Work and Health
https://www.sciltp.com/journals/wah

Article

Cardiometabolic Pattern of Workers Unfit for High-Altitude Occupational Exposure in Chile: A Large-Scale Retrospective Analysis Using a Random Forest Model ‡

Ricardo Jorquera [1], Guillermo Droppelmann [2,*,†], Gonzalo Blanco [1], Max Dollmann [1], Ignacio Ahumada [1] and Felipe Feijoo [3,†]

1 Workmed, Santiago, Región Metropolitana 7500994, Chile
2 Clínica MEDS, Santiago, Región Metropolitana 7691236, Chile
3 School of Industrial Engineering, Pontificia Universidad Católica de Valparaíso, Valparaíso 2340000, Chile
* Correspondence: guillermo.droppelmann@meds.cl
† These authors contributed equally to this work.
‡ Based on an oral presentation at the 2025 ICOH-SCOM Congress, Lima, Peru, 11–13 December 2025.

How To Cite: Jorquera, R.; Droppelmann, G.; Blanco, G.; et al. Cardiometabolic Pattern of Workers Unfit for High-Altitude Occupational Exposure in Chile: A Large-Scale Retrospective Analysis Using a Random Forest Model. *Work and Health* **2026**, *2*(2), 10. https://doi.org/10.53941/wah.2026.100010

Received: 14 April 2026
Revised: 20 May 2026
Accepted: 5 June 2026
Published: 18 June 2026

Abstract: Workers exposed to chronic intermittent hypobaric hypoxia at high altitude (HA) face substantial cardiometabolic demands that may compromise occupational safety. Fitness-for-work (FFW) assessments are routinely performed in Chile under nationally standardized guidelines, yet the internal structure of the unfit population and codependence among predictive biomarkers remain poorly characterized. This retrospective study analyzed 48,783 workers undergoing mandatory pre-employment FFW evaluations for HA exposure in Chile (2021–2024), of whom 8% were classified as unfit for work (UFW). A supervised Random Forest model, applied to more than 20 clinical, physiological, and laboratory variables, identified key predictors of FFW classification by capturing nonlinear interactions among variables that univariate approaches cannot detect. The model achieved precision 0.90 (95% CI: 0.89–0.92), sensitivity 0.93, specificity 0.88, and kappa 0.807. Body mass index was the most influential predictor, followed by fasting plasma glucose, triglycerides, and systolic blood pressure. Among unfit workers, severe obesity (BMI ≥ 35 kg/m^2) was the most prevalent condition (34%), followed by altered fasting glucose (16%), elevated systolic blood pressure (10%), and severe hypertriglyceridemia (9%). The unfit population was predominantly male with age-related distribution. These findings reveal a cardiometabolic pattern as the dominant driver of HA occupational unfitness. Targeted strategies addressing obesity, glycemia, and dyslipidemia, alongside risk-based monitoring aligned with Chile's national standards, may reduce exclusion rates and support more individualized FFW evaluations in HA settings. Aim: to characterize dominant cardiometabolic patterns in workers classified as unfit for HA occupational exposure in Chile and to quantify their relative weight using a Random Forest variable-importance framework. Methods: retrospective analysis of 48,783 pre-employment FFW evaluations (2021–2024) from a national occupational-health surveillance system; supervised Random Forest model with stratified 70/30 train-test split and repeated 10-fold cross-validation. Conclusion: targeted preventive strategies focused on obesity, glycemia, and dyslipidemia, combined with structured re-evaluation pathways, could reduce HA occupational exclusion and inform the future refinement of FFW criteria.

Keywords: artificial intelligence; biomarkers; cardiovascular risk; fitness-for-work; hypobaric hypoxia; occupational medicine; random forest

1. Introduction

High-altitude (HA) occupational environments expose workers to chronic intermittent hypobaric hypoxia, a physiological stressor that challenges cardiovascular, metabolic, and hematological regulation daily [1–3]. While many individuals adapt sufficiently to these conditions, a non-negligible proportion develops alterations that compromise health, functional capacity, and occupational safety. In countries with extensive mining and industrial activity at altitude, such as Chile, this reality affects a substantial workforce and has positioned fitness-for-work (FFW) evaluations as a central pillar of occupational health practice [4].

Within the Chilean context, mining represents one of the largest economic sectors of the country, historically contributing close to 10–15% of national GDP and around half of total exports, primarily through copper and, increasingly, lithium production. An estimated population of more than 80,000 workers is regularly exposed to chronic intermittent hypobaric hypoxia at operational altitudes between 3000 and 4500 m, working under rotational shift schedules (commonly 7 × 7, 14 × 14, or 4 × 4 days). High-altitude shift work is typically associated with a salary premium relative to comparable low-altitude positions, which compensates for the physical and physiological burden involved. Worker protection is structured through Law 16,744 on occupational accidents and diseases, complemented by the technical guideline on chronic intermittent hypobaria issued by the Ministry of Health (MINSAL) and by the compendium of regulations of the Superintendence of Social Security (SUSESO) [5,6].

Typical HA tasks include open-pit and underground mining operations, heavy-machinery operation, processing-plant duties, and maintenance work, performed under combined exposure to low oxygen partial pressure, cold temperatures, intense ultraviolet radiation, and very low humidity. These concurrent environmental stressors compound the cardiovascular and metabolic demands of chronic intermittent hypobaric hypoxia, making fitness-for-work (FFW) evaluations a central element of occupational health practice in this setting.

FFW assessments for HA exposure are regulated through national technical guidelines that define exclusion criteria based on predefined clinical, laboratory, and complementary examination thresholds [5,6]. These frameworks have undoubtedly contributed to risk reduction. However, they are largely built on static, single-parameter cutoffs and the isolated interpretation of health indicators. Such an approach may be poorly suited to reflect the multifactorial and dynamic nature of physiological vulnerability under hypoxic stress, where multiple cardiometabolic and cardiovascular factors often coexist and interact [7,8].

As a result, workers are commonly classified as unfit based on one or more abnormal findings, yet little is known about the internal structure of this group. Most occupational health studies in HA have focused on differentiating fit from unfit workers as a binary outcome, frequently emphasizing screening efficiency or predictive performance [9]. While this perspective is valuable for population-level surveillance, it provides limited insight into who the unfit workers are. Treating unfitness as a homogeneous state overlooks potential differences in age, cardiometabolic burden, severity of abnormalities, and, critically, the potential reversibility of the conditions leading to exclusion. Given the occupational, economic, and social consequences of being declared unfit for HA work, this lack of focused characterization represents a relevant and unresolved gap in literature.

Evidence consistently links cardiometabolic conditions, such as obesity, impaired glucose regulation, dyslipidemia, and elevated blood pressure, to reduced tolerance to hypoxic environments and increased cardiovascular strain [10–12]. Conditions involving intermittent hypoxia, including sleep-related breathing disorders, have also been associated with elevated cardiovascular risk, with physical activity emerging as a potential modifying factor [13]. Despite this growing body of evidence, the following key questions remain unanswered. Which conditions most frequently drive exclusion from HA work? Do these abnormalities cluster into recognizable profiles, or do they occur in isolation? And to what extent might different unfitness patterns imply different needs for follow-up, intervention, or re-evaluation?

Prior studies, including previous work from our group [14,15], have primarily addressed the discriminative question: which variables best separate workers who are fit from those who are unfit for HA exposure. While this approach is valuable for population-level screening, it treats unfitness as a homogeneous endpoint and provides no information about the clinical composition of the unfit group itself. Whether unfit workers share a common metabolic profile or represent a heterogeneous mix of conditions, whether specific abnormalities tend to co-occur, and whether different unfitness patterns carry different implications for intervention and re-evaluation, are questions that a discriminative model cannot answer by design. The present study therefore addresses a distinct and previously unexamined question: given that a worker has been classified as unfit for HA work, what does that population look like clinically? By concentrating exclusively on workers classified as UFW and applying a variable importance framework to characterize dominant health patterns within this subgroup, this work moves beyond the fit-versus-unfit binary and generates clinically actionable insight, specifically, the identification of modifiable metabolic targets that may support preventive strategies, structured re-evaluation pathways, and future refinement of FFW criteria in HA occupational settings. Although the predictive model was trained on the full evaluated cohort to optimize discrimination between fit and unfit workers, the interpretation of variable importance was specifically focused on characterizing the dominant clinical patterns within the unfit subgroup.

