



Article

# Covid-19 and Shift Work: A Preliminary Note from the COVISTRESS Online Survey

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**How To Cite:** Puligheddu, M.; Battaglia, E.; Lecca, R.; et al. Covid-19 and Shift Work: A Preliminary Note from the COVISTRESS Online Survey. *Work and Health* 2026, 2(2), 6. <https://doi.org/10.53941/wah.2026.100006>

Received: 11 January 2026

Revised: 19 March 2026

Accepted: 24 March 2026

Published: 15 April 2026

**Abstract:** Previous studies showed an increased risk of COVID-19 in several occupations, particularly healthcare workers. We aimed to explore whether night shift work, a possible determinant of immune suppression, might have contributed to COVID infection in the pre-vaccine months using data from 435 Italian participants (330 women, 105 men) to the COVISTRESS online survey. After adjusting for age, sex, and education, the risk of COVID-19 was elevated among night shift workers (OR = 5.5, 95% CI 2.92, 10.2), particularly among healthcare workers (OR = 8.7, 95% CI 4.07, 18.4). After excluding healthcare workers from the analysis, subjects working night shifts in other jobs also run a 5-fold elevated risk of COVID-19 (OR = 5.1, 95% CI 1.92, 18.4), which was confirmed in a sensitivity analysis excluding subjects who reported working remotely. Parenting school-aged children was also a significant predictor (OR = 2.5; 95% CI 1.20–5.21) of SARS-CoV-2 infection, but there was no interaction with night shift work. Education, marital status, smoking, and sleep quality did not account for the association with night shift work. Our results suggest that, during the 2020 COVID-19 pandemic, night shift workers run an excess risk of COVID-19 infection. Whether this was because of sleep loss-induced suppression of the immune system, confounding, or chance remains to be clarified.

**Keywords:** COVID-19; occupational exposure; shift work; sleep wake disorders; immunologic factors

## 1. Introduction

During the first wave of the COVID-19 pandemic, almost half of the cases occurred in a few occupations, including healthcare workers, taxi drivers, tourist guides, housekeepers, and cleaners [1,2]. Apart from the risk of contagion among healthcare and social workers, a major occupational risk factor is the high frequency of close contact with the public, which implies exposure to transmissible agents and a more likely occurrence of work-related infectious diseases [3]. Generic and specific host resistance to infection, which is strictly related to the state



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of the immune system, modulates the risk. However, in the pre-vaccine months, only generic immune defences against SARS-CoV-2 infection were in place; therefore, any workplace conditions that could suppress the immune response might have facilitated its spread. One such condition might be sleep deprivation among night shift workers. Indeed, sleep loss is associated with a reduction in peripheral blood NK-cell activity [4], and changes in the plasma levels of several cytokines [4], among sleep-deprived patients suffering from depression and in experimental animal studies. However, results among shift workers seem controversial, [4,5] and more likely related to innate immunity dysregulation than clinically relevant immunosuppression [4,6].

Since the beginning of the COVID-19 pandemic, previous findings of increased susceptibility to viral infections, driven by disruption of both the innate and acquired immune system, suggested that shift workers may be at particularly high risk [7]. Indeed, a recent systematic review and meta-analysis identified eight papers specifically investigating the association with night shift work. Although results were not always consistent, a 31% increase in the random effect estimate was observed (OR = 1.31, 95% confidence interval [CI] 1.08–1.58) [8]. Studies that did not observe the association mostly had a cross-sectional design. In contrast, the risk was consistently elevated in the three prospective cohort studies conducted on this subject. In particular, two large-size studies, based on the U.K. Biobank survey, consistently observed that night shift workers were almost 2-fold more likely to get COVID-19. [9,10] The risk was likewise elevated in healthcare and other than healthcare jobs, and independent of the type of shift work schedule, or confounders, such as sleep duration, chronotype, premorbid disease, body mass index, alcohol and smoking [10]. However, in one study, the baseline occupational information in the UK Biobank database, dating back 14 years with respect to the COVID-19 pandemic, was used, [9] and, in the second study, that from a 2017 survey was used [10]. As a consequence, possible changes in the job and fitness to night shift work, whether related to age or health status, might not have accounted for, resulting in biased findings. On the contrary, the COVISTRESS survey recorded the current occupation and remote working during the COVID-19 pandemic. As night shift workers were more likely to belong to the “essential job categories”, and therefore, might have been less protected against contagion, the COVISTRESS database offered the unique opportunity of double-checking the nature of the association with night shift work. We further examined the relationship between night shift work and the risk of SARS-CoV-2 infection applying a case-control study design to data from the large COVISTRESS online survey conducted during the COVID-19 pandemic.

