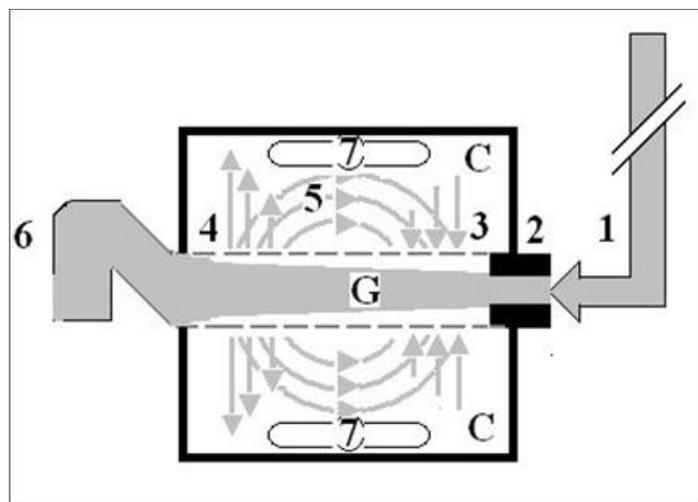


Figure 1: Shows a diagrammatic representation of the hydrodynamic of G tube based on G tubes and chamber C. This 38-years old diagrammatic representation of the hydrodynamic of G tube in chamber C is based on few photographs. The G tube is the plastic tube with narrow inlet and pores in its wall built on a scale to capillary ultra-structure of precapillary sphincter and wide inter cellular slit pores. The chamber C around it is another bigger plastic tube to form the G-C apparatus. The chamber C represents the ISF space. The diagram represents a capillary-ISF unit that should replace Starling's law in every future physiology, medical and surgical textbooks, and added to chapters on hydrodynamics in physics textbooks. The numbers should read as follows:
 1. The inflow pressure pushes fluid through the orifice
 2. Creating fluid jet in the lumen of the G tube**.
 3. The fluid jet creates negative side pressure gradient on the G tube's wall causing suction maximal over the proximal part of the G tube near the inlet that sucks fluid into lumen.
 4. The side pressure gradient turns positive pushing fluid out of lumen over the distal part maximally near the outlet.
 5. Thus, the fluid around G tube inside C moves in magnetic field-like circulation (5) taking an opposite direction to lumen flow of G tube.
 6. The inflow pressure 1 and orifice 2 induce the negative side pressure creating the dynamic G-C circulation phenomenon that is rapid, autonomous, and efficient in moving fluid and particles out

from the G tube lumen at 4, irrigating C at 5, then sucking it back again at 3,

7. Maintaining net negative energy pressure inside chamber C that is always lower than the distal pressure at 6.

****Note:** The shape of the fluid jet inside the G tube (Cone shaped), having a diameter of the inlet on right hand side and the diameter of the exit at left hand side (G tube diameter). I lost the photo on which the fluid jet was drawn, using tea leaves of fine and coarse sizes that runs in the center of G tube leaving the outer zone near the wall of G tube clear. This may explain the finding in real capillary of the protein-free (and erythrocyte-free) sub-endothelial zone in the Glycocalyx paradigm.

I also noted that fine tea leaves exit the distal pores in small amount maintaining a higher concentration in the circulatory system- akin to plasma proteins.

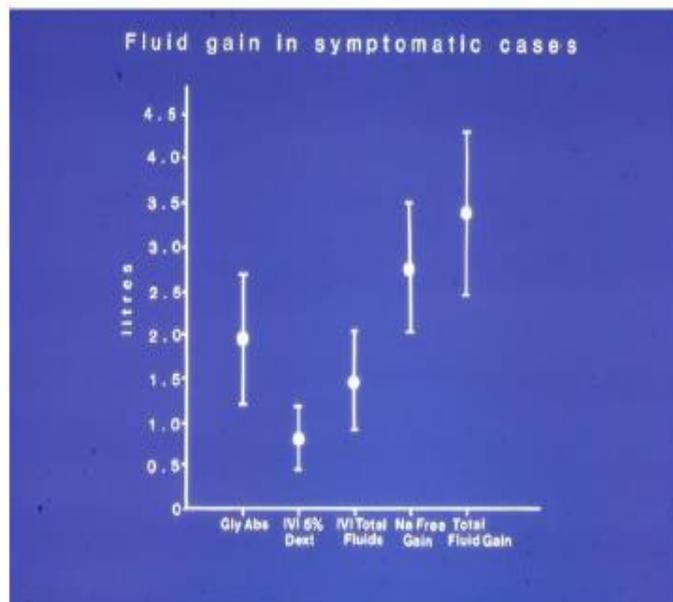


Figure 2: shows the means and standard deviations of volumetric overload in 10 symptomatic patients presenting with shock and Hyponatremia among 100 consecutive patients during a prospective study on transurethral resection of the prostate. The fluids were of Glycine absorbed (Gly abs), intravenously infused 5% Dextrose (IVI) Dext) Total IVI fluids, Total Sodium-free fluid gained (Na Free Gain) and total fluid gain in litres.