The aim of this study was to characterize the dominant clinical and cardiometabolic patterns of workers classified as unfit for HA occupational exposure in Chile, and to quantify the relative hierarchical weight of biomarkers driving this classification using a Random Forest variable-importance framework. The model is intended as an explanatory tool to inform preventive prioritisation and the design of structured re-evaluation pathways, not as a substitute for clinical judgement or for the regulatory criteria currently in force.

2. Materials and Methods

2.1. Study Design and Data Source

A retrospective observational study with an exploratory analytical approach was conducted using data collected during routine occupational medical assessments of workers evaluated for HA exposure in Chile. These assessments are part of mandatory fitness-for-work (FFW) procedures required by national regulations governing chronic intermittent hypobaric hypoxia. The study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.

Data were retrieved from Workmed's centralised occupational-health surveillance system, a harmonised electronic platform that consolidates pre-employment FFW evaluations conducted across multiple Chilean centers operating under MINSAL/SUSESO standards. Access was granted following Institutional Review Board approval, and all records were anonymized prior to analysis. The 2021–2024 study window was selected because it corresponds to the period in which the harmonised electronic record was fully deployed (ensuring uniform variable definitions and consistent laboratory reference ranges across centers) and because it captures the post-pandemic resumption of HA operations, which restored representative volumes and demographic structure of pre-employment FFW assessments.

2.2. Study Population

The study population comprised adult workers who underwent pre-employment medical evaluations for HA work between 2021 and 2024. FFW status was assigned during these evaluations based on standardized national criteria. Within the overall evaluated cohort, a minority of workers were classified as unfit for HA exposure. The primary analytical focus of this study was on workers classified as UFW. However, workers classified as FFW were retained within the dataset to enable comparative analyses and to support the training of the machine learning model used to derive variable importance estimates.

2.3. Determination of Unfitness for HA Work

Unfitness for HA exposure was determined during routine evaluations that included structured medical history, physical examination, laboratory testing, and complementary diagnostic procedures. Workers were classified as unfit when one or more assessed parameters exceeded contraindication thresholds established by national occupational health guidelines. These contraindications encompass metabolic, cardiovascular, renal, hematological, and other clinical conditions considered incompatible with safe HA exposure. Operationally, a worker was classified as unfit for HA exposure if at least one clinical, laboratory, or diagnostic parameter met or exceeded predefined contraindication thresholds established by national guidelines. These criteria were applied in a non-hierarchical manner, meaning that the presence of any single contraindication was sufficient to determine unfitness status. Specifically, the national instruments establish quantitative thresholds for cardiovascular (e.g., uncontrolled SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg, symptomatic ischaemic heart disease, decompensated arrhythmias), metabolic (e.g., BMI $\geq$ 35 kg/m^2, fasting plasma glucose $\geq$ 126 mg/dL, severe hypertriglyceridemia $\geq$ 500 mg/dL), respiratory (e.g., severe obstructive sleep apnoea, advanced COPD), hematological (e.g., hemoglobin > 18.5 g/dL in males or >16.5 g/dL in females; polycythaemia vera), renal (eGFR < 60 mL/min/1.73 m^2), neurological, ophthalmological, and otologic conditions. The post-evaluation pathway prescribed by the guidelines includes counselling on modifiable factors, optional re-evaluation after a defined interval, and redirection to non-HA roles when applicable, with the occupational-medicine physician retaining the final fitness decision.

2.4. Health Variables and Indicators

The analysis focused on clinical and laboratory variables most frequently implicated in unfitness determinations. These included age, sex, body mass index (BMI), fasting plasma glucose, triglycerides, systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, hemoglobin concentration, and serum creatinine. Lifestyle-related information, including smoking status and self-reported physical activity, was collected during standardized occupational health interviews.

For analytical purposes, age was treated both as a continuous variable and as a categorical variable. Age categories were defined a priori as ≤40 years, 41–55 years, and >55 years, reflecting commonly used strata in occupational and cardiovascular risk assessment. The ≤40-year group was used as the reference category for comparative analyses.

For descriptive analyses, variables were additionally categorized according to whether they met or exceeded regulatory cutoff values commonly used to define unfitness. This approach allowed estimation of the relative contribution of different health conditions to unfitness within the study population.

2.5. Data Management and Preprocessing

Data management procedures were implemented to ensure analytical reliability. Records were screened for duplication, extreme or implausible values were reviewed, and variable units were standardized across centers. Missing data were minimal (0.5% across all variables), and no variable exceeded 1% missingness. Missing values were addressed using median imputation for continuous variables and mode imputation for categorical variables, which was considered appropriate given the low proportion of missing data. Sensitivity analyses comparing models trained with imputed data and complete-case data showed no meaningful differences in performance, supporting the robustness of the imputation approach.

2.6. Artificial Intelligence Approach and Variable Importance Assessment

A supervised Random Forest model was applied to the full evaluated cohort to classify workers as fit or unfit for HA exposure and to evaluate the relative importance of clinical and laboratory variables in predicting FFW status. The model was trained on the full evaluated cohort (n = 48,783), using FFW classification as the binary outcome (fit vs. unfit), to identify which clinical and laboratory variables most strongly predicted occupational fitness status. Variable importance estimates derived from this model were subsequently interpreted to characterize the dominant health determinants of HA occupational exclusion within the unfit subpopulation. It should be emphasised that the Random Forest model is used here as an explanatory tool to estimate variable importance and to capture nonlinear cardiometabolic interactions; it is not intended to replace the regulatory criteria used to declare unfitness, nor to be deployed as an individual-level diagnostic classifier. Clinical judgement and the existing MINSAL/SUSESO criteria remain the primary basis for the FFW decision.

Random Forest was selected due to its capacity to model nonlinear relationships and complex interactions among variables without requiring parametric assumptions, which is particularly advantageous in the context of cardiometabolic data. Although other machine learning algorithms, such as logistic regression, support vector machines, and gradient boosting methods, are commonly used for classification tasks, the primary objective of this study was not to optimize predictive performance through model comparison but to obtain a robust and interpretable estimation of variable importance within a high-dimensional clinical dataset. Random Forest provides stable and well-established variable importance measures, such as Mean Decrease in Accuracy, which are less sensitive to model misspecification and multicollinearity compared to traditional regression-based approaches. Therefore, this model was considered the most appropriate for addressing the explanatory objective of the present analysis. The full evaluated cohort (n = 48,783) was divided into a training set (70%, n = 34,148) and a testing set (30%, n = 14,635). The full evaluated cohort (n = 48,783) was randomly partitioned into a training set (70%; n = 34,148) and a held-out testing set (30%; n = 14,635); the split was stratified by the FFW outcome so that the approximately 92%/8% (FFW/UFW) class ratio was preserved in both partitions. Hyper-parameter tuning and resampling were performed exclusively within the training set, and the held-out testing set was used only once for final evaluation.

To address class imbalance, defined as a higher proportion of fit workers compared to unfit workers (approximately 92% vs. 8%), multiple balancing strategies were evaluated, including oversampling, downsampling, and hybrid approaches. These techniques were implemented within the cross-validation framework to prevent information leakage and ensure robust model training. The final model was trained using a hybrid resampling approach, selected based on optimal performance during cross-validation, balancing sensitivity and specificity while minimizing overfitting. This approach ensured that both classes were adequately represented during training, improving model generalization and reducing bias toward the majority class.