## 2. Methods

The International COVISTRESS online survey was initiated by the University of Clermont-Ferrand, France, to study the impact of the COVID-19 pandemic on the international community, using a questionnaire focused on lifestyle, work environment, and stress. The survey and questionnaire were described in detail elsewhere [11]. Briefly, the COVISTRESS questionnaire was validated, translated into nine languages, and advertised to the general public for voluntary online access in 67 countries. The Ethical Committee of the University Hospital of Clermont Auvergne-France approved the research project on 9 March 2020 (Reference No. 2020/CE 06). The study complied with the provisions of the Declaration of Helsinki. COVID-19-positive and negative subjects were eligible for voluntary participation, irrespective of contact with a person infected with the virus, from 30 March to 10 June 2020. Data quality was maintained by ensuring that only one questionnaire was submitted per IP address.

Overall, 10,121 participants filled out the online questionnaire. For this study, we selected the 544 Italian participants. After excluding 109 questionnaires with missing relevant information, such as sex, age, education, occupation, and/or current or previous diagnosis of COVID-19, data from 435 participants (330 women and 105 men) were available for study, including 71 who self-reported a nasopharyngeal swab test positive for COVID-19 and 364 who didn't. We defined the first as cases and the second as controls.

### *Statistical Methods*

From the list of 290 COVISTRESS variables, we selected age, sex, body mass index (BMI), education (three categories: less than high school, high school, University), marital status, parental status and children's age, co-housing, home type and size, smoking, alcohol intake, use of sleeping pills, and physical activity in hours/day (ever/never), occupation, sleep quality, and night shift work (yes/no). The questionnaire listed broad occupational categories roughly corresponding to the major groups of the International Standard Classification of Occupations-2008 (ISCO-08), [12] with some more detail for healthcare and teaching occupations. For this analysis, we used the binary categorization of healthcare occupations vs. others. Sleep quality was self-defined by participants in a 0–100 Visual Analogue Scale (VAS) and arbitrarily categorized in bad and good quality according to whether the score was  $\leq 50$  or  $\geq 51$ , i.e., above or below the median value in the VAS scale.

The association between each variable and COVID-19 infection, independent of its severity, was tested using unconditional logistic regression models, adjusting for age (continuous), sex, and education. We used the odds ratio (OR) and its 95% confidence interval (95% CI) to measure the association of the independent covariates with COVID-19. The analysis was conducted with SPSSv20®.

### 3. Results

The mean age of participants was 47 years (*sd* 11.3), substantially similar by gender (men 46 yrs, *sd* 12.7; women 47 yrs, *sd* 10.9). The majority of participants were females (76%), with a high education level (graduate: 65%), married (48%). The majority reported some physical activity during the day (58%). Body mass index (BMI) and the other covariates did not vary significantly by case-control status; healthcare and night shift workers prevailed among the COVID-19 cases (Table 1). The results of the logistic regression analysis showed that COVID-19 risk was elevated for those having school-aged children (OR = 2.5; 95% CI 1.20–5.21) and, among the occupations, for medical doctors (OR = 3.0, 95% CI 1.20, 7.61) and nurses (2.3, 95% CI 1.38, 4.30) with reference to other jobs (Table 2). There was a 5.5-fold excess risk of COVID-19 among night shift workers (OR = 5.5, 95% CI 2.92, 10.2), which was highest for healthcare workers engaged in night shift work (OR = 8.7, 95% CI 4.07, 18.4). After excluding healthcare workers from the analysis, night shift workers in other jobs were still at risk (OR = 5.1, 95% CI 1.92, 18.4). Educational level, marital status, smoking, and sleep quality did not account for the association nor showed any interaction with night shift work.

