The lower limit for FEV_1/FVC in dive medical assessments: a retrospective study

Thijs T Wingelaar[1,2], Peter-Jan AM van Ooij[1,3], Edwin L Endert[1]

[1] *Diving and Submarine Medical Centre, Royal Netherlands Navy, the Netherlands*
[2] *Department of Anaesthesiology, Amsterdam University Medical Centres, Amsterdam Medical Centre, the Netherlands*
[3] *Department of Respiratory Medicine, Amsterdam University Medical Centres, Amsterdam Medical Centre, the Netherlands*

Corresponding author: *Dr Thijs Wingelaar, Royal Netherlands Navy Diving Medical Centre, Rijkszee en marinehaven, 1780 CA, Den Helder, the Netherlands*
tt.wingelaar@mindef.nl

Key words
Fitness to dive; Health surveillance; Lung function; Military diving

Abstract
(Wingelaar TT, van Ooij PJAM, Endert EL. The lower limit for FEV_1/FVC in dive medical assessments: a retrospective study. Diving and Hyperbaric Medicine. 2021 December 20;51(4):368–372. doi: 10.28920/dhm51.4.368-372. PMID: 34897602.)
Introduction: Interpreting pulmonary function test (PFT) results requires a valid reference set and a cut-off differentiating pathological from physiological pulmonary function; the lower limit of normal (LLN). However, in diving medicine it is unclear whether an LLN of 2.5% (LLN-2.5) or 5% (LLN-5) in healthy subjects constitutes an appropriate cut-off.
Methods: All PFTs performed at the Royal Netherlands Navy Diving Medical Centre between 1 January 2015 and 1 January 2021 resulting in a forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and/or FEV_1/FVC with a Z-score between -1.64 (LLN-5) and -1.96 (LLN-2.5) were included. Records were screened for additional tests, referral to a pulmonary specialist, results of radiological imaging, and fitness to dive.
Results: Analysis of 2,108 assessments in 814 subjects showed that 83 subjects, 74 men and nine women, mean age 32.4 (SD 8.2) years and height 182 (7.0) cm, had an FVC, FEV_1 and/or FEV_1/FVC with Z-scores between -1.64 and -1.96. Of these 83 subjects, 35 (42%) underwent additional tests, 77 (93%) were referred to a pulmonary specialist and 31 (37%) underwent high-resolution CT-imaging. Ten subjects (12%) were declared 'unfit to dive' for various reasons. Information from their medical history could have identified these individuals.
Conclusions: Use of LLN-2.5 rather than LLN-5 for FEV_1/FVC in asymptomatic individuals reduces additional investigations and referrals to a pulmonary specialist without missing important diagnoses, provided a thorough medical history is taken. Adoption of LLN-2.5 could save resources spent on diving medical assessments and protect subjects from harmful side effects associated with additional investigations, while maintaining an equal level of safety.

Introduction

Fitness to dive assessments are performed to identify potential medical risks that can lead to harm in diving.[1] Despite differences in fitness required for recreational, commercial and military diving, evaluating the pulmonary tract is paramount in these assessments, as the lungs and airways must adapt significantly to submersion.[2] Pulmonary function tests (PFTs), especially spirometry, are used frequently to evaluate pulmonary status.[1,3,4]

Because pulmonary functions are biological variables with significant variability, a valid set of reference values is necessary to separate physiologic from pathologic pulmonary function.[4,5] The acceptable lower limit of normal (LLN) in asymptomatic individuals has varied over the years and among reference sets.[6] Traditionally, fitness to dive standards have suggested that LLN be a percentage of a predicted value based on sex, age and height. This LLN was usually defined as between 70% and 80% of predicted value, as was common for pulmonary medicine.[7] With the introduction of the Global Lung Initiative (GLI-2012), spirometry results are regarded as normally distributed parameters, with the results for each individual represented as Z-scores.[8] Z-scores have been found to better represent pulmonary status than percentages of predicted values.[8,9] Several studies have shown that defining the lower limit of normal (LLN) as a fixed ratio leads to extensive under- and over diagnosing in younger and older adults respectively.[9,10]