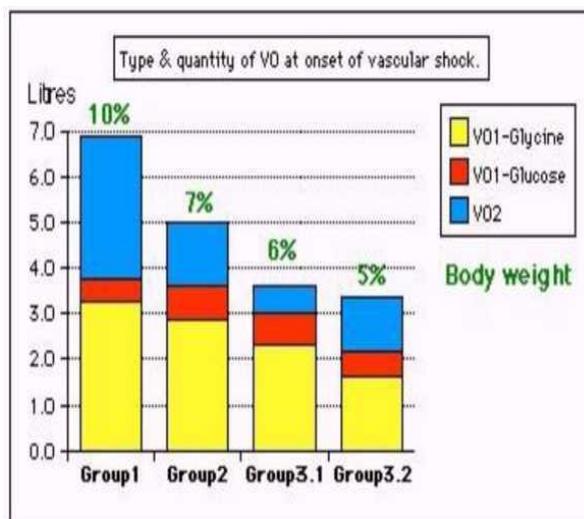




Figure 3: shows volumetric overload (VO) quantity (in litres and as percent of body weight) and types of fluids. Group 1 was the 3 patients who died in the case series as they were misdiagnosed as one of the previously known shocks and treated with further volume expansion. Group 2 were 10 patients from the series who were correctly diagnosed as volumetric overload shock and treated with hypertonic sodium therapy (HST). Group 3 were 10 patients who were seen in the prospective study and subdivided into 2 groups; Group 3.1 of 5 patients treated with HST and Group 3.2 of 5 patients who were treated with guarded volume expansion using isotonic saline.

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Declarations:

Ethical Approval:

Is not applicable. I consent to participate in and consent to publish this article.

Availability of data and materials:

The datasets used can be accessed from the given references of published articles and books.

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Abbreviations:

- ARDS Acute Respiratory Distress Syndrome
- TURP Syndrome Transurethral Resection of the Prostate Syndrome
- G Tube Porous Orifice Tube
- ISF Capillary-Interstitial Fluid
- VO Volumetric Overload
- VOS 1 Volumetric Overload Shock Type 1
- VOS 2 Volumetric Overload Shock Type 2
- AKI Acute Kidney Injury
- MODS The Multiple Organ Dysfunction Syndrome
- CVP Central Venous Pressure
- NaCl Sodium Chloride
- NaCO₃ Sodium Bicarbonate
- HST Hypertonic Sodium Therapy

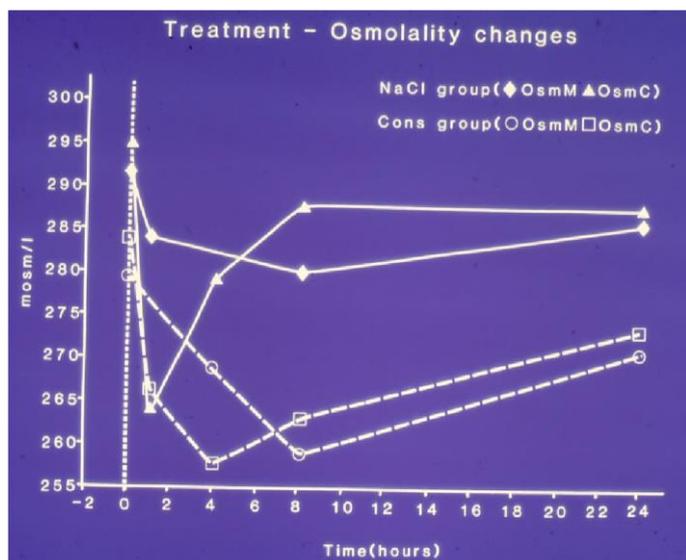


Figure 4: shows mean changes in measured serum osmolality (OsmM) and calculated osmolality (OsmC) in patients with the TURP syndrome comparing those infused with 5% hypertonic sodium (solid lines) and those treated conservatively (slashed lines). OsmC was calculated from the formula $2 \times \text{Na} + \text{urea} + \text{glucose}$ in mmol/l of serum concentration⁴⁸ thus reflecting changes in serum sodium concentration. The vertical dotted line represents the start of operation (Time B) followed by C, C1, C2 (end of treatment) and D, respectively.

References:

- Fernando G. Zampieri, MD, PhD; Sean M. Bagshaw, MD, MSc; Matthew W. Semler, MD, MSc Fluid Therapy for Critically Ill Adults With Sepsis: Review. JAMA .June 13, 2023; 329(22):1967-1980.
- Dull, R.O., Hahn, R.G. Hypovolemia with peripheral edema: What is wrong? Crit Care 27, 206 (2023).
- Ghanem AN. The Adult Respiratory Distress Syndrome: Volumetric Overload Shocks in Patho-Etiology, Correcting Errors and Misconceptions on Fluid Therapy, Vascular and Capillary Physiology. Surg Med Open Acc J. 2018; 2(2). SMOAJ.000534.2018.
- Ghanem AN. Magnetic field-like fluid circulation of a porous orifice tube and relevance to the capillary-interstitial fluid circulation: Preliminary report. Medical Hypotheses 2001 Mar; 56 (3): 325-334.
- Ahmed N Ghanem. Final Affirmative Proof Starling’s Law Wrong and G Tube Hydrodynamic is the Correct Replacement: New Results and Critical Analytical Criticisms of Impactful Landmark Articles. Biomed J Sci & Tech Res 33(5)-2021. BJSTR. MS.ID.005460.
- Ghanem AN. “New Scientific Basis of Fluid Therapy in Shock Management: The Complete Evidence Based on New