Model selection and hyperparameter tuning were performed using repeated 10-fold cross-validation, with resampling strategies applied within each training fold to prevent information leakage. The number of trees was varied across 1, 50, 100, and 500, while the mtry parameter was optimized through grid search. Variable importance was quantified using the Mean Decrease in Accuracy metric. In the classification framework, the unfit (UFW) class was treated as the positive class; sensitivity therefore reflects the proportion of unfit workers correctly identified, and specificity reflects the proportion of fit workers correctly classified.

2.7. Statistical Analysis

Descriptive analyses were performed to summarize demographic and clinical characteristics of the unfit population. Continuous variables were reported as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. The analytical strategy was exploratory and descriptive, and results were not intended to support causal inference. All analyses were conducted using R statistical software (R version 4.4.2 (2024-10-31 ucrt)) with reproducible analytical scripts.

2.8. Ethical Considerations

The study was based on anonymized secondary data obtained from routine occupational health assessments. All procedures complied with national ethical standards and the principles outlined in the Declaration of Helsinki. As no identifiable personal information was accessed and the study involved retrospective data analysis, the requirement for informed consent was waived.

3. Results

3.1. Study Population and General Characteristics

The study population was derived from a large-scale occupational health database comprising adult workers who underwent mandatory fitness-for-work medical evaluations for HA exposure. These evaluations were conducted as part of routine occupational health surveillance and followed standardized clinical and laboratory protocols across multiple centers within an integrated occupational health system.

Sample selection proceeded through successive filtering stages. From an initial dataset of 439,291 records, 12,934 cases were excluded due to incomplete evaluations, yielding a potential dataset of 426,357 individuals. An additional 5931 records were removed due to incomplete data, resulting in a preliminary dataset of 420,966 workers. Finally, 372,183 individuals without documented HA exposure were excluded, producing a final sample of 48,783 workers with confirmed HA exposure.

Of the total evaluated population, 3902 individuals, corresponding to 8% of all assessed workers, were classified as UFW, while the remaining 44,881 were deemed FFW. The UFW subgroup constituted the analytical population considered throughout the Results section, and all subsequent analyses were restricted to this population unless otherwise specified. Further details of the sample selection process are presented in Figure 1.

3.2. Baseline Characteristics and Clinical Profile

The demographic and clinical characteristics of the evaluated population are summarized in Table 1. UFW workers were significantly older than their FFW counterparts, with a mean age of 43.0 ± 11.2 years compared with 40.3 ± 10.5 years in the FFW group ($p < 0.001$). The sex distribution of the evaluated population was markedly skewed toward male workers, who accounted for 93.8% of all participants ($n = 45{,}743$), while females represented 6.2% ($n = 3040$). Within the UFW group, this disproportion was even more pronounced, with males comprising 94.0% ($n = 3668$) of unfit workers, reflecting the demographic composition of the occupational sectors evaluated for HA activities.

Regarding core metabolic biomarkers, UFW workers exhibited substantially higher mean values across all cardiometabolic variables compared with the FFW group. Mean BMI was 31.6 ± 5.4 kg/m^2 in the UFW group versus 28.1 ± 3.6 kg/m^2 in FFW workers ($p < 0.001$), while fasting glucose was markedly elevated in the UFW group (107 ± 38.4 mg/dL) relative to FFW workers (92.5 ± 10.1 mg/dL; $p < 0.001$). Mean systolic blood pressure was likewise higher among UFW workers (129 ± 13.6 mmHg) compared with FFW individuals (124 ± 10.5 mmHg; $p < 0.001$). Triglyceride levels followed a similar pattern, with UFW workers presenting a mean of 222 ± 114 mg/dL compared with 150 ± 78 mg/dL in the FFW group ($p < 0.001$).

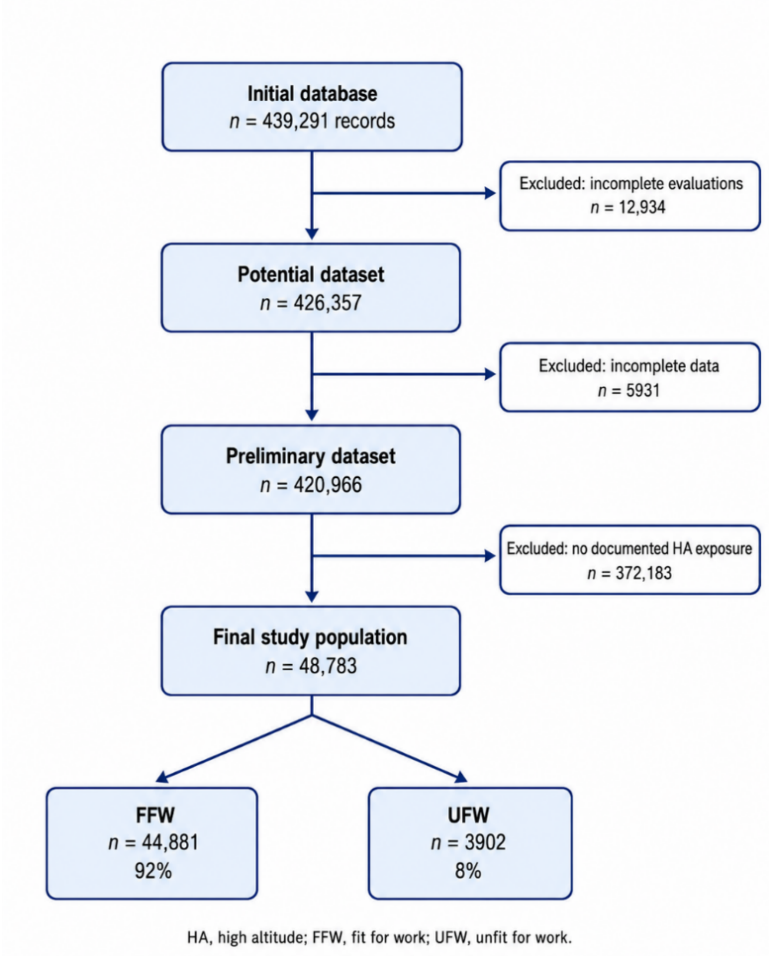

Figure 1. Flowchart of the study population selection process.

Among the 3902 UFW workers, four predominant disqualifying conditions were identified. Obesity, defined as BMI ≥ 35 kg/m^2, was the most frequent, affecting 1327 workers (34%), with mean BMI values of 38.8 kg/m^2 in females and 37.5 kg/m^2 in males ($p < 0.001$). Altered fasting glucose was present in 624 workers (16%), with mean values of 208 mg/dL in females and 174 mg/dL in males ($p < 0.001$). Severe systolic hypertension was identified in 390 workers (10%), with mean systolic blood pressure values of 156.5 mmHg and 155.8 mmHg in females and males, respectively ($p < 0.001$). Severe hypertriglyceridemia was recorded in 351 workers (9%), with markedly elevated mean triglyceride levels of 676.8 mg/dL in females and 768.7 mg/dL in males ($p < 0.001$). Across all four conditions, Chilean nationals constituted the vast majority of affected workers, ranging from 89.7% in the systolic hypertension subgroup to 92.4% in the hypertriglyceridemia subgroup, proportions broadly consistent with the nationality composition of the overall evaluated workforce. This finding suggests that nationality per se did not constitute an independent risk factor for UFW classification within these conditions.

