## O RIGINAL INVESTIGATIONS/COMMENTARIES

# Excess mortality in Mountain Areas of Emilia Romagna Region during the first months of SARS-CoV-2 pandemic: a "canary in the coal mine"?

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Abstract. Background. Because of their remoteness, Mountain Communities (MC) have been considered at advantage when dealing with infectious diseases. However, earlier reports have identified MC among the hotspots for early spreading of COVID-19 pandemic. Methods. Crude mortality rates (CMR) and Excess mortality rates (EMR) were calculated for 97 municipalities from MC in the Emilia Romagna Region (North-Eastern Italy), and resulting estimates were compared to the Parent Provinces. Notification and mortality rates for COVID-19 were also retrieved, and correlated with EMR estimates. Results. During 2020, a CMR of 150.3/100,000 (95% Confidence Interval [95%CI] 117-185.4) was identified, with substantial heterogeneities between the 8 provinces of Emilia Romagna Region that were included in the analyses. A pooled EMR of +20.3% (95%CI 10.6-30.1) for MC and 19.9% (95%CI 9.5-30.3) was identified. The monthly estimates were quite heterogenous across the various provinces, ranging between -79.7% and +307.4% during the assessed timeframe. Higher estimates were identified in the months of March and April in MC, and during the months of April and May for Parent Provinces. In bivariate analysis, EM in MC was loosely but positively correlated with estimates in the parent province (Spearman's r = 0.201, p = 0.049), and also with notification rates for COVID- (i.e. Piacenza, Parma, Reggio Emilia, Modena, Bologna, Ravenna, Rimini, and Forlì Cesena) (r = 0.225, p = 0.045), and particularly with mortality rates for COVID-19 at provincial level (r = 0.372, p < 0.001). Conclusions. In summary, the study highlights that small geographical and population size, along with remoteness, did not play a substantial advantage for MC against the spread and mortality rate of COVID-19. On the other hand, as the surge of EM in MC anticipated a similar habit in Parent Provinces of several weeks, improved surveillance interventions are also urgently in need. (www.actabiomedica.it)

Key words: case fatality rate, Coronavirus, Mountain, Apennines, mortality, syndemic, mortality rates, excess mortality rates

#### Introduction

Small geographical size and remoteness, even when facing restricted availability of medical resources, could represent a substantial advantage when dealing with epidemics of emerging infectious diseases (1–4). Regarding the ongoing SARS-CoV-2 pandemic, most of available evidence stems from Small Islands States of the Pacific, whose small geographical and population sizes, coupled with the appropriate implementation of non-pharmaceutical interventions (NPI), have guaranteed to the local communities some advantage in the early containment of viral spread (2–6).

Even though some Mountain Areas may be perceived as geographically isolated as island ones, local communities in Europe and North America have been initially identified as hotspots for viral spreading in the early stages of the pandemic, and several factors have contributed to this clearly unwanted role (1). First of all, in North America and Western Europe the earlier

stages of the "first wave" of SARS-CoV-2 pandemic (i.e. end February - May/June 2020, for most of Western Europe) occurred at the end of the winter tourist season (1,7,8). In this context, a combination of low risk perception among tourists and local Authorities, and the high influx of individuals from geographical areas that had been unbeknownst entry gates of this new pathogen in Western Countries, contributed to the rapid spread of the pathogen, not only locally but also at international level. Interestingly enough, even in the wake of the "First Wave", immediately after the implementation of NPI and lockdown measures, and the eventual shutdown of tourist resorts, some mountain municipalities have performed particularly well in containing the rate of new cases and incident deaths, stressing the advantage of remoteness when communities are asked to implement physical containment measures (7,8).

However, when dealing with such information, a precautionary approach is forcibly needed. In fact, the earlier stages of the pandemic were characterized by a substantial lack of diagnostic options, and a large share of incident cases and deaths were not properly identified (9,10). In this case, the remoteness of mountain areas may have contributed to a substantial underscoring of the actual SARS-CoV-2 burden of disease. A suitable option to cope with this potential issue is represented by the calculation of the "excess mortality" (EM), i.e. the percent difference between the reported number of deaths (RD) in a given month, and an estimate of the expected deaths (ED) for that period (11).