Parameter	Value	Std. Err	Std. Value	T Value	P
Intercept			0.773		
Fluid Gain (l)	0.847	0.228	1.044	3.721	0.0007
Osmolality	0.033	0.014	-0.375	2.42	0.0212
Na+ (C B)	0.095	0.049	0.616	1.95	0.0597
Alb (C B)	0.062	0.087	0.239	0.713	0.4809
Hb (C B)	-0.282	0.246	-0.368	1.149	0.2587
Glycine (C B)	-4.973E-5	5.975E-5	-0.242	0.832	0.4112

Table 1: shows the multiple regression analysis of total peri-operative fluid gain, drop in measured serum osmolality (OsmM), sodium, albumin, Hb and increase in serum glycine occurring immediately post-operatively in relation to signs of the TURP syndrome. Volumetric gain and hypoosmolality are the only significant factors. (Reproduced with the permission of author and editor of BJU Int. from reference 9).

Conflict of interest: None declared.



- Scientific Discoveries In Physics, Physiology, And Medicine. Book Publisher Austin Macauley Publishers Ltd ®, London (July 2023). Comes in 35 Chapters and 516 pages so far but may increase.
7. Ghanem AN. The scientific basis of fluid therapy in shock: Based on new scientific discoveries in physics, physiology, and medicine. Book. Eliva Press 2020. Comes in 12 Chapters and 207 pages.
 8. Ghanem AN. Volumetric overload shocks or volume kinetic shocks in clinical practice. Resolving the puzzles of the transurethral resection of the prostate (TURP) syndrome, acute dilution hyponatraemia (HN) and the acute respiratory distress syndrome (ARDS)". Book. Scholars Press USA .2018 1st edition and 2021 2nd edition. Comes in 16 Chapters and 289 pages.
 9. Ghanem AN, Ward JP. Osmotic and metabolic sequelae of volumetric overload in relation to the TURP syndrome. *Br J Uro.* 1990; 66: 71-78. (Winner of Princess Alice Memorial Award, UK 1988).
 10. Ghanem AN. New Theory on THE Capillary Physiology Based on 40-years Research Experience. *American Journal of Biomedical Science & Research.* 2022 7(2); 90-92
 11. Ahmed NM Ghanem and Khaled AN Ghanem. "Fluid Creep" in Critically Ill ARDS Surgical Patients: Time to Stop the Flood?!" *EC Emergency Medicine and Critical Care* 6.9 (2022): 09-13.
 12. Ghanem ANM, et al. Fluid Creep in ARDS after Shock Resuscitation of Trauma, Burns, Sepsis, and Acute Pancreatitis Patients: How Much, Where, and How to Find it? *J Cardiol* 2023, 7(1): 000176.
 13. Ghanem AN. "Volume Kinetic Shocks in Surgical Practice". *Journal of Emergency Medicine, Trauma and Surgical Care* 2 (2020): 010.
 14. Ghanem AN. "Update on Ghanem's New Scientific Discoveries in Physics, Physiology and Medicine". *Journal of Surgery and Anaesthesia* 4 (2020): 135.
 15. Ghanem AN. "What is Misleading Physicians into giving too much Fluid During Resuscitation of Shock and Surgery that Induces ARDS and/or AKI?" *Asploro Journal of Biomedical and Clinical Case Reports.*2020.
 16. Ghanem AN (2020) Twenty-one reasons affirming Starling's law on the capillary-interstitial fluid transfer wrong, and the correct replacement is the hydrodynamic of the porous orifice (G) tube. *Case Rep Open A J I*(1): 8-11.
 17. Rhodin JA (1967) The ultra-structure of mammalian arterioles and precapillary sphincters. *J Ultrastructure Research* 18(1): 181-222.
 18. Karnovsky MJ (1967) The ultra-structural basis of capillary permeability studied with peroxidase as a tracer. *J Cell Biol* 35(1): 213-236.
 19. Ghanem AN. and Ghanem KA. REVISED STARLING'S PRINCIPLE (RSP): A MISNOMER AS STARLING'S LAW IS PROVED WRONG. *Med. Res. Chronicles.*, 7(4), 198-206.
 20. Ghanem AN. Scientific Fraud Not Due to Fraudulent Research in Science. *International Journal of Science and Research (IJSR).* Volume 10 Issue 11, November 2021. 748-757. Paper ID: SR211112174358
 21. Ghanem ANM. What Exactly is the TUR Syndrome and How Should it be Treated? *J Urol Nephrol* 2022, 7(4): 000215.
 22. Ghanem ANM. The TUR Syndrome May Vanish from Urology but will be Re-Incarnating as ARDS after Saline Use as Irrigating Fluid in Endoscopic Surgery. *J Urol Nephrol* 2021, 6(2): 000195.
 23. Ghanem AN. Volumetric Overload Shocks Cause the Acute Respiratory Distress Syndrome: Building the Bridge Between Physics, Physiology, Biochemistry, and Medicine. *Biomed J Sci & Tech Res.* 2020; 29(1).
 24. Ghanem AN. Does Raising the Central Venous Pressure (CVP) in Treating Shock with Fluids Induce Volumetric Overload Shocks (VOS)? *Adv Card Res* 1(5)- 2019. ACR.MS.ID.000120.
 25. Ashbaugh DG., et al. "Acute respiratory distress in adults". *The Lancet Saturday* (1967).
 26. Rowan KM, Angus DC, Bailey M, Barnato AE, Bellomo R, et al. (2017) Early, Goal-Directed Therapy for Septic Shock - A Patient-Level Meta-Analysis. *The New England Journal of Medicine* 376(23): 2223-2234.
 27. Ghanem AN. (2022). Hypertonic Sodium Therapy Of 5%Nacl And 8.4%Naco3 for Acutely Ill and Shocked Patients. *International Journal of Clinical Therapeutics.* 1(1);