With respect to additional biomarkers, UFW workers showed higher total cholesterol, lower HDL cholesterol, elevated diastolic blood pressure, and increased heart rate compared with FFW workers, all with statistically significant differences ($p < 0.001$). Hemoglobin and creatinine values were also reported, with between-group differences reaching statistical significance. Abnormal ECG findings were present in 12.4% of the total population (n = 6033), with a significantly higher prevalence among males (12.7%) than females (6.3%; $p < 0.001$). Audiometric abnormalities were detected in 21.1% of workers (n = 10,282), also with a marked male predominance (21.9% vs. 8.3%; $p < 0.001$). Visual acuity abnormalities were observed in 8.4% of the total sample, with no statistically significant sex difference ($p = 0.65$). Regarding lifestyle factors, regular physical activity was reported by 66.9% of workers, tobacco use by 40.2%, alcohol consumption by 67.0%, and illicit drug use by 4.6%, all with significant sex-based differences ($p < 0.001$). For further details, see Table 1.

Table 1. Baseline characteristics of the study population by sex and fitness-for-work (FFW) status, and severe predominant conditions among unfit-for-work (UFW). Pre-employment FFW evaluations for high-altitude (HA) occupational exposure, Chile, 2021–2024 (*n* = 48,783).

1. Core Biomarkers						
Variable	**Female (*n* = 3040) Mean ± SD**	**Male (*n* = 45,743) Mean ± SD**	**Total (*n* = 48,783) Mean ± SD**	**FFW (*n* = 44,881) Mean ± SD**	**UFW (*n* = 3902) Mean ± SD**	***p*-Value**
Age (years)	36.3 ± 9.0	40.8 ± 10.6	40.52 ± 10.56	40.3 ± 10.5	43.0 ± 11.2	<0.001
BMI (kg/m^2)	27.4 ± 4.55	28.4 ± 3.84	28.34 ± 3.90	28.1 ± 3.6	31.6 ± 5.4	<0.001
Glucose (mg/dL)	89.1 ± 15.5	94.0 ± 15.0	93.69 ± 15.08	92.5 ± 10.1	107 ± 38.4	<0.001
Triglycerides (mg/dL)	115 ± 65.4	158 ± 110	155.32 ± 108.26	150 ± 78	222 ± 114	<0.001
Systolic BP (mmHg)	119 ± 11.6	125 ± 10.4	124.63 ± 10.58	124 ± 10.5	129 ± 13.6	<0.001
2. Predominant Conditions among UFW Workers *(n* = 3902)						
	Female Mean (%)	**Male Mean (%)**	**Total *n* (%)**	***p*-Value**		
Obesity	38.8 kg/m^2 (9%)	37.5 kg/m^2 (91%)	1327 (34%)	<0.001		
Altered glucose	208 mg/dL (3.2%)	174 mg/dL (96.8%)	624 (16%)	<0.001		
Hypertriglyceridemia	676.8 mg/dL (1.3%)	768.7 mg/dL (98.7%)	351 (9%)	<0.001		
Systolic hypertension	156.5 mmHg (2.3%)	155.8 mmHg (97.7%)	390 (10%)	<0.001		
3. Additional Biomarkers						
Total cholesterol (mg/dL)	181 ± 36.9	190 ± 40.2	189.44 ± 40.06	<0.001		
HDL cholesterol (mg/dL)	57.2 ± 16.0	47.2 ± 12.3	47.82 ± 12.79	<0.001		
	Female Mean (%)	**Male Mean (%)**	**Total *n* (%)**	***p*-Value**		
Diastolic BP (mmHg)	74.8 ± 9.26	78.9 ± 8.2	78.64 ± 8.33	<0.001		
Heart rate (bpm)	73.0 ± 10.5	70.3 ± 11.1	70.47 ± 11.08	<0.001		
Cardiovascular risk score (CVR)	0.011 ± 0.004	0.015 ± 0.008	0.014 ± 0.007	<0.001		
Hemoglobin (g/dL)	13.9 ± 2.93	15.9 ± 2.69	15.78 ± 2.75	<0.001		
Creatinine (mg/dL)	0.78 ± 2.18	0.99 ± 2.78	0.98 ± 2.75	<0.001		
ECG (abnormal findings)	193 (6.3%)	5840 (12.7%)	6033 (12.4%)	<0.001		
Audiometry (abnormal findings)	253 (8.3%)	10,029 (21.9%)	10,282 (21.1%)	<0.001		
Visual acuity (abnormal)	248 (8.2%)	3848 (8.4%)	4096 (8.4%)	0.65		
Regular physical activity	1554 (51.1%)	31,083 (68.0%)	32,637 (66.9%)	<0.001		
Tobacco use	1095 (36.0%)	18,521 (40.5%)	19,616 (40.2%)	<0.001		
Alcohol consumption	1764 (58.0%)	30,909 (67.6%)	32,673 (67.0%)	<0.001		
Illicit drug use	83 (2.77%)	2155 (4.69%)	2238 (4.6%)	<0.001		

BMI, body mass index; BP, blood pressure; CVR, cardiovascular risk score; ECG, electrocardiogram; FFW, fit for work; HDL, high-density lipoprotein; HR, heart rate; SD, standard deviation; SBP, systolic blood pressure; TRI, triglycerides; UFW, unfit for work. Section 1: continuous variables compared by independent-samples *t*-test or Mann–Whitney U test; categorical variables by χ^2 test; FFW and UFW columns show overall (non-sex-stratified) means. Section 2: Female and Male columns show mean biomarker value and percentage sex distribution within each condition; Total shows n and percentage of all UFW workers (n = 3902); *p*-value from χ^2 test comparing observed sex distribution against the expected population ratio (Female 6.23%/Male 93.77%). Severity cut-offs: Obesity, BMI ≥ 35 kg/m^2; Altered glucose, ≥125 mg/dL; Systolic hypertension, SBP ≥ 140 mmHg; Hypertriglyceridemia, TRI ≥ 500 mg/dL. Section 3: continuous variables reported as Mean ± SD; categorical as n (%). — = not applicable or not reported in source data.

3.3. Variable Importance Analysis and Model Performance

An exploratory analytical framework based on a Random Forest model was applied to characterize the relative contribution of clinical and laboratory variables to health patterns within the unfit population. The model was trained on the full evaluated cohort (FFW vs. UFW) and achieved high discriminative performance. Variable importance estimates were subsequently used to identify which health indicators most strongly differentiated fit from unfit workers, with particular focus on characterizing the dominant clinical determinants of HA occupational exclusion. The variable importance analysis revealed a well-defined hierarchical structure among the evaluated indicators. BMI emerged as the most influential predictor by a substantial margin, followed by fasting plasma glucose, triglycerides, and systolic blood pressure. Hemoglobin and ECG findings demonstrated intermediate importance, while age-related and cardiovascular risk variables contributed to a lesser extent. The complete importance ranking across all variables is presented in Figure 2. Of note, while the descriptive prevalence of crossed thresholds (Section 3) is expected to reproduce the regulatory criteria by construction, the variable-importance hierarchy described in this subsection conveys complementary information by quantifying the joint discriminative weight of each biomarker once all variables are considered simultaneously.

In contrast, variables related to cardiovascular assessment status, such as normal electrocardiographic findings and normal cardiac evaluation, showed comparatively low importance scores. Categorical age indicators also contributed minimally to the overall importance profile. Taken together, the variable importance analysis was characterized by a predominance of metabolic-related indicators, with non-metabolic and categorical variables playing a more limited role. Figure 2 illustrates the hierarchical distribution of the relative importance of the variables included in the model.