From this point of view, analysis of EM in Italian Mountain Communities may provide some interesting insights, and particularly in those from Emilia Romagna Region. Emilia Romagna is one of the 20 main administrative regions of Italy, with an area of 22,446 km<sup>2</sup> (8,666 sq mi), and a total population of around 4.4 million inhabitants. On the one hand, nearly more than half of the total surface of the region is either hilly (27%) or mountainous (25%), with a mountain range stretching for more than 300 km, and including a total of 97 Municipalities that were located at 600 m or more above sea level, being therefore acknowledged as "Mountain Communities" (MC) according to the Italian Law (Law 991/1952). On the other hand, during the first semester of 2020, western Acta Biomed 2022; Vol. 93, N. 4: e20222247

Provinces of Emilia Romagna Region (i.e. Piacenza, Parma, Reggio Emilia, and Modena) being extensively interconnected with nearby regions of Lombardy, Veneto and Piedmont, were severely involved in the "first wave" of SARS-CoV-2 pandemic, while eastern provinces of Bologna, Ferrara, Ravenna, Forlì-Cesena and Rimini were more marginally affected (10,12–15). Moreover, while other Regions of Northern Italy are substantially involved in the winter tourism, MC of Emilia Romagna do not represent significant tourist locations during the winter season: in other words, the characterization of the early stages of SARS-CoV-2 pandemic in these areas should limitedly depend on international influx of new infection, being rather an early index for the local dynamics of COVID-19 pandemic.

Still, few studies have specifically examined the impact of SARS-CoV-2 pandemic on Italian MC (16): in order to fill this information gap, this study will therefore compare mortality data from all cases over 12 months (January to December, 2020) in 97 municipalities from Emilia Romagna Region fulfilling the statutory definition of MC (Annex Figure A1).

## 2. Materials and Methods

#### 2.1. Background.

Italy has a total surface of 301,230 km<sup>2</sup>, with a total population of around 60,000,000 inhabitants. The first-level administrative entities are represented by the Regions (No. 20); each region is divided in a number of provinces (No. 107, including: 80 ordinary provinces, 2 autonomous provinces, 4 regional decentralization entities, 6 free municipal consortia, 14 metropolitan cities, as well as the Aosta Valley Region, where region and province coincide), that in turn include several municipalities (in Italian, "comune"; No. 7,904 by March 18, 2022), that vary considerably in size and population, both as for total population and population density. According to the Italian Law No. 991/1952, a municipality may be acknowledged as a Mountain Community if: a)  $\geq$  80% of the total surface is located 600 m or more above sea level, b) the difference between the highest and lowest points is equals

to 600 m or greater, irrespective of the total surface. In Emilia Romagna (Regional Law No. 2/2004, and No. 25/2017), a total of 97 municipalities in 2020 could be acknowledged as MC (See Supplementary Table A1 and Supplementary Figure A1).

#### 2.2. Population data.

Italian Institute of Statistics (ISTAT; https:// demo.istat.it) provides open-source data including population estimates at various administrative levels (i.e. National, Regional, Provincial and/or Municipality). More precisely, we retrieved monthly estimates from the timeframe 2018 – 2020 about: (a) resident population at Provincial and Municipality level; (b) monthly estimates for deaths among residents at Provincial and Municipality level.

## 2.3. Data about COVID-19.

Open-source provincial-level estimates for SARS-CoV-2 infections are regularly provided by the official website of the Italian National Institute for Nuclear Physics (INFN) at provincial level. In this study, monthly provincial estimates for COVID-19 notification rates were retrieved for 2020.