The process of making informed decisions around human relationships, sexual orientation and behaviour is an essential part of adolescents' upbringing, making an all-around approach to relevant matters an inescapable necessity. Sexual education covering fields such as human anatomy, human reproduction and reproductive health, legal consent and reproductive rights, safe sexual practice, birth control and sexually transmitted infections (STIs), as well as gender and sex differentiation is denoted under the term comprehensive sexual education. Such practices not only provide adolescents with the necessary valid information but, concurrently, remove barriers at a physical and emotional level in order for them to enjoy humane connection [7,8].

A different factor that made the introduction of official sexual education of utmost importance stems for the previous decades' outbreak of sexually transmitted infections, especially the surge in Human Immunodeficiency (HIV) infection and Acquired Immunodeficiency Syndrome (AIDS). In most affected nations worldwide where HIV infection arises at epidemic levels, including Kenya, Tanzania and Uganda, sexual education is regarded by healthcare advocates and academics as a viable public health strategy to combat the phenomenon [9,10]. Without a doubt, though, application of various techniques throughout the last decades shows that well-trained professionals offering a holistic and realistic approach to the matter yield the best results, as long as individual needs are covered in terms of varieties in age, religion, cultural and societal settings.

Sexual Education Around the World:

According to the World Health Organization (WHO), there exists no pattern regarding which countries worldwide offer compulsory sexual education as part of school curricula, with countries pertaining in the same geographical and socioeconomic groups presenting differences [11].

Europe is undoubtedly the continent along which the bigger differences among countries are observed. Romania does not include reproductive health education as a compulsory topic for the curriculum of different educational levels. Same rule applies for most of the countries of Southern Europe, which base their official education on laws and decrees from previous decades [12]. On the contrary, countries with more advanced educational systems like England, Netherlands, France and Wales have for decades implemented programs in schools based on policies for sexual education; openness about sex, society involvement, privacy and access to contraception [13].

Asia also presents wide variations among its countries when it comes to applying sexual education tactics. Nepal, Bangladesh, Myanmar and Pakistan offer no programs for their population whatsoever, while in Malaysia sex education was introduced in public schools in 2011, but this only happened after a long debate among conservative groups [14]. Indonesia still bases sexual education and sexual health on somewhat older beliefs and traditions. It is worth noting the existence of a presidential decree that condemns cohabitation and considers premarital sexual activities unethical or even illegal, leading sometimes to racism and discrimination against people choosing to go this way [15]. The China is becoming more and more liberal in various fields of everyday life and this is apparent on family planning, social and

sexual education. The national family planning program may give access to affordable contraception, but at the same time those services are mainly used by adults and rarely by students. Unmarried young people in China still live with the fear of stigma if they seek counselling from family planning workers [16]. Turkey also paints a very complex picture, as the large population combined with the cultural mosaic and the difference in attitudes of people from rural and urban areas create a hard task when it comes to implementing sexual education practices. Virginity is an important characteristic of a girl and negative consequences of sexual experiences reflect almost always on girls, leading to their marginalization. It seems that premarital sex demonization and gender inequity are still strong in the neighbouring country, although in some central areas like the capital and Istanbul, where tourism grows fast, traditional patterns show some change towards more liberal sexual attitudes [17].

In Africa, for lack of official sexual education by the state, sexual education lies upon the efforts of Non-Governmental Organizations and private parties. Local authorities in Uganda have been trying years to educate the general population more and more about safe sexual attitudes. The result is a very high rate in knowledge of transmitted infections, HIV/AIDS and their prevention/treatment among students [18]. On the other hand, in Madagascar, results among students paint a different image as the prevalence of Human Immunodeficiency Virus rose between 2000 and 2003 from 0.15% to 0.95%, with students representing almost 2% of the population living with the virus [19].

In USA sexual education is compulsory in schools since 1940, although up until now there has been no official program that covers the whole country. Every school is responsible for developing its own program and curriculum concerning sexual education, but it is important to note that most states offer official guidelines upon which schools can create their projects [20,21]. A 2016 publication from the United States tried to measure the penetration of sexual education among female and male school students in various states of the country, concluding a significant decline in receipt of education regarding sexually transmitted infections, HIV/AIDS, healthy relationships and other topics, especially for females [22].

Australia, with an education system often praised as one of the best in the world, offers widely accessible safe and effective family planning and sexual education programs [23].

Sexual Education in Greece:

According to the report 'Sexuality Education in Europe', school-based sexuality education in Greece began in 1980 with a pilot programme, carried out by the Ministries of Health and Education. Although these two ministries bear responsibility for devising the sexuality education programs to be incorporated in schools, there has not been a specific course taught or a comprehensive approach on the subject in the last years [24].

