PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Association between Spinal Curvature Disorders and Injury: A Nationwide Population-based Retrospective Cohort Study
AUTHORS	Kuo, Yen-Liang; Chung, Chi-Hsiang; Huang, Tsai-Wang; Tsao, Chang-Huei; Chang, Shan-Yueh; Peng, Chung-Kan; Cheng, Wei-Erh; Chien, Wu-Chien; Shen, Chih-Hao

VERSION 1 – REVIEW

REVIEWER	Yu Yamato Hamamatsu University School of Medicine, Japan
REVIEW RETURNED	15-May-2018

GENERAL COMMENTS	I would like to congratulate the authors that this paper is very interesting and well written report. In this manuscript the authors reported the effect of spinal curvature on the risk of injury based on a large number of patients in the National Health Insurance Research Database. The results clearly revealed that patients with spinal curvatures had a significantly higher risk of developing injury. General points: This manuscript revealed the significant effect of incidence of spinal curvatures on developing injury using statistical methods appropriately. I have no objection against the study methods and results but the interpretation of the result was slightly difficult to understand. Spinal curvatures include many kinds of pathologies and morphology; idiopathic scoliosis, degenerative kyphoscoliosis, kyphosis following vertebral fracture, and so on. Usually the spinal curvature disorders in patients aged 20-40 include idiopathic scoliosis and congenital spinal deformity. However in patients aged 60 and over, the disorders include degenerative or osteoporotic spinal disease. The authors' data showed the adjusted HR in relatively young patients were much higher than in those aged 65 and over; nevertheless the chest wall compliance decreased in only a few severe cases. (Besides,) the reduction in muscle strength and gait unsteadiness generally appeared in elderly patients, not in young patients with spinal curvature disorders. Why does spinal curvature have this large effect? Either more detailed analysis in stratified subgroups of or additional comments about age and pathology difference in "Discussion" section are necessary to clarify this issue. Specific points: Page 7, line 15; Kyphosis is the anterior….of the thoracic spine. The terminology of "kyphosis" and "lordosis" is not use only for thoracic spine or lumber spine. The definition of these words were incorrect.

	Page 16, line 7; Since spinal curvature was associated with higher risk of injury, … this sentence was not supported data or literatures.

REVIEWER	Raquel Vaquero-Cristóbal Department of Sport Science, Catholic University San Antonio of Murcia, Murcia, Spain
REVIEW RETURNED	16-May-2018

GENERAL COMMENTS	Firstly, congratulations for your paper. It has been an honor review this excellent study. Some recommendations are included: - Introduction. Line 38-40. Please, include a reference for "postural changes, muscle weakness, and intervertebral ligament degeneration". Please, include systematic physical activity practice as factor. - Materials and Methods. Study design and sampled participants. Please, include a reference for ICD-9 codes system. - Reference. "1. JR C. Outline for the study of scoliosis. . American...:" Delete the double point.

REVIEWER	José M Muyor University of Almería (Spain)
REVIEW RETURNED	24-May-2018

GENERAL COMMENTS	The effort of the authors when carrying out this cohort study is appreciated. However, it is necessary to make some considerations: ABSTRACT page 4, lines 8-9: "Spinal curvatures are deformities characterized by abnormal curves of the spine" Comment: Please, read reference such as Stagnara et al. In their conclusion, they recommended avoiding the words normal or " abnormal. " Stagnara P, De Mauroy JC, Dran G, et al. Reciprocal angulation of vertebral bodies in a sagittal plane: approach to references for the evaluation of kyphosis and lordosis. Spine. 1982; 7: 335-342. page 4, lines 24-26: "Patients with spinal curvatures" Comment: Please, reconsider change this sentence in the whole manuscript because it is incorrect or wrongly defined. All persons have spinal curvatures in the sagittal plane. The problem is when these curves are in angular values altered. Introduction Page 8, lines10-12: "lordosis, kyphosis, and scoliosis." Lordosis refers to anteroposterior angulation and inward curving of the lumbar spine. Comment: The same that the previous comments. Please, add bibliographic references that report this definition. Page 8, lines 38-40: postural changes, muscle weakness, and intervertebral ligament degeneration ". Comment: Please, add bibliographic references that report this statement. Statistical analysis: Comment: Please, add the power and sample size. Discussion from page 14, line 54 to page 15, lines 4-38 the information reported is the same that in the results.