### 2.4. Statistical analysis.

Firstly, a descriptive analysis of annual crude mortality rates at municipal level was performed. Municipality-level estimates were then pooled at provincial level in order to confront them with similar data from the parent province. Excess mortality (EM), i.e. the difference between the reported number of deaths (RD) in a given month in 2020, and an estimate of the expected deaths (ED) for that period, was then calculated as follows:

 $EM = (RD^{i} - ED^{i,a, 2018-2019}) / ED^{i,a, 2018-2019}$ 

 $RD^{i,a}$  = reported deaths in a given month i, at a specific administrative level a

 $ED^{i,a, 2018-2019}$  = average deaths in a given month *i* for the time period 2018-2019, at a specific administrative level a

Average monthly estimates for COVID-19 notification rates were then calculated at provincial level in order to compare correspondent estimates with mortality and EM from the MC after their pooling at provincial level. Comparisons of crude rates were performed by means of Mann-Whitney or Kruskal-Wallis test for multiple independent samples, while the association between continuous variables was assessed through Spearman's rank correlation coefficient.

All calculation were performed on R 4.0.3 (17), by means of packages epiR (v. 2.0.19), EpiReport (v 1.0.1), fmsb (0.7.0).

*Ethical approval*. No ethical approval was needed for this study, as no individual data were identifiable, and only aggregated data were analyzed and presented.

## 3. Results

## 3.1. Demographics of MC

Between January 1st, 2018, and December 31st, 2020, the average population of the 97 MC included in the study was  $313,048.0 \pm 1053.2$  inhabitants (Table 1, Annex Table A1), equals to 7.0% of the total population of Emilia Romagna Region. The greater share of sampled population (105120.3  $\pm$  131.0, 33.6% of the total) was from the Province of Bologna, that also encompassed the larger share of municipalities (21, 21.6%), followed by Modena (62644.6 ± 184.8, 20.0%), Reggio Emilia (43071.2 ± 243.4, 13.8%), Parma (38930.8 ± 290.9, 12.4%), Forlì Cesena  $(32080.5 \pm 223.4, 10.2\%)$ , Rimini  $(17023.8 \pm 123.6,$ 5.4%), Piacenza (11655.5  $\pm$  153.4, 3.7%), and eventually Ravenna, as the latter Province included only one municipality for a total of  $2521.1 \pm 29.7$  inhabitants (0.8%).

Similarly, the greater share of deaths was from the municipalities in province of Bologna (30.5%), followed by Modena (18.3%), Parma (15.6%), Reggio Emilia (14.5%), Forlì Cesena (9.6%), Piacenza (6.4%), Rimini (4.8%), and Ravenna (0.3%).

As shown in Table 2, pre-pandemic monthly mortality rates ranged from 99.3 per 100,000 (95%CI 83.8 to 114.8) for the province of Rimini in 2019, to 204.3 per 100,000 (95%CI 183.9 to 224.8) in the province of

	Mountainous Communities		Population (2018- 2020)		Deaths	
Province	(No.)	%	(Average [SD])	%	(No.)	%
Total	97	100%	313048.0 (1053.2)	100%	13889	100%
Piacenza	10	10.3%	11655.5 (153.4)	3.7%	890	6.4%
Parma	20	20.6%	38930.8 (290.9)	12.4%	2173	15.6%
Reggio Emilia	10	10.3%	43071.2 (243.4)	13.8%	2017	14.5%
Modena	17	17.5%	62644.6 (184.8)	20.0%	2537	18.3%
Bologna	21	21.6%	105120.3 (131.0)	33.6%	4238	30.5%
Ravenna	1	1.3%	2521.1 (29.7)	0.8%	36	0.3%
Forlì-Cesena	11	11.3%	32080.5 (223.4)	10.2%	1335	9.6%
Rimini	7	7.2%	17023.8 (123.6)	5.4%	663	4.8%

Table 1. General characteristics of the sampled communities.

Table 2. Monthly mortality rates (reported as events per 100,000 persons) with corresponding 95% Confidence intervals for the mountain communities of Piacenza, Parma, Reggio Emilia, Modena, Bologna, Ravenna, Rimini, and Forlì Cesena in 2018, 2019, and 2020.