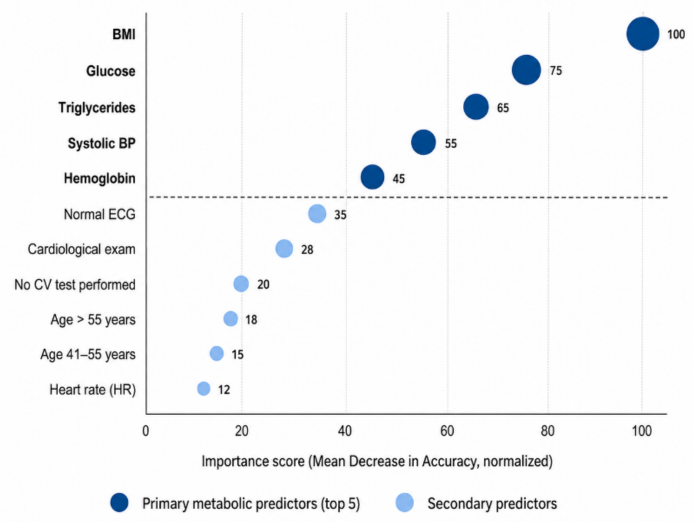

Figure 2. Variable importance derived from the Random Forest model trained on the full evaluated cohort (n = 48,783). Bubble position on the *x*-axis and bubble size both represent the Mean Decrease in Accuracy (MDA) importance score, normalised to BMI = 100. The five primary metabolic predictors (dark blue) account for the dominant share of the model's discriminative capacity. Secondary predictors (light blue) include electrocardiographic findings, cardiovascular risk score (CVR), age strata, and heart rate (HR).

On the other hand, the model performance was evaluated using a confusion matrix and standard classification metrics. The model demonstrated a high level of agreement between predicted and reference classifications. Specifically, 1086 individuals were correctly classified as negative and 1028 individuals as positive. Misclassification included 142 false negatives and 84 false positives, indicating a relatively low overall error rate. Overall classification accuracy reached 0.9034, with a 95% confidence interval ranging from 0.8907 to 0.9151 and significantly exceeded the no-information rate ($p < 0.001$). Balanced accuracy was also 0.9034, reflecting consistent performance across outcome categories. Agreement beyond chance was substantial, as indicated by a Cohen's kappa coefficient of 0.8068. Class-specific performance metrics showed a sensitivity of 0.9282 and a specificity of 0.8786. The positive predictive value was 0.8844, while the negative predictive value reached 0.9245, supporting the reliability of both positive and negative classifications. McNemar's test demonstrated a statistically significant asymmetry in misclassification patterns ($p < 0.001$). Model calibration was not formally assessed, which may limit interpretation of predicted probabilities despite strong classification performance.

Table 2 summarises the 2 × 2 confusion matrix obtained on the held-out testing set, together with the derived classification metrics.

Table 2. Confusion matrix and derived classification metrics for the Random Forest model on the held-out testing set (n = 2340 evaluated cases; UFW treated as the positive class).

	Predicted UFW (Positive)	**Predicted FFW (Negative)**
Actual UFW (positive)	True positives = 1028	False negatives = 142
Actual FFW (negative)	False positives = 84	True negatives = 1086
Derived metrics	Sensitivity = 0.928; Specificity = 0.879; PPV = 0.884; NPV = 0.925; Accuracy = 0.903 (95% CI 0.891–0.915); Balanced accuracy = 0.903; Cohen's kappa = 0.807.	

3.4. Predominant Clinical Conditions Associated with Unfitness

The distribution of clinical conditions contributing to unfitness showed clear patterns within the unfit population. The most frequently observed condition was severe obesity, defined as a body mass index of 35 kg/m^2 or higher, which affected 1327 individuals, representing 34% of all unfit workers. The second most common category comprised other clinical conditions grouped under a composite classification that included heterogeneous contraindications occurring at lower individual frequencies, accounting for 1210 cases (31%). Altered fasting plasma glucose, defined as 125 mg/dL or higher, was identified in 624 individuals (16%). Elevated systolic blood pressure, defined as 140 mmHg or higher, was observed in 390 cases (10%). Severe hypertriglyceridemia, defined as triglyceride levels of 500 mg/dL or higher, was present in 351 individuals (9%). Overall, the distribution of clinical conditions demonstrated a clear predominance of metabolic abnormalities among unfit workers, with obesity and dysglycemia accounting for a substantial proportion of unfitness determinations. Cardiovascular-related thresholds were also represented but occurred less frequently. As expected, because regulatory thresholds were used to assign UFW status, the descriptive distribution of crossed thresholds aligns with the criteria themselves; the analytical added value resides in the joint variable-importance hierarchy reported above, which incorporates nonlinear interactions among predictors.

The variable importance analysis derived from the random forest model confirmed this pattern, identifying body mass index, fasting plasma glucose, triglyceride levels, and systolic blood pressure as the four most influential contributors to unfitness classification, consistent with the clinical distribution described above. Figure 3 illustrates the distribution of these variables across fit and unfit populations, where the unfit group (target yes, shown in red) exhibited a rightward shift relative to the fit group (target no) across all four indicators.

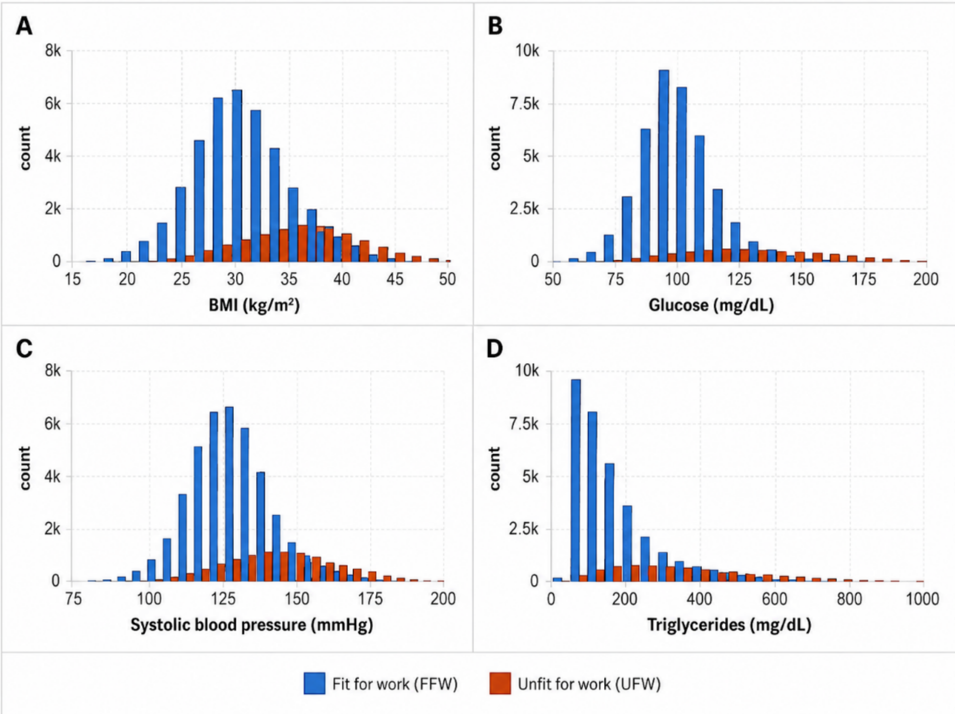

Figure 3. Distribution of core metabolic and physiological variables by fitness-for-work (FFW) classification. Each panel displays the frequency distribution for fit workers (FFW, blue) and unfit-for- worker (UFW, red), derived from pre-employment evaluations for high-altitude occupational exposure in Chile (2021–2024; n = 48,783). Panel **A**: body mass index (kg/m^2); Panel **B**: glucose (mg/dL); Panel **C**: systolic blood pressure (mmHg); Panel **D**: triglyceride levels (mg/dL). UFW workers consistently present right-shifted distributions across all four variables, reflecting higher metabolic burden relative to their FFW counterparts.

Body mass index showed pronounced differences between fit and unfit workers. Within the unfit population, 34% (n = 1327) met criteria for severe obesity. The distribution of body mass index values was markedly right-shifted, with a high concentration of observations within the obesity and severe obesity ranges. Among unfit individuals with severe obesity, 91% were male, with a mean body mass index of 37.5 kg/m^2, while female workers represented 9% and exhibited a slightly higher mean value of 38.8 kg/m^2, with a broader and more right-shifted distribution. Regarding nationality, 91.2% were Chilean nationals, with a mean body mass index of 37.6 kg/m^2, while 8.8% were foreign nationals, with a mean value of 38.1 kg/m^2. The distribution of body mass index values across fit and unfit populations is shown in Figure 3a.