	Conclusion The conclusion is obvious and generic. Any study related to spinal curvatures would report the same conclusion. References Please, correct the reference number 1.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1 (Comments to the Author):
1. Usually the spinal curvature disorders in patients aged 20-40 include idiopathic scoliosis and congenital spinal deformity. However in patients aged 60 and over, the disorders include degenerative or osteoporotic spinal disease. The authors' data showed the adjusted HR in relatively young patients were much higher than in those aged 65 and over; nevertheless the chest wall compliance decreased in only a few severe cases. (Besides,) the reduction in muscle strength and gait unsteadiness generally appeared in elderly patients, not in young patients with spinal curvature disorders. Why does spinal curvature have this large effect? Either more detailed analysis in stratified subgroups of or additional comments about age and pathology difference in "Discussion" section are necessary to clarify this issue.

Response: Thanks a lot for your valuable comment. According to your suggestion, we have added comments about age and pathology difference in the Discussion section:
"We found that older patients with spinal curvature disorders patients had more comorbidities than younger patients with these disorders (Table 2) in this study. Previous studies also showed that age and chronic illness are associated with disability in daily living activities50 51. Therefore, older patients with spinal curvature disorders may present less activity. On the other hand, previous studies also demonstrated that impaired balance control52 and changes in the capacity of maintaining position53 can be found in young scoliosis patients. It is possible that daily activities may be less limited in younger populations with spinal curvature disorders, which increases the risk of injury." (PDF proof P.16-P.17)

References:
50. Wu SC, Leu SY, Li CY. Incidence of and predictors for chronic disability in activities of daily living among older people in Taiwan. J Am Geriatr Soc 1999;47(9):1082-6.
51. Covinsky KE, Palmer RM, Fortinsky RH, et al. Loss of independence in activities of daily living in older adults hospitalized with medical illnesses: increased vulnerability with age. J Am Geriatr Soc 2003;51(4):451-8.
52. Gauchard GC, Lascombes P, Kuhnast M, et al. Influence of different types of progressive idiopathic scoliosis on static and dynamic postural control. Spine (Phila Pa 1976) 2001;26(9):1052-8.
53. Silferi V, Rougier P, Labelle H, et al. Postural control in idiopathic scoliosis: comparison between healthy and scoliotic subjects. Rev Chir Orthop Reparatrice Appar Mot 2004;90(3):215-25.

2. Page 7, line 15; Kyphosis is the anterior….of the thoracic spine. The terminology of "kyphosis" and "lordosis" is not use only for thoracic spine or lumber spine. The definitions of these words were incorrect.

Response: Thanks a lot for your valuable comment. We have revised the whole manuscript with definition of spinal curvature disorders including hyperkyphosis, hyperlordosis and scoliosis. Because hyperkyphosis and hyperlordosis are commonly referred to as kyphosis and lordosis by the medical community, we have reedited the Introduction section to clarify the definition of these words:
"The spine has a gentle curve when viewed from the side and a straight appearance when viewed from the back. This structure absorbs the stress from body movement and gravity. Kyphosis is a

convex curvature of the spine that creates a hunchback appearance. Lordosis refers to the inward concave curving of the cervical and lumbar regions of the spine (1,2). When disorders of the spine occur, the natural curvatures of the spine are misaligned or exaggerated in certain areas.
Possible spinal curvature disorders include scoliosis, hyperkyphosis, and hyperlordosis, which can be graded in severity by the Cobb angle (3). Scoliosis indicates a lateral displacement or curvature of the spine (4), which is defined by a curve in the spine with a Cobb angle of 10 degrees or greater in adults (5). Hyperkyphosis and hyperlordosis are commonly referred to as kyphosis and lordosis by the medical community. The evaluation of these conditions is challenging due to the lack of standardized diagnostic criteria. Generally, the Cobb angle of a normal thoracic spine ranges between 20 and 50 degrees in young people (1, 6).” (PDF proof P.7)