Despite the use of more reliable reference sets, such as the GLI-2012, the cut-off for LLN in fitness to dive assessments aiming to differentiate normal variations from potentially harmful findings remains unclear, especially in the absence of pulmonary complaints.[5] Pulmonologists have regarded the lowest 2.5% of the population (LLN-2.5), equivalent to a Z-score of -1.96 or lower, as potentially pathologic in asymptomatic individuals. By contrast, the Royal Netherlands Navy has adopted a more conservative cut-off, using the lowest 5% of the population (LLN-5), equivalent to a Z-score of -1.64 or lower, as the lower limit when transitioning from the European Respiratory Society

(ERS-1993) to the GLI-2012 dataset.[11] To determine whether LLNs below these cut-offs are potentially pathological, subjects must undergo additional testing, such as full-body plethysmography to determine the static lung volumes, bronchial challenge tests to exclude bronchial hyperreactivity and/or referral to a pulmonary specialist for additional tests like radiological imaging such as high-resolution computerized tomography (HRCT) or testing for dynamic hyperinflation.

This study was designed to determine the effect of using LLN-5 or LLN-2.5 as the cut-off value for PFTs in asymptomatic divers. We hypothesised that lowering the LLN to LLN-2.5 would not result in missing relevant diagnoses in fitness to dive assessments.

Methods

The Royal Netherlands Navy Diving Medical Centre medically assesses divers, submariners and inside chamber tender personnel (i.e., hyperbaric physicians and nurses) annually. All fitness to dive assessments were performed according to European Diving Technology Committee (EDTC) guidelines, except that PFT results have been interpreted relative to the GLI-2012 reference set beginning on 01 January 2015.[3,11] All data were stored in an electronic medical database.

All medical assessments of military divers between 01 January 2015 and 01 January 2021 showing a forced vital capacity (FVC), forced expiratory volume in one second (FEV_1) and/or FEV1/FVC with a Z-score between -1.64 (LLN-5) and -1.96 (LLN-2.5) were included in the analysis. Age, sex, ethnicity, height and smoking status were recorded. Medical assessments were evaluated to determine whether a subject had undergone additional testing at the Diving Medical Centre or was referred to a military pulmonary specialist at the Central Military Hospital (Utrecht, the Netherlands). Other parameters recorded including the results of radiological imaging and whether the subject was declared fit or unfit to dive.

According to national law and legislation, retrospective analyses are not required to be evaluated by a medical ethics committee. The methods used to handle personal details and privacy were in agreement with the guidelines of the Association of Universities in the Netherlands and the Declaration of Helsinki.

Results

During the 6-year study period, 814 subjects underwent 2,108 medical assessments. Of these 814 subjects, 83 (10%) had PFTs lower than LLN-5 but higher than LLN-2.5 (i.e., Z-scores between -1.96 and -1.64). These Z-scores may represent FVC, FEV_1, FEV_1/FVC-ratio or combinations of these variables. These 83 subjects included 74 (89%) men and nine (11%) women, of mean age 32.4 (SD 8.2) years and height 182 (7.0) cm. These results, as well as the PFT results, are shown in Table 1. None of the FVC and only four FEV_1 values were lower than LLN-5 (Z-score range FVC: -1.44 to +2.87, FEV_1: -2.25 to +1.27). Thus, the predominant variable with a Z-score in the targeted range was FEV_1/FVC. To give our population more context: 49 subjects of the total population (6%) had a FEV_1/FVC lower than LLN-2.5 (Z-score range -2.92 to -1.97, mean -2.33), with FVC ranging from -1.33 to 2.86 (mean 0.87) and FEV_1 from -2.8 to 1.04 (mean -0.92).

Of the 83 subjects with Z-scores between -1.64 and -1.96, 35 (42%) underwent additional investigations at the Diving Medical Centre (specified in Table 2) and 77 (93%) were referred to a pulmonary specialist in the military hospital, with 31 (37%) undergoing high-resolution computerised tomography (HRCT). Some of the included subjects may have undergone additional evaluations at the Diving Medical Centre before being referred to a pulmonary specialist.