Fasting plasma glucose showed increased variability and a pronounced rightward skew among unfit workers. Within the unfit population, 16% (n = 624) met criteria for elevated fasting plasma glucose. Men accounted for 96.8% of this subgroup, with a mean value of 174 mg/dL, while women represented 3.2% and showed higher mean values of 208 mg/dL with a broader distribution. Among Chilean nationals, who comprised 92% of this subgroup, the mean fasting plasma glucose was 175 mg/dL, compared with 172 mg/dL among foreign nationals, who accounted for the remaining 8%. The corresponding distribution across fitness-for-work categories is presented in Figure 3b.

Elevated systolic blood pressure was identified in 10% (n = 390) of unfit individuals. Men represented 97.7% of this subgroup and women 2.3%, with similar mean values of 155.8 mmHg and 156.5 mmHg, respectively. Chilean nationals accounted for 89.7% of cases, with a mean systolic blood pressure of 156 mmHg, while foreign nationals comprised 10.3%, with a mean value of 152 mmHg. The distribution of systolic blood pressure values by fitness-for-work classification is illustrated in Figure 3c.

Triglyceride levels showed the most extreme distributional asymmetry among the four conditions. Severe hypertriglyceridemia was identified in 9% (n = 351) of unfit individuals, with values concentrated at the far right tail of the distribution. Men accounted for 98.7% of this subgroup, with a mean triglyceride level of 768.7 mg/dL, while women represented 1.3%, with a mean value of 676.8 mg/dL. Chilean nationals comprised 92.4% of cases, with a mean of 769.6 mg/dL, compared with 703.3 mg/dL among foreign nationals, who accounted for 7.6%. Extreme triglyceride elevations were almost exclusively observed among male workers. The distribution of triglyceride levels across fitness-for-work categories is presented in Figure 3d.

Across all four conditions, the nationality distribution broadly reflected the composition of the overall evaluated workforce, with Chilean nationals consistently representing the vast majority of affected individuals. This pattern suggests that nationality was not a primary distinguishing factor within the evaluated conditions for unfitness classification within any of the evaluated conditions. For further details, see Table 1. This methodological check confirms that nationality did not act as an independent driver of UFW within this cohort; it was included exclusively to verify the absence of confounding by migrant-worker sub-populations and should not be interpreted as a substantive risk-factor question.

4. Discussion

This study provides one of the largest and most comprehensive characterizations of workers classified as unfit for HA occupational exposure reported to date. Among 48,783 workers evaluated over a four-year period, 8% were deemed UFW, with the unfit population defined predominantly by a dominant cardiometabolic pattern. Severe obesity was the leading disqualifying condition, affecting 34% of UFW workers, followed by altered fasting glucose (16%), elevated systolic blood pressure (10%), and severe hypertriglyceridemia (9%). Variable importance derived from a Random Forest model trained on the full evaluated cohort confirmed the hierarchical dominance of these metabolic biomarkers, with BMI emerging as the most influential variable, followed by fasting plasma glucose, triglycerides, and systolic blood pressure. The model achieved high classification accuracy (0.90), with a kappa coefficient of 0.81, supporting the internal validity of the observed patterns. Together, these findings support the presence of a dominant cardiometabolic pattern underlying unfitness for HA occupational exposure.

The central role of obesity in driving unfitness for HA work is consistent with evidence from other HA occupational cohorts. Studies in HA mining populations have shown that obesity and overweight are prevalent and closely associated with elevated blood pressure, cholesterol, and glucose levels, with obesity rates varying by occupational category [14,15]. Similarly, a prospective cohort study of workers at a gold mine in Kyrgyzstan operating at 3800–4500 m found that both age and BMI were independently associated with a greater likelihood of developing cardiovascular disease leading to unfitness, even after adjusting for lung function, baseline diagnoses, and blood pressure [13]. The convergence of these findings across geographically distinct populations reinforces the notion that elevated BMI represents a consistently identified and potentially modifiable risk factor in HA occupational health. Furthermore, recent evidence from Peruvian Andean mining workers suggests a dual physiological response to chronic intermittent hypobaric hypoxia, with erythropoietic adaptation coexisting with metabolic vulnerability, including a significantly greater prevalence of obesity compared to low-altitude controls [16–20]. This duality underscores the importance of metabolic surveillance beyond hematological markers in HA worker populations.

The co-occurrence of dysglycemia, hypertriglyceridemia, and hypertension within the unfit group points to a metabolic syndrome phenotype as a central driver of exclusion. Global data indicate that metabolic syndrome prevalence has approximately doubled between 2000 and 2023, now affecting an estimated 1.54 billion adults worldwide, with prevalence rising with age, urbanization, and income level [18]. In the Latin American context, a recent systematic review and meta-analysis of studies conducted between 2009 and 2024 found an overall metabolic syndrome prevalence of 40% across the region, with substantial variation by diagnostic criteria, sex, and country [19]. The patterns observed in our UFW population align with this regional burden and suggest that pre-employment HA evaluations are capturing workers who carry a substantial cardiometabolic risk profile that may not have been previously identified or managed. A systematic review examining metabolic syndrome prevalence at different altitudes found an overall prevalence of 30.3%, with an inverse relationship between altitude and metabolic syndrome prevalence, suggesting complex physiological interactions between hypoxia and metabolic dysregulation [20]. These findings support the interpretation that the metabolic profiles observed in our UFW population reflect a broader regional cardiometabolic burden rather than an altitude-specific phenomenon.

Several limitations of this study must be acknowledged. First, the retrospective cross-sectional design precludes any causal inference regarding the relationship between biomarker levels and unfitness outcomes. Second, the study population was derived from a single occupational health surveillance system operating within a specific regulatory framework, which may limit the generalizability of findings to other countries or industries with different HA exposure profiles and clinical evaluation protocols. Third, the analysis did not include information on treatment status or prior diagnoses, meaning that some workers classified as UFW may have had pre-existing managed conditions rather than newly identified abnormalities. Fourth, the predominantly male composition of the cohort, which reflects the occupational structure of the evaluated sectors, limits the ability to draw robust sex-stratified conclusions, particularly for female workers. Finally, while the Random Forest model demonstrated high internal performance, no external validation was performed, and model interpretability was limited to Mean Decrease in Accuracy. More advanced interpretability approaches, such as SHAP (SHapley Additive exPlanations), were not applied and may provide more granular insight into individual-level variable contributions in future analyses.

The predominance of modifiable metabolic conditions, including obesity, dysglycemia, and dyslipidemia, suggests that a substantial proportion of occupational exclusions may be preventable through targeted interventions. Evidence from HA occupational medicine suggests that existing pre-employment screening frameworks, while effective at identifying contraindications, are largely based on a nosological approach that may not adequately capture the cumulative risk attributed to a range of modifiable predictors such as age, BMI, and physical activity [15,16]. Reframing FFW evaluations to incorporate not only static exclusion criteria but also structured follow-up pathways and risk stratification tools could improve both worker health outcomes and occupational reintegration rates. In this regard, the application of data-driven approaches such as Random Forest to identify dominant health patterns represents a meaningful step toward more individualized and evidence-based occupational health assessments. Systematic reviews comparing machine learning models with conventional cardiovascular risk prediction algorithms have shown that such approaches can offer meaningful improvements in predictive performance, particularly in capturing complex interactions among multiple biomarkers [21,22]. Importantly, the objective of the present study was not to develop a predictive tool for clinical deployment, but to leverage machine learning as an exploratory framework to uncover latent structure and dominant patterns within a clinically defined subgroup. In this context, the use of Random Forest was not intended to outperform alternative models, but to provide a stable and interpretable estimation of variable importance capable of capturing nonlinear interactions among cardiometabolic variables.