References:
1. Fon GT, Pitt MJ, Thies AC, Jr. Thoracic kyphosis: range in normal subjects. AJR Am J Roentgenol. 1980;134(5):979-83.
2. Voutsinas SA, MacEwen GD. Sagittal profiles of the spine. Clin Orthop Relat Res. 1986(210):235-42.
3. J. C. Outline for the study of scoliosis. Amer Acad Orthop Surg Instructional Course Lectures. 1948;5:261–75.
4. Vasiliadis ES, Grivas TB, Kaspiris A. Historical overview of spinal deformities in ancient Greece. Scoliosis. 2009;4:6.
5. Kane WJ. Scoliosis prevalence: a call for a statement of terms. Clin Orthop Relat Res. 1977(126):43-6.
6. Boseker EH, Moe JH, Winter RB, Koop SE. Determination of "normal" thoracic kyphosis: a roentgenographic study of 121 "normal" children. J Pediatr Orthop. 2000;20(6):796-8.

3. Page 16, line 7; Since spinal curvature was associated with higher risk of injury, … this sentence was not supported data or literatures.

Response: Thanks a lot for your valuable comment. We have re-written this part in the Discussion section: “We found spinal curvature disorders were associated with higher risk of injury. However, whether providing assistive devices or protective gear to patients with spinal curvature disorders decreases the incidence of injury remains uncertain. Future studies focusing on the association between early detection, adequate treatment of spinal curvature disorders, and the prevention of injury are warranted.” (PDF proof P.17)
Reviewer #2 (Comments to the Author):
1. Introduction. Line 38-40. Please, include a reference for "postural changes, muscle weakness, and intervertebral ligament degeneration". Please, include systematic physical activity practice as factor.

Response: We thank reviewer for the valuable comment. We have included the references for postural changes, muscle weakness, and intervertebral ligament degeneration. We also reviewed literatures of systematic physical activity practice as spinal curvature disorders risk factor and re-edited the introduction section with including related references. (PDF proof P.7-P.8)
References:
13. Axenovich TI, Zaidman AM, Zorkoltseva IV, Kalashnikova EV, Borodin PM. Segregation analysis of Scheuermann disease in ninety families from Siberia. Am J Med Genet. 2001;100(4):275-9.
14. Schneider DL, von Muhlen D, Barrett-Connor E, Sartoris DJ. Kyphosis does not equal vertebral fractures: the Rancho Bernardo study. J Rheumatol. 2004;31(4):747-52.
15. Kado DM, Prenovost K, Crandall C. Narrative review: hyperkyphosis in older persons. Ann Intern Med. 2007;147(5):330-8.
16. Boyle JJ, Milne N, Singer KP. Influence of age on cervicothoracic spinal curvature: an ex vivo radiographic survey. Clin Biomech (Bristol, Avon). 2002;17(5):361-7.
17. Vialle R, Levassor N, Rillardon L, Templier A, Skalli W, Guigui P. Radiographic analysis of the