In total, 10 (12%) of the subjects did not meet the criteria for 'fit to dive'. Four of these subjects chose not to pursue a diving career after having failed to meet the PFT requirements (all had a FEV_1/FVC between LLN-5 and LLN-2.5) on their first assessment. The other six subjects were declared 'unfit to dive' after additional testing. Two

Table 1
Baseline characteristics of 83 study subjects; data are mean (SD). FVC – forced vital capacity; FEV_1 – forced expiratory volume in one second

Parameter	Total (*n* = 83)	Male (*n* = 74)	Female (*n* = 9)
Age (years)	32.4 (8.1)	32.3 (8.1)	33.2 (8.2)
Height (cm)	182 (6.8)	183 (6.6)	175 (4.4)
FVC (L)	6.14 (0.82)	6.32 (0.67)	4.77 (0.56)
FVC (Z-score)	0.75 (0.83)	0.77 (0.82)	0.58 (0.85)
FEV_1 (L)	4.30 (0.55)	4.42 (0.45)	3.41 (0.42)
FEV_1 (Z-score)	-0.52 (0.72)	-0.51 (0.71)	-0.61 (0.72)
FEV_1/FVC (%)	0.70 (0.02)	0.70 (0.02)	0.71 (0.02)
FEV_1/FVC (Z-score)	-1.80 (0.83)	-1.80 (0.82)	-1.75 (0.85)

Table 2
Tests and referrals performed after PFT results in 83 divers with spirometry Z-scores between -1.64 and -1.96

35 (42%) additional investigations at the Diving Medical Centre: - 35 spirometry - 5 end-expiratory lung volume tests during exercise - 2 bronchial challenge tests -2 exercise-induced bronchoconstriction tests
77 (93%) referrals to a pulmonary specialist at the Central Military Hospital: - 77 spirometry - 31 high-resolution computerised tomography • 26 subjects without clinically significant findings • 1 subject with minimal air trapping in secondary lobules, determined by the pulmonary specialist as not being a risk for diving • 1 subject with severe air trapping and a history that included pneumonia and pneumothorax • 3 unexpected findings: schwannoma, haemangioma and paraseptal emphysema.

of these subjects had FEV_1/FVC lower than LLN-2.5 after retesting and were declared medically unfit for diving. Two subjects failed bronchial challenge testing after having met the spirometry requirements at a later stage. One subject showed reversibility on spirometry after testing with salbutamol and was later diagnosed with asthma by a pulmonary specialist. Finally, one subject had a medical history that included pneumonia and traumatic pneumothorax, for which he was referred to a pulmonary specialist, with HRCT showing trapped air. All divers underwent bronchial challenge testing at the start of their diving career and are subjected to both spirometry and exercise tolerance testing annually to meet national legislation requirements.

Discussion

This study indicated that use of LLN-2.5 (Z-score of -1.96) rather than LLN-5 (Z-score of -1.64) as a cut-off point for spirometry would reduce the number of additional tests and referrals to a pulmonary specialist without missing significant diagnoses. Diagnoses that led to disqualification from diving were also identified through history taking or the finding of reversibility on spirometry. Adoption of the LLN-2.5 cut-off would have saved time and resources associated with additional investigations and referral to a pulmonary specialist in 10% of our diving population.

These results are in agreement with the recommendations of the GLI-2012 taskforce for evaluating asymptomatic individuals,[8,10] as well as with a study in aviators showing that using LLN-2.5 rather than LLN-5 reduced the number of referrals significantly.[12] In the latter study, the reduction of referrals was more profound in men aged > 40 years, but was also observed in men aged < 25 years and in women. Because men constituted 89% of our study population, with too few women included for subgroup analysis, we cannot validate these findings for female divers specifically.

A higher-than-expected percentage of our population (10%) fell within the range between LLN-5 and LLN-2.5. By definition this should constitute only 2.5% of the total population We could not find seasonal effects or other explanations for this finding. However, (Dutch) Navy divers cannot be considered a representative sample of the general population due to selection bias in the Armed Forces. With a FVC generally higher than normal and a regular FEV_1, the FEV_1/FVC-ratio tends to be lower. A long-standing military diving career does not seem to negatively affect pulmonary function, although sufficiently powered prospective research is not available.[13,14] Another remarkable observation in this study was the low percentage of clinically significant findings on HRCT, as previous studies have shown that this percentage could be as high as 34%.[15,16] While this could be expected, as PFTs are a functional test and imaging relates to structural changes, this contradicts earlier findings of frequent anomalies on HRCT in dive medical assessments of healthy subjects.[15,16] We feel these findings emphasise the safety of refraining from both additional testing and referral to a pulmonary specialist in subjects with a FEV_1/FVC between LLN-5 and LLN-2.5.