In 1999, the Ministry of Education decided for the production and use of educational material on health education and health promotion, and the relative project for 15–18-year-old pupils was assigned to the 2nd Gynaecology-Obstetrics Clinic of the University of Athens, in collaboration with the Greek Sexology Institute. In 2001, material was delivered in the forms of a school



book and a CD-ROM. The book was a quite structured approach, including chapters for bodily functions, sexuality, sex and gender [25]. In 2007, a publicly well-known sexologist was appointed by the Ministry of Education to be in charge of the chapter for “Sexuality Education-Intersexual Relationships” of a programme called “Social School” which was at the time run by the Ministry. The sexologist made an effort to create a network of educators, teachers and psychologists to convey some of the important sexuality topics to the adolescent children and their parents as well [26].

According to a 2011 publication from the Ministry of Education on the Greek high school curriculum, which are the latest available, pupils of the second-last and last high school class (aged 17-18 years old) can choose a non-obligatory class named “Family Orientation/Education” with duration of 4 hours a week. It remains unknown how many school units actually have trained personnel to teach this class and are capable of offering the class. It is important to note here that non-obligatory classes in the Greek school are offered rather more based on the availability of teachers and less in terms of demand from the pupils [27].

In a review from 2010 among Greek students about sources of information about sexual education, “friends and classmates” ranked first followed by “mass media and magazines” in second place, “family members and relatives” in third place, “school” ranked fourth in importance, and “other sources” (self-experimentation, books, partners) ranked last. It becomes apparent that schools do not even begin to cover the need of Greek students for sexuality education [28].

Aim and Objectives of the Study:

Aim:

To explore the experiences, perceptions and attitudes of freshmen university students in the city of Athens, concerning their sexual education knowledge and identify the strengths, weaknesses and barriers of the sexual education system.

Objectives:

1. Recognize the main sources of sexual education in Athens
2. Explore the role of family, culture, tradition, religion and formal education when it comes to shaping students’ opinions on sexuality
3. Point out which demographic characteristics play the biggest role when it comes to defining sexual behaviour
4. Identify some of these characteristics as the major determinants of sexual education provision and sexual behaviour

Study Methodology:

Research design:

For the purpose of this study, we proposed the realization of a qualitative research protocol that is exploratory, descriptive and contextual in order to gain a rich understanding of the phenomenon as it exists in the natural setting. Data for the research were collected through structured questionnaires, filled by students individually and privately.

Study population:

Freshmen students from higher educational Institutes of Athens were included as they embody the eligible population of sexual education receivers. The online population gave us the opportunity for a larger sample and therefore more accurate perception of ideas. Participating students were born in the digital age and are generally described as digital citizens. Social platforms are broadly used by students as a social technology tool, which helps them intergrade into university life, achieving an accepted social status at the beginning of their university life [29,30]. Meanwhile, they also offer support in the learning process through communication and interaction; therefore, they were chosen to be our main distribution platform for our online questionnaire.

The questionnaire was created based on the guidelines of WHO for performing sexual education surveys and on the conceptual framework of planned behaviour. The questionnaire consisted of a short description of our study objectives, followed by demographics that allowed us to weight our sample, while the main part consisted of approximately twenty closed-type questions. The development of the questionnaire was originally in English, following the back-to-back translation method to Greek by a bilingual Greek-English origin native speaker. A pilot trial was performed on students bearing the same characteristics as our sample but studying in the city of Patras, Greece [31].

After conducting the pilot study, we had to make the following changes:

- Point the importance of our closed age group and educational status
- Conversion of many open type questions into closed ones for better analysis
- Reduction of questions’ number for quicker participation

Data management and statistical analysis:

The data from the online questionnaires was gathered, arranged in the proper form and transferred into the statistical analysis platform ‘SPSS Statistics’ v. 26.0 (IBM, Armonk, USA).

Limitations of the study:

The main restriction of our research is the sensitivity of the topic we aim to explore. Due to that and the accessibility to the large population group of students, we decided to conduct the research online, based on the idea that almost all students are active on social media and the online groups of their departments. The attempted access only to tertiary education students with access to the Internet can be also described as a limitation. Finally, generalisations cannot be made for the whole population of Greek students, even if the capital houses the vast majority of university departments.

Results:

Demographics:

The recruited population sample consisted of two hundred and fifty-four (n=254) freshmen students with a female sex ratio of 61% and a mean age of 18.7 ± 2.3 years. 231 students (91%) were of Greek origin and 178 (70%) registered themselves as greek orthodox. Regarding sexuality, 85% of the students registered as heterosexual, 5% as homosexual, 9% as bisexual and 1% as



unspecified or other, while 70% of the sample had already initiated their sexual life. Full demographics for the participating sample can be found in Table 1.

Demographics Variables	Sample Representation
Age (years)	18.7 ± 2.3
Sex – nr. (%)	
Male	99 (39.0%)
Female	155 (61.0%)
Country of Birth – nr. (%)	
Greece	239 (94.1%)
Other	15 (5.9%)
Yearly Family Income – euros	
<5,000	15 (5.9%)
5,000-10,000	39 (15.4%)
10,000-20,000	45 (17.7%)
>20,000	84 (33.1%)
Do not know	71 (28.0%)
Religion – nr. (%)	
Orthodox	178 (70.1%)
Atheist	61 (24.0%)
Other	15 (5.9%)
Spoken Language in	
Greek	248 (97.6%)
Other	6 (2.4%)
Living Status – nr. (%)	
With family	143 (56.3%)
Alone	91 (35.8%)
With friends/partner/roommate	20 (7.9%)
Working Status – nr. (%)	
Employed	58 (22.8%)
Without occupation	196 (77.2%)
Sexual Orientation – nr. (%)	
Heterosexual	216 (85.0%)
Homosexual	13 (5.1%)
Bisexual	23 (9.1%)
Other/Do not know	2 (0.8%)
Sexual Life Initiation – nr. (%)	
Yes	178 (70.1%)
No	76 (29.9%)

Table 1: Demographic data of the participating population.