Beyond individual clinical management, these findings have broader implications for occupational health policy in HA industries. The male predominance of both the evaluated population and the UFW group reflects the structural demographics of extractive industries in Chile and across the Andes, where physical labor remains heavily gendered. The age-related distribution in unfitness, with older workers carrying a greater burden of metabolic abnormalities, raises important questions about workforce sustainability, the timing of preventive interventions, and the adequacy of current periodic health surveillance protocols. Longitudinal data from HA mines indicate that smoking, lowland residence, and obesity are associated with earlier exit from work, suggesting that cardiometabolic burden accumulates over occupational careers and may be detectable at earlier stages if appropriate monitoring strategies are in place [23]. The high proportion of Chilean nationals across all four disqualifying conditions, mirroring the nationality composition of the evaluated workforce, further suggests that population-level cardiometabolic trends, rather than occupation-specific or nationality-specific factors, are driving unfitness patterns at the national level [19,24].

Future research should prioritize several complementary directions. Prospective longitudinal studies are needed to evaluate whether workers classified as UFW who undergo structured metabolic interventions are able to achieve re-evaluation and eventual fitness for HA work, and on what timeline. The development and validation of risk stratification tools capable of identifying workers at high probability of future unfitness before their condition reaches exclusion thresholds would represent a significant advance in preventive occupational medicine. Studies incorporating additional biological markers, including inflammatory mediators, oxidative stress markers, and sleep-related parameters such as apnea screening, could further refine the characterization of high-risk metabolic profiles in this population. External validation of the Random Forest importance framework in independent HA worker cohorts, including populations from Peru, Bolivia, and other Andean countries, would strengthen the generalizability of the present findings [17,20]. Finally, the integration of occupational health data with electronic health records and national disease registries could enable more comprehensive follow-up of excluded workers and provide insight into long-term cardiovascular and metabolic trajectories following UFW classification. Collectively, these findings support a paradigm shift in fitness-for-work evaluation for high-altitude exposure, moving from static exclusion thresholds toward dynamic, risk-based frameworks that incorporate modifiable cardiometabolic profiles and enable targeted intervention, monitoring, and potential reintegration of affected workers.

Non-modifiable determinants. The patterns observed are also shaped by non-modifiable factors. UFW workers were on average three years older than their FFW counterparts (43.0 vs. 40.3 years), consistent with the well-documented age-related accumulation of cardiometabolic burden and with the rising global prevalence of metabolic syndrome with age. The marked male predominance (94% of UFW workers) reflects the structural demographics of Chilean extractive industries rather than a biological vulnerability per se, yet it limits the precision of sex-stratified inferences for female workers. Nationality distribution mirrored that of the overall evaluated workforce and did not independently flag a higher-risk subgroup. Genetic determinants of altitude tolerance and metabolic regulation (e.g., EPAS1, EGLN1, PPARA variants) could not be explored with the present dataset, but represent a promising avenue for future research integrating occupational-health surveillance with biobank-based information.

Workplace-level recommendations. From a preventive standpoint, the dominance of modifiable cardiometabolic conditions suggests that several concrete workplace interventions could reduce exclusion rates. We propose: (i) on-site structured weight-management programmes combining nutritional counselling and supervised physical activity adapted to rotational shift schedules; (ii) pre-shift metabolic screening enabling early identification and individualised management of glycemic and lipid abnormalities; (iii) workplace-wellness programmes promoting shift-compatible sleep hygiene and stress management; and (iv) transparent re-evaluation pathways that reward measurable improvement in modifiable biomarkers, supporting reintegration of workers who achieve adequate metabolic control.

Occupational, economic, and social implications. A UFW decision has consequences that extend well beyond the clinical encounter. The worker loses access to the salary premium associated with HA shift work, with tangible household-level economic effects, and may be redirected to lower-paid non-HA roles or, in some cases, lose the contract altogether. From the employer perspective, structured cardiometabolic prevention programmes have the potential to deliver a positive return on investment through reduced turnover, lower absenteeism, fewer adverse-event-related evacuations, and lower long-term insurance costs covered under Law 16,744. Embedding these programmes within periodic FFW surveillance aligns the financial interests of companies with the health interests of workers and the regulatory aims of MINSAL and SUSESO.

Practical implications and added value. The descriptive prevalence of abnormalities reproduces, by construction, the regulatory criteria used to assign UFW status. The added value of the present analysis lies in three applied dimensions: (a) it quantifies the joint hierarchical weight of cardiometabolic predictors at population level, identifying where preventive investment is most likely to reduce exclusion; (b) it provides an evidence base for designing structured re-evaluation pathways focused on the few biomarkers that account for most exclusions (BMI, fasting glucose, triglycerides, SBP); and (c) it offers a benchmark against which future refinements of the FFW criteria, including multi-parameter risk models, can be empirically compared. A logical follow-up agenda, suggested by one of the reviewers, would therefore involve prospective evaluation of whether composite multi-parameter risk scores outperform single-threshold rules in predicting medium-term occupational outcomes, and whether the current regulatory cut-offs are themselves empirically calibrated. Such an evaluation requires a prospective design and is beyond the scope of the present cross-sectional analysis.

5. Conclusions

This study provides a comprehensive characterization of workers classified as unfit for HA occupational exposure, based on one of the largest occupational health datasets reported in this context. The findings demonstrate that metabolic abnormalities, particularly severe obesity, dysglycemia, and hypertriglyceridemia, constitute the predominant drivers of unfitness for HA work in Chile. These conditions are not isolated but tend to cluster in older male workers, suggesting a dominant cardiometabolic pattern that may benefit from targeted preventive and rehabilitative strategies. The exploratory Random Forest model confirmed the dominant role of body mass index and related metabolic biomarkers in differentiating health patterns within this population, achieving high classification accuracy. Importantly, many of the conditions identified as primary contributors to unfitness are potentially modifiable through structured lifestyle and clinical interventions. These results suggest that reframing FFW assessments to incorporate not only exclusion criteria but also individualized follow-up and re-evaluation pathways could improve both worker health outcomes and occupational reintegration. Future studies should prospectively evaluate the reversibility of unfitness conditions and the long-term occupational trajectories of workers excluded from HA work.

Author Contributions

R.J.: conceptualization, data curation, formal analysis, writing—original draft preparation; G.D.: conceptualization, methodology, supervision, writing—reviewing and editing; G.B.: investigation, data curation, writing—reviewing and editing; M.D.: investigation, data curation, writing—reviewing and editing; I.A.: investigation, data curation, writing—reviewing and editing; F.F.: methodology, software, formal analysis, visualization, writing—reviewing and editing. All authors have read and agreed to the published version of the manuscript.

Funding

This research received no external funding.

Institutional Review Board Statement

The studies involving humans were approved by the Comité de Ética Científico Adultos del Servicio de Salud Metropolitano Oriente (Santiago, Chile, 4 March 2025; approval code SSMOriente040324-1; approval date 4 March 2025). The study was based on a retrospective analysis of anonymized secondary data obtained from routine occupational health assessments, with no identifiable personal information accessed and no experimental procedures performed on human participants. In accordance with national legislation and institutional requirements, written informed consent was waived. All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Informed Consent Statement

Not applicable. The requirement for individual informed consent was waived by the Ethics Committee because the study was based on a retrospective analysis of anonymized secondary data obtained from routine occupational health assessments, with no identifiable personal information accessed.

Data Availability Statement

The data underlying this study were obtained from a large-scale integrated occupational health surveillance system and are not publicly available due to privacy and confidentiality constraints applicable to occupational health records. Anonymized aggregate data supporting the reported findings may be made available upon reasonable request to the corresponding author, subject to applicable data protection regulations and institutional approval.