Fewer false-positive PFT results would save time and resources during the process of dive medical assessments, which in our military population reduces the downtime of important operational assets of the Royal Netherlands Navy. Additionally, every additional test may provide findings of unknown clinical significance, which could lead to disqualification of a diver due to legal issues. The findings of this study are in agreement with studies that emphasise the need for more clinically driven assessments of divers rather than a legal approach consisting of annual assessments with mandatory boxes that have to be ticked.[1] For instance, a Dutch Marine who recently broke the world record speed marching (i.e., running a full marathon in military attire and a 18 kg rucksack) still had to participate in an exercise tolerance test for his dive medical assessment to ensure his fitness met the professional standards.[1,17] The argument could be made that this could have been concluded from the history taking alone.

STRENGTHS AND LIMITATIONS

To our knowledge this is the first study that assesses the LLN of PFTs in military divers. PFTs are a cornerstone of dive medical assessments, and, due to the ongoing COVID-19 pandemic, are likely to remain of great value. This emphasises the great importance of separating physiologic from pathologic pulmonary function. Moreover, a sensible policy for additional investigations or referral to a pulmonary specialist, preferably with experience in diving medicine, can save resources and prevent exposure to the potentially harmful effects of radiation, as well as reducing the likelihood of clinically insignificant findings.

This study had several limitations. First, the study population was biased towards healthy and physically fit young adults, predominantly men. Although this makes the results more relevant to military diving personnel, care should be exercised in extrapolating these results to other populations. Although these results may not be applicable to leisure or sports diving or submariners, the study population resembles commercial divers, suggesting that our results may be relevant to this group. Moreover, it could be argued that the GLI-2012 does not optimally represent our population, as the Z-score of the FVC is on average 0.75, where 0 would be expected. However, our sample size of 83 is too small to conclude the GLI-2012 is invalid for the Dutch military diving population. We feel the GLI-2012 is currently the most appropriate dataset for evaluating PFTs in Dutch military personnel, although future research might lead to the development of a specific dataset, as has been proposed for other specific populations.[18]

Secondly, our results were gathered using our earlier published algorithm.[10] We are aware that other dive medical physicians use different reference sets for interpreting PFT results, as well as different strategies that prompt additional tests and referrals to pulmonary specialists. Studies are needed to determine whether our results can be replicated in other populations. As retrospective studies have their limitations, for instance in the case of incomplete records or unclear deviations from the algorithm, a prospective study with a sufficiently long follow-up is required to ensure the suggested more permissive range does not result in harm.

Finally, using slow vital capacity (SVC) rather than FVC to evaluate PFTs may yield more accurate results, because SVC is less affected by technique than FVC. However, at time of this study, the GLI has not published Z-scores associated with SVC, which would have required the use of the outdated ERS-1993 dataset for interpretation of the PFT results. Because the GLI-2012 dataset is more accurate than the ERS-1993 reference values, use of a more reliable dataset would likely provide better results. Additionally, PFTs are performed under supervision of qualified and experienced pulmonary function technicians until reliable end-of-test criteria are met. These findings indicate that the presented data using FVC are valid and support the conclusion of this study.

Conclusion

Adopting the GLI-2012 LLN-2.5 rather than LLN-5 as a cut-off point for FEV_1/FVC in asymptomatic individuals reduces the number of additional tests and referrals to a pulmonary specialist without missing important diagnoses. Taking a thorough history and performing spirometry according to professional standards would save time and resources spent on dive medical assessments and protect subjects from harmful side effects of additional tests, such as radiation. Use of LLN-2.5 for FEV_1/FVC would also avoid findings of unknown clinical significance, which often trigger further tests and potentially disqualify subjects for diving, while maintaining an equal level of safety for divers.

References

1 The medical examination and assessment of commercial divers. Health and Safety Executive; 2015 (revision 4). [cited 2021/08/01]. Available from: https://www.hse.gov.uk/pubns/ma1.htm.

2 Pendergast DR, Lundgren CEG. The physiology and pathophysiology of the hyperbaric and diving environments. J Appl Physiol (1985). 2009;106:274–5. doi: 10.1152/japplphysiol.91477.2008. PMID: 19023014.