Sexual Life Data and Information Sources:

Regarding the sexual life and information sources of the participating population, full data can be found in Table 2. Sexual initiation age for those that had already had at least one sexual intercourse was 17.0 ± 1.4 years of age, with the number of sexual partners being 2.4 ± 0.7 up to the date of the survey completion. Among those who had yet to participate in sexual intercourse, approximately half (55.1%) were not given the chance yet, and every fourth student (26.0%) did not feel ready, while another 9.8% characterized premarital intimacy as unethical and 9.1%

stated other reasons. First sexual information source for 35.8% of the participants was the family environment, with internet and school (25.2%) tying in the second place and friends coming last at 13.8%. Almost eight out of ten participants (78.0%) would have liked more information provided to them, mainly by an expert on the subject or via the education system. Among the 178 people who had already initiated their sexual life, the minority (40.4%) recalls using a contraceptive method on their first intercourse, with most used ones being condoms (78.1%). Although few participants actually contracted an STI so far (5.1%), only 38.5% of them admits to having sought medical help for the infection.

Sexual Life Variables	
Sexual initiation age (years)	17.0 ± 1.4
Number of sexual partners – nr.	2.4 ± 0.7
Reasons for no initiation of sexual	
‘I did not have the chance yet’	140 (55.1%)
‘I do not feel ready yet’	66 (26.0%)
‘Premarital sex is morally	25 (9.8%)
Other reason	23 (9.1%)
First information source – nr.	
Family	91 (35.8%)
Internet	64 (25.2%)
School	64 (25.2%)
Friends	35 (13.8%)
Belief that more info is necessary	198 (78.0%)
Preferred source – nr. (%)	
Expert on the subject	152 (59.8%)
School	89 (35.0%)
Other	13 (5.1%)
Contraceptive use on first	72 (40.4%)
Means of contraception on first	
Condom	139 (78.1%)
Coitus Interruptus	7 (3.9%)
Other	32 (18.0%)
STI contraction – nr. (%)	13 (5.1%)
Sought medical help after STI	
Yes	5 (38.5%)
No	8 (61.5%)

Table 2: Sexual life characteristics of the participating population.

Comparison between male and female students:

Independent sample student's t-testing was performed between male and female students for determination of possible differences regarding important topics of our questionnaire. Selected results are discussed below and relevant data is depicted in Table 3. Statistically important differences were found in sexual life initiation (p-value 0.032), number of sexual partners up to survey completion (p-value 0.013), as well as contraceptive use on first intercourse (p-value 0.005). On the other hand, no differences were noted between sexes for sexual initiation age (p-value 0.93) and STI contraction (p-value 0.329). The data suggests that more male students have already had sexual intercourse although among students who have already initiated their sexual life, no difference



in initiation age exists. Furthermore, males tend to have more partners but, at the same time, present riskier behaviour as shown by reduced contraceptive methods usage, though this is not mirrored upon STI contraction, where percentages do not differ significantly.

Independent Variable	Sex		P-value
Sexual life initiation – (%)	Male 77.2%	Female 60.8%	0.032
Sexual partners number	Male 2.6 ± 0.9	Female 2.3 ± 0.6	0.013
Contraceptive use on first intercourse – (%)	Male 37.6%	Female 47.4%	0.005
Sexual initiation age (years)	Male 16.8 ± 2.1	Female 17.4 ± 2.4	0.93
STI Contraction (%)	Male 5.5%	Female 4.9%	0.329

Table 3: Independent sample t-test for male and female students.

Discussion:

In the current study protocol, we used an original online questionnaire, consisting of both open- and closed-type questions, improvised by the authors, in order to assess sources of information as well as beliefs and behaviours around sexual practice of freshmen students in the capital city of Greece. Since available literature and official data revolving around sexual education within the greek borders are extremely scarce, we aimed to pinpoint areas in which young adults' knowledge appears insufficient, in order for them to be better implemented as part of future official sexual education practices. Recent literature reviews suggest that curriculum-based interventions yield efficient results, especially when incorporating the use of modern technologies [32,33].

First and foremost, sexual orientation and age of sexual initiation does not differ significantly between the sexes, with males having more partners throughout their early years of sexual life, while at the same time presenting riskier sexual behaviours, as shown by the rarer use of contraception. A balance exists in terms of general knowledge around sexual intercourse, with females appearing more knowledgeable in topics around sexually transmitted infections. One of the few recent studies on the topic also found young people of 18-30 years of age to be very informed on the subject of well-known STIs [34]. Since reports about sexual violence in the country are increasing, we consider the matters of consent and sexual safety of utmost significance in future sexual education endeavours [35,36].