	Monthly Mortality Rates (per 100,000, 95% Confidence Interval)					
	2018	2019	2020			
Piacenza	204.3 (183.9; 224.8)	192.9 (175.8; 210.1)	239.4 (180.9; 297.9)			
Parma	137.6 (125.4; 149.8)	147.5 (133.7; 161.3)	180.2 (124.7; 235.6)			
Reggio Emilia	129.0 (112.6; 145.4)	122.1 (112.6; 131.5)	139.2 (115.3; 163.1)			
Modena	110.4 (99.2; 121.6)	109.1 (100.2; 118.1)	117.9 (106.9; 129.0)			
Bologna	108.5 (96.8; 120.2)	103.5 (97.2; 109.9)	123.9 (109.8; 138.0)			
Ravenna	140.2 (100.7; 179.7)	125.8 (82.1; 169.6)	153.7 (117.8; 189.5)			
Forlì Cesena	110.1 (102.4; 117.7)	110.1 (95.0; 125.2)	126.7 (112.3; 141.2)			
Rimini	104.4 (89.6; 119.2)	99.3 (83.8; 114.8)	121.0 (107.2; 134.8)			
POOLED	130.6 (104.4; 156.7)	126.3 (101.5; 151.1)	150.3 (117.0; 183.5)			

Piacenza in 2018. Focusing on 2020, the lower mortality rates were reported from the MC of the province of Modena (117.9, 95%CI 106.9 to 129.0), with highest rates from the province of Piacenza (239.4, 95%CI 180.9-297.9).

Still, if the analyses were limited to the months of March and April 2020 (i.e. when lockdown measures were strictly implemented in the whole of Italy), mortality rates were substantially increased in Parent Provinces compared to MC (173.1 per 100,000, 95%CI 121.2-225.0 vs. 210.1 per 100,000, 95%CI 139.5-280.7, p = 0.025), while estimates for EM remained comparable (+56.7%, 95%CI 23.2-90.2 vs. +68.5%, 95%CI 4.1-132.8; p = 0.694), but not correlated (r = 0.103, p = 0.727).

Nonetheless, when the Risk Ratios (RR) for monthly deaths in mountain communities were plotted (Figure 1), a specific trend was seemingly suggested. In fact, RR for all-causes death was substantially increased in the sampled MC compared to the Parent Provinces, across the whole of the assessed timeframe, as it ranged between 1.193 (95%CI 1.064 to 1.338; September 2020) and RR 1.398 (April 2019, 95%CI 1.256 to 1.555), with a pooled estimate of 1.306, 95%CI 1.281-1.330 ( $I^2 = 8.4$ , Q = 38.2, p = 0.326).

#### 3.2. Excess Mortality

EM were initially pooled at provincial level (Figure 2), and a specific pattern was identified,



**Figure 1.** Time trend of the Risk Ratio (RR) for mortality in Mountain Communities compared to the Parent Provinces (Piacenza, Parma, Reggio Emilia, Modena, Bologna, Ravenna, Rimini, and Forlì Cesena) between January 2018 and December 2021. A pooled RR equals to 1.306, 95%CI 1.281- 1.330 ( $I^2 = 8.4$ , Q = 38.2, p = 0.326) was eventually calculated.

with a certain west-to-east trend. More precisely, the western provinces – and particularly Piacenza and Parma, and also Reggio Emilia were characterized by increased EM rates during the months of April (+347.4%, +275.7%, and +81.2%, respectively), and May (+112.4%, +111.2%, and +79.1%, respectively).

By moving eastwards, the increase of EM progressively diminished (+76.2% in March and +22.6% in April for Modena; +44.5% and +55.4% for Bologna; +25.6% and +23.3% in Ravenna), with a resurgence in the south-eastern provinces of Forlì Cesena (+50.1%, and 31.8%), and Rimini (+115.8%, and +43.6%).

Interestingly enough, MC of Piacenza and Parma were characterized by earlier surge of EM rates, that peaked in the month of March (+183.0%, and +136.3% for Piacenza and Parma, respectively), and then decreased in the following months of April (+75.7% and +133.9%, respectively), and May (-10.7%, and +5.9%).

While nearby provinces of Reggio Emilia (+68.8% in March, +48.7% in April, and -13.7% in May) and Modena (+25.2% in March, +27.1% in April, 8.3% in May) exhibited a similar but milder trend, it was unnoticeable in more eastern MC (i.e. areas that were more distant from the COVID-19 hotspots of Southern Lombardy).