Acknowledgments

The authors wish to thank the clinical and administrative teams at Workmed for their support in data management and coordination of occupational health evaluations. Special acknowledgment is due to the workers who participated in the occupational health surveillance program that generated the data supporting this study.

Conflicts of Interest

The authors declare no conflict of interest. The data used in this study were obtained from anonymized occupational health records, and the authors had full responsibility for the study design, data analysis, interpretation of results, manuscript preparation, and decision to submit the article for publication.

Use of AI and AI-Assisted Technologies

The authors disclose the use of OpenAI ChatGPT and Grammarly exclusively for language editing and grammar review purposes throughout all sections of this manuscript. These tools were used solely to improve readability, grammar, spelling, and overall linguistic clarity. All scientific ideas, study design, methodological development, analyses, interpretations, results, and conclusions presented in this work were independently developed and validated by the authors. The authors take full responsibility for the originality, accuracy, and integrity of the content of this manuscript.

References

1. Luks, A.M.; Swenson, E.R.; Bärtsch, P. Acute high-altitude sickness. *Eur. Respir. Rev.* **2017**, *26*, 160096. https://doi.org/10.1183/16000617.0096-2016.
2. Mallet, R.T.; Burtscher, J.; Richalet, J.-P.; et al. Impact of high altitude on cardiovascular health: Current perspectives. *Vasc. Health Risk Manag.* **2021**, *17*, 317–335. https://doi.org/10.2147/VHRM.S294121.
3. Aragón-Vela, J.; Bejder, J.; Huertas, R.J.; et al. Does intermittent exposure to high altitude increase the risk of cardiovascular disease in workers? A systematic narrative review. *BMJ Open.* **2020**, *10*, e041532. https://doi.org/10.1136/bmjopen-2020-041532.
4. Palmer, K.T.; Cox, R.A.; Brown, I. *Fitness for Work: The Medical Aspects*; Oxford University Press: Oxford, UK, 2007.
5. Ministerio de Salud de Chile. Guía Técnica: Exposición a Hipobaria Intermitente Crónica. (In Spanish). Available online: https://www.minsal.cl/sites/default/files/guia_hipobaria_altitud.pdf (accessed on 14 April 2026).
6. Superintendencia de Seguridad Social. Compendio de Normas del Seguro Social. Available online: https://www.suseso.gob.cl/613/w3-propertyname-647.html (accessed on 14 April 2026).
7. Serra, C.; Rodriguez, M.C.; Delclos, G.L.; et al. Criteria and methods used for the assessment of fitness for work: A systematic review. *Occup. Environ. Med.* **2007**, 64, 304–312. https://doi.org/10.1136/oem.2006.029397.
8. Vinnikov, D.; Krasotski, V. Healthy worker survival effect at a high-altitude mine. *Sci. Rep.* **2022**, *12*, 13903. https://doi.org/10.1038/s41598-022-18331-4.
9. Sarkar, S.; Maiti, J. Machine learning in occupational accident analysis: A review using science mapping approach with citation network analysis. *Saf. Sci.* **2020**, *121*, 104900. https://doi.org/10.1016/j.ssci.2020.104900.
10. Vandersmissen, G.J.; Schouteden, M.; Verbeek, C.; et al. Prevalence of high cardiovascular risk by economic sector. *Int. Arch. Occup. Environ. Health* **2020**, *93*, 843–853. https://doi.org/10.1007/s00420-019-01458-9.
11. Muñoz, S.; Nazzal, C.; Jimenez, D.; et al. Health effects of chronic intermittent hypoxia among Chilean miners: Rationale, design, and baseline results of a longitudinal study. *Ann. Work Expo. Health* **2021**, *65*, 908–918. https://doi.org/10.1093/annweh/wxab029.
12. Vinnikov, D.; Saktapov, A.; Romanova, Z.; et al. Work at high altitude and non-fatal cardiovascular disease associated with unfitness to work. *PLoS ONE* **2024**, *19*, e0306046. https://doi.org/10.1371/journal.pone.0306046.
13. Carrillo, J.; Mahecha-Matsudo, S.; Droppelmann, G.; et al. Riesgo de apnea obstructiva del sueño y nivel de actividad física y su asociación con riesgo cardiovascular elevado en adultos chilenos. *Rev. Chil. Enferm. Respir.* **2019**, *35*, 22–30. https://doi.org/10.4067/S0717-73482019000100022.
14. Jorquera, R.; Droppelmann, G.; Blanco, G.; et al. Data-driven identification of metabolic and cardiovascular biomarkers in high-altitude workers: A machine learning approach. *Front. Public Health* **2025**, *13*, 1652605. https://doi.org/10.3389/fpubh.2025.1652605.
15. Jorquera, R.; Droppelmann, G.; Dollmann, M.; et al. Mining the risk: Early cardiovascular detection in workers. *Front. Med.* **2025**, *12*, 1678172. https://doi.org/10.3389/fmed.2025.1678172.
16. Esenamanova, M.K.; Kochkorova, F.A.; Tsivinskaya, T.A.; et al. Chronic intermittent high altitude exposure, occupation, and body mass index in workers of mining industry. *High Alt. Med. Biol.* **2014**, *15*, 412–417. https://doi.org/10.1089/ham.2013.1150.
17. Montes-Madariaga, E.S.; Ortiz-Saavedra, B.; Mamani-Castillo, J.S.; et al. Cardiovascular risk and obesity in miner workers exposed to intermittent hypobaric hypoxia in the Peruvian Andes. *Front. Physiol.* **2026**, *17*, 1693470. https://doi.org/10.3389/fphys.2026.1693470.
18. Noubiap, J.J.; Nansseu, J.R.; Nyaga, U.F.; et al. Worldwide trends in metabolic syndrome from 2000 to 2023: A systematic review and modelling analysis. *Nat Commun.* **2025**, *17*, 573. doi: 10.1038/s41467-025-67268-5.
19. Parra-Gómez, L.A.; Rojas, J.P.; Vásquez, A.J.; et al. Prevalence of metabolic syndrome in Latin America: A systematic review and meta-analysis of observational studies. *Diabetes Metab. Syndr. Clin. Res. Rev.* **2025**, *19*, 103282. https://doi.org/10.1016/j.dsx.2025.103282.
20. Zila-Velasque, J.P.; Grados-Espinoza, P.; Challapa-Mamani, M.R.; et al. Prevalence of metabolic syndrome and its *Done*components according to altitude levels: A systematic review and meta-analysis. *Sci. Rep.* **2024**, *14*, 77928. https://doi.org/10.1038/s41598-024-77928-z.
21. Cappelli, F.; Castronuovo, G.; Grimaldi, S.; et al. Random Forest and feature importance measures for discriminating the most influential environmental factors in predicting cardiovascular and respiratory diseases. *Int. J. Environ. Res. Public Health* **2024**, *21*, 867. https://doi.org/10.3390/ijerph21070867.
22. Liu, T.; Krentz, A.; Lu, L.; et al. Machine learning based prediction models for cardiovascular disease risk using electronic health records data: Systematic review and meta-analysis. *Eur Heart J Digit Health* **2024**, *6*, 7–22. https://doi.org/10.1093/ehjdh/ztae080.

23. Burtscher, M.; Ponchia, A. The risk of cardiovascular events during leisure time activities at altitude. *Prog. Cardiovasc. Dis.* **2010**, *52*, 507–511. https://doi.org/10.1016/j.pcad.2010.02.008.
24. Richalet, J.-P.; Hermand, E.; Lhuissier, F.J. Cardiovascular physiology and pathophysiology at high altitude. *Nat. Rev. Cardiol.* **2024**, *21*, 75–88. https://doi.org/10.1038/s41569-023-00924-9.