sagittal alignment and balance of the spine in asymptomatic subjects. J Bone Joint Surg Am. 2005;87(2):260-7.
18. Hinman MR. Comparison of thoracic kyphosis and postural stiffness in younger and older women. Spine J. 2004;4(4):413-7.
19. Mika A, Unnithan VB, Mika P. Differences in thoracic kyphosis and in back muscle strength in women with bone loss due to osteoporosis. Spine (Phila Pa 1976). 2005;30(2):241-6.
20. Brocklehurst JC, Robertson D, James-Groom P. Skeletal deformities in the elderly and their effect on postural sway. J Am Geriatr Soc. 1982;30(8):534-8.
21. Chow RK, Harrison JE. Relationship of kyphosis to physical fitness and bone mass on post-menopausal women. Am J Phys Med. 1987;66(5):219-27.
22. Sinaki M, Itoi E, Rogers JW, Bergstralh EJ, Wahner HW. Correlation of back extensor strength with thoracic kyphosis and lumbar lordosis in estrogen-deficient women. Am J Phys Med Rehabil. 1996;75(5):370-4.
23. Sinaki M, Brey RH, Hughes CA, Larson DR, Kaufman KR. Balance disorder and increased risk of falls in osteoporosis and kyphosis: significance of kyphotic posture and muscle strength. Osteoporos Int. 2005;16(8):1004-10.
24. Birnbaum K, Siebert CH, Hinkelmann J, Prescher A, Niethard FU. Correction of kyphotic deformity before and after transection of the anterior longitudinal ligament--a cadaver study. Arch Orthop Trauma Surg. 2001;121(3):142-7.
25. Esparza FV-C, Raquel & Alacid, Fernando & Martínez-Ruiz, E & López-Miñarro, Pedro. Sagittal spinal curvatures in maximal trunk flexion of young female dancers. British journal of sports medicine. 2014;48.:595.
26. López-Miñarro PM, José & Alacid, Fernando & Manuel, Isorna & Vaquero-Cristóbal, Raquel. Sagittal spinal curvatures and pelvic inclination in kayakers. Revista Internacional de Medicina y Ciencias de la Actividad Fisica y del Deporte. 2014;14.:633-50.
27. Vaquero-Cristóbal RE, Francisco & Gómez-Durán, R & Martínez-Ruiz, E & Muyor, José & Alacid, Fernando & López-Miñarro, Pedro. Thoracic and lumbar morphology in standing, sitting and maximal trunk flexion with extended knees in dancers. Archivos de Medicina del Deporte. 2015;32.:87-93.
28. López-Miñarro PV-C, Raquel & Alacid, Fernando & Manuel, Isorna & Muyor, José. Comparison of sagittal spinal curvatures and pelvic tilt in highly trained athletes from different sport disciplines. Kinesiology. 2017;491:109-16.

2. Materials and Methods. Study design and sampled participants. Please, include a reference for ICD-9 codes system.

Response: We thank reviewer for reminding the critical point. We have included the reference for ICD-9 codes system. (PDF proof P.9)
Reference:
37. Organization GWH. World Health Organization, Manual of the International Classification of Diseases, Injuries, and Causes of Death, Ninth Revision. 1977.

3. Reference. "1. JR C. Outline for the study of scoliosis. . American...:" Delete the double point.

Response: We thank reviewer for pointing out this issue. We have corrected the 1st reference typing error. (PDF proof P.18)

Reviewer #3 (Comments to the Author):
1. ABSTRACT page 4, lines 8-9: "Spinal curvatures are deformities characterized by abnormal curves of the spine" Comment: Please, read reference such as Stagnara et al. In their conclusion, they recommended avoiding the words normal or " abnormal. " Stagnara P, De Mauroy JC, Dran G, et al. Reciprocal angulation of vertebral bodies in a sagittal plane: approach to references for the evaluation

of kyphosis and lordosis. Spine. 1982; 7: 335-342.

Response: We thank reviewer for pointing out this critical issue. We have reedited the whole manuscript with “spinal curvature disorders” for describing “excessive” curve of the spine rather than “abnormal”. We have re-edited the Introduction section for your comment 1, 2, 3. Please see the revised manuscript in response to the comment 3.

2. Page 4, lines 24-26: "Patients with spinal curvatures"
Comment: Please, reconsider change this sentence in the whole manuscript because it is incorrect or wrongly defined. All persons have spinal curvatures in the sagittal plane. The problem is when these curves are in angular values altered.