When estimates were pooled by the reporting month (see **Figure 3**), during March 2020 (i.e. the first wave of the pandemic), MC exhibited an increased EM (i.e. +57.8%, 95%CI +6.5 to +109.2 vs. -6.6%, 95%CI -1.8 to +11.4) compared to the other areas of the Parent Provinces, that were affected by a substantial surge of EM rates during the following months of April and May (+127.1%, 95%CI +38.0 to +216.1; +59.7%, 95%CI +32.5 to +86.9). Early months of the warm season (i.e. June and July) were characterized by higher rates for EM in MC (+48.6%, 95%CI +26.5 to +70.7, and +16.2%, 95%CI +3.9 to +28.5) than in







Figure 3. Excess Mortality (2020 vs. 2018-2019) for Mountain Communities (MC) vs. Parent Provinces of Piacenza, Parma, Reggio Emilia, Modena, Bologna, Ravenna, Rimini, and Forlì Cesena.

Parent Provinces (+10.7%, 95%CI +0.6 to 20.8, and +2.1%, 95%CI -5.6 to +9.8), and again in the months of October (+18.9%, 95%CI +2.3 to +35.5 vs. -7.6%, 95%CI -10.6 to 4.5) and November (+26.0%, 95%CI +7.4 to 44.5 vs. +17.1%, 95%CI +11.0 to +23.2). However, no substantial difference was eventually identified (Wilcoxon matched-pairs signed rank test p value = 0.622).

When monthly estimates were pooled at provincial level (Table 3), MC from Western Provinces of Piacenza and Parma (i.e. those that were more severely affected by SARS-CoV-2 in the early stages of the pandemic), but also Reggio Emilia and Modena, had lower EM rates than those reported in the parent province (i.e. +22.1% vs. +41.2%, p = 0.519 for Piacenza; +23.5% vs. +35.4% for Parma, p = 0.380; +11.4% vs. +15.5% for Reggio Emilia, p = 0.719; +8.6% vs. +14.1% for Modena, p = 0.622). On the contrary, in the MC of the Eastern areas of Bologna, Ravenna, Ferrara, Forlì-Cesena a specular trend was identified, with local municipalities exhibiting increasing estimates for EM across all of the calendar year 2020 compared to 2018-2019 (i.e. Bologna +17.7% vs. +9.9%, p = 0.064; Ravenna +37.9% vs. +8.4%, p = 0.519; Rimini +24.1% vs. 22.1%, p = 0.470; Forlì Cesena +17.4% vs. 12.5%, p = 0.910), and again the difference was not significant. In fact, correspondent pooled estimates of +20.3% (95%CI +10.6 to +30.1) for the whole of MC and +19.9% (+9.5 to +30.3) for Parent Provinces were eventually calculated, and the difference was not significant (p = 0.819).

### 3.3. Bivariate analysis

In bivariate analysis, as shown in Figure 4, both mortality rates (Spearman's r = 0.457, p < 0.001) and EM estimates of MC and Parent Provinces were positively correlated (r = 0.201, p = 0.049), i.e. higher the mortality in the parent province, higher the mortality rates in the mountain areas.

	Excess mortality (%, 95%CI), monthly average					
	Mountain Communities	Parent Province	P value			
Piacenza	+22.1% (-13.8; 58.0)	+41.2% (-23.8; 106.1)	0.519			
Parma	+23.5% (-10.3; 57.2)	+35.4% (-16.9; 87.7)	0.380			
Reggio Emilia	+11.4% (-6.4; 29.2)	+15.5% (-5.3; 36.2)	0.791			
Modena	+8.6% (-3.2; 20.5)	+14.1% (-3.4; 31.7)	0.622			
Bologna	+17.7% (3.0; 32.4)	+9.9% (-4.3; 24.1)	0.064			
Ravenna	+37.9% (-24.0; 99.7)	+8.4% (-1.2; 18.1)	0.519			
Forlì Cesena	+17.4% (-1.1; 35.8)	+12.5% (0.4; 24.5)	0.910			
Rimini	+24.1% (0.1; 48.2)	+22.1% (-1.5; 45.7)	0.470			
POOLED	+20.3% (10.6; 30.1)	+19.9% (9.5; 30.3)	0.819			

**Table 3.** Monthly average of excess mortality estimated in 2020 compared to the biennial estimates for 2018-2019 in mountain communities of Piacenza, Parma, Reggio Emilia, Modena, Bologna, Ravenna, Rimini, and Forlì Cesena, compared to the Parent Provinces. Comparisons were performed by means of Wilcoxon matched-pairs signed rank test.