3 Wendling J, Elliott D, Nome T, editors. Fitness to dive standards. Guidelines for medical assessment of working divers. Biele-Biene: European Diving Technology Committee; 2003. [cited 2011/08/01]. Available from: http://edtc.org/wp-content/uploads/2020/05/EDTC-Fitnesstodivestandard-2003.pdf.

4 Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26:948–68. doi: 10.1183/09031936.05.00035205. PMID: 16264058.

5 Celli BR, Halbert RJ, Isonaka S, Schau B. Population impact of different definitions of airway obstruction. Eur Respir J. 2003;22:268–73. doi: 10.1183/09031936.03.00075102. PMID: 12952259.

6 Quanjer PH, Brazzale DJ, Boros PW, Pretto JJ. Implications of adopting the Global Lungs Initiative 2012 all-age reference equations for spirometry. Eur Respir J. 2013;42:1046–54. doi: 10.1183/09031936.00195512. PMID: 23520323.

7 Singh D, Agusti A, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease: the GOLD science committee report 2019. Eur Respir J. 2019;53(5):1900164. doi: 10.1183/13993003.00164-2019. PMID: 30846476.

8 Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3–95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012;40:1324–43. doi: 10.1183/09031936.00080312. PMID: 22743675. PMCID: PMC3786581.

9 Swanney MP, Ruppel G, Enright PL, Pedersen OF, Crapo RO, Miller MR, et al. Using the lower limit of normal for the FEV1/FVC ratio reduces the misclassification of airway obstruction.

Thorax. 2008;63:1046–51. doi: 10.1136/thx.2008.098483. PMID: 18786983.
10 Hansen JE, Sun XG, Wasserman K. Spirometric criteria for airway obstruction: use percentage of FEV1/FVC ratio below the fifth percentile, not 70%. Chest. 2007;131:349–55. doi: 10.1378/chest.06-1349. PMID: 17296632.
11 Wingelaar TT, Clarijs P, van Ooij PA, Koch DA, van Hulst RA. Modern assessment of pulmonary function in divers cannot rely on old reference values. Diving Hyperb Med. 2018;48:17–22. doi: 10.28920/dhm48.1.17-22. PMID: 29557097. PMCID: PMC6467825.
12 Wingelaar-Jagt YQ, Wingelaar TT, Bülbül M, Vd Bergh PP, Frijters E, Staudt E. The effect of using the lower limit of normal 2.5 in pulmonary aeromedical assessments. Aerosp Med Hum Perform. 2020;91:636–40. doi: 10.3357/AMHP.5566.2020. PMID: 32693871.
13 Voortman M, van Ooij PJAM, van Hulst RA, Zanen P. Pulmonary function changes in Navy divers during their professional careers. Undersea Hyperb Med. 2016;43:649–57. PMID: 28768392.
14 Sames C, Gorman DF, Mitchell SJ, Zhou L. Long-term changes in spirometry in occupational divers: a 10–25 year audit. Diving Hyperb Med. 2018;48:10–6. doi: 10.28920/dhm48.1.10-16. PMID: 29557096. PMCID: PMC6467824.
15 de Bakker HM, Tijsterman M, de Bakker-Teunissen OJG, Soerdjbalie-Maikoe V, van Hulst RA, de Bakker BS. Prevalence of pulmonary bullae and blebs in postmortem CT imaging with potential implications for diving medicine. Chest. 2020;157:916–23. doi: 10.1016/j.chest.2019.11.008. PMID: 31759963.
16 Wingelaar TT, Bakker L, Nap FJ, van Ooij PJAM, Endert EL, van Hulst RA. Routine chest X-rays are inaccurate in detecting relevant intrapulmonary anomalies during medical assessments of fitness to dive. Front Physiol. 2021;11:613398. doi: 10.3389/fphys.2020.613398. PMID: 33488401. PMCID: PMC7816860.
17 Royal Netherland Navy. Livestream – Wereld Record Speedmars door Korps Mariniers. Streamed live on Oct 24 2020. Available from: https://www.youtube.com/watch?v=397MC1FwqCY.
18 Kainu A, Timonen KL, Toikka J, Qaiser B, Pitkäniemi J, Kotaniemi JT, et al. Reference values of spirometry for Finnish adults. Clin Physiol Funct Imaging. 2016;36:346–58. doi: 10.1111/cpf.12237. PMID: 25817817.

Conflicts of interest and funding: nil

Submitted: 10 August 2021
Accepted after revision: 02 October 2021