**Table 1.** Frequency of selected variables by case-control status in the COVISTRESS Italy study population.

Characteristics	COVID-19				Total Study Population		p-Value
	Cases (No. = 71)		Controls (No. = 364)		(No. = 435)		
Age (mean, <i>sd</i> )	46.2	9.85	47.1	11.6	47.0	11.3	0.546 *
BMI (mean, <i>sd</i> )	25.7	7.51	24.7	4.14	24.8	4.84	0.115 *
Sex							
Women (No., %)	60	84.5	270	74.2	330	75.9	0.063 **
Men (No., %)	11	15.5	94	25.7	105	24.1	
Education (Years)							
less than high school	14	19.7	59	16.2	73	16.8	0.969 **
high school	13	18.3	67	18.4	80	18.4	
university	44	62.0	238	65.4	282	64.8	
Marital status							
Married, stable partnership	35	49.3	175	48.1	210	48.3	0.173 **
Single, widowed, divorced	22	31.0	116	31.9	138	31.7	
Missing	14	19.7	73	20.0	87	20.0	
Children							
None	19	26.8	143	39.3	162	37.2	0.192 **
Aged 6–18 years	28	39.4	96	26.4	124	28.5	
Aged ≤ 5 years	10	14.1	54	14.8	64	14.7	
Missing	14	19.7	71	19.5	85	19.6	
Home							
Single home	5	7.0	32	8.8	37	8.5	0.934 **
Apartment > 50 m <sup>2</sup>	41	57.7	193	53.0	234	53.8	
Apartment ≤ 50 m <sup>2</sup>	7	9.9	25	6.9	32	7.4	
Missing	18	25.4	114	31.3	132	30.3	
Co-housing (family, partner, co-tenants)							
no	10	14.1	72	19.8	82	18.9	0.378 **
yes	33	46.5	169	46.4	202	46.4	
Missing	28	39.4	123	33.8	151	34.7	
Current smoking							
No	42	59.2	197	54.1	239	54.9	0.310 **
≤10 cigarettes	8	11.3	24	6.6	32	7.4	
≥11 cigarettes	2	2.8	32	8.8	34	7.8	
Missing	19	26.7	111	30.5	130	29.9	
Alcohol (regular intake)							
no	18	25.4	113	31.0	131	30.1	0.169 **
yes	34	47.9	138	38.0	172	39.5	
Missing	19	26.7	113	31.0	132	30.4	

Table 1. Cont.

Characteristics	COVID-19				Total Study Population (No. = 435)	p-Value
	Cases (No. = 71)		Controls (No. = 364)			
Physical activity						
no	6	8.4	51	14.0	57	13.1
yes	47	66.2	207	56.9	254	58.4
Missing	18	25.4	106	29.1	124	28.5
Sleeping pills						
no	68	95.8	357	98.1	425	97.8
yes	3	4.2	7	1.9	10	2.2
Sleep quality						
Score ≤ 50	29	38.0	190	30.8	139	32.0
Score ≥ 51	26	42.3	113	51.9	219	50.3
Missing	14	19.7	63	17.3	77	17.7
Occupation						
Healthcare workers	38	53.5	91	25.0	129	29.7
Other jobs	33	46.5	274	75.3	307	70.6
Night shift work						
no	43	60.6	315	86.5	358	82.3
yes	28	39.4	49	13.5	77	17.7

Footnote: \* *T* test; \*\* chi square.

**Table 2.** Results of the logistic regression analysis on risk of COVID-19 associated with occupation, night shift work, and personal and lifestyle covariates. Unless noted differently, all regression models include age (continuous), sex, and education.