**Figure 4.** Monthly estimates of mortality (2018-2020; a) and Excess Mortality (2020 vs. 2018-2019; b) for mountain communities of Piacenza, Parma, Reggio Emilia, Modena, Bologna, Ravenna, Rimini, and Forlì Cesena, compared to the Parent Provinces. Both mortality rates (Spearman's r = 0.457, p < 0.001) and Excess Mortality estimates (r = 0.201, p = 0.049) were positively correlated.

EM estimates in MC were positively correlated with notification rates for COVID-19 in the parent province (i.e. r = 0.225, p = 0.045), and more specifically with mortality rates, also at provincial level (r =0.372, p < 0.001) (Figure 5; Annex Figure A2 and Annex Figure A3). In other words, increased occurrence of SARS-CoV-2 infections in the whole of the province was associated with an increase in the excess mortality 2020 vs. 2018-2019 in the mountain communities.

#### 4. Discussion

In this ecological study on MC from Emilia Romagna Region in North-Eastern Italy, mortality rates increased from 130.6 per 100,000 in 2018, and 126.3 per 100,000 in 2019 to 150.3 in 2020, a surge that mostly affected western provinces of Parma and Piacenza – i.e. the areas of Emilia Romagna that were more directly involved in the "first wave" of the SARS-CoV-2 pandemic (13–15). In fact, an EM equals to +20.3%



**Figure 5.** Correlation between monthly excess mortality in mountain communities of Emilia Romagna Region and: (a) notification rates for COVID-19 in Parent Provinces (i.e. Piacenza, Parma, Reggio Emilia, Modena, Bologna, Ravenna, Rimini, and Forli Cesena) (Spearman's r = 0.225, p = 0.045); (b) mortality rates for COVID-19 at provincial level (Spearman's r = 0.372, p < 0.001).

(95%CI 10.6 to 30.1) was identified at regional level for the whole of MC, suggesting a substantial increase in incident deaths during 2020 compared to 2018 and 2019. Not only a similar increase was reported from the Parent Provinces (+19.9%, 95%CI 9.5 to 30.3, p = 0.819), but crude mortality rates and EM estimates in MC and Parent Provinces were each other positively correlated (Spearman's r = 0.457, p < 0.001; and r = 0.201, p = 0.049, respectively).

Unfortunately, detailed estimates at municipal level for SARS-CoV-2 infections are to date unavailable, but provincial-level data for incidence and mortality were positively correlated with monthly EM estimates in MC (r = 0.225, p = 0.045 for SARS-CoV-2 incidence, and r = 0.372, p < 0.001 for mortality rates). In summary, MC have been seemly involved in the SARS-CoV-2 pandemic in a similar way to the Parent Provinces. However, when focusing on the monthly estimates, some specificities of MC do appear.

First of all, MC have been characterized by an increased risk for all-cause mortality well before the inception of SARS-CoV-2 pandemic (RR 1.306, 95%CI 1.281- 1.330 for the timeframe 2018-2020). This was not unexpected, as mountain areas in all of the Italian Peninsula are increasingly depopulated, with a progressively increasing share of older age groups over the total population (18,19), and this secular trend

has most severely affected the Apennine ranges (20). Even if older mean age of MC compared to Parent Provinces should have resulted in the increased vulnerability of resident population to complications of SARS-CoV-2 infection (21–24), increased EM rates were identified only in the earlier stages of the pandemic, while estimates were highly comparable in the following months of 2020.