Secondly, as expected by the lack of not only scientific research but also official reporting, penetration of official sexual education within the national education system is extremely low. Only one fourth of asked students received their first piece of information on relevant subjects from an official school source, while family and internet were the lead providers, though students would have preferred for their educators to carry more expertise. Of note, both students with or without an active sex life opted for more formal sexual education programmes, with an approximate eight out of ten students expressing a wish for more school hours devoted to

the subject. Let it be pointed out here, that many European countries, including Greece, do not have official sexual education courses available even at the level of official medical training [37]. Regarding sexual practice, only every third student who had already initiated their sex life used a contraceptive method on their first sexual encounter, with condoms being the most prevalent method. Although few students out of our sample actually contracted a sexually transmitted infection, more than half of them never sought medical help. Another recent study estimated a moderate knowledge around Human Papillomavirus (HPV) and its vaccine [38]. Taken together, these results appear quite alarming, especially given the fact that older reports estimate use of contraception at higher levels [39]. Of note, a nationwide survey of almost 2,000 individuals showed that while sexual health and STIs do not make it in the top-three public health concerns, they are of great importance in younger generations, thus making correct information provision vital for these ages [40].

Conclusion:

While state efforts for implementation of structured official sexual education programmes currently remain scarce, some level of provision of information around the subject exists among Greek students, with home and internet being among the most used sources. As individuals nowadays begin to explore their sexuality and engage in sexual practice at younger ages, the need for organized sexual education appears greater than ever. Furthermore, young pupils, adolescents and students deserve to be in a position to make informed decisions when it comes to exploring their sexuality, participating in and enjoying sexual intercourse, and building healthy intrapersonal relationships. We consider the topic of vital importance when it comes to planning future school curricula and urge state authorities engaged in such planning to take action.

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Ethical Approval and Participant Consent:

Since the questionnaire was anonymous, no ethical approval was sought for the data to be made public. Participants in the study agreed to the statistical analysis as well as publication of their responses by filling out a relevant field in the questionnaire. The specific field was placed in the beginning of the questionnaire.

Conflict of Interest:

The authors declare no conflict of interest for the present study.

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References:

1. Leung H, Shek DTL, Leung E, Shek EYW. Development of contextually-relevant sexuality education: Lessons from a comprehensive review of adolescent sexuality education across cultures. *Int J Environ Res Public Health* [Internet].