Covariates	Cases/Controls	OR	(95% CI)
Age (per year)	71/364	1.0	0.97–1.02
Female Sex	60/270	1.7	0.83–3.61
Education			
less than high school	14/59	1.0	-
high school	13/67	0.2	0.03–1.71
university	44/238	0.2	0.03–1.55
Marital status (married in stable partnership)	35/175	1.1	0.58–1.94
Parenting children			
None	19/143	1.0	-
Aged 6–18 years	28/96	2.5	1.20–5.21
Aged ≤ 5 years	10/54	1.6	0.64–3.79
Home size			
Single home	5/32	1.0	-
Apartment > 50 m <sup>2</sup>	41/193	1.4	0.52–3.99
Apartment ≤ 50 m <sup>2</sup>	7/25	1.8	0.50–6.56
Co-housing (family, partner, co-tenants)	10/33	1.4	0.66–3.12
Current smoking			
No	19/143	1.0	-
≤10 cigarettes	8/24	1.4	0.55–3.36
≥11 cigarettes	2/32	0.2	0.05–1.15
Alcohol (regular intake)	34/138	1.6	0.83–2.97
Physical activity	6/51	0.5	0.21–1.30
Sleeping pills	3/7	2.3	0.56–9.25
Poor sleep quality	30/189	0.6	0.35–1.15
BMI			
≤24.9	35/168	1.0	-
25–29.9	32/169	0.9	0.47–1.59
≥30	4/27	0.7	0.23–2.16
Occupation			
Other jobs	33/274	1.0	-
Nurses	23/65	2.3	1.28–4.30
Medical doctors	8/19	3.0	1.20–7.61
Healthcare workers	38/91	4.8	2.59–8.94
Night shift work			
All	28/49	5.5	2.92–10.2
Night shift work in Health care jobs	22/31	8.7	4.07–18.4
Healthcare jobs not engaged in night shifts	22/78	4.7	2.19–9.88
Night shift work in other jobs	6/18	5.1	1.92–18.4

Among COVID-19 cases reporting an occupation other than healthcare, production jobs and a subgroup including housewives, retired and unemployed were more represented. Technical and production jobs were more represented among night shift workers. Subjects engaged in technical jobs were also relatively prevalent among the occupations other than healthcare, with 61 study subjects overall, including 7 COVID-19 cases and 11 night shift workers. Within this subgroup, the odds ratio of COVID-19 associated with night shift work was increased 3-fold (crude OR = 3.2, 95% CI 1.4–7.0). Although confirming the association, the small size of this subgroup caused an unreliably elevated OR in the multivariable analysis.

During the first wave of the COVID-19 pandemic, workers not belonging to the essential job categories were frequently requested to work remotely or shut down their professional or commercial activities. Because of that, they enjoyed significant protection against contagion: indeed, in our study, the OR for COVID-19 among those working remotely was 0.3 (95% CI 0.1–1.2). On the other hand, night shift workers were more likely to belong to essential job categories, and, therefore, might not have benefited from the protection against contagion provided by isolation at home. If this were the case, the association with shiftwork we observed among occupations other than healthcare might have been spurious. Therefore, we conducted a sensitivity analysis excluding all the subjects who had been working remotely during the COVID-19 pandemic. This analysis confirmed that night shift workers were more prone to develop COVID-19 (OR = 5.2, 95% CI 1.6–16.9).

#### 4. Discussion

Our results confirm that, in the pre-vaccine months of the COVID-19 pandemic, healthcare workers experienced an elevated risk of SARS-CoV-2 infection with respect to other occupations. Risk was particularly elevated among healthcare workers engaged in night shifts. However, working night shifts was a strong predictor of COVID-19 among other occupations as well. This was a heterogeneous array of broad occupational categories. Restricting the analysis to the relatively more homogenous group of technical jobs confirmed the association. Also, a sensitivity analysis excluding from these occupations those who worked remotely during the COVID-19 pandemic confirmed the excess risk of COVID-19 among night shift workers. Having school-aged children was also a risk factor, but did not explain the association. interact with night shift work or change after multiple adjustments.

Our findings are consistent with previous reports [7–13]. In previous reports among UK healthcare workers, night shift work was a significant risk factor for COVID-19 infection between December 2020 and March 2021 in the univariable analysis, but risk did not increase with the frequency of night shifts, and the multivariable analysis weakened the association [14]. Moreover, the authors did not explore whether the introduction of COVID-19 vaccines affected the risk associated with night shift work. It might be noteworthy that, in the UK Biobank project, the occupational information was collected at the time of recruiting, 10–14 years before the COVID-19 pandemic. Participants might have changed their jobs over time; others might have developed hypertension, diabetes, cardiovascular disease, renal failure, liver disease, asthma, and COPD and, therefore, referred to the occupational physician, possibly resulting in judgment of unfitness to night shift work. Therefore, bias might have resulted from referring to night shift work at recruitment.