Second, MC were characterized by a rapid increase of EM estimates during the earlier months of the pandemic, and particularly in western provinces of Emilia Romagna, i.e. Parma and Piacenza. The geographical continuity with Southern Lombardy (i.e. the "hotspot" of SARS-CoV-2 pandemic in Italy during the "first wave") may explain such estimates (10,25). In this regard, the analysis of EM rates in the calendar months of March and April 2020 seemly suggests that MC may have anticipated of around 30 days the surge in EM that has been linked to the COVID-19 pandemic in Parent Provinces (13,14,23). As our estimates are based on the all-causes mortality, we are unable to causally associate this surge with early introduction of SARS-CoV-2 infections. Moreover, MC in Emilia Romagna Region are hardly comparable to the mountain resorts that highly contributed to the earlier stages of the pandemic (1,26). Even though before the SARS-CoV-2 Pandemic Emilia Romagna region was

among the top European Tourism Destinations, as it welcomed more than 11.5 million visitors annually (i.e. 50 million overnight stays) (27), Apennine Mountains and local resorts are only marginally involved in the winter tourism. Therefore, the surge in EM that was associated with MC compared to Parent Provinces was unlikely associated with an earlier introduction of the pathogen in the local communities, as in some previous reports from mountain resorts (1,7,8). In fact, the EM rates in MC and Parent Provinces were correlated across the assessed timeframe, as well as EM in MC with estimates for COVID-19 in Parent Provinces, suggesting a common background. A possible explanation could rather be found in a combination of limited availability of medical resources in mountain areas impacting on highly vulnerable populations. In other words, the higher mortality in the first weeks of the pandemic may have been caused by an early shortage of medical resources (28-30), that other areas of Parent Provinces may have been more proficient in dealing with. In other words, the scarce or reduced availability of intensive medical treatment, or even a delayed referral to health care facility able to provide intensive care may explain the earlier evidence of increased EM among MC compared to Parent Provinces. For the very same reason, MC have reasonably benefited the most from the implementation of lockdown measures and physical distancing, which have reasonably led to a rapid "exhaustion" of the "first wave" (31,32).

Limits. Our study is affected by several limitation that should be taken in account before any further generalization of our results. First of all, the present report is based on an ecological study, being therefore affected by all of the implicit limits of this design, and particularly the potentially confounding factors represented by individual level variables (33-35). The lack of detailed notification rates at municipal level for COVID-19 may have further amplified the implicit "ecological fallacy" associated with all ecological studies. In this regard, it should be stressed that during the first stages of the pandemic both incidence (or better, notification) rates and mortality rates for COVID-19 may have been largely under-reported (3,6), with estimates for lacked diagnoses that in certain areas may have accounted to 96% of actual cases (10). Therefore, while EM may represent a reliable proxy for COVID-19 mortality in the first year of the pandemic, when appropriate diagnostic options were less frequently available, all comparisons including laboratory diagnosis for SARS-CoV-2 should be more cautiously assessed (11).

Another obvious shortcoming of this study design is forcibly represented by the quality of the available data from online sources (i.e. dashboards, platforms and other ministerial sites) (36). For example, even though the all-causes mortality appears at relatively low risk of reporting bias (21), mortality rates are calculated on the number of residents, and this specific variable may be affected by substantial uncertainties. For example, some residents of MC in Emilia Romagna are in fact commuters and spend most of their active life in the largest city centers of the parent province. Following the progressive depopulation of Apennines, a large share of residents has in fact left MC but may retain the original and formal residence for fiscal reasons, in fact impairing the reliability of cumulative estimates (20).

# 5. Conclusions

In conclusion, MC of the Emilia Romagna Region have been impacted by the "first wave" of the SARS-CoV-2 pandemic similarly to their Parent Provinces. Interestingly, the impact of the pandemic on EM was noticeable in MC some weeks earlier than in Parent Provinces, and several specificities of these communities may have contributed to this habit. In other words, while remoteness has been often advocated as a preventive factor against infectious diseases, MC may represent a sort of "early indicator" for the accelerated stages of SARS-CoV-2 pandemic, representing a sort of "canary in a coal mine". As a consequence, not only preventive measures are therefore forcibly required in order to protect resident population, but improved surveillance interventions may be quite useful in order to contribute to the quick characterization of the pandemic stages.

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