Response: We thank reviewer for pointing out this critical issue. As the previous comment, we have re-edited the whole manuscript with “spinal curvature disorders” for describing “excessive” curve of the spine. We also re-edited the Introduction section for your comment 1, 2, 3. Please see the revised manuscript in response to the comment 3

3. Introduction Page 8, lines10-12: "lordosis, kyphosis, and scoliosis." Lordosis refers to anteroposterior angulation and inward curving of the lumbar spine.
Comment: The same that the previous comments. Please, add bibliographic references that report this definition.

Response: Thanks a lot for your valuable comment. We have revised the whole manuscript with definition of spinal curvature disorders including hyperkyphosis, hyperlordosis and scoliosis. Because hyperkyphosis and hyperlordosis are commonly referred to as kyphosis and lordosis by the medical community, we have reedited the Introduction section to clarify the definition of these words: “The spine has a gentle curve when viewed from the side and a straight appearance when viewed from the back. This structure absorbs the stress from body movement and gravity. Kyphosis is a convex curvature of the spine that creates a hunchback appearance. Lordosis refers to the inward concave curving of the cervical and lumbar regions of the spine (1,2). When disorders of the spine occur, the natural curvatures of the spine are misaligned or exaggerated in certain areas.
Possible spinal curvature disorders include scoliosis, hyperkyphosis, and hyperlordosis, which can be graded in severity by the Cobb angle (3). Scoliosis indicates a lateral displacement or curvature of the spine (4), which is defined by a curve in the spine with a Cobb angle of 10 degrees or greater in adults (5). Hyperkyphosis and hyperlordosis are commonly referred to as kyphosis and lordosis by the medical community. The evaluation of these conditions is challenging due to the lack of standardized diagnostic criteria. Generally, the Cobb angle of a normal thoracic spine ranges between 20 and 50 degrees in young people (1, 6).” (PDF proof P.7)
References:
1. Fon GT, Pitt MJ, Thies AC, Jr. Thoracic kyphosis: range in normal subjects. AJR Am J Roentgenol. 1980;134(5):979-83.
2. Voutsinas SA, MacEwen GD. Sagittal profiles of the spine. Clin Orthop Relat Res. 1986(210):235-42.
3. J. C. Outline for the study of scoliosis. Amer Acad Orthop Surg Instructional Course Lectures. 1948;5:261–75.
4. Vasiliadis ES, Grivas TB, Kaspiris A. Historical overview of spinal deformities in ancient Greece. Scoliosis. 2009;4:6.
5. Kane WJ. Scoliosis prevalence: a call for a statement of terms. Clin Orthop Relat Res. 1977(126):43-6.
6. Boseker EH, Moe JH, Winter RB, Koop SE. Determination of "normal" thoracic kyphosis: a roentgenographic study of 121 "normal" children. J Pediatr Orthop. 2000;20(6):796-8.

4. Page 8, lines 38-40: postural changes, muscle weakness, and intervertebral ligament degeneration ". Comment: Please, add bibliographic references that report this statement.