In respect to the UK blood bank studies, the COVISTRESS survey offered the advantage of gathering data on participants' occupation at the same time as the outcome, so preventing bias from health- or life-related changes over the years. Also, information on remote working was available. This is an important variable, as night shift workers are more likely to belong to the "essential job categories", and therefore, might have been more subject to contagion than workers in non-essential jobs working remotely. On the other hand, the poor occupational details do not allow for the exclusion of bias from other factors associated with night shift work as previously suggested [14]. Still, our result of a similar association among night shift workers in jobs other than healthcare in our study and in the UK Biobank study [10], which was confirmed in the relatively more homogenous category of technical jobs and after excluding participants who worked remotely during the pandemic, reinforced our findings.

Consistent with the hypothesis, experimental studies showed that the expression of clock genes in NK cells of rats, mouse macrophages, and human leukocytes was affected by the sleep/wake rhythm and polymorphisms in those genes, and the circadian rhythm of hormones, such as melatonin and cortisol, affected the immune response [15]. Indeed, a good quality, resting sleep confers protection against infections [16]. Conversely, sleep loss and ageing induce immunological changes, such as an impaired T cell immune response, an increase in the innate immune activation, and a reduced immune response following vaccination [15]. In addition, sleep-deprived subjects have lowered plasma levels of interleukin-1 (IL-1) and 6 (IL-6), and tumour necrosis factor (TNF) [17].

The small study size is a reason for concern. We selected the Italians among the more than 10,000 COVISTRESS participants, first for a rapid preliminary exploration of the hypothesis, and secondly for the sake of homogeneity among the study population and the timing in the COVID-19 spread, which differed by country.

Our results suggest the opportunity to extend the analysis to the whole COVISTRESS data set. Also, we did not find an association between poor sleep quality and risk of COVID-19, which would contradict the excess risk among night shift workers. However, the COVISTRESS questionnaire assessed sleep quality with a simple 0–100 VAS scale answer to a single direct question about the level of sleep quality, instead of the validated Pittsburgh Sleep Quality Index (PSQI), which was strongly correlated with COVID-19 risk among Chinese healthcare workers working night shifts [13]. Furthermore, participation in the online survey was on a voluntary basis with over-representation of women, well-educated, and healthcare workers among participants. Therefore, our study population cannot be considered an independent sample of the general population, and the interpretation of the observed associations might not be generalizable. We aimed to minimize selection bias by selecting cases and controls from the same source, and performing multivariable analysis adjusted for age, sex, and education, and stratified by occupation, whether in healthcare or occupations other than healthcare. We are uncertain whether our strategy effectively reduced selection bias. Finally, results from the case-control study design need to be interpreted cautiously, as they can establish associations between variables, but not causality. For instance, an alternative explanation for the observed association might be the higher probability of being in contact with the SARS-CoV-2 virus during night shifts, due to reduced staff in the night hours. However, this might be plausible for healthcare workers but less so for other occupations, who might have been less scrupulous in respecting anti-COVID precautions, instead.

The diagnosis of COVID-19 was based on the self-report of a positive nasopharyngeal swab test. The regular nasopharyngeal swab testing among healthcare workers, particularly those in the frontline during the epidemic, might reflect their higher probability of contagion and greater worry, and therefore their over-representation among participants in the COVISTRESS survey with respect to other jobs. However, this does not diminish the results of the case-control analysis, as the association with night shift work was confirmed in the stratified analysis by occupational groups. If nonconfirmed asymptomatic cases were more frequent among occupations other than healthcare, this would have most likely diluted the association we observed.

## 5. Conclusions

Consistent with other reports, our results suggest that night shift workers run a high risk of COVID-19 during the first wave of the pandemic. Whether immune suppression due to circadian disruption or other conditions associated with night shift work explain the observed association remains to be clarified.

## Author Contributions

R.L., M.P., E.C. and MF oversight the protocol for submission to the Ethics Committee, E.B, R.L., E.C. and MF collected the data, S.D.M., and V.C. performed the statistical analyses. E.B., M.P., E.C. and MF drafted the manuscript. M.P., S.D.M., Ma.C., R.B., MoC., M.L.F. and F.D. reviewed the manuscript. The COVISTRESS Network, under the direction of F.D., designed the study and recruited the participants. F.D. coordinated the project and reviewed the manuscript. All authors have contributed to the manuscript and approved the submitted version. All authors have read and agreed to the published version of the manuscript.