- 2019;16(4):621.
2. Bungener SL, Post L, Berends I, Steensma TD, de Vries ALC, Popma A. Talking About Sexuality With Youth: A Taboo in Psychiatry? *J Sex Med* [Internet]. 2022;19(3):421–9.
 3. Ben Thabet J, Charfeddine F, Charfi N, Baati I, Zouari L, Zouari N, et al. Sexualité de la femme tunisienne: entre le religieux et le culturel. *Encephale* [Internet]. 2015;41(2):144–50.
 4. Hall KS, Moreau C, Trussell J. Lower use of sexual and reproductive health services among women with frequent religious participation, regardless of sexual experience. *J Womens Health (Larchmt)* [Internet]. 2012;21(7):739–47.
 5. Russell S, Mallory A, Bishop M, Dorri A. Innovation and integration of sexuality in family life education. *Fam Relat* [Internet]. 2020;69(3):595–613.
 6. Tupper KW. Sex, drugs and the honour roll: the perennial challenges of addressing moral purity issues in schools. *Crit Public Health* [Internet]. 2014;24(2):115–31.
 7. International technical guidance on sexuality education [Internet]. United Nations Population Fund. [cited 2022 Dec 29]. <https://www.unfpa.org/publications/international-technical-guidance-sexuality-education>
 8. Marques SS, Constantine NA, Goldfarb ES, Mauldon J. Sexuality Education. In: *International Encyclopedia of the Social & Behavioral Sciences*. Elsevier; 2015. p. 825–32.
 9. Sport and Culture and the Ministry of Higher Education, Training and Employment Creation of Namibia. National Policy on HIV/AIDS for the Education Sector. Solitaire Press; 2003.
 10. Wikipedia contributors. HIV/AIDS in Africa [Internet]. Wikipedia, The Free Encyclopedia. 2022. Available from: https://en.wikipedia.org/w/index.php?title=HIV/AIDS_in_Africa&oldid=1129085500
 11. The journey towards comprehensive sexuality education: global status report [Internet]. Who.int. [cited 2022 Dec 29].
 12. Blidaru IE, Furau G, Socolov D. Female Romanian university students' attitudes and perceptions about contraception and motherhood. *Eur J Contracept Reprod Health Care* [Internet]. 2016;21(1):39–48.
 13. Reis M, Ramiro L, Matos MG de, Diniz JA. The effects of sex education in promoting sexual and reproductive health in Portuguese university students. *Procedia Soc Behav Sci* [Internet]. 2011;29:477–85.
 14. Wong LP. An exploration of knowledge, attitudes and behaviours of young multiethnic Muslim-majority society in Malaysia in relation to reproductive and premarital sexual practices. *BMC Public Health* [Internet]. 2012;12(1):865.
 15. Hald GM, Mulya TW. Pornography consumption and non-marital sexual behaviour in a sample of young Indonesian university students. *Cult Health Sex* [Internet]. 2013;15(8):981–96.
 16. Ma Q, Ono-Kihara M, Cong L, Xu G, Pan X, Zamani S, et al. Early initiation of sexual activity: a risk factor for sexually transmitted diseases, HIV infection, and unwanted pregnancy among university students in China. *BMC Public Health* [Internet]. 2009;9(1):111.
 17. Aşci O, Gökdemir F, Kanbay Y. Examination of sexual attitudes of students in a university in Turkey. *Int J Health Sci Res*. 2016;6(6):245–53.
 18. Nsubuga H, Sekandi JN, Sempeera H, Makumbi FE. Contraceptive use, knowledge, attitude, perceptions and sexual behavior among female University students in Uganda: a cross-sectional survey. *BMC Womens Health* [Internet]. 2016;16(1):6.
 19. Hoque ME, Ntsipe T, Mokgatle-Nthabu M. Awareness and practices of contraceptive use among university students in Botswana. *SAHARA J* [Internet]. 2013;10(2):83–8.
 20. Adefuye AS, Abiona TC, Balogun JA, Lukobo-Durrell M. HIV sexual risk behaviors and perception of risk among college students: implications for planning interventions. *BMC Public Health* [Internet]. 2009;9(1):281.
 21. Buhi ER, Marhefka SL, Hoban MT. The State of the union: sexual health disparities in a national sample of US college students. *J Am Coll Health* [Internet]. 2010;58(4):337–46.
 22. Lindberg LD, Maddow-Zimet I, Boonstra H. Changes in adolescents' receipt of sex education, 2006–2013. *J Adolesc Health* [Internet]. 2016;58(6):621–7.
 23. Leung J, Pirovich R, Woods C, de Costa C. Knowledge of contraceptive methods and services among tertiary students in far North Queensland. *Aust N Z J Obstet Gynaecol* [Internet]. 2014;54(4):386–9.
 24. Parker R, Wellings K, Lazarus JV. Sexuality education in Europe: an overview of current policies. *Sex Educ* [Internet]. 2009;9(3):227–42.
 25. Gkatzamanis K, Papatthanasiou Z. Sexual Education - Intrasexual relationships. Athens: Ministry of National Education and Religious Affairs. 2000.
 26. Σεξουαλική Διαπαιδαγώγηση: 200 εκπαιδευτές μιλούν μαζί μου γι αυτό. | Θάνος Ασκητής - Ινστιτούτο Ψυχικής & Σεξουαλικής Υγείας [Internet]. Askitis.gr. [cited 2022 Dec 29].
 27. Ministry of Education and Culture of Greece. Athens: Lithostar Ltd; 2011 p. Selection of Classes in High School.
 28. Fakinos M. Sexuality education in Greek schools: Student experience and recommendations. *Electronic Journal of Human Sexuality*. 2010;
 29. Sánchez A, Cortijo R, Javed V. Students' perceptions of Facebook for academic purposes. *Computers & Education*. 2014;70:138–49.
 30. Yu AY, Tian SW, Vogel D, Chi-Wai Kwok R. Can learning be virtually boosted? An investigation of online social networking impacts. *Comput Educ* [Internet]. 2010;55(4):1494–503.
 31. Wilentz G. The importance of European standards and a human rights-based approach in strengthening the implementation of sexuality education in Ireland. *Sex Educ* [Internet]. 2016;16(4):439–45.
 32. Lameiras-Fernández M, Martínez-Román R, Carrera-Fernández MV, Rodríguez-Castro Y. Sex education in the spotlight: What is working? Systematic review. *Int J Environ Res Public Health* [Internet]. 2021;18(5):2555.
 33. Rabbitte M. Sex education in school, are gender and sexual minority youth included?: A decade in review. *Am J Sex Educ* [Internet]. 2020;15(4):530–42.
 34. Voyiatzaki C, Venetikou MS, Papageorgiou E, Anthouli-Anagnostopoulou F, Simitzis P, Chaniotis DI, et al. Awareness, knowledge and risky behaviors of sexually transmitted diseases among young people in Greece. *Int J Environ Res Public Health* [Internet]. 2021;18(19):10022.
 35. Chroni SA, Kavoura A. From silence to speaking up about sexual violence in Greece: Olympic journeys in a culture that neglects safety. *Front Psychol* [Internet]. 2022;13:862450.



36. Sakellari E, Berglund M, Santala E, Bacatum CMJ, Sousa JEXF, Aarnio H, et al. The perceptions of sexual harassment among adolescents of four European countries. *Children (Basel)* [Internet]. 2022;9(10):1551.
37. Kristufkova A, Pinto Da Costa M, Mintziori G, Vásquez JL, Aabakke AJM, Fode M. Sexual Health During Postgraduate Training-European Survey Across Medical Specialties. *Sex Med* [Internet]. 2018;6(3):255–62.
38. Sidiropoulou M, Gerogianni G, Kourti FE, Pappa D, Zartaloudi A, Koutelekos I, et al. Perceptions, knowledge and attitudes among young adults about prevention of HPV infection and immunization. *Healthcare (Basel)* [Internet]. 2022;10(9):1721.
39. Patseadou M, Galli-Tsinopoulou A, Goulis DG, Arvanitidou M. Factors associated with the onset of sexual activity among Greek high school students. *Eur J Contracept Reprod Health Care* [Internet]. 2010;15(5):357–66.
40. Tzortzi A, Kapetanstradaki M, Rachiotis G, Evangelopoulou V, Leventou E, Behrakis P. Perceived importance of public health risks in Greece: A nationwide survey of the adult population. *Int J Environ Res Public Health* [Internet]. 2021;18(16):8256.