Response: We thank reviewer for the valuable comment. We have included the references for postural changes, muscle weakness, and intervertebral ligament degeneration. (PDF proof P.7-P.8)
References:
13. Axenovich TI, Zaidman AM, Zorkoltseva IV, Kalashnikova EV, Borodin PM. Segregation analysis of Scheuermann disease in ninety families from Siberia. Am J Med Genet. 2001;100(4):275-9.
14. Schneider DL, von Muhlen D, Barrett-Connor E, Sartoris DJ. Kyphosis does not equal vertebral fractures: the Rancho Bernardo study. J Rheumatol. 2004;31(4):747-52.
15. Kado DM, Prenovost K, Crandall C. Narrative review: hyperkyphosis in older persons. Ann Intern Med. 2007;147(5):330-8.
16. Boyle JJ, Milne N, Singer KP. Influence of age on cervicothoracic spinal curvature: an ex vivo radiographic survey. Clin Biomech (Bristol, Avon). 2002;17(5):361-7.
17. Vialle R, Levassor N, Rillardon L, Templier A, Skalli W, Guigui P. Radiographic analysis of the sagittal alignment and balance of the spine in asymptomatic subjects. J Bone Joint Surg Am. 2005;87(2):260-7.
18. Hinman MR. Comparison of thoracic kyphosis and postural stiffness in younger and older women. Spine J. 2004;4(4):413-7.
19. Mika A, Unnithan VB, Mika P. Differences in thoracic kyphosis and in back muscle strength in women with bone loss due to osteoporosis. Spine (Phila Pa 1976). 2005;30(2):241-6.
20. Brocklehurst JC, Robertson D, James-Groom P. Skeletal deformities in the elderly and their effect on postural sway. J Am Geriatr Soc. 1982;30(8):534-8.
21. Chow RK, Harrison JE. Relationship of kyphosis to physical fitness and bone mass on post-menopausal women. Am J Phys Med. 1987;66(5):219-27.
22. Sinaki M, Itoi E, Rogers JW, Bergstralh EJ, Wahner HW. Correlation of back extensor strength with thoracic kyphosis and lumbar lordosis in estrogen-deficient women. Am J Phys Med Rehabil. 1996;75(5):370-4.
23. Sinaki M, Brey RH, Hughes CA, Larson DR, Kaufman KR. Balance disorder and increased risk of falls in osteoporosis and kyphosis: significance of kyphotic posture and muscle strength. Osteoporos Int. 2005;16(8):1004-10.
24. Birnbaum K, Siebert CH, Hinkelmann J, Prescher A, Niethard FU. Correction of kyphotic deformity before and after transection of the anterior longitudinal ligament--a cadaver study. Arch Orthop Trauma Surg. 2001;121(3):142-7.
25. Esparza FV-C, Raquel & Alacid, Fernando & Martínez-Ruiz, E & López-Miñarro, Pedro. Sagittal spinal curvatures in maximal trunk flexion of young female dancers. British journal of sports medicine. 2014;48.:595.

5. Statistical analysis:
Comment: Please, add the power and sample size.

Response: Thanks for your comments and we have calculated the statistical power by the injury rates of spinal curvature disorders subjects (17.59 %, in 20,566) and non-spinal curvature disorders control (15.20%, in 41,132), in two-tailed examination while $p < 0.05$, the estimated statistical power for this study is 0.999." We have added these data in the Result section. (PDF proof P.14)

6. Discussion from page 14, line 54 to page 15, lines 4-38 the information reported is the same that in the results.

Response: We thank reviewer for pointing out this issue. We try to figure out the relationship and possible etiology between the result and previous studies, so the key results were mentioned in discussion for fluency.

7. Conclusion: The conclusion is obvious and generic. Any study related to spinal curvatures would report the same conclusion.

Response: We thank reviewer for the insight comment. We are interested in whether sequential association between spinal curvature disorders and injury or not. The demonstration of this association of this study is pleasant and may play a role of public health field or prevention policy. Otherwise, this is the first nationwide population-based cohort study to assess the associations between spinal curvature and injury.

8. References: Please, correct the reference number 1.

Response: We thank reviewer for pointing out this issue. We have corrected the reference typing error. (PDF proof P.18)

VERSION 2 – REVIEW

REVIEWER	Yu Yamato Hamamatsu University School of Medicine, Japan
REVIEW RETURNED	29-Jul-2018

GENERAL COMMENTS	I confirmed the authors revision.

REVIEWER	José M. Muyor University of Almería (Spain)
REVIEW RETURNED	12-Aug-2018

GENERAL COMMENTS	Authors have answered all questions/suggestions that were reported in the first revision.