## Funding

The COVISTRESS survey was funded by the Centre National pour la Recherche Scientifique—Laboratoire de Psychologie Sociale et Cognitive and the Centre Hospitalière Universitaire Clermont Ferrand, France.

## Institutional Review Board Statement

The Ethical Committee of the University Hospital of Clermont Auvergne-France approved this research project on 9 March 2020 (Reference No. 2020/CE 06).

## Informed Consent Statement

The study complied with the provisions of the Declaration of Helsinki. Written informed consent was obtained from all participants before they accessed the online questionnaire.

## Data Availability Statement

All data generated or analysed during this study are included in this article. Further inquiries can be directed to the corresponding author. The raw data supporting the conclusions of this article are available from the authors upon reasonable request, and will be shared in accordance with ethical approvals and applicable data protection regulations, including EU GDPR requirements.

## Conflicts of Interest

The authors declare no conflict of interest.

## Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

## Appendix A

The COVISTRESS network is headed by Frédéric Dutheil (frederic.dutheil@uca.fr)—CHU Clermont-Ferrand, Occupational and Environmental Medicine, 58 rue Montalembert, 63000 Clermont-Ferrand, France. Members of the research group are Maëlys Clinchamps, Stéphanie Mestres, Cécile Miele, Valentin Navel, Lénise Parreira, Bruno Pereira, Karine Rouffiac—CHU Clermont-Ferrand, France; Yves Boirie, Jean-Baptiste Bouillon-Minois, Martine Duclos, Maria Livia Fantini, Jeannot Schmidt, Stéphanie Tubert-Jeannin—Université Clermont Auvergne / CHU Clermont-Ferrand, France; Mickael Berthon, Pierre Chausse, Michael Dambrun, Sylvie Droit-Volet, Julien Guegan, Serge Guimond, Laurie Mondillon, Armelle Nugier, Pascal Huguet—Université Clermont Auvergne, CNRS, LAPSCO, France; Samuel Dewavrin—WittyFit, France; Sébastien Couarraze, Louis Delamarre, Fouad Marhar—CHU Toulouse, France; Martial Mermillod—CHU Toulouse, France; Geraldine Naughton, Amanda Benson—Swinburne University, Australia; Claus Lamm—University of Vienna, Austria; Karen Gbaglo, Ministry of Health; Vicky Drapeau—Université de Laval, Canada; Raimundo Avilés Dorliac—Universidad Finis Terrae, Chile; Benjamin Bustos—Universidad de Los Andes, Chile; Gu Yaodong—Ningbo University, China; Haifeng Zhang—Hebei Normal University, China; Peter Dieckmann—Copenhagen Academy for Medical Education and Simulation (CAMES), Denmark; Julien Baker, Yanping Duan, Yang Gemma Gao, Yajun Wendy Huang, Jiao Jiao, Binh Quach, Chunqing Zhang, Hong Kong Baptist University, China; Hijrah Nasir, Indonesia; Perluigi Cocco, Rosamaria Lecca, Monica Puligheddu, Michela Figorilli, Università di Cagliari, Italia; Morteza Charkhabi, Reza Bagheri—University of Isfahan, Iran; Daniela Pfabigan—University of Oslo, Norway; Peter Dieckmann, University of Stavanger, Norway; Marek Zak, Tomasz Sikorski, Magdalena Wasik—Jan Kochanowski University of Kielce, Poland; Samuel Antunes, David Neto, Pedro Almeida—Ordem dos Psicólogos Portugueses, ISPA-Instituto Universitário, Portugal; Maria João Gouveia—ISPA-Instituto Universitário, Portugal; Pedro Quinteiro—William James Center for Research, ISPA-Instituto Universitário; Constanta Urzeala—UNEFIS, Romania; Benoit Dubuis—UNIGE, Switzerland; Juliette Lemaigen—Fondation INARTIS, Switzerland; Kuan-Chou Chen, National Taiwan University of Sport, Taiwan; Andy Su-I Liu—University of Taipei, Taiwan; Foued Saadaoui, King Abdulaziz University, Tunisia; Ukadike C Ugbole, University of the West of Scotland, United Kingdom; Keri Kulik—Indiana University of Pennsylvania, USA.

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